ELSEVIER

Contents lists available at ScienceDirect

Internet Interventions



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

Predictors of functional impairment at assessment and functional improvement after treatment at a national digital mental health service

Shane P. Cross^{a,b,*}, Eyal Karin^{a,b}, Lia Asrianti^a, Jennie Walker^a, Lauren G. Staples^{a,b}, Madelyne A. Bisby^{a,b}, Olav Nielssen^a, Rony Kayrouz^a, Alana Fisher^b, Blake F. Dear^{a,b}, Nickolai Titov^{a,b}

^a MindSpot Clinic, Macquarie University, Sydney, Australia

^b School of Psychological Sciences, Macquarie University, Sydney, Australia

ARTICLE INFO

Keywords: Digital mental health service Assessment Internet-delivered cognitive behavioural treatment (iCBT) Functioning

ABSTRACT

Mental disorders are associated with impairment to daily functioning, which affects both the individual and society. Despite this, most research on treatment outcome only report symptom change. Self-reported days out of role (DOR) is a simple measure of functional impairment used in many population studies. The current study sought to report on the degree of functional impairment measured by DOR in a clinical sample at assessment, the factors associated with this impairment, the predictors of functional improvement after treatment and the relationship between symptomatic and functional change. Using a prospective uncontrolled observational cohort study design with a sample of 17,813 patients accessing a digital mental health service (DMHS), we examined self-reported demographic, psychosocial and clinical data. Using a series of univariate regression models and multivariate classification algorithms, we found that baseline DOR was associated with age, employment and relationship status, symptom severity, symptom chronicity and with the presence of several psychosocial difficulties. Baseline DOR was best predicted by older age, disability payments, higher symptom severity and increasing number of endorsed psychosocial difficulties ($R^2 = 32.7$ %). Forty-one per cent of the sample experienced a >50 % or greater reduction in DOR following treatment. Those who were separated, unemployed or on disability payments, or with severe and chronic depression, experienced the greatest reductions in DOR after treatment. Changes in functioning were independent of changes in symptoms, highlighting the importance of functional impairment as a treatment outcome. This study found that many of the patients who access DMHS have significant levels of functional impairment, a large proportion obtain functional improvement after treatment, and improvement in function after treatment was independent of improvement in symptoms.

1. Introduction

Numerous population surveys and clinical cohort studies have shown that mental disorders are associated with significant disability and impairment to function. The 2013 Global Burden of Disease Study, for example, found that mental and substance use disorders are the leading cause of years lived with disability (YLDs) (Whiteford et al., 2013), accounting for 21.1 % of all YLDs and 11 % of all disability-adjusted life years (DALYs) (Vos et al., 2017). A recent Australian Government report highlighted that despite the large public investment in mental health services, mental disorders still result in significant loss of productivity, estimated at AUD\$39 billion/year (Productivity Commission, 2020).

There are a number of ways to measure functional impairment, the

simplest and most used of which is self reported 'days out of role' (DOR). The DOR measure asks a person how many days they have been unable to perform their usual daily occupational, caregiving, and other social roles due to poor physical or mental health in the past month (McCallum et al., 2019). DOR has been reported to be higher in people with common mental disorders, indicating greater disability (Alonso et al., 2011). Although it relies on retrospective self-report, DOR has good concordance with payroll records of employed people (Revicki et al., 1994), and prospective daily diary reports (Kessler et al., 2004).

A multi-centre international study of 62,971 respondents conducted by the World Health Organization (WHO) reported that mental disorders were among the most strongly associated with productivity loss when measured by average DOR over a year (Alonso et al., 2011). When

https://doi.org/10.1016/j.invent.2023.100603

Received 17 July 2022; Received in revised form 30 November 2022; Accepted 20 January 2023 Available online 21 January 2023 2214-7829/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/bync-nd/4.0/).

^{*} Corresponding author at: MindSpot Clinic, Macquarie University, Sydney, Australia. *E-mail address:* shane.cross@mq.edu.au (S.P. Cross).

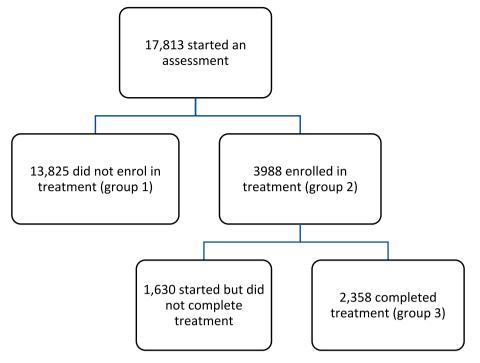


Fig. 1. Participant flow from assessment through to treatment completion.

adjusting for comorbid disorders, bipolar disorder, PTSD, panic disorder, generalized anxiety disorder, and social phobia were among the mental health conditions resulting in the greatest impairment (Alonso et al., 2011). The Australian mental health and wellbeing survey (NMHWBS) found that adults with mental disorders had an average of four days in which they reduced or were unable to carry out their normal activities in the past 30 days (Slade et al., 2009). A more recent Australian study with nearly 3000 participants found that adults with diagnosed mental disorders report significantly reduced capacity to carry out normal activities (McCallum et al., 2019) with an average DOR for participants with any disorder of 6.01 days, for those with Major Depressive Disorder (MDD) 11.4, Generalized Anxiety Disorder (GAD) 8.5, and no disorder 0.8.

