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1 **Lower socioeconomic status predicts higher mortality and morbidity in**
2 **patients with heart failure**

3
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29 **Abstract**

30 *Objective.* It is not fully understood whether and how socioeconomic status (SES)
31 has a prognostic impact in patients with heart failure (HF). We assessed SES and its
32 association with patient characteristics and outcomes in a contemporary and well-
33 characterised HF cohort.

34 *Methods.* Socioeconomic risk factors (SERF) were defined in the Swedish HF
35 Registry based on income (low vs. high according to the annual median value),
36 education level (no degree/compulsory school vs. university/secondary school), and
37 living arrangement (living alone vs. cohabitating).

38 *Results.* Of 44,631 patients, 21% had no, 33% one, 30% two and 16% three SERF.
39 Patient characteristics strongly and independently associated with lower SES were
40 female sex and no specialist referral. Additional independent associations were older
41 age, more severe HF, heavier comorbidity burden, use of diuretics and less use of
42 HF devices. Lower SES was associated with higher risk of HF
43 hospitalisation/mortality, and overall cardiovascular and non-cardiovascular events.
44 These associations persisted after extensive adjustment for patient characteristics,
45 treatments and care. The magnitude of the association increased linearly with the
46 increasing number of coexistent SERF: hazard ratio (95% confidence interval) 1.09
47 (1.05-1.13) for one, 1.16 (1.12-1.20) for two and 1.22 (1.18-1.28) for three SERF
48 ($p < 0.01$).

49 *Conclusions.* In a contemporary and well-characterised HF cohort and after
50 comprehensive adjustment for confounders, lower SES was linked with multiple
51 factors such as less use of HF devices and age, but most strongly with female sex
52 and lack of specialist referral; and associated with greater risk of morbidity/mortality.

53

54 Key words: Heart failure, socioeconomic status, income, education, living
55 arrangement, health inequality

56 **Key questions**

57 What is already known about the subject?

58 Lower socioeconomic status is suggested to be associated with high risk of
59 morbidity/mortality in heart failure, although it is debated whether this association is
60 mediated by differences in heart failure severity or differences in quality of care.

61

62 What does this study add?

63 This study showed that lower socioeconomic status is associated with a 9-22%
64 higher risk of morbidity/mortality independently of heart failure severity and quality of
65 care.

66

67 How might this impact on clinical practice?

68 These findings call for more awareness on health inequalities in heart failure.
69 Identifying factors leading to worse outcomes in patients with lower socioeconomic
70 status may contribute to attenuate health disparities.

71 **Introduction**

72 Heart failure (HF) affects approximately 2-3% of the western population and is
73 increasing in prevalence. It is characterised by high mortality/morbidity, impaired
74 quality of life and an heavy economic burden on healthcare systems worldwide[1].
75 Several factors, such as demographic and clinical characteristics linked with more
76 severe HF, comorbidities and poorly implemented use of treatment contribute to
77 explain the impaired prognosis characterising the HF population.[2] However, these
78 important factors only partially account for the total risk of adverse outcomes
79 observed in HF[3].

80 Lower socioeconomic status (SES) is associated with poorer outcome in the general
81 population as well as in patients with cardiovascular disease[4]. It might also play an
82 important role in HF disease progression and contribute to explain the total risk of
83 adverse outcomes which is not linked with well-established prognostic factors.

84 Previous studies have highlighted an interplay between different measures of SES
85 and outcomes in HF[5, 6, 7]. However, the lack of important phenotypic information
86 and of granular data on use of care and of HF treatments might have led to
87 overestimation of the prognostic role of SES, which might rather be explained by
88 unmeasured confounding, e.g. be a risk marker simply for less use of HF therapies[5,
89 6, 7]. How SES impacts on prognosis is not exactly known. Socioeconomic
90 disparities might foster differences in the distribution of comorbidities which are
91 prognostically relevant in HF (e.g. diabetes, hypertension, etc.), and/or might limit the
92 access to healthcare, influence the likelihood of receiving/using life-saving treatments
93 and also influence lifestyle patterns.

94 Therefore, we investigated in a large, well characterised and contemporary HF cohort
95 1) the clinical phenotype of HF patients with different SES; 2) whether lower SES is

96 associated with poorer outcome and 3) whether this potential association might be
97 explained by specific patient characteristics, or different use of care or treatments.

98 **Methods**

99 Study protocol and setting

100 The design of the Swedish Heart Failure Registry (SwedeHF, www.SwedeHF.se) has
101 been previously described[8]. Briefly, patients with clinician-judged HF have been
102 enrolled since May 11th, 2000. Approximately 80 variables are recorded at discharge
103 from hospital or after outpatient visit.

104 For this analysis, SwedeHF was linked to the National Patient Registry which
105 provided data on additional comorbidities and the outcomes HF, cardiovascular, non-
106 cardiovascular hospitalisation, to Statistics Sweden which provided data on
107 education level and income, and to the Cause of Death Registry which provided all-
108 cause, cardiovascular, non-cardiovascular mortality data.

109 The study was conducted in accordance with the Declaration of Helsinki. SwedeHF
110 as well as this analysis requiring the linking of the above-mentioned registries were
111 approved by a multi-site ethics committee. Individual patient consent was not
112 required, but patients were informed of entry into the registry and allowed to opt out.

113

114 Patient and public involvement

115 Patients or the public were not involved in this research project.

116

117 Determination of SES

118 In this study SES has been broadly defined, including different factors indicating the
119 level of social and economic resources.

120 *Income:* higher/lower income was defined as individual annual income at the index
121 date > or ≤ median annual income of all SwedeHF patients registered in the same
122 year, respectively.

