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2023-05-01

Malkki , V K , Rosenström , T H , Jokela , M M & Saarni , S E 2023 , ' Associations between specific depressive symptoms and psychosocial functioning in psychotherapy ' , Journal of Affective Disorders , vol. 328 , pp. 29-38 . https://doi.org/10.1016/j.jad.2023.02.021

http://hdl.handle.net/10138/356788
https://doi.org/10.1016/j.jad.2023.02.021

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Journal of Affective Disorders 328 (2023) 29–38

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Associations between specific depressive symptoms and psychosocial functioning in psychotherapy

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ARTICLE INFO

Keywords:
Social and occupational functioning
Depression symptoms
Psychotherapy
Hopelessness

ABSTRACT

Background: Psychotherapy for depression aims to reduce symptoms and to improve psychosocial functioning. We examined whether some symptoms are more important than others in the association between depression and functioning over the course of psychotherapy treatment.
Methods: We studied associations between specific symptoms of depression (PHQ-9) and change in social and occupational functioning (SOFAS), both with structural equation models (considering liabilities of depression and each specific symptom) and with logistic regression models (considering the risk for individual patients). The study sample consisted of adult patients (n = 771) from the Finnish Psychotherapy Quality Registry (FPQR) who completed psychotherapy treatment between September 2018 and September 2021.
Results: Based on our results of logistic regression analyses and SEM models, the baseline measures of depression symptoms were not associated with changes in functioning. Changes in depressed mood or hopelessness, problems with sleep, feeling tired, and feeling little interest or pleasure were associated with improved functioning during psychotherapy. The strongest evidence for symptom-specific effects was found for the symptom of depressed mood or hopelessness.
Limitations: Due to our naturalistic study design containing only two measurement points, we were unable to study the causal relationship between symptoms and functioning.
Conclusions: Changes in certain symptoms during psychotherapy may affect functioning independently of underlying depression. Knowledge about the dynamics between symptoms and functioning could be used in treatment planning or implementation. Depressed mood or hopelessness appears to have a role in the dynamic relationship between depression and functioning.

1. Introduction

Major Depressive Disorder (MDD) hinders the ability to fully function in many areas of daily life (Sheehan et al., 2017). Even symptoms below the diagnostic threshold of clinical depression can cause psychosocial burden and economic difficulties (Greer et al., 2010; Sadek and Bona, 2000). Psychotherapy and antidepressant treatment are both considered effective in treating depression, although psychotherapy appears to have more lasting effects (Furukawa et al., 2021). Evidence from a meta-analysis suggests that 62 % of depressed patients attending psychotherapy achieve remission (95 % CI 0.56–0.68 %), in contrast with 43 % of participants in control groups (95 % CI 0.34–0.52 %) (Cuijpers et al., 2014). However, there appears to be no consistent differences in effectiveness between different therapeutic frameworks (Barkham and Lambert, 2021). A strong need to further reduce the burden of depression remains (Cuijpers, 2017).

Evaluations of treatment outcome are often based solely on symptomatic change, even though the patient's social and occupational functioning is also relevant (Kamenov et al., 2015). From the patient's perspective, improving functioning may be even more important than relieving depressive symptoms as such (Zimmerman et al., 2006). While the mechanisms of change in psychotherapy are still largely unknown (Cuijpers et al., 2019), recent research suggests that psychotherapeutic treatments can be targeted and tailored for each patient to achieve better outcomes (e.g. Delgadillo et al., 2017; Schwartz et al., 2021). Targeting refers to treatment choices informed by patient's baseline characteristics, such as patterns of specific depressive symptoms. To improve treatment tailoring, more information is needed on how treatment

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https://doi.org/10.1016/j.jad.2023.02.021
Received 28 April 2022; Received in revised form 21 January 2023; Accepted 4 February 2023
Available online 9 February 2023
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response is related to changes in symptoms and functioning during treatment.

Some studies have suggested that different depressive symptoms change more readily than others in response to treatment, regardless of whether the treatment was psychotherapy (e.g. Fournier et al., 2013) or antidepressant medication (Iniesta et al., 2016; Komulainen et al., 2021). However, these symptom-specific changes may still be accounted for by a single underlying latent factor or syndrome (Rosenström et al., 2021; Stochl et al., 2020). Specific aspects of social and occupational functioning could also be differentially related to different depressive symptoms. The possible specificity related to functioning is an important question, as symptom severity is not directly associated with the level of disability, even though some symptom combinations are much more disabling than others (Fried and Nesse, 2014; García-Velázquez et al., 2017, 2021; Rosenström and Jokela, 2017; Zimmerman et al., 2018).

Psychotherapy improves psychosocial functioning of patients with depression, although evidence from a meta-analysis suggests that this effect is only moderate (d = 0.35, 95 % CI 0.24–0.46; Kamenov et al., 2017). It is not clear if the link between depression and functioning is explained by a depressive syndrome or whether it is more specific to some symptoms than to others. It is also unclear if these connections differ at the beginning and over the course of psychotherapy. Psychotherapy is often assumed to begin with the restoration of well-being; this is followed by alleviation of symptoms and eventually improvements in functioning (Howard et al., 1993; Stulz and Lutz, 2007). Empirical evidence for temporal or causal relationships between symptoms and functioning during psychotherapy remains unclear (Dunn et al., 2012; Lin et al., 2015).

This study sought to examine the associations between depression symptoms and functioning in the context of psychotherapy and to better understand the effectiveness of treatment and how specific symptoms are linked with social and occupational functioning. We determined (*i*) if specific pre-therapy depression symptoms are associated with changes in functioning during psychotherapy, despite adjusting for overall depression scores, and (*ii*) whether changes in specific symptoms during therapy are associated with changes in functioning, despite adjusting for change in overall depression scores. Further, we examined (*iii*) whether the results of the previous two questions differed if we used simpler sum scores or latent liabilities to adjust for overall depression. If the therapeutic change process starts before psychotherapy (Howard et al., 1993), baseline measures of depression should predict changes in functioning. In addition, we hypothesized that at least some of the symptom changes are partially independently linked to changes in social and occupational functioning.

