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Temporal trends in socioeconomic disparity in clinical outcomes for patients with acute coronary syndrome

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ABSTRACT

Aims: Socioeconomic factors are well-established determinants of clinical outcomes among patients with acute coronary syndrome (ACS) although quality of care has improved the last decades. This study aims to investigate 20-years temporal trends of socioeconomic disparity in 1-year incidence of major adverse cardiac events (MACE) among ACS patients in Denmark.

Methods: This population-based cohort study included all incident ACS patients in the Danish National Patient Registry during 1998–2017. Socioeconomic disparity was assessed by income and educational level. Patients were followed 1-year for MACE; defined as all-cause mortality, recurrent ACS, revascularization, stroke, or cardiac arrest. Adjusted MACE incidence rates (aIR) and hazard rate ratios (aHR) were computed with 95 % confidence intervals (CI) for five-year-periods. Changes in trends were examined from interaction analyses between the HR for five-year-periods and income and education, respectively.

Results: The study included 220,887 patients with first-time ACS. The incidence of MACE decreased within all income and education levels. In 1998–2002 the MACE aIR among patients with low income was 885[95%CI:863–907] versus 733[711–756]/1000-person-year among those with high income (aHR: 1.19[95%CI:1.15–1.23]). The aIRs decreased to 506[489–522] and 405[388–423]/1000-person-year, respectively, in 2013–2017 (aHR: 1.23[1.17–1.29]). The aIRs of MACE decreased correspondingly within all educational levels from 1998 to 2002 to 2013–2017. However, the socioeconomic disparity according to the interaction analyses persisted both according to income and educational level.

Conclusion: Although 1-year clinical outcomes following ACS has improved substantially over the last decades, socioeconomic disparity persisted both according to income and education level.

1. Introduction

Acute coronary syndrome (ACS) is the leading cause of mortality globally. The global incidence of ACS persists above 20 million cases yearly [1] and has a major impact on the disparity in life expectance [2]. Socioeconomic position (SEP), e.g. reflected by income and education, represent individual pathways for the disparity in health outcomes [3,4]. Low SEP is generally associated with worse clinical outcomes, i.e. higher mortality and morbidity in the patients with ACS [5,6].

Socioeconomic disparity in the incidence of ACS appear to have remained without significant improvements since the late eighties [7–9]. Short-and long-term major adverse cardiac events (MACE), including mortality, recurrent ACS, urgent need for revascularization, and stroke after ACS have decreased during the last four decades [10–12]. This has been accomplished e.g. by improvements in cardiovascular risk factors (e.g. decreased smoking prevalence) and by increasing use of guideline-recommended invasive treatments [13] (i.e., percutaneous coronary interventions or coronary artery bypass grafting) and secondary preventive medications [10,14,15]. However, considerable disparity in medical care and mortality after ACS, according to income, education, insurance, employment, and composite measures of SEP has been reported from most studies investigating this matter during the last decade [6]. Furthermore, socioeconomic disparity

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is presented in clinical outcomes after ACS, including recurrent ACS, subsequent stroke, urgent need for revascularization, and composite measures of these up to 10 years after the ACS diagnosis [16–20]. Studies on temporal trends in socioeconomic disparity in mortality after ACS have reported persistent or small declines in the socioeconomic disparity in the period 1976–2008 [10–12,21,22], and persistent disparity from 2008 to 2018 [12]. These trends could be affected by disparity in resources to act and initiate a healthier lifestyle or disparity in health care use [3,4]. However, the temporal trends in the socioeconomic disparity in MACE after ACS, including recurrent ACS, revascularization, stroke, and cardiac arrest, are yet unexplored.

The present study aims to investigate temporal trends of socioeconomic disparity in MACE within 30-days and 1-year after the ACS diagnosis among patients with incident ACS in Denmark from 1998 to 2017.

2. Methods

2.1. Settings

This historical population-based cohort study was conducted using data from national administrative registries covering all contacts to the healthcare sector and information on SEP on an individual level for the Danish population ($N = 4.5$ million aged ≥18 years in 2016) [23]. The study was reported according to the guidelines for Reporting of studies Conducted using Observational Routinely-collected health Data statement (RECORD) [24] and registered at the Danish Data Protection Agency (Journal number: 2019-899/10-0429).

2.2. Data sources

Person-linked data was accessed from several nationwide registries through Statistics Denmark [25]. Personal income were identified from the Income Statistic Registry and information about the highest completed level of education from the Population Education Register [25]. The Danish National Patient registry (DNPR) holds data on morbidity from hospital-based activities and procedures for all inpatients discharged from Danish somatic hospitals since 1977 and information from emergency departments and outpatient specialty clinics since 1995 [26]. Diagnoses was routinely recorded at all patient contacts, according to the International Classification of Diseases 8th revision (ICD-8) since 1977 and 10th revision (ICD-10) since 1994 [26]. The Register of Medicinal Products Statistics holds information on all prescription drugs, according to the Anatomical Therapeutic Chemical (ATC) classification system [27]. Data are available on a person-based level on drugs dispensed in Danish community pharmacies and hospital-based outpatient pharmacies since 1995. The Danish Civil Registration System (CRS) is an administrative register established in 1968 on individual-level information on all Danish residents, allowing cross-register-linkage, essential for the conduction of nationwide cohort studies. Daily updated data on migration and vital status holds almost complete long-term follow-up [23].

