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The male–female health–survival paradox: A survey and register study of the impact of sex-specific selection and information bias

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Running head: Selection and information bias in the Danish surveys

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Abstract

Background. There is a remarkable discrepancy between the health and survival of men and women: men are physically stronger and have fewer disabilities, but they still have excess mortality at all ages compared with women. A number of proposed explanations are rooted in biological, social and psychological interpretations. The present study examined whether the health–survival paradox could partially be due to sex-specific selection and information bias in surveys.

Methods. The study is based on the linkage of three population-based surveys of 15,401 Danes aged 45–102 years with health registers covering the total Danish population regarding hospitalizations within the last two years prior and prescription medicine use within the last six months prior to the baseline surveys.

Results. Men had higher participation rates than women at all ages. Non-hospitalized men had higher participation rates compared to hospitalized men in all age groups except the group of 90+ year-olds (difference 1.4-7.1%), while no consistent pattern was found for females according to hospitalization status. However, women taking medications had higher participation rates than female non-users (difference 0.8-7.6%), while no such pattern was seen in men. Men used fewer medications than women, but they underreported medication use to a similar degree as women.

Conclusions. Women using prescription medicine, as well as non-hospitalized men, were slightly over-represented in the surveys. This suggests that selection bias in surveys may contribute to the explanation of the health–survival paradox. However, there was no evidence for sex-specific reporting of medication use among the study participants.

Background

In almost all western countries, men report better health than females^{1,2}, but women still outlive men in all countries around the world³. Among the most widely cited explanations for this apparent contradiction are favorable effects of estrogen on serum lipids⁴, the compensatory effect of the second X chromosome^{5,6}, a lower ability of the male immune system to avoid the harmful effects of infections⁷, a relatively higher compatibility of sick roles with other female responsibilities, engagement in more risk-taking behavior among men, as well as better awareness of disease symptoms and timely seeking for medical advice among women^{8,9}. Research findings that women are more sensitive about disease symptoms, perceive and report more symptoms, physical or physically unexplained, suggest that excess morbidity among women may partially be attributed to over-reporting of worse health^{10,11}.

The distribution of chronic diseases has been proposed to contribute to the health–survival paradox^{2,12}. Women suffer more frequently from diseases that increase the risk of physical disabilities and that have a relatively low contribution to the overall mortality risk (e.g. musculoskeletal diseases), whereas men experience diseases that considerably impact both their health status and mortality risk – in particular, cardiovascular diseases. The distribution of many diseases depends on their definitions, diagnostic procedures and age-related changes in incident rates. For example, coronary heart disease (CHD) incidence is about twice as high in middle-aged men compared with same-aged women, but the male excess of CHD incidence and mortality declines after 60 years of age and, for 80-year-olds, the sex difference is small¹³.

Despite mounting research regarding sex differences in health and mortality, we still do not fully understand neither the reasons for the paradox nor its mechanisms. The health–survival paradox is likely to be due to multiple causes, including fundamental biological and behavioral

differences. Another consideration is that the paradox can partially be due to bias in surveys if men are more reluctant than women to participate and/or accurately report in surveys if they have disabilities or diseases. The Nordic countries, with their long tradition of surveys with high participation rates and national health registers, are excellent settings for testing this hypothesis.

In the present study we utilized a unique opportunity to link three Danish surveys covering 15,401 individuals aged 45–102 years with the extensive register information on the complete Danish population. We hypothesized that unhealthy men will be less willing to participate in surveys than their female counterparts. If so, this would lead to a bias, resulting in underestimation of the health problems in surveyed men. The study also aimed to test whether there is sex-specific information bias in the surveys by comparing self-reported medication use with prescribed medications recorded in the registers. We hypothesized that women and men will have a similar reporting pattern for major medications, e.g. cardiovascular medications, but women will have more accurate reporting of nervous and musculoskeletal system medications.

Materials and methods

The study is based on the linkage of the Study of Middle-Aged Danish Twins (MADT), the Longitudinal Study of Aging Danish Twins (LSADT), and the Danish 1905–Cohort Survey with registers within Statistics Denmark. The studies are described in detail elsewhere¹⁴⁻¹⁶. In brief, participants in the MADT and LSADT were identified in the Danish Twin Register¹⁷ and participants in the 1905-Cohort Survey were identified in the Danish civil registration system¹⁸.

