

The Male–Female Health–Survival Paradox: A Survey and Register Study of the Impact of Sex-Specific Selection and Information Bias

ANNA OKSUZYAN, MD, MPH, INGE PETERSEN, MSc, HENRIK STOVRRING, PhD,
PAUL BINGLEY, MA, PhD, JAMES W. VAUPEL, MPP, PhD, AND KAARE CHRISTENSEN, MD, PhD

PURPOSE: This study examined whether the health–survival paradox could be due partially to sex-specific selection and information bias in surveys.

METHODS: The study is based on the linkage of three population-based surveys of 15,330 Danes aged 46–102 years with health registers covering the total Danish population regarding hospitalizations within the last 2 years and prescription medicine within 6 months before the baseline surveys.

RESULTS: Men had higher participation rates than women at all ages. Hospitalized women and women taking medications had higher participation rate compared with nonhospitalized women (difference = 0.7%–3.0%) and female nonusers (difference = 0.8%–7.6%), respectively, whereas no consistent pattern was found among men according to hospitalization or medication use status. Men used fewer medications than women, but they underreported medication use to a similar degree as did women.

CONCLUSIONS: Hospitalized women, as well as women using prescription medicine, were slightly over-represented in the surveys. Hence, the study found some evidence that selection bias in surveys may contribute to the explanation of the health–survival paradox, but its contribution is likely to be small. However, there was no evidence for sex-specific reporting of medication use among study participants. *Ann Epidemiol* 2009;19:504–511. © 2009 Elsevier Inc. All rights reserved.

KEYWORDS: Sex Differences, Health, Mortality, Paradox, Nonresponse, Register Study, Healthcare Utilization, Hospitalization, Medication Use, Denmark.

INTRODUCTION

In almost all western countries, men report better health than females (1, 2), but women still outlive men in all countries around the world (3). Among the most widely cited explanations for this apparent contradiction are favorable effects of estrogen on serum lipids (4), the compensatory effect of the second X chromosome (5, 6), a lower ability of the male immune system to avoid the harmful effects of infections (7), 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, timely seeking for medical advice (8, 9) and overreporting of worse health among women (10, 11). The distribution of chronic diseases has been also proposed to contribute to the health–survival paradox (2, 12).

Despite mounting research regarding sex differences in health and mortality, we still do not fully understand the

reasons for the paradox or its mechanisms. In addition to the fundamental biological and behavioral differences, 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.

In this study, we utilized a unique opportunity to link three Danish surveys covering 15,330 individuals, 46–102 years of age, 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 underestimating 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, 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 Study with registers within Statistics Denmark. The studies are described in detail elsewhere (13–15). In brief, the MADT represented a random sample of 120

From the Max Planck Institute for Demographic Research, Rostock, Germany (A.O., J.W.V.); the Danish Aging Research Center, Institute of Public Health, University of Southern Denmark, Odense (A.O., I.P., K.C.); Research Unit of General Practice, University of Southern Denmark, Odense (H.S.); The Danish National Center for Social Research, Copenhagen, Denmark (P.B.); and The Danish Twin Registry, University of Southern Denmark, Odense (K.C.).

Address correspondence to: Anna Oksuzyan, Address: Max Planck Institute for Demographic Research, Konrad-Zuse Str.1, 18057 Rostock, Germany. Tel.: +49 381 2082 178; fax: +49 381 2082 478. E-mail: oksuzyan@demogr.mpg.de.

Received August 19, 2008; accepted March 2, 2009.

Selected Abbreviations and Acronyms

ATC = Anatomical Therapeutic Chemical classification system
ATC-C = cardiovascular system medications
ATC-M = musculoskeletal system medications
ATC-N = nervous system medications
ATC-R = respiratory system medications
c1905 = Danish 1905-Cohort Study
CHD = coronary heart disease
CPR number = Civil Personal Registration Number
CVD = cardiovascular disease
ICD = International Classification of Diseases
LSADT = Longitudinal Study of Aging Danish Twins
MADT = Study of Middle-Aged Danish Twins

