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Chapter 3

The effect of cognitive impairment on the predictive value of multimorbidity for the increase in disability in the oldest old: the Leiden 85-plus Study

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ABSTRACT

Background
Prevention of disability is an important aim of healthcare for older persons. Selection of persons at risk is a first crucial step in this process.

Objectives
This study investigates the predictive value of multimorbidity for the development of disability in the general population of very old people and the role of cognitive impairment in this association.

Design
The Leiden 85-plus Study (1997–2004) is an observational prospective cohort study with 5 years of follow-up.

Setting
General population of the city of Leiden, The Netherlands.

Subjects
Population based sample of 594 participants aged 85 years.

Methods
Disability in activities of daily living (ADL) was measured annually for 5 years with the Groningen Activity Restriction Scale (range 9–36, 9=optimal). Multimorbidity is defined as the presence of two or more chronic diseases at age 85 years. Cognitive function was measured at baseline with the mini-mental state examination (MMSE).

Results
At baseline participants with multimorbidity had higher ADL disability scores compared with those without [median 11 inter-quartile range (IQR 9–16) versus 9 (IQR 9–13) ADL points, Mann–Whitney U test p <0.001]. Stratified into four MMSE groups, ADL disability increased over time in all groups, even in participants without multimorbidity (p trend <0.001). Multimorbidity predicted accelerated increase in ADL disability in participants with MMSE of 28–30 points (n=205, 0.67 points/year, p <0.001), but not in participants with lower MMSE scores (all p >0.100).

Conclusion
The predictive value of multimorbidity for the increase in ADL disability varies with cognitive function in very old people. In very old people with good cognitive function,
multimorbidity predicts accelerated increase in ADL disability. This relation is absent in very old people with cognitive impairment.

**KEY POINTS**

- The predictive value of multimorbidity for the increase in disability in ADL varies with cognitive function.
- Multimorbidity does not predict accelerated increase in disability in ADL in older persons with cognitive impairment.
- Only in older persons with good cognitive function, multimorbidity predicts accelerated increase in disability in ADL.
- For selection of high-risk patients, multimorbidity can be used only in those older persons without cognitive impairment.
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INTRODUCTION

The aim of preventive programmes for older people is to enable them to live as independently as possible for as long as possible. For these programmes instruments are needed to identify older people at high risk to develop disability in the near future. When such instruments are available, older people can pro-actively be approached to prevent increase in disability.

It is known that chronic diseases\textsuperscript{1-7} and multimorbidity\textsuperscript{6-8} are strongly related with disability. However, most of these studies incorporated cognitive impairment or dementia in their multimorbidity scores. Because earlier studies showed strong associations between cognitive function and disability,\textsuperscript{2-4,6-13} the predictive value of multimorbidity for disability may differ between persons with and without cognitive impairment.

Therefore, we studied the predictive value of multimorbidity for the increase in disability in activities of daily living (ADL) in older persons with and without cognitive impairment.

METHODS

Setting and study population
The Leiden 85-plus Study is an observational population based prospective follow-up study of 85-year-old inhabitants of Leiden (The Netherlands). Between September 1997 and September 1999, all inhabitants of Leiden who reached the age of 85 years were invited to participate in the study.

Participants were followed for 5 years until the age of 90 years or until death. Date of death was obtained from the municipality. All participants were visited annually at their place of residence where face-to-face interviews were conducted, cognitive testing was performed, and disabilities in basic ADL were measured.

All participants gave their informed consent; for those with severe cognitive impairment, informed consent was obtained from a proxy. The Medical Ethics Committee of Leiden University Medical Centre approved the study. For the present study, participants with missing ADL measurements at baseline and participants with missing information on the presence of two or more chronic diseases at baseline were excluded.
Main study parameters

Determinants
Information on the presence of chronic diseases at baseline was obtained from the participant’s general practitioner (GP), nursing home physician and/or pharmacy records. We included common chronic diseases in the analyses, which are commonly used in multimorbidity scores: arthritis, chronic obstructive pulmonary disease (COPD), diabetes mellitus, heart failure, stroke, Parkinson disease, depressive symptoms reported in the previous year, and history of cancer or myocardial infarction. COPD was considered present when lung medication [Anatomical Therapeutic Chemical (ATC) code R03] was used at age 85 years. Multimorbidity was defined as the presence of two or more of the nine chronic diseases investigated.

Cognitive function was assessed with the mini-mental state examination (MMSE), with scores ranging from 0 to 30 (=optimal function) and was stratified in four groups: MMSE score <19 points (severe cognitive impairment), 19–23 points (moderate cognitive impairment), 24–27 points (mild cognitive impairment) and 28–30 points (optimal cognitive function).

