Heart failure in Norway, 2000-2014: analyzing incident, total and readmission rates using data from the Cardiovascular Disease in Norway (CVDNOR) Project

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Abstract

Aims: To examine trends in heart failure hospitalization rates and risk of readmissions following an incident HF hospitalization.

Methods and Results: During 2000-2014, we identified in "The Cardiovascular Disease in Norway Project" 142 109 hospitalizations with HF as primary diagnosis. Trends of incident and total (incident and recurrent) HF hospitalization rates were analyzed using negative binomial regression models. Changes over time in 30-day and three-year risk of HF recurrences or CVD-related readmissions were analyzed using Fine and Grey competing risk regression, with death as competing events.

Age-standardized rates declined on average 1.9% per year in men and 1.8% per year in women for incident HF hospitalizations (both $P_{trend}<0.001$) but did not change significantly in either men or women for total HF hospitalizations.

In men surviving the incident HF hospitalization, 30-day and three-year risk of a HF recurrent event increased 1.7% and 1.2% per year, respectively. Similarly, 30-day and three-year risk of a cardiovascular (CVD)-related hospitalization increased 1.5% and 1.0% per year, respectively (all $P_{trend}<0.001$). No statistically significant changes in the risk of HF recurrences or CVD-related readmissions were observed among women. In-hospital mortality for a first and recurrent HF episode declined over time in both men and women.

Conclusions: Incident HF hospitalizations rates declined in Norway during 2000-2014. An increase in the risk of recurrences in the context of reduced in-hospital mortality following an incident and recurrent HF hospitalization led to flat trends of total HF hospitalization rates.

Keywords: Heart failure, hospitalization rates, readmission rates, Norway, epidemiology

Introduction

Heart failure (HF) affects 38 million people worldwide and is the most common reason for hospitalization in patients ≥ 65 years in high-income countries.[1] HF places a considerable burden to health care systems due to multiple hospitalizations and high treatment costs.

Several factors influence HF occurrence in the general population. Decline in the incidence of heart disease reduces the risk of HF while improved survival following an acute event exposes survivors to more years at risk of developing HF.[2] Aging of the population also increases the risk of HF through various mechanisms. Aging is associated with structural and functional changes of the heart muscle and/or valves,[3] leading to increased risk of HF. Further, treatment of the underlying conditions are suboptimal[4] or less successful in the elderly, increasing the risk of adverse outcomes, including HF.

To add to the complexity, population trends in other risk factors for HF such as obesity, diabetes, hypertension, and smoking also influence HF rates.[5]

Previous publications have shown declines in first-time (incident) HF hospitalization rates in many Western countries during recent years.[6-9] Less consistent have been results of trend analyses for total (incidence and recurrent) HF hospitalization rates, showing declines in some countries[10-13] and increase in others.[14] Although incident events account for the majority of HF-related hospitalizations, recurrences are regarded as an indicator of hospital performance.[15] Nevertheless, information on the relationship between trends in incident and total HF hospitalization and the role of recurrences in this relationship is sparse.

Therefore, the current study aimed at exploring trends in incident and total HF hospitalization rates over a 15-year period using national data from Norway. In addition, we analyzed changes in

short (30 days) and long (three years) term risk of HF recurrences and CVD-related readmission following discharge from the incident HF hospitalization.

Methods

Data Sources

The Cardiovascular Disease in Norway Project (CVDNOR) contains information on all hospital stays with a CVD-related diagnosis [International Classification of Diseases (ICD) 9 codes 390-459 or ICD-10 codes, I00-I99] in Norway during 1994-2014. The information was retrieved directly from the Patient Administrative System (PAS) of all somatic hospitals during 1994-2009 and from the Norwegian Patient Registry after 2009. Detailed information on data collection, content and quality have been previously published.[16-18] A personal, unique project-specific number assigned to each individual allowed us to follow study participants at the individual level for subsequent hospitalizations and/or death. Information on deaths was retrieved from the Cause of Death Registry.

Study design, population and definitions

This is a nationwide, retrospective cohort study linking hospitalization data to several national registers and data sources in Norway.

For the main analyses, we identified all individuals 15+ years, hospitalized with HF as primary discharge diagnosis (ICD-9 codes, 402.01, 402.11, 402.3, 402.7, 402.91, 425.4, 425.5, 425.9, 428, 428.x; ICD-10 codes, I09.81, I11.0, I50 and I50.) in Norway, 1994-2014.

