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Activities of Daily Living at hospital admission associated with Mortality in Geriatric Patients with Dementia: A Danish Nationwide Population-based Cohort Study

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Key summary points

- **Aim:** What is the association between mortality and basic activities of daily living upon hospital admission among patients with dementia?
- **Findings:** Patients with dementia have high levels of dependency in basic activities of daily living on hospital admission

  Mortality increased with decreasing basic activities of daily living as assessed by Barthel-Index at hospital admission
- **Message:** Barthel-Index may be a helpful tool when discussing treatment and care strategies with patients and their families

Abstract

Purpose: Determining life expectancy in patients with dementia are challenging. We aimed at studying the association between basic activities of daily living as measured by the Barthel Index at hospital admission and mortality among older patients with dementia.

Methods: All patients aged ≥65 years with diagnosed dementia in the population-based National Danish Geriatric Database from 2005-2014 were included and followed until death, emigration, or study termination (31.12.2015). Data on Barthel-Index (BI) was used to assess ADL. Patients were categorized into four predefined standard BI subcategories according to the national Danish version of the statistical classification of diseases (BI=0-24 (very low ADL), BI=25-49 (low ADL), BI=50-79 (moderate reduced ADL), and BI=80-100 (independent ADL)). Association with mortality was assessed using multivariable Cox regression analysis adjusting for age, marital status, Charlson Comorbidity Index, BMI, prior hospitalizations, year of admission and polypharmacy.

Results: In total, 6,550 patients (women 62%) were included, median (IQR) age 84(79-88) years and BI 37(13-63). Mortality increased significantly with decreasing BI in both the crude and multivariable analysis. In subcategories BI=(80-100) and BI=(0-24) survival time (median(95%)) was 3.6(3.4-3.9) years and 0.8(0.7-0.9) years, respectively. Also, in patients with BI=(0-24), the overall mortality risk (HR(95%CI)) was 2.5(2.2-2.8), 30-day risk 11.8(5.8-23.9), and 1-year risk 4.4(3.6-5.5) when using BI=(80-100) as reference.

Conclusion: BI is independently associated with all-cause mortality among older patients with dementia admitted to hospital. BI may be a helpful tool for clinicians when discussing treatment and care strategies with patients and their families.

Key words: ADL, Barthel Index, mortality, dementia, population-based

Introduction

Life expectancy has increased worldwide since the beginning of the 19th century [1] and is still increasing steadily [2]. Age is one of the primary risk factors for developing dementia [3] and the number of patients with dementia is expected to increase due to the growing population of older people with improved survival at higher ages [2]. Even though mortality risk of dementia is increased compared to the general population [4], WHO estimates that dementia in 2030 will affect 75 million people worldwide [5]. Dementia is a condition with a huge impact on society in terms of cost and caregiver burden similar to that of heart disease and cancer [6, 7]. Besides dementia, the aging population suffers from an increasing amount of multimorbidity and polypharmacy, putting health care systems under further pressure with several challenges ahead [8].

Decline in physical functions is associated with increasing age and is objectively assessed by basic activities of daily living (ADL) [9-11]. Dementia is an umbrella term for many different diseases, all of which have a wide variety of clinical presentations, prognosis, and site of origin. In general, the disease progresses from mild cognitive impairment to its potentially severe stages with a corresponding gradual loss of ADL, with basic ADL being the last affected. The increase in mortality can both be attributed to the general neurodegeneration and cognitive decline, but probably also to the commonly seen trouble with eating and weight loss, difficulties in staying active, and adhere to medical treatment. When discussing future care with a patient with dementia and their relatives it is important to keep a holistic approach taking all aspects of the individual's health into account, including prognosis. However, dementia prognostication is difficult with no reliable way of determining life expectancy in patients with all types of dementia [12]. Therefore, helpful tools providing clinicians information on overall survival is valuable in the discussion of treatment and care strategies.

Previous studies have shown that basic ADL is a strong predictor of mortality in community dwelling older adults [13], in patients attending an emergency department [14], and among hospitalized geriatric patients [15]. Also, in patients with dementia associations between basic ADL and mortality in community dwellers [16, 17] and nursing home residents [18, 19] have been described. However, large studies from hospital settings exclusively evaluating patients with dementia are lacking. The Barthel-Index was first described in 1958 as a

way of measuring the level of dependency in ADL at the time of hospital admission in patients with chronic illness[11, 20]. Since then, it has been modified into various versions. The modified version Barthel-Index-100 (BI) developed by Shah et al. in 1989 with scores from 0-100 is the most elaborated[21]. BI as a way of assessing basic ADL is a fast, simple, low cost, and reliable assessment scale [9] used routinely in all Danish geriatric medicine departments at admission to hospital [15].

Therefore, the aim of this study was to investigate the association between basic ADL assessed by BI at hospital admission and mortality among patients with dementia admitted acutely to geriatric medicine departments.

Patients and methods

This study was a nationwide register-based longitudinal cohort study. We combined data from four different Danish national registers: the Danish civil registration system, the Danish National Database of Reimbursed Prescriptions, the Danish National Patient Registry, and the National Database of Geriatrics.