Despite the established relationship between mental disorders and functional impairment, change in function is rarely reported as a treatment outcome. The most frequently reported treatment outcome metric is group-level symptom reduction (van Os et al., 2019) and an umbrella review of over 90 meta-analyses reported that <5 % of clinical trials in depression report functional outcomes (Lam et al., 2011). Paradoxically, when people with MDD were asked to rate the factors most important to them when defining remission, the most frequently reported were 1) the presence of features of positive mental health such as optimism and selfconfidence; 2) a return to one's usual, normal self; and 3) a return to the usual level of function (Zimmerman et al., 2006). Although there is a positive relationship between functional impairment and symptom severity, functioning effect sizes after treatment are typically smaller than symptom effect sizes (de Groot et al., 2022), changes in symptoms and function are distinct outcomes (Becker et al., 2011) that may not change in the same way at the same time together. For example, a pooled analysis of three randomised, double-blind, 8-week acute treatment studies found that for MDD and GAD respectively, 38 % vs 30 % of patients achieved symptomatic remission, defined by the clinical threshold of the Hamilton depression scale, 32 % vs 45 % achieved functional remission defined according to the authors' disability scale, and 23 % vs 25 % achieved both symptomatic and functional remission (Sheehan et al., 2011). Other studies have shown that functional improvement lags behind the symptomatic improvement, suggesting that treatment specifically focused on functional impairments may be necessary to achieve both symptomatic and functional remission (Sheehan et al., 2017). Moreover, persistent impairment in function despite recovery from symptoms of depression has been shown to be a predictor of subsequent relapse (IsHak et al., 2013).

There are also few reports of functional outcome in psychological treatments delivered remotely by digital mental health services (DMHS). Most studies of internet-delivered cognitive behavioural therapy (iCBT) report symptom severity and symptom change as the primary, or only, outcomes. For example, in a recent meta-analysis and systematic review of 19 studies reporting the outcomes of iCBT treatment in routine care, not one reported on functional outcomes (Etzelmueller et al., 2020). Hence, despite large improvements in self-reported symptoms of both anxiety and depression achieved by DMHS delivering iCBT as part of routine care (Titov et al., 2018; Etzelmueller et al., 2020; Titov et al., 2020), questions still remain about the real world effectiveness of digital treatments, in particular, whether the improvement in symptoms translates to improvement in functional outcomes. Therefore, there is a clear need for the evaluation of functional outcomes from DMHS to overcome continuing scepticism about the functional benefit of this form of care.

The purpose of this study was to report on the levels of functional impairment and improvement across the natural service flow in a large sample of patients seeking assessment or treatment from a national DMHS. Our specific aims were to:

- 1. Describe baseline levels of functional impairment and compare to large scale community studies.
- 2. Identify predictors of functional impairment at assessment (baseline).
- 3. Identify predictors of functional impairment after iCBT treatment and identify treatment specific predictors compared to baseline.
- 4. Determine the relationship between symptom change and functional change.

2. Methods

2.1. Design and participants

This study was designed as a prospective uncontrolled observational cohort study and is reported according to STROBE guidelines (Erik von Elm et al., 2007). It includes all patients who registered for assessment, or enrolled in a transdiagnostic treatment course at the MindSpot Clinic from 1st January 2019 to 31st December 2019. As a naturalistic study, we aimed to follow the observed service flow through the pathway during that period, which resulted in three 'pathway' groups and one outcome group (Fig. 1). The 'assessment' group comprised all who started the online assessment to enter the service and did not enrol in treatment. The 'enrolment' group completed the assessment and elected to enrol in a treatment course, while the 'completion' group is a subset of the 'enrolment' group who completed the treatment, defined as reading four of the five lessons of the course. The outcome group was labelled the 'improvement' group, a subset of the treatment completion group reporting a 50 % reduction in DOR, as described below. A similar grouping model examining factors predicting treatment uptake, completion and symptom outcome has been previously reported (Cross et al., 2022). Ethical approval for the collection and use of the data was obtained from the Macquarie University Human Research Ethics Committee (5201200912) and registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12613000407796). All included patients consented to their non-identifiable, aggregated data being used for research purposes.

2.2. Procedure

MindSpot is a high volume, Australian Government funded Australian DMHS launched in December 2012, that has provided services at no cost to >160,000 Australian adults and enrolled >30,000 people in one of its 8-week iCBT-based treatment courses (Titov et al., 2016; Titov et al., 2020). MindSpot serves a highly diverse group of patients, obtains high treatment outcome effects (Titov et al., 2020) and is highly costeffective (Lee et al., 2017). People self-refer or are referred by health professionals. After registering with MindSpot, they provide answers to questions seeking demographic and clinical information, including about symptoms, suicidal thoughts and plans and current psychosocial difficulties. People who complete the online assessment are invited to discuss their results and treatment options with a MindSpot therapist. Depending on preference and suitability, participants can enrol into one of seven online treatment courses, unless they are considered unsuitable for digital treatment due to concerns about their immediate safety or the severity and complexity of their conditions. Four of the seven courses are 'transdiagnostic', in that they aim to treat symptoms of both depression and anxiety, adapted to suit different patient characteristics. Given the similarity in content, patients enrolled in the four transdiagnostic courses (Mood Mechanic for 18 to 25-year-olds (Dear et al., 2018), Wellbeing for 26-65-year-olds (Dear et al., 2016), Wellbeing Plus for 60+ (Staples et al., 2016) and the Indigenous Wellbeing course (Titov et al., 2019) were included in the current analysis.

2.3. Measures

Standardised and validated symptom questionnaires were administered to patients during assessment and treatment with the clinic. These included the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder 7-item Scale (GAD-7) and the Kessler Psychological Distress 10-Item Scale (K10).

2.3.1. Patient Health Questionnaire — 9 item

The PHQ-9 consists of nine items measuring symptoms of major depressive disorder according to criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (Kroenke et al., 2001). Scores

range from 0 to 27, with a score of 10 or more considered indicative of a diagnosis of depression, although this cut-off has been recently challenged (Titov and Andersson, 2022).

