

- 3 Parker G: Beyond major depression. *Psychol Med* 2005;35:467–474.
- 4 Parker G, Roy K, Mitchell P, Wilhelm K, Malhi G, Hadzi-Pavlovic D: Atypical depression: a reappraisal. *Am J Psychiatry* 2002;159:1470–1479.
- 5 Leventhal AM, Rehm LP: The empirical status of melancholia: implications for psychology. *Clin Psychol Rev* 2005;25:25–44.
- 6 Thase ME: Atypical depression: useful concept, but it's time to revise the DSM-IV criteria. *Neuropsychopharmacology* 2009;34:2633–2641.
- 7 Lurie SJ, Gawinski B, Pierce D, Rousseau SJ: Seasonal affective disorder. *Am Fam Physician* 2006;74:1521–1524.
- 8 Baumeister H, Kufner K: It is time to adjust the adjustment disorder category. *Curr Opin Psychiatry* 2009;22:409–412.
- 9 Sneed JR, Roose SP, Sackeim HA: Vascular depression: a distinct diagnostic subtype? *Biol Psychiatry* 2006;60:1295–1298.

Harald Baumeister
 Engelbergerstrasse 41
 DE-79085 Freiburg (Germany)
 Tel. +49 761 203 3044, Fax +49 761 203 3040
 E-Mail baumeister@psychologie.uni-freiburg.de

Psychother Psychosom 2010;79:389–391
 DOI: [10.1159/000320899](https://doi.org/10.1159/000320899)

Adverse Effects of Multiple Physical Symptoms on the Course of Depressive and Anxiety Symptoms in Primary Care

K.M.L. Huijbregts^{a,b,e}, H.W.J. van Marwijk^b, F.J. de Jong^{a,b},
 B. Schreuders^d, A.T.F. Beekman^c, C.M. van der Feltz-Cornelis^{a,f}

^aDepartment of Diagnosis and Treatment, Netherlands Institute of Mental Health and Addiction (Trimbos Institute), Utrecht, Departments of ^bGeneral Practice and ^cPsychiatry and the EMGO+ Institute for Health and Care Research, VU University Medical Center, and ^dFaculty of Psychology and Education, VU University, Amsterdam, ^eAltrecht, Center of Excellence for Psychosomatic Medicine, Zeist, and ^fDepartment of Developmental, Clinical and Transcultural Psychology, University of Tilburg, Tilburg, The Netherlands

Depression and anxiety are highly prevalent [1] and are often treated in the primary care setting [2]. The effectiveness of psychosocial treatments such as problem-solving treatment has been established [3–6], but results in the primary care setting are sometimes less than one would expect based on the outcomes of efficacy studies under more stringently controlled circumstances [7–9].

A potentially relevant factor with a negative influence on treatment outcome is the presence of multiple physical symptoms [10, 11]. Up to 70% of depressed patients present themselves to their general practitioner with such physical symptoms instead of psychological symptoms [12]. Given this frequent co-occurrence, it seems plausible that multiple physical symptoms interfere with the course and outcome of symptoms of depression and anxiety. This hypothesis is in line with findings regarding the influence of concomitant physical symptoms on the course of major depressive disorder [11].

It is often difficult to determine whether multiple physical symptoms are an expression of co-morbidity with chronic medical conditions, or whether they are an expression of co-syndromality [13] or somatization [10, 14–16]. This distinction however might not be relevant if there is no association between multiple physical symptoms and the course and outcome of depression and anxiety.

We hypothesized that multiple physical symptoms might have a generic, but also a differential, effect (interaction by type of treatment) on the outcome of treatment. This study aims to test both hypotheses in a secondary analysis of data from a recently completed randomized clinical trial (RCT). This RCT assessed the effectiveness of up to 6 sessions of problem-solving treatment compared to ‘care as usual’ for patients suffering from depressive or anxiety symptoms in primary care [9]. The design [6] and results [9] of this RCT have been published elsewhere.

Patients were included in the current analysis if they had filled out the Hospital Anxiety and Depression Scale (HADS; $n = 130$) [17] at baseline and at follow-up (after 3 months). The course of anxiety and depressive symptoms was defined as unfavorable if the improvement in HADS was $\leq 50\%$ at follow-up. Multiple physical symptoms were measured with the PHQ-15, a scale comprising 15 physical symptoms frequently reported in the outpatient setting (total score: 0–30) [18].

