- **1** Socioeconomic gradients in mortality following heart failure hospitalization in a country
- 2 with universal healthcare coverage
- Short title: Education, income and mortality following first-time hospitalization due to heart
 failure
- 5 Author list
- 6 Gerhard Sulo^{1,2} MD, PhD; Jannicke Igland³ PhD; Simon Øverland^{1,4} PhD; Enxhela Sulo⁵
- 7 MD, PhD; Jonas Minet Kinge^{1,6,7} PhD; Gregory A Roth⁸ MD, PhD; Grethe S. Tell^{3,9} MPH,
- 8 PhD.
- 9 Author affiliation(s)
- 10 1. Centre for Disease Burden, Division of Mental and Physical Health, Norwegian Institute of
- 11 Public Health, Norway
- 12 2. Oral Health Centre of Expertise in Western Norway-Hordaland, Bergen, Norway
- 13 3. Department of Global Public Health and Primary Care, University of Bergen, Norway
- 14 4. Department of Psychosocial Science, University of Bergen, Bergen, Norway.
- 15 5. Haraldsplass Diakonale Sykehus, Bergen, Norway.
- 16 6. Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway
- 17 7. Department of Health Management and Health Economics, University of Oslo
- 18 8. Institute for Health Metrics and Evaluation (IHME), University of Washington, WA, US.
- 19 9. Division of Mental and Physical Health, Norwegian Institute of Public Health, Norway
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- 22 Address for correspondence
- 23 Gerhard Sulo, MD, PhD
- 24 Centre for Disease Burden, Division of Mental and Physical Health, Norwegian Institute of
- 25 Public Health, Norway

26	Zander Kaaesgate 7, 5015 Bergen, Norway
27	Phone: + 47 21 07 80 17
28	E-mail: Gerhard.Sulo@fhi.no
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51 ABSTRACT

52 **OBJECTIVES**: We explored the association between socioeconomic position (SEP) and
53 long-term mortality following first heart failure (HF) hospitalization.

54 BACKGROUND: It is not clear to what extent education and income - individually or

- combined influence mortality among HF patients.
- 56 METHODS: We analyzed 49 895 patients, age 35+ years, with a first HF hospitalization in
- 57 Norway during 2000-2014 and followed them until death or December 31, 2014. The

58 association between education, income and mortality was explored using Cox regression

59 models, stratified by sex and age group (35-69 years and 70+ years).

- 60 **RESULTS**: Compared to patients with primary education, those with tertiary education had
- 61 lower mortality (adjusted hazard ratio [HR]: 0.89; 95% confidence interval [CI]: 0.78 to 0.99

62 in younger men; HR: 0.57; 95% CI: 0.43 to 0.75 in younger women; HR: 0.90; 95% CI: 0.84

to 0.97 in older men and HR: 0.87; 95% CI: 0.81 to 0.93 in older women). After adjusting for

64 educational differences, younger and older men and younger women in highest income

quintile had lower mortality compared to those in the lowest income quintile (HR: 0.63; 95%

66 CI: 0.55 to 0.72; HR: 0.78; 95% CI: 0.63 to 0.96 and HR: 0.91, 95% CI: 0.86 to 0.97,

67 respectively). The association between income and mortality was almost linear. No

68 association between income and mortality was observed in older women.

69 **CONCLUSIONS**: Despite the well-organized universal healthcare system in Norway,

- 70 education and income are independently associated with mortality in HF patients in a clear
- 71 sex and age group-specific pattern.

73 ABBREVIATION LIST

- 74 CI = confidence interval
- 75 CVD = cardiovascular disease
- 76 CVDNOR = "Cardiovascular disease in Norway"
- 77 COPD = chronic obstructive pulmonary disease
- 78 DM = diabetes mellitus
- F = ejection fraction
- HF = heart failure
- 81 ICD = international classification of disease
- 82 IQR = interquartile range
- HR = hazard ratio
- 84 SD = standard deviation