2.3.2. Generalized Anxiety Disorder — 7 item

The GAD-7 consists of seven items and is sensitive to the presence of generalized anxiety disorder, social phobia, and panic disorder (Spitzer et al., 2006). Scores range from 0 to 21, with a score of 8 or more indicating the probable presence of an anxiety disorder. For both the PHQ-9 and the GAD-7, patients were also asked a 'functional interference' question: "How much have the above problems interfered with your ability to do your work, take care of things at home, or get along with other people?"

2.3.3. Kessler Psychological Distress 10-item

The Kessler Psychological Distress 10-Item Scale (K-10) scores range from 10 to 50 and scores of 21 or more are associated with the presence of anxiety and depressive disorders (Kessler et al., 2002). The K10 also contained four additional disability and service utilisation questions, known as the K10+.

2.3.4. Functional impairment

The functional impairment question from the K10+ used in this study was measured as Days Out of Role (DOR): "In the last four weeks, how many days were you totally unable to work, study or manage your dayto-day activities because of these feelings?". Patients were also asked about the cause of DOR: "in the last 4 weeks, how often have physical health problems been the main cause of these feelings?". Functional improvement was defined as a 50 % or more reduction in DOR between assessment and treatment completion, as this definition allowed a comparison to the mean functional improvement reported in the larger national sample (Titov et al., 2020).

2.3.5. Psychosocial difficulties

Patients were asked, "*are you having significant difficulties with any of the following*?" and were required to endorse at least one of the 14 options listed in Table 2, which included an option for 'none of these'. Culminative difficulties were simply the total number of difficulties indicated.

2.4. Statistical analysis

Analysis and identification of participant characteristics that influence DOR in the three groups were explored in three steps. In the first step, a series of univariate logistic regression models examined the association of each variable (predictor) as a single (univariate) model against each outcome group. These models employed a binomial distribution with a logit link function to determine and test the event rate (% proportion) across the different groups. Power analyses were determined using a power analysis package that uses a binomial distribution and a sequence of Bernoulli trials.

The second step employed a classification algorithm to develop a multivariate model for each group. These models specified exhaustive Chi-square Automatic Interaction Detection classification algorithms (CHAID), which identify subgroups that are characterised with more than one variable (higher-order interactions), and without parametric assumptions (Bi et al., 2019; Aafjes-van Doorn et al., 2021). This multivariate analysis groups variables that characterise a more complex pattern of combined (multivariate profile) prediction against each of the groups, with variables that don't feature in the multivariate model redacted to emphasise the importance of variables over one another. The model evaluates the list of possible predictors and selects a combined, parsimonious model from a larger list of alternatives. The multivariate classification tree employed the decision tree procedure to classify cases into groups or predict values of a dependent (target) variable based on values of independent (predictor) variables. The assessment of predictor

Demographic characteristics of the assessment and treatment sample of patients.

Variable		Group 1: Assessment group	Group 2: Treatment enrolment group	Group 3: Treatment complete group
	Total	13,825 (100 %)	3988 (100 %)	2358 (100 %)
Age group	18–24	4228 (30.6 %)	491 (12.3 %)	229 (9.7 %)
	25–34	4180 (30.2 %)	1074 (26.9 %)	553 (23.5 %)
	35–44	2556 (18.5 %)	920 (23.1 %)	552 (23.4 %)
	45–54	1620 (11.7 %)	726 (18.2 %)	467 (19.8 %)
	55–64	873 (6.3 %)	513 (12.9 %)	373 (15.8 %)
	65+	368 (2.7 %)	264 (6.6 %)	184 (7.8 %)
Gender	Female	10,382 (75.1 %)	2729 (68.4 %)	1606 (68.1 %)
	Male	3331 (24.1 %)	1248 (31.3 %)	745 (31.6 %)
	Other	112 (0.8 %)	11 (0.3 %)	7 (0.3 %)
Locality	Capital city or	8403 (61.4	2223 (56.2	1314 (56.2
	surrounding suburbs	%)	%)	%)
	Other urban region	2801 (20.5 %)	812 (20.5 %)	490 (21 %)
	Rural or	2480 (18.1	922 (23.3 %)	533 (22.8 %)
Dama in	remote region	%)	0004 (75.0	1700 (75 5
Born in Australia	Born Australia	10,542	3024 (75.8	1780 (75.5
Australia	Born overseas	(76.3 %) 2862 (20.7 %)	%) 862 (21.6 %)	%) 520 (22.1 %)
	Not specified	421 (3 %)	102 (2.6 %)	58 (2.5 %)
Aboriginal and	Other	9972 (95.2	2924 (97.3	1727 (97.8
Torres Strait	Australian	%)	%)	%)
Islander	Aboriginal and Torres Strait Islander	507 (4.8 %)	82 (2.7 %)	38 (2.2 %)
Employment	Employed	8218 (59.9	2433 (61.3	1492 (63.7
status	(full time, part time)	%)	%)	%)
	Student (full	2439 (17.8	334 (8.4 %)	169 (7.2 %)
	time, part time)	%)		
	Home duties/ parenting	900 (6.6 %)	297 (7.5 %)	162 (6.9 %)
	Disability support	356 (2.6 %)	185 (4.7 %)	99 (4.2 %)
	payment Unemployed	1411 (10.3 %)	410 (10.3 %)	191 (8.2 %)
	Retired	391 (2.9 %)	310 (7.8 %)	230 (9.8 %)
Education	Other	5381 (38.9	1823 (45.7	1189 (50.4
	(education)	%)	%)	%)
	University	8444 (61.1	2165 (54.3	1169 (49.6
	degree	%)	%)	%)
Relationship	Married de	4725 (34.5	1818 (45.9	1181 (50.5
status	facto	%)	%)	%) 77((22.2.4)
	Never married	7372 (53.9	1468 (37.1	776 (33.2 %)
	Separated	%) 1453 (10.6 %)	%) 610 (15.4 %)	342 (14.6 %)
	Widowed	%) 122 (0.9 %)	63 (1.6 %)	37 (1.6 %)

robustness was analysed using the Categorical Regression Regularization package within SPSS.