2. Methods

2.1. Participants and study description

Participants were adult patients diagnosed with MDD, gathered from the Finnish Psychotherapy Quality Registry (FPQR) of the Hospital District of Helsinki and Uusimaa (HUS). Data for the study were collected from 12 September 2018 to 28 September 2021. Rationale, development, and baseline results concerning the Finnish psychotherapy quality register are described in elsewhere (Saarni et al., 2022). The FPQR works as a platform to support the planning of individual patient care and provides information on the availability and effectiveness of psychotherapies. The patient and therapist completed separate questionnaires to gather information about the patient's treatment experience and symptoms at the beginning and end of treatment. The therapists also reported the therapy framework. This naturalistic cohort study was non-profit research conducted as part of the HUS research project on the availability, effectiveness, and quality of psychosocial care. Permission was granted by the HUS Ethical Review Board. We focused on patients who were referred to short psychotherapy (<20 sessions) either from primary care or psychiatric specialty care and excluded those in extended therapy (40 or more sessions).

2.2. Measures and definitions

2.2.1. Background/control variables

Information on patients' work status, medication, and gender is based on self-reports, and therapy framework was reported by clinicians. Patients age and the site of referral (primary care vs. short specialty care) was recorded in the medical record system at the time of referral. Comorbidity was estimated based on the OASIS (The Overall Anxiety Severity and Impairment Scale; Norman et al., 2006) and AUDIT-C (The Alcohol Use Disorders Identification Test Consumption; Kriston et al., 2008) questionnaires, as both are included in the FPQR as a standard measures for all patients. OASIS consists of five questions, answered on a five-point scale (from 0 to 4), with the sum score ranging from 0 to 20 and higher values indicating stronger anxiety. AUDIT-C is a scale for detecting abuse of alcohol (five-point scale, sum score from 0 to 12) consisting of three questions, with higher levels corresponding to higher levels of alcohol consumption. The clinical cut-off for anxiety is OASIS score ≥8, and AUDIT-C ≥5 for women and ≥6 for men. The quality monitoring of psychotherapies acquired as outsourced services is systematically performed in the quality register. This is a contractual obligation for service providers; thus they also have a financial incentive to perform follow up. However, the results of the therapy did not affect the reimbursements received by the therapists.

2.2.2. Outcome variables

Assessment of psychosocial functioning often includes separate measures of mental, physical, and social functioning, and participation in work or other areas of life. In this study, functioning was measured with the SOFAS scale (Social and Occupational Functioning Assessment Scale) based on interview and assessment by a clinician (4th ed.; DSM–IV; American Psychiatric Association, 1994; Goldman et al., 1992). Previous research has shown that the SOFAS has acceptable reliability and validity (Hilsenroth et al., 2000; Jovanović et al., 2008; Smith et al., 2011). The SOFAS scale is highly similar to its parent scale Global Assessment of Functioning, (GAF, Lehman, 1983), with the difference that the former assess functioning separately from patients' symptoms (Samara et al., 2014). According to the study of Hay et al. (2003), SOFAS seems to have better validity among adult psychiatric inpatients, compared to the other DSM-IV axis V scales GAF and GARF (the Global Assessment of Relational Functioning Scale). However, more reliable and valid tools to assess functioning are still needed (Ro and Clark, 2009).

SOFAS includes an assessment of general psychosocial functioning in the present timeframe and separate estimates of functioning related to self-care, family life and relationships, work and study, and leisure activities. The scale ranges from 0 to 100, with higher values describing better functioning. More than 80 SOFAS points indicate normal or better than normal functioning, while less than 50 points indicate severe impairment (Current Care Guidelines, 2021). For example, 80 points from the area of work and study corresponds to the description: “No more than a slight impairment in occupational functioning”. In addition, zero is given when there is not enough information to complete the assessment, although there were no such cases in our data.

A ten-point change in SOFAS score can be considered clinically meaningful based on the structure and logic of the SOFAS scale and based on clinical practice. The scale is divided into ten sections (see supplements), where the level of functioning changes in intervals of ten points (Goldman et al., 1992). Therefore, also in the clinical practice, it is common to consider the change of ten points as a clinically meaningful change, when assessing functioning with SOFAS scale (Isometsä et al., 2008; Tuisku et al., 2012; Kuikka et al., 2014; Tiitola et al., 2016; Vuokko et al., 2012). We did not find any research articles that sought to identify the amount of SOFAS change associated with clinically relevant improvement, and therefore our decision to categorize change using 10-

point cut-off is based mainly on the structure of the SOFAS questionnaire. The SOFAS scores have been shown to be linearly linked with GAF scores measured both cross-sectionally and over time, thus the two being practically exchangeable measures of functioning (Samara et al., 2014). This means that a SOFAS measure is highly equivalent to a GAF measure. Like SOFAS, the GAF scale ranges from 0 to 100, with 10 interval anchor points describing different levels of functioning. The similar arrangement of the two scales, and the research evidence linking SOFAS and GAD measures together further validates our choice to interpret 10-point change in SOFAS scale as clinically meaningful.

Depression was measured with the PHQ-9 scale (Kroenke et al., 2001), which captures both DSM-V and ICD-10 diagnostic criteria of depression. Each of the nine questions resembles one symptom category in DSM-V (5th ed., American Psychiatric Association, 2013). The prevalence of each symptom during the last two weeks is evaluated on a four-point scale (0 = "never" to 3 = "nearly every day"). In addition, the estimate of the overall depression is calculated as a sum of the specific symptoms (range 0–27). A total score of 0–4 corresponds to normal mood, 5–9 points describe mild depressive symptoms, and points above 15 or 20 represent moderate or severe depression, respectively (Kroenke and Spitzer, 2002). A clinical cutoff point of 10 has diagnostic value in different settings (Moriarty et al., 2015). The validity and reliability of PHQ-9 is acceptable based on previous studies (Kroenke et al., 2001; Stochl et al., 2020). To improve readability, we refer to the PHQ-9 questions as symptoms. We used differences between baseline and follow up measures to depict change in PHQ-9 sum, PHQ-9 items and SOFAS.