123 *Education level:* higher education was defined as secondary school degree or higher
124 whereas lower education as compulsory school degree or no degree.

125 *Living arrangement:* defined as living alone vs. cohabitating.

126 SES was graded based on the prevalence/coexistence of the socioeconomic risk
127 factors (SERF) measured in our cohort, i.e. lower income, lower education level,
128 living alone. Therefore, a patient could have 0, 1, 2 or 3 SERF.

129

130 Patients

131 Patients registered in SwedeHF between 11th May 2000 and 31st December 2016
132 with available data on income, education level, living arrangement and ejection
133 fraction (which is a categorized variable in SwedeHF, i.e. <30%, 30-39%, 40-49%,
134 and ≥50%), were included in the analyses. Patients who died during the
135 hospitalisation/visit linked to their SwedeHF registration were excluded. If the same
136 patient had multiple registrations in SwedeHF, the last one was selected, since more
137 representative of contemporary care and socioeconomic context. The index date was
138 defined as either the day of the outpatient visit or the day of hospital discharge.

139

140 Statistical analyses

141 *Patient characteristics.* Baseline characteristics were compared across different SES
142 (i.e. different number of coexistent SERF) by ANOVA or Kruskal-Wallis tests for
143 continuous and by chi-squared for categorical variables.

144 To evaluate patient characteristics which were independently associated with lower
145 SES, a multivariable ordinal logistic regression model was fitted, with the number of
146 coexistent SERF as the dependent variable and the baseline characteristics reported
147 in *Table 1* as covariates. The proportional odds assumption was visually verified and

148 met. Odds ratio (OR) and 95% confidence interval (CI) were calculated for each
149 potential predictor.

150 *Outcome analysis.* The primary outcome was a composite of time to first HF
151 hospitalization or all-cause death. Secondary outcomes were HF hospitalisation (with
152 censoring at death) and all-cause death, separately, cardiovascular events (time to
153 first cardiovascular hospitalization or cardiovascular death, with censoring for non-
154 cardiovascular death) and non-cardiovascular events (time to first non-cardiovascular
155 hospitalisation or non-cardiovascular death; with censoring for cardiovascular death).
156 To investigate the association between SES and outcomes, the Kaplan-Meier
157 method was used to estimate unadjusted survivor functions in patients stratified by
158 the number of coexistent SERF. Separate Cox regression models were fitted with (1)
159 no adjustment; (2) adjustment for demographic characteristics; (3) for demographic +
160 clinical characteristics; (4) for demographic + clinical characteristics + comorbidities;
161 (5) for demographic + clinical characteristics + comorbidities + treatments (42
162 variables in total). Hazard ratio (HR) and 95% CI were calculated. The proportional
163 hazard assumption was verified by Schoenfeld residuals and met. To assess whether
164 SES was similarly associated with the different outcomes, the respective HRs were
165 compared based on their betas/standard errors by t-test.

166 In both multivariable ordinal logistic and Cox regression models, missing data were
167 handled by chained-equations multiple imputation (R-package *mice*). Analyses were
168 performed in 10 imputed datasets and then the estimates were combined by Rubin's
169 rules. Variables used for the multiple imputation are marked in *Table 1*.

170 All statistical analyses were performed by R3.5.3. A two-sided p-value <0.05 was
171 considered as statistically significant.

172 Variable definitions are provided in *Supplementary Table 1*, missing data is shown in
173 *Supplementary Table 2*.

175 **Results**

176 Prevalence of socioeconomic risk factors

177 Between 11th May 2000 and 31st December 2016, there were 130,420 registrations
178 from 76,506 unique patients in SwedeHF. After applying inclusion/exclusion criteria,
179 44,641 patients were eligible for this analysis.

180 As many as 9,362 patients (21%) had no SERF, 14,600 patients (33%) had one
181 SERF, 13,594 patients (30%) had two SERF and 7085 patients (16%) had all three
182 SERF. *Figure 1* illustrates the interrelationship across the different SERF.

183

184 Baseline characteristics (*Table 1*)

185 Patients with lower SES were more likely older and female, with higher ejection
186 fraction, more severe HF (i.e. higher New York heart association functional class, N-
187 terminal pro-B-type natriuretic peptide levels) and higher comorbidity burden. They
188 were less likely to receive guideline-recommended HF therapies and to have follow-
189 up in specialty care, but more likely to receive diuretics. Similar results were shown
190 when analyses were stratified by ejection fraction subtype or by individual SERF
191 (*Supplementary Tables 3-8*).

192 Results in *Table 1* are unadjusted. Therefore, we performed multivariable ordinal
193 logistic regression to identify patient characteristics independently associated with
194 lower SES (*Figure 2*).

195 Among the variables considered in our analyses, female sex (OR 2.97, 95%CI 2.85-
196 3.08, $p < 0.01$) and no referral to specialty care follow-up (OR 1.50, 95%CI 1.44-1.56,
197 $p < 0.01$) showed strong associations with lower SES. Other important patient
198 characteristics linked with lower SES were older age, more severe HF, higher
199 comorbidity burden (including smoking, ischaemic heart disease, obesity, liver
200 disease, diabetes, pulmonary disease, chronic kidney disease, anaemia, atrial

201 fibrillation, neurologic/psychiatric disorders), more use of diuretics but less use of HF
202 devices. Similar results were obtained when patients were stratified by ejection
203 fraction subtype (*Supplementary Figures 1-3*).