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INTRODUCTION 95

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96 The prevalence of heart failure (HF) has increased globally (1). This increase is expected to continue (2) due to aging of the population (3), improved survival following most cardiac 97 conditions and increasing trends of obesity and diabetes mellitus (DM). 98 In 2012, Hawkins and al. (4) pointed to the existence of social gradients in HF incidence 99 100 and prevalence while evidence on social gradients in mortality were less consistent, with some studies confirming (5-8) and others failing to show (6,9-11) their presence. 101 102 Methodological issues that may have contributed to the lack of consistency include use of area-level (5,7,9,10,12-14) rather than individual-level measurements for socioeconomic 103 104 position (SEP), small sample sizes (6), selected, high-risk cohorts (15,16), or narrow age groups (5,10,13). Most studies have analyzed short-term outcomes (30-day and up to one 105 year) (5,10,11,16), not allowing enough time for SEP-related mechanisms to operate. 106 107 The health care system in Norway is characterized by universal coverage with predominantly public provision of services. All Norwegian residents are entitled to full access 108 109 to medical care, regardless of their age, sex, race and employment status. 110 Copayments for health services are capped at 2460 NOK (approximately 246 US dollars) a year and additional measures are applied for people with permanent reduced health and work 111 capacities. 112 Despite this universal coverage and low copayment for medical services, social gradients 113 in health outcomes still exist in Norway (17,18). 114 Education and income are often used as indicators for SEP. Education captures the 115 knowledge-related assets of a person, is established during early adulthood and remains 116 relevant throughout life. Income on the other hand, relates to the material resources and can

influence health through one's ability to purchase health-enhancing commodities and services. 118

The complex interplay between the two is poorly described, especially with regard to HF. 119

- 120 To advance knowledge on the issue, and analyzed the independent and combined effects of
- education and income on long term mortality in a nationwide cohort of patients hospitalized
- 122 with an incident HF in Norway during 2000-2014.

124 METHODS

125 **Design and settings**

126 We used data from the CVDNOR project (19) to explore the association between education,

127 personal income and mortality. We included in the study all patients age 35+ years, with an

incident HF hospitalization between 1 January 2000 and 31 December 2014 (20).

129 Exposure and other covariates

130 The information on highest attained education was retrieved from the National Education

131 Database and categorized into primary (up to 10 years), secondary (high/vocational school) or

132 tertiary education (college/university).

133 Information on patients' personal income in the last three years preceding the HF

134 hospitalization was obtained from The National Registry for Personal Taxpayers. The

135 personal income reflects income generated from wages, self-employment, capital income,

136 pensions, and social benefits after tax deduction. The personal income for each year was

137 adjusted for inflation using the consumer price index (<u>https://www.ssb.no/en/kpi</u>) for the year

138 2015. The three-year average of adjusted income was used in the analyses as i) categorical

139 (applying sex and age-specific quintile cutoff points) and ii) continuous variables.

Information on relevant co-existing medical conditions during the HF hospitalization wasobtained from the corresponding ICD-10 codes.

142 Study outcome

143 Information on date, underlying cause and place of death was obtained from the Cause of

144 Death Registry. A personal, unique project-specific number assigned to each individual

allowed us to follow study participants until death or end of follow up (31 December 2014).

146 Statistical Analyses

147 Continuous variables are presented as means and SD or median and IQR. Categorical

148 variables are presented as proportions.

We used Cox proportional hazard regression models to explore the association of 149 education and personal income with mortality. The analyses were conducted separately for i) 150 men, 35-69 years, ii) women, 35-69 years, iii) men, 70+ years and iv) women, 70+ years. 151 152 First, we explored the association of education and income with mortality by introducing in the same model both education (primary education as reference category) and income in 153 quintiles, (first quintile as reference category). Then, we explored the combined effect of 154 education and income on mortality by combining education (primary/secondary versus 155 156 tertiary) and income (< median versus \geq median) into a four-category variable. The category 'primary/secondary education and income < median' was used as reference category in these 157 158 analyses. Schoenfeld residuals were used to evaluate Cox proportionality assumptions and no significant deviation from proportionality was observed. 159

All analyses were only adjusted for age in 'Model 1') and for age, calendar year, civil
status and ten most relevant medical conditions [atrial fibrillation (AF), valvular heart disease,
coronary heart disease (CHD), DM, COPD, anemia, hypertension, neoplasms, renal failure
(RF) and thyroid disease] in Model 2.

Lastly, we applied a Cox regression model with education (as three-category variable) and income (as continuous variable), using penalized cubic splines to allow for a non-linear association between income and mortality.

167 Additional analyses

To minimize the assumptive effect of spouse's income on the association between personal
income and mortality among women, we repeated the analyses including only unmarried
women.

