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Trajectories of depressive symptoms after a major cardiac event

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Abstract

Depression is a common comorbidity in cardiac patients. This study sought to document fluctuations of depressive symptoms in the 12 months after a first major cardiac event. In all, 310 patients completed a battery of psychosocial measures including the depression subscale of the Symptom Check List-90-Revised. A total of 252 of them also completed follow-up measures at 3 and 12 months. Trajectories of depressive symptoms were classified as none, worsening symptoms, sustained remission, and persistent symptoms. Although the prevalence of depressive symptoms was consistent at each assessment, there was considerable fluctuation between symptom classes. Regression analyses were performed to identify predictors of different trajectories.

Keywords

affect, coping, coronary artery disease, depression, outcomes

Introduction

Depressive symptoms are common in patients hospitalized for coronary heart disease (CHD) or revascularization interventions, with estimates ranging between 30 and 40 percent (Herrmann-Lingen and Buss, 2002; Lespérance and Frasure-Smith, 2000). In addition, depression disorders are reportedly prevalent in between 15 and 20 percent of CHD patients, indicating substantially higher prevalence than physically healthy populations (Härter et al., 2007). Moreover, the deleterious impact of depressive symptoms on prognosis, all-cause mortality, quality of life, and health care costs is well documented, representing a major public health burden (Barth et al., 2004; Baumeister and Härter, 2005; Härter et al., 2007). Consequently, several learned cardiology societies' guidelines recommend that all CHD patients should be routinely screened for depression after an acute cardiac event (e.g. American Association of Cardiovascular and Pulmonary Rehabilitation, 2004; Colquhoun et al., 2013; Giannuzzi et al., 2003; Ladwig et al., 2014; Piepoli et al., 2010). However, depression interventions in CHD patients have not yielded universally positive results with respect to depression remission and freedom from CHD events (e.g. Glassman et al., 2002; Writing Committee for the Enhancing Recovery in Coronary Heart Disease (ENRICHD) Investigators, Baumeister et al., 2011; Berkman et al., 2003), raising questions about the nature of depressive symptoms post cardiac events, the appropriate timing of interventions, and who would benefit most from interventions.

One possible reason for the lack of significant impact upon such interventions on CHD events is fluctuation of depressive symptoms (e.g. spontaneous remission, worsening depression) following cardiac events, thus obscuring the effects of interventions (cf. Schrader et al., 2004). For example, Kop (2012) argues that relapsing and treatment resistant depression provides an unresolved clinical dilemma in CHD patients, thus necessitating further investigation. Conversely, Lespérance and Frasure-Smith (2000) point out that a significant proportion of comorbid depression-CHD patients have a relatively rapid and spontaneous

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remission and do not require an intervention. Consequently, it is crucial to identify characteristics of CHD patients with persistent depression as well as those with sustained remission to better inform clinical practice and furthermore, to inform whom to include in clinical depression trials.

The longitudinal fluctuations in depression classes following cardiac events have been reported in two previous Australian studies. Schrader et al. (2004, 2006) showed that although the crude proportion of mild and moderate depression was similar between baseline, 3 and 12 months, there was considerable fluctuation at an individual level, emphasizing the importance of intra-individual variation. Specifically, only 50 percent of those who were depressed measured by the Centre of Epidemiology Scale for Depression (CES-D) during hospitalization remained depressed at 3 and 12 months while incident depression was reported in 26 percent of patients. Persistent depression was associated with depression scores at baseline, and past history of emotional problems. Taking a growth mixture modeling approach by examining trajectories after coronary artery bypass graft (CABG) surgery, Murphy et al. (2008) demonstrated that the majority of patients (72%) showed a remitted minor depression; two sub-groups showed either a (partially) remitted major depression or a worsening minor depression (14% each). In a second cohort, Murphy et al. (2013) examined depression and anxiety in 160 patients following a cardiac event (myocardial infarction (MI), acute coronary syndrome (ACS), percutaneous coronary intervention (PCI), CABG), as well as 2 and 6 months after hospital discharge. While anxiety scores tended to persist over time, in-hospital depression scores resolved for some patients (17%) and slightly worsened for others (29%); about half of the sample showed no depressive symptoms over time. Among others, a mental health history, poor self-rated health, social isolation, and younger age were predictors for persistent anxiety and worsening depression. However, one drawback of these studies is the paucity of analogous research in other settings especially in Western Europe.