In a third step, the roles of depressive, anxiety, and psychological distress symptoms were explored as potential mediators of the change in DOR that occurred within the treatment period. Mediation analysis was conducted with the Hayes bootstrapping approach using the PROCESS macro (Montoya and Hayes, 2017) and serial mediation models. These models enable a test of the indirect effects (mediation effects) of pre-post change in DOR via pre-post symptom change pathways. A statistical summary of the serial mediation and the indirect effects of changes in

Table 2

Clinical characteristics of the assessment and treatment sample of patients.

Clinical characte	ristics of the as	sessment and tre	eatment sample	
		Group 1: Assessment only group	Group 2: Treatment enrolment group	Group 3: Treatment complete group
	Total	13,825 (100 %)	3988 (100 %)	2358 (100 %)
Baseline K10	Mild (10–24)	%) 2491 (18 %)	%) 871 (21.8 %)	%) 596 (25.3 %)
severity	Moderate	2661 (19.2	971 (24.3 %)	602 (25.5 %)
categories	(25–29)	%)	0146 (50.0	11/0 //0 0
	Severe (30+)	8673 (62.7 %)	2146 (53.8 %)	1160 (49.2 %)
Baseline PHQ9	Mild (0–9)	3043 (22 %)	1072 (26.9	728 (30.9 %)
severity categories	Moderate	3605 (26.1	%) 1171 (29.4	709 (30.1 %)
0	(10–14)	%)	%)	
	Severe (15+)	7177 (51.9 %)	1745 (43.8 %)	921 (39.1 %)
Degree of	No	942 (9 %)	207 (7.2 %)	135 (7.6 %)
interference depression	interference Mild	4643 (44.6	1274 (44.4	828 (46.8 %)
	interference	%)	%)	
	Moderate interference	4833 (46.4 %)	1390 (48.4 %)	807 (45.6 %)
Baseline GAD7	Mild (0–9)	4201 (30.8	1343 (33.7	855 (36.3 %)
severity categories	Moderate	%) 4210 (30.8	%) 1289 (32.3	777 (33 %)
categories	(10–14)	%)	%)	/// (00 /0)
	Severe (15+)	5238 (38.4 %)	1356 (34 %)	726 (30.8 %)
Degree of	No	997 (9.6 %)	268 (9.2 %)	171 (9.5 %)
interference anxiety	Interference Mild	4509 (43.6	1267 (43.5	824 (45.9 %)
	interference	%)	%)	
	Moderate interference	4844 (46.8 %)	1377 (47.3 %)	799 (44.5 %)
Physical health	None of the	6443 (46.6	1716 (43 %)	1035 (43.9
as cause of DOR	time A little of the	%) 3420 (24.7	835 (20.9 %)	%) 489 (20.7 %)
	time Some of the	%) 2261 (171	746 (10 7 0/)	494 (19.0/)
	Some of the time	2361 (17.1 %)	746 (18.7 %)	424 (18 %)
	Most of the time	1117 (8.1 %)	487 (12.2 %)	282 (12 %)
	All of the time	484 (3.5 %)	204 (5.1 %)	128 (5.4 %)
Chronicity of	2 weeks or	369 (3.7 %)	104 (3.7 %)	63 (4 %)
depression	less >2 weeks	1756 (17.8	463 (16.5 %)	272 (17.2 %)
	<6 months >6 month	%) 1388 (14.1	341 (12.1 %)	196 (12.4 %)
	<1 year	%)		400 (07.1.0/)
	1 to 5 years	3109 (31.5 %)	776 (27.6 %)	429 (27.1 %)
	6 to 10 years	1247 (12.6 %)	356 (12.7 %)	183 (11.6 %)
	>10 years	2006 (20.3 %)	767 (27.3 %)	439 (27.7 %)
Chronicity of	2 weeks or	320 (2.7 %)	77 (2.2 %)	36 (1.8 %)
anxiety	less >2 weeks	1724 (14.4	508 (14.5 %)	301 (14.8 %)
	<6 months	%) 1560 (12 %)	378 (10.8 %)	212 (10 E 04)
	>6 month <1 year	1560 (13 %)	578 (10.8 %)	213 (10.5 %)
	1 to 5 years	4216 (35.2 %)	1078 (30.9 %)	644 (31.7 %)
	6 to 10 years	1628 (13.6 %)	439 (12.6 %)	236 (11.6 %)
	>10 years	2513 (21 %)	1014 (29 %)	604 (29.7 %)
Relationship difficulties	Endorsed	8240 (59.6 %)	2101 (52.7 %)	1160 (49.2 %)
Parenting	Endorsed	1875 (13.6	549 (13.8 %)	280 (11.9 %)
difficulties Vocational	Endorsed	%) 7156 (51.8	1935 (48.5	1070 (45.4
difficulties	Endorred	%)	%)	%)
	Endorsed		(continu	919 (39 %) ed on next page)
			Commu	ca on next page)

Table 2 (continued)

