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ORIGINAL ARTICLE
Heart failure

Influence of multimorbidity and socioeconomic position on long-term healthcare utilization and prognosis in patients after cardiac resynchronization therapy implantation

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Aims We aimed to investigate the influence of socioeconomic position (SEP) and multimorbidity on cross-sectional healthcare utilization and prognosis in patients after cardiac resynchronization therapy (CRT) implantation.

Methods and results We included first-time CRT recipients with left ventricular ejection fraction ≤35% implanted between 2000 and 2017. Data on chronic conditions, use of healthcare services, and demographics were obtained from Danish national administrative and health registries. Healthcare utilization (in- and outpatient hospitalizations, activities in general practice) was compared by multimorbidity categories and SEP by using a negative binomial regression model. The association between SEP, multimorbidity, and prognostic outcomes was analysed using Cox proportional hazards regression. We followed 2007 patients (median age of 70 years), 79% were male, 75% were on early retirement or state pension, 37% were living alone, and 41% had low education level for a median of 5.2 [inter-quartile range: 2.2–7.3) years. In adjusted regression models, a higher number of chronic conditions were associated with increased healthcare utilization. Both cardiovascular and non-cardiovascular hospital contacts were increased. Patients with low SEP had a higher number of chronic conditions, but SEP had limited influence on healthcare utilization. Patients living alone and those with low educational level had a trend towards a higher risk of all-cause mortality [adjusted hazard ratio (aHR): 1.17, 95% confidence interval (CI) 1.03–1.33, and aHR 1.09, 95% CI 0.96–1.24).

Conclusion Multimorbidity increased the use of cross-sectional healthcare services, whereas low SEP had minor influence on the utilizations. Living alone and low educational level showed a trend towards a higher risk of mortality after CRT implantation.

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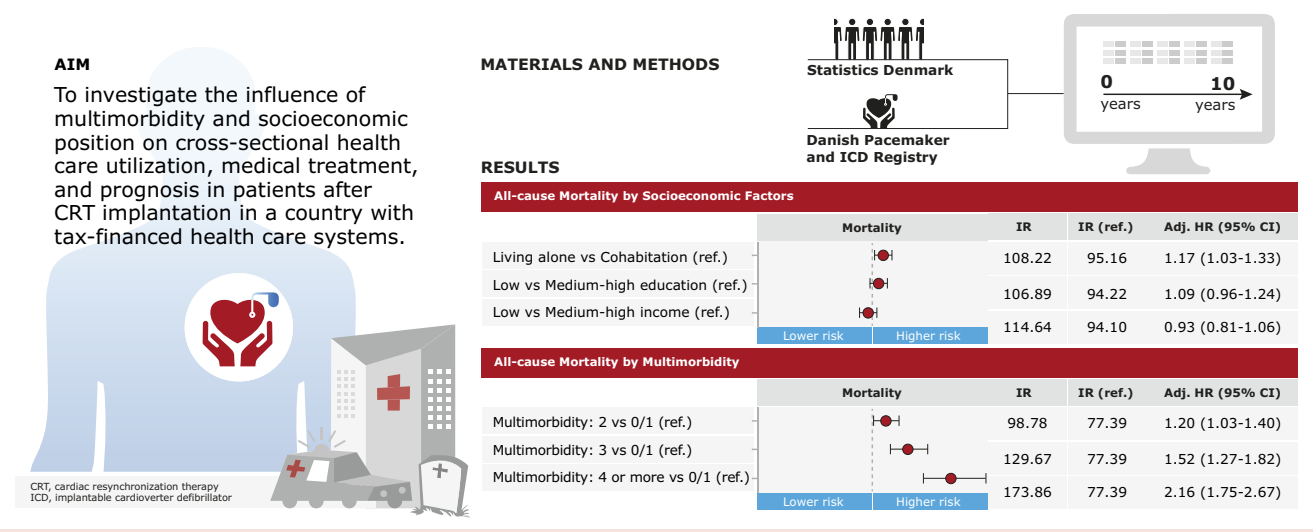
Graphical Abstract



Keywords Cardiac resynchronization therapy • Healthcare utilization • Multimorbidity • Heart failure • Prognosis • Socioeconomic position

Introduction

Multimorbidity is a part of daily life for a growing number of individuals, and long-term management is challenging for healthcare systems worldwide.[1,2] It becomes more prevalent with increasing age and is associated with functional difficulties, increased utilization of healthcare services, and higher mortality.[1,2] Management of patients with multimorbidity is a challenge for the highly specialized healthcare systems as these patients often will need a broader approach.[3] Consequently, these patients use many services to manage individual diseases in different parts of the healthcare system due to a lack of coordination.[4] Previous studies have also shown that low socioeconomic position (SEP) is associated with multimorbidity and increased use of healthcare utilization.[5,6]

Heart failure (HF) is a growing healthcare problem and an expensive condition to manage and thus places a growing strain on healthcare systems.[7,8] Prevalence of multimorbidity in patients with HF is high and associated with a higher risk of hospitalization and mortality.[9] Studies indicate that SEP can affect cardiovascular health and clinical outcomes.[10] However, socioeconomic variation in risk factors may contribute to these inequalities. In selected patients with HF, cardiac resynchronization therapy (CRT) is an effective treatment that leads to improved quality of life, reductions in HF hospitalization rates, and reduced all-cause mortality.[11,12] Post-implantation care of the patients is often confined by a lack of integration of cardiological and non-specialist care; thus, it may lead to suboptimal and variable post-implantation management.[13] The impact of multimorbidity and SEP on healthcare services utilizations and prognosis after CRT implantation is unknown. Identifying and addressing determinants of health inequalities is a major priority even in universal healthcare systems, and a better understanding could lead to improved follow-up strategies and survival in patients after CRT implantation.

Our aim was to investigate the influence of multimorbidity and SEP on cross-sectional healthcare utilization and prognosis in patients after CRT implantation in a country with tax-financed healthcare systems.

Methods

Study population

This cohort study was conducted in patients above 40 years and with a left ventricular ejection fraction (LVEF) ≤ 35% who had received their first implanted CRT device [with or without implantable cardioverter defibrillator (ICD)) between January 2000 and December 2017 at Aarhus University Hospital, Denmark. The patients were identified from the Danish Pacemaker and ICD Registry. The index date was defined as the date of primary CRT implantation. The patients were followed from the index date until 31 December 2018, emigration, loss of follow-up, or death, whichever occurred first.

Using the Danish Civil Registration System (CRS) and the unique personal identification number assigned to all Danish citizens, individual-level data from the Danish Pacemaker and ICD Registry were linked to Danish national registers.[14] The study was approved by the Danish Data Protection Agency (no.: 1-16-02-656-18) and the Danish Patient Safety Authority, authorizing access to information in medical records (no.: 3-3013-3173/1).

