Scandinavian Journal of Public Health, 1–8

ORIGINAL ARTICLE

Effects of screening for anxiety and depression in patients with ischaemic heart disease – a nationwide Danish register study

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Abstract

Aim: To investigate the effect of screening for anxiety and depression (AD) in patients with ischaemic heart disease (IHD) on the likelihood of receiving treatment for AD. *Methods:* We used a nationwide dataset of all Danish patients with an incident IHD diagnosis in the period 2015–2018 (N = 80,701) of which 20,461 (25%) were exposed to screening for AD as part of cardiac rehabilitation. A binary composite indicator for the use of any AD treatment (prescriptions of AD drugs, general practitioner (GP) counselling or referral to a psychologist), was modelled as the dependent variable. The probability of receiving AD treatment was estimated using linear probability and instrumental variable regression models. *Results:* Exposure to AD screening was lower for patients with low income (change in probability −0.67, 95% CI −0.76; −0.59), low education (change in probability −0.16, 95% CI −0.20; −0.13), and a high comorbidity burden (change in probability −0.09, 95% CI −0.10; −0.07). Screened patients had a lower conditional probability of AD treatment (change in probability −0.0061, $p < 0.001$) than non-screened patients. The patient's GP also had an impact on the probability of being referred for AD treatment. Using an instrumental variable approach did not affect the results. ***Conclusions:*** **Screening for AD was subject to selection at the patient level; patients at lower risk of AD had a higher probability of being screened. Hence, extending systematic screening to cover a larger population may not achieve a noticeable increase in the uptake of AD treatment if it is not supported by appropriate measures to reduce reverse selection into screening.**

Keywords: *Ischaemic heart disease, cardiac rehabilitation, anxiety, depression, screening, selection*

Introduction

A large share of patients with ischaemic heart disease (IHD) suffer from anxiety, depression or both (AD), some studies find that up to a third of IHD patients have symptoms of AD [1-4]. Studies show that these patients are at increased risk of dropout from cardiac rehabilitation [3,5], have more difficulty returning to work [6], and are at higher risk of morbidity and mortality [1,2]. Despite these increased risks, few IHD patients with symptoms of AD received adequate psychological or medical treatment.

Danish national guidelines, guidelines of the European Society of Cardiology, and the American Heart Association recommend that patients with a diagnosis of IHD are systematically screened for symptoms of AD [7-9]. National clinical guidelines, issued by the Danish Health Authority in 2013 and updated in 2015, recommend that patients with IHD – as part of cardiac rehabilitation (CR) – should be screened for symptoms of AD using a validated questionnaire, for example, the Hospital Anxiety and Depression Scale (HADS) [10]. The guidelines recommend that all patients should be informed about

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Date received 15 July 2021; reviewed 14 December 2021; accepted 24 December 2021

DOI: 10.1177/14034948221074972
journals.sagepub.com/home/sjp
SAGE

the results of their screening test, and in the case of a positive screening – a HADS score ⩾8 on either anxiety, depression, or both – patients are encouraged to contact their general practitioner (GP) for diagnostic assessment, and to seek further treatment if needed.

To support the implementation of screening for AD in the CR setting, a manual was developed to ensure that the screening procedure would be systematic. The manual was disseminated in 2016 to hospitals and municipalities through the Danish Heart Association, alongside short videos explaining the background, potential barriers and advantages of the systematic screening process [11]. The actual screening process is usually conducted by CR nurses at the starting point of the CR programme.

In Denmark, CR is offered by the regions as part of the publicly funded health care system. Formally, CR is offered to all patients with IHD that may benefit from rehabilitation. CR may be initiated at the hospital, however, currently in Denmark CR is increasingly becoming the responsibility of the municipalities, thus, procedures for referral and invitation to CR might vary across the country.

The aim of the present study was to investigate the effect of the screening programme for AD on patients with IHD and its effect on the likelihood of receiving treatment for elevated symptoms of AD 12 months after the screening procedure.

Methods

Data and population

The study was based on a retrospective nationwide cohort study of all patients aged 18 and above admitted to hospital with a diagnosis of IHD between January 2015 and December 2018, without any IHD hospitalisation within the past 12 months. A diagnosis of IHD was identified through the Danish National Patient Register in the period January 2015 to December 2018 using ICD-10 diagnostic codes (I20, I21,I23 I24, I25 as the main diagnosis or I21, I240, I248, I249 as a secondary diagnosis in combination with emergency admission).