Outcome
Disability in basic ADL was determined with the Groningen Activity Restriction Scale, which assesses an individual’s competence in the following nine basic activities: walk inside, get up out of bed, get into and out of a chair, visit the toilet, wash hands and face, wash body, dress and undress, eat and drink and make breakfast. Questions are phrased: “Can you, fully independently, …?” Answers range from “Fully independently, without any difficulty” (1 point) to “Not fully independently, only with someone’s help” (4 points). The total ADL disability score ranges from 9 to 36.

Data analysis
In the cross-sectional analysis, median scores of ADL disability at age 85 years between participants were compared using the Mann–Whitney U test.

Prospectively, the relation between individual chronic diseases and multimorbidity at baseline and changes in ADL-disability scores over time were analysed with linear mixed models. Each linear mixed model included the individual disease a term for time, and a term for the interaction between disease and time. The results of the linear mixed models are as follows: the effect of time on disability in ADL reflects the annual change in ADL disability in those without the disease, and is presented as basic annual change in ADL disability score. The interaction of an individual chronic disease and time reflects the
additional annual change in ADL disability for those with the disease and is presented as additional annual change in ADL disability score.

To assess the influence of cognitive impairment, participants were stratified into four groups according to their baseline MMSE score (0–18, 19–23, 24–27 and 28–30) and the predictive effect of multimorbidity on changes in disability in ADL were examined separately in these four groups.

Data were analysed using SPSS 16.0 (Chicago, IL, USA).

RESULTS

Study population
Between September 1997 and September 1999, 705 inhabitants of Leiden reached the age of 85 years and were eligible for participation in the study. A total of 14 persons died before enrolment in the study, 92 declined to participate, no ADL measures were available for two persons, and for three persons information on the presence of two or more chronic diseases was missing. Therefore baseline data were available for 594 participants. Appendix 1 shows the numbers of participants at the start of the study and annually over the 5-year follow-up period.

Cross-sectional analysis
Table 1 presents the baseline characteristics, the prevalence of the investigated chronic diseases, and the prevalence of multimorbidity among the participants at age 85 years. In total, 34% of the participants were male. The prevalence of multimorbidity was 39%. Arthritis was the most common chronic disease (33%).

At baseline, participants with arthritis, depressive symptoms, diabetes mellitus, stroke and Parkinson disease had higher scores of ADL disability than participants without these diseases (Appendix 2). The greatest differences in median ADL disability scores between participants with and without an individual chronic disease were seen for Parkinson disease (19 versus 10 points, p <0.001) and stroke (15 versus 10 points, p <0.001). Participants with multimorbidity had higher ADL disability scores compared with those without multimorbidity (11 versus 9 points, p <0.001).

At baseline, highest ADL disability scores were found in participants with an MMSE score <19 (Figure 1). In the groups with MMSE scores of 19–23, 24–27 and 28–30, higher baseline ADL disability scores were found for participants with multimorbidity than for
participants without multimorbidity (all p ≤0.010). However, in subjects with an MMSE score <19, no differences in ADL disability scores were found between participants with multimorbidity and those without multimorbidity (median ADL disability scores: 19 versus 19 points, p=0.950).

Prospective analyses
Appendix 3 presents the relation of individual chronic diseases and multimorbidity with additional annual changes in ADL performance. In participants without any of the investigated chronic diseases, the basic annual change in ADL disability score was 1.2 points per year (95% CI 1.0–1.4, p <0.001, data not shown). Depressive symptoms, heart failure, myocardial infarction and stroke predicted an additional annual change in ADL disability score during follow-up. Other individual chronic diseases did not predict an additional annual change in ADL disability score (all p >0.100). Participants with mul-

Table 1. Baseline characteristics of the study population at age 85 years (n=594*).

| Sociodemographic characteristics                  | n  | %  |
|---------------------------------------------------|----|----|
| Sex, male                                         | 201| 34 |
| Low level of education – primary school only      | 383| 65 |
| Prevalence of individual chronic diseases         |    |    |
| Arthritis                                         | 193| 33 |
| Depressive symptoms                               | 125| 21 |
| History of cancer                                 | 104| 18 |
| Diabetes mellitus                                 | 86 | 15 |
| Heart failure                                     | 75 | 13 |
| COPD                                              | 70 | 12 |
| Myocardial infarction                             | 63 | 11 |
| Stroke                                            | 61 | 10 |
| Parkinson disease                                 | 15 | 2.5|
| Total number of chronic diseases                  |    |    |
| None                                              | 147| 25 |
| One                                               | 213| 36 |
| Two or more (multimorbidity)                      | 234| 39 |
| Classification in the mini-mental state examination (MMSE) |    |    |
| MMSE <19 pts                                      | 97 | 16 |
| MMSE 19-23 pts                                    | 85 | 14 |
| MMSE 24-27 pts                                    | 207| 35 |
| MMSE 28-30                                        | 205| 35 |

*missing data in n=0 to n=11 per disease; of 568 participants the data on chronic diseases were complete. COPD = chronic obstructive pulmonary disease
timorbidity had an accelerated progression of ADL disability over time compared with those without multimorbidity: additional annual change 0.42 points (95% CI 0.21–0.63, p <0.001).

