BMJ Open

Influence of socio-economic status on the referral process to cardiac rehabilitation following acute coronary syndrome : a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036088
Article Type:	Original research
Date Submitted by the Author:	02-Dec-2019
Complete List of Authors:	Graversen, Christina Boesgaard; Aalborg University Hospital, Department of Cardiology, Department of Clinical Medicine Johansen, Martin; Aalborg University Hospital, Unit of Biostatistics Eichhorst, Regina; Slagelse Hospital, Department of Cardiology Johnsen, Søren Paaske; Aalborg University, Danish Center for Clinical Health Services Research, Department of Clinical Medicine Riahi, Sam; Aalborg University Hospital, Department of Cardiology, Department of Clinical Medicine Holmberg, Teresa; University of Southern Denmark, National Institute of Public Health Larsen, Mogens ; Aalborg University, Department of Clinical Medicine
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Adult cardiology < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title: Influence of socio-economic status on the referral process to cardiac rehabilitation following acute coronary syndrome: a cross-sectional study

Authors:

Christina Boesgaard Graversen*[a,b], Martin Nygård Johansen[c], Regina Eichhorst[d], Søren Paaske Johnsen[e], Sam Riahi[a,b], Teresa Holmberg[f], Mogens Lytken Larsen[b]

Affiliations:

a. Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark

b. Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

c. Unit of Clinical Biostatistics, Aalborg University Hospital, Aalborg, Denmark

d. Department of Cardiology, Slagelse Hospital, Slagelse, Denmark

e. Danish Center for Clinical Health Services Research, Department of Clinical Medicine, Aalborg University and Aalborg University Hospital, Aalborg, Denmark

f. National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark

Information about previous presentation of the whole or part of the work presented in the article:

Parts of the work has been presented in a poster format at the ESC Congress 2019.

Sources of support, for all authors, for the work in the form of grants:

This work was supported by grants from the Karen Elise Jensen's Foundation and the Danish Heart Foundation (18-R123-A8283-22081).

Disclaimers, if any:

None

Corresponding author:

Christina Boesgaard Graversen, postal address: Holger Danskes Vej 73, 2nd Floor Left, 2000 Frederiksberg, DK, mail: c.graversen@rn.dk

Word count: 2303 words

Abstract

Objective: to assess socio-economic predictors for referral to CR after incident ACS by dividing the entire referral process into three phases (1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting).

Design: Cross-sectional study

Setting: Department of Cardiology at a Danish University Hospital from 1 January 2011 to 31 December 2014

Participants: A total of 1229 patients assessed for CR during hospitalisation with ACS were prospectively registered in the Rehab-North Register from 2011-2014. Socio-economic status (SES) was assessed using data from national registers, concerning: personal income, occupational status, educational level, and civil status. Patients were excluded if in one of the following criteria were fulfilled: 1) missing data on SES, or 2) acceptable reason for not informing patients about CR, including treatment with coronary artery bypass graft, transfer to another hospital, still under treatment, or death.

Main outcome measures: Outcomes were defined by dividing the referral process into three phases: 1. being informed about CR, 2. willingness to participate, and 3. assigned CR setting (in-hospital /community centre) after ACS.

Results: A total of 854 (69.5 %) patients were referred to CR. After adjustment for age, gender, diagnosis and comorbidity, high income level had the strongest association of referral to CR in all three phases (informed about CR: OR 2.17, 95% CI: 1.0- 4.64; willingness to participate in CR: OR 1.55, 95% CI: 1.02-2.35; assigned in-hospital CR: OR 1.47, 95% CI: 0.91-2.36). High educational level showed similar tendencies but did not reach statistical significance. The results did not vary according to gender.

Conclusion: This is the first study to investigate the entire referral process to CR using a three-phase structure. It suggests income and education to influence all phases in the referral process to CR after suffering ACS.

Keywords: Myocardial Infarction, Adult Cardiology, Cardiac Epidemiology

Strengths and limitations of this study

- This is the first study to investigate the referral process to cardiac rehabilitation (CR) using a three phase structure (information about CR, willingness to participate in CR, assigned CR setting) rather than the person-level), which provides better knowledge in understanding why social inequality persists in referral to cardiac rehabilitation.
- Socio-economic variables were provided by highly validated Danish register data using the unique 10-digit civil registration number that is given to all Danish citizens.
- Multiple regression analyses were used to minimise potential confounding.
- Data was not gathered for specific scientific purposes and it cannot be ruled out that not all patients admitted with ACS were identified. However, such loss was considered unsystematic and unintended and should not pose a problem for bias introduction.

Introduction

Low socio-economic status (SES) is associated with higher risk of developing Ischemic Heart Disease and a poorer subsequent outcome, including a higher risk of recurrent cardiovascular events and cardiac-related mortality.(1–5) Cardiac rehabilitation (CR) is an important step to reduce disease outcomes and is an integral part of ischemic heart disease care as it aims to improve quality of life as well as patients' physical, psychological, and social functioning.(4)

CR comprises exercise therapy, psychological consulting, treatment-targeted therapy, and life-style changing modules (dietary modification, and smoking cessation).(4) The program is a coordinated effort made by cardiologists, nurses, physiotherapists, dietitians, and eventually occupational therapists. If needed, psychologists, social workers, or priests may be included as well.(4)

The efficacy of CR in reducing cardiovascular mortality and risk of hospital readmissions is well-documented.(6–8) It therefore seems irrational that international research in general continues to find CR referral, participation, and completion rates to be unsatisfactory.(9–13)

Different socio-economic characteristics (income, educational level, occupational status, cohabiting status) are shown to be associated with CR underutilization.(14) Low income and educational level have irrespectively of type of health care system repeatedly been associated with limited participation and completion rate.(11,15) It is consequently of major importance to eliminate the socio-economic differences in CR if the inequality in ischemic disease burden is to be reduced.

Obstacles in referral to CR among patients with lower SES may be due to both personal- and system-level barriers.(16) However, vulnerable elements in the referral process prone to socio-economic inequality among patients with acute coronary syndrome (ACS) remain unexplored. By dividing the referral process into three phases, it is possible to evaluate if such inequality is the result of selection of patients at the system-level (information about CR, place of referral) rather than the person-level (wish to participate in CR). To our knowledge, no study has analysed the entire referral process using such three-phase structure while controlling for confounders in a population of patients surviving ACS. Therefore, the objective of this study was to investigate how SES is associated with the patients' chances of 1) being informed about CR, 2) willingness to participate, and 3) assigned CR setting (in-hospital or community centre).

Methods

The study followed the STROBE guidelines for cross-sectional studies.(17)

Study design

This population-based study used data from the Rehab-North Register. Its content has previously been described.(16) In short, the Rehab-North Register holds data on all patients hospitalised at the

Department of Cardiology, Aalborg University Hospital from 1 January 2011 to 31 December 2014 with a diagnosis of ACS. All were assessed for eligibility to CR using a questionnaire.(16)

In Denmark, CR fully or partially takes place in-hospital or at community centres. In-hospital CR is reserved for high-risk patients and is structured with a more complex intervention. The Danish Public Health System is tax paid, enabling CR to be free of charge for the patient.

Patient and Public involvement statement

No patients were involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study Population

The study population was identified in the Rehab-North Register as patients diagnosed with ACS (ICD-10: DI200, DI21). The registered diagnosis by Rehab-North was verified by linking data from the Rehab-North register with the Danish National Patient Register (NPR) and the Danish Register of Causes of Death.(18) If any discrepancy arose, the diagnosis registered in the NPR was selected.
Patients were excluded if in one of the following criteria were fulfilled: 1) missing data on SES 2) acceptable reason for not informing patients about CR, including treatment with coronary artery bypass graft, transfer to another hospital, still under treatment, or death.

Socio-economic status

Different indicators of SES (personal income, occupational status, educational level, and civil status) were chosen, due to a priori knowledge about their proposed mechanisms associated to the outcome variable. Ascertainment of socio-economic variables from national registers was done by linkage of a unique personal number given to all Danish residents.
The Income Statistics Register provided information regarding both disposable personal income (low, medium, high) calculated for the calendar year before disease onset, and occupational status

(employed, unemployed/out of workforce) set for the calendar year before disease onset.(19) A person's highest obtained educational level (low, medium, high) was based on the International Standard Classification of Education (ISCED)(20) from the Student's Register(21), and civil status (married/partnership, divorced/unmarried /widow) from the Civil Registration System (CRS).(22)

Outcomes

Outcomes were defined by dividing the referral process into three phases: 1. being informed about CR, 2. willingness to participate, and 3. assigned CR setting (in-hospital /community centre) after ACS. All outcome information gathering were done during the patients' hospitalisation and included in the questionnaires that founded the Rehab-North Register.

As regional guidelines determined setting for CR: patients suffering ST-Elevated Myocardial Infarction (STEMI) or complicated Non-ST-Elevated Myocardial Infarction (NSTEMI) were offered in-hospital CR whereas patients with uncomplicated NSTEMI and Unstable Angina Pectoris (UAP) were offered CR in a community centre, we intended to investigate whether this structure was followed.

Covariates

The analysis model was constructed with a directed acyclic graph to reduce confounding (online supplementary material, figure 1).

Age was registered at time of diagnosis and categorized into three groups: < 65 years, 65-74 years, and ≥ 75 years. Information regarding age and gender was gathered from the CRS.(22) Comorbidity diagnoses were defined by the Charlson Comorbidity Index (CCI) and drawn from the NPR.(23)

Statistical analysis

Baseline characteristics of study population were summarised by frequencies and percentages. The association between socio-economic exposure variables and being informed about CR, willingness to participate, and assigned CR setting was assessed by crude (model 1) and multiple logistic regression adjusted for confounders (age, gender, diagnosis, CCI) (model 2). Results were presented in odds ratios

(OR) with 95% confidence intervals (95% CI). Potential effect modification by gender was assessed by stratification and likelihood-ratio tests as studies have found females to experience lower rates of referral to CR compared to males.(10,24) Statistical analyses were performed using Stata Software (v.15.1; Stata Corp. College Station, TX).

Results

Of the original cohort of 1721 patients diagnosed with ACS, only patients with no missing socio-economic variables, and no acceptable reasons for not being informed about CR were included in the study (online supplementary material, figure 2). This resulted in a study population comprising 1229 patients (73.8% male). The patients' baseline characteristics, stratified by diagnosis, are presented in table 1. STEMI patients were relatively younger and still an available workforce with higher income. In the study population, 1123 (91.4%) patients were informed about CR of which 854 (76.0%) patients subsequently agreed to participate in the program. Of those, 349 (40.9%) patients were referred to CR in a community centre and 505 (59.1%) patients were referred to in-hospital CR (figure 1).

Table 1: Characteristics of study population stratified by diagnosis

Characteristics	Full population n = 1229	STEMI n = 402	NSTEMI n = 711	UAP n = 116
Male (n, %)	907 (73.8)	322 (80.1)	503 (70.7)	82 (70.7)
Age Group (years)				
< 65	591 (48.1)	227 (56.5)	308 (43.3)	56 (48.3)
65-74	371 (30.2)	116 (28.9)	215 (30.2)	40 (34.5)
≥ 75	267 (21.7)	59 (14.7)	188 (26.4)	20 (17.2)
Civil status (n, %)				
Married/Partnership	793 (64.5)	253 (62.9)	449 (63.2)	91 (78.4)
Divorced/Unmarried/Widow	436 (35.5)	149 (37.1)	262 (36.8)	25 (21.6)
Occupational status (n, %)				
Employed	479 (39.0)	195 (48.5)	240 (33.8)	44 (37.9)
Unemployed/Retired	750 (61.0)	207 (51.5)	471 (66.2)	72 (62.1)
Educational level (n, %)				
Low	516 (42.0)	144 (35.8)	322 (45.3)	50 (43.1)
Medium	539 (43.9)	201 (50.0)	293 (41.2)	45 (38.8)
High	174 (14.2)	57 (14.2)	96 (13.5)	21 (18.1)
Gross income, tertile (n, %)				
Low	405 (33.0)	113 (28.1)	251 (35.3)	41 (35.3)
Medium	406 (33.0)	124 (30.8)	247 (34.7)	35 (30.2)
High	418 (34.0)	165 (41.0)	213 (30.0)	40 (34.5)
Charlson Comorbidity Index				
Low (0 points)	1088 (88.5)	358 (89.1)	630 (88.6)	100 (86.2)
Moderate/High (>0 points)	141 (11.5)	44 (10.9)	81 (11.4)	16 (13.8)

STEMI: ST-elevated myocardial infarction; NSTEMI: non-ST-elevated myocardial infarction; UAP: unstable angina pectoris

Phase 1: SES and being informed about CR

Higher income and educational level had positive crude associations with being informed about CR. Whereas, being unemployed/retired had a negative association (table 2). These associations were greatly reduced after adjustment for age, gender, diagnosis, and CCI. The adjusted regression analysis found high income to be associated with being informed about CR (OR 2.17, 95% CI: 1.01; 4.64). High educational level was also associated with being informed about CR although the association did not reach statistical significance.