Information on primary care utilisation and prescription of psychotropics was obtained from the Danish National Health Service Register and the Danish National Prescription Register, respectively. IHD patients were offered CR, which was initiated about 2–6 weeks after discharge for those who wished to participate. Screening for AD normally takes place at the onset of CR, however local variations may occur. Information on CR and the result of the screening process (i.e. HADS scores) were obtained from the Danish Cardiac Rehabilitation Database (DHRD) [12,13]. Registration of conducted screening was mandatory, while registering the actual score resulting from the screening was discretionary. Information on comorbidities were derived from the Danish National Patient Register. Information on sociodemographic variables was derived from the following registers in Statistics Denmark: the Population Register, the Income Register, and the Education Register.

Danish register data have high validity [14,15] and can be merged using the personal identification numbers. The data set was subject to neglective missing variables. The study was approved by the legal office at the University of Southern Denmark (reference number 10.302).

Dependent variable/primary endpoint

Use of AD treatment was measured by following the patients up to 12 months after their IHD diagnosis. We constructed an aggregate composite binary indicator for any AD treatment, including GP prescriptions of drugs used for the treatment of AD (ATC codes: N05B, N06A), GP counselling for AD, or GP referral to a psychologist.

Exposure variable

We used a binary indicator for whether the patient was screened with HADS. The screening test was provided only to a subgroup of IHD patients who were enrolled on a CR programme at the hospital. Only 37.3% of the IHD patients in our study were enrolled on a CR programme according to DHRD data. The share of patients screened varied across hospitals and over time consistent with the resources and effort allocated to the implementation of the programme by the respective hospitals.

Statistical analysis

Two distinct analyses were carried out. First, we investigated which patient characteristics predicted selection into the screening programme. This was analysed with a linear probability model with age, gender, living alone, national origin, income bracket, education, and comorbidity as independent variables.

Second, we examined the association between exposure to screening and the subsequent probability of treatment for AD. A rich set of confounder variables were included: age, gender, socioeconomic status (income, education, living alone, unemployed), comorbidity measures (Charlson Comorbidity Index score [16], history of diabetes, atrial fibrillation, heart failure and history of treatment for AD). GP fixed effects were included, and standard errors were

Table I. Descriptive statistics for the total IHD population (N = 80,701) over the period 2015–2018.

Variable	Total IHD population		CR population		Screened population	
Potential confounder variables		95% confidence interval		95% confidence interval		95% confidence interval
Age, mean	66.52	(66.47;66.58)	64.29	(64.20;64.38)	64.09	(63.98;64.20)
Charlson Comorbidity Index, mean	1.02	(1.01;1.03)	0.77	(0.76;0.78)	0.74	(0.73;0.75)
Non-Danish origin, percent	10.2%	(0.10;0.10)	9.3%	(0.09; 0.10)	8.5%	(0.08;0.09)
Low education, percent	31.6%	(0.31;0.32)	26.6%	(0.26;0.27)	25.4%	(0.25;0.26)
Living alone, percent	30.8%	(0.30;0.31)	25.4%	(0.25;0.26)	24.9%	(0.24;0.25)
Low income, percent	6.5%	(0.06;0.07)	3.8%	(0.04;0.04)	3.5%	(0.03;0.04)
Unemployed at index date, percent	2.8%	(0.03;0.03)	2.9%	(0.03;0.03)	2.8%	(0.03; 0.03)
Anxiety and depression treatment before index date, percent	2.5%	(0.02;0.03)	2.3%	(0.02;0.03)	2.4%	(0.02;0.03)
Cardiac comorbidity – arterial fibrillation, percent	8.1%	(0.08;0.08)	5.0%	(0.05;0.05)	5.0%	(0.05;0.05)
Cardiac comorbidity – heart failure, percent	7.1%	(0.07;0.07)	3.1%	(0.03;0.03)	2.7%	(0.02;0.03)
Diabetes, percent	10.4%	(0.10;0.11)	8.6%	(0.08;0.09)	7.9%	(0.08;0.08)
Gender – male, percent	72.6%	(0.72;0.73)	77.0%	(0.77;0.77)	77.2%	(0.77;0.78)
Endpoint						
Anxiety and depression treatment at 12 months, percent	3.1%	(0.03;0.03)	2.6%	(0.02;0.03)	2.4%	(0.02;0.03)
Exposure						
Screening for anxiety or depression	25.4%	(0.25;0.26)	68.0%	(0.67;0.68)	100.0%	(1.00; 1.00)
Cardiac rehabilitation	37.3%					
Total	80,701		30,104		20,461	

