© 2012 This manuscript version is made available under the CC-BY-NC-ND 4.0 license https:// creativecommons.org/licenses/by-nc-nd/4.0/

1	Symptoms of Heart Disease or its Treatment May Increase Beck Depression Inventory
2	Scores in Hospitalized Post-Myocardial Infarction Patients
3	
4	Running head: Depression Scores in Post-Myocardial Infarction Patients
5	
6	Vanessa C. Delisle, MSc <sup>1,6</sup> , Aaron T. Beck, MD <sup>7</sup> , Roy C. Ziegelstein, MD <sup>8</sup> , Brett D.
7	Thombs, PhD <sup>1-6</sup>
8	
9	Departments of <sup>1</sup> Counselling and Educational Psychology, <sup>2</sup> Epidemiology, Biostatistics, and
10	Occupational Health, <sup>3</sup> Medicine, and <sup>4</sup> Psychiatry, and <sup>5</sup> School of Nursing, McGill University,
11	Montréal, Québec, Canada; <sup>6</sup> Lady Davis Institute for Medical Research, Jewish General Hospital,
12	Montréal, Québec, Canada; <sup>7</sup> Department of Psychiatry, University of Pennsylvania, Philadelphia,
13	Pennsylvania, USA; <sup>8</sup> Department of Medicine, Johns Hopkins University School of Medicine,
14	Baltimore, Maryland, USA.
15	
16	Address for correspondence: Brett D. Thombs, PhD; Jewish General Hospital; 4333 Cote Ste
17	Catherine Road; Montréal, Québec, Canada, H3T 1E4; Tel (514) 340-8222 ext. 5112; E-mail:
18	brett.thombs@mcgill.ca
19	

### 20 ABSTRACT

21 **Objective:** The Beck Depression Inventory (BDI) is one of the most commonly used self-report 22 depression symptom questionnaires in medical settings. The revised BDI-II was developed in 23 1996, partially due to concerns about the influence of somatic symptoms from medical illness on 24 BDI scores. The BDI, however, continues to be frequently used in medical settings. The objective 25 of this study was to examine the degree to which somatic symptom items influence BDI scores 26 among hospitalized post-myocardial infarction (MI) patients with major depressive disorder 27 (MDD) compared to psychiatry outpatients with MDD matched on cognitive/affective scores, 28 sex, and age. 29 Methods: Somatic scores of post-MI patients with MDD and matched psychiatry outpatients 30 with MDD were compared using independent samples *t*-tests. 31 **Results:** 579 post-MI patients with MDD (mean age=54.4 years, SD=9.9) and 579 psychiatry 32 outpatients with MDD (mean age=51.2 years, SD=9.7) were matched on cognitive/affective 33 scores, sex, and age. Somatic symptoms accounted for 47% of BDI total scores among post-MI 34 patients (mean total=22.6, SD=8.8) versus 37% among psychiatry outpatients (mean total=19.2, 35 SD=9.7). Somatic scores of post-MI patients were 3.4 points higher than for matched psychiatry outpatients (95% confidence interval 3.0 to 3.9; p<.001), a difference that is equivalent to 15% of 36 37 total post-MI patient scores. 38 Conclusion: BDI scores of hospitalized post-MI patients with MDD may, in part, reflect 39 symptoms of the acute medical condition or its treatment, rather than depression. The BDI-II was 40 designed to reduce the influence of somatic symptoms on total scores and may be preferable to 41 the BDI among heart disease patients.

42 Keywords: Beck Depression Inventory; Cardiovascular disease; Depression, Myocardial

43 infarction; Psychometrics.

44

#### 45 **INTRODUCTION**

60

46 Major depressive disorder (MDD) is common among patients with chronic medical 47 disease and is associated with increased morbidity and mortality {{267 Katon, W.J. 2011; 265 48 Clarke, D.M. 2009; 266 Egede, L.E. 2007; 268 Moussavi, S. 2007; 269 Patten, S.B. 2006; 1 49 Evans, D.L. 2005}. Among patients with cardiovascular disease, the prevalence of MDD is 50 approximately 20% {{231 Thombs, B.D. 2006; 232 Rutledge, T. 2006}}. Depression following 51 acute myocardial infarction (MI) is associated with an increased risk of subsequent 52 cardiovascular events and mortality {{253 Nicholson, A. 2006; 251 Frasure-Smith, N. 2005; 236 53 Sorensenf, C. 2005; 238 Barth, J. 2004; 239 van Melle, J.P. 2004}, as well as greater disability 54 {{240 Ruo, B. 2003}}, reduced quality of life {{14 Rumsfeld, J.S. 2005}}, and higher health care 55 costs {{242 Frasure-Smith, N. 2000}}. 56 Concerns have been raised, however, about the validity of assessing symptoms of 57 depression with self-report questionnaires among patients with chronic medical disease because 58 symptoms that commonly occur in this context may be misinterpreted as mood-related {{274 59 Kathol,R.G. 1990; 273 Rodin,G. 1986}. Symptoms that occur in many patients hospitalized for

61 substantially with somatic symptoms of depression. This has led some experts to suggest that

an MI, including appetite disturbances, sleep disturbances, and fatigue, for example, may overlap

62 scores on self-report depression symptom questionnaires among post-MI patients may reflect

63 both symptoms of depression and cardiovascular disease severity and that this may artificially

64 increase the association between post-MI depressive symptoms and subsequent cardiovascular

65 events and mortality {{253 Nicholson, A. 2006; 236 Sorensenf, C. 2005; 247 Lane, D. 2003; 249

66 Mendes de Leon, C.F. 1999}. After adjustment for disease severity, symptoms of depression are

67 still associated with poorer cardiovascular prognosis, albeit to a reduced degree {{253

Nicholson,A. 2006; 235 Meijer,A. 2011}. Nonetheless, the likelihood of residual confounding
raises the possibility of overestimation of the strength of this relationship {{305 Macleod,J. 2003;
304 Macleod,J. 2003}}.