2.3. Statistical analyses

2.3.1. Logistic regression analysis

The symptom-specific effects on the change in social and occupational functioning were first studied with logistic regression analysis (here called "clinical model"). We used at least 10 points change in functioning as a binary outcome measure for a clinically meaningful change (see "Outcome variables" above). To distinguish the effects of specific symptom changes from the changes in PHQ-9 sum score, we constructed nine trimmed sum scores, one for each symptom (i.e., question in PHQ-9) by summing changes in all the other eight symptoms together. In separate models for each nine symptoms, we adjusted for the overall depression using these trimmed sum scores. First, we predicted functioning using only the sum of symptoms and other control variables and could therefore compare the results from symptom-specific models with this baseline model. The other controlled variables in all regression models were sex, age, therapy framework (solution-focused, cognitive, psychodynamic, cognitive-analytic, cognitive-behavioral, integrative, other), site of referral (primary care vs. short specialty care), comorbidity (anxiety; OASIS, or alcohol use; AUDIT-C, being above their clinical cut-off score), number of sessions, and the time between baseline and follow-up measures of psychosocial functioning. We performed 10 analyses for both baseline measures of symptoms and trimmed sum scores as predictors of change in social and occupational functioning ("prognostics"). In addition, we constructed another 10 analyses with change in corresponding measures (i.e. symptoms and trimmed sum scores) as predictors ("models of change"), resulting in a total of 20 regression models. In all models, we used standardized symptom and depression variables to facilitate cross-model comparisons. Multicollinearity between symptoms were measured by GVIF (generalized variance inflation factor) (Fox and Monette, 1992).

2.3.2. Structural equation model (SEM)

SEMs can be used to study how well theoretical models and hypotheses fit the observed data. Importantly, SEM techniques for ordinal-valued data can be utilized to model underlying continuous-valued phenomena from coarse-grained ordinal-valued item data, such as PHQ-9 items. This puts symptoms with different endorsement rates on a more equal footing when considering their etiologic roles rather than predictive value on observed data. Due to the model for the underlying continuity, different answer categories of an independent variable are not collapsed into one effect, like in e.g., in classic linear regression analysis, and therefore, more accurate (less biased) results from the relationship between independent and dependent variables can be obtained. With SEM models, it is possible to simultaneously consider a symptom as a reflection of shared factor for depressive disorder and of item-specific variance orthogonal to the syndrome. To avoid biased estimates of latent quantities, it is important to define the SEM on polychoric rather than product-moment correlations (Verhulst and Neale, 2021). We called our SEM models as "etiologic", as these should provide more information on the latent etiology of symptoms compared to the logistic regression.

We examined the associations between depression symptoms and social and occupational functioning by using both depression symptoms measured at the baseline (10 "prognostic models"), and by using the measures of change in depression symptoms (10 "models of change") as predictors in separate models. In our SEM models we used continuous measures of change in functioning as the dependent variable. We first constructed a model in which the functioning was predicted only by latent depression. We then built models separately for each of the nine PHQ-9 items.

Based on the recent studies of Rosenström et al. (2021) and Stochl et al. (2020), we assumed longitudinal measurement invariance to approximately hold for PHQ-9 and we focused on the differential associations of functioning with specific items versus depression factor (cf. external validity). For latent depression and underlying item-liabilities, we set the population mean at the beginning of the treatment to 0 and variance to 1 (along Rosenström et al., 2021) such that the estimated mean in the follow-up could be interpreted as changes in the standard deviations of the baseline values.

To implement these models, we used the mean- and variance-adjusted weighted least squares ("WLSMV") estimation method (Rosseel, 2012). We evaluated SEM fit based on χ^2 test and different fit indexes, such as the comparative fit index (CFI) (Bentler, 1990) and the root mean square error of approximation (RMSEA) (Steiger and Lind, 1980). We used R-Studio version 4.0.3 (2020-10-10, R Core Team, 2022) for all analyses and version 0.6–8 of the lavaan package for the SEM models (Rosseel, 2012). Because using dichotomized dependent variable in logistic regression is associated with loss of information, and because the SEM analysis without such dichotomization used other strong assumptions about the data, we did also a further sensitivity analysis with basic linear regression using a continuous-valued SOFAS outcome (see online supplements).

3. Results

The study sample (n = 771) consisted of adult patients diagnosed with major depression who had attended and completed psychotherapy. Patient age ranged from 19 to 86 (mean = 43.1 years, SD = 15.3) years; 75.0 % were women. The number of sessions ranged from 1 to 40, although 40.7 % of the treatments had a length of precisely 20 sessions, and only four patients received treatments longer than 20 sessions. Time between baseline and follow-up measures varied between 31 and 698 days. More information considering demographics and measures of depression and functioning are shown in Table 1. Distributions of PHQ-9 and SOFAS scales at the beginning and at the end of the treatment are shown in Fig. 1. Depression improved on average 3 PHQ-9 points during treatment, indicating medium-sized effect (mean = 3.28, SD = 5.12, Hedge's g = 0.59, 95 % CI = 0.52–0.67). Based on SOFAS changes, average functional improvement was nine points, indicating medium effect (mean = 9.32, SD = 10.14, Hedge's g = 0.76, 95 % CI = 0.70–0.83). From all participants, 735 (95.3 %) had measures of PHQ-9 at baseline and 699 (90.7 %) at follow up. Correspondingly, 751 (97.4 %) had data from SOFAS baseline and 735 (95.3 %) from follow up.

Table 1
Characteristics of adult depression patients from Finnish Psychotherapy Quality Registry (FPQR), n = 771.