		Group 1: Assessment only group	Group 2: Treatment enrolment group	Group 3: Treatment complete group
Physical		5562 (40.2	1652 (41.4	
difficulties Financial	Endorsed	%) 4123 (29.8	%) 1060 (26.6	510 (21.6 %)
difficulties	Endorsed	4123 (29.8 %)	1000 (20.0 %)	510 (21.0 %)
Housing difficulties	Endorsed	1617 (11.7 %)	325 (8.1 %)	143 (6.1 %)
Alcohol difficulties	Endorsed	1314 (9.5 %)	354 (8.9 %)	183 (7.8 %)
Drug difficulties	Endorsed	990 (7.2 %)	167 (4.2 %)	64 (2.7 %)
Religion difficulties	Endorsed	575 (4.2 %)	143 (3.6 %)	71 (3 %)
Cultural difficulties	Endorsed	360 (2.6 %)	73 (1.8 %)	39 (1.7 %)
Sexual difficulties	Endorsed	598 (4.3 %)	117 (2.9 %)	60 (2.5 %)
Grief difficulties	Endorsed	567 (4.1 %)	160 (4 %)	82 (3.5 %)
Carer difficulties	Endorsed	168 (1.2 %)	69 (1.7 %)	31 (1.3 %)
No difficulties	Endorsed	1957 (14.2 %)	619 (15.5 %)	415 (17.6 %)
Total number of	0	1957 (14.5 %)	619 (15.8 %)	415 (18.1 %)
difficulties	1	2500 (18.5 %)	879 (22.5 %)	573 (24.9 %)
	2	2977 (22 %)	867 (22.2 %)	548 (23.8 %)
	3	2646 (19.5 %)	714 (18.3 %)	383 (16.7 %)
	4	1757 (13 %)	424 (10.9 %)	201 (8.7 %)
	5	954 (7 %)	240 (6.1 %)	109 (4.7 %)
	6+	748 (5.5 %)	163 (4.2 %)	70 (3 %)

DOR is presented in Table 4. To determine evidence for a causal relationship, total indirect effects, specific indirect effects, and reverse pathways were explored (Valente and MacKinnon, 2017). All estimates were estimated using a bootstrap procedure from models that resampled 2000 cases from the treatment sample.

Missing cases in all three samples were not imputed to avoid uncertain, and potentially artificial, influences on the testing of large and specific models related to the natural clinical flow. Statistical analyses were performed using SPSS version 27. Alpha was set at 0.05, to balance the possibility of a type I error within the multiple contrasts and the need to detect possible marginal trends within more nuanced subgroups (as well as higher-order interactions). Statistical power was determined at 0.8.

3. Results

3.1. Sample characteristics

Within the recruitment period of one year, of the 17,813 participants who started the assessment 13,825 participants completed the assessment but did not enrol in treatment, forming the total 'assessment sample' (group 1) (Fig. 1). Of the participants that completed an assessment, 3988 (28.8 %) started treatment ('enrolment sample'/group 2). Post-treatment data were available for 2358 participants ('treatment sample'/group 3). Statistical power analyses confirmed that the sample was adequately powered to detect small subgroup differences in the rate of improvement events (min ORgroup $\Delta > 1.093$), or differences in the mean rate of DOR (Means SMDsubgroup $\Delta > 0.025$).

The sample characteristics are presented in Tables 1 and 2. The mean age of participants for the entire sample was 33.7 years. More females than males completed an assessment (75.1 % vs 24.1 %), with the ratio of males increasing in the treatment uptake (68.4 % vs 31.3 %) and treatment completed (68.1 % vs 31.6 %) groups. Most of the assessment

group lived in capital cities or surrounding urban areas (61.4 %), were single or never married (53.9 %) and had a university-level education (61.1 %). The majority scored in the severe range on the K10 (62.7 %), PHQ9 (51.9 %) and GAD7 (38.4 %). Only 14.2 % of the assessment group reported having no psychosocial difficulties. Most patients reported moderate functional interference associated with their depressive (46.4 %) and anxiety (46.8 %) symptoms respectively. Patients reported 5.5 days out of role (DOR) in the last month. A minority (11.6 %) of the sample reported that their impairment (DOR) was mostly caused by physical health problems.

3.2. Univariate analyses

Results from the series of univariate logistic regressions models, testing the joint association of each predictor to the DOR at assessment, treatment completion and functional improvement, are presented in Table 3 under "Univariate models". Tables 3, 4 and 5 show baseline DOR differences between the assessment group and those who complete treatment (5.49 vs 3.79) for each of the predictor variable types (demographic, clinical and psychosocial) with the treatment completion group experiencing 1.7 fewer DOR than the assessment group. DOR varied significantly within and across variables within each of the groups. For the assessment group, age shows that those aged between 25 and 34 years experience 3.74 DOR, compared to those aged between 55 and 64 years who experience 6.33 DOR with the variation in the group being statistically significant (p < 0.001). Similar large variations are also observed for employment status (3.4 employed vs 15.47 disability payments vs 11.49 unemployed, p < 0.001), being Aboriginal or Torres Strait Islander (10.45 vs 4.82; p < 0.001) and relationship status (7.17 separated vs 4.07 married, p < 0.001). Clinical variables including all baseline symptom scores (K10, GAD7 and PHQ9, all p < 0.001) and chronicity (depression and anxiety, p < 0.001) were positively related to DOR, as was the total number of reported psychosocial difficulties (p < p0.001). Employment status ($R^2 = 0.18$), baseline PHQ9 ($R^2 = 0.15$), and baseline K10 ($R^2 = 0.17$) had the highest degree of explained variance. DOR increased between assessment and treatment for those with mild symptoms (e.g. K10 mild severity at assessment 1.8 DOR vs posttreatment 3.5 DOR) and no reported interference due to anxiety or depressive symptoms (e.g. 'no interference' depression at assessment 0.4 DOR vs post-treatment 3.1 DOR). Appendix Table 1 shows similar relationships in both baseline DOR for treatment enrolment and treatment complete groups.

Regarding post-treatment DOR, 41 % of the post-treatment group achieved a >50 % reduction in DOR. Age was again significant (p < 0.001), but with less variability across groups. Chronicity of anxiety and depression were also predictive of lack of functional improvement (p < 0.001). The variables most predictive of a >50 % reduction in DOR were relationship status (married 37 % reduction versus separated 53 %; p < 0.001, AUC 0.55), employment status (employed 36 % reduction vs disability payments 66 %; p < 0.001, AUC 0.57), baseline symptom scores (for example PHQ9 mild severity 28 % reduction versus severe severity 61 %; p < 0.001, AUC 0.63), and chronicity of depression (2 weeks or less 35 % reduction versus >10 years 57 %; p < 0.001, AUC 0.54).