Using a fixed lookback (LP) period of six years, we identified individuals without prior hospitalizations with HF as either primary or secondary diagnosis (incident cases). Therefore, the study period was confined to 2000-2014. A 'recurrent' event was defined as a new hospitalization with HF as primary diagnosis following discharge from the incident HF hospitalization.

Statistical Analyses

Continuous variables are presented as means and standard deviations (SD) and categorical variables as proportions. Differences in baseline characteristics were tested using clustered linear (for continuous variables) and logistic (for categorical variables) regression models, adjusted for age, with patient ID as the cluster variable. This was done to account for the dependency caused by multiple hospitalizations for the same individual.

We calculated age-standardized HF hospitalization rates for men and women separately, using the direct standardization method and the age distribution of Norwegian population in year 2000 as standard population. The population 'at risk' for analyses involving incident HF hospitalizations included individuals without previous HF hospitalizations (HF-free population). The population 'at risk' for analyses involving total HF hospitalizations included the total population of Norway. We plotted the age-standardized rates [overall and by admission type (acute versus non-acute) for years with available data (2010-2014)] and joined them using *Lowess* smoothing lines.

Sex-specific trends of HF hospitalization rates were explored using negative binomial regression models and results are expressed as incidence rate ratios (IRRs) with corresponding 95% confidence intervals (CIs). They estimate the average annual change in rates over the study period.

In patients surviving the incident HF hospitalization, we assessed age-adjusted changes in short (30 days) and long (three years) term risk of a first HF recurrence or CVD-related readmission, using Fine and Grey competing risk regression, with death as a competing risk event. To ensure a minimal equal follow up time for all study participants, we included in 30-day analyses incident HF hospitalizations between January 1, 2000 and December 1, 2014. Consequently, incident HF

hospitalizations occurring between January 1, 2000 and December 31, 2011 were included in three-year analyses.

The proportional hazards assumption for the competing risk models were evaluated by tests of time-varying effects and inspection of Schoenfeld residuals and were not found to be violated. Lastly, we present changes over time in the proportion of patients experiencing one or multiple HF recurrences and analyzed changes over time in the odds of in-hospital mortality during an incident or recurrent HF hospitalization.

Analyses were conducted separately for men and women, using Stata (Stata Corp LP, 4905 Lakeway Drive, College Station, Texas, USA).

Results

Over the study period, 142 109 hospitalizations (54.7% among men; 38.8% due to incident HF episodes) with HF as primary diagnosis were registered in Norway.

Mean (SD) age at hospitalization was 77.8 (11.7) years. Men were on average younger than women (P<0.001) (Table 1). After adjusting for age, atrial fibrillation (AF), valvular heart disease, hypertension, anemia and thyroid diseases were more prevalent among women while coronary heart disease (CHD), cerebrovascular disease, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), renal failure and neoplasms were more prevalent among men (Table 1).

In men, the prevalence of AF, DM, hypertension, and renal failure increased while the prevalence of IHD, cerebrovascular disease, valvular heart disease, COPD and neoplasms decreased over time. The number of medical conditions also increased over time (Supplementary material online, Table 1).

In women, age at hospitalization increased over time, as did the prevalence of AF, hypertension, COPD, renal failure and anemia while the prevalence of CHD, cerebrovascular disease and DM decreased. Similar to men, we observed an increase over time in the number of medical conditions (Supplementary material online, Table 2).

Over the study period, we observed a slight increase in age at hospitalization, driven by increasing age at hospitalizations for recurrent events in men and all hospitalizations in women. (Supplementary material online, Table 3).

Trends in heart failure hospitalization rates

Incident hospitalizations

From 2000 to 2014, the number of hospitalizations decreased in men by 12.2% (from 2055 to 1805) and in women by 17.2% (from 1962 to 1625) (Supplementary material online, Table 3). Age-adjusted hospitalization rates decreased 1.9% per year (IRR=0.981, 95% CI: 0.976-0.987) in men and 1.8% per year (IRR=0.982, 95% CI: 0.972-0.991) in women ($P_{interaction} = 0.52$) (Figure 1, Table 2).