Table 2: Logistic regression model for being informed about cardiac rehabilitation

		Unadjusted		Multivariable adjusted*	
	n, (%)	OR	95% CI	OR	95% CI
Observations	1123 (100.0)				
Civil status					
Married/Partnership	469 (41.8)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	654 (58.2)	0.64	0.43-0.95	0.76	0.49-1.19
Occupational status					
Employed	735 (65.4)	1 (ref.)		1 (ref.)	
Unemployed/Retired	388 (34.6)	0.15	0.07-0.28	0.46	0.20-1.07
Educational level					
Low	452 (40.2)	1 (ref.)		1 (ref.)	
Medium	505 (45.0)	2.10	1.36-3.25	1.17	0.72-1.89
High	166 (14.8)	2.94	1.38-6.26	1.60	0.72-3.54
Income, tertiles					
Low	342 (30.5)	1 (ref.)		1 (ref.)	
Medium	374 (33.3)	2.15	1.37-3.38	1.40	0.86-2.28
High	407 (36.2)	6.82	3.54-13.14	2.17	1.01-4.64

* Adjusted for age, gender, diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Phase 2: SES and willingness to participate in CR

High income, high educational level, and being single-living (divorced/unmarried/widow) were all associated with a higher likelihood of willingness to participate in CR in the crude analyses (table 3). After adjustment, high income level had the highest OR (OR 1.55, 95% CI: 1.02; 2.35) in relation to willingness to participate. A similar pattern was observed for high educational level although the association was not statistically significant (OR 1.60, 95% CI: 0.78; 1.88). Likewise, being single-living was also associated with willingness to participate in CR, although, the estimates did not reach statistical significance (OR 1.28, 95% CI: 0.93; 1.76).

Table 3: Logistic regression model for willingness to participate in cardiac rehabilitation

		Unadjusted		Multiple adjustment*	
	n (%)	OR	95% CI	OR	95% CI
Observations	854 (100.0)				
Civil status					
Married/Partnership	388 (45.4)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	466 (54.6)	1.33	0.99-1.79	1.28	0.93-1.76
Occupational status					
Employed	546 (63.9)	1 (ref.)		1 (ref.)	
Unemployed/Retired	308 (36.1)	0.52	0.39-0.69	0.93	0.62-1.40
Educational level					
Low	322 (37.7)	1 (ref.)		1 (ref.)	
Medium	405 (47.4)	1.64	1.21-2.20	1.36	0.98-1.88
High	127 (14.9)	1.31	0.87-1.99	1.21	0.78-1.88
Income, tertiles					
Low	229 (26.8)	1 (ref.)		1 (ref.)	
Medium	288 (33.7)	1.65	1.19-2.30	1.35	0.94-1.94
High	337 (39.5)	2.38	1.69-3.34	1.55	1.02-2.35

* Adjusted for age, gender, diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Phase 3: SES and assigned CR setting

Table 4 shows the association of SES on being assigned to in-hospital CR compared to CR in a community centre. High income was associated with referral to being assigned to in-hospital CR (OR: 2.10, 95% CI: 1.49; 2.97) but the association was attenuated after adjustment for confounders (income: adjusted OR: 1.47, 95% CI: 0.91; 2.36).

Table 4: Logistic regression model for assigned cardiac rehabilitation setting

		Unadjusted		Multiple adjustment*	
	n (%)	OR	95% CI	OR	95% CI
Observations	505 (100.0)				
Civil status					
Married/Partnership	268 (53.1)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	237 (46.9)	1.13	0.85-1.51	1.20	0.84-1.69
Occupational status					
Employed	317 (62.8)	1 (ref.)		1 (ref.)	
Unemployed/Retired	188 (37.2)	0.46	0.35-0.61	0.75	0.49-1.15
Educational level					
Low	177 (35.0)	1 (ref.)		1 (ref.)	
Medium	248 (49.1)	1.29	0.96-1.74	0.90	0.63-1.30
High	80 (15.8)	1.39	0.91-2.13	1.20	0.72-1.99
Income, tertiles					
Low	115 (22.8)	1 (ref.)		1 (ref.)	
Medium	161 (31.9)	1.26	0.89-1.78	1.14	0.73-1.78
High	229 (45.3)	2.10	1.49-2.97	1.47	0.91-2.36

* Adjusted for age, gender, diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Supplementary analyses

The analyses were stratified by gender in a supplementary analysis. The results were not substantially different from the main analysis.

Discussion

In this study, the referral process to CR was assessed using a three-phase structure: 1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting. We observed patients with low SES to have lower odds of being informed about CR, lower willingness to participate in CR, and to be less often assigned in-hospital CR. Specifically, high income was associated with referral to CR in all phases of the referral process. Moreover, high educational level had a similar pattern, but the association did not reach statistical significance.

Overall, 69.5% of the patients were referred to CR, which is in accordance with earlier findings (22-81.5%).(9,10,24,25) Notably, in one study strikingly 86% was referred to CR after usage of a social differentiated intervention program.(26) However, it would be difficult to reproduce such a result in an observational study without this specific purpose.

In international studies younger age, male gender, living with a partner, high educational level, and high gross income were found to be predictors of CR referral.(10,25,27) This inequality in CR referral causes concern as participation helps patients implement needed behavioural changes, which reduces cardiac-related deaths.(6) Patients with low SES often have biological, behavioural, and psychosocial disadvantages that may accelerate risk of cardiovascular diseases. Therefore, the need of referral, attendance, and completion of CR should be prioritized in this patient group.(1,2) Our results found high income and high educational level to be associated with higher OR's throughout the referral process. We found single-living to be potentially associated with the willingness to participate in CR. If such an association is reproducible in later studies, then attention should focus on these patients without a partner, who less often receive referral to CR, which has been attributed to lack of social

support.(27) It is highly important that patients are well-informed about CR to make a well-considered decision regarding participation.

An earlier study, assessed by crude analyses the referral process to CR on patients hospitalised for a diverse range of incidental cardiac diseases and observed similar socio-economic determinants as predictors for referral as seen in this present study.(16)

Definition of SES is a conceptual challenge often solved by use of personal/family income, educational level, civil status, and/or occupation. There is no consensus on which parameters to use as indicators of SES. It has been argued to use single variables as proxy measurements for SES despite different causal pathways. However, others find it problematic only to estimate SES by one parameter, as this may increase the risk of residual confounding by unmeasured socio-economic circumstances.(1,28) Moreover, the effect of socio-economic variables seems rather outcome-related and is suggested not to be used interchangeably without thorough consideration.(29) As our central interest was to investigate the impact of SES on the referral process to CR, and therefore use SES as exposure variable, we a priori hypothesized the different variables all to be linked to our outcome measures. The risk of such an approach was the introduction of collinearity. However, research finds e.g. educational level, occupation, and income to measure different phenomena, to have different causal mechanisms, and in part to be explained by other socio-economic parameters.(29,30) Since literature finds income, educational level, occupational status, and civil status to be important determinants for referral, participation, and completion of CR, it seemed most appropriate to include all variables in order to answer our research questions. The consequence of this approach was that we cannot get a single estimate that illustrates the effect of SES.

Some caution must be taken when interpreting the results of our study. Firstly, data was not gathered for specific scientific purposes and it cannot be ruled out that some patients admitted with ACS were

not included in the Rehab-North Register. However, such loss was considered unsystematic and unintended and should not pose a problem for bias introduction. Secondly, use of register data minimized risk of information bias, due to nationwide good algorithms for correct diagnosis coding. Despite linkage to other registers, risk of residual or unmeasured confounding may be present.(31) Thirdly, there may be a risk of residual or unaccounted confounding, if data on confounding variables was not classified with adequate precision. Fourthly, several of the results only showed weak association, which most likely was a consequence of the rather small study population. Therefore, it cannot be assumed that there was no association and use of a national cohort may find more conclusive results.

Participation and completion rates of in-hospital CR and CR in community centres remained unexplored as our study only focused on the referral process to CR.

Conclusion

High income and educational level were associated with a larger chance of being informed about CR, willingness to participate in CR, and assigned in-hospital CR in patients with ACS.

Acknowledgements: None

Contributorship statement: CBG, RE, and MLL contributed to study design and acquisition of the data. CBG, MNJ, and MLL analysed and interpreted the data. SPJ, SR, and THO contributed to interpretation. CBG drafted the initial manuscript and all authors critically revised the manuscript and gave final approval.

Ethics: The study is approved by the Danish Data Protection Agency (project number: 2008-58-0028) and the Danish Patient Safety Authority (3-3013-2763/1). In Denmark, no written consent is needed for use of such register-based data.

Funding: This work was supported by the Karen Elise Jensen's Foundation, and the Danish Heart Foundation grant number: 18-R123-A8283-22081. The funders had no role in planning or conducting the study.

Competing interest: None declared

Data sharing statement: No additional data available

References

1. Havranek EP, Mujahid MS, Barr DA, et al. Social determinants of risk and outcomes for cardiovascular disease: A scientific statement from the American Heart Association. Circulation. 2015;132(9):873–98.

2. Schultz WM, Kelli HM, Lisko JC, et al. Socioeconomic Status and Cardiovascular Outcomes. Circulation [Internet]. 2018;137(20):2166–78.

3. Ohm J, Skoglund PH, Discacciati A, et al. Socioeconomic status predicts second cardiovascular event in 29,226 survivors of a first myocardial infarction. Eur J Prev Cardiol. 2018;25(9):985–93.

4. Piepoli MF, Corra U, Adamopoulos S, et al. Secondary prevention in the clinical management of patients with cardiovascular diseases . Core components , standards and outcome measures for referral and delivery. Eur J Prev Cardiol. 2014;21(6):664–81.

5. Rasmussen JN, Rasmussen S, Gislason GH, et al. Mortality after acute myocardial infarction according to income and education. J Epidemiol Community Health. 2006;60(4):351–6.

6. Anderson L, Oldridge N, Thompson DR, et al. Exercise-Based Cardiac Rehabilitation for Coronary Heart Disease. J Am Coll Cardiol. 2016;67(1):1–12.

7. Anderson LJ, Taylor RS. Cardiac rehabilitation for people with heart disease: An overview of

Cochrane systematic reviews. Int J Cardiol. 2014;177(2):348–61.

8. Rauch B, Davos CH, Doherty P, et al. The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: A systematic review and meta-analysis of randomized and non-randomized studies - The Cardiac Rehabilitation Outcome Study (CROS). Eur J Prev Cardiol. 2016;23(18):1914–39.

9. Sumner J, Grace SL, Doherty P. Predictors of Cardiac Rehabilitation Utilization in England : Results From the National Audit. J Am Heart Assoc. 2016;1–7.

10. Colella TJ, Gravely S, Marzolini S, et al. Sex bias in referral of women to outpatient cardiac rehabilitation? A meta-analysis. Eur J Prev Cardiol. 2015;22(4):423–41.

11. Martin B-J, Hauer T, Arena R, et al. Cardiac Rehabilitation Attendance and Outcomes in Coronary Artery Disease Patients. Circulation. 2012;126(6):677–87.

12. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2016;37(29):2315–81.

13. Smith SC, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011;124(22):2458–73.

14. Gaalema DE, Elliott RJ, Morford ZH, et al. Effect of Socioeconomic Status on Propensity to Change Risk Behaviors Following Myocardial Infarction : Implications for Healthy Lifestyle Medicine. Prog Cardiovasc Dis [Internet]. 2017;60(1):159–68.

15. Nielsen KM, Faergeman O, Foldspang A, et al. Cardiac rehabilitation: Health characteristics and socio-economic status among those who do not attend. Eur J Public Health. 2008;18(5):479–83.

16. Graversen CB, Eichhorst R, Ravn L, et al. Social inequality and barriers to cardiac rehabilitation in

the rehab-North register. Scand Cardiovasc J [Internet]. 2017;51(6):316–22.

17. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–9.

18. Madsen M, Davidsen M, Rasmussen S, et al. The validity of the diagnosis of acute myocardial infarction in routine statistics: A comparison of mortality and hospital discharge data with the Danish MONICA registry. J Clin Epidemiol. 2003;56(2):124–30.

19. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments. Scand J Public Health. 2011;39(7):103–5.

20. Eurostat Statistics Explained. International Standard Classification of Education (ISCED). URL: https://ec.europa.eu/eurostat/statistics-explained/index.php/International_Standard_Classification_of_Education_(ISCED).Access date: November 7, 2019.

21. Jensen VM, Rasmussen a. W. Danish education registers. Scand J Public Health. 2011;39(7 Suppl):91–4.

22. Pedersen CB. The Danish Civil Registration System. Scand J Public Health. 2011;39(7 suppl):22–5.

23. Thygesen SK, Christiansen CF, Lash TL, et al. Predictive value of coding of diagnoses in the charlson comorbidity index in the Danish national registry of patients. Pharmacoepidemiol Drug Saf. 2009;18 (S1):S189.

24. Colbert JD, Martin B-J, Haykowsky MJ, et al. Cardiac rehabilitation referral, attendance and mortality in women. Eur J Prev Cardiol. 2014;22(8):979–86.

25. Brown TM, Hernandez AF, Bittner V, et al. Predictors of Cardiac Rehabilitation Referral in Coronary Artery Disease Patients. Findings From the American Heart Association's Get With The

Guidelines Program. J Am Coll Cardiol. 2009;54(6):515–21.

26. Meillier LK, Nielsen KM, Larsen FB, et al. Socially differentiated cardiac rehabilitation: Can we improve referral, attendance and adherence among patients with first myocardial infarction? Scand J Public Health. 2012;40(3):286–93.

27. Cortés O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: A systematic review. Am Heart J. 2006;151(2):249–56.

28. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). J Epidemiol Community Health. 2006;60(1):7–12.

29. Geyer S, Hemström Ö, Peter R, et al. Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. J Epidemiol Community Health. 2006;60(9):804–10.

30. Lahelma E, Martikainen P, Laaksonen M, et al. Pathways between socioeconomic determinants of health. J Epidemiol Community Health. 2004;58(4):327–32.

31. Schmidt M, Schmidt SAJ, Sandegaard JL, et al. The Danish National patient registry: A review of content, data quality, and research potential. Clin Epidemiol. 2015;7:449–90.

Figure legends:

Figure 1: Flowchart of the referral process to cardiac rehabilitation

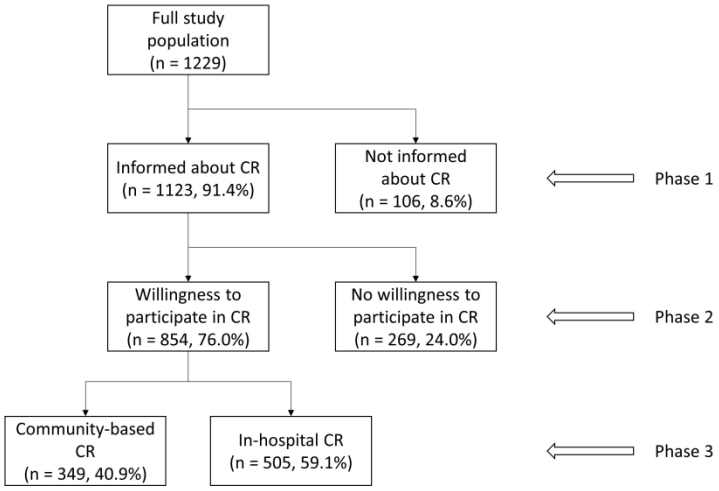


Figure 1: Flowchart of the referral process to cardiac rehabilitation

338x190mm (300 x 300 DPI)

Online supplementary material

Figure S1: Directed acyclic graph

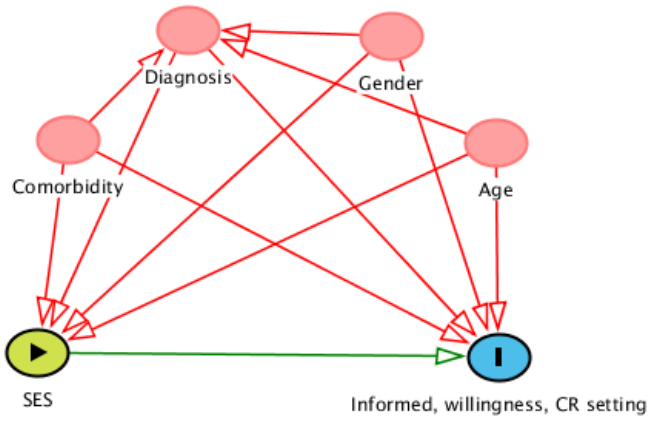
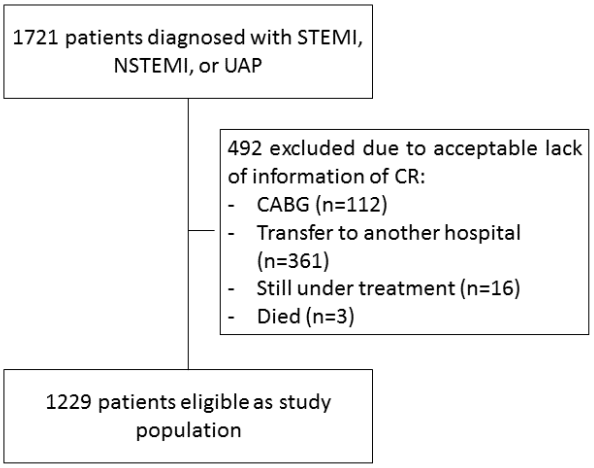


Figure S2: Flowchart of study population



STEMI: ST-Elevated Myocardial Infarction; NSTEMI: Non-ST-Elevated Myocardial Infarction; UAP: Unstable Angina Pectoris; CR: cardiac rehabilitation; CABG: coronary artery bypass graft

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Influence of socio-economic status on the referral process to cardiac rehabilitation following acute coronary syndrome: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036088.R1
Article Type:	Original research
Date Submitted by the Author:	22-Jan-2020
Complete List of Authors:	Graversen, Christina Boesgaard; Aalborg University Hospital, Department of Cardiology, Department of Clinical Medicine Johansen, Martin; Aalborg University Hospital, Forskningens Hus Eichhorst, Regina; Slagelse Hospital, Department of Cardiology Johnsen, Søren Paaske; Aalborg University, Danish Center for Clinical Health Services Research, Department of Clinical Medicine Riahi, Sam; Aalborg University Hospital, Department of Cardiology, Department of Clinical Medicine Holmberg, Teresa; University of Southern Denmark, National Institute of Public Health Larsen, Mogens Lytken; Aalborg University, Department of Clinical Medicine
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Adult cardiology < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title: Influence of socio-economic status on the referral process to cardiac rehabilitation following acute coronary syndrome: a cross-sectional study

Authors:

Christina Boesgaard Graversen[a,b*], Martin Berg Johansen[c], Regina Eichhorst[d], Søren Paaske Johnsen[e], Sam Riahi[a,b], Teresa Holmberg[f], Mogens Lytken Larsen[b]

Affiliations:

a. Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark

b. Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

c. Unit of Clinical Biostatistics, Aalborg University Hospital, Aalborg, Denmark

d. Department of Cardiology, Slagelse Hospital, Slagelse, Denmark

e. Danish Center for Clinical Health Services Research, Department of Clinical Medicine, Aalborg University and Aalborg University Hospital, Aalborg, Denmark

f. National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark

Information about previous presentation of the whole or part of the work presented in the article:

Parts of the work has been presented in a poster format at the ESC Congress 2019.

Sources of support, for all authors, for the work in the form of grants:

This work was supported by grants from the Karen Elise Jensen's Foundation and the Danish Heart Foundation (18-R123-A8283-22081).

Disclaimers, if any:

None

Corresponding author:

Christina Boesgaard Graversen, postal address: Holger Danskes Vej 73, 2nd Floor Left, 2000 Frederiksberg, DK, mail: c.graversen@rn.dk

Word count: 3349 words

Abstract

Objective: to evaluate the association between socio-economic status (SES) and referral to cardiac rehabilitation (CR) after incident acute coronary syndrome (ACS) by dividing the referral process into three phases (1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting).

Design: Cross-sectional study.

Setting: Department of Cardiology at a Danish University Hospital from 1 January 2011 to 31 December 2014.

Participants: A total of 1229 patients assessed for CR during hospitalisation with ACS were prospectively registered in the Rehab-North Register from 2011-2014. SES was assessed using data from national registers, concerning: personal income, occupational status, educational level, and civil status. Patients were excluded if in one of the following criteria were fulfilled: 1) missing data on SES, or 2) acceptable reason for not informing patients about CR (treatment with coronary artery bypass graft, transfer to another hospital, still under treatment, or death).

Main outcome measures: Outcomes were defined by dividing the referral process into three phases: 1. informed about CR, 2. willingness to participate, and 3. assigned CR setting (in-hospital /community centre) after ACS.

Results: A total of 854 (69.5 %) patients were referred to CR. After adjustment for age, gender, ACS diagnosis (ST-Elevated Myocardial Infarction, Non-ST-Elevated Myocardial Infarction, Unstable Angina Pectoris) and comorbidity, high income had the strongest association of referral to CR in all three phases (informed about CR: OR 2.17, 95% CI: 1.0- 4.64; willingness to participate in CR: OR 1.55, 95% CI: 1.02-2.35; assigned in-hospital CR: OR 1.47, 95% CI: 0.91-2.36). Educational level showed similar tendencies, however not statistically significant. The results did not vary according to gender.

Conclusion: This is the first study to investigate the referral process to CR using a three-phase structure. It suggests income and education to influence all phases in the referral process to CR after ACS.

Keywords: Acute Myocardial Infarction, Cardiac Rehabilitation, Referral Process, Socio-economic Status

Strengths and limitations of this study

- This is the first study to investigate the referral process to cardiac rehabilitation (CR) using a three phase structure (1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting) which provides better knowledge in understanding why social inequality persists in referral to CR.
- Socio-economic variables were provided by highly validated Danish register data using the unique 10-digit civil registration number that is given to all Danish citizens.
- Multivariable logistic regression analyses were used to minimise potential confounding.
- Data was not gathered for specific scientific purposes and it cannot be ruled out that not all patients admitted with Acute Coronary Syndrome were identified. However, such loss was considered unsystematic and unintended and should not pose a problem for bias introduction.

Introduction

Low socio-economic status (SES) is associated with higher risk of developing Ischemic Heart Disease (IHD) and poorer subsequent outcome, including higher risk of recurrent cardiovascular events and cardiac-related mortality.(1–5) Cardiac rehabilitation (CR) is an important step to reduce disease outcomes and is an integral part of IHD care as it aims to improve quality of life as well as patients' physical, psychological, and social functioning.(4)

CR comprises exercise therapy, psychological consulting, treatment-targeted therapy, and life-style changing modules (dietary modification, and smoking cessation).(4) The program is a coordinated effort made by cardiologists, nurses, physiotherapists, dietitians, and eventually occupational therapists. If needed, psychologists, social workers, or priests may be included as well.(4)

The efficacy of CR in reducing cardiovascular mortality and risk of hospital readmissions is well-documented.(6–8) It therefore seems irrational that international research in general continues to find CR "referral" or "participation and completion" rates to be unsatisfactory.(9–13)

Different socio-economic characteristics (income, educational level, occupational status, civil status) are shown to be associated with CR underutilization.(14) Low income and educational level have irrespectively of type of health care system repeatedly been associated with limited participation and completion rate.(11,15) It is consequently of major importance to eliminate the socio-economic differences in CR if the inequality in IHD burden is to be reduced.

Obstacles in referral and participation to CR among patients with lower SES may be due to system-level and personal barriers.(16) System-level barriers covers physicians recommendations, the interaction with the healthcare team, and misconceptions about CR. Personal barriers includes perception about IHD and CR, and belief about the ability to control IHD. (16) However, vulnerable elements in the referral process prone to socio-economic inequality among patients with ACS remain unexplored. By dividing the referral process into three phases, it is possible to evaluate if such inequality is the result of selection of patients at the system-level (the process of informing patients about CR and the setting of CR that patients are referred to) rather than the person-level (patients' own willingness to participate in CR). To our knowledge, no study has analysed the entire referral process using such three-phase structure while controlling for confounders in a population of patients surviving ACS. Therefore, the objective of this study was to investigate how SES is associated with the patients' chances of 1) being informed about CR, 2) willingness to participate, and 3) assigned CR setting (in-hospital or community centre). Phase 3 was determined by regional guidelines: patients suffering ST-Elevated Myocardial Infarction (STEMI) or complicated Non-ST-Elevated Myocardial Infarction (NSTEMI) were offered in-hospital CR whereas patients with uncomplicated NSTEMI and Unstable Angina Pectoris (UAP) were offered CR in a community centre).