Note: Binary variables are reported as percentages and continuous variables as means. Patients younger than 30 were excluded. Low income is defined by the 10th percentile for the total Danish population. Low education is defined as having completed primary school as the longest education. Anxiety and depression treatment is defined as a composite binary measure of GP counselling, prescriptions for anxiolytics and anti-depressants or treatment by a psychologist. The 95% confidence intervals were calculated around the mean using the ci function in Stata, assuming a binomial distribution of data except for age and the Charlson Comorbidity Index where a poisson distribution was assumed.

clustered at the GP level to allow for the potential confounding effect of the GP and the potential correlation of patients registered in the same GP practice. For instance, differences in GP propensity to prescribe drugs to treat AD or refer patients to a psychologist might have had a direct effect on the study outcome. In the present study, linear probability models were preferred to logistic regressions as the latter suffer from the incidental parameter problem when applying fixed effects [17], and estimated coefficients are directly comparable with instrumental variable (IV) models.

The effect of screening captured by our linear probability model might have been affected by selection bias not captured by the included confounder variables or the fixed effects. For instance, hospital doctors may have been more likely to screen patients who showed symptoms of AD, resulting in a positive association between screening and AD treatment. As a robustness check we estimated an IV model with the proportion of patients screened at the hospital as an instrument for the probability of screening a patient. The validity of the IV model relied on two conditions: the share of patients screened at the hospital (i.e. the instrument) must be a strong predictor of the probability of screening a patient (i.e. the instrumented variables) and also it must have no direct effect on the probability of taking AD treatment (i.e. the dependent variable). Our instrument satisfied both conditions as the share of patients screened at hospital was likely to depend on the total resources allocated to IHD patients and the administrative decisions taken by hospital management, rather than by potentially unmet needs for AD treatment in IHD patients treated at hospital, as the latter are usually unknown. The strength of the instrument in predicting the probability of being screened was formally assessed by an F-test of the first stage regression obtaining an F-score >10, which indicates sufficient strength to ensure validity of the IV approach. Further validation of the IV approach is available upon request. We used Stata/SE v.16 for all analyses.

Results

The final study population included 80,701 patients; 30,104 patients (37%) were enrolled on a CR programme, of which 20,461 (25% of the IHD population or 68% of the CR population) were exposed to screening for AD. The characteristics of the total IHD population, the CR population, and the screened population are presented in Table I. The proportion of patients screened varied across hospitals and over time.

Within 12 months from their diagnosis, 3.1% of patients had received treatment for anxiety and/or depression. Of all patients, about 25% were screened for AD during our study period. The screened patients represented a subgroup of the patients enrolled in the

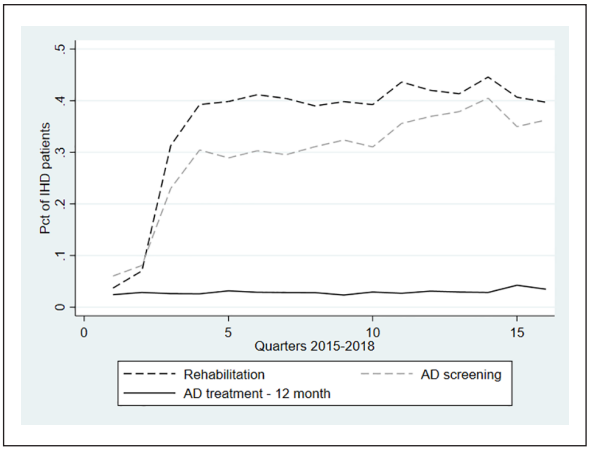

Figure 1. Time trends in rehabilitation, anxiety and depression screening and 12-month anxiety and depression treatment.