Hospitalization rates remained unchanged in patients < 50 years and declined 2.5%, 3.2% and 1.0% per year in men and 0.9%, 2.7% and 1.3% per year in women among patients 50-69 years, 70-79 years and 80+ years, respectively (all $P_{trend} <0.001$) (Figure 1, Table 2).

Total hospitalizations

From 2000 to 2014, the number of hospitalizations increased in men by 22.7% (from 4583 to 5623) and decreased in women by 4.7% (from 4229 to 4031) (Supplementary material online, Table 3). Age-adjusted hospitalization rates did not change significantly in either men or women (Figure 2, Table 2). In men, hospitalization rates increased 2.2% per year in age group 15-49 years and did not change across other age groups. In women, hospitalization rates declined 1.1% and 1.8% in age groups 50-69 years and 70-79 years, respectively (Figure 2, Table 2).

Readmissions following an incident heart failure hospitalization

Risk of heart failure recurrences

Table 3 summarizes the burden and time trends in the risk of the first HF recurrence at 30 days and three years of follow up. Overall, 6.1% of men and 5.6% of women surviving the incident HF hospitalization had a HF recurrence. The age-adjusted risk of recurrences at 30 days increased 1.7% per year ($P_{trend}<0.001$) in men but did not change in women.

Overall, 28.0% of men and 25.7% of women surviving the incident HF hospitalization had a HF recurrence at three years of follow up. The age-adjusted risk of recurrences increased 1.2% per year ($P_{trend}<0.001$) in men and did not change in women (Table 3).

The proportion of patients experiencing a recurrence at 30 days and three years was similar across age groups.

Age group-specific analyses revealed no statistically significant changes in the risk of recurrences, except for elderly (80+ years) men (for 30-day and three-year analyses) and women (only for three-year analyses) (Table 3).

Readmissions with a cardiovascular condition

The overall, sex and age group-specific proportions of patients with a CVD-related readmission at 30 days and three years of follow up are summarized in Table 4. The observed proportion of HF patients with a CVD-related readmission at 30 days was 11.7% in men and 10.2% in women. The age-adjusted risk of CVD-related readmissions at 30 days increased in men 1.5% per year ($P_{trend}<0.001$) but did not change significantly in women. The observed proportion of HF patients with a CVD-related readmission at three years was 55.6% in men and 49.7% in women. The risk of CVD-related readmissions at three years increased in men 1.0% per year ($P_{trend}<0.001$) but did not change significantly in women.

Age group-specific analyses revealed no statistically significant changes in the risk of CVD-related readmissions, except for men age 70-79 years (for three-year analyses) and 80+ years (for 30-day and three-year analyses) as well as women age 80+ years (only for three-year analyses) (Table 4).

In-hospital mortality

We analyzed changes over time in the odds of surviving each HF hospitalization and summarized the results in Table 4, Supplementary material online. The odds of surviving the incident HF hospitalization increased 4.7% per year in men and 3.6% per year in women (both $P_{trend}<0.001$). Similarly, the odds of surviving a second or later HF hospitalization increased 5.8% and 2.1% in men and 2.5% and 4.2% per year in women, respectively (all $P_{trend}<0.001$).

Discussion

In Norway, incident HF hospitalization rates declined in both men and women at a comparable pace from 2000 through 2014. Total HF hospitalization rates on the other hand did not decline in either men or women. We observed an increased risk of HF recurrences (confined to men) in the context of a reduced in-hospital mortality for each HF episode. The CVD-related readmissions following an incident HF hospitalization were frequent, and their risk increased over time only among men.

Declines in incident HF rates were reported from Olmsted County, Minnesota (2000-2010),[6] Ontario, Canada (1997-2007)[19] and more recently from England (2002-2014)[20] while in New Zealand (1988-2008)[8] and Denmark (1983-2012),[9] incident HF rates were characterized by a biphasic pattern (i.e. initial increase followed by decline). Total HF events rates declined in the US (2006-2014),[13] Western Australia (1990-2005),[11] Sweden (2002-2007)[21] and France (2000-2012)[12] but increased from 2003 up to 2007 and then flattened through 2013 in Spain.[14]

Of studies addressing both types of events, a decline in HF incidence and increased prevalence of HF was observed earlier in the US (1994-2003)[22] while in Western Australia, both incident and total HF hospitalization rates declined (1990-2005). [11]

The 30-day HF readmission rates did not change among Medicare beneficiaries in the US (2004-2006)[23] while one-year HF readmission rates increased in Scotland (1986-2003)[7] and declined in Ontario, Canada (1997-2007).[19]

Of patients discharged from an index HF hospitalization in the US and Canada (2005-2015), the 30-day CVD readmission rates were comparable to ours and declined modestly over time.[24] In Spain (2003-2013)[25] however, 30-day CVD-related readmission rates increased over time.