Methods

The study followed the STROBE guidelines for cross-sectional studies.(17)

Study design

This population-based study used data from the Rehab-North Register. Its content has previously been described.(18) In short, the Rehab-North Register holds data on all patients hospitalised at the Department of Cardiology, Aalborg University Hospital from 1 January 2011 to 31 December 2014 with a diagnosis of ACS. All were assessed for eligibility to CR using a questionnaire.(18)

In Denmark, CR fully or partially takes place in-hospital or at community centres. In-hospital CR is reserved for high-risk patients and is structured with a more complex intervention. The Danish Public Health System is tax paid, enabling CR to be free of charge for the patient.

Patient and Public involvement statement

No patients were involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study Population

The study population was identified in the Rehab-North Register as patients diagnosed with ACS (ICD-10: I20.0, I21.). The registered diagnosis was verified by linking data from the Rehab-North Register with the Danish National Patient Register (NPR) and the Danish Register of Causes of Death.(19) If any discrepancy arose, the diagnosis registered in the NPR was selected. Patients were excluded if in one of the following criteria were fulfilled: 1) missing data on SES 2) acceptable reason for not informing patients about CR, including treatment with coronary artery bypass graft, transfer to another hospital, still under treatment, or death. Patients who underwent coronary artery bypass grafting was informed about CR at the Thoracic Surgery Department performing the operation. Patients who were 'transferred

to another hospital' received information about CR at other cardiology departments. We were not able to receive confirmation regarding referral to CR in this patient group.

The study population and referral design using three phases is illustrated in figure 1.

Socio-economic status

Different indicators of SES (personal income, occupational status, educational level, and civil status) were chosen, due to a priori knowledge about their proposed mechanisms associated to the outcome variable. Ascertainment of socio-economic variables from national registers was done by linkage of a unique personal number given to all Danish residents.

The Income Statistics Register provided information regarding both disposable personal income (low, medium, high) calculated for the calendar year before disease onset, and occupational status (employed, unemployed/out of workforce) set for the calendar year before disease onset.(20) A person's highest obtained educational level (low, medium, high) was based on the International Standard Classification of Education (ISCED)(21) from the Student's Register(22), and civil status (married/partnership, divorced/unmarried /widow) from the Civil Registration System (CRS).(23)

Outcomes

Outcomes were defined by dividing the referral process into three phases: 1. informed about CR, 2. willingness to participate, and 3. assigned CR setting (in-hospital /community centre) after ACS.

All outcome information gathering were done during the patients' hospitalisation and included in the questionnaires that founded the Rehab-North Register.

Covariates

The selection of covariates to be included in the multivariable analyses was done based on directed acyclic graph (not shown).

Age was registered at time of diagnosis and categorized into three groups: < 65 years, 65-74 years, and ≥ 75 years. Information regarding age and gender was gathered from the CRS.(23) Comorbidity

diagnoses were defined by the Charlson Comorbidity Index (CCI), but only diagnoses from the year 2011 until hospitalisation were accessible. Comorbidity diagnoses was drawn from the NPR.(24) In general, patients with NSTEMI and UAP are less likely referred to CR compared to patients with STEMI.(25) Therefore, to get an accurate estimate of the impacts of patients' SES on CR referral, ACS diagnosis (STEMI, NSTEMI, UAP) were included as a covariate.(25)

Statistical analysis

Baseline characteristics of study population were summarised by frequencies and percentages. The association between socio-economic variables and being informed about CR, willingness to participate, and assigned CR setting was assessed by crude (model 1) and multivariable logistic regression adjusted for confounders (age, gender, ACS diagnosis, CCI) (model 2). Results were presented in odds ratios (OR) with 95% confidence intervals (95% CI). Potential effect modification by gender was assessed by stratification and likelihood-ratio tests as studies have found females to experience lower rates of referral to CR compared to males.(10,26) Statistical analyses were performed using Stata Software (v.15.1; Stata Corp. College Station, TX).

Results

Of the original cohort of 1822 patients diagnosed with ACS, only patients with no missing socio-economic variables, and no acceptable reasons for not being informed about CR were included in the study (figure 1). This resulted in a study population comprising 1229 patients (73.8% male). The patients' baseline characteristics, stratified by diagnosis, are presented in table 1. STEMI patients were relatively younger and still an available workforce with higher income. In the study population, 1123 (91.4%) patients were informed about CR of which 854 (76.0%) patients subsequently agreed to participate in the program. Of those, 349 (40.9%) patients were referred to CR in a community centre and 505 (59.1%) patients were referred to in-hospital CR (figure 1).

Table 1: Characteristics of study population stratified by diagnosis

Characteristics	Full population n = 1229	STEMI n = 402	NSTEMI n = 711	UAP n = 116
Male (n, %)	907 (73.8)	322 (80.1)	503 (70.7)	82 (70.7)
Age Group (years)				
< 65	591 (48.1)	227 (56.5)	308 (43.3)	56 (48.3)
65-74	371 (30.2)	116 (28.9)	215 (30.2)	40 (34.5)
≥ 75	267 (21.7)	59 (14.7)	188 (26.4)	20 (17.2)
Civil status (n, %)				
Married/Partnership	793 (64.5)	253 (62.9)	449 (63.2)	91 (78.4)
Divorced/Unmarried/Widow	436 (35.5)	149 (37.1)	262 (36.8)	25 (21.6)
Occupational status (n, %)				
Employed	479 (39.0)	195 (48.5)	240 (33.8)	44 (37.9)
Unemployed/out of workforce	750 (61.0)	207 (51.5)	471 (66.2)	72 (62.1)
Educational level (n, %)				
Low	516 (42.0)	144 (35.8)	322 (45.3)	50 (43.1)
Medium	539 (43.9)	201 (50.0)	293 (41.2)	45 (38.8)
High	174 (14.2)	57 (14.2)	96 (13.5)	21 (18.1)
Income, tertile (n, %)				
Low	405 (33.0)	113 (28.1)	251 (35.3)	41 (35.3)
Medium	406 (33.0)	124 (30.8)	247 (34.7)	35 (30.2)
High	418 (34.0)	165 (41.0)	213 (30.0)	40 (34.5)
Charlson Comorbidity Index				
Low (0 points)	1088 (88.5)	358 (89.1)	630 (88.6)	100 (86.2)
Moderate/High (>0 points)	141 (11.5)	44 (10.9)	81 (11.4)	16 (13.8)

STEMI: ST-elevated myocardial infarction; NSTEMI: non-ST-elevated myocardial infarction; UAP: unstable angina pectoris

Phase 1: SES and being informed about CR

Higher income and educational level had positive crude associations with being informed about CR whereas being unemployed/retired or single-living had a negative association (table 2). These associations were greatly reduced after adjustment for age, gender, ACS diagnosis, and CCI. The adjusted regression analysis found high income to be associated with being informed about CR (OR 2.17, 95% CI: 1.01; 4.64). High educational level was also associated with being informed about CR although the association did not reach statistical significance (OR: 1.60, 95% CI: 0.72-3.54).

Table 2: Logistic regression model for being informed about cardiac rehabilitation, n = 1229

		Unadjusted		Multivariable adjusted*	
	n, (%)	OR	95% CI	OR	95% CI
Observations	1123 (91.4)				
Civil status					
Married/Partnership	469 (38.2)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	654 (53.2)	0.64	0.43-0.95	0.76	0.49-1.19
Occupational status					
Employed	735 (59.8)	1 (ref.)		1 (ref.)	
Unemployed/out of workforce	388 (31.6)	0.15	0.07-0.28	0.46	0.20-1.07
Educational level					
Low	452 (36,8)	1 (ref.)		1 (ref.)	
Medium	505 (41.1)	2.10	1.36-3.25	1.17	0.72-1.89
High	166 (13.5)	2.94	1.38-6.26	1.60	0.72-3.54
Income, tertiles					
Low	342 (27.8)	1 (ref.)		1 (ref.)	
Medium	374 (30.4)	2.15	1.37-3.38	1.40	0.86-2.28
High	407 (33.1)	6.82	3.54-13.14	2.17	1.01-4.64

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Phase 2: SES and willingness to participate in CR

High income, high educational level, and being single-living (divorced/unmarried/widow) were all associated with a higher likelihood of willingness to participate in CR in the crude analyses (table 3). Being unemployed/retired was negatively associated with being willing to participate in CR. After adjustment, high income level had the highest OR (OR 1.55, 95% CI: 1.02; 2.35) in relation to willingness to participate. A similar pattern was observed for high educational level although the association was not statistically significant (OR 1.60, 95% CI: 0.78; 1.88). Likewise, being single-living was also associated with willingness to participate in CR, although, the estimates did not reach statistical significance (OR 1.28, 95% CI: 0.93; 1.76).

Table 3: Logistic regression model for willingness to participate in cardiac rehabilitation, n = 1123

		Unadjusted		Multivariable adjusted*	
	n (%)	OR	95% CI	OR	95% CI
Observations	854 (76.0)				
Civil status					
Married/Partnership	388 (34.6)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	466 (41.5)	1.33	0.99-1.79	1.28	0.93-1.76
Occupational status					
Employed	546 (48.6)	1 (ref.)		1 (ref.)	
Unemployed/out of workforce	308 (27.4)	0.52	0.39-0.69	0.93	0.62-1.40
Educational level					
Low	322 (28.7)	1 (ref.)		1 (ref.)	
Medium	405 (36.1)	1.64	1.21-2.20	1.36	0.98-1.88
High	127 (11.3)	1.31	0.87-1.99	1.21	0.78-1.88
Income, tertiles					
Low	229 (20.4)	1 (ref.)		1 (ref.)	

Medium	288 (25.6)	1.65	1.19-2.30	1.35	0.94-1.94
High	337 (30.0)	2.38	1.69-3.34	1.55	1.02-2.35

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Phase 3: SES and assigned CR setting

Table 4 shows the association of SES on being assigned to in-hospital CR compared to CR in a community centre. High income was significantly associated with assignment to in-hospital CR (OR: 2.10, 95% CI: 1.49; 2.97) but the association was attenuated after adjustment for confounders (income: adjusted OR: 1.47, 95% CI: 0.91; 2.36).

Table 4: Logistic regression model for assigned cardiac rehabilitation setting, n = 854

		Unadjusted		Multivariable adjusted*	
	n (%)	OR	95% CI	OR	95% CI
Observations	505 (59.1)				
Civil status					
Married/Partnership	268 (31.4)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	237 (27.8)	1.13	0.85-1.51	1.20	0.84-1.69
Occupational status					
Employed	317 (37.1)	1 (ref.)		1 (ref.)	
Unemployed/out of workforce	188 (22.0)	0.46	0.35-0.61	0.75	0.49-1.15
Educational level					
Low	177 (20.7)	1 (ref.)		1 (ref.)	
Medium	248 (29.0)	1.29	0.96-1.74	0.90	0.63-1.30
High	80 (9.4)	1.39	0.91-2.13	1.20	0.72-1.99
Income, tertiles					
Low	115 (13.5)	1 (ref.)		1 (ref.)	
Medium	161 (18.9)	1.26	0.89-1.78	1.14	0.73-1.78

High	229 (26.8)	2.10	1.49-2.97	1.47	0.91-2.36

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Supplementary analyses

The analyses were stratified by gender in a supplementary analysis. The results were not substantially different from the main analysis (not shown).

The baseline characteristics of patients being excluded from the study population was obtained (online supplementary material, table 1). After multivariable logistic regression, patients being excluded from the study population to have significantly lower SES compared to the patients being included (online supplementary material, table 2).

Discussion

In this study, the referral process to CR was assessed using a three-phase structure: 1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting. After adjustment, high income was the only variable statistical significantly associated with referral to CR in phase 1 and 2, and insignificantly associated with phase 3 of the referral process. High educational level had a similar pattern, but the association did not reach statistical significance.

Overall, 69.5% of the patients were referred to CR, which is in accordance with earlier findings (22-81.5%).(9,10,25,26) Notably, in one study strikingly 86% was referred to CR after usage of a social differentiated intervention program.(27) However, it would be difficult to reproduce such a result in an observational study without this specific purpose.