The Danish Heart Registry (DHR) holds medical and administrative data on patients referred for invasive cardiological procedures and heart surgery from 2003. Unique variables include demographic characteristics, prognostic factors, and procedure-related information on complications [28].

2.3. Study population

The study population was identified based on nationwide population-based data on hospital admissions. Subjects aged ≥18 years admitted to a hospital with a first episode of ACS in Denmark from 1998 to 2017 registered in the DNPR were included (*Supplemental Table S1*). Patients were excluded if they did not have an address in Denmark the year before the ACS diagnosis or if they had previous ACS diagnoses. All patients were followed from hospital admission until the date of a MACE, emigration, or administrative censoring, whichever appeared first. Administrative censoring was set at 30-days and 1-year of follow-up.

2.4. Socioeconomic position

The individual patient level SEP was applied based on two measures: equivalent personal income quartile [29] and education level [30]. Year-age- and sex-specific income equivalents quartiles, accessed in Statistics Denmark, were applied according to the entire Danish population to reduce the impact of inflation [29]. Personal education was categorized into three levels based on the International Standard Classification of Education (ISCED) 2011: 1) Low (ISCED 0–2), 2) medium (ISCED 3), 3) high (ISCED 5–8). ISCED 4 is not used in the Danish education system [30].

2.5. Major adverse cardiac events

Various definitions for MACE have been used in cardiovascular research [5,18,31]. In this study, MACE was defined as the first event registered ≥7 days after discharge from the primary ACS admission. The events included: all-cause mortality (from hospital admission), recurrent ACS, revascularization (Percutaneous Coronary Interventions or Coronary Artery Bypass Grafting), stroke (hemorrhagic or ischemic), or cardiac arrest *(Supplemental Table S2)* [31]. As secondary outcomes, the individual MACE, i.e., all-cause mortality, recurrent ACS, revascularization, stroke, and cardiac arrest, were individually investigated.

2.6. Covariates

Covariates included age, sex, employment, migrant-, civil-, or cohabitant status, and Charlsons Comorbidity Index (CCI). Age was applied as restricted cubic splines. Employment was categorized based on information from the Register-based Labour Force Statistics, defined as employed, retired (including early retirement), or unemployed. Migrant status was defined based on place of birth (Danish-born or Immigrant/descendant). CCI was calculated from the ICD-8 and ICD-10 diagnoses based on the 19 disease categories within ten years before the index date [32]. Patients were categorized according to one of three levels of CCI [32] defined as: a score of 0 (low), given to patients with no record of diseases; a score of 1–2 (medium); and a score of 3 or more (high) *(Supplemental Table S3)*.

2.7. Statistics

Statistical analyses were performed in Stata 17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC). Baseline characteristics for the patients were presented; continues variables as median and interquartile ranges and categorical variables as frequencies and percentages. This was presented according to income quartile, education level, and four five-year intervals. Numbers of missing observations were reported alongside these statistics and missing data were imputed in the analysis using multiple imputation chained equations. MACE incidence rates were computed, and cox-proportional hazards regression was used to estimate the hazard rate ratio (HR) of MACE associated with each income and education level. Analyses were repeated for income and education level in univariable, simple-, and complex-adjusted forms using inverse-probability of treatment weighting (IPTW) in accordance with the presented selected covariates from a causal diagram (*Supplemental Figs. S1 & S2*). Based on the identified pathways from these diagrams, the simple analyses were adjusted for age, sex, and migrant status. The complex model was adjusted for the covariates in the simple model and the patient's civil status, occupation status, and comorbidity level measured by the CCI, as well as income or education level (depending on the exposure). All main findings presented in the present study are based on the

simple-adjusted model. In both models, data were trimmed at the 0.5th percentiles of the propensity score, and balance was assessed after the propensity score weighting [33]. Doubly robust adjusting was performed for the cox-proportional hazards regression to compensate for imbalance following IPTW [34]. Interaction analyses were applied to examine the temporal trends as interactions over the five-year periods with regard to income and education. Furthermore, temporal trends in socioeconomic disparities were evaluated for all single events included in the MACE, represented by adjusted cause-specific HRs where appropriate. Analyses were stratified according to sex, age, and diagnoses and restricted using clinical data from the DHR from 2003. (*Supplemental Table S4)*.

3. Results

Overall, 220,887 patients aged ≥18, living in Denmark the year before diagnosis, were hospitalized with an incident ACS diagnosis during 1998–2017. Baseline characteristics for the patients are presented according to income quartile in Table 1, education level in Table 2, and the time of the incident ACS in *Supplemental Table S5*. Education data was missing for 29 % of the patients with ACS in 1998, whereas this data was only missing for 3 % of the patients in 2017. The mean follow-up time was 241 days. Overall, 43,832 (21 %) patients died, and 92,522 (42 %) had a MACE in the year after ACS. Over the 20-years, 231 (0.1 %) patients were lost to follow-up due to emigration. Balance diagnostics after the weighting according to the simple and the complex model are presented in *Supplemental Tables S6–9*. Not all variables could be perfectly balanced by the propensity score matching, especially according to education, and across the different measures of SEP, there was an imbalance.