A notable exception is the growth mixture modeling study of Romppel et al. (2012) who described individual trajectories of depressive classes measured by the Hospital Anxiety and Depression Scales (HADS) in over 650 German cardiac patients. With only two time points at baseline and 6 years later, they found four latent classes: low symptoms (60%), low increase of symptoms (26%), high increase (7%), and symptom decrease (7%). The latter was associated with female gender. However, this study is limited by only including two assessment time points.

A more general limitation of studies to date concerns the paucity of data concerning key predictors for worsening symptoms and persistent depression in CHD that might inform clinical treatment initiation. Notwithstanding previous reports regarding persistent depressive symptoms and social isolation (Murphy et al., 2013), it is also plausible that other factors such as coping styles and locus of control could serve as important moderator variables (Sanjuán et al., 2012; Vögele et al., 2012). Conversely, the dearth of data regarding sustained remission particularly makes decisions regarding trial inclusion and anti-depressant treatment difficult. Especially the latter might be initiated unnecessarily as CHD patients might remit spontaneously. Importantly, few studies have investigated serial depression classes in relation to major adverse cardiac events (MACEs).

In this study, we replicated the approach taken by Schrader et al. (2004, 2006) using classes of depression defined by clinical cut-offs rather than using a growth modeling approach to identify distinct trajectories. In this way, we also wanted to place emphasize on the clinical significance of our results. This study advances the understanding of CHD and depression in two ways: first, by examining predictors of depressive symptom trajectory classes for 12 months after a cardiac event with a focus on worsening symptoms and sustained remission, respectively. Second, this study examined varying serial depression classes with respect to MACEs.

Methods

Sample

Patients were recruited by trial staff members on a consecutive basis between October 1998 and June 2000 in seven hospitals (acute in-patient or rehabilitation) in northern Germany. Eligible patients were those admitted for a first cardiac event comprising acute MI, ACS, PCI, CABG. Exclusion criteria were age over 75 years, refused written consent, or inability to complete questionnaires (e.g. language difficulty, visual, or cognitive impairment). Approval for the study was obtained from the Ethics Committee of the Medical Association Schleswig-Holstein, and all patients provided written informed consent.

Measures

The baseline questionnaire was completed 1–3 weeks after the cardiac event. Depressive symptoms were assessed using the respective subscale of the Symptom Check List-90-Revised (SCL-90-R; Franke, 2002). This subscale comprises 13 items measuring only the affective or cognitive aspects of depression, and thus excluding somatic items which might be misleading especially in hospitalized CABG patients (Tully and Baker, 2012). Missing values for individual item responses were replaced with the variable mean. Total scores for the SCL-90-R depression subscale were calculated according to age and sex adjusted T scores, as outlined in the manual (Franke, 2002). In the first instance, patients were classified by T scores to either have no depressive symptoms ($T < 60$), mild to moderate

depressive symptoms ($60 \leqslant T < 70$), or severe depressive symptoms ($T \geqslant 70$). For easier interpretation, we then combined the depressive symptom classes, resulting in two baseline classes: "no depressive symptoms" and "mild to moderate/severe depressive symptoms." In a next step, we defined trajectory classes by watching patient depression progress at 3 and 12 months. Trajectories of depression were classified as no depressive symptoms, worsening depressive symptoms (i.e. elevation in T score $\geqslant 60$), sustained remission, and persistent depressive symptoms. Patients who did not fit the four mentioned classes were excluded from further analyses as they showed an unstable, more erratic (off-on/on-off) trajectory.