204

205 Outcome

206 Over a median follow-up of 1.98 (interquartile range 0.40-4.76) years, 30,402
207 (68.1%) all-cause death/HF hospitalisation events occurred, corresponding to an
208 event rate of 231 (95%CI: 229-234) per 1000 patient-years. Unadjusted event rates
209 of the composite outcome increased together with worsening SES: 157 (95%CI: 153-
210 161) per 1000 patient-years for no SERF, 207 (95%CI: 203-212) for one SERF, 275
211 (95%CI: 269-279) for two SERF, and 358 (95%CI: 348-367) for all three SERF
212 ($p < 0.001$; *Figure 3*).

213 Multivariable Cox regression models showed lower SES to be significantly
214 associated with a higher risk of HF hospitalisation/ all-cause death. This association
215 persisted after adjustment for demographics, clinical characteristics, comorbidities
216 and treatments. Risk of outcome steadily increased with the increasing number of
217 coexistent SERF. In the fully adjusted model, as compared with no SERF, HR for one
218 SERF was 1.09 (95%CI 1.05 - 1.13; $p < 0.001$); 1.16 (95%CI 1.12 - 1.20; $p < 0.001$) for
219 two SERF; and 1.22 (95%CI 1.18 - 1.28, $p < 0.001$) for three SERF (*Figure 4*). Similar
220 results were observed when all the different clusters/combinations of SERF and
221 individual SERF were analysed and when analyses were performed stratifying by
222 ejection fraction subtype (*Supplementary Table 9 and Supplementary Figures 4-5*).
223 We explored sex-interactions for the associations between SERF and outcome
224 showing that the relative risk in females was higher as compared to males when all
225 SERF were prevalent (p interaction < 0.01 , *Supplementary Figure 6*).

226 In the secondary outcome analysis, lower SES was associated with an increased risk
227 of all-cause mortality but not of HF hospitalisation, and was associated with a
228 similarly increased risk of cardiovascular vs. non-cardiovascular events
229 (*Supplementary Figure 7-8*).

230 **Discussion**

231 In this large, contemporary HF cohort, we observed that: 1) patients with lower SES
232 had more severe HF, but were less likely treated with HF therapies and to be referred
233 to specialty care follow-up; and 2) lower SES was associated with higher
234 mortality/morbidity, which was only partially attenuated by extensive adjustments for
235 multiple patient and treatment characteristics. Two critical and quantitatively very
236 strong associations with lower SES were female sex and no referral to specialist
237 follow-up.

238

239 Patient characteristics according to SES

240 Women with HF are older, have more variable symptoms and longer delay to
241 prognosis[9], and in most[10, 11] though not all[12] studies women are underserved
242 by many HF interventions, especially devices. Even independent of these factors,
243 women had an almost 3-fold greater odds of having low SES, and low SES was
244 associated with worse outcomes, independent of sex and other factors. Taken
245 together, these data suggest that strong and formal efforts are needed to improve HF
246 care in women. Similarly, lower SES was strongly and independently linked to not
247 being referred to specialist follow-up care, even independent of therapy and other
248 factors. It has previously been described that specialist care is critical to receiving
249 appropriate HF drug initiation and up-titration as well as device therapy[8, 10].
250 Additionally, these findings suggest that in this era of rapidly increasing HF
251 prevalence together with diminishing resources, it is critical to ensure access to
252 specialist care (e.g. cardiology or internal medicine). Furthermore, in recent years,
253 multiple new drugs, catheter-based interventions and procedures have proven
254 beneficial in HFrEF, and treatment optimisation is becoming increasingly difficult for
255 the generalist. Thus, it has been suggested that essentially all patients with

256 symptomatic HFrEF should be referred to the HF team for appropriate selection of
257 HF interventions[13, 14].

258 Another key finding was that patients with lower SES had more severe HF but were
259 less likely treated with HF therapies and referred to specialty care follow-up. In
260 principle, there should be no inequalities in quality or affordability of medical care in a
261 universal health care system, such as in Sweden. Nevertheless, health care
262 inequalities for patients with different SES have been previously reported in this and
263 similar health care systems.[4] This inconsistency might be at least partially
264 explained by the fact that patients are requested to pay a fee for drug dispensation or
265 health care access. Although costs are limited, fees may affect the likelihood of
266 seeking care or collecting prescribed drugs for patients with a low income. The higher
267 comorbidity burden, also linked to a poorer lifestyle, could be a likely explanation for
268 the observed more severe HF in patients with lower vs. higher SES. Indeed, in our
269 study, several comorbidities known to be linked with both HF disease progression
270 and overall impaired prognosis, e.g. diabetes, renal disease, ischaemic heart
271 disease, anaemia, and atrial fibrillation, were independently associated with lower
272 SES.[2] However, lower SES does not only drive disease progression in HF patients,
273 but it is also associated with incident HF in the general population[15]. Important
274 factors such as alcohol and drug abuse, smoking, unhealthy diet, physical inactivity
275 and systemic inflammatory response can contribute per se or by fostering the onset
276 of comorbidities linked to HF onset.[16, 17, 18, 19]. Poor treatment of or adherence
277 to therapies for comorbidities (e.g. hypertension, diabetes, dyslipidaemia), delayed
278 access to revascularisation in case of myocardial infarction leading to greater
279 myocardial damage, are further factors which may contribute to explain the
280 association between lower SES and both incident and more severe HF.[20, 21]

281 Another potential explanation for our finding might be linked to the association
282 between SES and health literacy. Lower health literacy, which is more likely in
283 patients with lower SES, might limit self-care in HF and therefore contribute to
284 disease progression[22]. Additionally, lower SES and lower health literacy can also
285 be barriers to adequate use of health care resources, as they negatively influence the
286 use of preventive measures or treatments in several cardiovascular diseases[22, 23],
287 or simply delay the first contact with primary/secondary care and prevent an
288 adequate follow-up. Finally, present bias and naivete, where patients avoid short-
289 term inconvenience or discomfort at the cost of long-term complications, has been
290 described in conditions such as type 1 diabetes[24] and may be linked with SES.