3.1. Socioeconomic disparity in major adverse cardiac events

When comparing patients from the lowest income quartile to those from the highest and patients with low education level to those with the highest, disparity in MACE within 30-days and 1-year after ACS was present across the entire period *(Supplemental Table S10)*. Within all levels of income and education, the risk of MACE at 30-days and 1-year after ACS decreased over the 20-year period. However, the disparity according to income and education remained unchanged (Fig. 1). The interaction analyses showed no significant temporal trends in the disparities according to income or education. However, when adjusting for the patient's civil status, employment status, and comorbidity level, as well as income or education level in the complex model, the disparity in MACE both within 30-days and 1-year after ACS appeared to diminish, especially according to education level *(Supplemental Table S10)*.

3.2. Socioeconomic disparity in all-cause mortality

The socioeconomic disparity in MACE after ACS was particularly present as a disparity in the 30-day and 1-year mortality, according to income quartile and education level. Moreover, income and educational disparities in all-cause mortality within 1-year after ACS were present for the entire period. The overall aHR was 1.46 [1.42–1.50] for patients in the low- compared to the high-income quartile, and the aHR was 1.41[1.35–1.47] for patients with low compared to high education level. The overall risk of mortality within 30-days and 1-year after ACS also decreased over the 20-years within all levels of income and education, but the disparity according to income quartile and education level remained (Fig. 2). The interaction analyses showed no significant changes in the socioeconomic disparities in mortality.

Table 1
Baseline characteristics of patients with incident ACS according to personal income.

	Personal income					
	Q1	Q2	Q3	Q4	Missing	Total
Patients with ACS, n	64,795	59,669	52,333	43,314	776	220,887
Age, median (IQR)	68 (57–78)	70 (59–79)	70 (60–80)	71 (60–80)	64 (54–76)	70 (59–79)
Male, n (%)	39,429 (61)	36,171(61)	32,215 (62)	27,239 (63)	497 (64)	135,551 (61)
Diagnosis, n (%)						
MI	52,777 (81)	48,902 (82)	42,472 (81)	34,191 (79)	639 (82)	178,981 (81)
UAP	12,018 (19)	10,767 (18)	9861 (19)	9123 (21)	137 (18)	41,906 (19)
Civil status, n (%)						
Married/cohabiting	28,703 (44)	30,536 (51)	29,897 (57)	27,015 (62)	266 (34)	116,417 (53)
Unmarried/Single living	32,635 (50)	26,001 (44)	19,547 (37)	13,996 (32)	456 (59)	92,635 (42)
Missing	3457 (5)	3132 (5)	2889 (6)	2303 (5)	54 (7)	11,835 (5)
Migrant status, n (%)						
Danish	55,989 (86)	56,446 (95)	50,010 (96)	41,188 (95)	625 (81)	204,258 (92)
Immigrant/descendant	8016 (12)	2523 (4)	1707 (3)	1679 (4)	116 (15)	14,041 (6)
Missing	790 (1)	700 (1)	616 (1)	447 (1)	35 (5)	2588 (1)
CCI, n (%)						
Low (0)	28,380 (44)	27,754 (47)	26,325 (50)	23,497 (54)	408 (53)	106,364 (48)
Medium (1–2)	23,704 (37)	21,103 (35)	17,502 (33)	13,812 (32)	251 (32)	76,372 (35)
High (>2)	12,711 (20)	10,812 (18)	8506 (16)	6005 (14)	117 (15)	38,151 (17)
Employment, n (%)						
Employed	14,679 (23)	20,004 (34)	20,638 (39)	20,494 (47)	357 (46)	76,172 (34)
Unemployed	4872 (8)	905 (2)	533 (1)	418 (1)	158 (20)	6886 (3)
Retired	45,244 (70)	38,760 (65)	31,162 (60)	22,402 (52)	261 (34)	137,829 (62)
Education, n (%)						
Low	32,921 (51)	27,033 (45)	18,426 (35)	8843 (20)	239 (31)	87,462 (40)
Medium	18,632 (29)	20,165 (34)	19,453 (37)	14,548 (34)	271 (35)	73,069 (33)
High	3845 (6)	4546 (8)	7204 (14)	13,970 (32)	77 (10)	29,642 (13)
Missing	9397 (15)	7925 (13)	7250 (14)	5953 (14)	189 (24)	30,714 (14)
Year, n (%)						
1998–2002	18,349 (28)	17,334 (29)	15,433 (30)	12,538 (29)	311 (40)	63,965 (29)
2003–2007	17,581 (27)	16,276 (27)	14,607 (28)	12,016 (28)	139 (18)	60,619 (27)
2008–2012	15,051 (23)	13,754 (23)	11,702 (22)	9905 (23)	203 (26)	50,615 (23)
2013–2017	13,814 (21)	12,305 (21)	10,591 (20)	8855 (20)	123 (16)	45,688 (21)

Abbreviations: ACS: Acute Coronary Syndrome, CCI: Charlsons comorbidity index, IQR: Inter Quartile ranges, MI: Myocardial Infarction, n = number of patients, UAP: Unstable angina pectoris, Q: Income quartile (1: low, 2: medium-low, 3: medium-high, 4: high. The cutoffs for the applied quartiles were year-, age group-, and sex-specific, available from Statbank[33]).

