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### Somatic depression in the picture

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# Chapter 6

## The association between cardiac rehabilitation and mortality risk for myocardial infarction patients with and without depressive symptoms

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## Abstract

**Objective:** Post-myocardial infarction (MI) depression is associated with reduced adherence to cardiac rehabilitation (CR) and increased mortality risk. The present observational study investigated whether all-cause mortality reduction associated with CR is different for MI-patients with and without depression.

**Methods:** Data of 2198 post-MI patients from the Depression after Myocardial Infarction (DepreMI) study and Myocardial Infarction and Depression Intervention Trial (MIND-IT) was used. Depression was assessed at hospitalization, defined as a score  $\geq 10$  on the Beck Depression Inventory (BDI). Participation in CR was assessed with a self-report questionnaire, 12 months post-MI. Cox regression was used to estimate hazard ratios (HR) for all-cause mortality, up till 10 years post-MI. Missing data was imputed, using multiple imputation.

**Results:** 878 (52%) patients attended CR, 517 (26%) patients had a BDI score  $\geq 10$ , and 379 (18%) patients died during the follow-up period. Overall, CR was not associated with a lower mortality risk (HR: 0.83; 0.54-1.30;  $p=0.41$ ), adjusted for age, sex, left ventricle ejection fraction, previous MI, and past or current heart failure. However, there was a significant interaction between depression and CR on mortality (HR: 0.49; 0.27-0.90;  $p=0.02$ ). CR was significantly associated with reduced mortality in depressed patients (HR: 0.48; 0.28-0.84;  $p=0.01$ ), but not in non-depressed patients (HR: 1.09; 0.63-1.89;  $p=0.74$ ).

**Conclusions:** CR was associated with reduced mortality risk only for MI-patients with depression. Clinicians should therefore particularly encourage MI-patients with depression to participate in CR.

## Introduction

Depression is common among myocardial infarction (MI) patients and is associated with an increased risk of mortality.<sup>1</sup> To date, the mechanisms behind this association are still unclear. Cardiac rehabilitation (CR) aims to improve the cardiovascular health and well-being of patients with cardiac disease. CR is considered essential in the treatment of MI and has been shown to reduce mortality.<sup>2-5</sup> Most probably, the effect of CR is not homogeneous across groups of patients. Benefits of CR are likely to be low in depressed patients, as depression in cardiac patients is associated with poorer rates of completion and adherence in CR.<sup>6-9</sup> If patients with depressive symptoms profit less from CR programs than those without, e.g. through less intense participation, this could be an explanation for the association between post-MI depression and mortality.<sup>1</sup> On the other hand, patients with depressive symptoms could show a relatively higher degree of CR-associated mortality reduction than patients without depressive symptoms, because they have higher pre-treatment mortality risks and consequently there is more cardiovascular health to gain.

Exercise and counseling on risk factor modification are important components of CR, that have been extensively researched and shown to improve cardiovascular prognosis.<sup>3,10-12</sup> However, these components are likely to be less effective in the presence of some common depressive symptoms, such as feelings of helplessness, lack of energy, or anhedonia.<sup>6,13</sup> Thus, less intensive participation in CR, as a result of depression, may be associated with worse prognosis. In line with this hypothesis, a randomized controlled trial (RCT) performed in heart failure (HF) patients showed that a disease management program (DMP) even resulted in a tendency towards a *higher* mortality and HF readmission for depressed patients compared to care as usual, whereas the opposite was observed for patients without depressive symptoms.<sup>7</sup> In contrast, in an observational study, depressed coronary artery disease (CAD) patients seemed to benefit more from CR than non-depressed CAD patients,<sup>14</sup> which supports the hypothesis that in depressed patients there may be more to gain. However, the authors did not statistically test for an interaction between depression and CR.

To our knowledge, no studies have directly investigated whether depressed and non-depressed MI patients benefit differently from cardiac rehabilitation with regard to long-term prognosis. In the current study, we therefore investigated the association of CR with all-cause mortality and compared the size and direction of this association between patients with and without depressive symptoms.