The method of analysis applied by us to determine the association between multiple physical symptoms and the course and outcome of depression and anxiety was that of logistic regression analysis. The outcome variable was improvement on the HADS of $\leq 50\%$ (yes or no) and the determinant of focus was the PHQ-15 score at baseline. The analysis was adjusted for severity on the HADS at baseline, and for other variables that are associated with a higher number of physical symptoms (therefore likely to influence the association of the PHQ-15 with an unfavorable course on the HADS), namely gender [18], ethnicity and age [19]. Additional variables for which the analysis was adjusted were a diagnosis of depression and hypochondriasis, and whether or not psychopharmacological treatment was initiated between baseline and follow-up. A diagnosis of depression and hypochondriasis was based on the MINI neuropsychiatric interview [20].

The results of the adjusted logistic regression analysis, as shown in table 1, indicate that when the baseline PHQ-15 score of a patient in our sample increases by 1 point, the odds on an unfavorable course increase 1.17 times (95% CI: 1.019–1.351). The higher the score on the PHQ-15 at baseline, the less likely a patient was to experience a symptom reduction of at least 50% on the HADS. The likelihood of such an unfavorable course was about twice as high for patients scoring 1 SD above average on the PHQ-15. The adjusted odds ratio (OR) was 2.12 per 4.7 points (one SD) on the PHQ-15. The unadjusted OR, with only the PHQ-15 score as an independent variable, was 1.94 per SD ($p = 0.012$).

Adding the interaction term ‘randomization status times PHQ-15 score’ to the logistic regression model resulted in no significant improvement ($p = 0.823$). This implies that the outcome was similar in both treatment groups, although this should be interpreted with caution due to the relatively small sample size. This suggests a generic negative influence of multiple physical symptoms on the effectiveness of treatment for symptoms of depression and anxiety in primary care.

Two alternative explanations should be considered for this effect. Firstly, concomitant physical symptoms could be an expres-

Table 1. Results of the logistic regression analysis with response on the HADS at T1 as outcome variable

Independent variables	OR	p value	95% CI (of the OR)
PHQ-15	1.173 ¹	0.027	1.019–1.351
HADS at baseline	0.977 ¹	0.626	0.891–1.072
Female gender	0.746	0.580	0.263–2.110
Non-Dutch ethnicity	4.101	0.194	0.488–34.452
Age	0.981	0.293	0.947–1.016
MDD	1.683	0.506	0.363–7.789
Psychotropic medication	0.571	0.312	0.192–1.694
Hypochondriasis	1.257	0.763	0.285–5.538
Constant	0.851	0.948	0.007–109.710

T1 = Three months follow-up; MDD = major depressive disorder.

¹ OR per point on a continuous scale; an increase or decrease of 1 point on this scale means that the probability of a favorable response increases or decreases with the OR that is represented in the table.

sion of severity of depression or anxiety. However, in that case, the negative association would have disappeared after adjustment for baseline severity on the HADS and a MINI classification of MDD. As this was not the case, this explanation seems improbable.

Secondly, concomitant physical symptoms might be an independent factor, such as somatization (in the sense of somatic worry), with a negative impact on the course of depression and anxiety. In that case, the effect should have diminished at least partly after adjustment for a MINI classification of hypochondriasis. This was not the case either.

It is still unclear whether the physical symptoms were due to medical conditions, or whether they were medically unexplained symptoms. Our data did not allow us to make such a distinction, but this should be the topic of further research. Either way, the present data suggest that concomitant physical symptoms in patients with depression and anxiety are associated with a poorer prognosis of symptoms of depression and anxiety.

Our data thus show that it might prove worthwhile to pay attention to the role of multiple physical symptoms in the process of tailoring interventions to meet the needs of depressed and anxious patients in primary care. A useful tool might be the Diagnostic Criteria for use in Psychosomatic Research (DCPR) [21] that have recently been evaluated in primary care [22]. The DCPR classify 12 psychosomatic syndromes that may play a mediating role in the course and outcome of psychiatric disorders [23]. A thorough assessment according to these can be made by a general practitioner alone or together with a consultant-liaison psychiatrist who can also assist with the choice of treatment. Consultant-liaison models have been found to enhance the effectiveness of treatment in primary care for depression [24], anxiety [25] and medically unexplained symptoms [26]. Patients suffering from symptoms of depression and anxiety as well as multiple physical symptoms might reap the benefits of these services.

Conflict of Interest

All authors report that no conflicts of interest have occurred within the last 3 years (except C.F.C., who has received royalties for books that she wrote on the subject of psychiatry).

