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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.

Keywords: *disability, multimorbidity, cognitive impairment, prediction, elderly*

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 [1–7] and multimorbidity [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 [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 [14, 15]: 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) [16] 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 [17, 18]. 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

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

	n	$\%$
Sociodemographic characteristics		
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 patients	97	16
MMSE 19–23 patients	85	14
MMSE 24–27 patients	207	35
MMSE 28–30	205	35

^{a}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.

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) [19] 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, Supplementary data are available in *Age and Ageing* online, 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 (Supplementary data are available in *Age and Ageing* online, 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 $P \leq 0.010$). 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, Supplementary data are available in *Age and Ageing* online, 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 multimorbidity 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, Supplementary data are available in *Age and Ageing* online, 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–
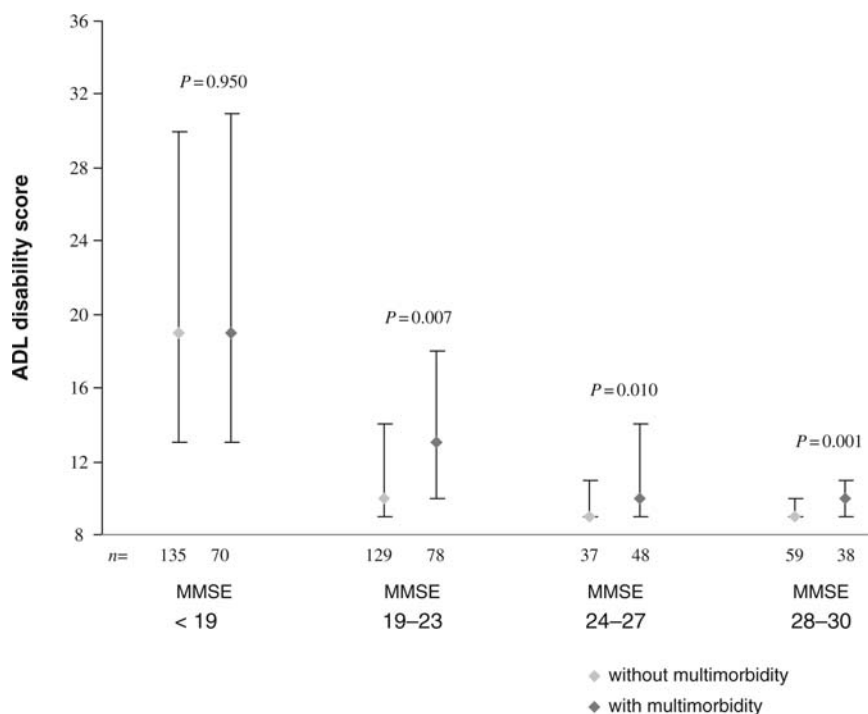
Figure 1. ADL disability scores dependent on the presence of multimorbidity at age 85 years stratified for cognitive function. Data were presented as medians and corresponding inter-quartile ranges, *P*-values estimated with the Mann–Whitney *U* test; ADL, activities of daily living; MMSE, mini-mental state examination.
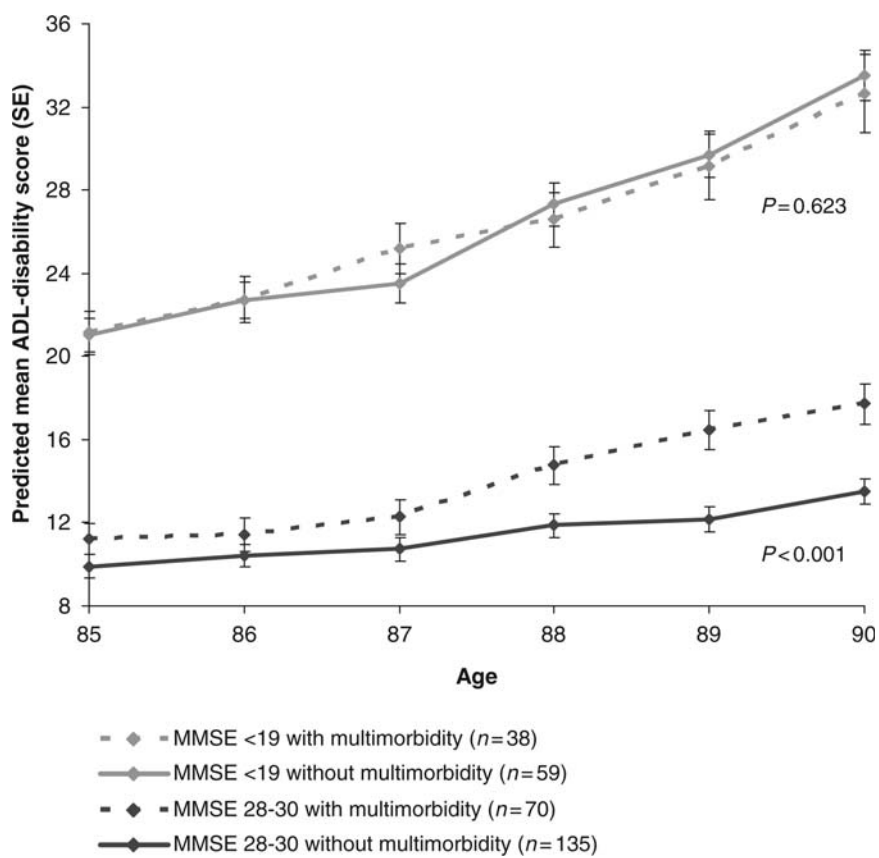

Figure 2. Changes in ADL-disability points over time depending on multimorbidity in participants from age 85 years onwards, for strata of cognitive function. ADL, activities of daily living; MMSE, mini-mental state examination.

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).

Comment

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 [9–11, 13, 15, 20]. 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.

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 [21] and the prevalence of disability in ADL increases with age [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 [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.

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.

Author contributions

Gussekloo had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Studyconcept and design: de Craen and Gussekloo.

Acquisition of data: de Craen and Gussekloo.

Analysis and interpretation of data: Drewes, den Elzen, de Craen, Mooijaart, Assendelft and Gussekloo.

Drafting of the manuscript: Drewes and den Elzen.

Critical revision of the manuscript for important intellectual content: Drewes, den Elzen, de Craen, Mooijaart, Assendelft and Gussekloo.

Obtained funding: Gussekloo.

Conflicts of interest

None declared.

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Ethical approval

The medical ethical committee of Leiden University Medical Center approved the study in 1997.

Independence of researchers

All researchers were independent from the funder.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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