The finding of patients' income and educational level to be associated with all three phases the referral process to CR may be explained by 'the Nordic Paradox' observed in the Nordic European countries.(28,29) These countries, covering Denmark, Norway, Sweden, and Finland, are 'welfare states' with equal access to health care which theoretically ought to diminish the importance of patients' level of income and education regarding access to health care services. However, this is not

the case as inequality e.g. in mortality, persists.(29) Although income inequality is smaller in the Nordic countries, this still covers over inequality in wealth, housing condition, and material living conditions, and are used together with educational level to assess latent socio-economic factors (health literacy, greater burden of behavioral and biological risk factors, and reduced access to quality care and medication).(30) Thus, our finding may imply such latent socio-economic factors to be important in the referral process to CR.

We found single-living to be potentially associated with the willingness to participate in CR. If such an association is reproducible in later studies, then attention should focus on these patients without a partner, who less often receive referral to CR, which has been attributed to lack of social support.(31)

International studies find younger age, male gender, living with a partner, high educational level, and high gross income to be predictors of CR referral.(10,25,31) This inequality in CR referral causes concern as participation helps patients implement needed behavioural changes, which reduces cardiac-related deaths.(6) Patients with low SES often have biological, behavioural, and psychosocial disadvantages that may accelerate risk of cardiovascular diseases. Therefore, the need of referral, attendance, and completion of CR should be prioritized in this patient group.(1,2)

By splitting the referral process into three phases, new insights regarding importance of taking patients SES into consideration when referring them to CR was gained. Our results show the importance of being aware of system-level barriers present in the referral process. Moreover, identifying those patients who need more motivation before being willing to enter a CR programme is highly important. In that way, patients are well-informed about CR and able to make a well-considered decision regarding participation.

Definition of SES is a conceptual challenge often solved by use of personal/family income, educational level, civil status, and/or occupation. There is no consensus on which parameters to use as indicators of SES. It has been argued to use single variables as proxy measurements for SES despite different causal

pathways. However, others find it problematic only to estimate SES by one parameter, as this may increase the risk of residual confounding by unmeasured socio-economic circumstances.(1,32) Moreover, the effect of socio-economic variables seems rather outcome-related and is suggested not to be used interchangeably without thorough consideration.(33) As our central interest was to investigate the impact of SES on the referral process to CR, and therefore use SES as exposure variable, we a priori hypothesized the different variables all to be linked to our outcome measures. The risk of such an approach was the introduction of collinearity. However, research finds e.g. educational level, occupation, and income to measure different phenomena, to have different causal mechanisms, and in part to be explained by other socio-economic parameters.(33,34) Since literature finds income, educational level, occupational status, and civil status to be important determinants for referral, participation, and completion of CR, it seemed most appropriate to include all variables in order to answer our research questions. The consequence of this approach was that we cannot get a single estimate that illustrates the effect of SES.

Some caution must be taken when interpreting the results of our study. Firstly, data was not gathered for specific scientific purposes and it cannot be ruled out that some patients admitted with ACS were not included in the Rehab-North Register. However, such loss was considered unsystematic and unintended and should not pose a problem for bias introduction. Moreover, the non-response analysis found excluded patients to have lower SES compared to the included study population. As exclusion was due to clinical implications (patients were to receive CR referral elsewhere), this should not pose a problem for participation bias introduction in our study population.

Secondly, use of register data minimized risk of information bias, due to nationwide good algorithms for correct diagnosis coding. Despite linkage to other registers, risk of residual or unmeasured confounding may be present.(35) Thirdly, there may be a risk of residual or unaccounted confounding, if data on confounding variables was not classified with adequate precision. The CCI variable may be inaccurate

which is caused by the limited time-frame for inclusion of comorbidities. This increases the risk of unaccounted confounding and should be taken into consideration when interpreting the results. Participation and completion rates of in-hospital CR and CR in community centres remained unexplored as our study only focused on the referral process to CR.

Conclusion

High income and educational level were associated with a larger chance of being informed about CR, willingness to participate in CR, and assigned in-hospital CR in patients with ACS.

Acknowledgements: None

Contributorship statement: CBG, RE, and MLL contributed to study design and acquisition of the data. CBG, MNJ, and MLL analysed and interpreted the data. SPJ, SR, and THO contributed to interpretation. CBG drafted the initial manuscript and all authors critically revised the manuscript and gave final approval.

Ethics: The study is approved by the Danish Data Protection Agency (project number: 2008-58-0028) and the Danish Patient Safety Authority (3-3013-2763/1). In Denmark, no written consent is needed for use of such register-based data.

Funding: This work was supported by the Karen Elise Jensen's Foundation, and the Danish Heart Foundation grant number: 18-R123-A8283-22081. The funders had no role in planning or conducting the study.

Competing interest: None declared

Data sharing statement: No additional data available

References

1. Havranek EP, Mujahid MS, Barr DA, Blair I V., Cohen MS, Cruz-Flores S, et al. Social determinants of risk and outcomes for cardiovascular disease: A scientific statement from the American Heart Association. Circulation. 2015;132(9):873–98.

2. Schultz WM, Kelli HM, Lisko JC, Varghese T, Shen J, Sandesara P, et al. Socioeconomic Status and Cardiovascular Outcomes. Circulation. 2018;137(20):2166–78.

3. Ohm J, Skoglund PH, Discacciati A, Sundström J, Hambraeus K, Jernberg T, et al. Socioeconomic status predicts second cardiovascular event in 29,226 survivors of a first myocardial infarction. Eur J Prev Cardiol. 2018;25(9):985–93.

4. Piepoli MF, Corra U, Adamopoulos S, Benzer W, Bjarnason-wehrens B, Cupples M, et al. Secondary prevention in the clinical management of patients with cardiovascular diseases . Core components , standards and outcome measures for referral and delivery. Eur J Prev Cardiol. 2014;21(6):664–81.

5. Rasmussen JN, Rasmussen S, Gislason GH, Buch P, Abildstrom SZ, Køber L, et al. Mortality after acute myocardial infarction according to income and education. J Epidemiol Community Health. 2006;60(4):351–6.

6. Anderson L, Oldridge N, Thompson DR, Zwisler A-D, Rees K, Martin N, et al. Exercise-Based Cardiac Rehabilitation for Coronary Heart Disease. J Am Coll Cardiol. 2016;67(1):1–12.

7. Anderson LJ, Taylor RS. Cardiac rehabilitation for people with heart disease: An overview of Cochrane systematic reviews. Int J Cardiol. 2014;177(2):348–61.

8. Rauch B, Davos CH, Doherty P, Saure D, Metzendorf MI, Salzwedel A, et al. The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: A systematic review and meta-analysis of randomized and non-randomized studies - The Cardiac

Rehabilitation Outcome Study (CROS). Eur J Prev Cardiol. 2016;23(18):1914–39.

9. Sumner J, Grace SL, Doherty P. Predictors of Cardiac Rehabilitation Utilization in England : Results From the National Audit. J Am Heart Assoc. 2016;5:1–8.

10. Colella TJ, Gravely S, Marzolini S, Grace SL, Francis JA, Oh P, et al. Sex bias in referral of women to outpatient cardiac rehabilitation? A meta-analysis. Eur J Prev Cardiol. 2015;22(4):423–41.

11. Martin B-J, Hauer T, Arena R, Austford LD, Galbraith PD, Lewin a. M, et al. Cardiac Rehabilitation Attendance and Outcomes in Coronary Artery Disease Patients. Circulation. 2012;126(6):677–87.

12. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2016;37(29):2315–81.

13. Smith SC, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011;124(22):2458–73.

14. Gaalema DE, Elliott RJ, Morford ZH, Higgins ST, Ades PA. Effect of Socioeconomic Status on Propensity to Change Risk Behaviors Following Myocardial Infarction : Implications for Healthy Lifestyle Medicine. Prog Cardiovasc Dis. 2017;60(1):159–68.

15. Nielsen KM, Faergeman O, Foldspang A, Larsen ML. Cardiac rehabilitation: Health characteristics and socio-economic status among those who do not attend. Eur J Public Health. 2008;18(5):479–83.

16. Neubeck L, Freedman S Ben, Clark AM, Briffa T, Bauman A, Redfern J. Participating in cardiac rehabilitation: A systematic review and meta-synthesis of qualitative data. Eur J Prev Cardiol. 2012;19(3):494–503.

17. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–9.

18. Graversen CB, Eichhorst R, Ravn L, Christiansen SR, Johansen MB, Larsen ML, et al. Social inequality and barriers to cardiac rehabilitation in the rehab-North register. Scand Cardiovasc J. 2017;51(6):316–22.

19. Madsen M, Davidsen M, Rasmussen S, Abildstrom SZ, Osler M. The validity of the diagnosis of acute myocardial infarction in routine statistics: A comparison of mortality and hospital discharge data with the Danish MONICA registry. J Clin Epidemiol. 2003;56(2):124–30.

20. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments. Scand J Public Health. 2011;39(7):103–5.

21. Eurostat Statistics Explained. International Standard Classification of Education (ISCED) [Internet]. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php/International_Standard_Classification_of_Education_%28ISCED%29

22. Jensen VM, Rasmussen a. W. Danish education registers. Scand J Public Health. 2011;39(7 Suppl):91–4.

23. Pedersen CB. The Danish Civil Registration System. Scand J Public Health. 2011;39(7 suppl):22–5.

24. Thygesen SK, Christiansen CF, Lash TL, Christensen S, Sorensen HT. Predictive value of coding of diagnoses in the charlson comorbidity index in the Danish national registry of patients. Pharmacoepidemiol Drug Saf. 2009;18 (S1):S189.

25. Brown TM, Hernandez AF, Bittner V, Cannon CP, Ellrodt G, Liang L, et al. Predictors of Cardiac Rehabilitation Referral in Coronary Artery Disease Patients. Findings From the American Heart Association's Get With The Guidelines Program. J Am Coll Cardiol. 2009;54(6):515–21.

26. Colbert JD, Martin B-J, Haykowsky MJ, Hauer TL, Austford LD, Arena RA, et al. Cardiac rehabilitation referral, attendance and mortality in women. Eur J Prev Cardiol. 2014;22(8):979–86.

27. Meillier LK, Nielsen KM, Larsen FB, Larsen ML. Socially differentiated cardiac rehabilitation: Can we improve referral, attendance and adherence among patients with first myocardial infarction? Scand J Public Health. 2012;40(3):286–93.

28. Mackenbach JP. The persistence of social inequalities in modern welfare states: the explanation of a paradox. Soc Sci Med. 2012;75:761–9.

29. Mackenbach JP. Nordic paradox, Southern miracle, Eastern disaster: Persistence of inequalities in mortality in Europe. Eur J Public Health. 2017;27:14–7.

30. Tromp J, Collins S. Universal healthcare but not universal access? Eur J Prev Cardiol. 2019;27(1);75-8.s

31. Cortés O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: A systematic review. Am Heart J. 2006;151(2):249–56.

32. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Smith GD. Indicators of socioeconomic position (part 1). J Epidemiol Community Health. 2006;60(1):7–12.

33. Geyer S, Hemström Ö, Peter R, Vågerö D. Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. J Epidemiol Community Health. 2006;60(9):804–10.

34. Lahelma E, Martikainen P, Laaksonen M, Aittomäki A. Pathways between socioeconomic determinants of health. J Epidemiol Community Health. 2004;58(4):327–32.

35. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National patient registry: A review of content, data quality, and research potential. Clin

376 Epidemiol. 2015;7:449–90.

377

378 **Figure legends:**

379 Figure 1: Flowchart of the referral process to cardiac rehabilitation

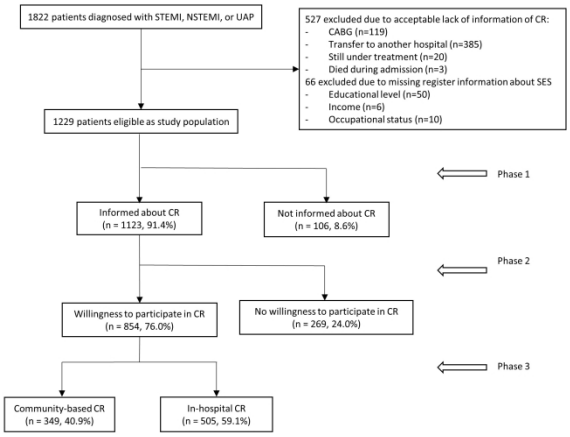


Figure 1: Flowchart of the referral process to cardiac rehabilitation

338x190mm (300 x 300 DPI)

ONLINE SUPPLEMENTARY MATERIAL

Table S1: Baseline Characteristics of excluded patients

	Excluded
Characteristics	n = 593
Male (n, %)	423
Age Group (years)	
< 65	242
65-74	171
≥ 75	180
Civil status (n, %)	
Married/Partnership	378
Divorced/Unmarried/Widow	>210
Missing	<5
Occupational status (n, %)	
Employed	158
Unemployed/out of workforce	417
Missing	18
Educational level (n, %)	
Low	256
Medium	200
High	52
Missing	72
Income, tertile (n, %)	
Low	245
Medium	197
High	>145
Missing	<5
Charlson Comorbidity Index	
Low (0 points)	421
Moderate/High (>0 points)	75
Missing	97

Table S2: Logistic regression model for those excluded compared with those included in the study population, n = 1822

		Unadjusted		Multivariable adjusted*	
	n, (%)	OR	95% CI	OR	95% CI
Observations	593 (32.5)				
Civil status					
Married/Partnership	378 (20.7)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	>210 (>11.5)	1.02	0.83-1.25	0.85	0.67-1.07
Missing	<5 (<1)				
Occupational status					
Employed	158 (8.7)	1 (ref.)		1 (ref.)	
Unemployed/Retired	417 (22.9)	1.69	1.36-2.09	1.54	1.14-2.08
Missing	18 (1.0)				
Educational level					
Low	256 (14.1)	1 (ref.)		1 (ref.)	
Medium	200 (10.1)	0.77	0.61-0.96	0.77	0.61-0.97
High	49 (2.7)	0.59	0.42-0.84	0.60	0.41-0.87
Missing	72 (4.0)				
Income, tertiles					
Low	245 (13.4)	1 (ref.)		1 (ref.)	
Medium	197 (10.8)	0.71	0.56-0.90	0.77	0.59-1.01
High	>145 (>7.9)	0.46	0.36-0.59	0.55	0.40-0.75
Missing	<5 (<0.3)				

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	7-8
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6+8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-12
		(*b*) Report category boundaries when continuous variables were categorized	9-12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Influence of socio-economic status on the referral process to cardiac rehabilitation following acute coronary syndrome: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036088.R2
Article Type:	Original research
Date Submitted by the Author:	19-Feb-2020
Complete List of Authors:	Graversen, Christina Boesgaard; Aalborg University Hospital, Department of Cardiology, Department of Clinical Medicine Johansen, Martin; Aalborg University Hospital, Unit of Clinical Biostatistics Eichhorst, Regina; Slagelse Hospital, Department of Cardiology Johnsen, Søren Paaske; Aalborg University, Danish Center for Clinical Health Services Research, Department of Clinical Medicine Riahi, Sam; Aalborg University Hospital, Department of Cardiology, Department of Clinical Medicine Holmberg, Teresa; University of Southern Denmark, National Institute of Public Health Larsen, Mogens Lytken; Aalborg University, Department of Clinical Medicine
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Adult cardiology < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title: Influence of socio-economic status on the referral process to cardiac rehabilitation following acute coronary syndrome: a cross-sectional study

Authors:

Christina Boesgaard Graversen[a,b*], Martin Berg Johansen[c], Regina Eichhorst[d], Søren Paaske Johnsen[e], Sam Riahi[a,b], Teresa Holmberg[f], Mogens Lytken Larsen[b]

Affiliations:

a. Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark

b. Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

c. Unit of Clinical Biostatistics, Aalborg University Hospital, Aalborg, Denmark

d. Department of Cardiology, Slagelse Hospital, Slagelse, Denmark

e. Danish Center for Clinical Health Services Research, Department of Clinical Medicine, Aalborg University and Aalborg University Hospital, Aalborg, Denmark

f. National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark

Information about previous presentation of the whole or part of the work presented in the article:

Parts of the work has been presented in a poster format at the ESC Congress 2019.

Sources of support, for all authors, for the work in the form of grants:

This work was supported by grants from the Karen Elise Jensen's Foundation and the Danish Heart Foundation (18-R123-A8283-22081).

Disclaimers, if any:

None

Corresponding author:

Christina Boesgaard Graversen, postal address: Holger Danskes Vej 73, 2nd Floor Left, 2000 Frederiksberg, DK, mail: c.graversen@rn.dk

Word count: 3373 words

Abstract

Objective: to evaluate the association between socio-economic status (SES) and referral to cardiac rehabilitation (CR) after incident acute coronary syndrome (ACS) by dividing the referral process into three phases (1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting).

Design: Cross-sectional study.

Setting: Department of Cardiology at a Danish University Hospital from 1 January 2011 to 31 December 2014.

Participants: A total of 1229 patients assessed for CR during hospitalisation with ACS were prospectively registered in the Rehab-North Register from 2011-2014. SES was assessed using data from national registers, concerning: personal income, occupational status, educational level, and civil status. Patients were excluded if in one of the following criteria were fulfilled: 1) missing data on SES, or 2) acceptable reason for not informing patients about CR (treatment with coronary artery bypass graft, transfer to another hospital, still under treatment, or death).

Main outcome measures: Outcomes were defined by dividing the referral process into three phases: 1. informed about CR, 2. willingness to participate, and 3. assigned CR setting (in-hospital /community centre) after ACS.

Results: A total of 854 (69.5 %) patients were referred to CR. After adjustment for age, gender, ACS diagnosis (ST-Elevated Myocardial Infarction, Non-ST-Elevated Myocardial Infarction, Unstable Angina Pectoris) and comorbidity, high income had the strongest association of referral to CR in all three phases (informed about CR: OR 2.17, 95% CI: 1.0- 4.64; willingness to participate in CR: OR 1.55, 95% CI: 1.02-2.35; assigned in-hospital CR: OR 1.47, 95% CI: 0.91-2.36). Educational level showed similar tendencies, however not statistically significant. The results did not vary according to gender.

Conclusion: This is the first study to investigate the referral process to CR using a three-phase structure. It suggests income and education to influence all phases in the referral process to CR after ACS.

Keywords: Acute Myocardial Infarction, Cardiac Rehabilitation, Referral Process, Socio-economic Status

Strengths and limitations of this study

- This is the first study to investigate the referral process to cardiac rehabilitation (CR) using a three-phase structure (1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting) which provides better knowledge in understanding why social inequality persists in referral to CR.
- Socio-economic variables were provided by highly validated Danish register data using the unique 10-digit civil registration number that is given to all Danish citizens.
- Multivariable logistic regression analyses were used to minimise potential confounding.
- Data was not gathered for specific scientific purposes and it cannot be ruled out that not all patients admitted with Acute Coronary Syndrome were identified. However, such loss was considered unsystematic and unintended and should not pose a problem for bias introduction.

Introduction

Low socio-economic status (SES) is associated with higher risk of developing Ischemic Heart Disease (IHD) and poorer subsequent outcome, including higher risk of recurrent cardiovascular events and cardiac-related mortality.(1–5) Cardiac rehabilitation (CR) is an important step to reduce disease outcomes and is an integral part of IHD care as it aims to improve quality of life as well as patients' physical, psychological, and social functioning.(4)

CR comprises exercise therapy, psychological consulting, treatment-targeted therapy, and life-style changing modules (dietary modification, and smoking cessation).(4) The program is a coordinated effort made by cardiologists, nurses, physiotherapists, dietitians, and eventually occupational therapists. If needed, psychologists, social workers, or priests may be included as well.(4)

The efficacy of CR in reducing cardiovascular mortality and risk of hospital readmissions is well-documented.(6–8) It therefore seems irrational that international research in general continues to find CR "referral" or "participation and completion" rates to be unsatisfactory.(9–13)

Different socio-economic characteristics (income, educational level, occupational status, civil status) are shown to be associated with CR underutilization.(14) Low income and educational level have irrespectively of type of health care system repeatedly been associated with limited participation and completion rate.(11,15) It is consequently of major importance to eliminate the socio-economic differences in CR if the inequality in IHD burden is to be reduced.

Obstacles in referral and participation to CR among patients with lower SES may be due to system-level and personal barriers.(16) System-level barriers covers physicians recommendations, the interaction with the healthcare team, and misconceptions about CR. Personal barriers includes perception about IHD and CR, and belief about the ability to control IHD.(16) However, vulnerable elements in the referral process prone to socio-economic inequality among patients with Acute Coronary Syndrome (ACS) remain unexplored. By dividing the referral process into three phases, it is possible to evaluate if such inequality is the result of selection of patients at the system-level (the process of informing patients about CR and the setting of CR that patients are referred to) rather than the person-level (patients' own willingness to participate in CR). To our knowledge, no study has analysed the entire referral process using such three-phase structure while controlling for confounders in a population of patients surviving ACS. Therefore, the objective of this study was to investigate how SES is associated with the patients' chances of 1) being informed about CR, 2) willingness to participate, and 3) assigned CR setting (in-hospital or community centre). Phase 3 was determined by regional guidelines: patients suffering ST-Elevated Myocardial Infarction (STEMI) or complicated Non-ST-Elevated Myocardial Infarction (NSTEMI) were offered in-hospital CR whereas patients with uncomplicated NSTEMI and Unstable Angina Pectoris (UAP) were offered CR in a community centre).

Methods

The study followed the STROBE guidelines for cross-sectional studies.(17)

Study design

This population-based study used data from the Rehab-North Register. Its content has previously been described.(18) In short, the Rehab-North Register holds data on all patients hospitalised at the Department of Cardiology, Aalborg University Hospital from 1 January 2011 to 31 December 2014 with a diagnosis of ACS. All were assessed for eligibility to CR using a questionnaire.(18)

In Denmark, CR fully or partially takes place in-hospital or at community centres. In-hospital CR is reserved for high-risk patients and is structured with a more complex intervention. The Danish Public Health System is tax paid, enabling CR to be free of charge for the patient.

Patient and Public involvement statement

No patients were involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study Population

The study population was identified in the Rehab-North Register as patients diagnosed with ACS (ICD-10: I20.0, I21.). The registered diagnosis was verified by linking data from the Rehab-North Register with the Danish National Patient Register (NPR) and the Danish Register of Causes of Death.(19) If any discrepancy arose, the diagnosis registered in the NPR was selected. Patients were excluded if in one of the following criteria were fulfilled: 1) missing data on SES 2) acceptable reason for not informing patients about CR, including treatment with coronary artery bypass graft, transfer to another hospital, still under treatment, or death. Patients who underwent coronary artery bypass grafting was informed about CR at the Thoracic Surgery Department performing the operation. Patients who were 'transferred

to another hospital' received information about CR at other cardiology departments. We were not able to receive confirmation regarding referral to CR in this patient group.

The study population and referral design using three phases is illustrated in figure 1.

Socio-economic status

Different indicators of SES (personal income, occupational status, educational level, and civil status) were chosen, due to a priori knowledge about their proposed mechanisms associated to the outcome variable. Ascertainment of socio-economic variables from national registers was done by linkage of a unique personal number given to all Danish residents.

The Income Statistics Register provided information regarding both disposable personal income (low, medium, high) calculated for the calendar year before disease onset, and occupational status (employed, unemployed/out of workforce) set for the calendar year before disease onset.(20) A person's highest obtained educational level (low, medium, high) was based on the International Standard Classification of Education (ISCED)(21) from the Student's Register(22), and civil status (married/partnership, divorced/unmarried /widow) from the Civil Registration System (CRS).(23)

Outcomes

Outcomes were defined by dividing the referral process into three phases: 1. informed about CR, 2. willingness to participate, and 3. assigned CR setting (in-hospital /community centre) after ACS.

All outcome information gathering were done during the patients' hospitalisation and included in the questionnaires that founded the Rehab-North Register.

Covariates

The selection of covariates to be included in the multivariable analyses was done based on directed acyclic graph (not shown). Age was registered at time of diagnosis and categorized into three groups: < 65 years, 65-74 years, and ≥ 75 years. Information regarding age and gender was gathered from the CRS.(23) Comorbidity diagnoses were defined by the Charlson Comorbidity Index (CCI), but only

diagnoses from the year 2011 until hospitalisation were accessible. Comorbidity diagnoses was drawn from the NPR.(24) In general, patients with NSTEMI and UAP are less likely referred to CR compared to patients with STEMI.(25) Therefore, to get an accurate estimate of the impacts of patients' SES on CR referral, ACS diagnosis (STEMI, NSTEMI, UAP) were included as a covariate.(25)

Statistical analysis

Baseline characteristics of study population were summarised by frequencies and percentages. The association between socio-economic variables and being informed about CR, willingness to participate, and assigned CR setting was assessed by crude (model 1) and multivariable logistic regression adjusted for confounders (age, gender, ACS diagnosis, CCI) (model 2). Results were presented in odds ratios (OR) with 95% confidence intervals (95% CI). Potential effect modification by gender was assessed by stratification and likelihood-ratio tests as studies have found females to experience lower rates of referral to CR compared to males.(10,26) Statistical analyses were performed using Stata Software (v.15.1; Stata Corp. College Station, TX).