The Danish civil registration system has been used for 50 years to link information on the individual using a unique 10-digit number. The number is given to each Danish citizen at birth and provides information on death, migration, and marital status [22]. The Danish civil registration system links information on an individual level making it possible for us to account for the individual throughout the different databases. The National Database of Geriatrics is a Danish national clinical quality database that includes all patients admitted to a geriatric department in Denmark. It was established in 2005 and contains information on BI and body mass index. The database has a completeness of >90% [23]. The Danish National Patient Registry contains information on hospital admissions, discharge diagnosis, and dates of admission and discharge [24]. It does not contain any data on disease burden unless specified within the codes. We extracted ICD-8 and ICD-10 codes from this registry up to 10 years prior to index date in order to identify patients with dementia and evaluate comorbidities. The Danish National Database of Reimbursed Prescriptions is a prescription database. The database contains data on all redeemed prescriptions from any pharmacy in Denmark for the past 15 years. The data are reported at an individual level and only medications that are reimbursed are covered by the database

[25]. We extracted the ATC-codes for medications used to treat dementia and evaluated polypharmacy from this database. BI is a widely acknowledged way of assessing basic ADL functions. It consists of 10 domains (feeding, transfer, grooming, toilet use, bathing, mobility, stair climbing, dressing, bowel function, and bladder function) and one can achieve a total score of 0-100 with lower score indicating higher degree of dependence [15]. The highest score within each domain vary between 5, 10 and 15. BI is routinely assessed at time of admission to geriatric department by a nurse [11, 15]. In Denmark, BI is categorized into four standard subcategories according to the national Danish version of the statistical classification of diseases: BI score = 80-100 (independent ADL), BI score = 50-79 (moderately reduced ADL), BI score = 25-49 (low ADL), and BI score = 0-24 (very low ADL) [15].

Study population

We included patients with dementia aged ≥65 years who were identified in the Danish National Database of Geriatrics during 2005-2014. Dementia diagnosis was defined as a patient with relevant ICD-codes up to 10 years prior to index date using relevant ICD-10 codes (F00.0, F00.1, F00.2, F00.9, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, F02.0, F03.9, G30.0, G30.1, G30.8, G30.9, G31.8, G31.9) or ICD-8 codes (290.10, 290.11, 290.09-19, 293.09-19) and/or redeemed prescriptions of anti-dementia medical treatment up to three years prior to index date using relevant ATC-codes (N06DA04, N06DA02, N06DA03, N06DX01) which have previously been proven acceptable for epidemiological studies [26]. Patients were followed until death, emigration, or study termination (31.12.2015).

Statistics

The primary outcome was overall all-cause mortality and the secondary outcome was 30-days and 1-year mortality. BI was categorized into the predefined four subcategories (0-24, 25-49, 50-79, and 80-100). The following variables were defined as confounders: body mass index (BMI) calculated using measured height and weight, age, marital status, year of admission, polypharmacy, prior hospital admissions, and the Charlson comorbidity index (CCI) [27], which was categorized in three groups (0, 1-2, ≥3).

The data was reported either as median with IQR (25-75% percentile) or mean with SD according to data distribution. Chi-squared test was used to test for differences in categorical variables, and differences in the numerical variables were tested using either Wilcoxon rank-sum test for the median differences or Student's *t*-test for the mean differences. Kaplan-Meier survival curves were calculated for the four subcategories of the BI. Cox regression was used for estimating hazard ratios in the univariable and multivariable analyses, which included adjustment for age, marital status, BMI, CCI, polypharmacy, and prior hospital admissions. The Cox regression model was tested using Wald statistics. In case of missing data (BI and BMI) we performed a robustness analysis placing these patients in either the highest or lowest BI- or BMI-group. P-value of ≤ 0.05 indicated statistical significance.

Ethics

According to Danish medical ethics, informed consent was not necessary due to the use of register-based retrospective data only. The Danish Data Protection Agency approved the study allowing linkage of data on an individual level (2012-58-0018, J.nr. 16/23359). Data is reported according to the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines [28].

Results

A total of 6,550 patients (women 62%) were included (Figure 1). Patients had a median (IQR) age of 84 (79-88) years, a median (IQR) BI-score of 37 (13-63), a normal BMI (mean (SD) 23.4 (4.5)), a median (IQR) CCI of 1 (0-2), and 20% used ten or more medications at admission (Table 1). BI was missing in 539 patients upon admission leaving 6,008 patients available for analysis.

During the study period 5,156 patients died yielding a total of 13,761 person-years of follow-up. The median (95% CI) survival of the cohort was 2.0 (1.9-2.1) years with women living longer (2.2 (2.1-2.4) years) compared to men (1.5 (1.4-1.6) years). Mortality increased significantly with decreasing BI (Figure 2) ($p<0.001$). In women, survival (median (95% CI)) was 3.8 (3.5-4.3) years in subcategory BI score = 80-100, 2.8

(2.5-3.1) years in subcategory BI score = 50-79, 2.4 (2.1-2.5) years in subcategory BI score = 25-49, and 0.9 (0.8-1.1) years in subcategory BI score = 0-24. In men, survival time (median (95% CI)) was 3.1 (2.8-3.6) years in subcategory BI score = 80-100, 2.2 (1.9-2.5) years in subcategory BI score = 50-79, 1.6 (1.4-1.8) years in BI score = 25-49, and 0.6 (0.5-0.8) years in subcategory BI score = 0-24.

Low BI score = 0-24 was significantly associated with increased overall mortality HR (95% CI) in the total cohort (2.71 (2.46-2.98)) when using BI score = 80-100 as reference in the univariable analysis (Table 2). The BI stayed significantly associated with 30-days (11.79 (5.82-23.90)), 1-year (4.41 (3.55-5.48), and overall (2.46 (2.21-2.75)) mortality in the fully adjusted multivariable analysis (Table 2).