3.3. Multivariate analyses

In the second step, the multivariate analyses of DOR at assessment, DOR at treatment completion, and functional improvement were conducted, with the results collated in Table 3, under the column "multivariate models". Outcomes for baseline DOR for the treatment enrolment and treatment completion groups are outlined in Appendix Table 1. The multivariate analyses of DOR at assessment identified a combined list of patient features, including age, employment status, baseline symptom severity categories (PHQ-9, GAD7 and K10) and the total number of endorsed psychosocial difficulties ($R^2 = 32.7$ %). The

Univariate and multivariate estimates of DOR at assessment, treatment completion and significant improvement for demographic predictors.

Variable	Variable sub-	Univariate estimate	Univariate estimates			tes	
	group	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement* (N = 2358)	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement (N = 2358)
	Total sample	5.49 (5.36 to	3.79 (3.5 to	41 % (39 to 43.1)	5.49 (5.42 to	3.79 (3.74 to	45.9 % (45.3 to 46.4
	estimate	5.61)	4.09)		5.56)	3.83)	
Demographic	10.04	464(271 +	4 46 (2 E4 to	$0.51(0.46 \pm 0.56)$	6 1E (6 04 to	4 20 (4 22 40	
Age group	18–24	4.64 (3.71 to 5.56)	4.46 (3.54 to 5.39)	0.51 (0.46 to 0.56)	6.15 (6.04 to 6.25)	4.39 (4.23 to 4.54)	-
	25–34	3.74 (3.14 to	3.92 (3.33 to	0.44 (0.41 to 0.47)	5.17 (5.04 to	4.07 (3.96 to	_
		4.33)	4.52)	,	5.29)	4.17)	
	35–44	4.13 (3.53 to	3.08 (2.48 to	0.43 (0.39 to 0.46)	4.89 (4.72 to	3.27 (3.21 to	-
		4.73)	3.67)		5.06)	3.34)	
	45–54	5.2 (4.55 to 5.85)	4.34 (3.68 to 5)	0.48 (0.45 to 0.52)	5.35 (5.11 to 5.59)	4.26 (4.17 to 4.35)	-
	55–64	6.33 (5.6 to 7.06)	3.54 (2.82 to	0.47 (0.43 to 0.52)	5.73 (5.39 to	3.08 (3.02 to	_
		,	4.27)	(6.07)	3.14)	
	65+	5.32 (4.29 to	3.89 (2.84 to	0.45 (0.39 to 0.52)	5.64 (5.18 to	3.96 (3.86 to	-
		6.35)	4.94)		6.11)	4.06)	
	<i>p</i> -Value	<i>p</i> < 0.001	p < 0.001	<i>p</i> = 0.044	5.49 (5.42 to	3.79 (3.74 to	-
		$R^2 = 0.006$	$R^2 = 0.005$	AUC 0.52 (0.49, 0.54)	5.56)	3.83)	
Gender	Female	4.53 (4.18 to	3.78 (3.43 to	0.46 (0.44 to 0.48)	_	_	_
		4.88)	4.13)				
	Male	5.15 (4.64 to	3.85 (3.34 to	0.46 (0.43 to 0.49)	-	-	-
		5.67)	4.37)				
	Other	9.14 (3.81 to	0.71 (-4.39 to	0.64 (0.34 to 0.86)	-	-	-
	<i>p</i> -Value	14.48) p = 0.039	5.81) $p = 0.483$	p = 0.51			
	p-value	p = 0.039 $R^2 = 0.001$	p = 0.485 $R^2 = 0.001$	p = 0.51 AUC 0.50 (0.48, 0.52)			
Relationship status	Married de facto	4.07 (3.66 to	3.52 (3.1 to	0.37 (0.34 to 0.4)	_	3.46 (3.42 to	_
*		4.48)	3.93)			3.51)	
	Never married	4.67 (4.17 to	4.41 (3.91 to	0.42 (0.38 to 0.46)	-	4.34 (4.26 to	-
	Compared a 1	5.17)	4.91)	0.50 (0.47 += 0.50)		4.43)	