twin pairs from each birth cohort from 1931 to 1952, 46–68 years of age in 1998 when the survey was implemented. The LSADT involved the Danish twins 75 years of age and older by January 1995, and residing in Denmark. Twins at least 70 years of age were added to the 1997, 1999, and 2001 follow-ups (16). The 1905-Cohort Study included all Danes born in 1905 and alive in 1998. 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 instrument consisted of various questions on health, lifestyle and socio-economic conditions, tests of cognitive and physical functioning, and the collection of biological samples. Data collection in each wave was carried out within approximately 3 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. All individuals who were invited to participate in the three studies 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, diagnoses (8th International Classification of Diseases (ICD-8) until 1993 and ICD-10 since 1994), and other information for nonpsychiatric illnesses since 1977); and the Prescription Medicine Register (contains the Anatomical Therapeutic Chemical classification system (ATC) codes of prescribed medications, dates of purchase, and other related information since 1995). The drugs administered in hospitals are reported on the ward level rather than individual

and, therefore, were omitted in this analysis. Using CPR numbers the register data were combined with variables identifying participation in the surveys.

Nonresponse Variables

Nonresponse was defined as nonparticipation in the intake survey for any reason other than death or emigration from the country. Proxy interviews were considered to be nonrespondents, 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 2 years before the baseline 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 Study. All-cause hospitalization included all inpatient admissions except ICD-8 Y-list (unique for the Danish healthcare system) and ICD-10 Z00-Z99. 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. 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-cause and cardiovascular system medications use (ATC-C) was assessed within 6 months before the intake, as the information letter was usually sent weeks before the interview. Due to the availability of the Prescription Medicine Register only since 1995, the nonparticipation analyses for LSADT start with 1997 wave for medicine use. The interview dates were used to define the start and end of the 2-year/6-month interval. For nonrespondents the first dates of the corresponding surveys were used.

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 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, except alternative medications and vitamins. The number of prescribed all-cause medications from the register data was calculated as a total count of all medications prescribed within the 6 months after intake.

To account for possible changes of a medication within a pharmacological group, a medication was counted only once if the person was prescribed different drugs of the same pharmacological subgroup or the same drug multiple times within the selected time period. We also estimated a number of prescribed all-cause medications 6 months before and 3 months before and after the baseline, but the three methods yielded similar results. Previous research in Demark suggests that medication use within 6 months after the survey represents a more accurate measurement of actual medicine use (17).

Statistical Analysis

Logistic regression was used to analyze the impact of prior hospitalization and medication use on response pattern, adjusted for age and sex, where appropriate. The estimates are presented in odds ratios (OR) and 95% confidence intervals (CI). All diagnosis-specific hospitalization/system-specific medication use variables were grouped as follows: (1) nonhospitalized/nonuser, (2) hospitalized for specific diagnosis (cancer or total CVD)/ATC-C user, and (3) other diagnoses/other-ATC user. To elucidate sex differences in the response pattern the interaction between hospitalization or medication use variables and sex was included using nonhospitalized men or male nonusers as the reference category. 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, 5203 individuals were invited to participate in the MADT (mean age $\pm$ standard deviation [SD]: 56.9 ± 6.3) and 6535 eligible individuals were invited for the LSADT intake participation (77.4 ± 5.6). In the 1905-Cohort Study, 3600 elderly individuals (92.9 ± 0.41) were invited to intake survey. We were unable to track in the Statistics Denmark registers only six individuals from the MADT and eight from the LSADT.

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 showed that hospitalized women had higher participation rates compared with nonhospitalized women at all age groups except the 80–89 age group. Nonhospitalized men had higher participation rates in the

TABLE 1. Participation rates in MADT, LSADT, and c1905

Study	Age groups (yr)	Men (% [n])	Women (% [n])	Total (% [n])
MADT		n = 2597	n = 2606	n = 5203
	46–49	82.4 (398)	81.4 (393)	81.9 (791)
	50–54	86.3 (515)	83.0 (499)	84.6 (1014)
	55–59	85.2 (506)	80.5 (467)	82.9 (973)
	≥60	84.1 (776)	80.2 (755)	82.1 (1531)
LSADT	Total	84.5 (2195)	81.1 (2114)	82.8 (4309)
		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)
c1905	Total	72.4 (1845)	65.9 (2622)	72.4 (4467)
		n = 849	n = 2751	n = 3600
	92–93	58.2 (494)	47.9 (1320)	50.4 (1814)

c1905 = Danish 1905-Cohort Study; LSADT = Longitudinal Study of Aging Danish Twins; MADT = Study of Middle-Aged Danish Twins.