Coping styles were assessed by a German questionnaire measuring cognitive, emotional and behavioral aspects of coping with illness (FKV-LIS; Muthny, 1989), locus of control was assessed by a questionnaire to survey control beliefs concerning disease and health (KKG; Lohaus and Schmitt, 1989), and perceived social support was assessed by the F-SOZU (Sommer and Fydrich, 1991). Follow-up depressive symptom and coping style questionnaires were sent via mail at 3 and 12 months after discharge from hospital.

Endpoints

MACEs during follow-up were defined as recurrent acute myocardial infarction (AMI), ACS, PCI, or CABG between baseline and 12 months. Mortality was confirmed from patient's local physician. Other medical data were obtained from a questionnaire completed by the hospital physicians at baseline, and from the family doctors at follow-up (12 months).

Data analysis

Statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS)® Version 22.0. Logistic regression analyses were performed in order to identify predictors (e.g. demographic, medical, social, and psychological variables from the baseline questionnaire) for trajectories of depressive classes. In each case, depression at 12 months, sustained remission (vs. persistent depressive symptoms), and worsening depressive symptoms (vs. no depressive symptoms) were employed as dependent variables. Age and sex were forced into regression models considering these demographic variables are related to depression and cardiac outcome (Tully et al., 2015). Otherwise, only covariates yielding statistical significant bivariate associations $p < 0.05$ with the outcome variables (trajectory classes) were entered into the analyses. Major adverse cardiac outcome (binary coded) was assessed with the Chi-square statistic in order to identify associations with trajectory classes of depression. All statistical tests were two-tailed with significance defined as $p < 0.05$.

Table 1. Baseline patient demographic and clinical characteristics.

Characteristics	$N = 252$	
	Mean	SD
Age	58.15	9.67
	n	%
Sex		
Male	169	67.1
Female	83	32.9
Marital status		
Single	18	7.2
Married	193	76.9
Divorced/separated	24	9.5
Widowed	16	6.4
Years of schooling		
Up to 9 years	148	59.9
More than 9 years	95	38.5
No graduation	2	0.8
Type of cardiac event		
ACS/MI	159	63.9
CABG	71	28.5
PCI	19	7.6

SD: standard deviation; ACS: acute coronary syndrome; MI: myocardial infarction; CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention.

Results

Sample descriptive characteristics

Initially, 310 patients were recruited, and 252 patients (81%) returned the follow-up questionnaires at 3 and 12 months. Analysis of attenuation showed that drop-outs were younger, and their cardiac status was not significantly different from study completers. Table 1 shows baseline patient demographic and clinical characteristics of completers. Average age of the patients in the sample was 58 years. One-third was female, approximately 75 percent were married, and almost 40 percent had more than 9 years of schooling. About two-thirds of patients were admitted to hospital following MI, 29 percent had undergone CABG, and 8 percent received PCI.

Depressive symptom classes over 12-month follow-up

At baseline, prevalence rates of depression classes were 45 percent for "no depressive symptoms," and 32 or 23 percent for the categories "mild to moderate depressive symptoms" and "severe depressive symptoms," respectively. These proportions were almost identical at all time points (Figure 1).

For easier interpretation, we had dichotomized baseline depression scores into patients who either experienced no depressive symptoms or mild to moderate/severe depressive