	Separated	7.17 (6.41 to 7.92)	3.28 (2.51 to 4.04)	0.53 (0.47 to 0.59)	-	3.56 (3.45 to 3.67)	-
	Widowed	4.73 (2.43 to	5.09 (2.71 to	0.38 (0.23 to 0.55)	_	4.19 (3.84 to	_
		7.03)	7.48)			4.55)	
	p-Value	<i>p</i> < 0.001	p = 0.16	<i>p</i> < 0.001			
		$R^2 = 0.024$	$R^2 = 0.005$	AUC 0.55 (0.53, 0.57)			
Employment status	Employed (full	3.40 (3.27 to	3.67 (3.30 to 4.04)	0.36 (0.33 to 0.39)	3.35 (3.31 to 3.39)	3.67 (3.63 to 3.72)	40.3 (39.7 to 40.8)
	time, part time) Student (full time,	3.53) 6.30 (6.05 to	4.38 (3.31 to	0.46 (0.38 to 0.54)	6.45 (6.35 to	4.23 (4.08 to	51.7 (49.6 to 53.9)
	part time)	6.55)	5.44)		6.56)	4.39)	
	Home duties/	7.98 (7.61 to	3.53 (2.44 to	0.42 (0.35 to 0.50)	8.52 (8.19 to	3.58 (3.44 to	45.8 (44.2 to 47.3)
	parenting	8.36)	4.62)		8.84)	3.72)	
	Disability support	15.47 (14.9 to	4.17 (2.77 to	0.66 (0.56 to 0.75)	16.05 (15.52 to	3.69 (3.49 to	64 (62 to 66)
	payment Unemployed	16.03) 11.49 (11.18 to	5.58) 3.99 (2.97 to	0.61 (0.53 to 0.68)	16.57) 11.34 (11.14 to	3.9) 4.62 (4.33 to	65.1 (63.3 to 66.8)
	onemployed	11.79)	5.02)	0.01 (0.33 (0 0.08)	11.54)	4.91)	05.1 (05.5 10 00.8)
	Retired	6.11 (5.61 to 6.6)	4.11 (3.18 to	0.41 (0.35 to 0.48)	6.16 (5.71 to 6.6)	3.64 (3.54 to	47.1 (45 to 49.2)
			5.05)			3.73)	
	<i>p</i> -Value	<i>p</i> < 0.001	p = 0.745	<i>p</i> < 0.001			
Aboriginal Torra-	No	$R^2 = 0.181$	$R^2 = 0.001$	AUC 0.57 (0.54, 0.59)			16 E (1E 9 to 17 1)
Aboriginal, Torres Strait Islander	No	4.82 (4.47 to 5.17)	3.69 (3.36 to 4.02)	0.46 (0.44 to 0.48)	-	-	46.5 (45.8 to 47.1)
Strait islander	Yes	10.45 (8.1 to	4.89 (2.66 to	0.67 (0.56 to 0.77)	_	_	52.3 (48.7 to 55.9)
		12.79)	7.11)	,			
	p-Value	<i>p</i> < 0.001	p = 0.297	<i>p</i> < 0.001			
		$R^2 = 0.010$	$R^2 = 0.001$	AUC 0.51 (0.50, 0.52)			
Education	Other (education)	5.95 (5.54 to	3.93 (3.52 to	0.51 (0.49 to 0.53)	-	3.75 (3.68 to	49.3 (48.6 to 50.1)
	University degree	6.36) 3.55 (3.14 to	4.35) 3.69 (3.27 to	0.39 (0.37 to 0.42)	_	3.81) 3.82 (3.76 to	41.8 (41 to 42.5)
	Survey degree	3.95)	4.1)	2.02 (0.07 to 0.72)		3.82 (3.70 to 3.87)	110 (11 (0 12:0)
	<i>p</i> -Value	<i>p</i> < 0.001	<i>p</i> = 0.407	<i>p</i> < 0.001		-	
		$R^2 = 0.033$	$R^2 = 0.000$	AUC 0.55 (0.53, 0.57)			
Locality	Capital city/	4.39 (4 to 4.78)	3.64 (3.25 to	0.45 (0.43 to 0.48)	-	-	-
	suburbs Other urban	5.21 (4.57 to	4.03) 4 5 (3 87 to	0.47 (0.44 to 0.51)			
	other urban region	5.21 (4.57 to 5.85)	4.5 (3.87 to 5.13)	0.47 (0.44 (0 0.51)	-	-	-
	Rural or remote	5.21 (4.6 to 5.83)	3.51 (2.9 to	0.46 (0.42 to 0.49)	_	_	_
	region		4.13)				
	region <i>p</i> -Value	<i>p</i> =0.023	<i>p</i> =0.046	<i>p</i> = 0.608			
Born in Australia	-	p = 0.023 $R^2 = 0.001$		<i>p</i> = 0.608 AUC 0.51 (0.49, 0.53) 0.44 (0.4 to 0.47)			