70–79 and 80–89 age groups, whereas the reverse pattern was observed in the youngest and oldest-old ages (Table 2).

Logistic regression showed that women regardless of hospitalization status had increased risks of nonresponse in the three studies (Table 3), but the risk of nonresponse was the highest in nonhospitalized women. Only in the LSADT women with all-cause hospitalizations and nonhospitalized women had similar risks of nonresponse. Men with all-cause hospitalizations had lower risks of nonresponse in the MADT and 1905-Cohort Study, but they had an elevated risk of nonresponse (OR = 1.18, 95% CI: 0.99, 1.42) in the LSADT.

The analysis of diagnosis-specific hospitalizations before intake showed that men with cancer hospitalizations had higher risks of nonresponse than nonhospitalized men, whereas there was no clear pattern among men with total CVD hospitalization. Women regardless of diagnose-specific hospitalization status had consistently elevated risks of nonresponse compared with nonhospitalized men, being the highest among women hospitalized for cancer or CVD in the twin samples (Supplementary Tables 1 and 2).

All-Cause and System-Specific Medications and Response Pattern

Descriptive analysis showed that women taking medications had higher participation rates than female nonusers, whereas no such a pattern was seen in men (Table 2). Logistic regression indicated that female nonusers and women taking all-cause medications had increased risks of nonresponse than male nonusers. However, the risk of nonresponse was highest among women with medication use in all three studies (Table 4). Men taking medications had a similar or lower risk of nonresponse in the MADT (OR = 1.02, 95% CI: 0.82, 1.27) and oldest sample (OR = 0.85, 95% CI: 0.53, 1.38), and a higher risk in the LSADT (OR = 1.18, 95% CI: 0.93, 1.50) than male nonusers.

TABLE 2. Participation rates at the intake by all-cause hospitalization and medication use status in MADT, LSADT, and c1905

		Men (95% CI)		Women (95% CI)	
Hospitalization status		Nonhospitalized	Hospitalized	Nonhospitalized	Hospitalized
Age groups (yr)					
46–59		84.4 (82.5, 86.2)	87.2 (81.9, 91.4)	81.2 (79.1, 83.3)	84.2 (79.9, 88.6)
60–69		83.7 (80.8, 86.2)	84.8 (78.7, 89.8)	79.7 (76.7, 82.5)	80.8 (74.0, 86.5)
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		Nonusers	All-cause users	Nonusers	All-cause users
Age groups (yr)					
46–59		85.7 (83.2, 88.0)	83.8 (81.1, 86.2)	79.2 (75.5, 82.5)	82.9 (80.5, 85.0)
60–69		82.0 (77.5, 86.0)	84.9 (81.8, 87.7)	77.1 (71.1, 82.4)	80.8 (77.7, 83.6)
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; c1905 = Danish 1905–Cohort Study; LSADT = Longitudinal Study of Aging Danish Twins; MADT = Study of Middle-Aged Danish Twins.

Similar results were shown in the analysis of ATC-C medications use (Supplementary Table 3). Compared to the reference group the highest risk of nonresponse was found among female nonusers, followed by women taking ATC-C and other medications, and, finally, by men taking ATC-C and other medications in the older samples. Only in the MADT women taking ATC-C medications were at the highest risk of nonresponse.

All findings remained unaltered when all-cause and system-specific medication use was evaluated within 2 years before the intake and when all-cause medication use of at least 2 or 3 medications within 6 months before intake was considered. The results were also unchanged when sex-specific conditions and sex hormones 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 (no proxy respondents were in the MADT that included the youngest participants).

Sex Differences in the Reporting of Medication Use

The registry data and self-reports showed that women consume more all-cause (Table 5), ATC-M and ATC-N medication medications compared with same-aged men. The use of ATC-C medications was similar in men and women. Sex differences in the mean number of respiratory medications differed by age, such that middle-aged women used more respiratory medicines than the same-aged men, but at older ages men used more respiratory medications.