The effect of cognitive function on the predictive value of multimorbidity for disability in ADL was investigated by stratifying the participants into four groups according to their MMSE scores at baseline (Figure 2; Appendix 4). In all MMSE groups, ADL disability increased over time, independent of the presence of multimorbidity (basic annual change, p for trend <0.001).

Multimorbidity was associated with an additional annual change in ADL disability of 0.67 points (95% CI 0.39–0.95, p <0.001) in subjects with an MMSE score of 28–30. In participants with an MMSE score <28, multimorbidity did not predict the change in ADL disability (additional annual change, p for trend <0.001).

Figure 1. ADL disability scores dependent on the presence of multimorbidity at age 85 years stratified for cognitive function.
Data were presented as medians and corresponding inter-quartile ranges, p-values estimated with the Mann-Whitney U test; ADL, activities of daily living; MMSE, mini-mental state examination.
Principal findings

This population-based study of very old people demonstrates that disability in ADL increases over time in older persons of the general population. Multimorbidity only predicted accelerated increase in disability in ADL in older people with an optimal cognitive function (MMSE score ≥28 points). In persons with lower MMSE scores, this relation was not observed.

Our findings are in agreement with earlier studies showing that both cognitive impairment and multimorbidity are associated with the development of disability in ADL in older persons. However, these studies did not report that this relation is only present in older people with MMSE scores ≥28 points. A possible explanation for these findings is that the effect of cognitive impairment on ADL performance overwhelms the effect of multimorbidity. Another possible explanation is the possibility that cognitive performance at the age of 85 years is a marker for the total health condition, with a high sensitivity to detect detrimental effects on ADL disability. In persons with cognitive impairment, we found large basic annual changes in ADL disability score, indicating that in persons with cognitive impairment ADL disability increases, independent of the presence of multimorbidity.

Figure 2. Changes in ADL-disability points over time depending on multimorbidity in participants from age 85 years onwards, for strata of cognitive function.

ADL, activities of daily living; MMSE, mini-mental state examination.
Strength and limitations

Our study has several strengths. The population-based setting and almost complete follow-up of the participants allow to generalise the conclusions to older people (aged 85 years and over) in the general population. It is important to study the development of disability in ADL in old age, because the very old are the fastest growing segment of the general population\textsuperscript{21} and the prevalence of disability in ADL increases with age.\textsuperscript{12,22,23} Therefore, disability in ADL in old age can have a significant effect on quality-of-life, healthcare needs and costs in our ageing society. Furthermore, the study stratified on cognitive function, allowing to investigate the predictive value of multimorbidity for disability in ADL at different levels of cognitive function.

A possible limitation of the present study is that we used a selection of only nine diseases, as diagnosed by physicians. The prevalence of multimorbidity might have been different when other chronic diseases had been included, or when more specific diagnostic tests had been used. In addition, we did not take the severity of the chronic diseases into account. However, our approach of multimorbidity, by using only data of the GPs, nursing home physicians and pharmacy records, reflects clinical practice and similar systems of adding individual diseases have been applied in many other studies.\textsuperscript{8}

Clinical implications and future research

The most important clinical implication is that multimorbidity can only be used as a predictor for disability in ADL in older people with optimal cognitive function. Older people with an MMSE score less than 28 are at the highest risk for disability in ADL. However, multimorbidity is no longer an additional predictor of disability in ADL in this group. Preventive programmes to promote older people to live as independently as possible may use a two-stage screening test, which contains MMSE screening as a first step and multimorbidity screening as the second, to select older people at risk for disability.

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Independence of researchers: All researchers were independent from the funder.

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REFERENCES

1. Puts MT, Deeg DJ, Hoeymans N, Nusselder WJ, Schellevis FG. Changes in the prevalence of chronic disease and the association with disability in the older Dutch population between 1987 and 2001. Age Ageing 2008; 37: 187–93.

2. Spiers NA, Matthews RJ, Jagger C et al. Diseases and impairments as risk factors for onset of disability in the older population in England and Wales: findings from the Medical Research Council Cognitive Function and Ageing Study. J Gerontol A Biol Sci Med Sci 2005; 60: 248–54.