Performing robustness analysis for patients with missing data on either BI or BMI did not alter the significant association between BI and mortality (data not shown).

Discussion

In this nationwide register-based longitudinal cohort study of 6,550 hospitalized patients with dementia, we found that BI assessed at hospital admission was independently associated with overall, 30-days, and 1-year mortality.

The associations between basic ADL, mortality, and dementia have previously been evaluated in other studies, but most of them were either small, did not specifically address dementia, or were performed in settings outside the hospital. Two studies assessed basic ADL in a hospital setting (emergency department [14]; general hospital [29]), and found similar associations with mortality. But both studies used a non-specific general patient population, making conclusions less applicable to patients with a dementia diagnosis. However, in our previous study using the entire hospitalized population of the Danish National Database of Geriatrics we found, similar to the present study, an association between low BI and increased mortality, which supports the importance of including a functional assessment when discussing treatment and care strategies [15].

In the US, a small study of 399 nursing home residents described an association between low basic ADL and increased mortality especially among the cognitively impaired residents [18]. However, the study did not adjust

for other risk factors of mortality and described nursing homes setting in the 1990-ies making it less reliable in today's setting. Another large prospective cohort-study among institutionalized older adults and with a follow-up of only one year also showed an association between low BI and increased mortality [19]. Yet, only a few residents had verified dementia making it more difficult to draw conclusions even though undiagnosed dementia probably is more common among the institutionalized.

Two studies on older community-dwelling adults have also examined functional decline and an association between dementia and mortality [16, 17], but both studies were, compared to our study, relatively small in number (<800 patients) [16, 17]. A Danish population-based birth cohort study of an unselected population of 2,262 very old adults (92+ year-olds) also found an association between low basic ADL and increased mortality [13]. Even though this study does not apply to patients admitted to hospital, it supports our findings and is indicative of an association outside hospitals as well.

Our study has several limitations. First, by using data from the national registers we have no data on disease severity. Even though a prior validation study showed that the diagnoses of dementia in registers are valid and can be used to perform epidemiological research [26] we cannot address disease impact, nor can we be sure that all patients with dementia were registered with a dementia diagnosis in the registers. It may be the case that only the most obvious dementia cases were registered, i.e. the patients with more severe forms of dementia. The assessed ICD-10 codes cover Alzheimer's disease, Pick's disease, vascular dementia, and unspecified dementia thereby covering the most common causes of dementia. Some forms of dementia have a rapid deterioration and quick death whereas other forms progress slowly and the clinical stage of dementia is known to be one of the most important prognostic factors. There was no way of determining the clinical state based on the ICD-10 code alone. If we have included a higher proportion of patients with the most severe forms of dementia, we increase the risk of overestimating the association between basic ADL and mortality among patients with dementia.

Second, we had missing data on BMI in 27.6% of the cases and for BI in 8.2% of the cases. Patients with all kinds of dementia are known to change eating behavior and diet, and are therefore also known to lose weight. Because of this, we would expect more patients with dementia in the lower BMI groups, which could

potentially overestimate mortality due to missing data on BMI. However, our robustness analysis did not change the results significantly when adding patients with missing data in either the lowest or highest BMI category group. Third, we looked at prescribed and collected medication only. Whether the patients take their medications or not is unknown which might affect the results in either direction. Fourth, cause of admission may vary from serious conditions with a high mortality to less serious conditions such as mild dehydrations. The current dataset did not include data on cause of admission or severity of comorbidities. However, we used CCI to adjust for diseases known to have an impact on mortality. Finally, our data do not allow us to look into the different domains of BI. We only had the final score and are not able to address if any subdomains of the BI have more impact than others. Also, we had no data on BI at discharge or later in the course of care and can therefore not address impact of potential changes in BI during admission or after discharge.

Our study also had some strengths. We used four national registers that have been proven valid for use in epidemiological studies [22-25]. This allowed us not only to account for all patients during the entire study period with no patients lost to follow-up, but also to include several important register-based co-factors in our analyzes. Furthermore, we had access to objective measurements of basic ADL and BMI, which both are performed routinely at the geriatric departments. Using BI allowed us to evaluate the actual level of dependency.

As the natural course of dementia is a progressive decline until death, it is helpful for clinicians to identify when a patient is approaching end of life to initiate advanced care planning discussions with the patient and relatives. However, estimating how long a patient with dementia will live can be challenging [30]. In this population-based study we provide information on expected survival after hospital admission among older geriatric patients with dementia. Those with high BI at hospital admission have a median life expectancy of more than three years whereas survival in those with low BI is less than one year, for some close to six months. It is well known that patients with dementia have increased mortality rates compared to the general population. It is also well known that they have increasing difficulties in basic ADL. Our study shows that identification of these difficulties by using BI are directly associated to survival even when adjusting for multiple other common risk factors. This

information could, together with other prognostic tools, such as the SPICT guidelines, be a valuable tool to the clinician and be included in discussions on advanced care planning and end-of-life care, and influence future medical decisions on hospitalization or not [31].