The MADT represented a random sample of 120 twin pairs from each birth cohort from 1931 to 1952, aged 45-68 years in 1998 when the survey was implemented. The LSADT

involved the Danish twins aged 75 years and older by January 1995, and residing in Denmark. Twins aged at least 70 years were added to the 1997, 1999 and 2001 follow-ups¹⁹.

The 1905-Cohort Survey included all Danes born in 1905 and alive in 1998 (aged 92–93 years). The consecutive waves in 2000, 2003 and 2005 were follow-up assessments of survivors from previous waves. In all surveys the individuals residing in nursing homes or sheltered accommodation were considered eligible to participate in the study. If persons refused or were unable to participate in the face-to-face interview, a proxy respondent, usually a close relative, was sought.

All three studies are comparable with regard to the design, implementation and data collection instrument with only minor differences, mainly related to age distributions in the three surveys. The questionnaire consisted of an extensive battery of questions on health, lifestyle and socioeconomic conditions, and tests of cognitive and physical functioning, as well as the collection of biological samples. Data collection in each survey wave was carried out within approximately three months.

Register linkage

Since 1968 all residents of Denmark have been identified by a unique 10-digit identification number – the Civil Registration Number (CPR number) – that can be linked to thematically organized databases (called ‘registers’) within Statistics Denmark. In the present study all individuals who were invited to participate in the MADT, LSADT and 1905-Cohort Survey were identified and linked to the Danish Demographic Database (includes information on birth, sex, death and migration); the National Patient Register (includes type and date of hospital admissions, primary diagnoses (International Classification of Diseases 8 (ICD-8) until 1993 and

ICD-10 since 1994), and number of hospital days and other information for non-psychiatric illnesses since 1977); and the Prescription Medicine Register, which contains the Anatomical Therapeutic Chemical classification system (ATC) codes of prescribed medications, dates of purchase and other drug-related information since 1994. The Register contains the individual-level information on all prescription medications purchased at all commercial pharmacies in Denmark, but the drugs administered in hospitals are reported on the ward level and, therefore, omitted in the present analysis. Using CPR numbers, the register data on hospitalization and medication use were combined with demographic characteristics and variables identifying participation in the surveys.

Non-response variables

The outcome variable of interest – non-response – was defined as non-participation in the intake survey for any reason other than death or emigration from the country. Proxy interviews were considered to be non-respondents, as proxies are often spouses and could confound the analysis of sex differences in the response pattern.

Hospitalization and medication use variables

All-cause and diagnosis-specific hospitalizations within two years prior to the baseline surveys were selected as the operational measures of morbidity. This time period was selected in accordance with a 2-year interval between consecutive waves in the LSADT and 1905-Cohort Survey. All-cause and system-specific medication use was assessed within six months prior to the intake. The interview dates were used to define the beginning and end of the 2-year interval. For non-respondents the first dates of the corresponding surveys were used.

All-cause hospitalization included all inpatient admissions except ICD-8 Y-list (unique for the Danish healthcare system, e.g. Y0099 – general examination of endocrine and metabolic system, Y4009 – contact with tuberculosis) and ICD-10 Z00-Z99 (e.g. Z00 - general examination and investigation of persons without complaint and reported diagnosis). The total cardiovascular diseases (CVDs) hospitalization included all inpatient admissions with primary diagnoses ICD-8 390-459, 745-747 and ICD-10 I00-I99, Q20-Q28. The major CVD hospitalization included all admissions with ICD-8 390–459 and ICD-10 I00-I99 diagnoses. Cancer hospitalization (apart from skin cancer) included all admissions for primary diagnoses ICD-8 140-171, 174-199, 201-207 and ICD-10 C00-C41, C45-C97. All diagnosis-specific hospitalization variables were grouped as follows: 1- non-hospitalized, 2-hospitalized for specific diagnosis (cancer or total/major CVD) and 3- other diagnoses.

The all-cause medication use indicator included all prescribed medications. System-specific medication use included the cardiovascular system medications (ATC-C) and was categorized as: 1- non-users, 2- ATC-C medications and 3- all others. As the information letter is usually sent weeks before the interview, we used medicine prescribed during the six months before the interview in the analyses of non-participation. Due to the availability of the Prescription Medicine Register only since 1995, the non-participation analyses for LSADT begin with the 1997 wave for medicine use. In all analyses non-hospitalized groups or non-users were taken as the reference category.