## Methods

### *Design and participants*

The present study was conducted as part of the Depression after Myocardial Infarction (DepreMI) study and the Myocardial Infarction and Depression Intervention Trial (MIND-IT). DepreMI is an observational prospective cohort study evaluating the association of post-MI depression with cardiovascular prognosis, including 528 patients who were hospitalized for MI between September 1997 and September 2000 in one of four hospitals in the North of the Netherlands. In MIND-IT, 2176 patients diagnosed with an acute MI were recruited from 10 hospitals in the Netherlands between September 1999 and November 2002. From the MIND-IT sample, 331 depressed patients were randomized to examine the effects of antidepressant treatment compared to usual care. Details of both studies have been described before.<sup>15,16</sup> In brief, patients in both studies were enrolled if they met at least two of the following criteria: 1) chest pain for at least 20 min, 2) typical electrocardiographic changes, and 3) a documented increase in cardiac enzyme levels. Exclusion criteria were inability to participate in study procedures (e.g. unable to communicate or unavailable for follow-up), another disease likely to influence short-term survival, and already receiving psychiatric treatment for depression (only in MIND-IT). All patients gave written informed consent before enrolment and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Although DepreMI was an observational study and MIND-IT a randomized intervention study for post-MI depression, the protocols were largely similar. Because the patients in the intervention arm of the MIND-IT study had no better long-term outcomes than those in the usual-care-arm,<sup>17</sup> it would not bias the results when combining both arms of this study with DepreMI. We therefore pooled the results from the MIND-IT and DepreMI studies to gain more power, as we did previously.<sup>18</sup>

### *Assessment of predictors: depression and participation in cardiac rehabilitation*

All patients were assessed for the presence of depressive symptoms during hospitalization, using the Beck Depression Inventory (BDI).<sup>19</sup> This questionnaire consists of 21 items assessing the presence and severity of depressive symptoms. The total BDI-score can range from 0 to 63, with higher scores indicating more severe symptoms. Whether a patient was referred to CR was determined by the discretion of the patient's cardiologist. The contents of a CR program, also determined by the cardiologist, varied per patient and could consist of the following components: exercise training, relaxation training, information meetings, group discussions, and individual meetings with a physician, nurse, social worker, or psychologist. At 12 months post-MI, patients received a questionnaire in which they were asked to report whether they participated in CR. CR participation was

recorded as a dichotomous variable (yes/no). In MIND-it, only participants who were enrolled in the study before February 1, 2002 were asked to report this. Therefore, MIND-it patients enrolled after this date (N=506) were excluded from the analysis. The remaining combined sample consisted of 2198 MI-patients.

### ***Assessment of outcomes: mortality and cardiovascular readmissions***

The Dutch Central Bureau of Statistics provided data on all-cause mortality (ACM) and cardiovascular (CV) readmissions, which was evaluated up till 10 years post-MI (mean: 6 years). We used ACM as primary outcome and CV readmissions as secondary outcome, because CR is more consistently associated with a reduced ACM than with CV readmissions.<sup>2</sup> CV readmissions comprise hospital readmissions with the following ICD-9 primary discharge diagnoses: ischemic heart disease (410, 411, 413, 414), cardiac arrhythmia (427.1, 427.4, 427.5), heart failure (428, 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93), cerebrovascular disease (433, 434, 435, 437.0, 437.1) and peripheral vascular disease (440, 443.9).

### ***Potential confounders***

Characteristics associated with ACM may differ for patients who did and did not participate in CR and for depressed and non-depressed patients, i.e. confounding may have occurred. Therefore, we adjusted for the following characteristics: age, sex, left ventricular ejection fraction (LVEF), past or current heart failure (CHF), and MI before index-MI. These characteristics were assessed during hospitalization and obtained from medical records. The recorded categorization of LVEF was different for MIND-IT and DepreMI. Therefore, we used a dichotomized score for LVEF, which was chosen to be as close as possible to the LVEF categories in the two studies, i.e. at 45% for MIND-IT and at 40% for DepreMI, as previously reported.<sup>18</sup>