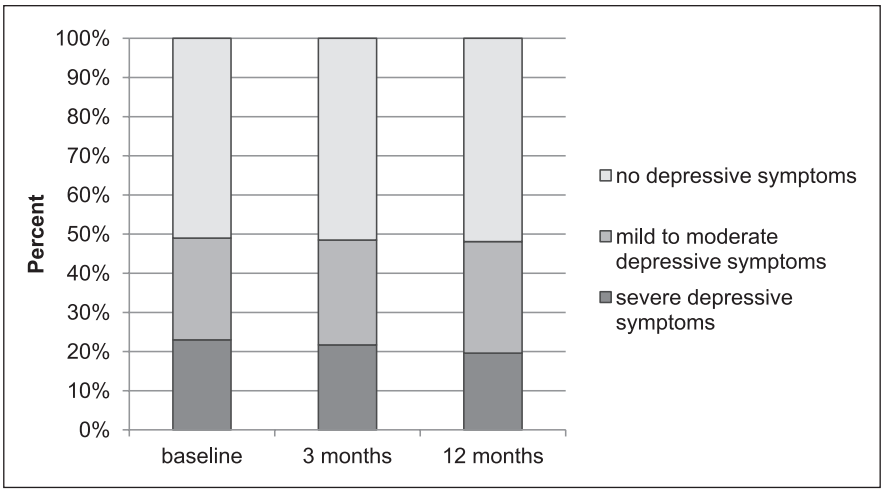

Figure 1. Prevalence rates within each depression category at all three time points ($N = 252$).

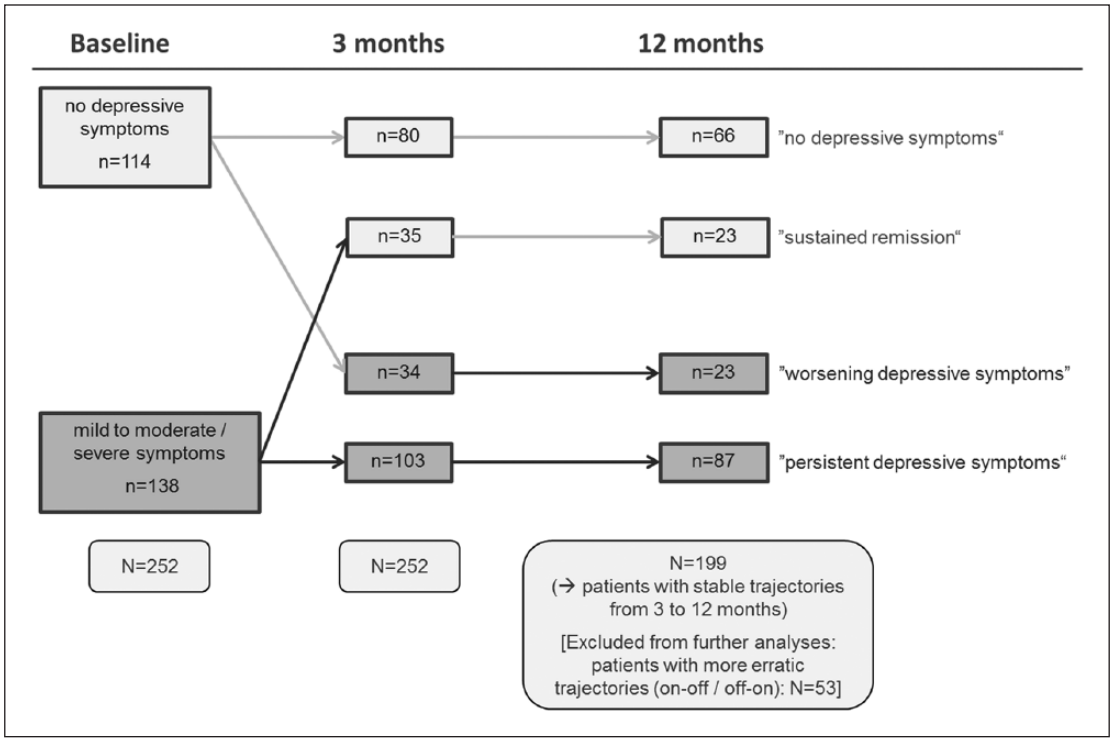

Figure 2. Trajectories of depression symptom classes over 12 months.

symptoms. While proportions remained stable, individual patient trajectories did not. Collectively, 27 percent (69/252) of the patients switched from one class of depression severity to another during the first 3 months, and approximately 40 percent (99/252; including patients with erratic trajectories) switched between depressive symptom classes over the 12-month follow-up.