Variables	Mean/%	SD
Age (years)	43.1	15.3
Sex (women, %)	75.0	–
Site of referral (%)		
Primary-care referrals	54.2	–
Specialty-care referrals	45.8	–
Time between baseline and follow-up (days)	192.8	73.3
Number of sessions	12.5	8.0
Comorbidity, OASIS (%)	69.1	–
Comorbidity, AUDIT-C (%)	5.2	–
Framework (%)		
Integrative therapy	11.1	–
Cognitive therapy	19.8	–
Cognitive-behavioral therapy	11.0	–
Cognitive-analytic therapy	11.0	–
Solution-focused therapy	29.2	–
Psychodynamic therapy	13.2	–
Other	4.7	–
Baseline of depression scores (PHQ-9)	11.0	5.6
Baseline functioning (SOFAS)	65.9	12.3
Work status (%)		
Retirement	9.4	–
Student	10.5	–
Unemployed	10.0	–
Working	41.5	–
Unable to work	15.7	–
Other	12.8	–
Psychotropic medication (%)		
Yes	57.1	–
No	42.9	–

Depression was measured by PHQ-9 (the Patient Health Questionnaire, scale = 0–27) and functioning by SOFAS (The Social and Occupational Functioning Assessment Scale, scale = 0–100). OASIS = The Overall Anxiety Severity and Impairment Scale, AUDIT-C = The Alcohol Use Disorders Identification Test Consumption. Patients attending long-term therapies are excluded from analyses. SD=Standard deviation.

Those missing PHQ-9 data either at baseline or follow up (11.4 %) did not differ in gender (31.8 % men among those who were missing PHQ-9 values, vs. 24.2 % men among those who did not, $\chi^2 = 2.05$, d.f. = 1, p = .15) or average age (41.5 vs. 43.3 years, $t = 0.93$, p = .36) from others. They also had similar levels of SOFAS at baseline (65.8 vs. 65.9 points at SOFAs scale, $t = -0.03$, p = .97) and at follow up (73.3 vs. 75.6 points at SOFAS scale, $t = 1.40$, p = .16) compared to participants without missing PHQ-9 values.

Polyserial correlations between symptoms and trimmed sum score were stronger at baseline when compared with measures of change. The symptoms most strongly associated with trimmed sum scores (both at baseline and over time) were little interest or pleasure, feeling depressed or hopeless, feeling tired, and feeling bad about oneself (items 1, 2, 4, and 6 in PHQ-9, correspondingly). The covariation in symptomatic changes was greatest between the diagnostic core symptoms, i.e., little interest or pleasure and feeling depressed or hopeless (polychoric R^2 = 28.8 %) and between feeling depressed or hopeless and feeling bad about oneself (polychoric R^2 = 27.3 %). Compared with other symptom items, changes in suicidal ideation and feeling slow or restless (items 8 and 9 in PHQ-9) occurred more rarely and had less variation, thus having lower correlations with changes in other symptoms and with changes in their trimmed sum scores.

3.1. Associating baseline measures of depression symptoms with functional improvement

3.1.1. Are symptoms clinically relevant for prognosis?

Baseline measures of overall depression or depression symptoms were not associated with change in patient's social and occupational functioning during psychotherapy (see supplementary materials). In logistic regression analyses, only poor appetite or overeating was associated with less frequent improvement in functioning ($OR_5 = 0.82$, 95 % CI = 0.68–0.98), but this finding did not withstand a correction for nine independent tests on nine depressive symptoms. None of the controlled variables in regression analyses were significant predictors for change in social and occupational functioning.

3.1.2. Are symptom-liabilities etiologically prognostic?

Results for the prognostic SEM models showed that, when adjusted for the baseline latent depression, none of the baseline symptoms were associated with improvement in social and occupational functioning gained during psychotherapy.

3.2. Associating changes in specific depression symptoms with functional improvement

3.2.1. Are symptom-specific changes associated with clinically significant functional improvement?

Change in sum of symptoms was a statistically significant predictor for improvement in social and occupational functioning in all 10 logistic regression models. From specific depression symptoms, improvements in little interest or pleasure ($OR_1 = 1.31$, 95 % CI = 1.08–1.59), feeling depressed or hopeless ($OR_2 = 1.54$, 95 % CI = 1.25–1.90), and feeling tired ($OR_4 = 1.31$, 95 % CI = 1.08–1.60) were statistically significantly associated with positive change in functioning after adjusting for change in overall depression using trimmed sum scores. Nagelkerke R^2 (Nagelkerke, 1991) values ranged from 0.29 (model 0) to 0.31 (model 2), indicating only small differences between the models, on how close the values predicted by each model was compared to the true observed value of the dependent variable. According to the ANOVA comparisons between each symptom model (models 1–9) and model 0, only models 5 and 2 differed from the baseline model 0 ($p\text{-value}_{model\ 5} = .004$, $p\text{-value}_{model\ 2} = .002$). Table 2 shows odds ratios for changes in specific symptoms and sum of symptoms in the regression models. For example, holding the trimmed sum score constant, the odds for experiencing clinically significant improvement in functioning increased by 54 % (95 % CI = 25–90 %) for each point reduction of one standard deviation in feeling depressed or hopeless. None of the controlled variables were associated with change in functioning and the measures of multicollinearity were acceptable (GVIF<2). Odds ratios for depression and symptom changes are summarized in Fig. 2.

3.2.2. Are latent symptom-specific liabilities associated with functional improvement?

Results of the SEM models of change are shown in Table 3 and summarized in Fig. 2. From specific symptom items, changes in feeling depressed or hopeless ($beta_2 = -0.20$, p < .001) and trouble sleeping ($beta_3 = 0.10$, p = .04) was associated with positive change in functioning, while enhancement of latent depression predicted improved functioning in all the models (beta = −0.28 to −0.31, p < .001). Model fit was acceptable for all SEM models of change [$\chi^2(79) = 57.68$–262.34, p-values <.001, CFI = 0.96, RMSEA = 0.06].