### ***Statistical analysis***

The percentages of missing data of the variables used for the analyses ranged between 0.6% (MI before index-MI) and 22.6% (CR); for 64.4% of the sample we had complete information on all variables. The potentially distorting effect of missing data as well as its unfavorable effect on the precision of our estimates was dealt with by using multiple imputation by chained equations. To this end we created 20 imputed data sets, which were pooled for the analyses using Rubin's rules.<sup>20</sup> This approach is valid under the assumption that missing values were missing at random (MAR) or missing completely at random. To investigate whether data were at least partly MAR we predicted the value being missing (yes/no) for all variables of main interest separately using logistic regression. As predictors variables we selected all variables that were considered potential



predictors of missingness.<sup>21</sup> The explained variance (Nagelkerke's R<sup>2</sup>) from these analyses ranged from 7% to 62% suggesting that the data in the present study were to some extent MAR. Consequently, multiple imputation likely increased the validity of our results, although the MAR assumption cannot be proved. The final imputation model included those variables that predicted the value of the incomplete variable and whether the incomplete variable was missing or not.<sup>21</sup>

We compared demographical and clinical characteristics between patients who had and had not participated in CR. In addition, this was done separately for patients with and without depression (in Supplement). With Cox regression, the risk for mortality (primary outcome) and CV readmissions (secondary outcome) was compared between patients who had and had not participated in CR. To test whether CR was differently associated with long term prognosis for depressed and non-depressed patients, an interaction term CR × depression (BDI $\geq$ 10) was added to the model. The analyses were repeated for depressed (BDI $\geq$ 10) and non-depressed (BDI $<$ 10) patients separately. All analyses were performed in an unadjusted model; a model which was adjusted for age and sex; and a model which was additionally adjusted for all potential confounders. Kaplan-Meier curves were used to depict the cumulative mortality with follow-up time, according to participation in CR for depressed and non-depressed patients separately. The proportional hazards assumption in each analysis was checked by inspecting the log-minus-log plot of the survival function. The level of statistical significance was set at 0.05, two-sided. All analyses and the multiple imputation were performed using SPSS, version 20.0.

## Results

### *Sample characteristics*

Of the total sample, 517 patients (26%) had a BDI score  $\geq$ 10, 878 (52%) patients had participated in CR (51% of the non-depressed and 55% of the depressed MI patients), and 379 patients (18%) had died during follow-up period. Patients who did not respond to the CR questionnaire (and who were still alive 12 months post-MI) were more often female, more often depressed, and had a higher mortality rate (in the period after 12 months post-MI) compared to responders. They did not differ with respect to age.

Table 1 shows baseline characteristics for patients who did and who did not participate in CR. Patients who did participate in CR were significantly younger, less likely to be female, to live alone, to have had a MI before the index-MI, to have past or current CHF, to be a previous smoker, and to die within the follow up period. In addition, they were significantly more likely to currently smoke and to have a family history of coronary artery disease (CAD), compared to patients who did not participate in CR. Participating and non-participating

**Table 1.** Baseline characteristics for both patients participating and non-participating in cardiac rehabilitation.

	<b>No CR N=824</b>	<b>CR N=878</b>	<b>p</b>	<b>Fraction of missing data</b>
Female	25%	17%	<.001	-
Age (SD)	65 (11)	57 (10)	<.001	-
Living alone	21%	15%	.003	20.8%
Family history of CVD	39%	46%	.003	1.7%
Current smoker	45%	53%	.002	4.5%
Previous smoker	34%	27%	.003	4.9%
BMI (SD)	26.5 (4.0)	26.7 (3.9)	.24	6.8%
MI before index-MI	17%	10%	<.001	0.6%
Low LVEF	24%	24%	.81	6.2%
Past or current CHF	12%	8%	.006	2.5%
BDI score (SD)	6.2 (5.7)	6.5 (5.5)	.17	8.8%
BDI score ≥ 10	22%	25%	.14	8.8%
All-cause mortality	20%	9%	<.001	6.0%
CV readmissions	44%	41%	.27	8.1%

CR = cardiac rehabilitation; SD = standard deviation; CVD = cardiovascular disease; BMI = body mass index; MI = myocardial infarction; LVEF = left ventricle ejection fraction (low LVEF was ≤ 45% for MIND-IT and ≤ 40% for DePreMI); CHF = congestive heart failure; BDI = Beck Depression Inventory; CV = cardiovascular. Note: all numbers are reported based on original data; fraction missing on the CR variable was 23%.