Measurement of information bias

Information bias was evaluated by comparing the mean number of registered and reported medications. The comparison was made for all-cause, ATC-C, musculoskeletal (ATC-

M), nervous (ATC-N) and respiratory (ATC-R) system medications. The number of prescribed all-cause medications from the register data was calculated as a total count of all medications prescribed within the six months after intake.

The information on medication use in surveys was obtained by asking the participants to list all medicines that they take on a regular basis or to present to an interviewer their drug storage. All prescribed medications reported by the participants were assigned the ATC code by a pharmacologist and the number of reported medications was calculated as a total count of all prescribed medications. Alternative medications and vitamins were excluded.

A medication was counted only once if the person was prescribed different drugs of the same pharmacological subgroup (3rd level of ATC classification system) or the same drug multiple times within the selected time period. We also estimated a number of prescribed all-cause medications six months before and three months before and after the baseline. However, as the three methods yielded similar results, the number of system-specific medications was calculated within six months after the baseline surveys only. Previous research in Denmark suggests that medication use within six months after the survey represents a more accurate measurement of actual medicine use²⁰.

Statistical analysis

Logistic regression was used to analyze the impact of prior hospitalization and medication use on response pattern. All regression analyses in the total samples were adjusted for age and sex. The estimates are presented in odds ratios (ORs) and 95% confidence intervals (CIs). To elucidate sex differences in the response pattern, the interaction between hospitalization or medication use indicators and sex was included using non-hospitalized men or

male non-users, respectively, as the reference category. Additional analysis was carried out for sex-specific samples. Age was categorized into four groups as follows: 46–49, 50–54, 55–59, ≥ 60 years old in the MADT, and 70–74, 75–79, ≥ 80 years in the LSADT. The youngest groups were taken as the reference category throughout the whole analysis. To correct for the correlated nature of twin data, the robust regression for all equations was used controlling for cluster by twin pair (Intercooled Stata 9.0, StataCorp, College Station, TX).

Results

Response rate

In total, 5,280 individuals were invited to participate in the MADT (mean age \pm standard deviation [SD]: 56.9 [6.3], range: 45.8 – 68.1) and 6,535 eligible individuals were invited for the LSADT intake participation (77.4 [5.6], 69.9-102.1). There were 3,095 twins invited in the LSADT 1995 baseline survey, 784 twins were added in 1997, 2001 twins in 1999 and 655 persons in the 2001 intake. Fourteen individuals – six from the MADT and eight from the LSADT – were excluded from the analysis because we were unable to track them in the Statistics Denmark registers. In the 1905-Cohort Survey, 3,600 elderly individuals (92.9 [0.41], 92.1-93.8) were invited to participate in the baseline survey.

The age- and sex-specific response rates are presented in Table 1. Generally, men had higher participation rates than women. Participation rates tended to decrease with advanced age except for the LSADT.

All-cause and diagnosis-specific hospitalization and response pattern

The data analysis revealed that non-hospitalized men had higher participation rates compared with hospitalized men in all age groups except the oldest, while no consistent pattern was found for women based on hospitalization status (Table 2). Non-hospitalized women aged 60-69 and 80-89 years had higher participation rates than hospitalized women, whereas the reverse pattern was found in the 70-79 and 90+ age groups.

Logistic regression showed that in the MADT and LSADT samples men with all-cause hospitalization had 18-29% higher risk of non-response (OR=1.29 CI: 0.99, 1.69 and OR=1.18, CI: 0.99, 1.42, respectively) compared with non-hospitalized men who were at the lowest risk of non-response (Table 3). In the MADT, hospitalized women had the highest risk of non-response, but the difference diminished in the older twin sample and among the oldest individuals non-hospitalized women had the highest risk of non-response.

The analysis of cancer-specific hospitalization prior to intake revealed that the risk of non-response was lowest among non-hospitalized men except in the 1905-Cohort Study (results not presented). The middle-aged men and women hospitalized for cancer diagnosis had a substantially higher risk of non-participation (OR=7.84, CI: 4.12, 14.9 and OR=6.61, CI: 3.85, 11.4, respectively). The effect of cancer hospitalization was smaller in the LSADT (OR=1.47, CI: 0.94, 2.31 and OR=1.56, CI: 0.98, 2.49, in men and women respectively). In the 1905-cohort sample non-hospitalized women had 43% higher risk (OR=1.43, 95% CI: 1.17, 1.74) of non-response than their male counterparts.