It is important to consider that our results are based on population level data and may therefore not be directly applicable to the individual, e.g. some of the patients with low BI in our study exceeded the median life expectancy and some of these patients may very well benefit from hospitalization and treatment. Therefore, the BI should only be used as an add-on tool when discussion treatment and care strategies. Also, although the BI is significantly associated with mortality, it does not provide information on the individual's quality of life. However, a recent large study of more than 470,000 patients ≥65 years showed that the onset of ADL difficulties significantly reduces the health-related quality of life [32].

Various sophisticated prognostic tools and frailty scales are available today, but this study shows that even simple assessment of ADL might still provide valuable information. BI is a robust, fast, efficient, and reliable assessment tool that has widely been proven valid for determining basic ADL [9-11]. It is routinely used in geriatric departments in Denmark, and could easily be applied to other hospital departments, maybe even to individuals with dementia living in the community with home care support, since other studies have found a similar association between ADL and mortality in non-hospitalized older adults [13, 16-19]. Yet, our results from this hospitalized study population cannot be validly extended to non-hospitalized community-dwelling older citizens. Also, future studies should address whether interventions aimed at increasing BI may potentially change the trajectory of mortality.

Conclusion

Basic activity of daily living is independently associated with all-cause mortality among geriatric patients with dementia admitted to hospital, even when adjusting for multiple known risk factors. Using the BI may be valuable for clinicians when discussing treatment and care strategies with patients and their families.

Author contributions

JR and PLA had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. TV, PLA, and JR designed the study. PLA performed the statistical analyzes in dialogue with TV and JR. All authors (TV, KAR, FW, PLA, TM, JR) were involved in the interpretation of data. TV wrote the first manuscript draft and all authors (TV, KAR, FW, PLA, TM, JR) were involved in the critical revision of the manuscript. JR had the primary responsibility for the final content but all authors (TV, KAR, FW, PLA, TM, JR) are accountable for the aspects of the work. All authors (TV, KAR, FW, PLA, TM, JR) read and approved the final manuscript.

Disclosure and Funding

All authors have completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and declare no personal conflict of interest regarding the present study. The study was supported by the Program for Clinical Research Infrastructure (PROCRIN) established by the Lundbeck Foundation and the Novo Nordisk Foundation. The funders were not involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data availability

According to the Danish Law on personal data, we are not allowed to make the dataset publicly available. Access to data from the Danish Health Data Authority requires association with a Danish research unit and approval from the Danish Data Protection Agency (www.datatilsynet.dk/english/) and the National Health Service Register (www.sundhedsdatastyrelsen.dk/da/forskerservice (in Danish)).

Compliance with ethical standards

Conflict of interest

All authors have completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and declare no personal conflict of interest regarding the present study.

Ethical approval

Approval from local ethical committee was not needed due to the epidemiological design of this study.

Informed consent

Informed consent was not necessary according to Danish legislation due to the register-based study design

Data sharing statement

According to the Danish Law on personal data, we are not allowed to make the dataset publicly available. Access to data from the Danish Health Data Authority requires association with a Danish research unit and approval from the Danish Data Protection Agency (www.datatilsynet.dk/english/) and the National Health Service Register (www. sundhedsdatastyrelsen.dk/da/forskerservice (in Danish))

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Legends

Figure 1 Flow chart of the study population and follow-up

Figure 2 Survival for the total cohort (A) and stratified by gender (women (B), men (C)). Illustrated for each of the four predefined Barthel-Index (BI) subcategories (0-24, 25-49, 50-79, 80-100)