4. Discussion

We examined whether specific depression symptoms, adjusted for overall depression, were associated with changes in social and occupational functioning during psychotherapy. Baseline measures of depression or any of the nine symptoms assessed via PHQ-9 were not associated with change in functioning. Thus, assessing specific depression symptoms at the beginning of treatment did not provide additional information regarding prognosis on social and occupational functioning when compared to the measures of overall depression alone. However, the results from our models concerning associations between changes in depressive symptoms and changes in functional capacity showed symptom-specific effects.

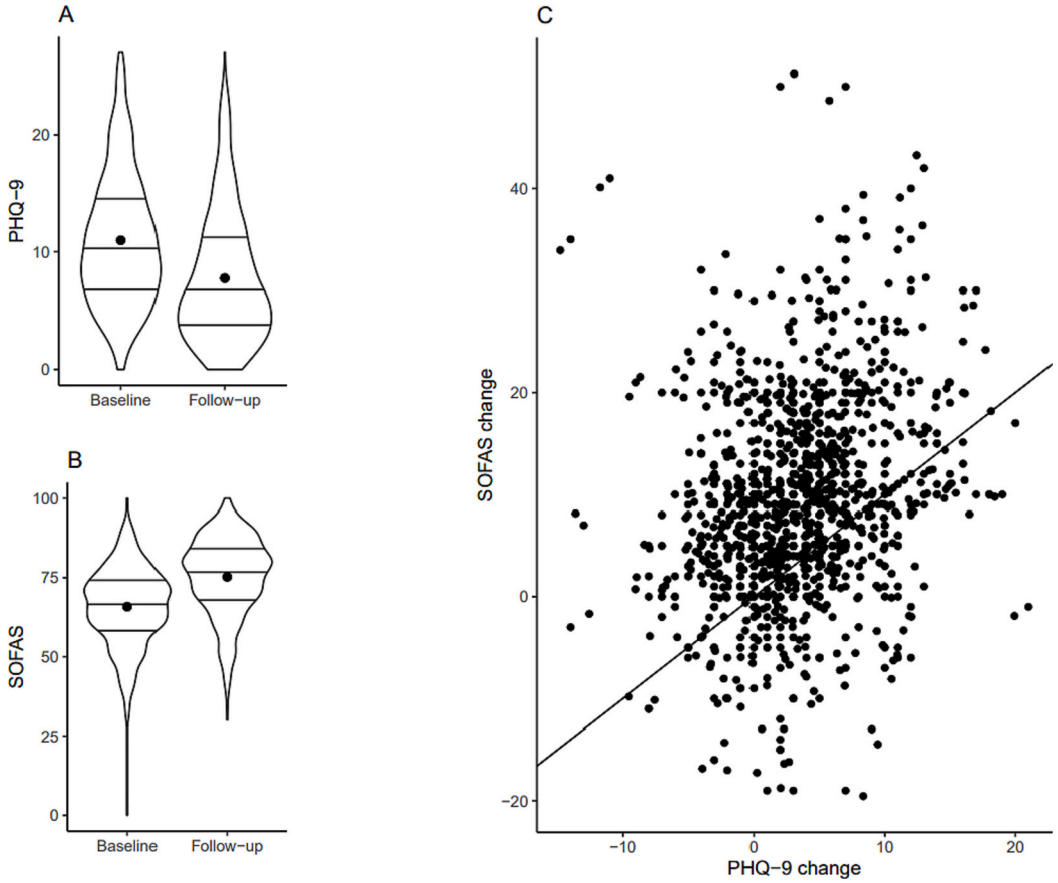

Fig. 1. Distributions of PHQ-9 (the Patient Health Questionnaire, scale = 0–27) and SOFAS (The Social and Occupational Functioning Assessment Scale, scale = 0–100) at the beginning and at the end of the treatment (panels A and B). A scatterplot of observed PHQ-9 changes and SOFAS changes are shown in panel C. The scale for SOFAS change is inverted, so positive numbers indicate improvement in both scales.

Table 2
Results from the logistic regression models of change predicting change in functioning (n = 771).

Model	OR $_{symptom}$	95 % Confidence interval		OR $_{depression}$	95 % Confidence interval	
0 Sum of symptoms	–	–	–	1.75	1.47	2.10
1 Little interest or pleasure	1.31	1.08	1.59	1.49	1.23	1.82
2 Feeling depressed or hopeless	1.54	1.25	1.90	1.32	1.08	1.62
3 Trouble sleeping	1.06	0.89	1.27	1.71	1.42	2.09
4 Feeling tired	1.31	1.08	1.60	1.47	1.20	1.80
5 Poor appetite	0.86	0.71	1.03	1.98	1.62	2.46
6 Feeling bad about oneself	1.11	0.91	1.35	1.64	1.34	2.02
7 Difficulty concentrating	1.11	0.93	1.34	1.66	1.37	2.02
8 Slow or restless	0.93	0.78	1.10	1.83	1.52	2.21
9 Suicidal ideation	0.97	0.82	1.17	1.78	1.48	2.17

In logistic regression model 0, change in social and occupational functioning is predicted by the change of depression sum score. In models 1–9, predictive variables are single-symptom changes and the trimmed sum score; numbers correspond to PHQ-9 symptom categories. In all models none of the measured adjusted variables were significant. As an example, adjusted variables for model 0 are shown in supplements (table S3). OR $_{symptom}$ = odds ratio for specific symptom corresponding the PHQ-9 items, OR $_{depression}$ = odds ratio for trimmed sum scores of depression symptoms.