To show 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. Fig. 1 shows 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. 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. However, the degree of underreporting was similar in both sexes for all-cause and system-specific medication use. Only underreporting of the ATC-R medications was higher among women.

DISCUSSION

This 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. Further, hospitalized women had higher participation rates than their nonhospitalized counterparts at almost all ages, whereas less consistency was indicated in participation rates among men based on hospitalization status. We also found that women taking all-cause medications had higher participation rates than female nonusers, whereas no such a pattern was observed among men. Likewise, compared with the reference group women with all-cause hospitalization and medication use were at lower risks of nonresponse than nonhospitalized women or female nonusers, respectively. The risk of nonresponse among men based on hospitalization and medication use had inconsistent pattern across the samples.

These results indicate that women with all-cause hospitalization and women taking prescription medications were slightly overrepresented in surveys. Selective nonparticipation of healthier women in surveys may result in overestimating health problems among surveyed women and, thus, contribute to the explanation of the health–survival paradox, although its contribution is likely to be small.

This study showed higher nonresponse rates in women that is in agreement with previous research findings in Denmark,

TABLE 3. Risk of nonresponse at intake by all-cause hospitalization in MADT, LSADT, and c1905

Surveys	Sample n (%)	Model 1 total OR (95% CI)*	Model 2 total OR (95% CI)	Men OR (95% CI)	Women OR (95% CI)
MADT	5203				
None		1		1	1
Hospitalization	788 (15.2)	0.85 (0.69, 1.05)		0.84 (0.61, 1.15)	0.85 (0.64, 1.14)
Women	2606 (50.1)	1.27 (1.09, 1.49)			
46–49 yr		1	1	1	1
50–54 yr		0.82 (0.64, 1.06)	0.82 (0.64, 1.06)	0.75 (0.52, 1.07)	0.89 (0.63, 1.28)
55–59 yr		0.94 (0.73, 1.21)	0.94 (0.73, 1.21)	0.82 (0.57, 1.17)	1.06 (0.75, 1.51)
≥60 yr		0.99 (0.79, 1.25)	0.99 (0.79, 1.25)	0.89 (0.65, 1.24)	1.09 (0.79, 1.51)
Nonhospitalized men	2209 (42.5)		1		
Hospitalized men	388 (7.5)		0.84 (0.61, 1.15)		
Nonhospitalized women	2206 (42.4)		1.27 (1.07, 1.50)		
Hospitalized women	400 (7.7)		1.09 (0.81, 1.46)		
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 yr		1	1	1	1
75–79 yr		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 yr		0.78 (0.68, 0.90)	0.79 (0.68, 0.90)	0.78 (0.62, 0.98)	0.78 (0.65, 0.93)
Nonhospitalized men	1702 (26.1)		1		
Hospitalized men	846 (13.0)		1.18 (0.99, 1.42)		
Nonhospitalized women	2830 (43.4)		1.46 (1.27, 1.69)		
Hospitalized women	1149 (17.6)		1.49 (1.26, 1.77)		
c1905	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)			
Nonhospitalized men	497 (13.8)		1		
Hospitalized men	352 (9.8)		0.83 (0.63, 1.10)		
Nonhospitalized women	1680 (46.7)		1.43 (1.17, 1.74)		
Hospitalized women	1071 (29.8)		1.36 (1.10, 1.68)		

CI = confidence interval; c1905 = Danish 1905–Cohort Study; LSADT = Longitudinal Study of Aging Danish Twins; MADT = Study of Middle-Aged Danish Twins; OR = odds ratio.

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

Sweden, the Netherlands, and Canada (18–20). Other studies found no or weak evidence for sex differential participation in surveys (21, 22) or even higher participation rates in women compared with men (23, 24). Surveys in Denmark and the Netherlands showed that sex differences in response rates varied by age such that men until 60–65 years had lower participation rates, whereas at older ages women had higher risks of nonparticipation (25, 26). In a longitudinal survey of elderly in Australia more women refused to participate in the study at the baseline, but no sex difference in participation rates was observed during follow-up surveys (27). In our study, however, women at all ages had lower participation rates than men, which is consistent with other studies (21).