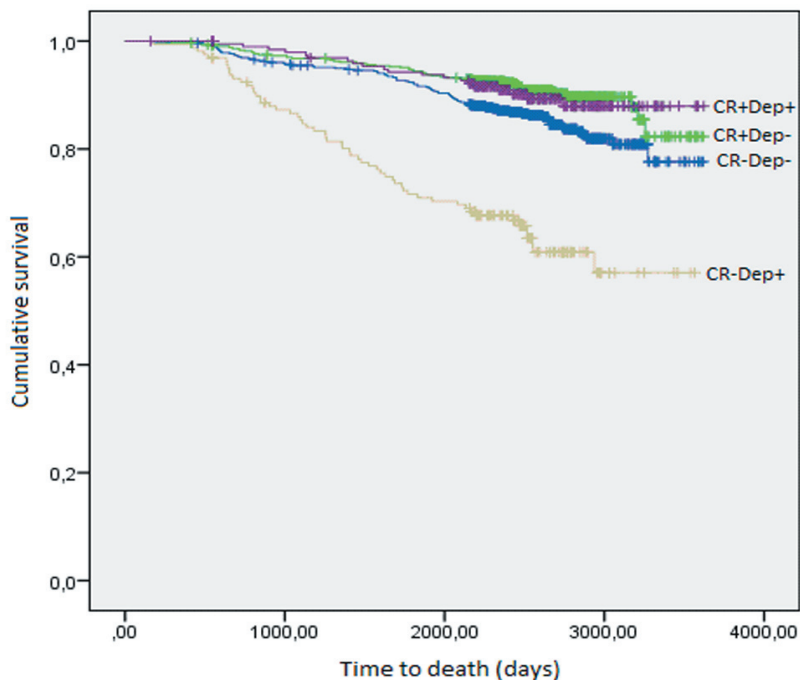
patients did not differ with respect to body mass index, LVEF, depression status, depression severity, and CV readmissions during follow up. In order to compare baseline characteristics for depressed and non-depressed separately, we included a supplementary table showing the baseline characteristics for the four groups (supplementary Table 1).

Participating patients started CR on average 2 months after the index-MI and the mean duration of CR was 9 weeks. Of the patients that attended CR, 88% attended (at least once) exercise training, 65% relaxation training, 58% information meetings, 43% group discussions, and 44% individual meetings with a physician, nurse, social worker, or psychologist.

### **Survival analyses**

The Kaplan-Meier curves (Figure 1) show that at each instance during follow-up, the cumulative risk of mortality was highest among those who did not participate in rehabilitation and who were depressed. It also shows that the difference in this risk between those who did and did not participate was considerably larger among the depressed patients. The results of the Cox regression analyses are





**Figure 1.** Kaplan Meier curves of the cumulative survival during follow-up of all-cause mortality for participating and non-participating MI patients, thereby also divided for depressed and non-depressed patients. The curves are based on the original data.

depicted in Table 2. Overall, in the unadjusted model, patients that participated in CR had a significant 50% lower mortality risk within the follow up period compared to patients who did not participate. After adjusting for age and sex, this difference decreased to 15% and was no longer statistically significant. Results hardly changed after additional adjustment for LVEF, MI before index-MI, and past or current CHF (HR=0.83; confidence interval (CI): 0.54-1.30;  $p=0.41$ ). There was a statistically significant interaction between depression status and CR participation using the fully adjusted model (HR=0.49; CI: 0.27-0.90;  $p=0.02$ ). In analyses stratified for depression status, CR participation was only significantly associated with a lower mortality rate for depressed patients (HR=0.48; CI: 0.28-0.84;  $p=0.01$ ) and not for non-depressed patients (HR=1.09; CI: 0.63-1.89;  $p=0.74$ ). Furthermore, all covariates, except for CR and sex, were significantly related to mortality rate in multivariable analyses (Table 3). Of note, the imputed results did not differ from the results based on the original data.