Factors associated with the observed trends

HF represents the impairment of cardiac function secondary to various cardiac and non-cardiac diseases and reflects the severity of the underlying condition and quality of care for the underlying event. CHD is the main underlying cause of HF.[26] In Norway, incident acute myocardial infarction (AMI) incident[17] and recurrence[27] rates have declined at a comparable magnitude in both men and women while invasive treatment during the early phase of the disease has improved significantly.[28] These changes led to a reduction in the proportion of HF incidence cases attributable to CHD. Further, the observed reduction in HF incidence rates is attributed to reductions in systolic and diastolic blood pressure and prevalence of hyperlipidemia.[29 30] A recent publication reported a decline in the incidence of type 2 DM in Norway.[31] On the other hand, increases in the prevalence of atrial fibrillation, valvular heart disease,[32] overweight[30] and obesity[33] have a negative impact on incident HF hospitalization rates.

Readmission rates are influenced by burden of medical conditions, quality of treatment (of both HF symptoms and the underlying condition) as well as secondary prevention measures. In our study, the prevalence of conditions that can cause HF was high, ranging from 42.6% for atrial fibrillation to 18.6% for valvular heart disease and DM. Further, 51.9% of HF patients had two or more (up to seven) other medical conditions. The prevalence of these conditions increased over time (except for CHD), as did the number of medical conditions. Clustering of many medical conditions renders the management of the incident HF episode challenging, leading to suboptimal results and eventually increased risk for other HF recurrences.

The observed increase in the risk of readmissions should be interpreted in the context of a continuous improvement in survival following hospitalization for a HF episode. We observed a significant increase in the odds of surviving hospitalization for both first and recurrent HF

episode(s), likely reflecting increased use of evidence-based treatment. These findings are in line with a previous publication showing increases in number of days alive following an incident HF hospitalization.[8] Taking together, these findings underline the importance of preventing HF recurrences in order to reduce the economic burden of HF in the community. Combined efforts to target metabolic risk factors, optimize timely treatment of the underlying condition and strengthen secondary prevention measures would help reducing mortality associated due to cardiometabolic diseases while keeping the risk of heart failure low.

Strength and limitations

The national coverage, ability to distinguish between incident and recurrent events, evaluation of both short and long-term outcomes as well as complete follow up of the study participants strengthen our study.

When interpreting our results one need to take into account some limitations inherent to study design and data content. Administrative databases do not contain information on clinical indicators of severity such as ejection fraction (EF) or type of HF (systolic versus diastolic). However, data from the US indicate that changes in the rates of HF with preserved and reduced EF have followed similar patterns.[6] Further, we did not have information on some relevant lifestyle factors such as smoking, lipid profile and diabetes. Nor did we have information on treatment while at hospital and/or following HF discharge.

Trends of incident HF hospitalization rates may not capture the true incidence of HF in the community. In the last decades, there has been a shift in HF diagnostic setting from hospitals toward outpatient clinics.[34, 35] A study conducted in Ontario[19] demonstrated a decline in rates of both hospitalized and not hospitalized new HF cases, but whether these findings are generalizable

to other locations is not known. Nevertheless, HF hospitalization is a god measure of severe HF episodes and capture the hospital-associated economic burden of the disease.

Although the quality of coding CVD conditions in administrative data in Norway is good,[36, 37] no previous study has specifically focused on HF in Norway. Based on studies from other Nordic countries, the positive predictive value and specificity of HF is high but its sensitivity is lower.[38, 39]

Lastly, the definition of 'incident' hospitalizations was based on the premise that no previous hospitalization with the same discharge diagnosis was identified up to 6 years prior to the index event. Although this method carries the risk of misclassifying a proportion of prevalent cases as incident, it avoids changes over time in the accuracy of identifying true incident event.