171 Analyses were performed using Stata (Stata Corp LP, 4905 Lakeway Drive, College Station,

172 Texas, USA) and the survival-package in R, version 3.6.0.

173

174 **RESULTS**

175 Study population characteristics

We included in the analyses 49 895 patients, age [mean (SD)] 78.1 (11.1) years (Table 1).

177 Nearly half (49.8%) of patients had completed only primary education. The majority were

178 either married (44.4%) or widow/widowed (36.2%). The proportion of comorbidities varied

179 widely, from 1.6% for asthma up to 43.0% for AF.

180 Patients with primary education were older, more often women and had a longer

181 hospitalization (in days) compared to those with higher education (Table 2). Lower education

182 was associated with lower prevalence of AF, valvular heart disease and neoplasms and higher

183 prevalence of CHD, COPD, anemia and mental disorders (Table 2).

Higher education was associated with higher income in both men and women. Within each
education and age category, men earned more than women (Figure S1, online supplemental
material).

187 Mortality

188 During a median follow up time of 27.8 months [interquartile range (IQR), 7.8 - 61.5 months;

189 maximal, 180 months), 34 127 patients died (Table S1, online supplementary material).

190 CVD deaths accounted for 58.1% of all deaths. Deaths occurring in hospitals and those

191 occurring in nursing homes accounted for 45.3% and 40.4% of total deaths. The majority

192 (91.2%) of patients survived the hospitalization for the incident HF.

193 Compared to patients who were alive at the end of follow up, those who died were older,

194 more often men, less educated, earned less and had a greater burden of comorbidities (Table

195 S2, online supplementary material).

196 The mortality (per 100 000) among HF patients was much higher than that observed in the

197 general population (Table S3, online supplementary material).

198 Education and mortality

- 199 Compared to primary education, tertiary education was associated with 11% (HR: 0.89; 95%
- 200 CI: 0.78 to 0.99) lower mortality in younger men, 43% (HR: 0.57; 95% CI: 0.43 to 0.75) in
- 201 younger women, 11% (HR: 0.89, 95% CI: 0.83 to 0.99) in older men and 10% (HR: 0.90;
- 202 95% CI: 0.84 to 0.97) in older women (Table 3).

203 Income (in quintiles) and mortality

- 204 The fifth income quintile was associated with lower mortality compared to the first income
- 205 quintile (Table 3). The magnitude varied from 37% (HR: 0.63; 95% CI: 0.55 to 0.72) in
- 206 younger men to 22% (HR: 0.78; 95% CI: 0.63 to 0.96) in younger women and 9% (HR: 0.91;
- 207 95% CI: 0.86 to 0.97) in older men. In older women, we observed no association between
- 208 income and risk of dying following first HF hospitalization.

209 Additional analyses

- 210 When restricting the analyses to unmarried women, the highest income quintile was
- associated with lower mortality compared to the lowest income quintile only in older women
- 212 (Table S4, online supplementary material).

213 Income (continuous variable) and mortality

- Figure 1 depicts results of adjusted analyses where income was introduced as a continuous
- variable. Income was inversely and nearly linearly associated with mortality in all sex and age
- 216 groups except for older women.

217 The combined effect of education and income (Figure 2)

- Among men, higher income was associated with reduced mortality, regardless of education
- 219 level (categories II and IV versus category I). In younger women, *either* highest education or
- 220 higher income were associated with reduced mortality (categories II, III and IV versus
- 221 category I). In older women, only highest education and higher income was associated with
- 222 lower mortality (category IV versus category I)
- 223

224 **DISCUSSION**

225 Summary of findings

Our study is among the first to demonstrate an inverse association between education and mortality, which is stronger in women compared to men. Income was inversely and, nearly linearly associated with mortality in all men and younger women. When education and income were combined, the later appeared to override education with regard to mortality in men. In younger women, each component *per se* was associated with reduced mortality. In older women, we observed reduced mortality only when highest education was combined with higher income.

233 **Published literature**

A recent study from Denmark (16) using reported an association between family income and
one-year mortality among 17 122 HF patients with reduced (≤ 40%) ejection fraction (EF).
Median household income was inversely associated with 30-day mortality among 48 338
elderly with HF enrolled in 'Get With The Guidelines-HF' database (13) and longer-term
(maximum follow up, 72 months) mortality among 1415 patients with incident HF enrolled in
the ARIC community study (7).