The effect of total CVD hospitalization prior to intake was small in all three studies (results not presented). In the twin samples, men with total CVD hospitalization had 4-43%

higher risk of non-response (OR=1.43, CI: 0.88, 2.33 in the MADT and OR=1.04, CI: 0.77, 1.41 in the LSADT) than non-hospitalized men. In the oldest sample hospitalized men were at a lower risk of non-response than their non-hospitalized counterparts. Non-hospitalized women and women hospitalized for total CVD or other diagnoses had consistently elevated risks of non-response compared with non-hospitalized men in all three surveys.

All-cause and system-specific medications and response pattern

The analysis of participation rates by medication use revealed that women taking medications had higher participation rates than female non-users, while no such a pattern was seen in men (Table 2). Participation rate was higher in male non-users aged 45-59, 70-79, and 80-89 years, but it was lower in male non-users aged 60-69 and 90+ years than in men taking medications.

Regression analysis indicated that female non-users and women taking all-cause medications had increased risks of non-response than male non-users. However, compared with male non-users, the degree of the increased risk was smaller among women with medication use than among female non-users in the MADT, LSADT and 1905-Cohort Study (Table 4). Men taking medications had a lower risk of non-response in the MADT (OR=0.88, CI: 0.71, 1.08) and oldest sample (OR=0.85, CI: 0.53, 1.38), but they had a higher risk in the LSADT (OR=1.18, CI: 0.93, 1.50) than male non-users.

Similarly, men using ATC-C medications had lower risks of non-response in the MADT (OR=0.93, CI: 0.69, 1.23) and 1905-Cohort Study (OR=0.77, CI: 0.47, 1.26), but they had 29% (CI: 0.99, 1.69) higher risk of non-response than male non-users in the LSADT (results not presented). Compared to the reference group the highest risk of non-response was found among

female non-users, followed by women taking ATC-C, and women with other medication use in all three surveys.

All findings remained unaltered when all-cause and system-specific medication use was evaluated within two years prior to the intake, when all-cause medication use of at least two or three medications within six months prior to intake and when major CVD hospitalization were considered as measures of morbidity. The results were also unchanged when sex-specific conditions (ICD-10 N40-N51, N60-N64, and N70-N77) and sex hormones (ATC G03) were excluded from all-cause hospitalization and medication use in the MADT sample and when proxy interviews were considered as participants in the LSADT and 1905-Cohort Study.

Sex differences in the reporting of medication use

Table 5 compares the mean number of self-reported and registered medications by sex and age group in each sample. The registry data indicated that women consume more all-cause, ATC-M and ATC-N medications and there was no sex-specific pattern in the use of the ATC-C medications. Sex differences in the mean number of respiratory medications differed by age, such that middle-aged women used more respiratory medicines than same-aged men, but at older ages men used more respiratory medications (results not presented).

To reveal potential sex differences in reporting pattern we plotted the absolute difference between the sex-age-specific mean number of reported medications and the number of registered medications versus number of registered medications (Figure 1). The comparison between self-reports and registered data showed that both women and men underreported the number of used medications compared with the register data. It was higher in younger cohorts and increased with increasing number of registered drugs. The degree of underreporting was the smallest for the

ATC-C and largest for the ATC-M medications in the twin samples and the ATC-R medications in the 1905-Cohort Study (results are not presented). However, the degree of underreporting was similar in both sexes for all-cause and system-specific medication use, but for ATC-R medications it was higher among women.

Discussion

The present study used a combination of survey and national health register data to test whether sex-specific selection and information biases in surveys contribute to the explanations of the health–survival paradox. We found that men had higher participation rates than women at all ages. Furthermore, the results revealed that non-hospitalized men had higher participation rates than men with all-cause hospitalization within two years prior to intake at all ages except for individuals aged 90 years and over (difference 1.4-7.1%), whereas no consistent pattern was found among women. Likewise, men with diagnose-specific hospitalizations had an increased risk of non-response compared with non-hospitalized men. The risk of non-response in women was consistently higher than in non-hospitalized men regardless of hospitalization status. We also found that women taking all-cause medications had higher participation rates than female non-users (difference 0.8-7.6%), while no such a pattern was observed among men. Compared with male non-users the risk of non-response was higher in women regardless of medication use, but still the risk of non-response in women taking all-cause and ATC-C medications was lower than that in female non-users.