Conclusion: Over a 15-year period, incident HF hospitalization rates declined at a comparable pace in both men and women in Norway. However, increased risk of experiencing recurrences in the context of reduced in-hospital mortality following an HF episode swept away the positive effect of trends in incident HF hospitalizations, leading to no improvements in total HF hospitalization rates.

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Disclaimers

Data from the Norwegian Patient Registry have been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Patient Registry is intended, nor should be inferred. This study used data from the Norwegian Cause of Death Registry. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Cause of Death Registry is intended, nor should be inferred.

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Conflict of interest

None declared

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Figure legends

Figure 1

Age-standardized rates of hospitalizations with an incident heart failure episode in men (upper panel) and women (lower panel) in Norway, 2000-2014: overall and by admission type.

Figure 2

Age-standardized rates of hospitalizations with any (incident or recurrent) heart failure episode in men (upper panel) and women (lower panel) in Norway, 2000-2014: overall and by admission type.

Table 1. Baseline characteristics of patients hospitalized with heart failure as primary diagnosis in Norway, 2000-2014

	All (n=142 109)	Men (n=77 706)	Women (n=64 403)	*P* value [a]
Age, mean (SD)	77.8 (11.7)	74.9 (11.9)	81.2 (10.5)	<0.001
Type of event, n (%)				<0.001
Incident (first)	55 119 (38.8)	28 222 (36.3)	26 897 (41.8)	
Recurrent	86 990 (61.2)	49 484 (63.7)	37 506 (58.2)	
Admission type [b]				0.002
Acute	41 830 (85.2)	22 857 (81.4)	18 973 (90.4)	
Non-acute	7238 (14.8)	5226 (18.6)	2012 (9.6)	
Medical conditions, n (%)				
Atrial fibrillation	60 481 (42.6)	32696 (42.1)	27785 (43.1)	<0.001
Coronary heart disease	57 637 (40.6)	35532 (45.7)	22105 (34.3)	<0.001
Hypertension	30 860 (21.7)	14 791 (19.0)	16 069 (25.0)	<0.001
Valvular heart disease	26 385 (18.6)	12108 (15.6)	14277 (22.2)	<0.001
Diabetes mellitus	26 588 (18.6)	15332 (19.7)	11256 (17.5)	0.057
Renal failure	23 344 (16.4)	14764 (19.0)	8580 (13.3)	<0.001
Chronic obstructive pulmonary disease	18 298 (12.9)	10633 (13.7)	7665 (11.9)	<0.001
Anemia	7565 (5.3)	3706 (4.8)	3859 (6.0)	<0.001
Neoplasms	7565 (4.8)	4403 (5.7)	2354 (3.9)	<0.001
Cerebrovascular disease	5690 (4.0)	3205 (4.1)	2485 (3.9)	0.001
Number of medical conditions, n (%)				<0.001
0	19 810 (13.9)	10 168 (13.0)	9642 (15.0)	
1	48 549 (34.2)	25 794 (33.2)	22 755 (35.3)	<0.001
2	43 430 (30.6)	24 057 (31.0)	19 373 (30.1)	<0.001
≥3	30 320 (21.3)	17 687 (22.8)	12 633 (19.6)	<0.001

[a] Adjusted for age.
[b] Information valid only during 2010-2014.

Table 2. Age-adjusted average annual changes of incident and total (incident and recurrent) heart failure hospitalization rates in Norway, 2000-2014

Age group		Incident hospitalizations				Total hospitalizations			
		Men		Women		Men		Women	
		No.	IRR (95% CI)	No.	IRR (95% CI)	No.	IRR (95% CI)	No.	IRR (95% CI)
All ages		28 222	0.981 (0.976-0.987)	26 897	0.982 (0.972-0.991)	77 706	1.004 (0.993-1.016)	64 403	0.995 (0.982-1.008)
	15-49y	1214	0.995 (0.981-1.009)	510	0.984 (0.960-1.008)	2583	1.022 (1.008-1.037)	1057	1.018 (0.996-1.041)
	50-69y	7169	0.975 (0.969-0.982)	2923	0.981 (0.973-0.989)	19 606	0.997 (0.991-1.003)	6383	0.989 (0.981-0.997)
	70-79y	7948	0.968 (0.962-0.974)	5627	0.973 (0.965-0.982)	23 384	0.996 (0.991-1.002)	13 726	0.982 (0.976-0.988)
	80+y	11 891	0.990 (0.982-0.999)	17 837	0.987 (0.977-0.997)	32 133	1.007 (0.998-1.016)	43 237	1.001 (0.987-1.013)

IRR: incidence rate ratio, CI: confidence interval.