71 The Beck Depression Inventory (BDI) {{270 Beck, Aaron. T. 1987}} is commonly used 72 in medical settings and has been used more than any other self-report depression symptom 73 questionnaire in studies of patients with cardiovascular disease {{231 Thombs, B.D. 2006; 239 74 van Melle, J.P. 2004; 235 Meijer, A. 2011; 244 Davidson, K.W. 2006}. In part due to concerns 75 that the BDI may be unduly influenced by somatic symptoms not necessarily related to 76 depression, the revised BDI-II {{271 Beck, A. T. 1996}} was developed. The BDI-II includes 77 three fewer somatic symptom items than the BDI. Specifically, items 15 (work difficulty), 19 78 (weight loss), and 20 (somatic preoccupation) on the BDI were removed in developing the 79 revised BDI-II. In addition, changes were made in the response options of items 16 (insomnia) 80 and 18 (loss of appetite) in an attempt to reduce the effect of somatic symptoms on total scores. 81 Consistent with this, a study of the BDI {{278 Delisle, VC. In press}} found that the relative 82 influence of somatic symptoms on the BDI total scores was significantly higher for 296 83 hospitalized post-MI patients than for psychiatry outpatients matched on cognitive/affective 84 symptom scores, sex, and age, equivalent to 14% of total BDI scores of post-MI patients. On the 85 other hand, a study of the BDI-II {{250 Thombs, B.D. 2010}} found no difference in BDI-II 86 somatic symptom scores between 209 hospitalized post-MI patients and psychiatry outpatients 87 similarly matched on cognitive/affective symptom scores, sex, and age. A limitation of both of 88 those studies, however, was that psychiatry outpatients were matched with post-MI patients, most 89 of whom did not have depression. Thus, BDI and BDI-II scores of matched post-MI and 90 psychiatry outpatients in the two studies were relatively low. To address this issue, the present

study compared BDI somatic symptom scores of post-MI patients with MDD and psychiatry

92 outpatients with MDD matched exactly on individual cognitive/affective symptom scores, as well

as sex and age.

94 **METHOD** 

## 95 **Patients and Procedure**

96 This study was a secondary analysis of existing datasets. Post-MI patient data was from
97 the Enhancing Recovery in Coronary Heart Disease (ENRICHD) study {{286 Berkman,L.F.
98 2003}} and was obtained from the National Heart, Lung, and Blood Institute Biologic Specimen
99 and Data Repository Information Coordinating Center. Psychiatry outpatient data was obtained
100 from Center of Cognitive Therapy of the University of Pennsylvania in Pennsylvania, USA.
101 Ethics approval for this study was obtained from the Research Ethics Committee of the Jewish
102 General Hospital, Montréal, Québec, Canada.

The methods of this study closely replicate the methods that were used in two previous studies that compared somatic symptoms scores on the BDI {{278 Delisle, VC. In press}} and the BDI-II {{250 Thombs,B.D. 2010}} of post-MI patients and psychiatry outpatients. In this study, however, unlike in those previous studies, only post-MI and psychiatry patients with a diagnosis of MDD were included.

108 Post-MI Patients. The post-MI sample consisted of baseline data from patients admitted 109 with an MI to 1 of 73 hospitals in the USA who were enrolled in the ENRICHD depression 110 treatment trial {{286 Berkman,L.F. 2003}}. Patients recruited between October 1996 and 111 October 1999 were eligible for the trial if they had a diagnosis of MDD or minor depression, or 112 were determined to have low social support. Patients with active substance abuse, bipolar 113 disorder, severe dementia or schizophrenia, or who were at imminent risk for suicide were excluded from the study. Before April 1998, patients taking an antidepressant medication were
also excluded from the study. Following April 1998, patients who were taking an antidepressant
for longer than two weeks but who met other eligibility criteria were included in the study.
Research nurses approached potentially eligible patients for informed consent and

enrollment within 28 days of the acute MI, at which time study assessments of depression and
social support were conducted. MDD, minor depression, and dysthymia were diagnosed
according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSMIV) criteria using the Depression Interview and Structured Hamilton {{284 Freedland,K.E.
2002}}. ENRICHD methods have previously been described {{286 Berkman,L.F. 2003; 301
ENRICHD Investigators 2001}}. In the present study, only patients from ENRICHD with MDD,
with or without low perceived social support, were included in analyses.

125 *Psychiatry Outpatients.* The psychiatry outpatient sample consisted of patients seeking 126 treatment for mental health problems at the Center of Cognitive Therapy of the University of 127 Pennsylvania in Pennsylvania, USA between July 1972 and February 1998. Patients provided 128 informed consent and were administered a standard intake battery of psychological measures, 129 including the BDI. In addition, patients received a psychiatric diagnosis based on a clinical 130 interview. Patients recruited from 1983 forward were interviewed and diagnosed by a doctoral-131 level clinician with consecutive editions of the Structured Clinical Interview for the DSM-III or 132 DSM-III-R {{279 Spitzer, R. L. 1990}}. All diagnoses were translated into diagnoses based on 133 the DSM-IV following guidelines and comparative listings presented in consecutive issues of the 134 DSM. Only patients with a diagnosis of MDD were included in analyses.