Secondary, the analyses were repeated with CV readmissions as an outcome. Regardless of depression status, CR participation was not associated with reduced risk for CV readmissions, in adjusted and unadjusted analyses (Table 4).

**Table 2:** Univariable and multivariable Cox regression analyses for all-cause mortality according to participation in cardiac rehabilitation. Analyses were performed on the whole sample and for depressed and non-depressed separately, in addition the interaction between CR and BDI was tested (values represent hazard ratios with 95% confidence intervals).

Model	All MI patients	p	MI patients with BDI<10	p	MI patients with BDI ≥ 10	p	Interaction CR x BDI	p
1 <sup>a</sup>	0.53 (0.34 - 0.84)	.009	0.69 (0.41 - 1.17)	.16	0.32 (0.18 - 0.59)	<.001	0.46 (0.25-0.84)	.01
2 <sup>b</sup>	0.84 (0.52 - 1.33)	.44	1.11 (0.64 - 1.92)	.70	0.47 (0.26 - 0.86)	.01	0.47 (0.26-0.85)	.01
3 <sup>c</sup>	0.83 (0.54 - 1.30)	.41	1.09 (0.63 - 1.89)	.74	0.48 (0.28 - 0.84)	.01	0.49 (0.27-0.90)	.02

BDI= Beck Depression Inventory; CR = cardiac rehabilitation.

<sup>a</sup> Unadjusted model

<sup>b</sup> Model adjusted for age and sex

<sup>c</sup> Model adjusted for age, sex, LVEF, MI before index-MI, and past or current heart failure

**Table 3:** Multivariable Cox regression analyses of all predictors for all-cause mortality.

Covariates	Multivariable HR	p
CR	0.83 (0.53 - 1.29)	.40
BDI≥10	1.45 (1.14 - 1.83)	.003
Age	1.06 (1.05-1.07)	<.001
Sex	0.79 (0.61 - 1.01)	.06
Low LVEF	1.87 (1.50-2.34)	<.001
Past or current CHF	2.14 (1.70-2.71)	<.001
MI before index-MI	1.68 (1.31-2.14)	<.001

BDI = Beck Depression Inventory; CR = cardiac rehabilitation; LVEF = left ventricle ejection fraction (low LVEF was ≤ 45% for MIND-IT and ≤ 40% for DePreMI); CHF = congestive heart failure; MI = myocardial infarction; HR = hazard ratio.

**Table 4:** Univariate and multivariable Cox regression analyses for cardiovascular readmissions according to participation in cardiac rehabilitation. Analyses were performed on the whole sample and for depressed and non-depressed separately, in addition the interaction between CR and BDI was tested (values represent hazard ratios with 95% confidence intervals).

Model	All patients	p	Patients with BDI<10	p	Patients with BDI ≥ 10	p	Interaction CR x BDI	p
1 <sup>a</sup>	0.90 (0.73 - 1.11)	.31	0.90 (0.71 - 1.14)	.37	0.91 (0.68 - 1.21)	.51	1.01 (0.72-1.41)	.97
2 <sup>b</sup>	0.98 (0.79 - 1.21)	.82	0.98 (0.77 - 1.24)	.83	0.98 (0.72 - 1.34)	.91	1.01 (0.72-1.42)	.94
3 <sup>c</sup>	1.00 (0.82 - 1.22)	1.0	0.99 (0.79 - 1.25)	.95	1.02 (0.75 - 1.37)	.92	1.03 (0.74-1.44)	.85

BDI= Beck Depression Inventory; CR = cardiac rehabilitation.

<sup>a</sup> Unadjusted model

<sup>b</sup> Model adjusted for age and sex

<sup>c</sup> Model adjusted for age, sex, LVEF, MI before index-MI, and past or current heart failure

## Discussion

Depressed MI patients significantly benefited more from CR than non-depressed MI patients. We observed that CR was associated with significantly reduced mortality risk only for MI patients with depressive symptoms. These findings suggest that MI patients with depressive symptoms should particularly be encouraged to engage in CR programs. The secondary analyses showed that CR was not associated with CV readmissions, regardless of depression status.