Table 3. Age-adjusted annual average changes in 30-day and three-year risk of recurrences following discharge from the incident heart failure hospitalization in Norway, 2000-2014

Age group	Men			Women		
	HF recurrence / Population at risk (%)	Follow up, days mean (SD)	SHR (95% CI)	HF recurrence / Population at risk (%)	Follow up, days mean (SD)	SHR (95% CI)
Within 30 days						
All ages	1589 / 25 902 (6.1)	26.8 (8.5)	1.017 (1.007-1.030)	1363 / 24 566 (5.6)	26.4 (8.9)	1.011 (0.998-1.023)
15-49y	72 / 1131 (6.4)	27.9 (6.9)	1.056 (0.997-1.119)	35 / 486 (7.0)	27.6 (7.4)	1.032 (0.954-1.117)
50-69y	477 / 6755 (7.1)	28.0 (6.7)	1.019 (0.997-1.041)	154 / 2748 (5.6)	28.0 (6.8)	1.011 (0.974-1.048)
70-79y	435 / 7360 (5.9)	27.3 (7.8)	1.003 (0.982-1.024)	286 / 5209 (5.5)	27.2 (7.9)	1.006 (0.979-1.033)
80+y	605 / 10 656 (5.7)	25.6 (9.7)	1.025 (1.006-1.044)	888 / 16 123 (5.5)	25.9 (9.5)	1.011 (0.995-1.027)
Within three years						
All ages	5833 / 20 792 (28.1)	627.2 (461.1)	1.012 (1.005-1.020)	5136 / 19 942 (25.8)	603.3 (460.5)	1.007 (0.999-1.015)
15-49y	219 / 908 (24.1)	814.4 (438.8)	1.004 (0.965-1.043)	81 / 394 (20.6)	823.5 (442.4)	1.026 (0.957-1.099)
50-69y	1511 / 5372 (28.1)	761.3 (448.2)	1.009 (0.993-1.023)	514 / 2158 (23.8)	771.2 (446.2)	1.012 (0.986-1.038)
70-79y	1792 / 6083 (29.5)	664.5 (452.4)	1.008 (0.994-1.021)	1160 / 4306 (26.9)	694.7 (445.9)	1.000 (0.983-1.017)
80+y	2311 / 8429 (27.4)	502.6 (443.3)	1.024 (1.011-1.036)	3381 / 13 084 (25.8)	541.1 (451.2)	1.012 (1.002-1.022)

HF: heart failure, SD: standard deviation, SHR: sub-hazard ratio, CI: confidence interval.

Table 4. Age-adjusted annual changes in 30-day and three-year risk of cardiovascular-related readmissions following discharge from the incident heart failure hospitalization in Norway, 2000-2014

Age group	Men			Women		
	CVD readmission / Population at risk (%)	Follow up, days mean (SD)	SHR (95% CI)	CVD readmission / Population at risk (%)	Follow up, days mean (SD)	SHR (95% CI)
Within 30 days						
All ages	3025 / 25 902 (11.7)	26.0 (9.1)	1.015 (1.007-1.023)	2491 / 24 566 (10.2)	25.8 (9.4)	1.006 (0.996-1.015)
15-49y	173 / 1131 (15.3)	26.6 (8.3)	1.017 (0.982-1.053)	68 / 486 (14.0)	26.6 (8.4)	1.001 (0.946-1.057)
50-69y	944 / 6755 (14.0)	27.0 (7.6)	1.005 (0.991-1.020)	331 / 2748 (12.0)	27.1 (7.8)	0.989 (0.965-1.014)
70-79y	852 / 7360 (11.6)	26.5 (8.5)	1.014 (0.999-1.030)	556 / 5209 (10.7)	26.6 (8.6)	1.005 (0.986-1.024)
80+y	1056 / 10 656 (9.9)	25.1 (10.1)	1.024 (1.010-1.039)	1536 / 16 123 (9.5)	25.3 (9.9)	1.009 (0.997-1.021)
Within three years						
All ages	11 589 / 20 792 (55.7)	457.3 (441.1)	1.010 (1.005-1.016)	9924 / 19 942 (49.8)	478.2 (444.1)	1.005 (0.999-1.011)
15-49y	514 / 908 (56.6)	528.2 (484.4)	1.012 (0.986-1.037)	191 / 394 (48.5)	582.0 (494.7)	1.008 (0.967-1.053)
50-69y	3276 / 5372 (61.0)	497.4 (465.8)	1.003 (0.993-1.013)	1180 / 2158 (54.7)	541.3 (473.4)	0.997 (0.981-1.014)
70-79y	3538 / 6083 (58.2)	484.0 (443.4)	1.014 (1.005-1.024)	2306 / 4306 (53.6)	530.5 (454.7)	1.005 (0.993-1.016)
80+y	4261 / 8429 (50.6)	407.8 (415.3)	1.017 (1.008-1.026)	6247 / 13 084 (47.8)	449.0 (431.9)	1.009 (1.002-1.017)