Matching Procedure. Post-MI patients and psychiatry outpatients who completed all BDI
 items were matched exactly on individual cognitive/affective symptom scores, sex, and age.

137 Matching on sex was undertaken since gender may influence the proportion of cognitive/affective 138 and somatic symptoms reported {{276 Delisle, V.C. 2012}}, and matching on age was 139 undertaken because the post-MI patients were, on average, older than psychiatry patients. Thus, 140 for males and females separately, for each individual cognitive/affective score on the BDI (0, 1, 1)141 2, and so forth), all post-MI patients or psychiatry outpatients were included from the group with 142 fewer patients with that score. Then, the same number of participants from the other group with 143 the same cognitive/affective score was included. We selected the youngest patients for each 144 cognitive/affective score for the post-MI sample and the oldest for the psychiatry outpatient 145 sample. For example, if there were 10 post-MI patients and 15 psychiatry outpatients with a 146 cognitive/affective score of 5, then all 10 post-MI patients were selected along with the oldest 10 147 psychiatry outpatients.

# 148 Measure

149 Symptoms of depression were assessed using the 21-item BDI [24]. BDI items consist of 150 four statements, scored 0 to 3, with higher scores indicating increasing symptom severity. 151 Respondents are instructed to describe the way they have been feeling during the past week. 152 There is extensive evidence for the reliability and validity of the BDI in both psychiatric and non-153 psychiatric populations {{263 Beck, Aaron T. 1988}}, including post-MI patients {{244 154 Davidson,K.W. 2006}}. 155 Based on a review of existing factor models {{263 Beck, Aaron T. 1988}} and item 156 content, scores on items 1-10 and 12-14 (sadness, pessimism, sense of failure, self-dissatisfaction,

157 guilt, punishment, self-dislike, self-accusations, suicidal ideas, crying, social withdrawal,

158 *indecisiveness, body image change*) were summed to calculate cognitive/affective symptom

scores. Items 11 and 15-21 (irritability, work difficulty, insomnia, fatigability, loss of appetite,

*weight loss, somatic preoccupation, loss of libido*) were summed to calculate somatic symptom
scores.

## 162 Analysis of the Data

163 To test whether somatic symptom scores on the BDI differed between post-MI patients 164 with MDD and matched psychiatry outpatients with MDD at different levels of 165 cognitive/affective symptom scores and overall, independent samples 2-tailed *t*-tests were used. 166 The standardized mean difference for overall somatic scores was calculated using the Hedges's g 167 statistic {{275 Hedges, L. V. 1982}}. Differences in somatic symptom item scores between post-168 MI patients and matched psychiatry outpatients were similarly compared with independent 169 samples 2-tailed t-tests. Hochberg's Sequential Method was used to maintain a family-wise Type 170 I error rate of  $\alpha < .05$  for multiple item comparisons. Hochberg's Sequential Method is a 171 modified Bonferroni approach that is more powerful than the standard Bonferroni correction. In 172 Hochberg's Sequential Method, comparisons are conducted and then ordered according to their 173 p-values (largest to smallest). The first comparison is evaluated at  $\alpha = .05$ , the second 174 comparison is evaluated at  $\alpha = .025$  (i.e., .05/2), the third comparison is evaluated at  $\alpha = .017$ 175 (i.e., .05/3), and so forth. Once a comparison in this sequence is found to be statistically 176 significant, the procedure stops and all comparisons with smaller p-values are also deemed to be 177 statistically significant.

Several sensitivity analyses were conducted. First, to supplement the main analysis, we analyzed data from all patients, rather than just matched patients, by regressing somatic symptom scores on group, controlling for cognitive/affective symptom scores. Second, because item 11 (*irritability*) may not be a somatic symptom, we analyzed whether removing this item from calculations of somatic symptom scores would change the main results of the study. To do this, 183 we calculated somatic scores using only items 15 to 21 (*work difficulty, insomnia, fatigability,* 184 loss of appetite, weight loss, somatic preoccupation, loss of libido) and then tested whether these 185 scores differed between post-MI patients and matched psychiatry outpatients overall, using 186 independent samples 2-tailed *t*-tests. Third, because of a post-matching difference in age between 187 the two groups, the overall somatic symptom scores of post-MI patients and matched psychiatry 188 outpatients were compared using ANCOVA to adjust for age. Fourth, because psychiatry 189 outpatients completed the BDI between 1972 and 1998, whereas post-MI patients completed the 190 BDI from 1996 to 1999, we tested whether the year of evaluation was associated with somatic 191 symptom scores among psychiatry outpatients, by regressing somatic scores on year of 192 evaluation, controlling for cognitive/affective symptom scores. Finally, we tested whether, 193 among post-MI patients, cardiac disease severity markers were associated with somatic symptom 194 scores. To do this, we separately regressed somatic symptom scores on diabetes mellitus (present 195 versus absent), history of MI (present versus absent), hypercholesterolemia (present versus 196 absent), hypertension (present versus absent), and Killip class (II, III or IV versus I), controlling 197 for cognitive/affective symptom scores in each case.