Other studies in Denmark that used register data to investigate selection bias in surveys in terms of healthcare use did not specifically report sex-specific results. In a Danish 1936-cohort study nonrespondents had higher mortality and hospitalization rates than participants before the survey at age of 60 years (28). Others found that nonrespondents had higher hospitalization rates shortly before and

throughout data collection, although participants and nonrespondents had similar hospital admission rates when healthcare use was measured over a longer period before or after the survey (14, 18, 25). Research in the Dutch population showed similar use of hospital care among participants and nonrespondents or even more frequent use of other health services by the participants (20, 29). Possible explanations for such inconsistent results are differences in time periods within which the use of health services was measured, age structure of study populations, selected morbidity indicators, and data sources (supplementary survey of nonrespondents or register).

This study adds to the previous research evidence that women use medications more frequently than men—especially nervous system medications (30, 31). Our finding of a slightly higher use of respiratory medications in women at younger ages and in men at older ages corresponds 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

TABLE 4. Risk of nonresponse at intake by total medication use in MADT, LSADT, and c1905

Surveys	Sample n (%)	Model 1 total OR (95% CI)*	Model 2 total OR (95% CI)	Men OR (95% CI)	Women OR (95% CI)
MADT	5203				
Nonusers		1		1	1
All-cause users	3263 (62.7)	0.89 (0.77, 1.05)		1.04 (0.83, 1.29)	0.78 (0.63, 0.98)
Women	2606	1.29 (1.09, 1.52)			
46–49 yr		1	1	1	1
50–54 yr		0.83 (0.64, 1.07)	0.83 (0.64, 1.07)	0.74 (0.52, 1.07)	0.91 (0.64, 1.31)
55–59 yr		0.95 (0.73, 1.22)	0.95 (0.74, 1.22)	0.81 (0.57, 1.16)	1.09 (0.76, 1.55)
≥60		1.00 (0.79, 1.27)	1.00 (0.79, 1.27)	0.88 (0.63, 1.22)	1.12 (0.81, 1.56)
Male nonusers	1175 (22.6)		1		
Male users	1422 (27.3)		1.02 (0.82, 1.27)		
Female nonusers	765 (14.7)		1.51 (1.18, 1.93)		
Female users	1841 (35.4)		1.19 (0.97, 1.48)		
LSADT	5292 [†]				
Nonusers		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 (59.9)	1.36 (1.18, 1.55)			
70–74 yr		1	1	1	1
75–79 yr		0.64 (0.54, 0.75)	0.64 (0.55, 0.75)	0.74 (0.57, 0.96)	0.58 (0.48, 0.72)
≥80 yr		0.58 (0.49, 0.69)	0.58 (0.50, 0.69)	0.66 (0.50, 0.86)	0.54 (0.44, 0.67)
Male nonusers	483 (9.13)		1		
Male users	1639 (30.9)		1.18 (0.93, 1.50)		
Female nonusers	515 (9.7)		1.65 (1.23, 2.22)		
Female users	2655 (50.2)		1.52 (1.20, 1.93)		
c1905	3600				
Nonusers		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 (76.4)	1.51 (1.29, 1.77)			
Male nonusers	75 (2.1)		1		
Male users	774 (21.5)		0.85 (0.53, 1.38)		
Female nonusers	225 (6.3)		1.65 (0.98, 2.79)		
Female users	2526 (70.2)		1.28 (0.81, 2.03)		

CI = confidence interval; c1905 = Danish 1905–Cohort Study; LSADT = Longitudinal Study of Aging Danish Twins; MADT = Study of Middle-Aged Danish Twins; OR = odds ratio.

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

[†]Due to the availability of Prescription Medicine Register since 1995, the analysis of nonresponse by medication use starts from the LSADT 1997.

smoking remained stable in men and tended to increase in women (32).