CR programme, as screening was delivered as part of the programme. The average age of all IHD patients was 66.5 years, 72.6% of the patients were male, and the average Charlson Comorbidity Index score in historical admissions was 1.02 (range 0–22). Previously, 8.1% had received atrial fibrillation, 7.1% had experienced heart failure, and 10.4% had diabetes, according to their hospital records. With respect to socioeconomic characteristics, 30.8% were living alone, 2.8% were unemployed, and 6.5% had a low income, defined as being among the 10% with the lowest income in Denmark. Of the screened patients, 31.6% had primary school as their highest educational achievement (low education). Of all patients, 10.2% had a national origin other than Denmark.

Figure 1 shows the variation over time in the percentage of patients receiving treatment for AD against the variation in the share of patients screened with HADS using calendar quarters as time units. Despite the rapid increment in the share of patients screened, the trend in treatment use remained quite flat, showing no time correlation with the former.

Table II shows the results of the linear regression model estimating the probability of receiving screening for AD. Patients aged 60–69 were more likely to be screened than younger or older patients ($p < 0.001$). Men had a higher probability of being screened (conditional change in probability 0.17 (0.13; 0.21), $p < 0.001$). Several indicators of deprived socioeconomic status were associated with a lower probability of screening: people living alone (conditional change in probability −0.20 (−0.24; −0.16), $p < 0.001$), people of an ethnic origin other than Danish (conditional change in probability −0.31 (−0.37; 0.25), $p < 0.001$), people with low education (conditional change in probability −0.16 (−0.20; −0.13), $p < 0.001$), and people with a low income (conditional change in probability −0.67 (−0.76; −0.59), $p < 0.001$). Except for diabetes, which was not statistically significant, all comorbidities impacted negatively on the probability of screening: Charlson Comorbidity Index (conditional change in probability −0.9 (−0.10; −0.07), $p < 0.001$), atrial fibrillation (conditional change in probability −0.29 (−0.37; −0.22), $p < 0.001$), and heart failure (conditional change in probability −0.82 (−0.92; −0.72), $p < 0.001$).

Table III reports the effect of screening for AD on the probability of receiving AD treatment, estimated by our statistical models. Columns 1–3 report the results from three different specifications of the linear probability model including an increasingly larger set of covariates. Column 1 includes the minimum set of covariates in order to capture the full association between screening and treatment. Column 2 includes controls for socioeconomic characteristics. Column 3 adds controls for GP fixed effects. Column 6, which includes the results of IV model, displays similar results to Column 3. Remarkably, the effect of screening on treatment was very small (conditional change in probability less than 1%, $p < 0.01$) and negative across all model specifications, showing that patients exposed to screening were less likely to obtain treatment than patients who were not screened. Different models produced similar predictions in terms of the patient characteristics associated with treatment: male patients and patients living alone were less likely to receive treatment. Among the socioeconomic characteristics examined, low income was negatively associated with treatment after controlling for GP fixed effects, suggesting that patients with a low income were less likely to receive treatment. Other characteristics, such as education, unemployment, and marital status were not associated with the treatment in any of our model specifications. Finally, our fixed effect model (Model 3) showed that around 12% of the total variance in treatment could be explained by variation at the level of the patient's GP. This suggests that GPs might play an important role in whether a patient is offered and agrees to engage in treatment, although the patient has to take the first step and contact their GP for advice.

Table IV focuses on treatment for the screened population only. Patients that are screened receive an AD score that indicates the need for treatment. Scores above 7 usually indicate a need for treatment. About half of the screened population had no registered HADS score, hence Table IV only comprises 11,979 patients.

Table IV shows that 156 (6%) of the 2563 screened patients with a HADS >8 received treatment for AD, although treatment guidelines recommend otherwise.

Table II. Regression on the probability of being exposed to screening for anxiety and depression. $N = 80{,}701$.