Of note, education was not associated with one-year mortality in patients hospitalized with an incident episode of HF in the Danish study (16). No association between education and mortality was found either in two sub-analyses of RCTs; the first enrolling 541 ambulatory patients with chronic HF (6) and the second enrolling 2331 patients with chronic HF and reduced EF (15).

245 Potential mechanisms involved

HF represents the end-stage of various cardiac and metabolic conditions. Therefore, risk
factor burden and configuration, clinical expression of the underlying conditions and delays in
seeking medical assistance are crucial factors in the development and severity of HF, which in

turn influence mortality. Studies point to the existence of socioeconomic gradients in lifestylerelated factors (21,22), including smoking habits (23). Further, low social status is associated
with lower health literacy (24) and delayed help seeking (25). The net effect of these
determinants operating outside heath system are likely to generate social gradients in disease
severity of the underlying conditions (often being coronary heart disease) and its optimal
treatment (26).

255 Little is known on other features through which health care systems themselves may contribute maintaining, or even perpetuating the observed social gradients in health outcomes. 256 An optimal prescription (27) and adherence (28) the guideline-directed drug therapy for HF, 257 improves patients' outcomes. Despite this evidence, real-world studies point to a suboptimal 258 prescription and/or adherence to treatment among HF patients (29), even in countries with 259 260 universal healthcare and low copayment such as the Netherlands (30), the UK (31) and 261 Sweden (32). Factors influencing suboptimal drug prescription are not fully understood, but it has been suggested that these gradients can originate from more comorbidities and more 262 severe HF among socially deprived patients (33). 263

The interaction between health care providers and HF patients is not to be neglected either. The observed social gradients in participation in rehabilitation programs (34) risk behavior modification (35), follow up rates (36), or even access to specialized care (37) could be narrowed if closer follow with more dedicated time were to be offered to socioeconomicallydeprived patients.

Lastly, due to its complexity, HF is a costly disease. While direct expenses related to
treatment are capped, other indirect costs (such as those related to transportation
arrangements, interventions and lifestyle modification, including diet) may accumulate and
become a burden for patients with low income. Moreover, lack of sufficient material

273 resources may induce stress which is linked to poor outcomes. Lastly, low income is often274 associated with poor social network and social support.

275 Differences between previously published studies and our study

Previous publications (6,15,16) did not find an association between education and
mortality among HF patients. These discrepancies could stem from a number of factors,
including differences in study populations' structure and size, length of follow up, time period
and study settings and data analyses.

280 To illustrate, study population in the other studies comprised patients with reduced EF

281 (6,15,16) and previous HF hospitalizations (6,15) while in our study we included individuals

with no previous HF hospitalizations and a mixture of reduced and preserved EF. Both

reduced EF and previous hospitalizations for HF increase the odds of dying.

The Danish study included 17 122 participants, but restricted the follow up time to one year (16). The number of participants and subsequently events of interest were much smaller in the two other studies; 2331 (15) and 571 (6) participants, respectively.

287 The Danish study (16) was observational, with no active follow up of study participants. The second largest study (15) was a post hoc analysis of HF-ACTION (a randomized 288 controlled clinical trial), including patients with moderate to severe HF receiving either i) 289 290 education or ii) education plus supervised exercise training program. Optimized therapy prior to study enrollment was a requirement. Further, both income and education was self-reported. 291 The third study (6) was a propensity score matched analysis of a small sample of HF patients 292 enrolled in DIG (Digitalis Investigation Group) trial in 1995. Information on education was 293 self-reported and included the participants or spouses' education level. We believe that shorter 294 follow up time, severity of HF and study settings (in the two RCTs) may have implied closer 295 medical follow up of patients (often in hospitals or other specialized care structures) and 296

- 297 optimization of therapies, leaving thus little room for education-related mechanisms to
- 298 operate and display educational gradients in mortality.

299 Sex and age group-specific patterns

300 Income was more strongly associated with mortality among men while education among

- 301 women. Although our study cannot fully explain the observed patterns, we believe they are
- 302 influenced by multiple, non-mutually exclusive potential factors.
- 303 *The effect of using personal rather than household income*

Generally, women earn less than men. Further, women married to partners with high earnings may in some cases choose to work part-time. Hence, the personal income in married women would underestimate the household income, dominated by partners' income. As a result, the observed association between personal income and mortality in women would underestimate the true association we would observed among them, had we been able to adjust for partner's income.