We were able to classify 79 percent of the sample (199/252) into the four stable trajectories of depressive symptoms (Figure 2). A total of 30 percent (34/114) of those not initially depressed were found to report depressive symptoms at 3 months, reducing to 20 percent (23/114) by 12-month follow-up, thus constituting the worsening depressive symptoms group. Out of the 138 patients (55%) with depressive symptoms at baseline, 75 percent (103/138) still showed depressive symptoms at 3 months, and 63 percent (87/138) remained depressed by 12 months, constituting the persistent depressive symptoms group. In all, 17 percent (23/138) showed a transient and sustained remission which had resolved at 3 months and did not recur. Out of the 114 patients (45%) with no

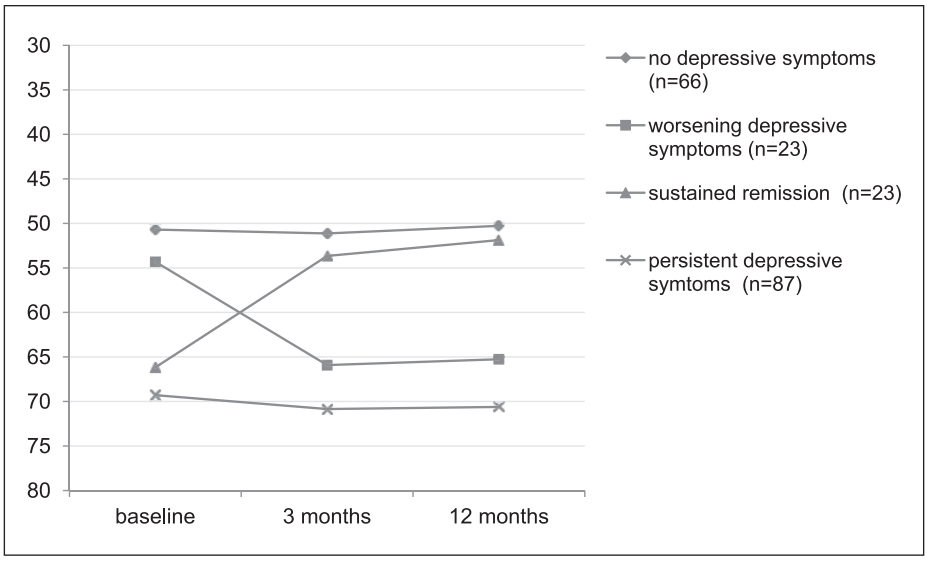

Figure 3. Trajectory means (only patients remaining stable from 3 to 12 months).

Table 2. Results of logistic regression analyses, odds ratios (95% CI).

Predictor	Depression at 12 months		Transient depression[a]		Worsening symptoms[b]	
Depression score at baseline	1.07*	(1.03; 1.11)	0.94	(0.84; 1.06)	1.15*	(1.02; 1.30)
Gender	0.78	(0.40; 1.49)	5.58*	(1.33; 23.45)	1.78	(0.40; 7.82)
Age	0.99	(0.96; 1.02)	1.01	(0.93; 1.09)	0.98	(0.90; 1.06)
CABG	0.94	(0.48; 1.84)	6.16*	(1.35; 28.15)	2.36	(0.57; 9.81)
PCI	0.67	(0.22; 1.99)	6.06	(0.92; 40.14)	0.71	(0.02; 20.66)
Social support	0.90*	(0.83; 0.98)	1.17	(0.98; 1.41)	0.86	(0.70; 1.07)
Internal LOC	1.00	(0.96; 1.05)	0.97	(0.86; 1.08)	1.00	(0.90; 1.11)
External LOC (social)	1.05	(0.98; 1.09)	0.97	(0.88; 1.08)	1.12	(1.00; 1.26)
Depressive coping	1.08	(0.97, 1.21)	0.74*	(0.58; 0.96)	0.82	(0.59; 1.12)
Distractive coping	1.05	(0.97; 1.13)	1.07	(0.88; 1.30)	1.17	(1.00; 1.38)
Trust in physicians	0.89	(0.74; 1.07)	1.23	(0.84; 1.81)	0.56*	(0.32; 0.96)
Nagelkerke's R^2	0.288		0.430		0.412	