291

292 Morbidity/mortality according to SES

293 An association between SES and outcome has been previously reported in HF, but
294 with limited adjustment for important clinical factors and treatments likely to influence
295 the relationship between SES and prognosis.[5, 6, 7] In this study, we showed that
296 the association between SES and mortality/morbidity persisted even after extensive
297 adjustments for relevant confounders, including demographics, clinical
298 characteristics, comorbidities and treatments. We combined different indicators of
299 SES and thus we could show that the magnitude of SES-associated risk of outcomes
300 was greater when several SERF coexisted. Importantly, our definition of SES did not
301 only include classical measures such as income and education, but also living status,
302 which is a measure for social connectedness. This is of relevance, as it has been
303 shown that individuals with lower social connectedness might not use the full range
304 of available medical measures (ranging from preventive to therapeutic
305 measures).[23] Our findings highlight the importance of assessing SES in patients

306 with HF, but also lead to important questions regarding potential mechanisms or
307 mediators.

308 As we reported for the association between SES and more severe HF, it is unlikely
309 that worse morbidity/mortality with lower SES might be mainly explained by
310 differences in affordability or availability of care in the Swedish health care system.
311 Dedicated follow-up care, as well as comorbidity burden and HF severity have been
312 considered for adjustments and, thus, might not explain the independent association
313 between SES and morbidity/mortality. Furthermore, lower SES was associated with
314 all-cause mortality but not HF hospitalization, which might be explained by the
315 adjustments for several variables linked with HF severity. This is consistent with UK
316 data showing lower SES to be associated with a higher risk of all-cause death, but
317 not with HF hospitalisation, in 1,802 HFrEF patients.[25] As for the primary outcome,
318 we observed increased risk of cardiovascular and non-cardiovascular events in
319 patients with lower SES. Health behaviours, such as unhealthy diet, sedentary
320 lifestyle, alcohol/drug abuse, which have not been considered, might contribute to
321 explain the overall worse prognosis in patients with lower SES[26, 27, 28, 29].
322 Additionally, for adjustments we considered treatments as prescribed, but lower
323 health literacy, social support and self-care which are more likely in lower SES could
324 have negatively impacted on adherence leading to higher mortality/morbidity[22].
325 Limited patient participation to follow-up care might have prevented the correct up-
326 titration of HF treatment in those with lower SES, which is known to be linked to
327 worse outcomes.[30] Additionally, lower SES is linked to a lower likelihood of being
328 engaged in preventive measures[23], and comorbidity status might have further
329 worsened over time, which could not be captured in our analysis where comorbidities
330 were considered at the baseline. Finally, although we adjusted for several
331 cardiovascular comorbidity-related therapies (e.g. antiplatelets), we could not adjust

332 for treatments required for many other comorbidities considered and not considered
333 in this analysis.

334

335 Limitations

336 Strengths include the use of a large, well-characterised and contemporary HF cohort
337 with data on several measures of SES, which allowed to perform extensive
338 adjustments, and a detailed characterisation of HF patients according to SES.

339 Limitations are linked with the observational nature of this analysis, and therefore
340 with residual/unmeasured confounding, which is likely to explain the significant
341 association between SES and outcome. SES was defined based on income,
342 education and living arrangement, but different definitions might provide different
343 results. Income and living arrangement, but not education, are dynamic and might
344 thus have varied during the follow-up, resulting in misclassification. Few variables
345 such as New York heart association functional class and N-terminal pro-B-type
346 natriuretic peptide levels had a considerable amount of missing data (25.6% and
347 64.2% missing, respectively), which was handled by multiple imputation. Data on
348 accessibility to specialty care were not available. Notably, clustering of such facilities
349 in neighbourhoods with a higher SES might contribute to explain less referral to
350 specialty care in patients with lower SES. Finally, our study is based on a national
351 cohort and generalisability to other countries/healthcare systems might be limited.

352

353

354 **Conclusions and clinical implications**

355 In this large and contemporary HF cohort from universal tax-financed healthcare
356 system, patients with lower SES had more severe HF but were less likely to receive
357 HF treatments and care. Lower SES was associated with worse prognosis, even
358 after extensive adjustment for demographics, clinical characteristics, comorbidities
359 and treatments.

360 Our findings call for more awareness on health inequalities in HF. Identifying factors
361 leading to worse outcomes in patients with lower SES may contribute to attenuate
362 health disparities. Additionally, assessing SES-related factors, such as health literacy
363 and social support, could improve risk stratification in HF. Specifically, there were two
364 findings of critical importance that can be easily addressed: (1) female sex was
365 associated with a nearly 3-fold higher odds of low SES, suggesting that extra effort
366 should be expended on optimising care for women with HF; and (2) referral to
367 specialist follow-up was less common with lower SES, suggesting that proper
368 specialty care should be offered to and ideally accepted by all patients who need it
369 and that community interventions in primary care setting are needed.

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374

375 **Conflict of Interest**

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395 The other authors do not report relevant conflicts of interest.