Figures

Figure 1

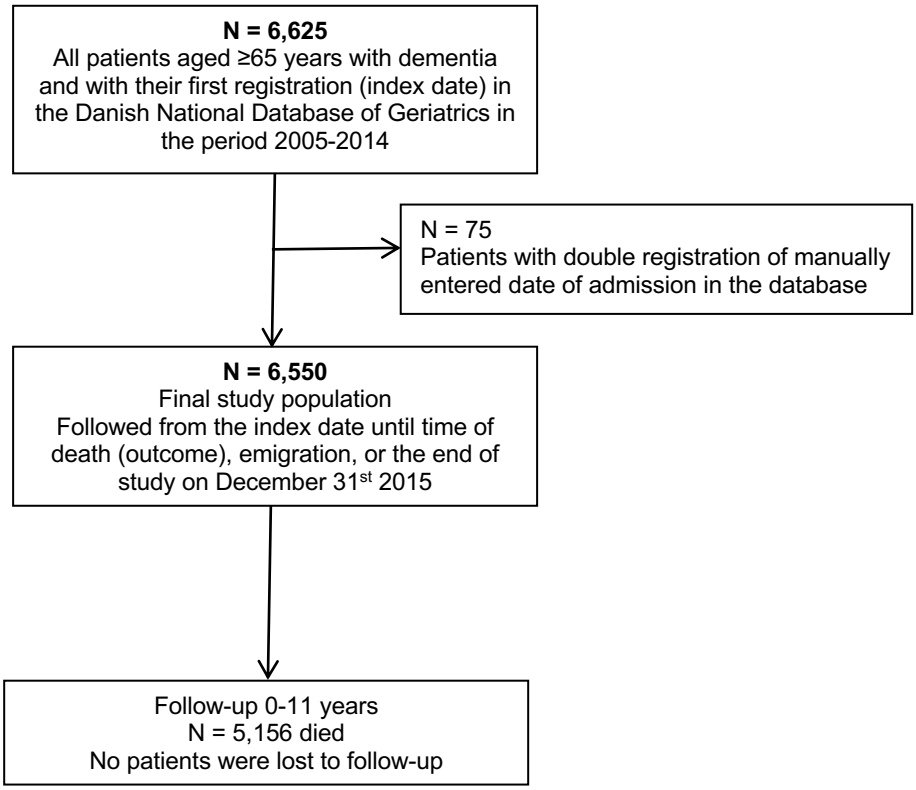
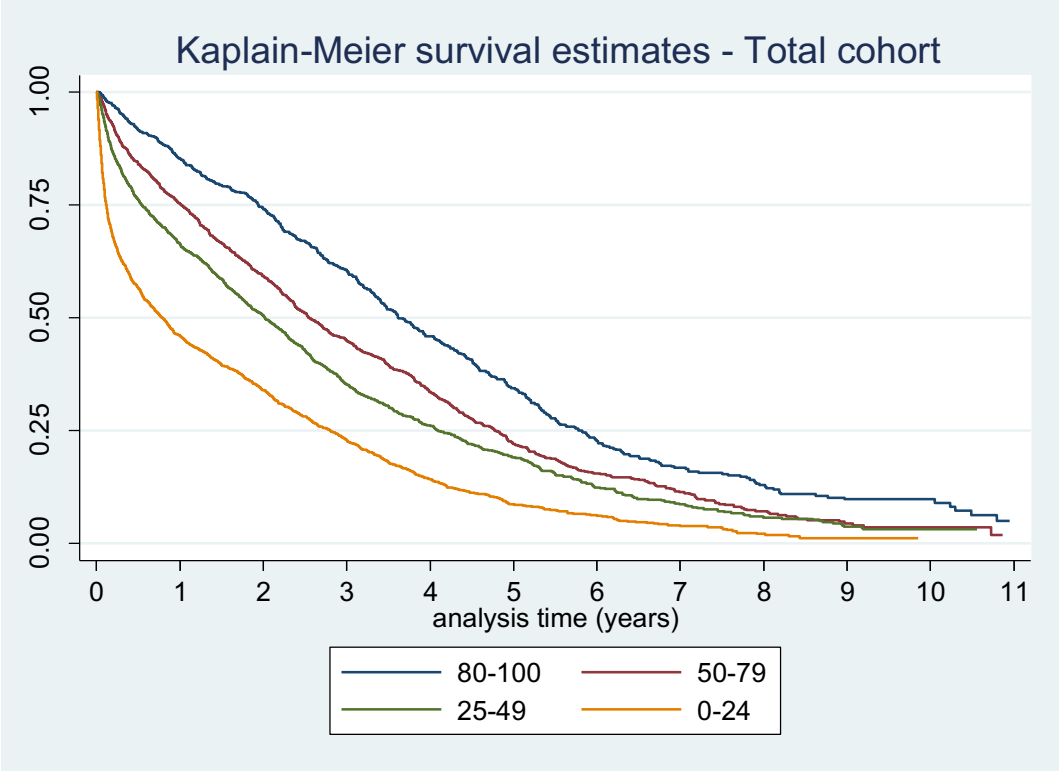
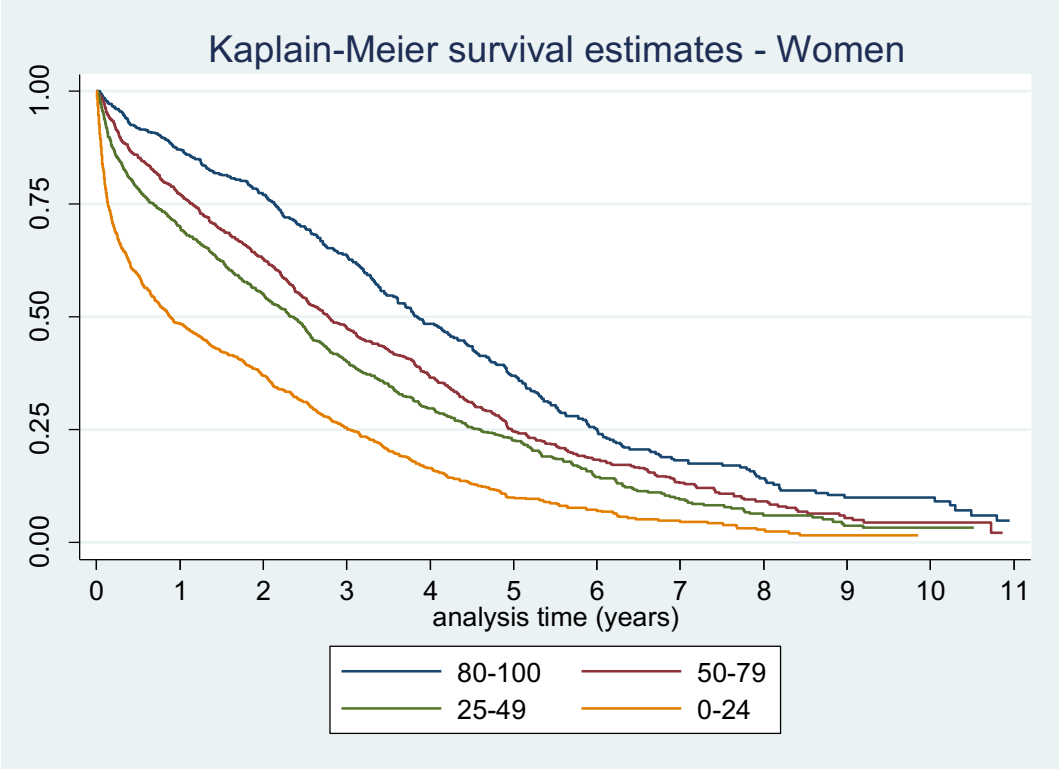