Results

Of the original cohort of 1822 patients diagnosed with ACS, only patients with no missing socio-economic variables, and no acceptable reasons for not being informed about CR were included in the study (figure 1). This resulted in a study population comprising 1229 patients (73.8% male). The patients' baseline characteristics, stratified by diagnosis, are presented in table 1. STEMI patients were relatively younger and still an available workforce with higher income. In the study population, 1123 (91.4%) patients were informed about CR of which 854 (76.0%) patients subsequently agreed to participate in the program. Of those, 349 (40.9%) patients were referred to CR in a community centre and 505 (59.1%) patients were referred to in-hospital CR (figure 1).

Table 1: Characteristics of study population stratified by diagnosis

Characteristics	Full population n = 1229	STEMI n = 402	NSTEMI n = 711	UAP n = 116
Male (n, %)	907 (73.8)	322 (80.1)	503 (70.7)	82 (70.7)
Age Group (years)				
< 65	591 (48.1)	227 (56.5)	308 (43.3)	56 (48.3)
65-74	371 (30.2)	116 (28.9)	215 (30.2)	40 (34.5)
≥ 75	267 (21.7)	59 (14.7)	188 (26.4)	20 (17.2)
Civil status (n, %)				
Married/Partnership	793 (64.5)	253 (62.9)	449 (63.2)	91 (78.4)
Divorced/Unmarried/Widow	436 (35.5)	149 (37.1)	262 (36.8)	25 (21.6)
Occupational status (n, %)				
Employed	479 (39.0)	195 (48.5)	240 (33.8)	44 (37.9)
Unemployed/out of workforce	750 (61.0)	207 (51.5)	471 (66.2)	72 (62.1)
Educational level (n, %)				
Low	516 (42.0)	144 (35.8)	322 (45.3)	50 (43.1)
Medium	539 (43.9)	201 (50.0)	293 (41.2)	45 (38.8)
High	174 (14.2)	57 (14.2)	96 (13.5)	21 (18.1)
Income, tertile (n, %)				
Low	405 (33.0)	113 (28.1)	251 (35.3)	41 (35.3)
Medium	406 (33.0)	124 (30.8)	247 (34.7)	35 (30.2)
High	418 (34.0)	165 (41.0)	213 (30.0)	40 (34.5)
Charlson Comorbidity Index				
Low (0 points)	1088 (88.5)	358 (89.1)	630 (88.6)	100 (86.2)
Moderate/High (>0 points)	141 (11.5)	44 (10.9)	81 (11.4)	16 (13.8)

STEMI: ST-elevated myocardial infarction; NSTEMI: non-ST-elevated myocardial infarction; UAP: unstable angina pectoris

Phase 1: SES and being informed about CR

Higher income and educational level had positive crude associations with being informed about CR whereas being unemployed/out of workforce or single-living had a negative association (table 2). These associations were greatly reduced after adjustment for age, gender, ACS diagnosis, and CCI. The adjusted regression analysis found high income to be associated with being informed about CR (OR 2.17, 95% CI: 1.01; 4.64). High educational level was also associated with being informed about CR although the association did not reach statistical significance (OR: 1.60, 95% CI: 0.72-3.54).

Table 2: Logistic regression model for being informed about cardiac rehabilitation, n = 1229

	Full study population	Informed about CR	Unadjusted		Multivariable adjusted*	
	n, (%)	n, (%)	OR	95% CI	OR	95% CI
Observations	1229 (100)	1123 (91.4)				
Civil status						
Married/Partnership	793 (64.5)	735 (59.8)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	436 (35.5)	388 (31.6)	0.64	0.43-0.95	0.76	0.49-1.19
Occupational status						
Employed	479 (39.0)	469 (38.2)	1 (ref.)		1 (ref.)	
Unemployed/out of workforce	750 (61.0)	654 (53.2)	0.15	0.07-0.28	0.46	0.20-1.07
Educational level						
Low	516 (42.0)	452 (36,8)	1 (ref.)		1 (ref.)	
Medium	539 (43.9)	505 (41.1)	2.10	1.36-3.25	1.17	0.72-1.89
High	174 (14.2)	166 (13.5)	2.94	1.38-6.26	1.60	0.72-3.54
Income, tertiles						
Low	405 (33.0)	342 (27.8)	1 (ref.)		1 (ref.)	
Medium	406 (33.0)	374 (30.4)	2.15	1.37-3.38	1.40	0.86-2.28

High	418 (34.0)	407 (33.1)	6.82	3.54-13.14	2.17	1.01-4.64

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Phase 2: SES and willingness to participate in CR

High income, high educational level, and being single-living (divorced/unmarried/widow) were all associated with a higher likelihood of willingness to participate in CR in the crude analyses (table 3). Being unemployed/retired was negatively associated with being willing to participate in CR. After adjustment, high income level had the highest OR (OR 1.55, 95% CI: 1.02; 2.35) in relation to willingness to participate. A similar pattern was observed for high educational level although the association was not statistically significant (OR 1.21, 95% CI: 0.78; 1.88). Likewise, being single-living was also associated with willingness to participate in CR, although, the estimates did not reach statistical significance (OR 1.28, 95% CI: 0.93; 1.76).

Table 3: Logistic regression model for willingness to participate in cardiac rehabilitation, n = 1123

	Full study population	Willingness to participate in CR	Unadjusted		Multivariable adjusted*	
	n, (%)	n, (%)	OR	95% CI	OR	95% CI
Observations	1229 (100)	854 (76.0)				
Civil status						
Married/Partnership	793 (64.5)	546 (48.6)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	436 (35.5)	308 (27.4)	1.33	0.99-1.79	1.28	0.93-1.76
Occupational status						
Employed	479 (39.0)	388 (34.6)	1 (ref.)		1 (ref.)	
Unemployed/out of workforce	750 (61.0)	466 (41.5)	0.52	0.39-0.69	0.93	0.62-1.40
Educational level						
Low	516 (42.0)	322 (28.7)	1 (ref.)		1 (ref.)	
Medium	539 (43.9)	405 (36.1)	1.64	1.21-2.20	1.36	0.98-1.88

High	174 (14.2)	127 (11.3)	1.31	0.87-1.99	1.21	0.78-1.88
Income, tertiles						
Low	405 (33.0)	229 (20.4)	1 (ref.)		1 (ref.)	
Medium	406 (33.0)	288 (25.6)	1.65	1.19-2.30	1.35	0.94-1.94
High	418 (34.0)	337 (30.0)	2.38	1.69-3.34	1.55	1.02-2.35

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Phase 3: SES and assigned CR setting

Table 4 shows the association of SES on being assigned to in-hospital CR compared to CR in a community centre. High income was significantly associated with assignment to in-hospital CR (OR: 2.10, 95% CI: 1.49; 2.97) but the association was attenuated after adjustment for confounders (income: adjusted OR: 1.47, 95% CI: 0.91; 2.36).

Table 4: Logistic regression model for assigned cardiac rehabilitation setting, n = 854

	Full study population	Assigned CR-setting	Unadjusted		Multivariable adjusted*	
	n, (%)	n, (%)	OR	95% CI	OR	95% CI
Observations	1229 (100)	505 (59.1)				
Civil status						
Married/Partnership	793 (64.5)	317 (37.1)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	436 (35.5)	188 (22.0)	1.13	0.85-1.51	1.20	0.84-1.69
Occupational status						
Employed	479 (39.0)	268 (31.4)	1 (ref.)		1 (ref.)	
Unemployed/out of workforce	750 (61.0)	237 (27.8)	0.46	0.35-0.61	0.75	0.49-1.15
Educational level						
Low	516 (42.0)	177 (20.7)	1 (ref.)		1 (ref.)	
Medium	539 (43.9)	248 (29.0)	1.29	0.96-1.74	0.90	0.63-1.30

High	174 (14.2)	80 (9.4)	1.39	0.91-2.13	1.20	0.72-1.99
Income, tertiles						
Low	405 (33.0)	115 (13.5)	1 (ref.)		1 (ref.)	
Medium	406 (33.0)	161 (18.9)	1.26	0.89-1.78	1.14	0.73-1.78
High	418 (34.0)	229 (26.8)	2.10	1.49-2.97	1.47	0.91-2.36

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

Supplementary analyses

The analyses were stratified by gender in a supplementary analysis. The results were not substantially different from the main analysis (not shown).

The baseline characteristics of patients being excluded from the study population was obtained (online supplementary material, table 1). After multivariable logistic regression, patients being excluded from the study population to have significantly lower SES compared to the patients being included (online supplementary material, table 2).

Discussion

In this study, the referral process to CR was assessed using a three-phase structure: 1. informed about CR, 2. willingness to participate in CR, and 3. assigned CR setting. After adjustment, high income was the only variable statistical significantly associated with referral to CR in phase 1 and 2, and insignificantly associated with phase 3 of the referral process. High educational level had a similar pattern, but the association did not reach statistical significance.

Overall, 69.5% of the patients were referred to CR, which is in accordance with earlier findings (22-81.5%).(9,10,25,26) Notably, in one study strikingly 86% was referred to CR after usage of a social differentiated intervention program.(27) However, it would be difficult to reproduce such a result in an observational study without this specific purpose.

The finding of patients' income and educational level to be associated with all three phases the referral process to CR may be explained by 'the Nordic Paradox' observed in the Nordic European

countries.(28,29) These countries, covering Denmark, Norway, Sweden, and Finland, are 'welfare states' with equal access to health care which theoretically ought to diminish the importance of patients' level of income and education regarding access to health care services. However, this is not the case as inequality e.g. in mortality, persists.(29) Although income inequality is smaller in the Nordic countries, this still covers over inequality in wealth, housing condition, and material living conditions, and are used together with educational level to assess latent socio-economic factors (health literacy, greater burden of behavioral and biological risk factors, and reduced access to quality care and medication).(30) Thus, our finding may imply such latent socio-economic factors to be important in the referral process to CR.

We found single-living to be potentially associated with the willingness to participate in CR. If such an association is reproducible in later studies, then attention should focus on these patients without a partner, who less often receive referral to CR, which has been attributed to lack of social support.(31)

International studies find younger age, male gender, living with a partner, high educational level, and high gross income to be predictors of CR referral.(10,25,31) This inequality in CR referral causes concern as participation helps patients implement needed behavioural changes, which reduces cardiac-related deaths.(6) Patients with low SES often have biological, behavioural, and psychosocial disadvantages that may accelerate risk of cardiovascular diseases. Therefore, the need of referral, attendance, and completion of CR should be prioritized in this patient group.(1,2)

By splitting the referral process into three phases, new insights regarding importance of taking patients SES into consideration when referring them to CR was gained. Our results show the importance of being aware of system-level barriers present in the referral process. Moreover, identifying those patients who need more motivation before being willing to enter a CR programme is highly important. In that way, patients are well-informed about CR and able to make a well-considered decision regarding participation.

Definition of SES is a conceptual challenge often solved by use of personal/family income, educational level, civil status, and/or occupation. There is no consensus on which parameters to use as indicators of SES. It has been argued to use single variables as proxy measurements for SES despite different causal pathways. However, others find it problematic only to estimate SES by one parameter, as this may increase the risk of residual confounding by unmeasured socio-economic circumstances.(1,32) Moreover, the effect of socio-economic variables seems rather outcome-related and is suggested not to be used interchangeably without thorough consideration.(33) As our central interest was to investigate the impact of SES on the referral process to CR, and therefore use SES as exposure variable, we a priori hypothesized the different variables all to be linked to our outcome measures. The risk of such an approach was the introduction of collinearity. However, research finds e.g. educational level, occupation, and income to measure different phenomena, to have different causal mechanisms, and in part to be explained by other socio-economic parameters.(33,34) Since literature finds income, educational level, occupational status, and civil status to be important determinants for referral, participation, and completion of CR, it seemed most appropriate to include all variables in order to answer our research questions. The consequence of this approach was that we cannot get a single estimate that illustrates the effect of SES.

Some caution must be taken when interpreting the results of our study. Firstly, data was not gathered for specific scientific purposes and it cannot be ruled out that some patients admitted with ACS were not included in the Rehab-North Register. However, such loss was considered unsystematic and unintended and should not pose a problem for bias introduction. Moreover, the non-response analysis found excluded patients to have lower SES compared to the included study population. As exclusion was due to clinical implications (patients were to receive CR referral elsewhere), this should not pose a problem for participation bias introduction in our study population.