These results indicate that women taking prescription medications and non-hospitalized men were slightly over-represented in surveys. Selective participation of healthier men in surveys may result in underestimating health problems among surveyed men and, thus,

contribute to the explanation of the health–survival paradox, though its contribution is likely to be small.

The present study revealed higher non-response rates in women which is in agreement with previous research findings in Denmark, Sweden, the Netherlands, and Canada²¹⁻²³. Other studies found no or weak evidence for sex differential participation in surveys^{24,25}, or higher participation rates in women compared with men were indicated^{26,27}. Surveys in Denmark and the Netherlands showed that sex differences in response rates varied by age such that men until the age of 60-65 had higher participation rates, whereas women at older ages were at a higher risk of non-participation^{28,29}. In a longitudinal survey of elderly people in Australia, more women than men refused to participate in the study at the baseline, but no sex difference in participation rates was observed during follow-up surveys³⁰. In our study, however, women at all ages had lower participation rates than men, although participation improved at follow-up compared with the baseline surveys in the LSADT and 1905-Cohort Survey, which is consistent with other studies²⁴.

Other studies in Denmark that used register data to test whether there is selection bias in surveys in terms of healthcare use did not specifically report sex-specific results. In a Danish cohort study non-respondents had more hospitalizations due to somatic (1991-95) and psychiatric diseases (1969-95) and longer hospital stays than participants prior to the survey at the age of 60 years³¹. Other registry studies in Denmark found that non-respondents had higher hospitalization rates within one year or six months before and throughout data collection, although participants and non-respondents had similar hospital admission rates when healthcare use was measured over a longer period before or after the survey^{15,21,28}. Research in the Dutch population revealed similar utilization of hospital care among participants and non-respondents

or even more frequent use of health services by the participants^{23,32}. Other studies conducted to assess the representativeness of study samples reported that participants tend to be healthier than non-respondents with respect to psychological problems, cognitive function, and physical abilities^{22,27,30}. Possible explanations for such inconsistent results are differences in time periods within which the utilization of health services was measured, age structure of study populations, selected morbidity indicators and data sources (supplementary survey of non-respondents or register).

Using a unique opportunity to compare medication use in the survey with register data, we found that men and women tended to underreport medication use. The Danish men, contrary to our expectation, tended to underreport all-cause medication use similarly to women, and there was no sex-specific pattern in the reporting of system-specific medication use except that the degree of underreporting of the ATC-R medications was higher among women. The degree of underreporting was higher in the younger cohorts and increased with increasing number of registered drugs.

The present analysis adds to the previous research evidence that women use medications more frequently than men - especially nervous system medications^{33,34}. Our finding of a slightly higher use of respiratory medications in women at younger ages and in men at older ages corresponds well with the trends of smoking prevalence in Denmark in 1964-94, when the decline in smoking prevalence was more pronounced in men, whereas the prevalence of heavy smoking remained stable in men and tended to increase in women³⁵.

Our results partially agree with other studies of congruence of self-reports with pharmacy records. Caskie et al. indicated that the proportion of major drugs (e.g. CVD, antihistamine, anti-infective, gastrointestinal, hormones and synthetic substitutes, etc), as well as specific CVD

medications registered in pharmacy records and omitted from self-reports was similar in women and men, but male participants had higher levels of agreement for nervous system medications³⁶. In a more recent study, these researchers found that being women were predictive of less accurate reporting of medication use at older ages³⁷. Van den Brandt found that women were more often long-term drug users than men, but no sex differences in the drug recall were indicated³⁸. Other researchers also failed to find substantial sex differences in the recall of nonsteroid anti-inflammatory or cardiovascular drugs^{39,40}.

The current study was well suited for testing the impact of non-response on the health-survival paradox. First, the data on healthcare utilization were obtained for all eligible individuals (except 14 individuals, 0.1%) through linkage of the surveys with registry data rather than through supplementary surveys of non-respondents, which allowed avoiding biased estimates due to the initial pattern of non-response. Second, we used the data from three large nationwide population-based surveys previously conducted in Denmark that covered the age range of 45–102 years and included persons living in nursing homes or alternative accommodation. Finally, the present study had a considerable sample size and, consequently, good power to detect the sex differential impact of hospitalization and medication use on response pattern.