Figure 2

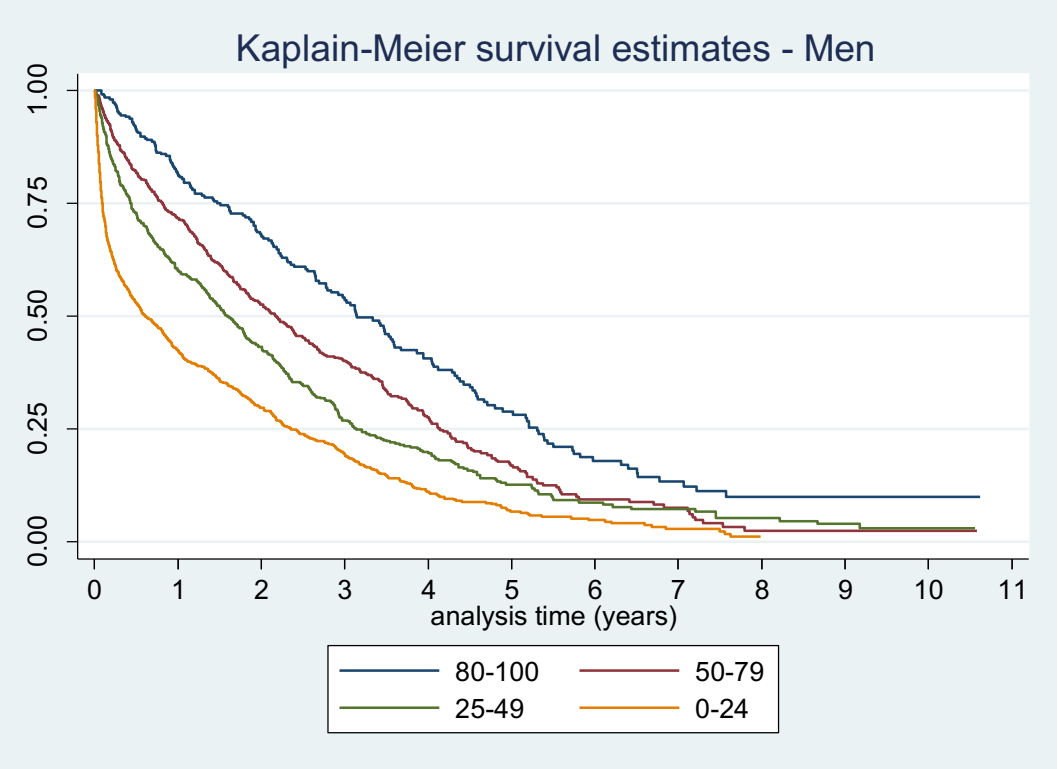
A


Kaplain-Meier survival estimates - Total cohort
1.00
0.75
0.50
0.25
0.00
0
1
2
3
4
5
6
7
8
9
10
11
analysis time (years)
80-100
50-79
25-49
0-24

B


Kaplain-Meier survival estimates - Women
1.00
0.75
0.50
0.25
0.00
0
1
2
3
4
5
6
7
8
9
10
11
analysis time (years)
80-100
50-79
25-49
0-24

C


Kaplain-Meier survival estimates - Men
1.00
0.75
0.50
0.25
0.00
0
1
2
3
4
5
6
7
8
9
10
11
analysis time (years)
80-100
50-79
25-49
0-24

Tables

Table 1 Baseline characteristics of the study population

	Total cohort N = 6,550	Women N = 4,062	Men N = 2,488
Barthel Index median	37 (13-63)	39 (15-65)	32 (10-59)
80-100 n (%)	776 (11.8)	521 (12.8)	255 (10.2)
50-79 n (%)	1,490 (22.7)	967 (23.8)	523 (21.0)
25-49 n (%)	1,479 (22.6)	927 (22.8)	552 (22.2)
0-24 n (%)	2,266 (34.6)	1,325 (32.6)	941 (37.8)
Missing n (%)	539 (8.2)	322 (7.9)	217 (8.7)
Age (years) median	84 (79-88)	85 (80-88)	82 (77-86)
65-74 n (%)	741 (11.3)	341 (8.4)	400 (16.1)
75-84 n (%)	2,892 (44.2)	1,664 (41.0)	1,228 (49.4)
85-94 n (%)	2,738 (41.8)	1,910 (47.0)	828 (33.3)
≥95 n (%)	179 (2.7)	147 (3.6)	32 (1.3)
Marital status n (%)			
Unmarried	338 (5.2)	205 (5.0)	133 (5.3)
Married	2,275 (34.7)	820 (20.2)	1,455 (58.5)
Divorced	727 (11.1)	449 (11.1)	278 (11.2)
Widowed	3,207 (49.0)	2,586 (63.7)	621 (25.0)
Missing	3 (0.0)	2 (0.0)	1 (0.0)
Period of admission			
2005-2009	2,720 (41.5)	1,778 (43.8)	942 (37.9)
2010-2014	3,830 (58.5)	2,284 (56.2)	1,546 (62.1)
BMI (kg/m^2) mean			
(SD)	23.4 (4.5)	22.9 (4.7)	24.2 (4.1)
<16.5 n (%)	192 (2.9)	159 (3.9)	33 (1.3)
16.5-18.4 n (%)	383 (5.8)	299 (7.4)	84 (3.4)
18.5-24.9 n (%)	2,656 (40.5)	1,689 (41.6)	967 (38.9)
25-29.9 n (%)	1,120 (17.1)	576 (14.2)	544 (21.9)
≥30 n (%)	388 (5.9)	248 (6.1)	140 (5.6)