198 **RESULTS** 

## **Sample Characteristics**

200 Prior to matching, mean BDI total scores were 21.1 (SD = 8.5) for 783 post-MI patients 201 with MDD and 23.1 (SD = 10.5) for 2,232 psychiatry outpatients with MDD (p < .001). Mean 202 age for the post-MI patients was 59.1 years (SD = 12.2), and 396 (51%) were male. For the 203 psychiatry outpatients, mean age was 36.6 years (SD = 12.0), and 839 (38%) were male. 204 There were 579 post-MI patients (74% of all post-MI patients) and 579 psychiatry 205 outpatients (26% of all psychiatry outpatients) successfully matched based on BDI cognitive/affective symptom scores, sex, and age. Post-match mean BDI total scores were 22.6 (SD = 8.8) for post-MI patients and 19.2 (SD = 9.7) for psychiatry outpatients (p < .001). Mean age was 54.4 years (SD = 9.9) for post-MI patients and 51.2 years (SD = 9.7) for psychiatry outpatients (p < .001). There were 300 (52%) males in both samples. Sociodemographic and clinical characteristics of the matched post-MI patients and psychiatry outpatients are shown in Table 1.

# 212 BDI Somatic Symptoms of Post-MI Patients versus Psychiatry Outpatients

213 Somatic symptoms accounted for 47% of BDI total scores for the 579 post-MI patients 214 versus 37% for the matched psychiatry outpatients, a raw difference of 10%. BDI somatic 215 symptom scores of post-MI patients were on average 3.4 points higher than those of psychiatry 216 outpatients (95% confidence interval [CI] = 3.0 to 3.9; p < .001), a difference that is equivalent to 217 15% of the total BDI scores of post-MI patients. The standardized mean difference in somatic 218 scores corresponded to a Hedges's g of 0.87. The results of the analysis were similar when item 219 11 (irritability) was removed from calculations of somatic symptom scores (somatic score 220 difference = 3.1, 95% CI = 2.7 to 3.6, p < .001) or when controlling for age (somatic score 221 difference = 3.1, 95% CI = 2.7 to 3.5, p < .001). In addition, the results did not change 222 substantively when somatic scores were regressed on cognitive/affective scores and group for all 223 patients, rather than just matched patients (somatic score difference = 3.3, 95% CI = 3.0 to 3.6, p 224 < .001). Post-MI patients had statistically significantly higher somatic scores than psychiatry 225 outpatients at all cognitive/affective symptom score levels (Table 2). Among psychiatry 226 outpatients, year of evaluation was correlated equally with somatic (r = -0.1) and 227 cognitive/affective (r = -0.1) scores. Year of evaluation was not significantly associated with

somatic scores, controlling for cognitive/affective scores (p = 0.143). As shown in Table 3,

adjusting for multiple analyses, post-MI patients had statistically significantly higher scores on

somatic symptom items 11(*irritability*), 15 (*work difficulty*), 16 (*insomnia*), 17 (*fatigability*), 18

231 (loss of appetite), 19 (weight loss), and 20 (somatic preoccupation), but not on item 21 (loss of

232 *libido*).

Among post-MI patients, the presence of diabetes mellitus was associated with a 0.8 point increase (95% CI = 0.3 to 1.4, p = .004) in somatic symptom scores, controlling for cognitive affective scores. There were also significantly higher somatic symptom scores among patients with a previous MI (0.7 points, 95% CI 0.0 to 1.3, p = .037), hypertension (0.9 points, 95% CI 0.4 to 1.5, p = .002), and Killip class II-IV (1.7 points, 95% CI 1.0 to 2.4, p < .001).

Hypercholesterolemia was not significantly associated with somatic symptom scores (p = .813).
DISCUSSION

240 The main finding of this study was that somatic symptom scores on the BDI of post-MI 241 patients with MDD were, on average, more than 3 points higher than those of psychiatry 242 outpatients with MDD who were matched exactly on individual cognitive/affective symptom 243 scores, as well as sex and age. This 3-point difference is equivalent to almost 9/10 of a standard 244 deviation (standardized mean difference = 0.86), which is a large difference based on Cohen's 245 operational definitions (small = 0.2, medium = 0.5, large = 0.8) { $\{277 \text{ Cohen, J. } 1988\}$ }. This 246 difference was equivalent to 15% of total post-MI patient BDI scores. There were significant 247 differences between post-MI patients and matched psychiatry outpatients on all somatic symptom 248 items, with the exception of item 21 (loss of libido). Among post-MI patients, somatic symptom 249 scores were significantly associated with diabetes mellitus, previous MI, hypertension, and Killip 250 class > I. Patients with Killip class > I scored almost 2 points higher on BDI somatic symptom

251 scores, controlling for cognitive/affective symptom scores.

252 These findings are consistent with results reported in a previous study that compared 253 somatic symptom reporting on the BDI among post-MI patients and psychiatry outpatients 254 without MDD {{278 Delisle, VC. In press}}. In that study, somatic symptom scores of post-MI 255 patients were, on average, more than one point higher than those of psychiatry outpatients 256 matched on cognitive/affective symptom scores, sex, and age, a difference that was equivalent to 257 14% of total BDI scores of post-MI patients. The findings of these two studies differ, however, 258 from a study that used similar methods to compare somatic symptom reporting on the revised 259 BDI-II among post-MI patients and psychiatry outpatients {{250 Thombs, B.D. 2010}}. That 260 study found no difference in somatic symptom reporting between the two groups. Taken together, the findings of these studies suggest that scores on the BDI, but not the BDI-II, of hospitalized 261 262 post-MI patients may disproportionately reflect symptoms that commonly result from the acute 263 medical event or its treatment, rather than from depression.