Dependent variable: Anxiety and depression screening	Regression coefficient	*p*-value	CI lower	CI upper
Age -49	−0.10	0.0010	−0.1602	−0.0388
Age (50–59)	−0.08	0.0030	−0.1275	−0.0255
Age (60–69) (reference)				
Age (70–79)	−0.06	0.0100	−0.1041	−0.0138
Age (80 -)	−0.76	0.0000	−0.8297	−0.6890
Gender – male	0.17	0.0000	0.1311	0.2099
Living alone	−0.20	0.0000	−0.2398	−0.1628
Ethnicity other than Danish	−0.31	0.0000	−0.3711	−0.2537
Low income	−0.67	0.0000	−0.7593	−0.5870
Low education	−0.16	0.0000	−0.2024	−0.1259
Unemployed	0.00	0.9630	−0.1086	0.1035
Charlson Comorbidity Index	−0.09	0.0000	−0.1022	−0.0689
Cardiac comorbidity – atrial fibrillation	−0.29	0.0000	−0.3675	−0.2208
Diabetes	0.02	0.4920	−0.0442	0.0920
Cardiac comorbidity – heart failure	−0.82	0.0000	−0.9177	−0.7233
Constant	−0.59	0.0000	−0.6460	−0.5326

Note: Low income defined by the 10th percentile for the total Danish population. Low education is defined as having completed primary school as the longest education.

Table III. Regression on the probability of using mental health treatment after an IHD diagnosis. $N = 80{,}701$, number of GPs = 2,115.

Dependent variable: Anxiety and depression treatment 12 months after IHD diagnosis	Linear probability			IV¶
	1	2	3	4
Anxiety and depression screening	−0.0076***	−0.0059***	−0.0061***	−0.0067***
Age -49	0.0057*	0.0076*	0.0089***	0.0078*
Age (50–59)	0.0037*	0.0045*	0.0044*	0.0043*
Age (60–69) (reference)	–	–	–	–
Age (70–79)	0.0001	−0.0014	−0.0008	−0.0014
Age (80 -)	0.0104***	0.0079*	0.0085***	0.0078*
Gender – male	−0.0089***	−0.0101***	−0.0104***	−0.0101***
Living alone		−0.0036*	−0.0032*	−0.0035*
Ethnicity other than Danish		0.0033	0.0056*	0.0033
Low income		−0.0046	−0.0058*	−0.0044
Low education		0.0004	0.0001	0.0003
Unemployed		0.0004	0.0035	0.0007
Charlson Comorbidity Index		0.0072***	0.0074***	0.0072***
Cardiac comorbidity – atrial fibrillation		0.0122***	0.0117***	0.0122***
Diabetes		−0.0019	−0.0019	−0.0021
Cardiac comorbidity – heart failure		−0.0028	−0.0027	−0.0028
Constant	0.0348***	0.0312***	0.0313***	0.0315***
Standard errors clustered at GP level	Yes	Yes	Yes	Yes
GP Fixed effect	No	No	Yes	No
GP random effects	No	No	No	No
Rho			0.12	

Note: Low income defined by the 10th percentile for the total Danish population. Low education is defined as having completed primary school as the longest education.

¶ The share of patients screened at the hospital treating the patients. IHD index diagnosis was used as an instrument. ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.

In comparison, around 1% of the patients with a HADS score below 8 (i.e. 140 out of 9416) actually received treatment for AD.

Discussion

In the current explorative retrospective cohort study of a population of patients with IHD referred for CR, we examined the effect of screening for AD on the likelihood of receiving treatment for AD, defined as prescriptions of AD drugs, GP counselling, or referral to a psychologist. Of the total CR population, a subsample of 68% was screened and received their test result. We found no evidence that screening for AD and providing patients with their test result as well as a recommendation to see their GP increased

Table IV. Anxiety and depression treatment status for screened IHD patients by HADS score.

	Screened population anxiety and depression score <8	Screened population anxiety and depression score ⩾8	
Receiving no treatment for anxiety and depression	9276 (99%)	2407 (94%)	11,683 (98%)
Receiving treatment for anxiety and depression	140 (1%)	156 (6%)	296 (2%)
Total	9416 (100%)	2563 (100%)	11,979 (100%)

Note: In patients where the a HADS score has been registered.

the likelihood that they would receive treatment for AD. The proportion of patients receiving treatment remained unchanged during the first 2 years of the implementation of the screening programme; we found no association between screening and treatment in our statistical models in the early phase of introducing the screening programme based on national clinical guidelines. Moreover, only 6% of screened patients with a HADS AD score ⩾8 (i.e. the recommended threshold for treatment) received treatment against an average of 3% in the total IHD population and 1% in the screened population with HADS <8. This suggests that only a small percentage of CR staff and/or patients acted on the information provided by an elevated HADS score. Possible explanations could be that patients were not sufficiently encouraged to act by health care professionals, or they did not have sufficient energy and motivation to contact their GP when suffering from AD. It is also possible that the GP did not react adequately in terms of prescribing treatment, corresponding to our findings that 12% of the variation in the probability of taking up AD treatment could be explained at the GP level. This finding could also relate to a possible shortcoming in the HADS score, being a generic tool and thus not specifically targeted at IHD patients [18].