Our findings indicated that poor adherence on CR programs<sup>6,8</sup> is not likely to explain the increased mortality risk for post-MI depressed patients.<sup>1</sup> Instead, we observed that in terms of mortality risk, depressed MI patients benefited significantly more from CR compared to non-depressed patients. We have several putative explanations for this finding. Possibly, the findings can be explained by a so-called ceiling effect, i.e., the potential of any intervention to exert an effect is larger in those who have more to gain. For instance, if depressed MI patients initially had a less healthy lifestyle than non-depressed patients (e.g. smoked more often, had worse dietary habits, and exercised less frequently), they might have benefited more from education on lifestyle modification and from exercise programs. However, baseline data showed no substantial differences for the lifestyle indicators including smoking status and BMI between depressed and non-depressed patients (see Supplementary Table 1). Unfortunately, information on other lifestyle factors, including physical activity and diet habits, was only available for a minority of the participants (only for DepreMI participants). Of these participants, depressed patients less often did odd jobs and/or gardening in leisure time, compared to non-depressed patients. No significant differences for other lifestyle factors (other physical activities and diet habits) were observed between depressed and non-depressed patients (data not shown). As regards to CR participation, depressed and non-depressed patients were equally likely to participate in CR, but depressed patients had significantly poorer rates of CR completion.<sup>6,8</sup> Nevertheless, the average duration of CR did not differ between depressed and non-depressed patients (Supplementary Table 1) and excluding patients that did not complete CR had no effect on the results.

Interestingly, of the patients that attended CR, depressed patients considered CR consistently more effective on all kinds of behavioral, social, and psychological aspects, compared to non-depressed patients. For example, they regarded CR significantly more helpful to adopt a healthier lifestyle, to better cope with stress, to learn to accept their situation, to talk about their problems with others, and to better adhere to medication (data not shown). Of note, we had this information only for MIND-IT participants.

Furthermore, depressed patients might particularly benefit from the exercise component of CR, as physical exercise has been found to reduce inflammation and sympathetic nervous system activity, and to increase heart

rate variability.<sup>10</sup> These physiological factors are suggested to be more disturbed in depressed than in non-depressed patients and are associated with adverse clinical outcomes.<sup>22</sup> Further, in addition to improving cardiovascular health, CR has been demonstrated to reduce many aspects of psychosocial stress, including depression, anxiety and hostility.<sup>4,23,24</sup> Therefore, the beneficial effects of CR on mortality may be mediated by their positive effects on depression. This has also been suggested by previous studies in CAD and HF patients.<sup>14,25,26</sup> These studies indicated that most of the benefit from CR was in those who either reduced their psychosocial stress or improved their fitness with CR. Of interest, previous studies in patients with post-MI depression have shown that particularly somatic symptoms of depression were related with high disease severity and adverse cardiovascular prognosis.<sup>27,28</sup> Perhaps, CR targets especially somatic depressive symptoms, as one of its main aims is to intervene in the physical health of MI patients. This would be an interesting avenue for further research. To date, traditional depression interventions in CAD patients had only a modest effect on depression outcomes, and were not successful in improving CAD prognosis.<sup>29</sup> Because CR aims to improve both well-being and cardiovascular health of cardiac patients, it may be more effective than traditional anti-depressant treatments in terms of improving medical prognosis.

It should be noted that in contrast to our results, a RCT in HF patients showed that a disease management program resulted in a trend for *higher* incidence of mortality in depressed patients and a trend for *lower* incidence of mortality for non-depressed patients.<sup>7</sup> Furthermore, we did not find a significant effect of CR on mortality for the sample as a whole. Although previous meta-analyses reported a significant effect of CR in CAD patients,<sup>25</sup> a large recent RCT reported negative findings as well.<sup>30</sup> The authors argued that the benefit of CR might have declined as current medical management has advanced. Finally, in contrast to our findings with mortality as outcome, we did not find any effect of CR on CV readmissions, the secondary outcome in this study. Notably, previous studies reported conflicting findings regarding the effectiveness of CR in reducing CV readmissions.<sup>24</sup>