264 Many previous studies show that higher scores on the BDI in hospitalized post-MI 265 patients are associated with worse prognosis {{235 Meijer, A. 2011}}. If these scores at least 266 partially reflect symptoms of the cardiac event or its treatment rather than depressed mood, it is 267 reasonable to consider whether the prognostic value of the BDI in this context may, at least in 268 part, relate to factors other than depression. It is interesting to note that no prior study has shown 269 that higher scores on the BDI-II in hospitalized post-MI patients are significantly associated with 270 prognosis, adjusting for other cardiac risk factors. Among studies included in a recent meta-271 analysis of post-MI depression and cardiovascular outcomes {{235 Meijer, A. 2011}}, only two 272 studies {{307 Steeds, R.P. 2004; 295 Lauzon, C. 2003}} used the BDI-II and neither study found a 273 significant relationship between symptoms of depression and cardiovascular prognosis. It should

be noted that one of the two studies incorrectly reported using the BDI, rather than the BDI-II, in
the original study {{295 Lauzon,C. 2003}}, but that it was later clarified that the BDI-II had been
used {{250 Thombs,B.D. 2010}}.

277 Results from the two studies on the BDI also raise the possibility that estimates of the 278 prognostic association of symptoms of depression assessed with the BDI and outcomes following 279 MI could be inflated due to biases in the measurement of depressive symptoms. Four studies 280 {{257 Roest, A.M. 2011; 256 Martens, E.J. 2010; 255 Linke, S.E. 2009; 254 de Jonge, P. 2006}} 281 have compared the prognostic association of somatic and cognitive/affective symptoms of 282 depression assessed with the BDI with post-MI outcomes and all have reported that somatic 283 symptoms, but not cognitive/affective symptoms, predicted negative cardiovascular outcomes. In 284 a recent study of 528 hospitalized post-MI patients, BDI somatic symptoms overlapped with vital 285 exhaustion to such a high a degree that the authors proposed they may represent the same 286 construct. A factor comprised of BDI somatic symptoms and vital exhaustion significantly 287 predicted new cardiovascular events, whereas BDI cognitive/affective symptoms did not {{302 288 Vroege, E.M. 2012}. In contrast to the findings of studies with the BDI, a study of 226 coronary 289 artery bypass graft patients that used the BDI-II found that cognitive/affective symptoms but not 290 somatic symptoms predicted cardiac morbidity and mortality {{262 Tully, P.J. 2011}}.

The degree to which somatic symptoms from medical illness may influence depression scores on self-report measures is likely measure-specific and should be assessed on a measureby-measure basis. For instance, both the BDI and the BDI-II assess somatic symptoms of depression, but, unlike the BDI, the BDI-II does not appear to be unduly influenced by inclusion of these symptoms. One possible reason for this is that there are fewer somatic symptom items included in the BDI-II compared to the BDI. Indeed, the number of somatic symptoms was intentionally reduced in developing the BDI-II {{271 Beck, A. T. 1996}}. Another possible
reason is that the BDI requires that symptoms be present for one week or longer, whereas the
BDI-II requires that they be present for a minimum of two weeks. The longer time period of
assessment built into the BDI-II may reduce the influence of acute symptoms from an MI or its
treatment.

302 Given that somatic symptoms from medical illness may influence scores on some 303 depression measures, it is tempting to consider excluding somatic symptoms from depression 304 symptom assessments. Indeed, self-report depression symptom questionnaires that do not include 305 somatic symptoms have been developed. The Hospital Anxiety and Depression Scale (HADS) 306 {{280 Zigmond, A.S. 1983}} is an example of one of these measures. The HADS is a 14-item self-report anxiety and depression symptom questionnaire that was developed based on the belief 307 308 that anhedonia is the core symptom of biologically influenced depression and the most robust 309 indicator of when antidepressant medications should be prescribed {{281 Snaith, R.P. 1987}}. 310 Consistent with this, 5 out of the 7 depression symptom items on the HADS assess anhedonia. 311 The HADS has been criticized, however, because it does not sufficiently differentiate between 312 anxiety and depression in some studies and because of and its poor performance in identifying 313 patients with depression in many patient groups {{283 Coyne, J.C. 2012; 282 Cosco, T.D. 2012}}. 314 Depression is a multifaceted construct, and validated instruments that assess the full spectrum of 315 symptoms without being overly influenced by somatic symptoms not necessarily related to 316 depression are preferable. Clinically, however, it is important to take care to not weigh somatic 317 symptoms such as appetite and fatigue too heavily without first clarifying the origin of these 318 symptoms.

319

Several limitations should be considered in interpreting results from this study. One is that

320 the post-MI and psychiatry outpatient samples were drawn from different settings. Although both 321 samples were closely matched on key variables (cognitive/affective symptom scores, sex, and 322 age), it is possible that differences in other variables, such as co-morbid physical and psychiatric 323 problems and differences in the method of diagnosing MDD, may have influenced the results. 324 However, the most likely bias, given the age of the psychiatry outpatients, would have been with 325 regard to physical problems, and this would actually be expected to dampen the difference 326 between the groups. Furthermore, the results of this study and a study that used a different 327 comparison sample were highly similar {{278 Delisle, VC. In press}}. In addition, the results of 328 this study, as well as those from a study on the BDI-II that did not find differences in somatic 329 symptom reporting {{250 Thombs, B.D. 2010}}, are consistent with what would be expected 330 given that the BDI was revised to reduce the influence of somatic symptoms on depression 331 symptom scores. A second limitation is that data for the post-MI and psychiatry outpatient 332 samples were collected over somewhat different time periods. While it is possible that the time of 333 assessment may have affected the number of symptoms reported, there is no obvious reason that 334 it would have affected the composition of symptoms. Furthermore, a sensitivity analysis showed 335 that the year of evaluation did not influence the relationship between BDI somatic scores and 336 BDI cognitive/affective scores among psychiatry outpatients. A third possible limitation is that 337 information on the clinical comorbidities of psychiatry outpatients was not available. To the 338 degree to which psychiatry outpatients may have had medical conditions, this may have reduced 339 potential differences in somatic symptom reporting between hospitalized post-MI and psychiatry 340 outpatients, suggesting that the difference we reported from this study may be conservative. In summary, this study found that somatic symptom scores on the BDI are significantly 341 342 higher among post-MI patients with MDD than among psychiatry outpatients with MDD