Clinical characteristics

Clinical data were collected at index date on age, sex, LVEF, ICD treatment, and QRS morphology from the Danish Pacemaker and ICD Registry and CRS. The following age categories were defined: 40–59, 60–69, 70–79, and ≥80 years. The Danish National Patient Registry (DNPR) was used to obtain information on discharge diagnoses recorded within 10 years before the index date.[15] From the Danish National Prescription Registry (NPR), all prescriptions were retrieved at substance level using the Anatomical Therapeutic Chemical Classification.[16] Information on baseline use of medication was defined as one or more redeemed prescriptions within 6 months before the index date.

Multimorbidity

Data on chronic conditions were obtained from the DNPR and the Danish Psychiatric Central Research Register.[14] Chronic conditions were collected 10 years before the index date and during follow-up. We used a previously

Table 1 Baseline characteristics of patients with cardiac resynchronization therapy implantation, Aarhus University Hospital, Denmark, 2000–2017

	Patients with cardiac resynchronization therapy implantation				
	Total ($n = 2007$)	Number of chronic conditions at baseline			
		≤1 ($n = 753$)	2 ($n = 656$)	3 ($n = 386$)	>3 ($n = 212$)
Gender					
Female	416 (21)	139 (18)	145 (22)	92 (24)	40 (19)
Male	1591 (79)	614 (82)	511 (78)	294 (76)	172 (81)
Age at index date in years					
40–59	367 (18)	193 (26)	106 (16)	46 (12)	22 (10)
60–69	599 (30)	236 (31)	191 (29)	110 (29)	62 (29)
70–79	791 (39)	241 (32)	268 (41)	176 (46)	106 (50)
≥ 80	250 (12)	83 (11)	91 (14)	54 (14)	22 (10)
Follow-up time in years					
0–1	181 (9)	42 (6)	63 (10)	36 (9)	40 (19)
> 1–3	514 (26)	172 (23)	147 (22)	120 (31)	75 (35)
> 3–5	420 (21)	141 (19)	149 (23)	89 (23)	41 (19)
> 5–10	655 (33)	263 (35)	225 (34)	121 (31)	46 (22)
CRT-D	1098 (55)	418 (56)	350 (53)	215 (56)	115 (54)
Left bundle branch block	1214 (60)	455 (60)	406 (62)	225 (58)	128 (60)
Prior cardiac implantable electrical device	474 (24)	167 (22)	150 (23)	96 (25)	61 (29)
Coronary artery disease		285 (38)	266 (41)	201 (52)	125 (59)
Chronic neurological disorder	42 (2)	0	10 (2)	18 (5)	14 (7)
Inflammatory bowel disease	24 (1)	0	12 (2)	7 (2)	5 (2)
Chronic liver disease		0	<5	<5	18 (8)
Chronic kidney disease	179 (9)	0	35 (5)	51 (13)	93 (44)
Diabetes		<5	111 (17)	179 (46)	152 (72)
Chronic obstructive pulmonary disease		<5	113 (17)	111 (29)	110 (52)
Obesity	160 (8)	23 (3)	36 (5)	49 (13)	52 (25)
Cancer		<5	68 (10)	70 (18)	63 (30)
Highest obtained educational level					
Low degree	840 (42)	293 (39)	274 (42)	174 (45)	99 (47)
Medium degree	876 (44)	341 (45)	283 (43)	159 (41)	93 (44)
High degree	242 (12)	100 (13)	84 (13)	43 (11)	15 (7)
Missing	49 (2)	19 (3)	15 (2)	10 (3)	5 (2)
Cohabitation status					
Living alone	748 (37)	253 (34)	237 (36)	168 (44)	90 (42)
Cohabitation	1259 (63)	500 (66)	419 (64)	218 (56)	122 (58)
Personal income group					
Low income	604 (30)	213 (28)	209 (32)	118 (31)	64 (30)
Intermediate–high income	1403 (70)	540 (72)	447 (68)	268 (69)	148 (70)
Labour market affiliation					
Employed	447 (22)	231 (31)	145 (22)	55 (14)	16 (8)
Unemployed	48 (2)	16 (2)	17 (3)	11 (3)	<5
Early retirement	318 (16)	121 (16)	105 (16)	52 (13)	40 (19)
State pension	1194 (59)	385 (51)	389 (59)	268 (69)	152 (72)
Cardiovascular medication					
Beta-blocker	1587 (79)	559 (74)	528 (80)	325 (84)	175 (83)
Renin–angiotensin system inhibitors	1770 (88)	653 (87)	591 (90)	349 (90)	177 (83)
Mineralocorticoid receptor antagonists	991 (49)	391 (52)	334 (51)	176 (46)	90 (42)

Values are *n* (%).
CRT-D, cardiac resynchronization therapy—defibrillator.