The Danish men, contrary to our expectation, tended to underreport medication use similarly to women except that underreporting of the ATC-R medications was higher among women. Our results partially agree with other studies of congruence of self-reports with pharmacy records. Caskie et al. (33) indicated that the proportion of major drugs (e.g., CVD, gastrointestinal, hormones, etc.) registered in pharmacy records but omitted from self-reports was similar in women and men, although men had higher levels of agreement for nervous system medications. Van den Brandt et al. (34) found that women were more often long-term drug users than men, but no sex differences in the drug recall were indicated. Other researchers also failed to find substantial sex differences in the recall of nonsteroid antiinflammatory or cardiovascular drugs (35, 36).

The current study was well suited for testing the impact of nonresponse on the health–survival paradox. The data on

healthcare use were obtained for almost all eligible individuals through linkage of the surveys with registry data rather than through supplementary surveys of nonrespondents, which allowed avoiding biased estimates due to the initial pattern of nonresponse. Second, we used the data from three large nationwide population-based surveys previously conducted in Denmark that included individuals 46–102 years of age and persons living in nursing homes or alternative accommodation. Finally, this 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 considered rather crude measures of health. To assure that health was similarly defined in women and men we further considered diagnosis-specific hospitalizations and system-specific medication use that only slightly alter the initial results. Furthermore, to minimize possible errors related to over-the-counter

TABLE 5. The number of self-reported and registered medications in MADT, LSADT, and c1905

Study	Persons (n)		Mean number of registered medications (SE)		Mean number of reported medications (SE)	
	Men	Women	Men	Women	Men	Women
MADT						
Age groups (yr)						
46–49	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						
Age groups (yr)						
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						
92–93	448	1235	4.48 (0.15)	5.16 (0.10)	2.74 (0.11)	3.26 (0.07)

c1905 = Danish 1905–Cohort Study; LSADT = Longitudinal Study of Aging Danish Twins; MADT = Study of Middle-Aged Danish Twins; SE = standard error.

medication we excluded vitamins and alternative medicines from the number of self-reported medications and carried out the analysis for several system-specific medications requiring prescription. All three studies were conducted within

approximately the same time period and in a single country and may not be representative for other settings.

In conclusion, the study suggests that selection in surveys may contribute to explaining the health–survival paradox,