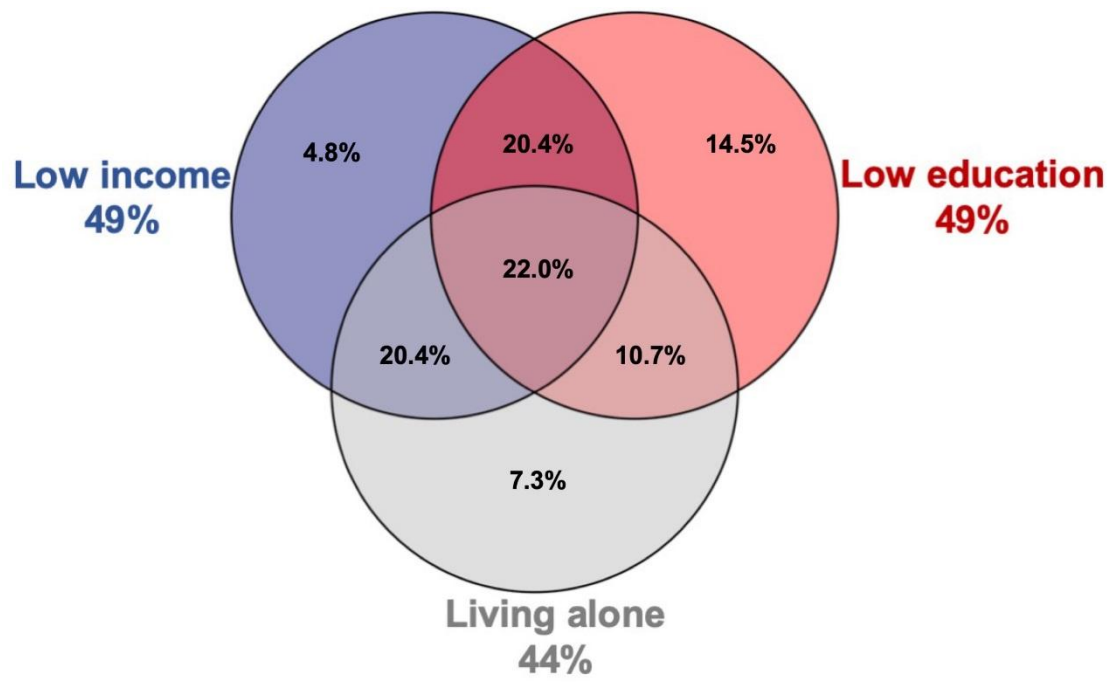
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484 **Figure legends**

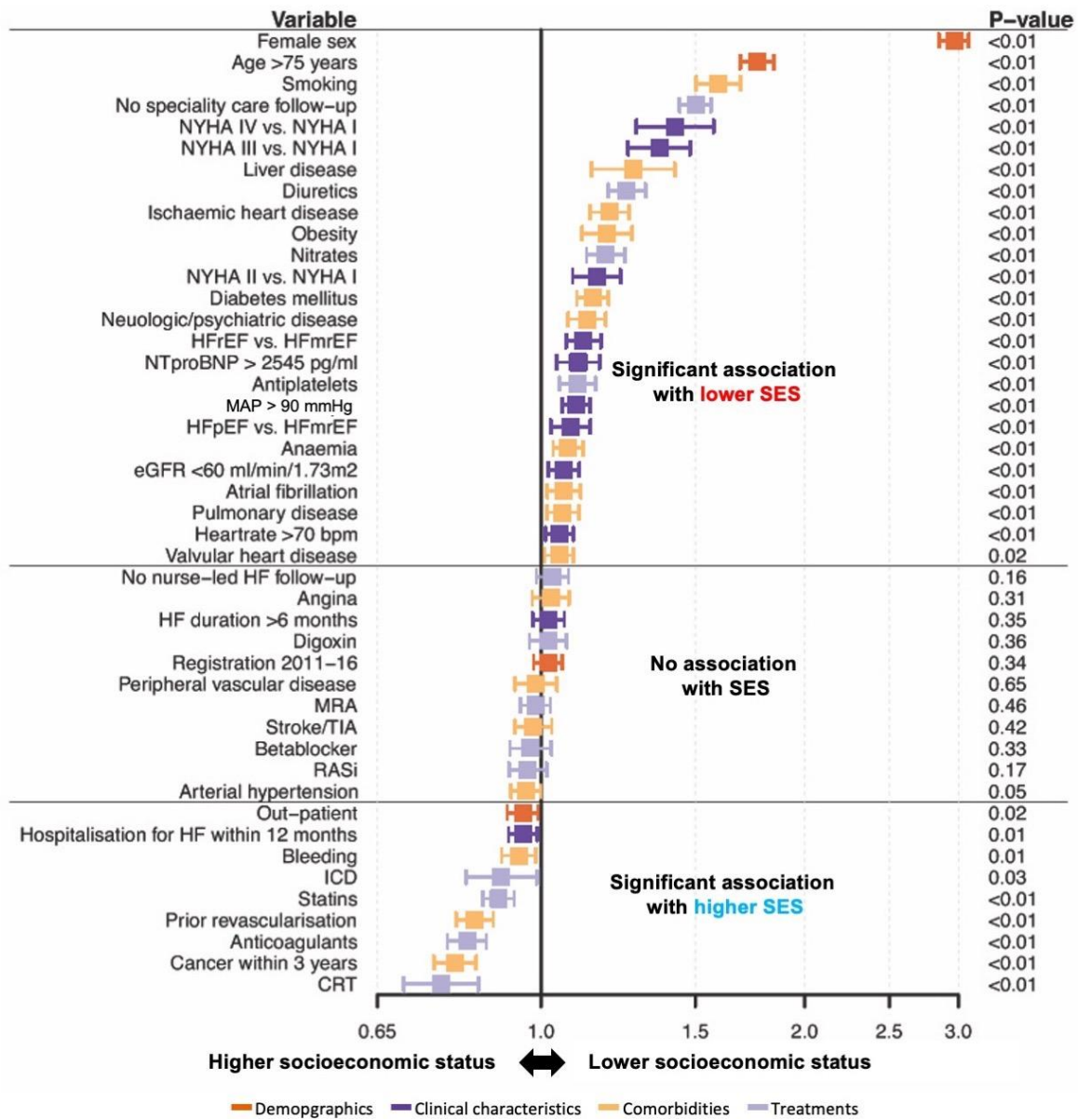
485 **Figure 1: Interrelationship between socioeconomic risk factors**