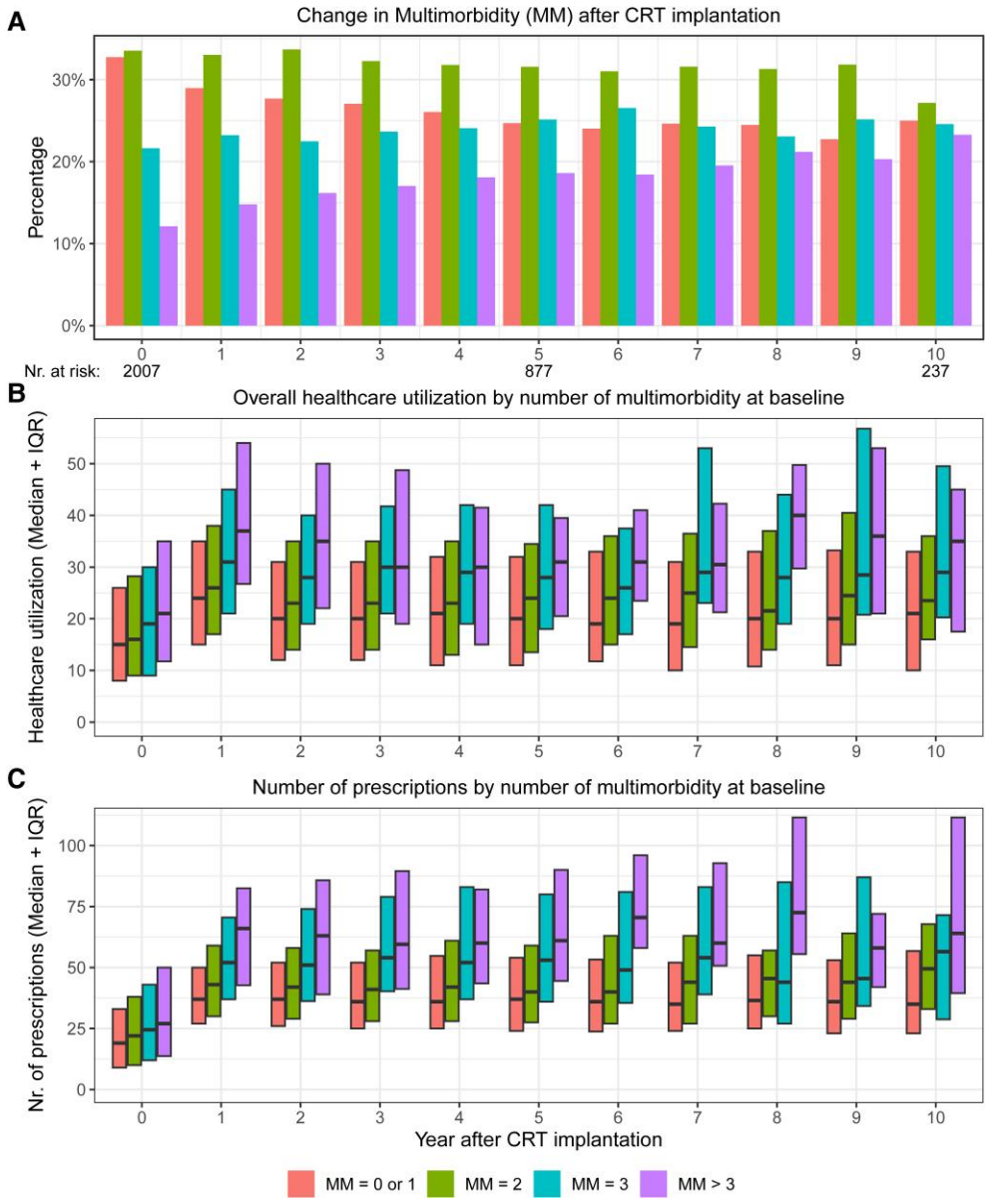


Figure 1 Annual number of chronic conditions (*A*) and overall healthcare utilization and total number of prescriptions by the number of chronic conditions after cardiac resynchronization therapy implantation (*B* and *C*). Annual estimates within the first 10 years after cardiac resynchronization therapy implantation presented as median and inter-quartile range (25th and 75th percentiles). CRT, cardiac resynchronization therapy; IQR, inter-quartile range; MM, multimorbidity.

described Danish algorithm to measure multimorbidity.[17,18] The algorithm included a large number of specific chronic conditions grouped into 11 comprehensive chronic disease groups. The number of chronic conditions was defined into four groups according to a number of chronic conditions: ≤ 1, 2, 3, and >3. A low number of patients ($n = 34$) had no diagnoses registered in the DNPR before CRT implantation. We did not generate a specific variable identifying mental multimorbidity due to Danish law on data protection (see Supplementary material online, *Table S1*).

Socioeconomic position

Information on SEP was collected from Statistics Denmark.[14] Level of education was obtained from the Education Registry. It was divided into five groups according to the highest completed educational level in the calendar year before the index date: low degree, medium degree, high degree, not finished education, or missing (see Supplementary material online, *Table S2*). Data on personal gross income were obtained from the Income Statistics Register, and they were collected in the calendar year before the index date and categorized as: low (≤25th percentile) and intermediate–high (>25th percentile). Family income was not included as these data were only available after 2004. Cohabitation status is registered in the CRS, and the patients were categorized as either living alone or cohabitating at index date.

Healthcare utilization

Healthcare utilization included all contacts to the primary (general practice) and secondary (hospital contact) healthcare systems. Hospital activity was

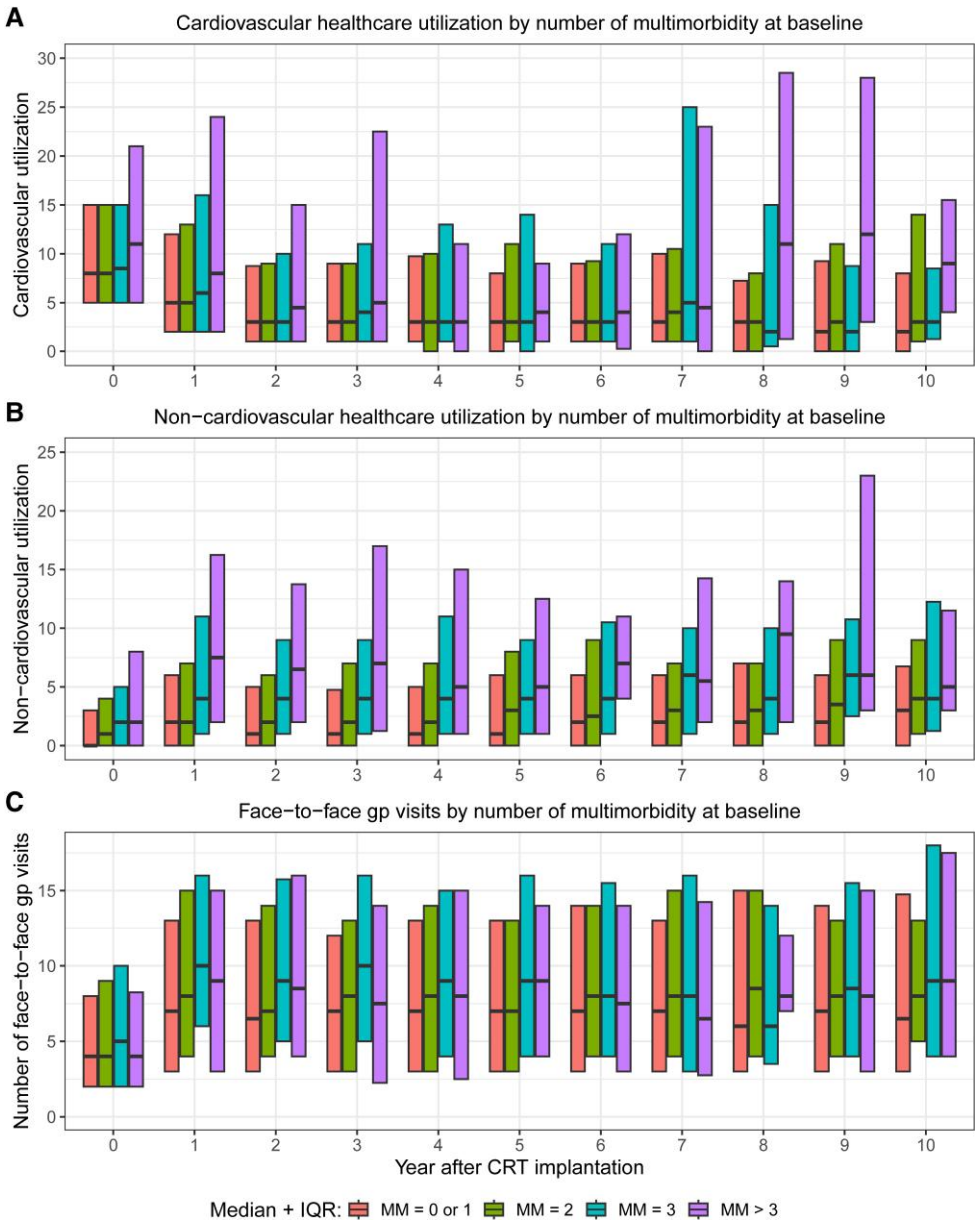


Figure 2 Healthcare utilization by the number of chronic conditions after cardiac resynchronization therapy implantation. (*A*) Cardiovascular hospital visits, (*B*) non-cardiovascular hospital visits, and (*C*) face-to-face general practitioner visits. Annual estimates within the first 10 years after cardiac resynchronization therapy implantation presented as median and inter-quartile range (25th and 75th percentiles). CRT, cardiac resynchronization therapy; IQR, inter-quartile range; MM, multimorbidity.