The major weakness of this study is that all-cause hospitalization and medication use indicators could be rather crude measures of health. To assure that health was similarly defined in women and men, we also considered diagnosis-specific hospitalizations and system-specific medication use that did not alter the initial results. Furthermore, to minimize possible errors related to over-the-counter (OTC) medication we excluded vitamins and alternative medicines when computing the number of self-reported medications, and we performed the analysis for

several system-specific medications requiring prescription. In addition, the comparison between all-cause medication use in the register and survey data was also performed at the 3rd level of the ATC classification system to account for possible changes of a medication within a pharmacological group. A limitation of our study is that the MADT, the LSADT and the 1905-Cohort Study were conducted within approximately the same time period and in a single country and these studies may therefore not be representative for other settings.

In conclusion, the study suggests that selection in surveys may contribute to explaining the health–survival paradox, but this contribution is likely to be small. It is also proposed that once in the study, men do not underreport medication use compared with women.

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Table 1. Participation rates in the Study of Middle-Aged Danish Twins, the Longitudinal Study of Aging Danish Twins and the Danish 1905-Cohort Survey*

Study	Age groups (y)	Males % (n)	Females % (n)	Total % (n)
MADT[†]		n=2637	n=2637	n=5274
	45–49	82.1 (398)	81.2 (393)	81.6 (791)
	50–54	85.8 (515)	82.9 (499)	84.4 (1014)
	55–59	84.1 (506)	79.3 (467)	81.7 (973)
	≥60	81.7 (776)	78.5 (755)	80.1 (1531)
	Total	83.2 (2195)	80.2 (2114)	81.7(4309)
LSADT		n=2548	n=3979	n=6527
	70–74	70.4 (816)	61.1 (909)	65.2 (1725)
	75–79	73.3 (576)	70.7 (905)	71.2 (1481)
	≥80	75.1 (453)	66.7 (808)	69.5 (1261)
	Total	72.4 (1845)	65.9 (2622)	72.4 (4467)
c1905		n=849	n=2751	n=3600
	92–93	58.2 (494)	47.9 (1320)	50.4 (1814)

* Proxy interviews are considered here as non-respondents

† MADT – the Study of Middle-Aged Danish Twins, LSADT – Longitudinal Study of Aging Danish Twins, c1905– the Danish 1905-Cohort Survey, 1FU – 1st follow-up survey

Table 2. Participation rate at the intake by hospitalization within the last 2 years and medication use within the last 6 months in the Study of Middle-Aged Danish Twins, the Longitudinal Study of Aging Danish Twins and the Danish 1905-cohort study

Hospitalization status	Men (95%CI)*		Women (95%CI)	
	Non-hosp.	Hospitalized	Non-hosp.	Hospitalized
<i>Age groups (y)</i>				
45-59	84.3 (82.3, 86.1)	82.9 (77.3, 87.6)	81.1 (79.0, 83.1)	81.1 (75.6, 85.8)
60-69	83.0 (80.1, 85.6)	75.9 (69.3, 81.6)	79.4 (76.4, 82.2)	73.4 (66.4, 79.6)
70-79	72.7 (70.2, 75.1)	69.3 (65.5, 72.9)	65.4 (63.3, 67.5)	66.1 (62.4, 69.5)
80-89	76.2 (71.4, 80.6)	74.2 (67.8, 79.9)	69.1 (65.4, 72.6)	66.6 (61.7, 71.2)
90+	57.5 (53.1, 61.7)	60.8 (55.6, 65.9)	47.8(45.5, 50.2)	49.2 (46.3, 52.2)
Medication use status	Non-users	All-cause users	Non-users	All-cause users
<i>Age groups (y)</i>				
45-59	84.6 (82.0, 86.9)	83.6 (80.9, 86.0)	77.9 (74.2, 81.3)	82.7 (80.4, 84.9)
60-69	76.9 (72.2, 81.2)	84.2 (81.0, 87.1)	73.5 (67.4, 79.0)	79.8 (77.7, 82.6)
70-79	73.3 (68.8, 77.6)	72.0 (69.5, 74.5)	65.1 (60.3, 69.7)	65.9 (63.8, 68.1)
80-89	90.0 (80.5, 95.9)	75.5 (70.5, 80.1)	73.7 (63.6, 82.2)	76.7 (73.2, 79.9)
90+	55.1 (43.4, 66.4)	59.7 (56.3, 63.1)	41.6 (35.3, 48.1)	49.2 (47.3, 51.1)