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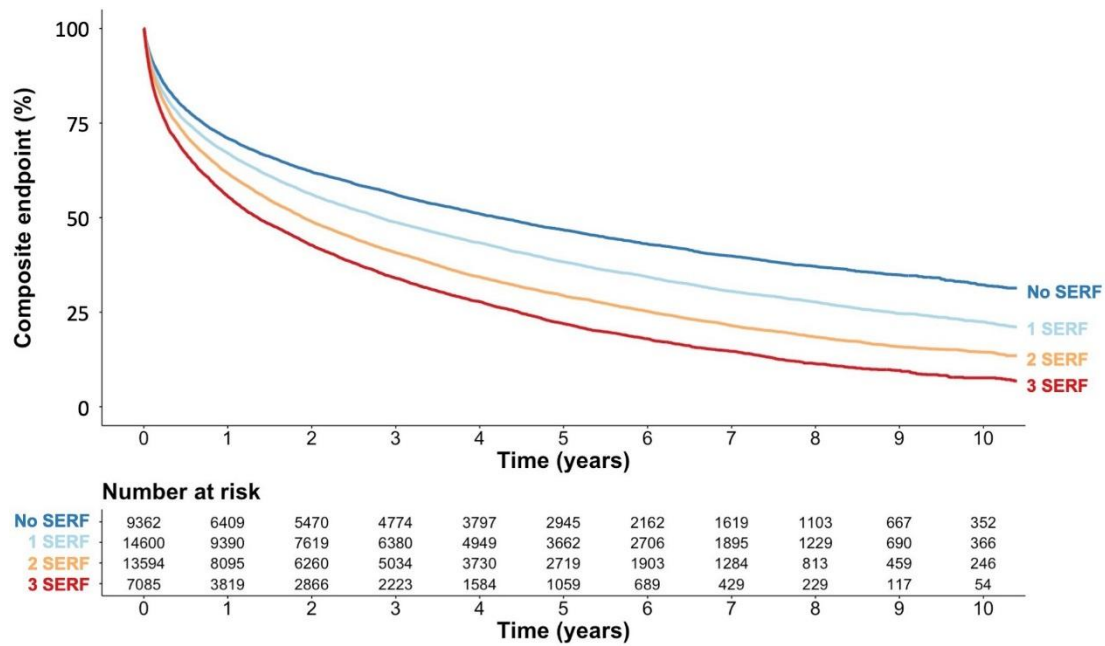
488 **Figure 2: Independent associations between patient characteristics and**
 489 **socioeconomic status**



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 491 Odds ratios from the multivariable ordinal logistic regression are shown on the x-axis, with an odds ratio below 1.0 indicating an
 492 association with higher socioeconomic status and an odds ratio above 1.0 indicating an association with a lower socioeconomic
 493 status. Specialty care follow-up refers to planned follow-up in a specialty care (e.g. cardiology, internal medicine) institution.
 494 Similarly, nurse-led HF follow-up refers to planned follow-up in a nurse-led HF clinic. HFpEF: heart failure with preserved
 495 ejection fraction; HFmrEF: heart failure with mid-range ejection fraction; HFrEF: heart failure with reduced ejection fraction;
 496 NYHA: New York Heart Association; NTproBNP: N-terminal pro-B-type natriuretic peptide; HFrEF: heart failure hospitalisation;
 497 MAP: mean arterial pressure; eGFR: estimated glomerular filtration rate (calculated by Chronic Kidney Disease Epidemiology
 498 Collaboration formula); ICD: implantable cardioverter-defibrillator; CRT: cardiac resynchronisation therapy; RASi: renin-
 499 angiotensin-system inhibitor; MRA: mineralocorticoid receptor antagonist; TIA: transient ischemic attack.

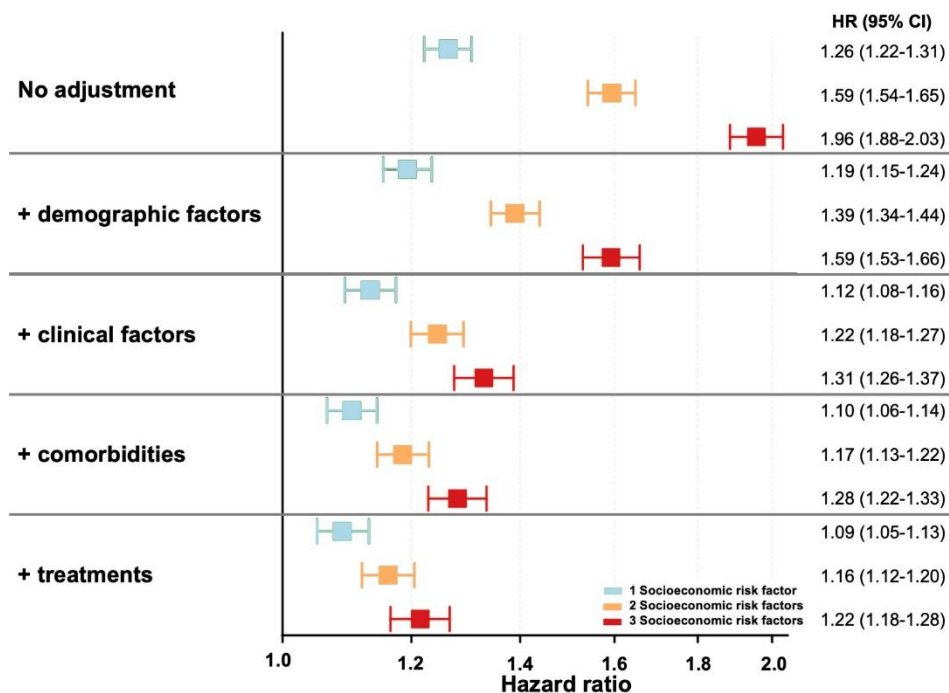
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501 **Figure 3: Kaplan Meier curves for heart failure hospitalisation or all-cause**
 502 **death according to the number of socioeconomic risk factors**