Missing n (%)	1,811 (27.6)	1,091 (26.9)	720 (28.9)
Charlson Comorbidity Index median *	1 (0-2)	1 (0-2)	1 (0-3)
0 n (%)	2,217(33.8)	1,493 (36.8)	724 (29.1)
1-2 n (%)	2,8455 (43.4)	1,796 (44.2)	1,049 (42.2)
≥3 n (%)	1,487 7 (22.7)	772 (19.0)	715 (28.7)
Missing n (%)	1 (0.0)	1 (0.0)	0
Number of drugs purchased (120 days) median ‡	6 (4-9)	6 (4-9)	6 (4-9)
0 n (%)	135 35 (2.1)	82 (2.0)	53 (2.1)
1-4 n (%)	1,878 78 (28.7)	1,153 (28.4)	725 (29.1)
5-9 n (%)	3,218 18 (49.1)	2,017 (49.7)	1,201 (48.3)
≥10 n (%)	1,288 288 (19.7)	790 (19.4)	498 (20.0)
Missing n (%)	31 (0.5)	20 (0.5)	11 (0.4)
Prior hospital admission (1 year) ¤	0 (0-1)	0 (0-1)	1 (0-1)
0 n (%)	3,279 (50.1)	2,117 (52.1)	1,162 (46.7)
1-2 n (%)	2,588 (39.5)	1,580 (38.9)	1,008 (40.5)
≥3 n (%)	682 (10.4)	364 (9.0)	318 (12.8)
Missing n (%)	1 (0.0)	1 (0.0)	0

Notes: * The Charlson Comorbidity Index was calculated based on hospital discharge diagnoses during ten years before baseline. ‡ All redeemed prescriptions were included, except from the following ATC codes: B05x (Blood substitutes and perfusion solutions), B06x (Other hematological agents), D09x (Medicated dressings), J07x (Vaccines), N01x (Anesthetics) and Vx (Various). Medications were counted at the fourth level of the ATC code, ie including the first 5 digits of the ATC code (eg Salicylic acid and derivates: N02BA). ¤ Based on hospital admissions during one year before baseline. Normal distributed data are presented with mean (SD) whereas non-normal distributed data are presented with both median (IQR) and mean (SD)

Abbreviations: ATC, Anatomical Therapeutic Chemical; BMI, Body Mass Index; IQR, Inter Quartile Range

Table 2 Univariable and multivariable* Hazard Ratios and corresponding 95% confidence intervals for overall mortality according to the Barthel Index by gender, using the Barthel Index subcategory 80-100 as the reference

Exposure	Total cohort HR (95% CI)		Women HR (95% CI)		Men HR (95% CI)	
	Univariable	Multivariable	Univariable	Multivariable	Univariable	Multivariable
Barthel index						
80-100	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
50-79	1.37 (1.24-1.52)	1.29 (1.15-1.44)	1.34 (1.18-1.52)	1.28 (1.11-1.47)	1.43 (1.19-1.71)	1.22 (1.00-1.49)
25-49	1.67 (1.51-1.85)	1.56 (1.39-1.75)	1.60 (1.41-1.82)	1.52 (1.32-1.75)	1.78 (1.49-2.13)	1.58 (1.29-1.92)
0-24	2.71 (2.46-2.98)	2.46 (2.21-2.75)	2.66 (2.35-2.99)	2.45 (2.14-2.81)	2.71 (2.29-3.20)	2.33 (1.93-2.82)
Age group						
65-74	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
75-84	1.26 (1.14-1.39)	1.27 (1.13-1.43)	1.29 (1.11-1.49)	1.21 (1.02-1.43)	1.37 (1.20-1.56)	1.40 (1.19-1.65)
85-94	1.65 (1.49-1.81)	1.73 (1.53-1.95)	1.79 (1.55-2.06)	1.69 (1.43-2.01)	1.82 (1.59-2.09)	1.92 (1.61-2.28)
95+	2.22 (1.85-2.65)	2.16 (1.73-2.71)	2.56 (2.06-3.19)	2.37 (1.81-3.10)	2.37 (1.62-3.48)	1.57 (0.94-2.64)
Marital status						
Unmarried	0.90 (0.79-1.02)	0.87 (0.75-1.02)	1.02 (0.85-1.21)	0.95 (0.77-1.16)	0.89 (0.73-1.09)	0.91 (0.71-1.16)
Married	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Divorced	0.85 (0.78-0.94)	0.84 (0.75-0.95)	0.94 (0.82-1.07)	0.90 (0.76-1.06)	0.92 (0.79-1.06)	0.96 (0.80-1.15)
Widowed	0.91 (0.86-0.97)	0.86 (0.80-0.93)	1.06 (0.97-1.16)	0.99 (0.88-1.11)	1.03 (0.93-1.14)	1.03 (0.90-1.17)
Period of admission						
2005-2009	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
2010-2014	1.16 (1.10-1.23)	1.06 (0.99-1.14)	1.19 (1.10-1.28)	1.04 (0.95-1.14)	1.07 (0.98-1.17)	1.09 (0.97-1.22)
BMI (kg/m^2)						
<16.5	1.74 (1.48-2.03)	1.69 (1.44-1.98)	1.90 (1.59-2.26)	1.86 (1.55-2.23)	1.89 (1.32-2.71)	1.81 (1.24-2.63)
16.5-18.4	1.41 (1.25-1.58)	1.33 (1.18-1.49)	1.47 (1.28-1.68)	1.41 (1.23-1.62)	1.68 (1.33-2.12)	1.40 (1.09-1.80)
18.5-24.9	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
25-29.9	0.84 (0.77-0.91)	0.83 (0.77-0.91)	0.83 (0.75-0.93)	0.83 (0.74-0.93)	0.75 (0.66-0.84)	0.75 (0.66-0.85)
≥30	0.77 (0.68-0.87)	0.74 (0.65-0.84)	0.85 (0.73-1.00)	0.83 (0.70-0.97)	0.62 (0.51-0.77)	0.60 (0.49-0.75)
Charlson Comorbidity Index^						
0	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
1-2	1.12 (1.05-1.19)	1.20 (1.11-1.30)	1.12 (1.04-1.22)	1.15 (1.05-1.27)	1.08 (0.97-1.20)	1.24 (1.09-1.41)
≥3	1.32 (1.23-1.42 3)	1.40 (1.27-1.54)	1.38 (1.25-1.52)	1.48 (1.31-1.68)	1.14 (1.02-1.28)	1.21 (1.04-1.40)