3. Reynolds SL, Silverstein M. Observing the onset of disability in older adults. Soc Sci Med 2003; 57: 1875–89.

4. Tas U, Verhagen AP, Bierma-Zeinstra SM et al. Incidence and risk factors of disability in the elderly: the Rotterdam Study. Prev Med 2007; 44: 272–8.

5. Wang L, van Belle G, Kukull WB, Larson EB. Predictors of functional change: a longitudinal study of nondemented people aged 65 and older. J Am Geriatr Soc 2002; 50: 1525–34.

6. Cigolle CT, Langa KM, Kabeto MU, Tian Z, Blaum CS. Geriatric conditions and disability: the Health and Retirement Study. Ann Intern Med 2007; 147: 156–64.

7. Kriegsman DM, Deeg DJ, Stalman WA. Comorbidity of somatic chronic diseases and decline in physical functioning: the Longitudinal Aging Study Amsterdam. J Clin Epidemiol 2004; 57: 55–65.

8. Stuck AE, Walthert JM, Nikolaus T, Bula CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. Soc Sci Med 1999; 48: 445–69.

9. Njegovan V, Hing MM, Mitchell SL, Molnar FJ. The hierarchy of functional loss associated with cognitive decline in older persons. J Gerontol A Biol Sci Med Sci 2001; 56: M638–43.

10. Greiner PA, Snowdon DA, Schmitt FA. The loss of independence in activities of daily living: the role of low normal cognitive function in elderly nuns. Am J Public Health 1996; 86: 62–6.

11. Raji MA, Ostir GV, Markides KS, Goodwin JS. The interaction of cognitive and emotional status on subsequent physical functioning in older mexican americans: findings from the Hispanic established population for the epidemiologic study of the elderly. J Gerontol A Biol Sci Med Sci 2002; 57: M678–82.

12. Tas U, Verhagen AP, Bierma-Zeinstra SM, Odding E, Koes BW. Prognostic factors of disability in older people: a systematic review. Br J Gen Pract 2007; 57: 319–23.

13. Orsitto G, Cascavilla L, Franceschi M et al. Influence of cognitive impairment and comorbidity on disability in hospitalized elderly patients. J Nutr Health Aging 2005; 9: 194–8.

14. Bootsma-van der Wiel A, Gussekloo J, De Craen AJ, Van Exel E, Bloem BR, Westendorp RG. Common chronic diseases and general impairments as determinants of walking disability in the oldest-old population. J Am Geriatr Soc 2002; 50: 1405–10.

15. Marengoni A, von Strauss E, Rizzuto D, Winblad B, Fratiglioni L. The impact of chronic multimorbidity and disability on functional decline and survival in elderly persons. A community-based, longitudinal study. J Intern Med 2009; 265: 288–95.

16. Heeren TJ, Lagaay AM, von Beek WC, Rooymans HG, Hijmans W. Reference values for the Mini-Mental State Examination (MMSE) in octo- and nonagenarians. J Am Geriatr Soc 1990; 38: 1093–6.

17. Bootsma-van der Wiel A, Gussekloo J, De Craen AJ et al. Disability in the oldest old: ‘can do’ or ‘do do’? J Am Geriatr Soc 2001; 49: 909–14.

18. Kempen GI, Miedema I, Ormel J, Molenaar W. The assessment of disability with the Groningen Activity Restriction Scale. Conceptual framework and psychometric properties. Soc Sci Med 1996; 43: 1601–10.
19. Izaks GJ, Gussekloo J, Dermout KM, Heeren TJ, Ligthart GJ. Three-year follow-up of mini-mental state examination score in community residents aged 85 and over. Psychol Med 1995; 25: 841–8.
20. Fried LP, Bandeen-Roche K, Kasper JD, Guralnik JM. Association of comorbidity with disability in older women: the Women’s Health and Aging Study. J Clin Epidemiol 1999; 52: 27–37.
21. Oeppen J, Vaupel JW. Demography. Broken limits to life expectancy. Science 2002; 296: 1029–31.
22. Hoogerduijn JG, Schuurmans MJ, Duijnstee MS, de Rooij SE, Grypdonck MF. A systematic review of predictors and screening instruments to identify older hospitalized patients at risk for functional decline. J Clin Nurs 2007; 16: 46–57.
23. Winblad I, Jaaskelainen M, Kivela SL, Hiltunen P, Laippala P. Prevalence of disability in three birth cohorts at old age over time spans of 10 and 20 years. J Clin Epidemiol 2001; 54: 1019–24.