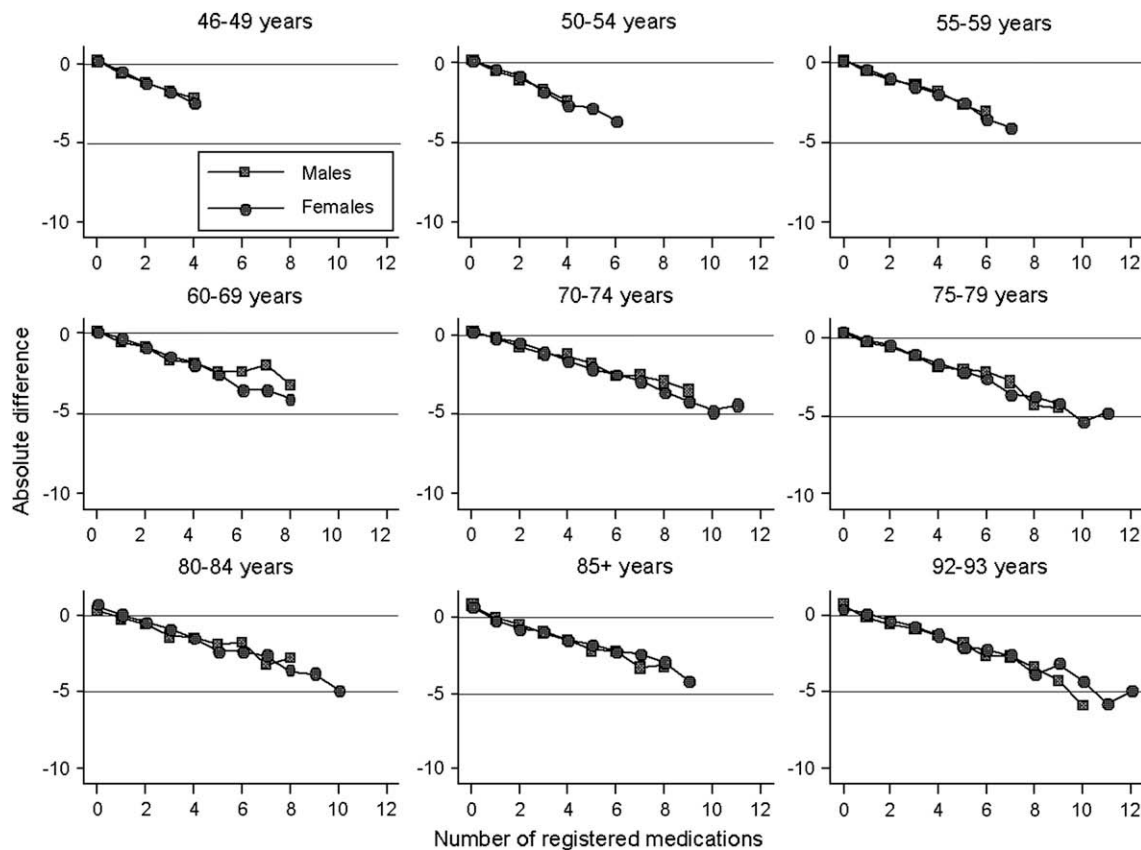


FIGURE 1. Reporting of medication use in the study of Middle-Aged Danish Twins, Longitudinal Study of Aging Danish Twins, and Danish 1905–Cohort Study.

but its contribution is likely to be small. It also proposed that once in the study men do not underreport medication use more than women do.

Financial support is provided by the research grants from the National Institute on Aging (Grant NIA-PO1-AG08761) and the VELUX Foundation.