Table 2
Baseline characteristics of patients with incident ACS according to education level.

	Education level				
	Low	Medium	High	Missing	Total
Patients with ACS, n	87,462	73,069	29,642	30,714	220,887
Age, median (IQR)	71 (61–78)	64 (55–73)	64 (55–73)	86 (82–90)	70 (59–79)
Male, n (%)	47,950 (55)	53,353 (73)	20,558 (69)	13,690 (45)	135,551 (61)
Diagnosis, n (%)					
MI	71,625 (82)	57,907 (79)	22,517 (76)	26,932 (88)	178,981 (81)
UAP	15,837 (18)	15,162 (21)	71,25 (24)	3782 (12)	30,714 (14)
Civil status, n (%)					
Married/cohabiting	43,205 (49)	45,044 (62)	19,362 (65)	8806 (29)	116,417 (53)
Unmarried/Single living	397,8 8(45)	25,079 (34)	9250 (31)	18,518 (60)	92,635 (42)
Missing	4469 (5)	2946 (4)	1030 (3)	3390 (11)	11,835 (5)
Migrant status, n (%)					
Danish	82,675 (95)	68,314 (93)	26,717 (90)	26,552 (86)	204,258 (92)
Immigrant/descendant	4001 (5)	4368 (6)	2798 (9)	2874 (9)	14,041 (6)
Missing	786 (1)	387 (1)	127 (0)	1288 (4)	2588 (1)
CCI, n (%)					
Low (0)	10,363 (34)	39,758 (54)	17,683 (60)	10,363 (34)	106,364 (48)
Medium (1–2)	31,963 (37)	22,247 (30)	8265 (28)	13,897 (45)	76,372 (35)
High (>2)	16,939 (19)	11,064 (15)	3694 (12)	6454 (21)	38,151 (17)
Employment, n (%)					
Employed	23,028 (26)	34,609 (47)	16,402 (55)	2133 (7)	76,172 (34)
Unemployed	2668 (3)	2361 (3)	972 (3)	885 (3)	6886 (3)
Retired	61,766 (71)	36,099 (49)	12,268 (41)	27,696 (90)	137,829 (62)
Personal income, n (%)					
Q1	32,921 (38)	18,632 (25)	3845 (13)	9397 (31)	64,795 (29)
Q2	27,033 (31)	20,165 (28)	4546 (15)	7925 (26)	59,669 (27)
Q3	18,426 (21)	19,453 (27)	7204 (24)	7250 (24)	52,333 (24)
Q4	8843 (10)	14,548 (20)	13,970 (47)	5953 (19)	43,314 (20)
Missing	239 (0)	271 (0)	77 (0)	189 (1)	776 (0)
Year, n (%)					
1998–2002	24,905 (28)	17,089 (23)	6033 (20)	15,938 (52)	63,965 (29)
2003–2007	24,723 (28)	19,147 (26)	7424 (25)	9325 (30)	60,619 (27)
2008–2012	20,549 (23)	18,471 (25)	7756 (26)	3839 (12)	50,615 (23)
2013–2017	17,285 (20)	18,362 (25)	8429 (28)	1612 (5)	45,688 (21)

Abbreviations: ACS: Acute Coronary Syndrome, CCI: Charlsons comorbidity index, IQR: Inter Quartile ranges, MI: Myocardial Infarction, n = number of patients, UAP: Unstable angina pectoris, Q: Income quartile (1: low, 2: medium-low, 3: medium-high, 4: high).