Secondly, use of register data minimized risk of information bias, due to nationwide good algorithms for correct diagnosis coding. Despite linkage to other registers, risk of residual or unmeasured confounding

may be present.(35) Thirdly, there may be a risk of residual or unaccounted confounding, if data on confounding variables was not classified with adequate precision. The CCI variable may be inaccurate which is caused by the limited timeframe for inclusion of comorbidities. This increases the risk of unaccounted confounding and should be taken into consideration when interpreting the results. Participation and completion rates of in-hospital CR and CR in community centres remained unexplored as our study only focused on the referral process to CR.

Conclusion

High income and educational level were associated with a larger chance of being informed about CR, willingness to participate in CR, and assigned in-hospital CR in patients with ACS.

Acknowledgements: None

Contributorship statement: CBG, RE, and MLL contributed to study design and acquisition of the data. CBG, MBJ, and MLL analysed and interpreted the data. SPJ, SR, and THO contributed to interpretation. CBG drafted the initial manuscript and all authors critically revised the manuscript and gave final approval.

Ethics: The study is approved by the Danish Data Protection Agency (project number: 2008-58-0028) and the Danish Patient Safety Authority (3-3013-2763/1). In Denmark, no written consent is needed for use of such register-based data.

Funding: This work was supported by the Karen Elise Jensen's Foundation, and the Danish Heart Foundation grant number: 18-R123-A8283-22081. The funders had no role in planning or conducting the study.

Competing interest: None declared

Data sharing statement: No data are available. Danish law dictates data access only to be available to researchers directly responsible for study conduction.

References

1. Havranek EP, Mujahid MS, Barr DA, Blair I V., Cohen MS, Cruz-Flores S, et al. Social determinants of risk and outcomes for cardiovascular disease: A scientific statement from the American Heart Association. Circulation. 2015;132(9):873–98.

2. Schultz WM, Kelli HM, Lisko JC, Varghese T, Shen J, Sandesara P, et al. Socioeconomic Status and Cardiovascular Outcomes. Circulation. 2018;137(20):2166–78.

3. Ohm J, Skoglund PH, Discacciati A, Sundström J, Hambraeus K, Jernberg T, et al. Socioeconomic status predicts second cardiovascular event in 29,226 survivors of a first myocardial infarction. Eur J Prev Cardiol. 2018;25(9):985–93.

4. Piepoli MF, Corra U, Adamopoulos S, Benzer W, Bjarnason-wehrens B, Cupples M, et al. Secondary prevention in the clinical management of patients with cardiovascular diseases . Core components , standards and outcome measures for referral and delivery. Eur J Prev Cardiol. 2014;21(6):664–81.

5. Rasmussen JN, Rasmussen S, Gislason GH, Buch P, Abildstrom SZ, Køber L, et al. Mortality after acute myocardial infarction according to income and education. J Epidemiol Community Health. 2006;60(4):351–6.

6. Anderson L, Oldridge N, Thompson DR, Zwisler A-D, Rees K, Martin N, et al. Exercise-Based Cardiac Rehabilitation for Coronary Heart Disease. J Am Coll Cardiol. 2016;67(1):1–12.

7. Anderson LJ, Taylor RS. Cardiac rehabilitation for people with heart disease: An overview of Cochrane systematic reviews. Int J Cardiol. 2014;177(2):348–61.

8. Rauch B, Davos CH, Doherty P, Saure D, Metzendorf MI, Salzwedel A, et al. The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: A systematic review and meta-analysis of randomized and non-randomized studies - The Cardiac Rehabilitation Outcome Study (CROS). Eur J Prev Cardiol. 2016;23(18):1914–39.

9. Sumner J, Grace SL, Doherty P. Predictors of Cardiac Rehabilitation Utilization in England : Results From the National Audit. J Am Heart Assoc. 2016;5:1–8.

10. Colella TJ, Gravely S, Marzolini S, Grace SL, Francis JA, Oh P, et al. Sex bias in referral of women to outpatient cardiac rehabilitation? A meta-analysis. Eur J Prev Cardiol. 2015;22(4):423–41.

11. Martin B-J, Hauer T, Arena R, Austford LD, Galbraith PD, Lewin a. M, et al. Cardiac Rehabilitation Attendance and Outcomes in Coronary Artery Disease Patients. Circulation. 2012;126(6):677–87.

12. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2016;37(29):2315–81.

13. Smith SC, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011;124(22):2458–73.

14. Gaalema DE, Elliott RJ, Morford ZH, Higgins ST, Ades PA. Effect of Socioeconomic Status on Propensity to Change Risk Behaviors Following Myocardial Infarction : Implications for Healthy Lifestyle Medicine. Prog Cardiovasc Dis. 2017;60(1):159–68.

15. Nielsen KM, Faergeman O, Foldspang A, Larsen ML. Cardiac rehabilitation: Health characteristics and socio-economic status among those who do not attend. Eur J Public Health. 2008;18(5):479–83.

16. Neubeck L, Freedman S Ben, Clark AM, Briffa T, Bauman A, Redfern J. Participating in cardiac rehabilitation: A systematic review and meta-synthesis of qualitative data. Eur J Prev Cardiol. 2012;19(3):494–503.

17. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–9.

18. Graversen CB, Eichhorst R, Ravn L, Christiansen SR, Johansen MB, Larsen ML, et al. Social inequality and barriers to cardiac rehabilitation in the rehab-North register. Scand Cardiovasc J. 2017;51(6):316–22.

19. Madsen M, Davidsen M, Rasmussen S, Abildstrom SZ, Osler M. The validity of the diagnosis of acute myocardial infarction in routine statistics: A comparison of mortality and hospital discharge data with the Danish MONICA registry. J Clin Epidemiol. 2003;56(2):124–30.

20. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments. Scand J Public Health. 2011;39(7):103–5.

21. Eurostat Statistics Explained. International Standard Classification of Education (ISCED) [Internet]. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php/International_Standard_Classification_of_Education_%28ISCED%29

22. Jensen VM, Rasmussen a. W. Danish education registers. Scand J Public Health. 2011;39(7 Suppl):91–4.

23. Pedersen CB. The Danish Civil Registration System. Scand J Public Health. 2011;39(7 suppl):22–5.

24. Thygesen SK, Christiansen CF, Lash TL, Christensen S, Sorensen HT. Predictive value of coding of diagnoses in the charlson comorbidity index in the Danish national registry of patients. Pharmacoepidemiol Drug Saf. 2009;18 (S1):S189.

25. Brown TM, Hernandez AF, Bittner V, Cannon CP, Ellrodt G, Liang L, et al. Predictors of Cardiac Rehabilitation Referral in Coronary Artery Disease Patients. Findings From the American Heart Association's Get With The Guidelines Program. J Am Coll Cardiol. 2009;54(6):515–21.

26. Colbert JD, Martin B-J, Haykowsky MJ, Hauer TL, Austford LD, Arena RA, et al. Cardiac rehabilitation referral, attendance and mortality in women. Eur J Prev Cardiol. 2014;22(8):979–86.

27. Meillier LK, Nielsen KM, Larsen FB, Larsen ML. Socially differentiated cardiac rehabilitation: Can we improve referral, attendance and adherence among patients with first myocardial infarction? Scand J Public Health. 2012;40(3):286–93.

28. Mackenbach JP. The persistence of social inequalities in modern welfare states: the explanation of a paradox. Soc Sci Med. 2012;75:761–9.

29. Mackenbach JP. Nordic paradox, Southern miracle, Eastern disaster: Persistence of inequalities in mortality in Europe. Eur J Public Health. 2017;27:14–7.

30. Tromp J, Collins S. Universal healthcare but not universal access? Eur J Prev Cardiol. 2019;27(1);75-8.s

31. Cortés O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: A systematic review. Am Heart J. 2006;151(2):249–56.

32. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Smith GD. Indicators of socioeconomic position (part 1). J Epidemiol Community Health. 2006;60(1):7–12.

33. Geyer S, Hemström Ö, Peter R, Vågerö D. Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. J Epidemiol Community Health. 2006;60(9):804–10.

34. Lahelma E, Martikainen P, Laaksonen M, Aittomäki A. Pathways between socioeconomic

determinants of health. J Epidemiol Community Health. 2004;58(4):327–32.

35. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National patient registry: A review of content, data quality, and research potential. Clin Epidemiol. 2015;7:449–90.

Figure legends:

Figure 1: Flowchart of the referral process to cardiac rehabilitation.
STEMI: ST-Elevated-Myocardial Infarction, NSTEMI: Non-ST-Elevated-Myocardial Infarction, UAP: Unstable Angina Pectoris, CR: Cardiac rehabilitation, CABG: Coronary artery bypass graft, SES: Socio-economic Status

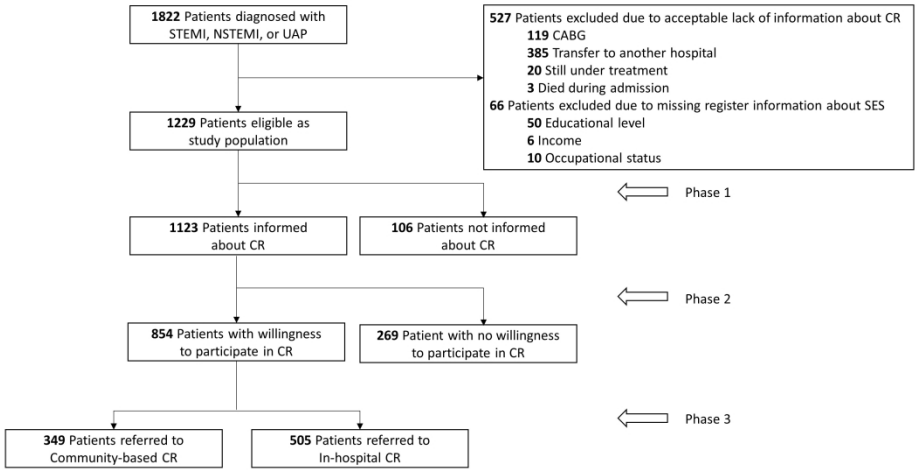


Figure 1: Flowchart of the referral process to cardiac rehabilitation.
STEMI: ST-Elevated-Myocardial Infarction, NSTEMI: Non-ST-Elevated-Myocardial Infarction, UAP: Unstable Angina Pectoris, CR: Cardiac rehabilitation, CABG: Coronary artery bypass graft, SES: Socio-economic Status

338x190mm (300 x 300 DPI)

ONLINE SUPPLEMENTARY MATERIAL

Table S1: Baseline Characteristics of excluded patients

	Excluded
Characteristics	n = 593
Male (n, %)	423
Age Group (years)	
< 65	242
65-74	171
≥ 75	180
Civil status (n, %)	
Married/Partnership	378
Divorced/Unmarried/Widow	>210
Missing	<5
Occupational status (n, %)	
Employed	158
Unemployed/out of workforce	417
Missing	18
Educational level (n, %)	
Low	256
Medium	200
High	52
Missing	72
Income, tertile (n, %)	
Low	245
Medium	197
High	>145
Missing	<5
Charlson Comorbidity Index	
Low (0 points)	421
Moderate/High (>0 points)	75
Missing	97

Table S2: Logistic regression model for those excluded compared with those included in the study population, n = 1822

		Unadjusted		Multivariable adjusted*	
	n, (%)	OR	95% CI	OR	95% CI
Observations	593 (32.5)				
Civil status					
Married/Partnership	378 (20.7)	1 (ref.)		1 (ref.)	
Divorced/Unmarried/Widow	>210 (>11.5)	1.02	0.83-1.25	0.85	0.67-1.07
Missing	<5 (<1)				
Occupational status					
Employed	158 (8.7)	1 (ref.)		1 (ref.)	
Unemployed/Retired	417 (22.9)	1.69	1.36-2.09	1.54	1.14-2.08
Missing	18 (1.0)				
Educational level					
Low	256 (14.1)	1 (ref.)		1 (ref.)	
Medium	200 (10.1)	0.77	0.61-0.96	0.77	0.61-0.97
High	49 (2.7)	0.59	0.42-0.84	0.60	0.41-0.87
Missing	72 (4.0)				
Income, tertiles					
Low	245 (13.4)	1 (ref.)		1 (ref.)	
Medium	197 (10.8)	0.71	0.56-0.90	0.77	0.59-1.01
High	>145 (>7.9)	0.46	0.36-0.59	0.55	0.40-0.75
Missing	<5 (<0.3)				

* Adjusted for age, gender, ACS diagnosis, Charlson Comorbidity Index. OR: odds ratio; CI: confidence interval

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	7-8
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6+8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-12
		(*b*) Report category boundaries when continuous variables were categorized	9-12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.