REFERENCES

- Olsen KM, Dahl S-A. Health differences between European countries. *Soc Sci Med*. 2007;64:1665–1678.
- Case A, Paxson C. Sex differences in morbidity and mortality. *Demography*. 2005;42:189–214.
- Barford A, Dorling D, Smith GD, Shaw M. Life expectancy: women now on top everywhere. *BMJ*. 2006;332:808.
- Waldron I, Johnston S. Why do women live longer than men? *J Human Stress*. 1976;2:19–30.
- Austad S. Why women live longer than men: sex differences in longevity. *Gend Med*. 2006;3:79–92.
- Christensen K, Kristiansen M, Hagen-Larsen H, Skytthe A, Bathum L, Jeune B, et al. X-linked genetic factors regulate hematopoietic stem-cell kinetics in females. *Blood*. 2000;95:2449–2451.
- Owens IPF. Ecology and evolution: sex differences in mortality rate. *Science*. 2002;297:2008–2009.
- Nathanson CA. Illness and the feminine role: a theoretical review. *Soc Sci Med*. 1975;9:57–62.
- Galdas PM, Cheater F, Marshall P. Men and health help-seeking behavior: literature review. *J Adv Nurs*. 2005;49:616–623.
- Verbrugge LM, Wingard DL. Sex differentials in health and mortality. *Women Health*. 1987;12:103–145.
- Kroenke K, Spitzer RL. Gender differences in the reporting of physical and somatoform symptoms. *Psychosom Med*. 1998;60:150–155.
- Wingard DL, Cohn BA, Kaplan GA, Cirillo PM, Cohen RD. Sex differentials in morbidity and mortality risk examined by age and cause in the same cohort. *Am J Epidemiol*. 1989;130:601–610.
- Gaist D, Bathum L, Skytthe A, Jensen TK, McGue M, Vaupel JW, et al. Strength and anthropometric measures in identical and fraternal twins: no evidence of masculinization of females with male co-twins. *Epidemiology*. 2000;11:340–343.
- Christensen K, Holm NV, McGue M, Corder L, Vaupel JW. A Danish population-based twin study on general health in the elderly. *J Aging Health*. 1999;11:49–64.
- Nybo H, Gaist D, Jeune B, Bathum L, McGue M, Vaupel JW, et al. The Danish 1905 Cohort: a genetic-epidemiological nationwide survey. *J Aging Health*. 2001;13:32–46.
- Christensen K, Frederiksen H, Vaupel JW, McGue M. Age trajectories of genetic variance in physical functioning: a longitudinal study of Danish twins aged 70 years and older. *Behav Genet*. 2003;33:125–136.
- Størvring H. Selection bias due to immigration in pharmacoepidemiologic studies. *Pharmacoepidemiol Drug Safety*. 2007;16:681–686.
- Osler M, Schroll M. Differences between participants and non-participants in a population study on nutrition and health in the elderly. *Eur J Clin Nutr*. 1992;46:289–295.
- von Strauss E, Fratiglioni L, Jorm AF, Viitanen M, Winblad B. Attitudes and participation of the elderly in population surveys: data from a longitudinal study on aging and dementia in Stockholm. *J Clin Epidemiol*. 1998;51:181–187.
- Boshuizen HC, Viet AL, Picavet HSJ, Botterweck A, van Loon AJM. Non-response in a survey of cardiovascular risk factors in the Dutch population: determinants and resulting biases. *Public Health*. 2006;120:297–308.
- Zunzunegui MV, Beland F, Gutierrez-Cuadra P. Loss to follow-up in a longitudinal study on aging in Spain. *J Clin Epidemiol*. 2001;54:501–510.
- Launer LJ, Wind AW, Deeg DJH. Nonresponse pattern and bias in a community-based cross-sectional study of cognitive functioning among the elderly. *Am J Epidemiol*. 1994;139:803–812.
- Korkeila K, Suominen S, Ahvenainen J, Ojanlatva A, Rautava P, Helenius H, et al. Non-response and related factors in a nationwide health survey. *Eur J Epidemiol*. 2001;17:991–999.
- van den Akker M, Buntinx F, Metsemakers JF, Knottnerus JA. Morbidity in responders and non-responders in a register-based population survey. *Fam Pract*. 1998;15:261–263.
- Kjoller M, Thoning H. Characteristics of non-response in the Danish Health Interview Surveys, 1987–1994. *Eur J Public Health*. 2005;15:528–535.
- Lamers LM. Medical consumption of respondents and non-respondents to a mailed health survey. *Eur J Public Health*. 1997;7:267–271.
- Jacomb P, Jorm A, Korten A, Christensen H, Henderson AS. Predictors of refusal to participate: a longitudinal health survey of the elderly in Australia. *BMC Public Health*. 2002;2:4.
- Drivsholm T, Eplöv LF, Davidsen M, Jorgensen T, Ibsen H, Hollnagel H, et al. Representativeness in population-based studies: a detailed description of non-response in a Danish cohort study. *Scand J Public Health*. 2006;34:623–631.
- Reijneveld SA, Stronks K. The impact of response bias on estimates of health care utilization in a metropolitan area: the use of administrative data. *Int J Epidemiol*. 1999;28:1134–1140.
- Barat I, Andreassen F, Damsgaard EM. The consumption of drugs by 75-year-old individuals living in their own homes. *Eur J Clin Pharmacol*. 2000;56:501–509.
- Roe CM, McNamara AM, Motheral BR. Gender- and age-related prescription drug use patterns. *Ann Pharmacother*. 2002;36:3–39.
- Osler M, Prescott E, Gottschau A, Bjerg A, Hein HO, Sjørl A, et al. Trends in smoking prevalence in Danish adults, 1964–1994. The influence of gender, age, and education. *Scand J Soc Med*. 1998;26:293–298.
- Caskie GIL, Willis SL. Congruence of self-reported medications with pharmacy prescription records in low-income older adults. *Gerontologist*. 2004;44:176–185.
- Van den Brandt PA, Petri H, Dorant E, Goldbohm RA, Van de Crommert S. Comparison of questionnaire information and pharmacy data on drug use. *Pharm Weekbl Sci*. 1991;13:91–96.
- West SL, Savitz DA, Koch G, Strom BL, Guess HA, Hartzema A. Recall accuracy for prescription medications: self-report compared with database information. *Am J Epidemiol*. 1995;142:1103–1112.
- Sjahid SI, van der Linden PD, Stricker BHC. Agreement between the pharmacy medication history and patient interview for cardiovascular drugs: The Rotterdam Elderly Study. *Br J Clin Pharmacol*. 1998;45:591–595.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.annepidem.2009.03.014](https://doi.org/10.1016/j.annepidem.2009.03.014).