3.3. Disparity in recurrent ACS, revascularization, stroke, and cardiac arrest

The socioeconomic disparity in recurrent ACS, and revascularization presented patterns of disparity similar to the overall composite MACE outcome. Disparity in having a recurrent ACS within 1-year after ACS was presented for the entire period according to income quartile (aHR for those with low compared to those with high income: 1.04 [1.01–1.08]) and education level (aHR for those with low compared to high education level 1.07[1.03–1.11]). The incidence of recurrent ACS within 1-year after ACS decreased over the 20-years within all levels of income and education *(Supplemental Fig. 3)*, but the disparity according to income and education level remained. Disparity in undergoing a revascularization procedure after discharge but within 1-year after ACS was presented for the entire period according to income (aHR: 1.05[1.01–1.10]) and education (aHR: 1.18[1.13–1.23]). The risk of undergoing revascularization after discharge, within 1-year after ACS decreased over the 20-years within all levels of income and education *(Supplemental Fig. 4)*, but the disparities according to income and education level remained. When looking at the entire period, socioeconomic disparity in the risk of having a stroke within 1-year after ACS was present according to income (aHR: 1.25[1.16–1.34]) and education (aHR: 1.22[1.12–1.34]). However, when looking at the periods over time, the disparity was insignificant, with a tendency of a decrease within all income groups and a tendency towards a decline in disparity according to education *(Supplemental Fig. 5)*, which could not be verified in the interaction analysis. Opposite to the other MACE outcomes, hospitalization with cardiac arrest within 1-year after ACS presented an increasing incidence over the 20-years *(Supplemental Fig. 6)*. Overall, there was a tendency towards a higher incidence among the patients from the high-income quartile (aHR: 0.83[0.68–1.01]) or higher education level (aHR: 0.76[0.62–0.94]) compared to those from the low-income quartile or low education level. No temporal trends in the disparity were identified. Temporal trends in socioeconomic disparity in recurrent ACS, revascularization, stroke, or cardiac arrest within 30 days after ACS could not be demonstrated, and few outcomes were observed (*Supplemental Figs. S3–6)*.

3.4. Socioeconomic disparity in MACE according to sex, age, diagnosis, comorbidities, and severity

A similar pattern in socioeconomic disparity and temporal trends in incidence was displayed both among men and women *(Supplements Figs. S7 & S8)*. Patterns in socioeconomic disparity and temporal trends in MACE incidence was also similar among both patients younger than 70 years and patients aged 70 or more *(Supplements Figs. S9 & S10)*. Among the patients with a registered ST-elevation MI diagnoses ($N = 53{,}341$) or non-ST-elevation MI diagnoses ($N = 56{,}497$), the pattern in socioeconomic disparity and temporal trends in incidence of MACE was similarly displayed *(Supplements Figs. S11 & S12)*. Among the patients with ACS and known diabetes ($N = 29{,}400$) or hypertension ($N = 47{,}019$) before the incident ACS, the incidence of 30-day and 1-year MACE was higher than in the general ACS population. Still, a similar pattern in socioeconomic disparity and temporal trends in incidence was displayed *(Supplements Figs. S13 & S14)*. When restricting the analyses to the ACS population from the Danish Heart Registry from 2003 to 2017, only 64,806 (41 %) of the identified patients from 2003 to 2017 had data on the number of coronary lesions, coronary vessels, or number of applied stents in the coronary arteries. However, there were still similar tendencies across the period towards socioeconomic disparity in 1-year MACE after the ACS, independent of whether the patients were registered to have had 1 or >1 affected lesions, vessels, or applied stents. Thus, income and educational disparities in MACE presented