Strengths of this study are the large sample size of 2198 MI patients, the long follow-up period of up till 10 years, and the adjustment for important confounders. The most important limitation is that patients were not randomized to CR. However, it would be unethical to have a randomized control group not receiving CR, as studies demonstrated the effectiveness of CR to reduce mortality risk.<sup>25</sup> Unfortunately, we had no information about the specific reasons of clinicians to offer CR and about the patients' motives to participate. Therefore the group that participated in CR may have had a different initial prognosis compared with the group that did not, despite adjustment for confounders. Although depression severity was not different for depressed patients that did and did not participate in CR (Supplementary table 1), patients that attended CR could have had a

higher initial intrinsic motivation to improve their health. This may have led to an overestimation of the effect of CR on mortality in depressed patients. In line with this, supplementary table 1 showed that depressed CR-attenders demonstrated more help-seeking behavior, as they were more likely to be treated for their depression than depressed non-attenders. Nevertheless, including treatment as additional covariate did not influence the results. Notably, a previous report in the MIND-it sample showed that MI-patients that were treated for their depression, irrespective of randomization, had reduced mortality risk.<sup>17</sup> Potentially, this finding can be explained by the fact that these patients participated more often in CR, as these analyses were not adjusted for CR participation.

Furthermore, patients with a relatively mild or relatively severe MI were possibly less likely to attend CR, which could have led to respectively an under- and overestimation of the effect. Another limitation is the long period between depression measurement and the start of CR; attenders started CR on average 2 months after hospitalization, therefore depression status changed for some participants at the time they attended CR. Nevertheless, the results indicated that a depression measurement at hospitalization appears an important predictor for the effect of CR on mortality, which is clinically relevant information.

To conclude, we observed that depressed MI patients benefited significantly more from CR than non-depressed patients, in terms of mortality rates. CR was associated with a reduced mortality rate only for MI patients with depressive symptoms. Based on these findings, MI patients with depressive symptoms should particularly be encouraged to engage in CR programs. As this was the first study to directly compare the association between cardiac rehabilitation and mortality risk for depressed and non-depressed MI-patients, more replicative studies are needed. In addition, the mechanisms that could account for the observed differences across depressed and non-depressed patients should be evaluated.

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**Supplementary table 1:** Baseline characteristics for both patients participating and non-participating in cardiac rehabilitation.

	No Depression N=1219			Depression N=370		
	No CR N=587	CR N=622	p	No CR N=165	CR N=205	p
Female	22%	16%	.007	32%	21%	.01
Age (SD)	64 (11)	57 (10)	<.001	67	57	<.001
Living alone	18%	12%	.005	29%	23%	.18
Family history of CAD	40%	48%	.005	37%	42%	.41
Current smoker	46%	52%	.03	44%	53%	.09
Previous smoker	33%	27%	.02	35%	29%	.22
BMI (SD)	27 (4)	27 (4)	.29	26 (4)	26 (4)	.52
MI before index-MI	16%	9%	<.001	21%	12%	.02
Low LVEF	22%	23%	.58	31%	26%	.32
Past or current CHF	11%	6%	.007	16%	12%	.26
All-cause mortality	15%	9%	.002	36%	10%	<.001
CV readmissions	43%	40%	.26	44%	45%	.81
Treatment depression	-	-	-	12%	31%	<.001
BDI score (SD)	-	-	-	14.9 (5.0)	14.3(4.6)	.27
CR duration (weeks) (SD)	-	9.5 (7.8)	-	-	8.9 (7.0)	.41
CR non-completion	-	9%	-	-	20%	<.001

CR = cardiac rehabilitation; SD = standard deviation; CVD = cardiovascular disease; BMI = body mass index; MI = myocardial infarction; LVEF = left ventricle ejection fraction (low LVEF was  $\leq 45\%$  for MIND-IT and  $\leq 40\%$  for DepreMI); CHF = congestive heart failure; CV = cardiovascular; BDI = Beck Depression Inventory. Note: all numbers are reported based on original data; Data on CR completion was only available for MIND-IT.