CVD: cardiovascular disease, SD: standard deviation, SHR: sub-hazard ratio, CI: confidence interval.

Figure 1 - revised

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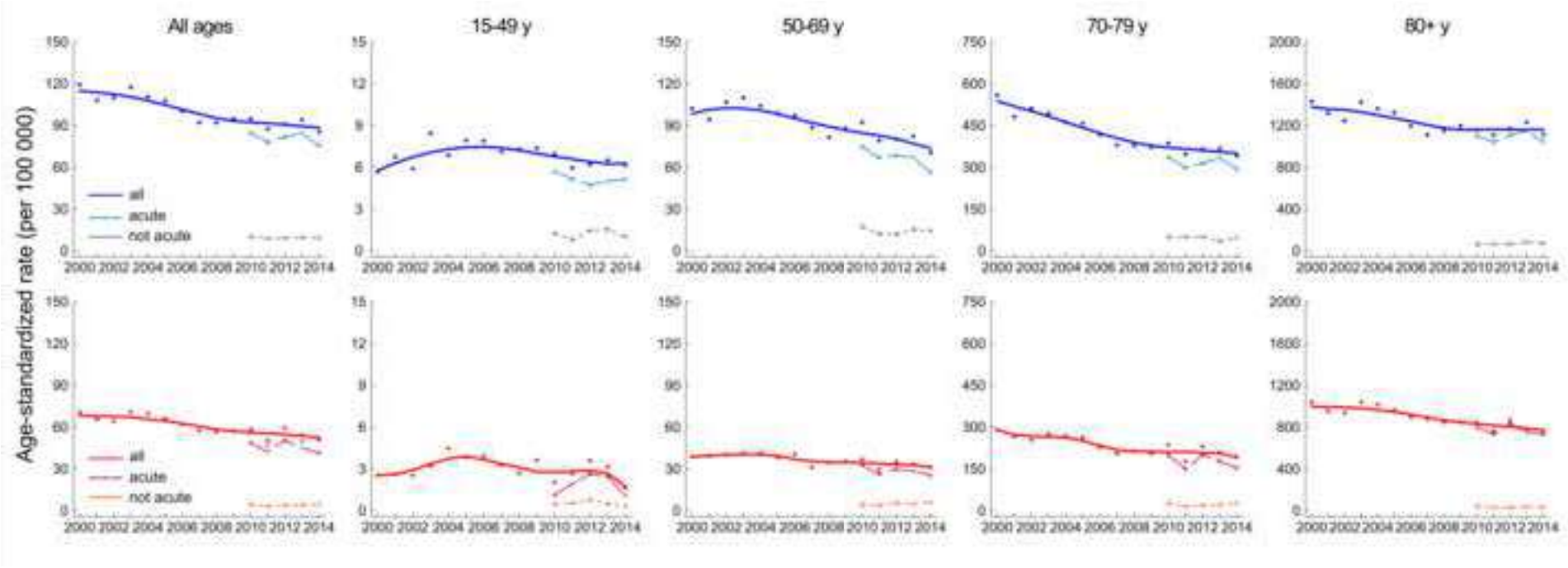

Figure 2 - revised

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