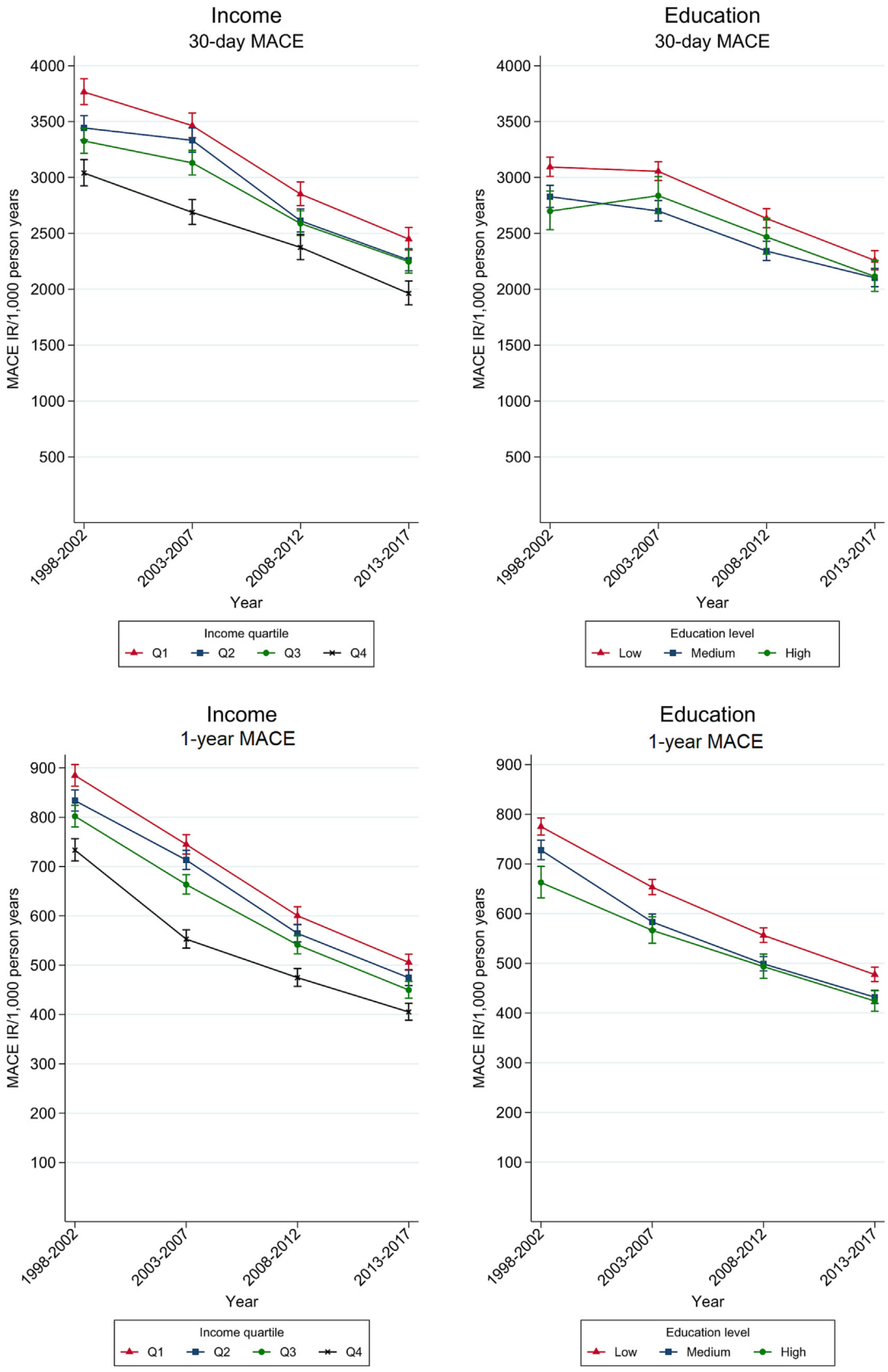

Fig. 1. Adjusted incidence rates for MACE within 30-days and 1-year after ACS, according to income and education. The presented results were adjusted for age, sex, and migrant status. Abbreviations: ACS: acute coronary syndrome, IR: incident rate, MACE: major adverse cardiovascular events, Q: Income quartile (1: low, 2: medium-low, 3: medium-high, 4: high).