* CI – confidence interval

Table 3. Risk of non-response at intake by all-cause hospitalization in the Study of Middle-Aged Danish Twins, the Longitudinal Study of Aging Danish Twins and the Danish 1905-Cohort Survey

Surveys	Sample No (%)	Total, model 1* OR (95% CI)	Total, model 2 OR (95% CI)	Men OR (95% CI)	Women OR (95% CI)
MADT†	5274				
None		1		1	1
Hospitalization	846 (16.0)	1.22 (1.02, 1.47)		1.30 (1.00, 1.69)	1.16 (0.89, 1.49)
Women	2637 (50.0)	1.23 (1.05, 1.43)			
45-49		1	1	1	1
50-54		0.82 (0.64, 1.06)	0.82 (0.64, 1.06)	0.75 (0.53, 1.07)	0.89 (0.62, 1.27)
55-59		0.99 (0.77, 1.27)	0.99 (0.77, 1.27)	0.86 (0.60, 1.22)	1.12 (0.79, 1.59)
>=60		1.09 (0.87, 1.36)	1.09 (0.87, 1.36)	1.00 (0.73, 1.36)	1.17 (0.85, 1.61)
Non-hosp. men	2217 (42.0)		1		
Hosp. men	420 (8.0)		1.29 (0.99, 1.69)		
Non-hosp. women	2211 (41.9)		1.25 (1.06, 1.48)		
Hosp. women	426 (8.1)		1.45 (1.12, 1.90)		
LSADT	6527				
None		1		1	1
Hospitalization	1995 (30.6)	1.08 (0.96, 1.21)		1.18 (0.99, 1.42)	1.02 (0.88, 1.18)
Women	3979 (60.9)	1.39 (1.24, 1.57)			
70-74		1	1	1	1
75-79		0.72 (0.63, 0.83)	0.72 (0.63, 0.83)	0.86 (0.69, 1.07)	0.65 (0.55, 0.78)
>=80		0.78 (0.68, 0.90)	0.79 (0.68, 0.90)	0.78 (0.62, 0.98)	0.78 (0.65, 0.93)
Non-hosp. men	1702 (26.1)		1		
Hosp. men	846 (13.0)		1.18 (0.99, 1.42)		
Non-hosp. women	2830 (43.4)		1.46 (1.27, 1.69)		
Hosp. women	1149 (17.6)		1.49 (1.26, 1.77)		
1905-cohort	3600				
None		1		1	1
Hospitalization	1423 (39.5)	0.92 (0.81, 1.05)		0.83 (0.63, 1.10)	0.95 (0.82, 1.11)
Women	2751 (76.4)	1.51 (1.29, 1.76)			
Non-hosp. men	497 (13.8)		1		
Hosp. men	352 (9.8)		0.83 (0.63, 1.10)		
Non-hosp. women	1680 (46.7)		1.43 (1.17, 1.74)		
Hosp. women	1071 (29.8)		1.36 (1.10, 1.68)		

* Model 1 – all-cause hospitalization, sex, age, Model 2 – Model 1 + all-cause hospitalization*sex interaction

† MADT – Middle-Age Danish Twins Study, LSADT – Longitudinal Study of Aging Danish Twins, 1905-cohort – the Danish 1905-cohort study, OR – odds ratio; CI – confidence interval

Table 4. Risk of non-response at intake by total medication use in the Study of Middle-Aged Danish Twins, the Longitudinal Study of Aging Danish Twins and the Danish 1905-Cohort Survey