defined as inpatient hospital admissions, length of stay (bed days), and outpatient contacts. Cardiovascular hospital activity was identified as a cardiovascular diagnosis (International Classification of Diseases 10th code: I05-I99 and Z95) registered in the DNPR. Outpatient activity was defined as a number of visits, identified by the action diagnosis, and a number of different dates for outpatient visit. Activity in general practice was received from the Danish National Health Service Register and included face-to-face-consultations, home consultations, as well as telephone and E-mail contacts (see Supplementary material online, *Table S3*).[19] Information on redeemed prescriptions for all pharmacotherapies was obtained from the NPR. After CRT implantation, the patients had an outpatient device interrogation after 1–3 months and a regularly scheduled visit every 6–12 months during follow-up.

Prognostic outcomes

Information on all-cause mortality was collected from the CRS.[14] The composite outcome of first-time major cardiovascular event (MACE) was defined as the first occurrence of HF readmission, heart transplantation, or all-cause mortality (see Supplementary material online, *Table S4*). Heart failure readmission was defined as a primary discharge diagnosis of HF collected from the DNPR. Heart transplantation was identified from the DNPR.

Statistical analysis

Descriptive information on categorical data was reported by number and percentage, and for continuous and count data, we reported mean with

Table 2 Overall healthcare utilizations and contacts to the secondary healthcare system divided into cardiovascular or non-cardiovascular disease-related visits after cardiac resynchronization therapy implantation by multimorbidity

Number of chronic conditions at baseline	Overall healthcare utilization	Cardiovascular disease-related			Non-cardiovascular disease-related		
		Inpatient visits	Bed days	Outpatient visits	Inpatient visits	Bed days	Outpatient visits
Follow-up between 0 and <1 year							
≤1	28 (19–41)	1 (1–2)	2 (2–7)	5 (3–10)	0 (0–0)	0 (0–0)	1 (0–4)
2	33 (22–46)	1 (1–2)	3 (2–8)	6 (3–11)	0 (0–1)	0 (0–0)	2 (0–5)
3	38 (27–53)	1 (1–2)	4 (2–11)	6 (3–11)	0 (0–1)	0 (0–2)	4 (1–8)
>3	45 (32–59)	2 (1–3)	8 (2–20)	6 (3–12)	0 (0–1)	0 (0–3)	6 (2–11)
Follow-up between 1 and <3 years							
≤1	38 (24–57)	0 (0–1)	0 (0–3)	5 (2–10)	0 (0–0)	0 (0–0)	2 (0–6)
2	44 (30–65)	0 (0–1)	0 (0–5)	5 (2–9)	0 (0–1)	0 (0–1)	4 (1–8)
3	58 (41–78)	0 (0–2)	2 (0–8)	6 (2–11)	0 (0–1)	0 (0–4)	6 (2–12)
>3	76 (57–92)	1 (0–3)	5 (0–16)	7 (2–14)	0 (0–2)	0 (0–6)	10 (5–19)
Follow-up between 3 and <5 years							
≤1	36 (22–58)	0 (0–1)	0 (0–4)	4 (2–7)	0 (0–1)	0 (0–0)	2 (0–5)
2	42 (27–63)	0 (0–1)	0 (0–5)	4 (1–8)	0 (0–1)	0 (0–1)	3 (1–8)
3	55 (39–79)	1 (0–2)	2 (0–8)	5 (1–9)	0 (0–1)	0 (0–3)	6 (2–12)
>3	66 (47–90)	1 (0–2)	4 (0–17)	4 (1–11)	0 (0–2)	0 (0–7)	10 (3–18)
Follow-up between 5 and 10 years							
≤1	75 (47–120)	1 (1–3)	3 (2–11)	10 (4–20)	0 (0–1)	0 (0–2)	6 (2–13)
2	109 (80–157)	2 (1–3)	6 (2–15)	12 (6–19)	1 (0–2)	3 (0–9)	13 (5–21)
3	146 (117–199)	2 (1–4)	6 (3–21)	13 (4–22)	1 (0–5)	4 (0–15)	25 (12–38)
>3	164 (129–225)	3 (1–6)	18 (5–46)	17 (8–35)	2 (1–6)	6 (3–18)	24 (17–46)

Median values with percentiles (25th and 75th inter-quartile range) within each follow-up period.

standard deviation or median with percentiles [25th and 75th inter-quartile range (IQR)].

Outcomes were assessed periodically within four follow-up periods after the index date: 0–<1 year, 1–<3 years, 3–<5 years, and 5–10 years. To describe long-term healthcare utilization by multimorbidity at index date, we used the four categories according to the number of chronic conditions. The proportion of patients within each chronic disease group was displayed graphically at the index year and for every year after CRT implantation. For each follow-up period, total healthcare utilization was presented by the degree of multimorbidity and SEP at baseline and compared with regression analyses. Socioeconomic variables were dichotomized as follows: educational level [low (low degree) vs. higher (medium/high degree)], personal income [(low (≤25th percentile) vs. intermediate–high (>25th percentile)], and cohabitation status (living alone vs. cohabitating). The healthcare utilization [count of in- and outpatient hospitalizations and general practitioner (GP) visits] by follow-up time was compared by multimorbidity categories and SEP using a negative binomial regression model with a robust variance estimator to account for overdispersion, and the logarithm of follow-up time was used as an offset parameter. In the analyses comparing the different multimorbidity categories, patients with ≤1 condition were used as the reference group, and the analyses were adjusted for calendar period (implanted between 2000 and 2006, 2007 and 2012, and after 2012), age, sex, device type (CRT with or without ICD), cohabitation status, educational level, and personal income. In the regression analysis comparing different socioeconomic variables, the reference group was cohabitation, higher educational level, or intermediate–high income. These analyses were adjusted for calendar period, age, sex, QRS morphology, device type, and multimorbidity groups. We graphically displayed overall healthcare system utilization and the total number of redeemed prescriptions in boxplots, presenting annual estimates for the first 10 years after CRT implantation. The association between the dichotomized socioeconomic factors and multimorbidity index on prognostic outcomes was analysed using Cox proportional hazards regression. The proportional hazards assumption was evaluated for all exposure and outcome combinations by comparing estimated log-minus-log curves. In the analyses comparing the different multimorbidity categories, patients with 1 condition were used as the reference group, and the hazard ratios (HRs) were adjusted for calendar period (implanted between 2000 and 2006, 2007 and 2012, and after 2012), age, sex, device type (with or without ICD), QRS morphology, atrial fibrillation, cohabitation status, and personal income. In the regression analysis comparing different socioeconomic factors, the reference group was cohabitation, higher educational level, or intermediate–high income. Sensitivity analyses only including patients with left bundle branch block (LBBB) were conducted. All statistical analyses were performed using SAS statistical software package (version 9.4, SAS Institute Inc., Cary, NC, USA) and R statistical software.