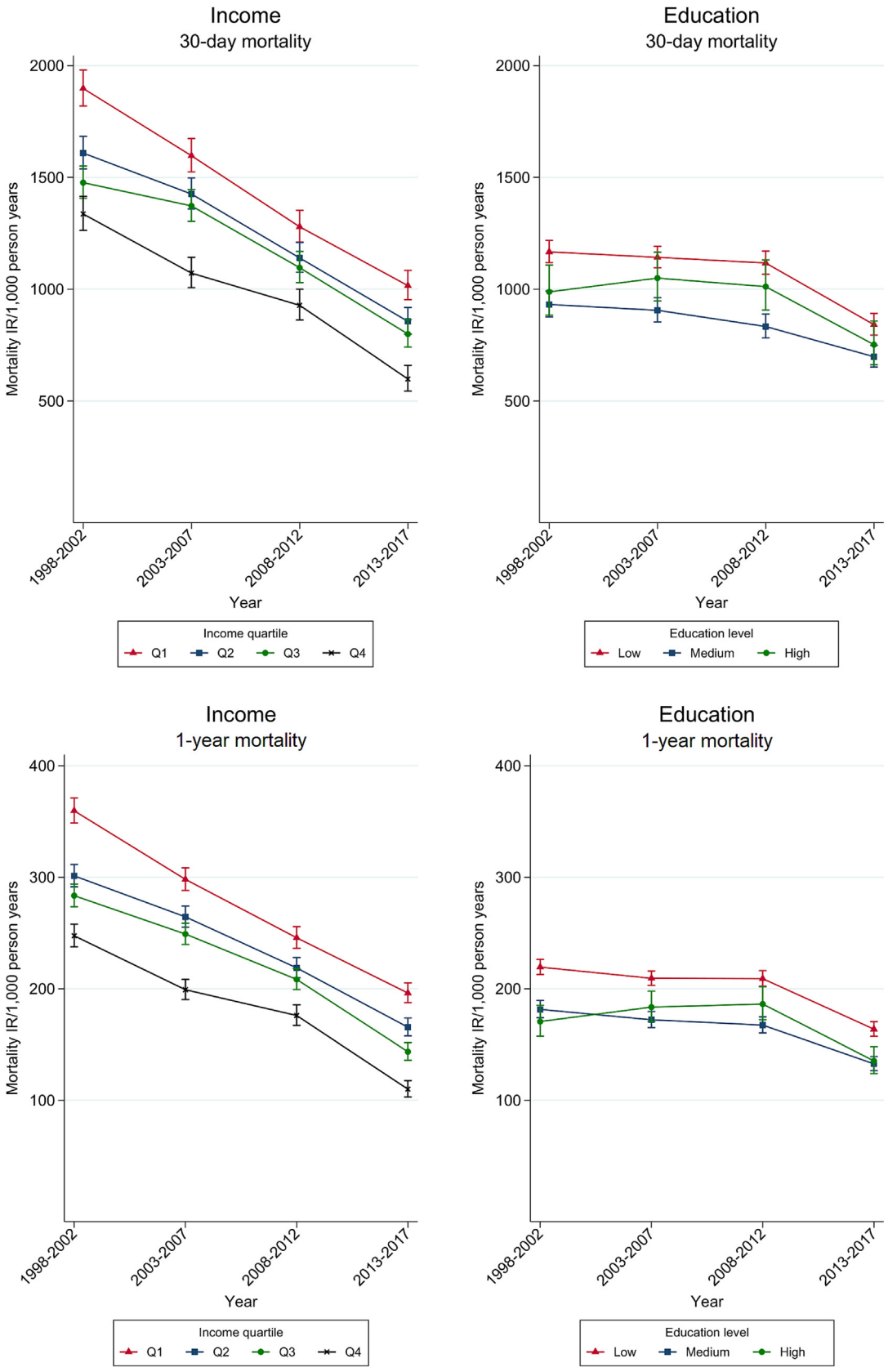

Fig. 2. Adjusted incidence rates for all-cause mortality within 30-days and 1-year after ACS, according to income and education. The presented results were adjusted for age, sex, and migrant status. Abbreviations: ACS: acute coronary syndrome, IR: incident rate, Q: Income quartile (1: low, 2: medium-low, 3: medium-high, 4: high).

without tendencies for changes in temporal trends among the patients with ACS independent of the registered severity. The interaction analyses showed no significant changes in the socioeconomic disparities in MACE in any of the analyses stratified according to sex, age, diagnosis, comorbidities, or severity.

4. Discussion

This nationwide cohort study found socioeconomic disparity in MACE the year after ACS, with a higher incidence among patients with a low compared to high income or education level. The incidence of MACE during the year after ACS has decreased substantially within all income and education levels over the last two decades; however, the socioeconomic disparity has persisted. The disparity in MACE the year after ACS was primarily explained by disparity in all-cause mortality but similar patterns were also observed for recurrent ACS, revascularization, and stroke.

The unique findings from the present study include the substantially decline in the MACE incidence among patients within all levels of SEP during the 20 years, and the yet persistent socioeconomic disparity. The general decline in incidence of MACE after ACS is probably related to major improvements in the treatment of ACS, including more extensive use of invasive coronary procedures and improved medical prophylaxis. In addition, changes in the diagnostic criteria, including improved specificity of the biomarkers defining MI, may have contributed [14,15]. Since this treatment is standardized, according to national clinical guidelines, it could be expected that the disparity in the clinical outcomes would be reduced over time. However, the reason behind the declining incidence of MACE could not be investigated based on the available data in the present study. The results from the present study illustrate a persistent socioeconomic disparity in MACE within the year after ACS during 1998–2017. Disparity in MACE has previously been illustrated in a multi-center study in China, investigating educational disparity in 1-year MACE, defined as all-cause mortality, stroke, or heart failure, after MI, identifying a higher risk of MACE among patients with low education [19]. The socioeconomic disparity in the clinical outcomes after the patients present with incident ACS is especially unfortunate, as patients with lower income or education level are already at higher risk of having the incident ACS in the first place [6–8]. The simple model used in the present study aims to evaluate the general association between SEP and MACE after ACS using income and education level as proxies, based on the identified pathways from the causal diagrams. The complex model aims to estimate the causal effect of income and education on MACE after ACS, respectively. Thus, it is noticeable that the disparity in MACE after ACS appeared to diminish when adjusted according to complex model, especially according to education level.

Studies have illustrated socioeconomic disparities in mortality after an incident ACS across high-income countries [6]. The present study found considerable socioeconomic disparity in mortality, both according to income and education level without significant changes in the temporal trends. ACS have been reported to play a significant role in the socioeconomic disparity in mortality and life expectancy in the general population, which still presents an unsolved issue [2]. This illustrates the magnitude of the disparity of clinical outcomes among patients with ACS, and the consequences regarding public health.

The present study illustrated persistent socioeconomic disparity in recurrent ACS, revascularization, and stroke after discharge within the first year after ACS in favor of those with a high income or education. Socioeconomic disparities in these outcomes have formerly been illustrated in a long-term perspective, up to 10 years after the ACS [16–18,20]. Furthermore, the present study investigated the temporal trends in this disparity within the year after ACS, without identifying any significant changes. The incidence of cardiac arrest within the first year after ACS presented a different pattern, with an increasing incidence. However, since cardiac arrest is diagnosed in the DNPR at hospital admission, this probably represents increasing incidence of patients with out-of-hospital cardiac arrest reaching the hospital rather than an increase in cardiac arrest after ACS [26,35]. This is in line with studies on the general Danish population, presenting a major increase in survival until hospitalization from 2001 to 2017 [35,36]. No disparity pattern was identified over the period, but patients with higher income or education tended to present the highest incidence of hospital registered diagnoses for cardiac arrest. This could associate with the fact that a higher proportion of out-of-hospital cardiac arrest patients with higher income level receive bystander cardiopulmonary resuscitation and defibrillation [36].