343 matched exactly on individual cognitive/affective symptom scores, sex, and age. Somatic 344 symptom scores were also substantially higher among post-MI patients with more severe cardiac 345 disease (e.g., Killip class). These results, as well as those from two previous studies {{278 346 Delisle, VC. In press; 250 Thombs, B.D. 2010}, suggest that assessing depressive symptoms 347 with the BDI, compared to the BDI-II, following an MI may be more likely to inflate depression 348 symptom severity scores due to the misattribution of somatic symptoms from the MI to 349 depression. Furthermore, these results suggest that the BDI-II is preferable among cardiovascular 350 disease patients and that the BDI would ideally not be used in this setting.

351

#### 352 **ACKNOWLEDGEMENTS**

353 Ms. Delisle was supported by a Master's Training Award from the Fonds de la Recherche 354 en Santé Québec. Dr. Thombs was supported by a New Investigator Award from the Canadian 355 Institutes of Health Research. Dr. Ziegelstein was supported by the National Center for 356 Complementary and Alternative Medicine (Grant no. R24AT004641) and the Miller Family 357 Scholar Program of the Johns Hopkins Center for Innovative Medicine. The content is solely the 358 responsibility of the authors and does not necessarily represent the official views of the National 359 Center for Complementary & Alternative Medicine or the National Institutes of Health. This 360 manuscript was prepared using Enhancing Recovery in Coronary Heart Disease (ENRICHD) 361 Research Materials obtained from the National Heart, Lung, and Blood Institute (NHLBI) 362 Biologic Specimen and Data Repository Information Coordinating Center and does not 363 necessarily reflect the opinions or views of the ENRICHD or NHLBI. 364

#### 365 **REFERENCES**

- 366 [1] Katon WJ. Epidemiology and treatment of depression in patients with chronic medical illness.
- 367 Dialogues Clin Neurosci 2011;13:7-23.
- 368 [2] Clarke DM, Currie KC. Depression, anxiety and their relationship with chronic diseases: a
- review of the epidemiology, risk and treatment evidence. Med J Aust 2009;190:S54-60.
- 370 [3] Egede LE. Major depression in individuals with chronic medical disorders: prevalence,
- 371 correlates and association with health resource utilization, lost productivity and functional
- disability. Gen Hosp Psychiatry 2007;29:409-16.
- 373 [4] Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic
- diseases, and decrements in health: results from the world health surveys. Lancet 2007;370:851-8.
- 376 [5] Patten SB, Wang JL, Williams JV, Currie S, Beck CA, Maxwell CJ, et al. Descriptive
- epidemiology of major depression in Canada. Can J Psychiatry 2006;51:84-90.
- 378 [6] Evans DL, Charney DS, Lewis L, Golden RN, Gorman JM, Krishnan KR, et al. Mood
- 379 disorders in the medically ill: scientific review and recommendations. Biol Psychiatry

380 2005;58:175-89.

- 381 [7] Thombs BD, Bass EB, Ford DE, Stewart KJ, Tsilidis KK, Patel U, et al. Prevalence of
- depression in survivors of acute myocardial infarction. J Gen Intern Med 2006;21:30-8.
- 383 [8] Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure: a meta-
- analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am
- 385 Coll Cardiol 2006;48:1527-37.
- 386 [9] Nicholson A, Kuper H, Hemingway H. Depression as an aetiologic and prognostic factor in
- 387 coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54

- 388 observational studies. Eur Heart J 2006;27:2763-74.
- 389 [10] Frasure-Smith N, Lesperance F. Reflections on depression as a cardiac risk factor.
- 390 Psychosom Med 2005;67:S19-25.
- 391 [11] Sorensen C, Friis-Hasche E, Haghfelt T, Bech P. Postmyocardial infarction mortality in
- relation to depression: a systematic critical review. Psychother Psychosom 2005;74:69-80.
- 393 [12] Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in
- patients with coronary heart disease: a meta-analysis. Psychosom Med 2004;66:802-13.
- [13] van Melle JP, de Jonge P, Spijkerman TA, Tijssen JG, Ormel J, van Veldhuisen DJ, et al.
- 396 Prognostic association of depression following myocardial infarction with mortality and
- 397 cardiovascular events: a meta-analysis. Psychosom Med 2004;66:814-22.
- 398 [14] Ruo B, Rumsfeld JS, Hlatky MA, Liu H, Browner WS, Whooley MA. Depressive symptoms
- and health-related quality of life: The Heart and Soul Study. JAMA 2003;290:215-21.
- 400 [15] Rumsfeld JS, Ho PM. Depression and cardiovascular disease: a call for recognition.
- 401 Circulation 2005;111:250-3.
- 402 [16] Frasure-Smith N, Lesperance F, Gravel G, Masson A, Juneau M, Talajic M, et al.
- 403 Depression and health-care costs during the first year following myocardial infarction. J
- 404 Psychosom Res 2000;48:471-8.
- [17] Kathol RG, Noyes R, Williams J, Mutgi A, Carroll B, Perry P. Diagnosing depression in
  patients with medical illness. Psychosomatics 1990;31:434-40.
- 407 [18] Rodin G, Voshart K. Depression in the medically ill: an overview. Am J Psychiatry
  408 1986;143:696-705.
- 409 [19] Lane D, Carroll D, Lip GY. Anxiety, depression, and prognosis after myocardial infarction:
- 410 is there a causal association? J Am Coll Cardiol 2003;42:1808-10.