310 *Income distribution in men and women*

The difference [in Norwegian Kroner (NOK)] from one income quintile to another is greaterin men compared to women. To illustrate, younger men in the fifth income quintile earned

292 000 NOK (approximately 29 200 US dollars) more than younger men in the first income

314 quintile while. In younger women, the difference between the corresponding income quintiles

315 was 195 000 NOK (approximately 19 500 US dollars). Hence, a stronger association between

- income and mortality in men compared to women (when using income quintiles) may reflect
- the absolute differences in earnings between income quintiles in men versus women.

318 Sex differences in etiology, clinical expression and type of HF

In men, HF is more often of ischemic origin, with reduced EF, and often more with more

320 typical symptoms. In women, HF's underlying conditions include more often slowly-evolving

and less fulminant conditions such as hypertension (38), obesity, diabetes (39) or anemia. The

dominant HF form in women is the diastolic, with preserved EF. Women are often 322 323 underrepresented in clinical trials (40), leading to insufficient understanding of mechanisms involved and HF treatment efficacy among them. This is also reflected in the lack of sex-324 specific treatment strategies for HF in international guidelines. The challenges in recognizing 325 symptoms and timely diagnosing HF in women, as well as uncertainties with regard to 326 treatment efficiency among them, may leave more room to knowledge-related assets of 327 328 patients, which, in a universal health care setting, are captured by education. Other potential explanations include the fact that income and education may capture 329 health-relevant behaviors to different extents in men and women, or that the set of risk factors 330 331 operating along with education and income are different across sexes.

The lack of an association between income and mortality among older women may be further related a higher burden of comorbidities and the fact that they reside more often in nursing homes, where, due to collective arrangements, personal income may not play an important role.

336 Strengths and limitations

We measured exposure at the individual level in a well-defined nationwide cohort of HF patients, thus minimizing the risk of selection bias. The long (up to 15 years) and complete follow up of study participants add to the value of our study. Further, we analyzed the individual and combined effects of education and income on mortality, describing for the first time sex and age group patterns characterizing this relationship.

Some limitations inherent to the structure and content of administrative data need to be kept in mind when interpreting the findings such as lack of information on lifestyle factors including smoking, physical activity, body mass index or family history of disease. Further, no information on medication taken during or after discharge and participation in rehabilitation programs was available. We could not stratify the analyses on EF (preserved vs.

reduced EF) as such information was not available. Information on comorbidities wascollected during the incident HF hospitalization.

Income measured at the personal level carries the risk of underestimating the true financial 349 resources of a family, especially among women and diluting the association between personal 350 income and mortality among them. We addressed this issue by conducting separate analyses 351 352 among unmarried women and found an association between personal income and mortality. However, the 'unmarried' category may include a fraction of population who live with a 353 partner without being formally married. Further, the personal income measured a few years 354 ahead of the first HF episode may not represent well the real lifelong financial situation of 355 356 individuals as it may be influenced by declining health prior to HF hospitalization (41).

Lastly, as in all observation studies, potential residual confounding cannot be completelyruled out.

359 Conclusions: Using an unselected population of patients hospitalized with incident HF, we found that education and income were independently and inversely associated with long-term 360 mortality. When combined, income was decisive among men. Among younger women, either 361 higher education or higher income was associated with lower mortality. In older women, 362 lower mortality was observed only among those with higher education and higher income. 363 The observed mortality gradients in a country with universal healthcare and low copayments 364 such as Norway should encourage more studies in order to identify factors responsible for 365 these gradients. 366

367 Perspectives

368 Competency in medical knowledge: Our results point to a significant mortality following the

369 first HF hospitalization and identify education and income as two independent, yet

370 complementary SEP dimensions involved in this process.

371	Translational outlook: We need more studies focusing on i) identifying mechanisms through
372	which education and income operate, ii) providing evidence on the best possible way to
373	reduce the observed SEP gradients in mortality following HF.
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517	Figure Legends
518	Figure 1: Penalized cubic spline plot for the association between income and mortality among
519	patients hospitalized with an incident heart failure in Norway, 2000-2014: the CVDNOR
520	project
521	Figure 2: Combined educational and income-related gradients in mortality among patients
522	hospitalized with an incident heart failure episode in Norway, 2000-2014: the CVDNOR
523	project
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542 Table 1. Baseline characteristics of patients hospitalized with incident heart failure in Norway, 2000-2014: the CVDNOR project