503
 504 Kaplan Meier curves are shown per number of socioeconomic risk factors (income \leq median, living alone, compulsory school
 505 degree/no degree). SERF: socioeconomic risk factor.

506 **Figure 4: Association between socioeconomic status and heart failure**
 507 **hospitalisation or all-cause death**



510 Models were adjusted for demographic factors: Age >75 vs. ≤75 years, sex, registration 2000-10 vs. 2011-16; clinical factors:
511 Outpatient, ejection fraction, New York Heart Association class, NT-proBNP >2545 vs. ≤2545 pg/ml (median), hospitalisation for
512 heart failure within the last 12 months, heart rate ≥70 vs. <70 bpm, mean arterial pressure ≥90 vs. <90 mmHg, duration of heart
513 failure <6 months vs. ≥6 months; comorbidities: Current smoking, obesity, estimated glomerular filtration rate <60 vs. ≥60
514 ml/min/1.73m², liver disease, cancer within past 3 years, anaemia, atrial fibrillation, diabetes mellitus, prior revascularization,
515 ischaemic heart disease, arterial hypertension, valvular heart disease, stroke/transient ischemic attack, pulmonary disease,
516 neurologic/psychiatric disease, history of bleeding, history of angina; treatments: Implantable cardioverter defibrillator, cardiac
517 resynchronisation therapy, betablocker, renin-angiotensin-system inhibitors, mineralocorticoid-receptor-antagonists, digoxin,
518 stations, anticoagulants, antiplatelets, nitrates, diuretics, planned nurse-led heart failure follow-up, planned specialty care follow-
519 up. Reference category was not having any socioeconomic risk factors. Hazard ratios are shown for comparison of having 1,2
520 or 3 socioeconomic risk factors vs. not having any socioeconomic risk factors. HR: hazard ratio; CI: confidence interval.
521

522 **Table 1: Baseline characteristics stratified by number of socioeconomic risk**
 523 **factors**

	Number of socioeconomic risk factors				P
	0 (N=9362, 21%)	1 (N=14600, 33%)	2 (N=13594, 30%)	3 (N=7085, 16%)	
Demographic factors					
Age (years)	69.94 (±12.39)	72.93 (±11.86)	76.23 (±10.89)	80.38 (±10.12)	<0.01
>75 years*	3489 (37.3%)	7005 (48.0%)	8297 (61.0%)	5402 (76.2%)	<0.01
Female*	1411 (15.1%)	4421 (30.3%)	5882 (43.3%)	4527 (63.9%)	
Registration*					<0.01
2000-10	4018 (42.9%)	6225 (42.6%)	6166 (45.4%)	3171 (44.8%)	
2011-16	5344 (57.1%)	8375 (57.4%)	7428 (54.6%)	3914 (55.2%)	
Clinical factors					
Out-patient*	5523 (59.0%)	7866 (53.9%)	6309 (46.4%)	2486 (35.1%)	<0.01
Ejection fraction*					<0.01
Preserved (≥50%)	1716 (18.3%)	3090 (21.2%)	3344 (24.6%)	2217 (31.3%)	
Mid-range (40-49%)	2179 (23.3%)	3272 (22.4%)	2941 (21.6%)	1457 (20.6%)	
Reduced (<40%)	5467 (58.4%)	8238 (56.4%)	7309 (53.8%)	3411 (48.1%)	
HF duration (days)	308 [38, 1660]	404 [40, 1800]	475 [41, 1814]	460 [29, 1702]	<0.01
>6 months*	4803 (56.3%)	7952 (58.8%)	7676 (60.5%)	3996 (59.7%)	<0.01
NYHA*					<0.01
Class I	1245 (16.4%)	1349 (12.1%)	880 (9.0%)	359 (7.8%)	
Class II	3718 (48.9%)	5196 (46.4%)	4261 (43.4%)	1858 (40.1%)	
Class III	2352 (31.0%)	4164 (37.2%)	4135 (42.1%)	2100 (45.4%)	
Class IV	283 (3.7%)	479 (4.3%)	537 (5.5%)	312 (6.7%)	
NT-proBNP (pg/ml)	1960 [762, 4695]	2347 [940, 5637]	2880 [1180, 6800]	3430 [1525, 8320]	<0.01
>2545 pg/ml*	1480 (42.0%)	2601 (47.5%)	2535 (54.0%)	1378 (60.2%)	<0.01
Hospitalization for HF within 12 months*	5398 (57.7%)	7874 (53.9%)	6781 (49.9%)	3183 (44.9%)	<0.01
Heart rate (bpm)	71.53 (±14.73)	72.94 (±15.01)	74.20 (±15.45)	75.05 (±15.66)	<0.01
≥70 bpm*	4642 (52.4%)	7864 (57.0%)	7699 (59.7%)	4196 (62.5%)	<0.01
MAP (mmHg)	89.88 (±13.17)	90.02 (±13.12)	90.34 (±13.31)	90.84 (±13.34)	<0.01
≥90 mmHg*	4671 (50.7%)	7359 (51.2%)	6953 (52.0%)	3713 (53.4%)	<0.01
Comorbidities					
eGFR (ml/min/1.73m ²)	64.52 (±23.58)	60.93 (±23.75)	56.49 (±23.38)	52.72 (±22.39)	<0.01
<60 ml/min/1.73m ² *	3949 (42.5%)	7194 (49.7%)	7920 (58.6%)	4584 (65.0%)	<0.01
Current smoking*	726 (9.1%)	1620 (13.2%)	1508 (13.8%)	669 (12.7%)	<0.01
Obesity*	1161 (21.6%)	2051 (25.2%)	1711 (24.3%)	794 (23.2%)	<0.01
Angina*	2725 (29.1%)	4746 (32.5%)	4607 (33.9%)	2459 (34.7%)	<0.01
PVD*	967 (10.3%)	1675 (11.5%)	1688 (12.4%)	823 (11.6%)	<0.01
Liver disease*	209 (2.2%)	381 (2.6%)	385 (2.8%)	181 (2.6%)	0.05
Cancer within 3 years*	1172 (12.5%)	1701 (11.7%)	1455 (10.7%)	634 (8.9%)	<0.01
Bleeding*	1675 (17.9%)	2869 (19.7%)	2781 (20.5%)	1426 (20.1%)	<0.01
Anaemia*	2999 (32.5%)	5168 (35.9%)	5234 (39.0%)	2899 (41.3%)	<0.01
Atrial fibrillation*	5336 (57.0%)	8575 (58.7%)	8175 (60.1%)	4405 (62.2%)	<0.01
Diabetes mellitus*	2281 (24.4%)	4173 (28.6%)	4170 (30.7%)	2115 (29.9%)	<0.01
Prior revascularization*	3254 (34.8%)	4908 (33.6%)	4249 (31.3%)	1682 (23.7%)	<0.01
Ischaemic heart disease*	5011 (53.5%)	8359 (57.3%)	8127 (59.8%)	4201 (59.3%)	<0.01