CI: confidence interval; CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention; LOC: locus of control.
[a]Versus "persistently depressed."
[b]Versus "no depression."
*$p < 0.05$.

depressive symptoms at baseline, 70 percent (80/114) stayed free of depression at 3 months, and 58 percent (66/114) continued reporting no depressive symptoms at 12 months, constituting the no depression group. Trajectory means are pictured in Figure 3. The remaining 21 percent (53/252) of the sample showed more erratic (off-on/on-off) trajectories (not represented in Figures 2 and 3).

Regression model to determine predictors of depression class over time

Predictors for persistent depressive symptoms were baseline depression scores and low social support (Table 2). A sustained remission was associated with female gender, CABG at baseline assessment, and low depressive coping styles. Females had a fourfold greater chance of depression remission, and probability of diminishing symptomatology in patients following CABG was six-fold compared to patients following AMI or PCI. A worsening course of depressive symptoms over time was associated with higher depression scores at baseline, and lower baseline trust in physicians measured by three items ("strictly following medical advice," "having confidence in the doctors," and "distrusting doctors; looking for another doctor to confirm diagnosis").

Depressive symptom classes and MACE

Major cardiac events were more frequent in patients with persistent depressive symptoms versus those with sustained remission ($\chi^2 = 5.99$, $df = 1$, $p = 0.014$); 29 percent of those in

the former group experienced at least one cardiac event while only 4 percent in those with sustained remission experienced clinical events. There was no difference as to clinical events between those with worsening symptoms versus patients with no depressive symptoms at baseline; here, 17 and 18 percent of patients, respectively, had at least one adverse cardiac event ($\chi^2 = 0.01$, $df = 1$, $p = 0.932$).

Discussion

First, this study showed that almost 40 percent of patients switched depressive symptom classes in the 12 months following their first serious cardiac event (including those with more erratic trajectories). It is particularly concerning that 44 percent of all observed patients displayed either persistent or worsening depressive symptoms. By contrast, only 9 percent of patients were found to experience a sustained remission from 3 months onwards. The second major finding of this study was the association between depressive symptom response and discrete factors, especially depression at baseline, low social support, and little trust in physicians. And third, study results found persons with a persistent depressive episode at greatest risk for MACE over 12 months. In general, our findings regarding depressive symptom trajectories correspond to those reported by Schrader et al. (2004, 2006) who utilized a similar methodology and time-frame, and also to those studies modeling change in cardiac (Murphy et al., 2008, 2013; Romppel et al., 2012) and non-patient samples (Kuchibhatla et al., 2012). Moreover, several studies have reported that a new increase in depressive symptoms or treatment resistant depression is associated with MACE. Collectively, the consistency in findings across studies points to the fluctuating nature of depressive symptoms after a major cardiac event.

The finding that baseline depression scores were associated with depression at 12 months is in accordance to earlier studies (Schrader et al., 2006). Depressive coping styles, distrust in physicians, and low social support were indicators of adverse developments of depressive symptoms. In contrast, female gender or antecedent CABG were strong predictors of a transient depressive response (=sustained remission). With respect to the former, a more favorable course of depression in women was reported by Romppel et al. (2012); however, their cohort was only assessed on two occasions. Similarly, Bjerkeset et al. (2005) found that although women had a high initial risk for anxiety and depression after AMI, they showed a significant decrease in depressive symptoms after 2 years, whereas in men the risk for depression increased. Similarly, Shanmugasegaram et al. (2012) found a two times greater prevalence of major depression in women than men directly following cardiac events, whereas 1 year later men and women showed hardly any differences as to depressive symptoms any more (Grace et al., 2014).