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	Total 35-69 years			70+ years			
	(n=49 895)	Men (n=7642)	Women (n=3105)	P value	Men (n=17 987)	Women (n=24 266)	P valu
Age, mean (SD)	78.1 (11.1)	60.7 (7.8)	61.3 (7.9)	<0.001	81.5 (5.8)	83.9 (5.8)	< 0.00
Mode of hospitalization				0.522			< 0.00
Emergency	92.4	86.6	87.4		92.5	95.2	
Planned	7.6	13.4	12.6		7.4	4.7	
Education				< 0.001			< 0.00
Primary	49.8	35.5	45.7		45.3	59.6	
Secondary	40.0	48.6	42.2		42.6	34.2	
Tertiary	10.2	15.9	12.1		12.1	6.3	
Income (in 1000 NOK), median (IQR)	188 (147-244)	258 (201-336)	192 (141-245)	< 0.001	204 (162-254)	159 (132-197)	< 0.00
Civil status, %				< 0.001			< 0.00
Unmarried/Cohabitants	9.7	19.7	12.0		8.2	6.9	
Married	44.4	55.1	51.9		62.4	24.0	
Widow	36.2	3.3	12.4		22.8	63.1	
Divorced	9.7	21.9	23.7		6.6	6.0	
Readmission due to HF	29.6	35.2	29.4	< 0.001	30.9	28.8	< 0.00
HF hospitalization (days), median (IQR)	6 (3-9)	6 (3-10)	6 (3-10)	0.007	5 (3-9)	6 (3-9)	0.00
Medical conditions, %							
Atrial fibrillation	43.0	37.4	27.6	< 0.001	46.4	44.5	< 0.00
Valvular heart disease	17.8	13.8	15.8	0.009	16.3	20.9	< 0.00
Coronary heart disease	34.5	41.3	32.6	< 0.001	38.9	28.6	< 0.00
Hypertension	26.5	27.6	27.8	0.801	22.7	29.2	< 0.00
Diabetes mellitus	14.8	19.1	18.5	0.408	14.0	13.4	0.05
Renal failure	10.0	6.8	5.4	0.006	13.9	8.6	< 0.00
Chronic obstructive pulmonary disease	11.5	11.2	17.0	< 0.001	13.2	9.5	< 0.00
Neoplasms	5.4	3.7	6.1	< 0.001	7.8	3.9	< 0.00
Anemia	4.9	2.1	3.5	< 0.001	5.1	5.9	< 0.00
Thyroid disease	3.2	0.9	5.0	< 0.001	1.4	5.3	<0.00
Mental disorders	3.8	1.9	2.2	0.572	3.8	4.1	0.1
Asthma	1.6	1.3	3.2	< 0.001	1.0	2.1	< 0.00
Pulmonary hypertension	2.2	1.7	3.6	< 0.001	1.9	2.4	0.00

544 SD = standard deviation; IQR = interquartile range; NOK = Norwegian kroner (0.11 EU or 0.12 USD in 2015).

	Primary	Secondary	Tertiary	Р
	(n=24 881)	(n=19 914)	(n=5100)	for trend
Age, mean (SD)	79.5 (10.3)	77.0 (11.3)	75.3 (12.5)	< 0.001
Sex, (male)	43.6	57.1	66.6	< 0.001
Mode of hospitalization				< 0.001
Emergency	93.6	91.8	90.4	
Planned	6.4	8.2	7.6	
Income (in 1000 NOK), median (IQR)	166 (135-203)	206 (160-261)	294 (235-367)	< 0.001
Length of hospitalization, median (IQR)	6 (3-9)	6 (3-9)	5 (3-9)	< 0.001
Civil status				< 0.001
Married	37.5	49.5	57.1	
Unmarried	10.3	8.9	9.8	
Widow	43.5	31.1	21.3	
Divorced	8.7	10.5	11.8	
Readmission due to HF, %	32.4	32.8	32.0	0.063
Medical conditions, %				
Atrial fibrillation	41.2	44.5	46.8	< 0.001
Valvular heart disease	17.7	17.7	19.9	< 0.001
Coronary heart disease	34.0	35.3	33.8	< 0.001
Hypertension	26.2	26.7	27.3	0.002
Diabetes mellitus	15.6	14.3	12.5	< 0.001
Renal failure	10.2	10.0	9.4	0.091
Chronic obstructive pulmonary disease	12.7	11.1	7.6	< 0.001
Neoplasms	5.0	5.8	6.1	0.010
Anemia	5.5	4.4	3.7	< 0.001
Thyroid diseases	3.5	2.9	2.7	0.803
Mental conditions	8.4	7.3	6.5	0.004
Asthma	1.8	1.5	1.6	0.571
Pulmonary hypertension	2.3	2.1	2.1	0.152

545 Table 2. Characteristics of the study participants by education: the CVDNOR project

SD = standard deviation; NOK = Norwegian kroner (0.11 EU or 0.12 USD in 2015); IQR = interquartile range.