The present study neither identified any temporal trends in socioeconomic disparity in MACE incidence among patients with ACS and known diabetes or hypertension nor among the patients with data on severity by affected vessels. As could be expected, the incidence of MACE after ACS was higher in the comorbid population than in the general ACS population. Comorbidities associate to the risk of MACE including mortality, but the findings from the present study illustrated that the socioeconomic disparities are not limited to disparities in comorbidities. Other factors after ACS, including resources to take action and initiate a healthier lifestyle and adherence to cardiac rehabilitation and medications after hospital admission, which presents socioeconomic disparity, could affect the disparity in MACE after the incident ACS [3,4]. However, this has not been investigated in the present study. Considerable disparity in medical care according to income and education presents in many studies, including studies in the Danish setting [6]. These studies indicate disparity in access to coronary angiography, rehabilitation programs, and non-acute revascularization in patients with ACS [6,20,21,37,38]. However, socioeconomic disparities in acute invasive revascularization after ACS could not be identified in the Danish health care in previous studies [6,20,37], and the disparity in coronary angiography was eliminated from 2001 to 2009 [21,37]. Thus, possible disparities in the Danish health care, including the acute care, cannot account for the socioeconomic disparities in MACE after ACS in this study.

4.1. Study strengths and limitations

All data in this study originated from routinely collected data within the Danish tax-financed health service system which provides health care for the entire population, financing about 85 % of all health care costs [23]. Thus, patient selection and collection of other variables should not derive from economic barriers in access to health care or willingness to participate, which makes these data ideal for the study of socioeconomic disparities. However, the results are not necessarily representative for countries without similar social security-based hospital care, where one could hypothesize that the disparities could be even more dominant. Furthermore, a Danish national strategy for acute invasive treatments of ACS according to diagnosis have been successfully implemented, since 2003 [39]. The patients with ACS were included based on hospital diagnoses from the DNPR. The positive predictive value for MI in DNPR was almost 100 % from 1996 to 2012. For angina pectoris, it was around 42 % in the beginning of the period increasing to 88 % in 2010–2012 [26,40]. The positive predictive values for capturing ST-elevation MI or non-ST-elevation MI were 96 % and 92 %, respectively [40]. However, if patients died from ACS without hospital admission or survived an unrecognized ACS, this would not be captured in the DNPR, and data on ST-elevation/non-ST-elevation was lacking for a large part of the hospitalized patients [26].

Data on SEP was collected as equivalent personal income quartile and education level to reflect socioeconomic disparities through separate possible pathways. The personal income was only collected one year before the year of the incident ACS. Hence, this measure could be sensible to life changes, including acute or chronic illnesses affecting the personal income. On the other hand, this enabled the use of nation-based income quartiles from the Danish background population according to age, sex, and specific year [29]. Thus, the personal income quartiles reflect the SEP according to the general population rather than

a quartile of the ACS population, which is not representative, since ACS incidence presents income disparities [9]. This measure reflects actual purchasing power and takes salary changes and inflation into account in a more concise manner [3]. The education level was defined as the highest completed education level before incident ACS, and is a strong socioeconomic indicator from early adulthood [3]. However, from 1998 to 2002 information on education level was missing for 37 % and missing information was strongly correlated with age. Furthermore, substantial changes in the education system and culture appeared when these patients were juveniles, meaning that education level according to ISCED classification as an indication for SEP may have changed [30]. However, overall, the education level represented the same disparity and temporal trends regarding MACE the year after ACS as the income level. Some variables could not be balanced from the propensity score matching, especially according to education level and across the measures of SEP, which seemed highly correlated. This was managed using doubly robust adjusting in the HR model, and generally, the same patterns were presented in the IR and HR for MACE the year after ACS.

All-cause mortality was included in the MACE outcome to overcome the competing risk of death. However, when presenting IRs separately for recurrent ACS, revascularization, stroke, and cardiac arrest, the competing risk of death could not be considered. Hence, aHR were also calculated, presenting the same disparity pattern, indicating socioeconomic disparities within the year after the incident ACS.

5. Conclusion

The present study found a socioeconomic disparity in severe clinical outcomes within the first year after ACS, according to personal income and education level in Denmark from 1998 to 2017. Thus, the patients with a low income or education level had a higher incidence of MACE within the first year after ACS compared to the patients with high income or education. Although the incidence of mortality, recurrent ACS, revascularization, and stroke within the first year after an incident ACS has decreased substantially, the socioeconomic disparity persisted.

Data statement

Permission to access the data used on this study can be obtained following approval from the Danish Health Authority.

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CRediT authorship contribution statement

Amalie H. Simoni: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Data curation, Project administration, Visualization, Writing – original draft. **Jan B. Valentin:** Investigation, Data curation, Formal analysis, Methodology, Writing – review & editing. **Kristian H. Kragholm:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing. **Henrik Bøggild:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing. **Svend E. Jensen:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing. **Søren P. Johnsen:** Conceptualization, Funding acquisition, Data curation, Investigation, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary material associated with this paper is available online. Results from the interaction analyses for changes in the socioeconomic disparities in 30-day and 1-year MACE, including all secondary individual MACE outcomes and stratified analyses can be accessed by request to the corresponding author. Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2023.05.012.

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