Results

A total of 2007 patients underwent *de novo* CRT implantation between 2000 and 2017. Baseline characteristics are presented in *Table 1*. They had a median age of 70 (IQR: 62–77) years, most were male (79%), they had a high prevalence of multimorbidity at index date (62% had ≥2 chronic conditions), and most patients were on early retirement or state pension (75%). They were followed for a median of 5.2 (IQR: 2.2–7.3) years. When the patients were divided according to a number of chronic conditions at baseline, 38% had ≤1, 33% had 2, 19% had 3, and 11% had >3 chronic conditions. Patients with ≥2 chronic conditions were more likely to be older, living alone, on early retirement or state pension, and to have lower education level and lower personal income compared with patients with ≤1 conditions. The number of chronic conditions increased after CRT implantation; percentage of

Table 3 Association between cross-sectional healthcare service utilization within each follow-up period in cardiac resynchronization therapy recipients according to the number of chronic conditions at baseline

Chronic conditions	Cross-sectional healthcare service utilization											
	Time intervals since cardiac resynchronization therapy implantation											
	0–<1 years			1–<3 years			3–<5 years			5–10 years		
	Median within the time period	Crude RR	Adjusted RR[a]	Median within the time period	Crude RR	Adjusted RR[a]	Median within the time period	Crude RR	Adjusted RR[a]	Median within the time period	Crude RR	Adjusted RR[a]
≤1	30 (20–44)			37 (22–58)			36 (20–59)			63 (29–115)		
2	33 (22–47)	1.40 (1.25–1.56)	1.37 (1.23–1.52)	43 (26–66)	1.20 (1.10–1.31)	1.18 (1.08–1.29)	41 (22–64)	1.18 (1.07–1.30)	1.15 (1.05–1.27)	60 (27–116	1.06 (0.93–1.20)	1.11 (0.99–1.24)
3	37 (25–52)	1.67 (1.48–1.90)	1.54 (1.37–1.74)	51.5 (31–75)	1.53 (1.38–1.69)	1.43 (1.29–1.58)	53.5 (32–76)	1.56 (1.39–1.75)	1.50 (1.34–1.69)	51 (22–122)	1.13 (0.96–1.33)	1.28 (1.10–1.48)
> 3	41 (30–57)	3.05 (2.60–3.58)	2.78 (2.38–3.24)	64 (33–88)	2.14 (1.86–2.45)	2.10 (1.83–2.40)	49 (27–70)	1.48 (1.26–1.75)	1.48 (1.26–1.74)	72.5 (26–165)	1.31 (1.04–1.65)	1.51 (1.22–1.87)

RR, relative risk.
[a]Adjusted for gender, age at CRT implantation, socioeconomic factors, QRS morphology, ICD.

patients with >3 conditions increased from 10% at baseline to 24% at 10 years after implantation (*Figure 1*). With increasing number of chronic conditions, there was a greater proportion of patients who were living alone (34, 36, and 43% in patients with 0, 1, and ≥2 chronic conditions, respectively) and who had low educational level (39, 42, and 46% in patients with 0, 1, and ≥2 chronic conditions, respectively), but the difference was smaller regarding patients with low income (28, 32, and 31% in patients with 0, 1, and ≥2 chronic conditions, respectively).

Healthcare utilization and medical treatment by multimorbidity

Across the different follow-up periods, median numbers of overall healthcare contacts increased with the number of chronic conditions at time of CRT implantation (*Figure 1*, *Table 3*), and the difference was seen in contacts to both the primary and secondary healthcare systems (*Figure 2*). Additionally, an increase in cardiovascular and non-cardiovascular hospital contacts was observed with a higher number of chronic conditions (*Table 2*). In adjusted regression models, an increasing number of chronic conditions were associated with higher healthcare utilization within the first 5 years after CRT implantation (*Table 3*). In the follow-up period between 5 and 10 years, only patients with 3 or >3 chronic conditions had a significant higher healthcare utilization [adjusted (aHR): 1.28, 95% confidence interval (CI): 1.10–1.48, and aHR: 1.51, 95% CI: 1.22–1.87, respectively], whereas smaller differences were observed in patients with 2 chronic conditions (aHR: 1.11, 95% CI: 0.99–1.24). During follow-up, the median number of all redeemed prescriptions was increasing in CRT recipients with a higher number of chronic conditions (*Figure 1*).

Healthcare utilization and medical treatment by socioeconomic position

In the different follow-up periods, usage of health care stratified by SEP showed minor differences (*Figure 3*, *Table 4*). In the adjusted analyses, patients living alone had a higher healthcare utilization within the first year (aHR: 1.11, 95% CI: 1.01–1.21) (*Table 4*). A total number of redeemed prescriptions seemed higher in patients with low educational level and low personal income during follow-up (*Figure 4*).

Prognostic outcomes

During follow-up, a total of 1043 (52%) patients died from any cause during follow-up with 1-year and 5-year survivals of 91% (95% CI: 90–92%) and 62% (95% CI: 60–65%) (see Supplementary material online, *Figure S1*) (*Figure 5*). Patients living alone and those with low educational level had a trend towards a higher risk of MACE and all-cause mortality, while this was not the case for low income (*Figure 5*) (see Supplementary material online, *Tables S5* and *S6*). Higher multimorbidity burden at time of CRT implantation was associated with an increased risk of both all-cause mortality and first-time MACE after CRT implantation (*Figure 6*). The sensitivity analyses only including patients with LBBB showed comparable results.