The association between antecedent CABG and sustained remission is potentially related to the invasive nature of the surgical procedure, pain, and pronounced physical and activity limitations (Chapman et al., 2012; Tully and Baker, 2012). Indeed, evidence suggests that somatic symptoms are largely artificially inflated after CABG (Contrada et al., 2006), and may include somatic complaints following thoracic surgery such as loss of appetite, fatigue, or pain. However, it is important to note that the depression subscale of the SCL-90-R does not include somatic items, thus making it suitable for measuring depression in persons with physical illnesses. Notwithstanding the absence of somatic depressive symptoms, it is likely that early mobility and physical improvements following CABG are related to decreasing depression symptoms. Along the same line, the favorable cardiac prognosis of patients with sustained remission might be attributable to the antecedent bypass surgery and not their emotional wellbeing considering that CABG is associated with a favorable prognosis in persons with two or more diseased coronary arteries (Hannan et al., 2005).

The importance of identifying persistent depression classes is emphasized by the finding that these patients reported a significantly higher proportion of adverse cardiac events during the first 12 months after initial hospitalization. A recent case-control study also showed that treatment resistant and insufficiently treated depression were associated with increased risk for cardiac events after an index AMI (Scherrer et al., 2012). In our sample, more than 50 percent of the patients showed symptoms of depression at every time point over 1 year, about 20 percent of them with severe symptoms. Evidently, change in depression over time may deserve specific monitoring by physicians and mental health specialists alike. The fluctuating course of depressive symptoms highlights the possibility that persons initially identified with depressive symptoms are free from depression some months later and vice versa. Indeed, although the American Heart Association guidelines (Lichtman et al., 2008) give no clear guidance as to the timing of initial depression assessment or follow-up monitoring, the recent National Heart Foundation of Australia guidelines suggest monitoring 1 month apart in the first instance, and annually subsequently (Colquhoun et al., 2013).

This study shows that almost one-fifth of the patients experienced a sustained remission after the cardiac event that resolved during the first 3 months and did not recur. This might partly explain the divergence in findings of depression interventions such as those initiated within hospital (ENRICHD) versus those targeting sustained depressive episodes (Davidson et al., 2013). Moreover, randomization into intervention trials of persons who would otherwise spontaneously remit might partly explain why trials initiating psychological treatment at least 2 months after a cardiac event have shown greater benefits to depression than those initiating treatment sooner (Linden

et al., 2007). Watchful-waiting before commencing antidepressive treatment or mental health professional referral seems prudent unless immediate treatment is required by the particular circumstances of the individual patient (Lespérance and Frasure-Smith, 2000; Schrader et al., 2006). Nevertheless, with respect to clinical trials of depression interventions, our findings support other scholars' suggestion that patients should not necessarily be included unless depressive symptoms are measured repeatedly (Davidson et al., 2006).

The study has several limitations including the inability to determine whether patients experienced symptomatic depressive symptoms before the index cardiac event. Past history of depression was found to increase the risk of incident depression symptoms (Schrader et al., 2006), but was not asked for in this study. Non-fatal clinical cardiac outcomes were assessed primarily by self-report in survivors, thus possibly limiting the validity of the data. Furthermore, our findings cannot verify the temporal association between depressive symptoms and cardiac events. Specifically, we could not establish whether recurring cardiac events preceded a worsening episode of depressive symptoms. Another limitation is surely the modest numbers of patients in two of the classes (sustained remission and worsening depressive symptoms). Finally, by participating in an observational psychological study, it is possible that patients were prompted to pay attention to their wellbeing and seek depression treatment outside the study. This was not monitored and might underestimate depression prevalence. Further research should consider these limitations.

In conclusion, this study emphasizes the fluidity of depressive symptoms following a cardiac event. Results show distinct depression trajectories after a cardiac event which were associated with discrete characteristics. The collective findings suggest that vigilance to patients' mental health after a cardiac event is warranted potentially through serial assessment of depressive symptoms.

Declaration of conflicting interests

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