Table 3. Educational and income-related gradients in mortality among patients hospitalized with incident heart failure in Norway, 2000-2014: the CVDNOR project

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	Men			Women			
	Deaths /	Hazard ratio		Deaths /	Hazard ratio		
	Person - Years	(95% CI)		Person - Years	(95% CI)		
		Model 1	Model 2		Model 1	Model 2	
Age group, 35-69 years							
Education							
Primary	1217 / 13 989	1 ^{reference}	1 ^{reference}	648 / 7311	1 reference	1 ^{reference}	
Secondary	1346 / 19 963	0.88 (0.82 - 0.96)	0.95 (0.88 - 1.03)	461 / 6904	0.79 (0.70 - 0.90)	0.84 (0.74 - 0.94)	
Tertiary	351 / 6826	0.82 (0.72 - 0.93)	0.89 (0.78 - 0.99)	68 / 2045	0.46 (0.36 - 0.60)	0.57 (0.43 - 0.75)	
Income							
1 st quintile	744 / 7709	1 ^{reference}	1 reference	271 / 3551	1 ^{reference}	1 ^{reference}	
2 nd quintile	654 / 7727	0.90 (0.81 - 1.00)	0.92 (0.81 - 1.01)	268 / 3155	1.09 (0.92 - 1.29)	0.99 (0.85 - 1.17)	
3 ^d quintile	582 / 8018	0.78 (0.70 - 0.87)	0.84 (0.74 - 0.93)	245 / 3180	1.01 (0.85 - 1.20)	0.88 (0.75 - 1.06)	
4 th quintile	503 / 8617	0.64 (0.57 - 0.72)	0.72 (0.64 - 0.81)	225 / 3205	0.98 (0.82 - 1.17)	0.85 (0.73 - 1.03)	
5 th quintile	431 / 8707	0.55 (0.48 - 0.62)	0.63 (0.55 - 0.72)	168 / 3168	0.84 (0.69 - 1.03)	0.78 (0.63 - 0.96)	
Age group, 70+ years							
Education							
Primary	6546 / 22 048	1 reference	1 reference	10 110 / 36 612	1 reference	1 reference	
Secondary	5705 / 21 680	0.94 (0.90 - 0.98)	0.96 (0.93 - 0.99)	5247 / 21 553	0.92 (0.89 - 0.96)	0.94 (0.90 - 0.98)	
Tertiary	1497 / 6381	0.85 (0.80 - 0.91)	0.90 (0.84 - 0.97)	904 / 4025	0.83 (0.77 - 0.89)	0.87 (0.81 - 0.93)	
Income							
1 st quintile	2914 / 9933	1 reference	1 reference	3334 / 13 144	1 reference	1 reference	
2 nd quintile	2838 / 9568	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)	3309 / 12 570	1.02 (0.97 - 1.07)	0.96 (0.92 - 1.02)	
3 ^d quintile	2711 / 9930	0.95 (0.91 - 1.00)	0.94 (0.90 - 0.99)	3291 / 12 165	1.05 (1.00 - 1.10)	0.98 (0.93 - 1.04)	
4 th quintile	2704 / 10 012	0.95 (0.90 - 1.00)	0.95 (0.90 - 0.99)	3227 / 12 163	1.04 (0.99 - 1.09)	0.97 (0.92 - 1.03)	
5 th quintile	2581 / 10 595	0.91 (0.86 - 0.97)	0.91 (0.86 - 0.97)	3127 / 12 131	1.06 (1.01 - 1.12)	0.98 (0.93 - 1.04)	

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553 Model 1 includes education, income and age (continuous variable).

554 Model 2 includes education, income, age (continuous variable), calendar year, civil status, atrial fibrillation, valvular heart disease, coronary heart disease, hypertension, diabetes mellitus, renal

failure, chronic obstructive pulmonary disease, neoplasms, anemia and thyroid diseases.

556 CI = confidence interval.