<i>Arterial hypertension*</i>	5567 (59.5%)	9197 (63.0%)	8950 (65.8%)	4819 (68.0%)	<0.01
<i>Valvular heart disease*</i>	2698 (28.8%)	4385 (30.0%)	4586 (33.7%)	2593 (36.6%)	<0.01
<i>Stroke/TIA*</i>	1339 (14.3%)	2230 (15.3%)	2223 (16.4%)	1278 (18.0%)	<0.01
<i>Pulmonary disease*</i>	1678 (17.9%)	3351 (23.0%)	3533 (26.0%)	1701 (24.0%)	<0.01
<i>Neurologic/psychiatric disease*</i>	1022 (10.9%)	2045 (14.0%)	2219 (16.3%)	1186 (16.7%)	<0.01
Treatments					
<i>ICD*</i>	696 (7.5%)	862 (6.0%)	503 (3.7%)	140 (2.0%)	<0.01
<i>CRT*</i>	619 (6.7%)	741 (5.1%)	473 (3.5%)	148 (2.1%)	<0.01
<i>Betablocker*</i>	8299 (89.0%)	12885 (88.7%)	11854 (87.5%)	5965 (84.5%)	<0.01
<i>RASi*</i>	8141 (87.4%)	12329 (84.9%)	10936 (80.8%)	5365 (76.2%)	<0.01
<i>MRA*</i>	3046 (32.8%)	4766 (32.9%)	4311 (31.9%)	2186 (31.1%)	0.03
<i>Digoxin*</i>	1510 (16.2%)	2502 (17.2%)	2329 (17.2%)	1265 (17.9%)	0.03
<i>Statins*</i>	4669 (50.1%)	7170 (49.3%)	6222 (45.9%)	2609 (37.0%)	<0.01
<i>Anticoagulants*</i>	4436 (47.6%)	6328 (43.6%)	5409 (40.0%)	2362 (33.6%)	<0.01
<i>Antiplatelets*</i>	4005 (43.1%)	6939 (47.9%)	6816 (50.4%)	3748 (53.2%)	<0.01
<i>Nitrates*</i>	1104 (11.9%)	2176 (15.0%)	2605 (19.3%)	1578 (22.4%)	<0.01
<i>Diuretics*</i>	6675 (71.3%)	11400 (78.1%)	11344 (83.4%)	6229 (87.9%)	<0.01
<i>Planned nurse-led HF follow-up*</i>	3701 (40.0%)	5282 (36.2%)	4226 (31.1%)	1675 (23.6%)	<0.01
<i>Planned specialty care follow-up*</i>	6431 (68.7%)	8716 (59.7%)	6703 (49.3%)	2455 (34.7%)	<0.01

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Summary statistics shown in Table 1 are based on unimputed data. Continuous variables are presented as mean (\pm standard deviation) and compared by one-way analysis of variance if normally distributed, and as median (25th, 75th percentile) and compared by Kruskal-Wallis test if non-normally distributed. Categorical variables are presented as absolute (relative) frequencies and compared by Chi²-test. Marked variables (*) were used for the multiple imputation together with the number of socioeconomic risk factors and the composite endpoint. HF: heart failure; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-B-type natriuretic peptide; MAP: mean arterial pressure; eGFR: estimated glomerular filtration rate (calculated by Chronic Kidney Disease Epidemiology Collaboration formula); ICD: implantable cardioverter-defibrillator; CRT: cardiac resynchronisation therapy; RASi: renin-angiotensin-system inhibitor; MRA: mineralocorticoid receptor antagonist; PVD: peripheral vascular disease; TIA: transient ischemic attack.