Discussion

This study examined the impact of SEP and multimorbidity on healthcare utilization and long-term prognostic outcomes after CRT implantation in patients with HF with reduced LVEF (≤35%) in a tax-financed universal healthcare system. We observed no strong associations between SEP and cross-sectional healthcare utilization. The median number of redeemed prescriptions was higher in patients within the lowest income group and lower educational level. The prevalence of multimorbidity was high in patients at time of CRT implantation, and a higher number

Table 4 **Association between cross-sectional healthcare service utilization within each follow-up period in** cardiac resynchronization therapy **recipients according to socioeconomic factors**

	Cross-sectional healthcare service utilization											
	Time intervals since cardiac resynchronization therapy implantation											
	0–<1 years			1–<3 years			3–<5 years			5–10 years		
	Median	Crude RR	Adjusted RR[a]	Median	Crude RR	Adjusted RR[a]	Median	Crude RR	Adjusted RR[a]	Median	Crude RR	Adjusted RR[a]
Cohabitation status												
Cohabitation	32 (22–47)			43 (25–66)			39 (23–65)			66 (27–126)		
Living alone	35 (24–49)	1.13 (1.02–1.24)	1.11 (1.01–1.21)	45 (26–70)	1.06 (0.98–1.15)	1.05 (0.98–1.13)	44 (24–65)	1.04 (0.96–1.14)	1.06 (0.97–1.15)	57.5 (24–107)	0.92 (0.82–1.03)	0.93 (0.84–1.03)
Personal income												
Intermediate–high income	33 (22–47)			42 (24–66)			40 (22–65)			62 (26–115)		
Low income	34 (22–48)	1.04 (0.94–1.15)	1.01 (0.92–1.11)	46 (28–70)	1.07 (0.99–1.16)	1.07 (0.99–1.15)	43 (25–66)	1.06 (0.97–1.15)	1.01 (0.93–1.10)	59 (25–123)	1.02 (0.91–1.14)	1.01 (0.91–1.12)
Highest obtained educational level												
High	34 (23–49)			43 (26–68)			41 (23–65)			62 (26–119)		
Low	33 (21–46)	1.01 (0.91–1.12)	0.91 (0.83–1.01)	44 (26–64.5)	1.02 (0.94–1.11)	0.93 (0.86–1.01)	44 (24–66)	1.09 (0.99–1.19)	1.00 (0.92–1.10)	55 (27–123)	0.98 (0.87–1.11)	1.00 (0.89–1.13)

RR, relative risk.
[a]Adjusted for gender, age at CRT implantation, multimorbidity, QRS morphology, ICD.

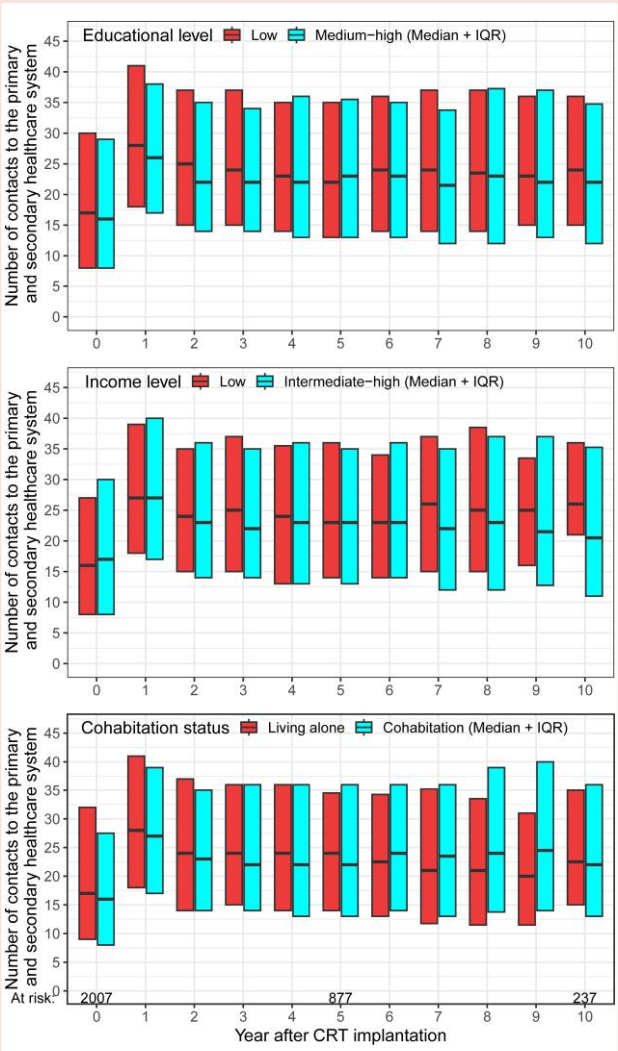


Figure 3 Annual overall healthcare utilization by socioeconomic position after cardiac resynchronization therapy implantation. (*A*) Education level, (*B*) personal income, and (*C*) cohabitation status. Annual estimates within the first 10 years after cardiac resynchronization therapy implantation presented as median and inter-quartile range (25th and 75th percentiles). CRT, cardiac resynchronization therapy; IQR, inter-quartile range.

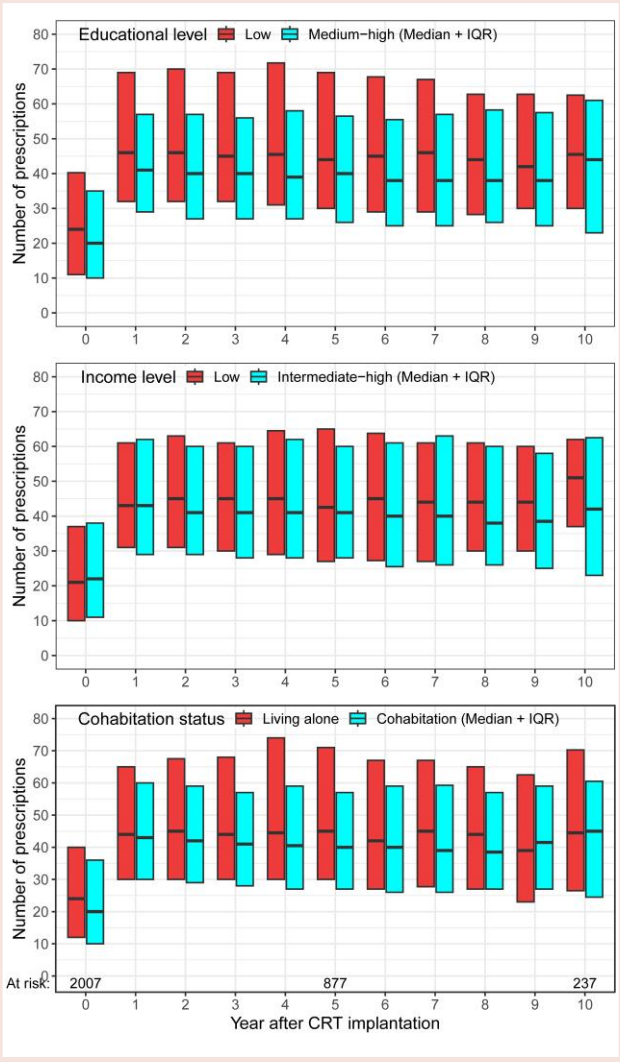


Figure 4 Annual total number of prescriptions by socioeconomic position after cardiac resynchronization therapy implantation. (*A*) Education level, (*B*) personal income, and (*C*) cohabitation status. Annual estimates within the first 10 years after cardiac resynchronization therapy implantation presented as median and inter-quartile range (25th and 75th percentiles). CRT, cardiac resynchronization therapy; IQR, inter-quartile range.

of chronic conditions were strongly associated with a higher utilization of cross-sectional health care, especially within the first 5 years of follow-up, as well as with a higher risk of the MACE and mortality independent of SEP. Patients living alone and with a low educational level seemed to have an increased risk of both MACE and mortality, while this was not observed for the low-income group.