References

- 1 Bijl RV, Ravelli A, Van Zessen G: Prevalence of psychiatric disorder in the general population: results of the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Soc Psychiatry Psychiatr Epidemiol* 1998;33:587–595.
- 2 Braspenning JCC, Schellevis FG, Grol RPTM: Second National Study of illnesses and treatment in general practice. Focus on the quality of primary care [Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Kwaliteit huisartsenzorg belicht. In Dutch]. Utrecht/Nijmegen, The Netherlands, NIVEL/WOK, 2004.
- 3 Mynors-Wallis L: Problem-solving treatment for anxiety and depression. A practical guide. Oxford, Oxford University Press, 2005.
- 4 Mynors-Wallis LM, Gath DH, Day A, Baker F: Randomised controlled trial of problem solving treatment, antidepressant medication, and combined treatment for major depression in primary care. *BMJ* 2000; 320:26–30.
- 5 Mynors-Wallis L, Davies I, Gray A, Barbour F, Gath D: A randomised controlled trial and cost analysis of problem-solving treatment for emotional disorders given by community nurses in primary care. *Br J Psychiatry* 1997;170:113–119.
- 6 Schreuders B, van Oppen P, van Marwijk HW, Smit JH, Stalman WA: Frequent attenders in general practice: problem solving treatment provided by nurses [ISRCTN51021015]. *BMC Fam Pract* 2005;6:42.
- 7 Cuijpers P, van Straten A, Warmerdam L: Problem solving therapies for depression: A meta-analysis. *Eur Psychiatry* 2007;22:9–15.
- 8 Huibers MJ, Beurskens AJ, Bleijenberg G, van Schayck CP: Psychosocial interventions by general practitioners. *Cochrane Database Syst Rev* 2007;3:CD003494.
- 9 Schreuders B, Van Marwijk HWJ, Smit JH, Rijmen F, Stalman WAB, Van Oppen P: Primary care patients with mental health problems. Outcome of a randomised clinical trial. *Br J Gen Pract* 2007;57:886–891.
- 10 Crombez G, Beirns K, Van Damme S, Eccleston C, Fontaine J: The unbearable lightness of somatisation in empirical studies of pain. *Pain* 2009;145:31–35.
- 11 Huijbregts KML, Van der Feltz-Cornelis CM, Van Marwijk HWJ, De Jong FJ, Van der Windt DAWM, Beekman ATF: Negative association of concomitant physical symptoms with the course of major depressive disorder: A systematic review. *J Psychosom Res* 2010, in press.
- 12 Simon GE, Vonkorff M, Piccinelli M, Fullerton C, Ormel J: An international study of the relation between somatic symptoms and depression. *N Engl J Med* 1999;341:1329–1335.
- 13 Van der Feltz-Cornelis CM: Unexplained or undiagnosed? Towards a DSM-V for somatoform disorder. Comment on Van Dieren and Vingerhoets (Article in Dutch: Onverklaard of ondoordacht? Naar een DSM-V voor somatoforme stoornissen). *Tijdschr voor Psychiatr* 2007; 49:839–842.
- 14 Lieb R, Meinlschmidt G, Araya R: Epidemiology of the association between somatoform disorders and anxiety and depressive disorders: An update. *Psychosom Med* 2007;69:860–863.
- 15 Henningsen P, Zimmermann T, Sattel H: Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review. *Psychosom Med* 2003;65:528–533.
- 16 Löwe B, Spitzer RL, Williams JB, Mussell M, Schellberg D, Kroenke K: Depression, anxiety and somatization in primary care: syndrome overlap and functional impairment. *Gen Hosp Psychiatry* 2008;30:191–199.
- 17 Bjelland I, Dahl AA, Haug TT, Neckelmann D: The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52:69–77.
- 18 Kroenke K, Spitzer RL, Williams JB: The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med* 2002;64:258–266.

- 19 Hoedeman R, Krol B, Blankenstein N, Koopmans PC, Groothoff JW: Severe MUPS in a sick-listed population: a cross-sectional study on prevalence, recognition, psychiatric co-morbidity and impairment. *BMC Public Health* 2009;9:440.
- 20 Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC: The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59(suppl 20):22-33.
- 21 Fava GA, Freyberger HJ, Bech P, Christodoulou G, Sensky T, Theorell T, Wise TN: Diagnostic Criteria for Use in Psychosomatic Research. *Psychother Psychosom* 1995;63:1-8.
- 22 Ferrari S, Galeazzi GM, Mackinnon A, Rigatelli M: Frequent Attenders in Primary Care: Impact of Medical, Psychiatric and Psychosomatic Diagnoses. *Psychother Psychosom* 2008;77:306-314.
- 23 Porcelli P, Bellomo A, Quartasan R, Altamura M, Luso S, Ciannameo I, Piselli M, Elisei S: Psychosocial Functioning in Consultant-Liaison Psychiatry Patients: Influence of Psychosomatic Syndromes, Psychopathology and Somatization. *Psychother Psychosom* 2009;78:352-358.
- 24 Unutzer J, Katon W, Williams JW Jr, Callahan CM, Harpole L, Hunkeler EM, Hopping M, Areal P, Hegel MT, Schoenbaum M, Oishi SM, Langston CA: Improving primary care for depression in late life: the design of a multicenter randomized trial. *Med Care* 2001;39:785-799.
- 25 Katon WJ, Roy-Byrne P, Russo J, Cowley D: Cost-effectiveness and cost offset of a collaborative care intervention for primary care patients with panic disorder. *Arch Gen Psychiatry* 2002;59:1098-1104.
- 26 Van der Feltz-Cornelis CM, van Oppen P, Adèr H, van Dyck R: Randomised Controlled Trial of a Collaborative Care Model with Psychiatric Consultation for Persistent Medically Unexplained Symptoms in General Practice. *Psychother Psychosom* 2006;75:282-289.