- 411 [20] Mendes de Leon CF. Depression and social support in recovery from myocardial infarction:
- 412 confounding and confusion. Psychosom Med 1999;61:738-9.
- 413 [21] Meijer A, Conradi HJ, Bos EH, Thombs BD, van Melle JP, de Jonge P. Prognostic
- 414 association of depression following myocardial infarction with mortality and cardiovascular
- 415 events: a meta-analysis of 25 years of research. Gen Hosp Psychiatry 2011;33:203-16.
- 416 [22] Macleod J, Davey Smith G. Depression as a risk factor for mortality after coronary artery
- 417 bypass surgery. Lancet 2003;362:1500-1.
- 418 [23] Macleod J, Davey Smith G. Psychosocial factors and public health: a suitable case for
- 419 treatment? J Epidemiol Community Health 2003;57:565-70.
- 420 [24] Beck AT, Steer RA. Manual for the revised Beck Depression Inventory. Texas:
- 421 Psychological Corporation; 1987.
- 422 [25] Davidson KW, Kupfer DJ, Bigger JT, Califf RM, Carney RM, Coyne JC, et al. Assessment
- 423 and treatment of depression in patients with cardiovascular disease: National Heart, Lung, and
- 424 Blood Institute Working Group Report. Psychosom Med 2006;68:645-50.
- 425 [26] Beck AT, Steer RA, Brown GK. Manual for the Beck Depression Inventory-II. Texas:
- 426 Psychological Corporation; 1996.
- 427 [27] Delisle V, Abbey S, Beck A, Dobson K, Dozois D, Grace S, et al. The influence of somatic
- 428 symptoms on Beck Depression Inventory scores in hospitalized post-myocardial infarction
- 429 patients. Can J Psychiatry. In press.
- 430 [28] Thombs BD, Ziegelstein RC, Pilote L, Dozois DJ, Beck AT, Dobson KS, et al. Somatic
- 431 symptom overlap in Beck Depression Inventory-II scores following myocardial infarction. Br J
- 432 Psychiatry 2010;197:61-6.
- 433 [29] Berkman LF, Blumenthal J, Burg M, Carney RM, Catellier D, Cowan MJ, et al. Effects of

- 434 treating depression and low perceived social support on clinical events after myocardial
- 435 infarction: the Enhancing Recovery in Coronary Heart Disease patients (ENRICHD) randomized
- 436 trial. JAMA 2003;289:3106-16.
- 437 [30] Freedland KE, Skala JA, Carney RM, Raczynski JM, Taylor CB, Mendes de Leon CF, et al.
- 438 The Depression Interview and Structured Hamilton (DISH): rationale, development,
- 439 characteristics, and clinical validity. Psychosom Med 2002;64:897-905.
- 440 [31] ENRICHD Investigators. Enhancing Recovery in Coronary Heart Disease (ENRICHD):
- 441 baseline characteristics. Am J Cardiol 2001;88:316-22.
- 442 [32] Spitzer RL, Williams JBW, Gibbon M, First MB. User's guide for the Structured Clinical
- 443 Interview for DSM-III-R. Washington, DC: American Psychiatric Press; 1990.
- [33] Delisle VC, Beck AT, Dobson KS, Dozois DJ, Thombs BD. Revisiting gender differences in
  somatic symptoms of depression: much ado about nothing? PLoS One 2012;7:e32490.
- 446 [34] Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory:
- twenty-five years of evaluation. Clin Psychol Rev 1988;8:77-100.
- [35] Hedges LV. Estimation of effect size from a series of independent experiments. Psychol Bull
  1982;92:490-9.
- 450 [36] Cohen J. Statistical power analysis for the behavioral sciences. New Jersey: Lawrence
- 451 Erlbaum Associates; 1988.
- 452 [37] Steeds RP, Bickerton D, Smith MJ, Muthusamy R. Assessment of depression following
- 453 acute myocardial infarction using the Beck Depression Inventory. Heart 2004;90:217-8.
- 454 [38] Lauzon C, Beck CA, Huynh T, Dion D, Racine N, Carignan S, et al. Depression and
- 455 prognosis following hospital admission because of acute myocardial infarction. CMAJ
- 456 2003;168:547-52.

457 [39] Roest AM, Thombs BD, Grace SL, Stewart DE, Abbey SE, de Jonge P. Somatic/affective

458 symptoms, but not cognitive/affective symptoms, of depression after acute coronary syndrome

459 are associated with 12-month all-cause mortality. J Affect Disord 2011;131:158-63.

460 [40] Martens EJ, Hoen PW, Mittelhaeuser M, de Jonge P, Denollet J. Symptom dimensions of

post-myocardial infarction depression, disease severity and cardiac prognosis. Psychol Med
2010:40:807-14.

463 [41] Linke SE, Rutledge T, Johnson BD, Vaccarino V, Bittner V, Cornell CE, et al. Depressive

464 symptom dimensions and cardiovascular prognosis among women with suspected myocardial

465 ischemia: a report from the National Heart, Lung, and Blood Institute-sponsored women's

466 ischemia syndrome evaluation. Arch Gen Psychiatry 2009;66:499-507.