The relatively small share of patients being treated for AD suggests that extending the screening programme to cover a larger percentage of the population is unlikely to be a sufficient measure in itself to ensure that a large proportion of patients who screen positive actively receive treatment. Hence, these findings point to the relevance of implementing automatic referral – based on joint decision making with the patient and including the HADS score as well as other relevant assessments – from CR to psychological treatment, as well as indicating the potential for integrating treatment for AD in the CR setting, as is the case for patient education, physical training, and risk factor management. With this approach, the implicit message to patients is that treatment of both the underlying somatic condition and their psychological challenges – heart and mind – matter and are considered equally important [19]. At least the evidence is clear that AD is associated with increased risk of morbidity and mortality [20,21] and also with increased costs, as a patient with IHD and comorbid depression costs society 33% more than a patient with IHD alone [22]. In addition, several behavioural and physiological mechanisms have been identified, providing plausible links for how psychological distress, such as AD, may lead to adverse outcomes in patients with IHD [3].

Moreover, we found evidence that screened patients constituted a very small sample (25%) of the population of IHD patients, and had different characteristics than the IHD patients receiving treatment for their AD. This suggests that patients who are at high risk of AD might not be captured by the current AD screening and CR programme. At present, AD screening is designed to reach patients enrolled in CR only, which may be a selected sample of the total IHD population. Such a selection criterion might filter out less motivated patients who might be at higher risk of AD, thus defeating the purpose of the screening programme [23].

Limitations and strengths

The results of the current study should be interpreted with the following limitations in mind. We had no way of verifying whether all patients are informed about their screening results, only that the screening test has been performed. Since DHRD is a new quality register that was implemented during the start of the study period, there might have been a gap between the actual- and registered proportion of screened patients. The organisation of CR, registration practices, and compliance with practices may have differed substantially between hospitals, leading to large heterogeneity in the register. In addition, screening might not have been conducted systematically at all hospitals, despite being registered as such, and therefore we expected a minor attritition for screening among those in CR. Some patients might have received psychological treatment through, for example, private health

insurance or have paid for it themselves, which is not identifiable in the national registers.

The strengths of the study included the rich data set where administrative-, clinical- and socioeconomic data were linked at the individual patient level. In addition, because we relied on national register data for this analysis, we anticipated little attrition, although it could not be ruled out entirely. Furthermore, we obtained a precise estimate of compliancewith the screening and CR services. Further, we were able to estimate the impact of the patients' GPs on the propensity for treatment. This was a major strength because normally this GP effect would be attributed to the patient.

Conclusion

In conclusion, we conducted a nationwide study of screening for AD in a cohort of IHD patients, and found evidence of selection into screening at the patient level, indicating that patients at lower risk of AD had a higher probability of being screened. Hence, an extension of the screening effort to cover a larger proportion of the population might not be sufficient to achieve a noticeable increase in the use of AD treatment, if the reverse selection into screening is not addressed.

Acknowledgements

This study is part of the eMindYourHeart (www.sdu.dk/en/om_sdu/institutter_centre/institut_psykologi/forskning/forskningsprojekter/emindyourheart) project that develops a therapist-assisted online treatment programme for patients referred for cardiac rehabilitation with ischaemic heart disease and comorbid depression and/or anxiety by means of a participatory design and the involvement of patients. This study has made use of data from The Danish Clinical Quality Program – National Clinical Registries (RKKP) – notably the Danish Cardiac Rehabilitation Database [12].

Author contributions

All authors contributed to the analysis plan, drafting and finalising of the manuscript.

MK conducted the data management; MK, KRO and ML conducted the statistical analysis; ADOZ, CH and SSP contributed clinical expertise and information.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The authors acknowledge the University of Southern Denmark for an unrestricted grant covering access to data for this study. Funding from Helsefonden (grant # 19-B-0257) supported the work on the paper for authors MK, KRO and ML.

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