Social inequalities in health care are a major challenge, and this potential social gradient has been investigated extensively, and they are a potential goal for health policy. Socioeconomic position has been identified as a risk factor for HF, hospital readmission, and mortality.[10] Moreover, studies have indicated that inequalities are seen in both universal and private insurance healthcare systems, suggesting that differences in access to treatment or specialist care are not solely responsible. Previous studies in patients with HF have demonstrated that multimorbidity increases healthcare service utilization.[20–22] Similarly, our study in CRT recipients showed that a higher number of chronic conditions lead to higher long-term usage of services in both the primary and secondary healthcare systems as well as the number of both cardiovascular and non-cardiovascular healthcare utilization. Previous studies have linked low socioeconomic status with level of multimorbidity and healthcare utilization.[1,5,6] We observed that the prevalence of multimorbidity increased with lower SEP, revealing a pronounced inverse socioeconomic gradient. However, we observed only weak association between SEP and overall healthcare utilization, when adjusting for multimorbidity level, gender, age, and clinical variables at time of implantation. Income may, however, inadequately reflect SEP, particularly after retirement.[23] This would be in line with a previous study, which observed an interaction between age and annual income on risk of HF hospitalizations and the effect of income being greater in younger patients.[24] The impact of SEP varies during life course, and the association between income or education and HF might diminish with increasing age. In the present study, we sought to adjust for differences in income in relation to age by categorizing income according to income for the Danish population born on the same

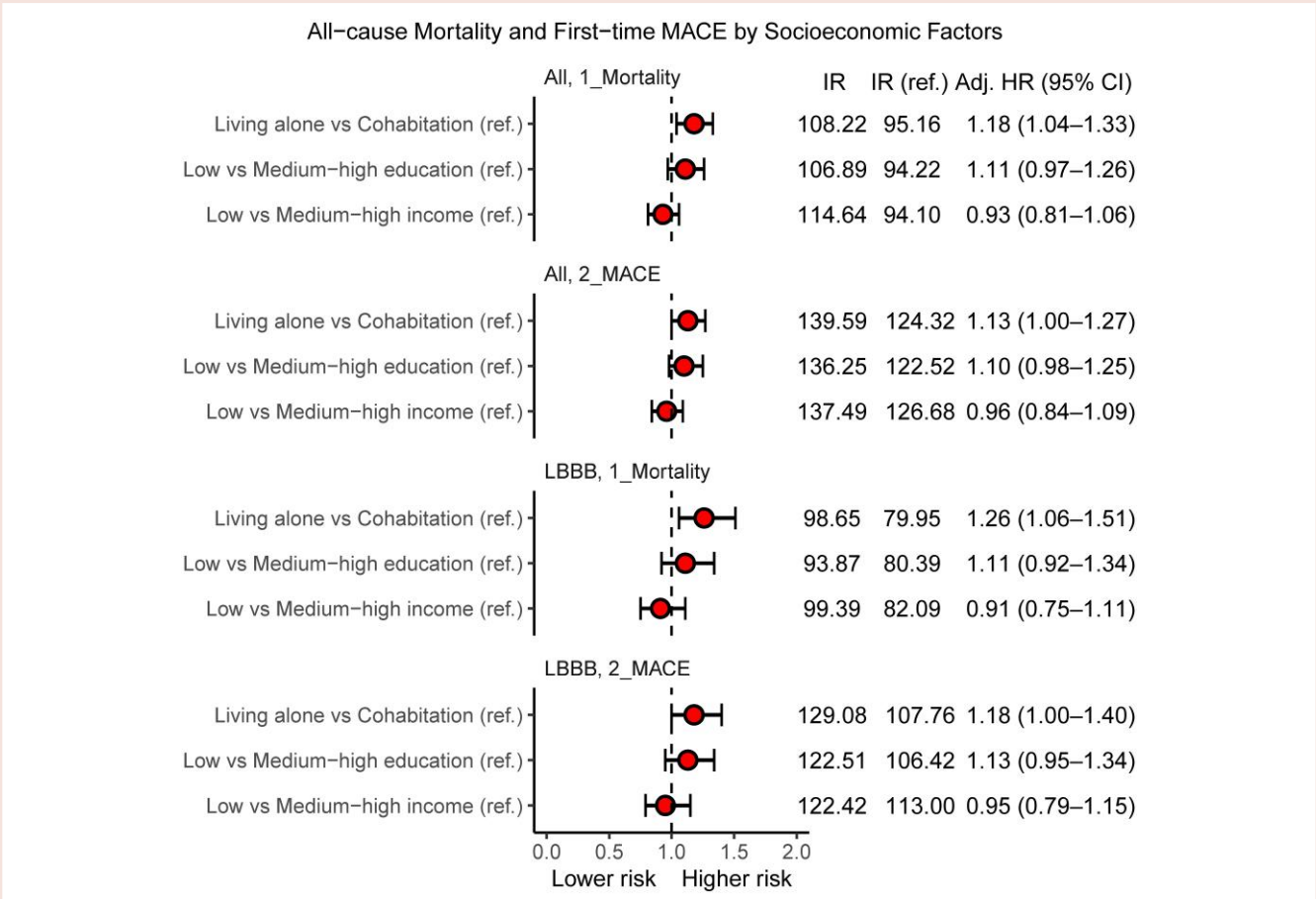


Figure 5 The risk of all-cause mortality and first-time major cardiovascular event according to socioeconomic position in the total cohort (*A*) and in the patients with left bundle branch block morphology (*B*). In multivariate analysis, the hazard ratios are adjusted for calendar period, age, sex, device type, coronary artery disease, QRS morphology, and multimorbidity groups. MACE, major adverse cardiovascular events (composite of readmission heart failure, heart transplantation, and all-cause mortality).

year. Furthermore, post-implantation follow-up requires regular outpatient visits for device interrogation, and within the last decade, most patients are being followed with remote monitoring; thus, all patients have a regular contact to the secondary healthcare system.[25] Thus, patients with CRT are more frequently in contact with the secondary healthcare system, making it easier to keep them compliant to their medical treatment and encourage them to seek their GP in the case of non-cardiac symptoms.

People with multimorbidity have poorer functional status, quality of life, and health outcomes and a higher usage of outpatient and inpatient healthcare services than those without multimorbidity.[1,2,5] High prevalence of multimorbidity is common in patients with HF and found to increase disease burden, risk of hospitalization, and mortality.[9,26] In the present study, patients had a high number of chronic conditions at time of CRT implantation and it increased during follow-up. Multimorbidity was progressively more common with age, but the lower level seen in patients older than 80 years was probably induced by selection bias by the referring and implanting physicians. After CRT implantation, patients had a high number of annual healthcare contacts in both the primary and secondary healthcare systems, and it increased with a number of chronic conditions. These findings indicate a high complexity in long-term management of patients with CRT, and previous studies have found that a fragmentation of care is burdensome for the patients and potentially harmful.[27,28] Improvement in the continuity and coordination of care for people with multimorbidity is a key challenge for healthcare systems worldwide, and healthcare professionals have to face the challenge of managing multiple chronic conditions simultaneously.