467 [42] de Jonge P, Ormel J, van den Brink RH, van Melle JP, Spijkerman TA, Kuijper A, et al.

468 Symptom dimensions of depression following myocardial infarction and their relationship with

somatic health status and cardiovascular prognosis. Am J Psychiatry 2006;163:138-44.

470 [43] Vroege EM, Zuidersma M, de Jonge P. Vital exhaustion and somatic depression: the same

471 underlying construct in patients with myocardial infarction? Psychosom Med 2012;74:446-51.

472 [44] Tully PJ, Winefield HR, Baker RA, Turnbull DA, de Jonge P. Confirmatory factor analysis

473 of the Beck Depression Inventory-II and the association with cardiac morbidity and mortality

474 after coronary revascularization. J Health Psychol 2011;16:584-95.

[45] Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand
1983;67:361-70.

477 [46] Snaith RP. The concepts of mild depression. Br J Psychiatry 1987;150:387-93.

478 [47] Coyne JC, van Sonderen E. No further research needed: abandoning the Hospital and

479 Anxiety Depression Scale (HADS). J Psychosom Res 2012;72:173-4.

- 480 [48] Cosco TD, Doyle F, Ward M, McGee H. Latent structure of the Hospital Anxiety and
- 481 Depression Scale: a 10-year systematic review. J Psychosom Res 2012;72:180-4.

		Psychiatry
	<b>Post-MI Patients</b>	Outpatients
	(N = 579)	(N = 579)
Sociodemographic Characteristics		
Age in years, mean (SD)	54.4 (9.9)	51.2 (9.7)
Male, n (%)	300 (51.8)	300 (51.8)
Clinical Characteristics <sup>a</sup>		
Diabetes mellitus, n (%)	216 (37.9) <sup>b</sup>	
History of MI, n (%)	153 (27.3) <sup>c</sup>	
Hypercholesterolemia, n (%)	325 (63.0) <sup>d</sup>	
Hypertension, n (%)	365 (64.4) <sup>e</sup>	
Killip class I, n (%)	402 (78.1) <sup>f</sup>	

Table I. Sociodemographic and Clinical Characteristics of Matched Post-MI patients andPsychiatry Outpatients

MI = myocardial infarction.

<sup>a</sup>Clinical characteristics of post-MI patients were obtained via their hospital charts by a research nurse. <sup>b</sup>n = 570. <sup>c</sup>n = 560. <sup>d</sup>n = 516. <sup>e</sup>n = 567. <sup>f</sup>n = 515.

									Somatic	Score
		Post-M	I Patients			Psychiatry	Outpatien	ts	Compa	rison
_		Mean		Somatic as		Mean		Somatic as	Difference	
Cognitive/		Cognitive/	Mean	Proportion		Cognitive/	Mean	Proportion	in	
Affective		Affective	Somatic	of Total		Affective	Somatic	of Total	Somatic	
Scores	n	Scores <sup>a</sup>	Scores <sup>a</sup>	Scores	n	Scores <sup>a</sup>	Scores <sup>a</sup>	Scores	Scores	p-value
0-6	114	3.87	8.30	68.2%	114	3.87	3.34	46.3%	4.96	< .001
7-9	108	8.04	9.41	53.9%	108	8.04	5.50	40.6%	3.91	< .001
10-12	117	10.90	10.75	49.7%	117	10.90	6.85	38.6%	3.90	< .001
13-17	134	14.68	11.39	43.7%	134	14.68	8.87	37.7%	2.52	< .001
18+	106	22.58	13.01	36.6%	106	22.58	11.22	33.2%	1.79	.001
Total	579	11.99	10.58	46.9%	579	11.99	7.17	37.4%	3.41	< .001

Table II. Comparison of BDI Somatic Symptom Scores of Post-MI Patients and Matched Psychiatry Outpatients

BDI = Beck Depression Inventory. MI = myocardial infarction.

<sup>a</sup>Definitions of cognitive/affective and somatic scores in text. Mean cognitive/affective scores were the same for post-MI patients and psychiatry outpatients across cognitive/affective score categories because patients were matched exactly on individual cognitive/affective scores, as well as sex and age.

		Psychiatry	Difference in	
	<b>Post-MI Patients</b>	Outpatients	Somatic Item	
BDI Item	(Mean/SD)	(Mean/SD)	Scores <sup>a</sup>	p-value
11. Irritability	1.19/0.81	0.92/0.77	0.27	<.001 <sup>b</sup>
15. Work difficulty	1.58/0.85	1.26/0.81	0.32	<.001 <sup>b</sup>
16. Insomnia	1.70/1.03	1.27/1.04	0.43	<.001 <sup>b</sup>
17. Fatigability	1.72/0.83	1.10/0.82	0.62	<.001 <sup>b</sup>
18. Loss of appetite	1.06/1.00	0.49/0.77	0.57	<.001 <sup>b</sup>
19. Weight loss	0.88/1.12	0.32/0.73	0.56	<.001 <sup>b</sup>
20. Somatic preoccupation	1.26/0.95	0.66/0.81	0.60	<.001 <sup>b</sup>
21. Loss of libido	1.18/1.21	1.15/1.10	0.03	.647

Table III. Comparison of BDI Somatic Symptom Item Scores of Post-MI Patients and Matched Psychiatry Outpatients

BDI = Beck Depression Inventory. MI = myocardial infarction.

<sup>a</sup>Definition of somatic scores in text. <sup>b</sup>Statistically significant based on Hochberg's Sequential Method.