Medications at admission‡						
0	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
1-4	1.13 (0.92-1.38)	0.90 (0.72-1.14)	1.10 (0.85-1.44)	0.93 (0.67-1.29)	1.20 (0.88-1.64)	0.92 (0.66-1.30)
5-9	1.19 (0.97-1.44)	0.91 (0.72-1.15)	1.21 (0.93-1.57)	0.98 (0.71-1.35)	1.20 (0.88-1.62)	0.93 (0.66-1.30)
≥10	1.35 (1.10-1.65)	1.02 (0.80-1.30)	1.38 (1.05-1.80)	1.10 (0.79-1.53)	1.33 (0.97-1.83)	1.09 (0.76-1.56)
Prior (1 year) hospital admission ¤						
0	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
1-2	1.07 (1.01-1.13)	1.04 (0.97-1.12)	1.09 (1.01-1.17)	1.09 (0.99-1.19)	1.00 (0.91-1.10)	0.92 (0.82-1.04)
≥3	1.18 (1.07-1.29)	1.05 (0.93-1.18)	1.15 (1.02-1.31)	1.05 (0.89-1.22)	1.13 (0.98-1.29)	1.01 (0.84-1.21)

Notes: ^ The Charlson Comorbidity Index was calculated based on hospital discharge diagnoses during ten years before baseline. ‡ All redeemed prescriptions were included, except from the following ATC codes: B05x (Blood substitutes and perfusion solutions), B06x (Other hematological agents), D09x (Medicated dressings), J07x (Vaccines), N01x (Anesthetics) and Vx (Various). Medications were counted at the fourth level of the ATC code, ie including the first 5 digits of the ATC code (eg Salicylic acid and derivates: N02BA). ¤ Based on hospital admissions during one year before baseline. * Adjusted for age, marital status, body mass index, Charlson Comorbidity Index, number of different medications purchased in the 120 days prior to index date, number of hospital admissions during 1 year before baseline, and period of index admission. Women: n=2,865; Men: n=1,696.

Abbreviation: ATC, Anatomical Therapeutic Chemical; CI, confidence interval; HR, Hazard Ratio

Table 3 Multivariable* Hazard Ratios and corresponding 95% confidence intervals for 30-day and 1-year mortality according to the Barthel Index by gender, using the Barthel Index subcategory 80-100 as the reference

Barthel Index	Total cohort HR (95% CI) *	Women HR (95% CI) *	Men HR (95% CI) *
30-day			
BI 80-100	1 (reference)	1 (reference)	1 (reference)
BI 50-79	2.27 (1.06-4.87)	1.84 (0.74-4.55)	3.49 (0.80-15.13)
BI 25-49	3.99 (1.91-8.33)	3.41 (1.44-8.11)	5.88 (1.40-24.27)
BI 0-24	11.79 (5.82-23.90)	9.07 (3.97-20.70)	18.49 (4.5-74.91)
p	< .001	< .001	< .001
1-year			
BI 80-100	1 (reference)	1 (reference)	1 (reference)
BI 50-79	1.66 (1.32-2.9)	1.74 (1.28-2.37)	1.47 (1.02-2.11)
BI 25-49	2.37 (1.88-2.98)	2.47 (1.83-3.34)	2.17(1.53-3.08)
BI 0-24	4.41 (3.55-5.48)	4.82 (3.61-6.44)	3.69(2.64-5.15)
p	< .001	< .001	< .001

Notes: * Adjusted for age, marital status, body mass index, Charlson Comorbidity Index, number of different medications purchased in the 120 days prior to index date, number of hospital admissions during 1 year before baseline, and period of index admission. Women: n=2,865; Men: n=1,696.

Abbreviation: BI, Barthel-Index