Surveys	Sample No. (%)	Total, model 1* OR (95% CI)	Total, model 2 OR (95% CI)	Men OR (95% CI)	Women OR (95% CI)
MADT†	5274				
Non-users		1		1	1
All-cause users	3281 (62.2)	0.79 (0.68, 0.92)		0.88 (0.71, 1.09)	0.72 (0.58, 0.88)
Women	2637	1.28 (1.09, 1.49)			
45-49		1	1	1	1
50-54		0.84 (0.65, 1.08)	0.84 (0.65, 1.08)	0.76 (0.53, 1.08)	0.92 (0.64, 1.32)
55-59		1.02 (0.79, 1.31)	1.02 (0.79, 1.31)	0.88 (0.62, 1.25)	1.17 (0.83, 1.66)
>=60		1.15 (0.91, 1.44)	1.15 (0.91, 1.44)	1.05 (0.76, 1.44)	1.25 (0.91, 1.72)
Male non-users	1208 (22.9)		1		
Male users	1429 (27.1)		0.88 (0.71, 1.08)		
Female non-users	785 (14.9)		1.43 (1.13, 1.81)		
Female users	1852 (35.1)		1.03 (0.85, 1.26)		
LSADT	5292‡				
Non-users		1		1	1
All-cause users	4294 (81.1)	1.03 (0.87, 1.20)		1.18 (0.92, 1.49)	0.93 (0.75, 1.15)
Women	3170	1.36 (1.18, 1.55)			
70-74		1	1	1	1
75-79		0.64 (0.54, 0.75)	0.64 (0.54, 0.75)	0.74 (0.57, 0.96)	0.58 (0.48, 0.72)
>=80		0.58 (0.50, 0.69)	0.58 (0.50, 0.69)	0.66 (0.51, 0.86)	0.54 (0.44, 0.67)
Male non-users	483 (9.13)		1		
Male users	1639 (30.9)		1.18 (0.93, 1.50)		
Female non-users	515 (9.7)		1.65 (1.23, 2.22)		
Female users	2655 (50.2)		1.52 (1.20, 1.93)		
1905-cohort	3600				
Non-users		1		1	1
All-cause users	3300 (91.7)	0.79 (0.63, 1.01)		0.85 (0.53, 1.37)	0.78 (0.59, 1.02)
Women	2751	1.51 (1.29, 1.77)			
Male non-users	75 (2.1)		1		
Male users	774 (21.5)		0.85 (0.53, 1.38)		
Female non-users	225 (6.3)		1.65 (0.98, 2.79)		
Female users	2526 (70.2)		1.28 (0.81, 2.03)		

* Model 1 – all-cause medication use, sex, age, Model 2 – Model 1 + all-cause medication use*sex interaction

† MADT – Middle-Age Danish Twins Study, LSADT – Longitudinal Study of Aging Danish Twins, 1905-cohort – the Danish 1905-cohort study, OR – odds ratio; CI – confidence interval

Table 5. The number of self-reported and registered medications in the Study of Middle-Aged Danish Twins, the Longitudinal Study of Aging Danish Twins and the Danish 1905-Cohort Survey

Study	No. of persons		Mean No. of registered medications (SE)		Mean No. of reported medications (SE)	
	Males	Females	Males	Females	Males	Females
MADT[†]						
<i>Age groups</i>						
45–49	397	393	0.90 (0.07)	1.69 (0.10)	0.43 (0.04)	0.77 (0.06)
50–54	514	497	1.02 (0.07)	1.99 (0.10)	0.51 (0.04)	0.92 (0.06)
55–59	506	467	1.40 (0.08)	2.33 (0.11)	0.74 (0.06)	1.22 (0.07)
≥60	769	750	2.01 (0.09)	2.69 (0.10)	1.13 (0.06)	1.41 (0.06)
Total	2186	2107	1.44 (0.08)	2.26 (0.11)	0.77 (0.05)	1.13 (0.06)
LSADT						
<i>Age groups</i>						
70–74	804	901	2.92 (0.10)	3.51 (0.10)	1.93 (0.07)	2.17 (0.07)
75–79	562	894	2.88 (0.12)	3.49 (0.10)	1.75 (0.08)	2.08 (0.07)
80–84	258	442	3.26 (0.19)	3.90 (0.16)	2.01 (0.13)	2.46 (0.11)
≥85	178	344	4.20 (0.25)	3.86 (0.17)	2.63 (0.17)	2.45 (0.12)
Total	1802	1899	3.08 (0.14)	3.62 (0.12)	1.96 (0.09)	2.23 (0.08)
c1905						
Total	448	1235	4.48 (0.15)	5.16 (0.10)	2.74 (0.11)	3.26 (0.07)

* MADT - The Study of Middle-Aged Danish Twins, LSADT - Longitudinal Study of Aging Danish Twins, c1905- the Danish 1905-Cohort study

Figure 1. Reporting of the all-cause medications in the Study of Middle-Aged Danish Twins, the Longitudinal Study of Aging Danish Twins and the Danish 1905-Cohort Survey