The phase model of behavior change in psychotherapy suggests that changes in symptoms precedes changes in functioning (Howard et al., 1993). Had the change process been in progress already when some patients entered therapy, we would have expected to see a prognostic effect of symptoms on functioning. This was not observed. Others have also found no temporal precedence of symptoms on functioning during treatment (Dunn et al., 2012; Lin et al., 2015). However, our finding of associations between the change in depression and change in functioning is consistent both with the phase model during psychotherapy and with findings on the opposite temporal ordering of changes (Dunn et al., 2012) but not with a study that did not find associated changes in symptoms and functioning (Lin et al., 2015). However, the latter study focused on antidepressant treatment instead of psychotherapy, and the mechanisms of change could differ between the treatment forms. To the contrary, behavioral activation treatments are built on the hypothesis that functional activation would lead into improved mood and alleviated depression symptoms (Lewinsohn, 1974). However, empirical evidence for treatment-mediating effect of activation is still lacking (Janssen et al., 2021). Thus, future research could elucidate the causal relationship between functioning and symptoms. With a better understanding of temporal sequence, treatment could be targeted to either functioning or symptoms depending on the stage of the change process.

Using logistic regression models on observed data, changes in feeling depressed or hopeless, in little interest or pleasure, and in feeling tired were associated with changes in social and occupational functioning independently of the changes in overall depression. Among these symptoms, feeling depressed or hopeless was the most prominent predictor. However, for latent liabilities (presumed underlying etiology), only changes in feeling depressed or hopeless and trouble sleeping were

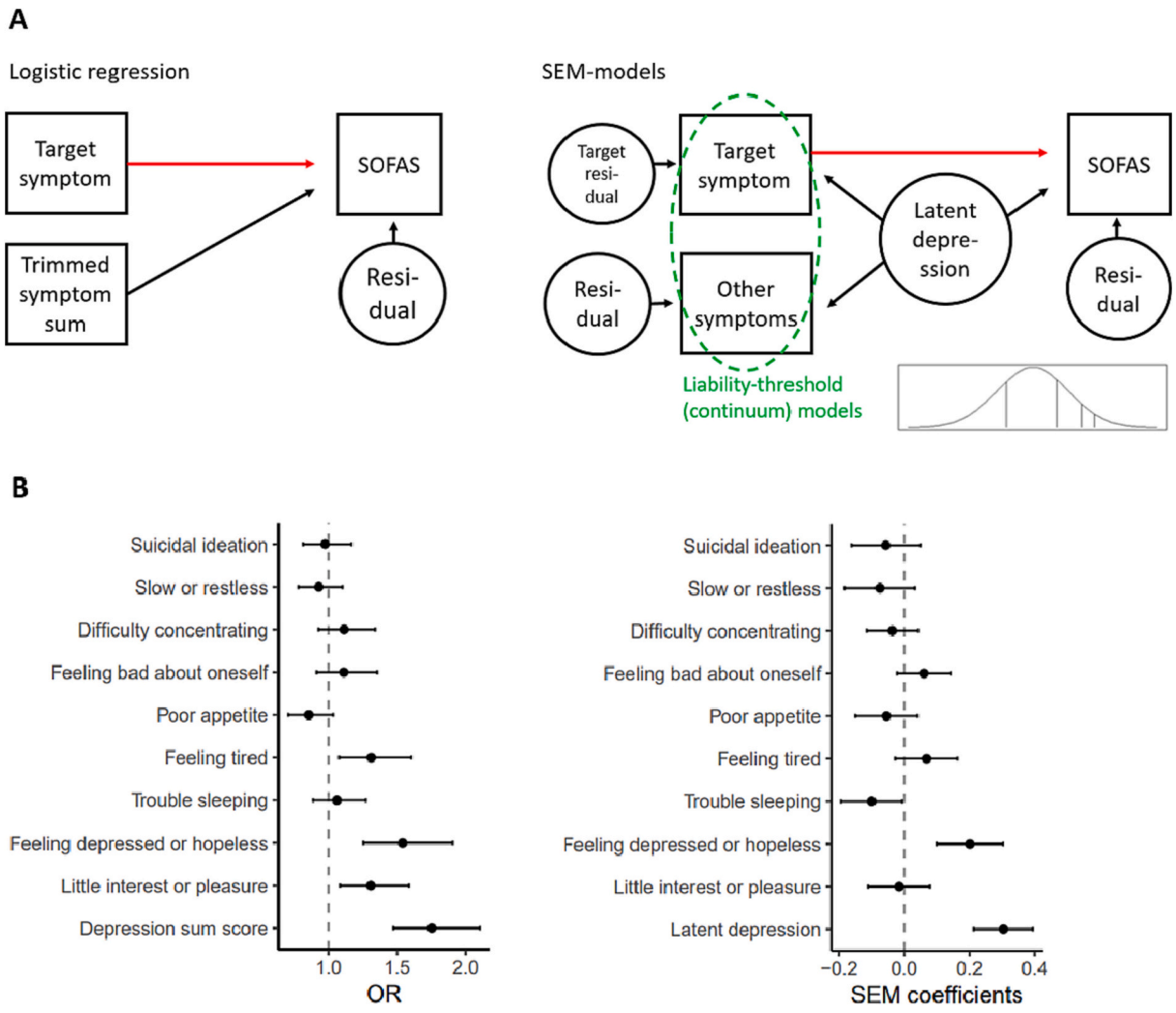

Fig. 2. Change in depression symptoms as predictors for improved functioning during psychotherapy. Panel A: Simplified path diagrams, to illustrate the methodological differences between logistic regression analysis and SEM models. Detailed descriptions of the models can be found in the text and supplementary materials. The normal distribution in the picture is an example of how the different answer categories (likert 0–4) of each item are not of equal size, and how mild symptoms are more frequent (more likely) than severe symptoms in the general population. With SEM models it is possible to consider these symptom liabilities behind the ordinal-valued PHQ-9 symptom items, and simultaneously consider a symptom as a reflection of latent depression and of item-specific variance orthogonal to the syndrome. Logistic regression analysis does not account for this population variance, but instead is better able to predict outcomes for individual patients. Panel B: On the left side is a forest plot showing odds ratios from 10 different logistic regression analysis predicting changes in social and occupational functioning (SOFAS) by decreases in depression symptoms (PHQ-9) and trimmed sum score (sum of other eight symptoms) or PHQ-sum score only (Depression sum score). Logistic regression analyses are adjusted for age, sex, comorbidity, site of referral, framework, number of sessions, and time between baseline and follow-up measures. On the right side is a forest plot displaying results from the 10 different SEM models, where decreases in depression symptoms (PHQ-9) predicted change in functioning (SOFAS). For visualization we used additive inverse of beta coefficients. Both methods show that depression or hopelessness is related to improved functioning.