K.M.L. Huijbregts
 Department of Diagnosis and Treatment
 Netherlands Institute of Mental Health and Addiction
 (Trimbos Institute), PO Box 725
 NL-3500 AS Utrecht (The Netherlands)
 Tel. +31 30 297 1185, Fax +31 30 297 1111
 E-Mail khuijbregts@trimbos.nl

Psychother Psychosom 2010;79:391-392
 DOI: [10.1159/000320897](https://doi.org/10.1159/000320897)

Major Depression in Cardiac Patients Is Accurately Assessed Using the Cardiac Depression Scale

William Y. Shi, Andrew G. Stewart, David L. Hare

Department of Cardiology, Austin Health,
 University of Melbourne, Melbourne, Vic., Australia

The Cardiac Depression Scale (CDS) was initially developed specifically for cardiac patients. Its purpose is to allow measurement over the continuum between low-level depressive symptomatology and major depression [1]. The CDS has not yet been validated against categorical diagnoses of depression by a structured clinical interview. We aimed to evaluate the criterion-related validity of the CDS and thus determine optimal CDS cutoff scores

These findings have been presented at the European Society of Cardiology Annual Congress, Munich, September 2008. There are no conflicts of interest.

for detecting major depression for both two-stage screening in clinical settings and single-stage screening in epidemiological research settings. Two hundred and fifteen patients were recruited from the cardiology service of a major secondary and tertiary referral hospital.

The CDS comprises 26 items, each answered on a 7-point Likert-type scale, with responses ranging from 'strongly disagree' (1) to 'strongly agree' (7) [1]. To avoid a response set, 7 of the 26 items are worded in a positive direction and the overall score is calculated by summing across all items after reversing positively worded items, with scores ranging from 26 to 182. A higher total score reflects more severe depressive symptoms. Because of our own experience and that in other cultures [2], for the present study it was decided to exclude the 26th item of the CDS – which asks about sexual activity – from the analysis. Some patients find answering this item embarrassing or intrusive. For others, the interpretation of the question varies considerably from patient to patient, resulting in an overall lower factor loading associated with blurring rather than refining of the construct.

The Mini International Neuropsychiatric Interview (MINI) was used as the external criterion measure to determine the categorical presence of major depression. The MINI is a diagnostic structured interview compatible with the ICD-10 and DSM-IV. It has excellent psychometric properties when validated using the Structured Clinical Interview for DSM-III-R as the external criterion [3].

Participants were recruited from cardiology outpatient clinics prior to their appointment. They completed the questionnaires and underwent clinical assessment of depression contemporaneously during the same 1-hour visit. The MINI interview was conducted by a trained interviewer who was blinded to the questionnaire scores. Data were analyzed using SPSS 16.0 for Windows (Rel. 16.0.1. 2007, Chicago, SPSS Inc.). The concurrent component of criterion validity was examined by assessing how well the CDS was able to detect the category of major depression using the structured interview as the external criterion. Receiver operating characteristic curves were constructed for determining the optimal sensitivity and specificity and the area under the curve.

In clinical settings, two-stage screening typically occurs where patients who initially obtain a positive result on an instrument undergo further investigation (such as an interview) to confirm the presence of depression. The two-stage approach is also relevant in clinical trials where screening is used to assess eligibility. For clinical two-stage screening, it is suggested that a cutoff score should provide maximum sensitivity with at least 75% specificity [4] so as to limit false negatives while also preventing an inordinate number of false positives.

On the other hand, in research settings, where follow-up interviewing may not be possible or feasible, an accurate single-stage screening estimate of depression prevalence is usually required. In this instance, a cutoff score must provide a good trade-off between sensitivity and specificity. It has been suggested that the maximal Youden index (sensitivity + specificity – 1) should be used to select the appropriate cutoff [4] for such research settings.

It is also important to propose cutoff scores which are rounded and recognizable numbers in order to aid administration and interpretation of a scale. We chose to recommend CDS cutoff scores that are a multiple of 5 rather than cumbersome scores based solely on the statistics.