We believe our study has several important findings in patients after CRT implantation based on a large cohort of patients with extended follow-up in a tax-financed healthcare system. The results of the present study are based on individual-level data on the SEP in a well-defined HF cohort, treated according to current evidence-based guidelines for HF medications and device follow-up. We found a satisfying prognosis after CRT implantation with around 62% being alive after 5 years and that comorbidities carry important clinical impact in CRT recipients regarding healthcare utilization, hospitalization, and mortality. However, SEP has a limited influence on the healthcare utilization and long-term clinical outcome. A high number of visits to the GP and outpatient visits illustrate the complex follow-up that patients with multimorbidity encounter; thus, there may be a need for better coordination of chronic management of patients with CRT.

Limitations

This study has an observational design, and its major limitations are inherent to this nature. The Danish healthcare system provides publicly financed free care for all patients; thus, these findings are not applicable to healthcare system different from ours. Data were collected retrospectively from hospital and primary care electronic medical records, and we were able to select all medical diagnoses in CRT recipients by

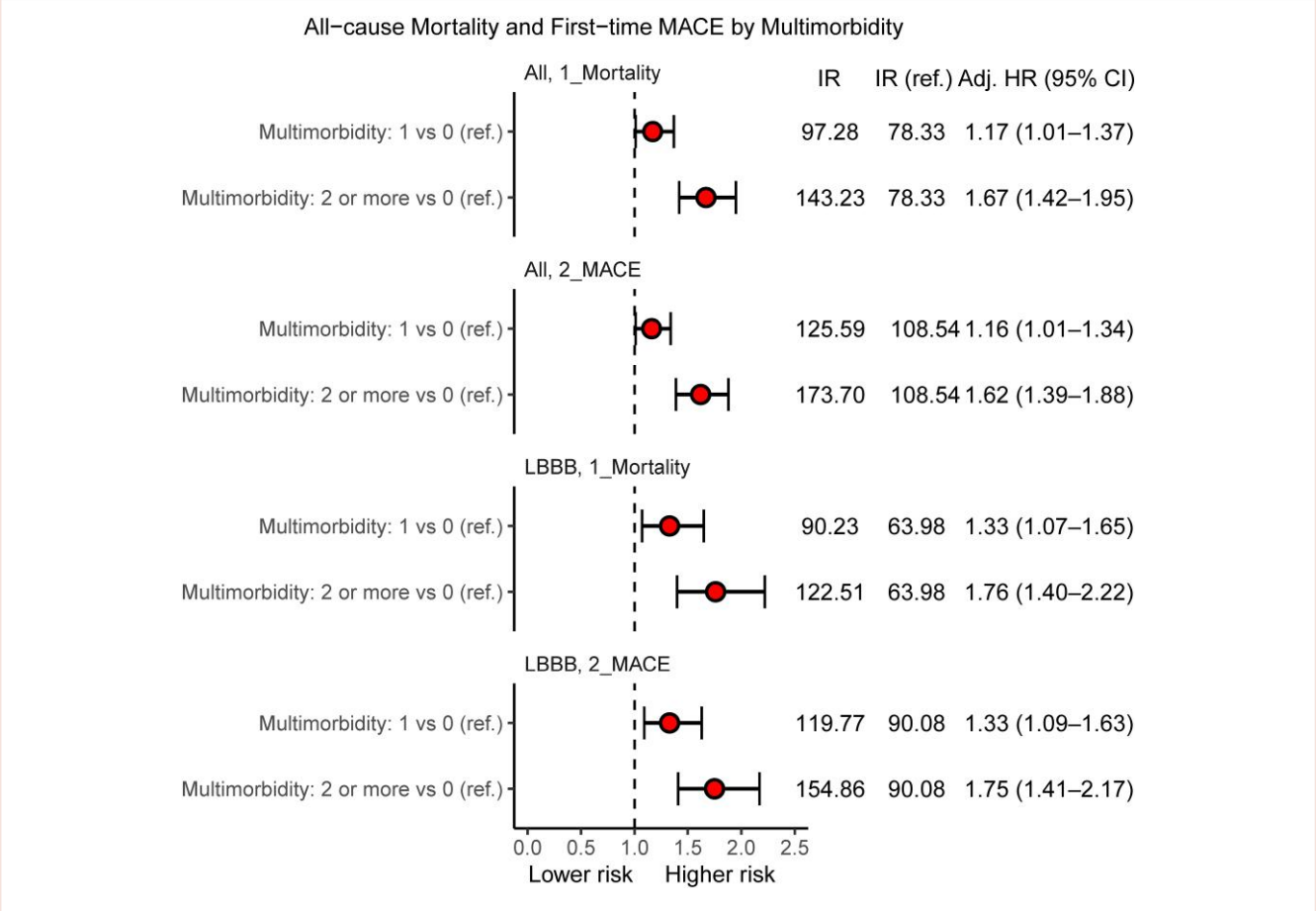


Figure 6 The risk of all-cause mortality and first-time major cardiovascular event according to multimorbidity in the total cohort (*A*) and in the patients with left bundle branch block morphology (*B*). In multivariate analysis, the hazard ratios are adjusted for calendar period (implanted between 2000 and 2006, 2007 and 2012, and after 2012), age, sex, device type (with or without ICD), coronary artery disease, QRS morphology, cohabitation status, and personal income. MACE, major adverse cardiovascular events (composite of readmission heart failure, heart transplantation, and all-cause mortality).

national hospital and psychiatric registries. With the linkage between registries, our study provides reliable register-based data on the pattern of multimorbidity 10 years before CRT implantation and during follow-up and usage in both the primary and secondary healthcare systems.[15] The quality of information on baseline variables and outcome depends on the validity of the data available. All information on SEP was measured at baseline, so any changes during follow-up were not examined. We used a simple disease count to define multimorbidity, and thus, all disorders were weighted equally; however, the effect of multimorbidity on individuals will likely vary with combination and severity of disorders. As the severity of the included diseases was not evaluated, the number of chronic conditions would indicate the complexity of follow-up of the patients. Because we used registry data and therefore relying on the quality of data recording, some morbidities are probably under-recorded, implying that the findings underestimate the true prevalence of multimorbidity. Information on diseases was derived from hospital-requiring treatment and does not include diseases diagnosed and treated in general practice, which in general are less severe.

Conclusions

In patients treated with CRT, increased multimorbidity is strongly associated with an increase in the healthcare utilization and a higher risk of MACE or death. Low SEP is associated with higher multimorbidity but less with healthcare utilization, while living alone and low educational level are associated with an increased risk of MACE or death after CRT implantation.

Lead author biography

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Data availability

The data underlying this article cannot be shared publicly due to the Danish law.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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