associated with functional change independently of the overall depression. Feeling depressed or hopeless was thus most consistently associated with changes in functioning among the specific depressive symptoms. The increase in trouble sleeping was associated with improved functioning in an etiologic (SEM) model but not in a clinical (logistic regression) model, whereas the specific associations of little interest or pleasure and feeling tired with functioning were observable in a clinical model but not in an etiologic model.

Some differences between clinical and etiologic approaches were expected on methodological grounds. By modeling item-specific phenomena in a unit comparable to the latent overall depression, we could use a fuller range of population variance than is directly visible from ordinal-valued item endorsements. This perspective could reveal effects that are meaningful at a population level. However, some symptom effects may be relevant for individual patients, even if the effects are too weak to be detected when adjusted for population-level variance. Whereas specific effects of sleep problems may not be clinically observable, a more fine-grained analysis of continuous-valued functioning and subjective sleep quality (latent liability) may still have detected a genuine effect. For example, sleep-quality changes may be associated with pressures on sleep inflicted by an increased (i.e., improved) social and occupational life independent of the overall depression. Conversely, some symptoms may have favorable properties in ("clinical") regression prediction without having etiologic significance. Such properties could include a comparatively favorable range of variation being captured by the item categories and population sampling, or competition for overlapping outcome variance with the index of overall depression when item-specific residuals are not modeled, or both. Notably, feeling depressed or hopeless was the only specific depression item having both the qualities of etiologic and clinical

Table 3
Results from the SEM models of change predicting change in functioning (n = 771).

SEM-model	Symptom change			Change in latent depression		
	Beta	Std. error	p-value	Beta	Std. error	p-value
0 Latent depression	–	–	–	−0.30	0.05	<.001
1 Little interest or pleasure	0.02	0.05	.73	−0.31	0.05	<.001
2 Feeling depressed or hopeless	−0.20	0.05	<.001	−0.28	0.05	<.001
3 Trouble sleeping	0.10	0.05	.04	−0.32	0.05	<.001
4 Feeling tired	−0.07	0.05	.16	−0.30	0.05	<.001
5 Poor appetite	0.06	0.05	.26	−0.31	0.05	<.001
6 Feeling bad about oneself	−0.06	0.04	.15	−0.30	0.05	<.001
7 Difficulty concentrating	0.04	0.04	.36	−0.31	0.05	<.001
8 Slow or restless	0.08	0.06	.17	−0.31	0.05	<.001
9 Suicidal ideation	0.06	0.05	.29	−0.31	0.05	<.001

In SEM model 0, change in social and occupational functioning is predicted by change in latent depression. In models 1–9, functioning is predicted by change in specific PHQ-9 symptom (corresponding to the number of the model) and by change in latent depression.

prediction relevance.

Given the null effects from the prognostic models, results from the models of change are likely to be specific to phenomena of change. Furthermore, changes in symptoms may provide important information about the trajectory of depression during the psychotherapy process. Similar results obtained from different analytical approaches confirm this interpretation. In a network study measuring symptom-specific effects of antidepressant treatments for depression, depressed mood and insomnia were the most central symptoms along suicidality when predicting recovery from depression (Komulainen et al., 2021). However, whether the "feeling depressed or hopeless" and "trouble sleeping" items play a central role in the dynamics of depression in the context of psychotherapy requires further examination.

According to the cognitive theory of depression, negative views of oneself, the world, and the future are descriptive for all depressed people (Beck, 1963; Haaga et al., 1991). Further, experiencing one's situation as final generates hopelessness and promotes depressive symptoms. Negative believes, including hopelessness, is therefore relevant also from the treatment perspective. For example, dysfunctional believes have shown to mediate the relationship between personality dysfunction and depression and other negative emotional outcomes (McDermut et al., 2019). In addition, negative believes related to depression are often resistant to change (Kube and Rozenkrantz, 2021). In accordance with "the hopelessness theory of depression", hopelessness is associated with past adverse life events and negative inferential styles, making individuals vulnerable to depression and more resistant to treatment (Liu et al., 2015). In the study of Serafini et al. (2020) patients with major affective disorders suffering hopelessness reported more depressive symptoms and more previous antidepressant or psychotherapy treatments compared to those without hopelessness symptoms. Here, hopelessness might have aroused from unsuccessful past treatment experiences or indicate treatment resistance. In other studies, hopelessness is linked to treatment-resistant depression (Maalouf et al., 2011; Papakostas et al., 2005) and elevated risk for suicide (Lew et al., 2019; Ribeiro et al., 2018). Thus, more broadly than just from a symptomatic perspective, hopelessness is associated with severe and enduring clinical conditions that are themselves associated with poor functioning. This could explain why, in our results, decreased hopelessness produced its own specific positive effect on functioning in addition to the decreases in overall depression symptoms. In addition, one could assume that impaired functioning in itself is frustrating and may evoke feelings of hopelessness.

Building hope is seen as an important catalyst in the therapy process, promoting the patient's agency and ability to generate pathways towards their therapeutic goals (Bartholomew et al., 2021; Irving et al., 2004; Snyder et al., 2000). Considering the dynamics between symptoms and hopelessness, the study of Vittengl et al. (2014) showed that in cognitive therapy, changes in cognitive contexts, including hopelessness, may drive changes in depression symptoms, or vice versa. "Feeling down, depressed, or hopeless" is also associated with experienced lack of social support, which may be relevant when considering efficacy of psychotherapy (Jokela et al., 2019). To summarize, hopelessness seems to have an important role in the etiology of depression, both as a risk factor for more persistent depression, or when alleviated, as a precursor to positive change.

It is also possible that the observed effect on social and occupational functioning was mainly due to the changes in depressed mood instead of hopelessness. For example, Hieronymus et al. (2016) examined the sensitivity of the Hamilton Depression Rating scale (HDRS-17) to detect changes between placebo and antidepressant treatments by comparing the effect sizes of HDRS-17 sum, depressed mood item, and other subscales. In this post-hoc study, antidepressant treatment was significantly more often superior to placebo when differences between these settings were measured by the depressed mood item than by HDRS-17 sum (Hieronymus et al., 2016). As an analogy to this study, the depressed mood item might be more unidimensional and thus sensitive to detect changes in the core features of depression compared to the combination of all PHQ-9 symptoms and therefore produced its own effect.

The diagnostic definition of depression is based on the assumption that most observable symptoms and symptom combinations are interchangeable representations of the underlying latent syndrome (American Psychiatric Association, 2013). However, the high heterogeneity of MDD impairs the validity of this assumption (Fried and Nesse, 2015; Olbert et al., 2014). Some efforts to clarify the definition of depression have relied on creating different subcategories on the basis of, for example, the time of disease onset, symptom combinations, etiology, severity, or treatment response (Beijers et al., 2019; Harald and Gordon, 2012; Ulbricht et al., 2018). Other research efforts seek diagnostic clarification by placing depression into a wider hierarchy of psychiatric etiologic factors (Kotov et al., 2017), where specific depressive symptoms can nevertheless contain specific variance not fully attributable to measurement errors (Waszczuk et al., 2020). Still other research efforts consider depressive symptoms as reflecting a network of symptom-to-symptom influence (Borsboom, 2017; Bringmann et al., 2015; García-Velázquez et al., 2020; Komulainen et al., 2021). All these recent etiologic research approaches align with possible symptom-specific influences on treatment outcome. Therefore, our present empiric investigation is relevant to the aforementioned etiologic approaches, without a priori assuming any of the models.

Our findings should be interpreted considering certain limitations. On the PHQ-9 scale, each symptom is measured with only one question, which likely implies higher measurement error for specific symptoms compared to the overall depression. Use of trimmed sum scores in logistic regression analyses is also not equal to the total sum or latent depression, and thus introduces some bias to our analyses. In addition, each PHQ-9 question assesses more than one symptom, three of them including opposite descriptions (e.g., fifth item: "poor appetite or overeating"). Opposite symptom descriptions associate differently with functioning (Fried and Nesse, 2014). Thus, even though composite questions are common in all scales measuring mental disorders, more precise measures of symptoms would be needed when studying symptom effects. It should also be noted that clinician-rated measures of functioning may cause overestimated effects sizes (Kamenov et al., 2017). Though it is possible that the patients' functional capacity in our sample is therefore overestimated, if this error were systematic by nature, it may not be relevant in measuring the relationship between symptoms and functioning.

In future studies that include data collection as a part of the research

process, a more accurate picture of possible symptom effects could be attained via repeated measurements. Other perspectives to better understand the causality between depression symptoms and functioning would also be welcome. However, as a methodological strength, in addition to using simple (trimmed) sum scores, we modeled overall depression by observed liabilities, which allowed us to compare effects of symptoms and overall depression simultaneously. Our complementary analyses made it possible to study symptom effects both at the population level and from the perspective of individual patients. Furthermore, our results showed that symptom effects may vary, depending on whether underlying symptom liabilities are considered or not. Although naturalistic study designs are in many ways weaker than randomized trials, this does not apply to our research questions as we did not assess treatment efficacy per se. Instead, FPQR provides valuable and current information from psychotherapy processes in real-life settings in an ecologically valid manner.

Improving psychosocial functioning is an important aim of psychotherapy. As the effect size of psychotherapy on functioning is only moderate (Kamenov et al., 2017), it would be important to identify the factors that drive functional improvements and treatment efficacy. Using readily measurable patient data in predicting treatment outcomes and optimal treatment allocation seems a promising way forward (Iniesta et al., 2016; Schwartz et al., 2021). Further, understanding the dynamics between depressive symptoms and functioning may be useful in treatment planning and implementation. Utilizing symptom data to tailor treatment improves efficacy of psychotherapy (Bone et al., 2021; Delgadillo et al., 2022). Unraveling the relationship between symptoms and functioning could facilitate timely tailoring of interventions and techniques used in the treatment of an individual patient. For example, should the treatment aim to actively resolve the patient's problems (e.g., behavioral activation, cognitive reframing), or help the patient to focus on things that bring joy and meaningfulness despite the current symptoms or functional deficits (e.g., acceptance and mindfulness-based strategies)?

According to our results, changes in certain symptoms during treatment affects functioning independently of underlying depression, possibly reflecting differential etiologic mechanisms. The strongest evidence for symptom specific effects was observed for one of the core symptoms of depression, depressed mood or hopelessness. In our study, changes in depressed mood or hopelessness clearly contributed to the dynamic relationship between depression and functioning.

Funding sources

VM was supported by the Department of Psychiatry, Helsinki University Hospital. TR was funded by the Academy of Finland (grant numbers 334057 and 335901), MJ was funded by the by the Academy of Finland (grant number 3115789), and SS was funded by the Social Insurance Institution of Finland (Kela 140/331/2021).

CRediT authorship contribution statement

VM, TR and SS contributed to the study conception and design. VM and TR performed the statistical analysis and all authors contributed to the interpretation of the data. VM drafted the first version of the manuscript and all authors critically revised it for important intellectual content and approved the final version to be published.

Conflict of interest

None of the authors have any conflicts of interest to declare.

Acknowledgements

We would like to thank the Academy of Finland, the Helsinki University Hospital and the Social Insurance Institution of Finland for supporting this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.02.021.

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