(continued on next page)

Table 3 (continued)

	Variable sub-	Univariate estimate	Univariate estimates			Multivariate estimates		
	group	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement* (N = 2358)	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement (N = 2358)	
		4.07 (3.45 to	3.79 (3.17 to					
		4.69)	4.41)					
	Born overseas	4.98 (4.65 to	3.77 (3.43 to	0.47 (0.45 to 0.48)	-	-	-	
		5.32)	4.1)					
	Not specified	3.29 (1.44 to	4.61 (2.77 to	0.44 (0.35 to 0.55)	-	-	-	
		5.15)	6.45)					
	p-Value	p = 0.012	p = 0.676	p = 0.319				
	-	$R^2 = 0.001$	$R^2 = 0.000$	AUC 0.51 (0.49, 0.52)				

 $^{\ast}\,$ Cox and Snell R squared. Significance set at p < 0.001, significant values in bold.

Table 4

Univariate and multivariate estimates of DOR at assessment, treatment completion and significant improvement for clinical predictors.

Variable Variable sub-		Univariate estimate	s		Multivariate estimates			
	group	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement* (N = 2358)	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement (N = 2358)	
	Total sample estimate	5.49 (5.36 to 5.61)	3.79 (3.5 to 4.09)	41 % (39 to 43.1)	5.49 (5.42 to 5.56)	3.79 (3.74 to 3.83)	45.9 % (45.3 to 46.4)	
Baseline PHQ9 severity	Mild (0–9)	1.82 (1.33 to 2.31)	3.27 (2.75 to 3.79)	0.28 (0.25 to 0.31)	1.96 (1.91 to 2.01)	-	28 (27.4 to 28.6)	
categories	Moderate (10–14)	3.48 (2.99 to 3.97)	3.89 (3.36 to 4.42)	0.39 (0.36 to 0.42)	3.08 (3.02 to 3.14)	-	39 (38.4 to 39.6)	
	Severe (15+)	8.01 (7.58 to 8.45)	4.14 (3.67 to 4.6)	0.61 (0.59 to 0.64)	8.19 (8.1 to 8.28)	-	61.4 (60.9 to 62)	
	p-Value	p < 0.001	<i>p</i> = 0.049	p < 0.001				
		$R^2 = 0.153$	$R^2 = 0.003$	AUC 0.63 (0.61, 0.66)				
Chronicity of depression	2 weeks or less	2.9 (0.99 to 4.82)	4.25 (2.46 to 6.03)	0.35 (0.27 to 0.45)	-	-	-	
	>2 weeks <6 months	4.99 (4.07 to 5.91)	3.5 (2.61 to 4.4)	0.47 (0.42 to 0.52)	-	-	-	
	>6 month <1 year	5.45 (4.37 to 6.54)	3.8 (2.74 to 4.85)	0.46 (0.41 to 0.52)	-	-	-	
	1 to 5 years	5.52 (4.79 to 6.26)	3.91 (3.21 to 4.61)	0.48 (0.45 to 0.52)	-	-	-	
	6 to 10 years	6.27 (5.14 to 7.39)	4.39 (3.31 to 5.48)	0.54 (0.48 to 0.59)	-	-	-	
	>10 years	7.07 (6.34 to 7.79)	4.48 (3.78 to 5.18)	0.57 (0.53 to 0.6)	-	-	-	
	<i>p</i> -Value	p < 0.001 $R^2 = 0.027$	p < 0.001 $R^2 = 0.003$	p < 0.001 AUC 0.54 (0.51, 0.57)				
Interference depression	None of these	0.38 (–0.38 to 1.14)	3.13 (1.96 to 4.3)	0.1 (0.07 to 0.15)	-	-	-	
	Mild	1.77 (1.46 to	3.63 (3.15 to	0.31 (0.28 to 0.33)	-	-	-	
	interference	2.08)	4.11)					
	Moderate interference	4.1 (3.79 to 4.41)	3.71 (3.22 to 4.19)	0.48 (0.45 to 0.51)	-	-	-	
	<i>p</i> -Value	<i>p</i> < 0.001	p = 0.674	p < 0.001				
		$R^2 = 0.091$	$R^2 = 0.000$	AUC 0.64 (0.61, 0.66)				
Baseline GAD7 severity	Mild (0–9)	3.04 (2.56 to 3.51)	3.51 (3.03 to 4)	0.35 (0.32 to 0.38)	3.2 (3.11 to 3.29)	3.43 (3.37 to 3.48)	-	
categories	Moderate	4.55 (4.05 to	3.43 (2.93 to	0.45 (0.42 to 0.48)	5.16 (5.04 to	3.53 (3.46 to	-	
	(10–14)	5.04)	3.94)		5.27)	3.59)		
	Severe (15+)	6.95 (6.44 to 7.46)	4.51 (3.99 to 5.03)	0.58 (0.55 to 0.6)	7.63 (7.51 to 7.75)	4.49 (4.4 to 4.58)	-	
	p-value	p < 0.001 $R^2 = 0.080$	p = 0.005 $R^2 = 0.005$	p < 0.001 AUC 0.58 (0.56, 0.61)				
Chronicity of anxiety	2 weeks or less	2.5 (0.1 to 4.9)	3.97 (1.65 to 6.29)	0.38 (0.28 to 0.49)	-	-	-	
	>2 weeks <6 months	4.12 (3.29 to 4.95)	3.83 (3.01 to 4.65)	0.42 (0.38 to 0.47)	-	-	-	
	>6 month <1 year	5.05 (4.06 to 6.04)	2.97 (1.98 to 3.97)	0.5 (0.44 to 0.55)	-	-	-	
	1 to 5 years	5.22 (4.65 to 5.78)	4.21 (3.65 to 4.78)	0.48 (0.44 to 0.51)	-	-	-	
	6 to 10 years	4.79 (3.85 to 5.73)	4.33 (3.39 to 5.28)	0.46 (0.41 to 0.51)	-	-	-	
	>10 years	5.15 (4.57 to 5.74)	3.8 (3.22 to 4.38)	0.49 (0.46 to 0.52)	-	-	-	

(continued on next page)

Table 4 (continued)

Variable	Variable sub-	Univariate estimates			Multivariate estimates		
	group	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement* (N = 2358)	Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement (N = 2358)
	<i>p</i> -Value	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> = 0.069			
		$R^2 = 0.013$	$R^2 = 0.003$	AUC 0.50 (0.48, 0.53)			
Interference anxiety	None of these	1.19 (0.44 to 1.94)	3.58 (2.54 to 4.61)	0.14 (0.1 to 0.19)	_	-	-
	Mild interference	2.01 (1.67 to 2.35)	3.33 (2.86 to 3.8)	0.33 (0.3 to 0.35)	-	-	-
	Moderate interference	4.49 (4.14 to 4.84)	3.76 (3.28 to 4.24)	0.49 (0.46 to 0.51)	-	-	-
	p-Value	p < 0.001	<i>p</i> = 0.451	<i>p</i> < 0.001			
		$R^2 = 0.065$	$R^2 = 0.001$	AUC 0.61 (0.59, 0.64)			
Baseline K10 severity	Mild (10–24)	1.75 (1.2 to 2.3)	3.47 (2.89 to 4.04)	0.25 (0.22 to 0.28)	1.61 (1.55 to 1.66)	-	-
categories	Moderate (25–29)	3.26 (2.71 to 3.8)	3.47 (2.9 to 4.05)	0.42 (0.38 to 0.45)	3.5 (3.39 to 3.6)	-	-
	Severe (30+)	7.04 (6.65 to 7.44)	4.13 (3.72 to 4.55)	0.56 (0.54 to 0.59)	7.21 (7.12 to 7.3)	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.116$	p = 0.082 $R^2 = 0.002$	<i>p</i> < 0.001 AUC 0.62 (0.60, 0.64)			
Physical health as cause	None of the time	3.3 (2.88 to 3.73)	3.87 (3.43 to 4.31)	0.34 (0.31 to 0.37)	-	-	-
cuuse	A little of the time	3.97 (3.35 to 4.59)	3.74 (3.1 to 4.38)	0.41 (0.36 to 0.45)	-	-	-
	Some of the time	5.58 (4.92 to 6.24)	4 (3.31 to 4.68)	0.45 (0.4 to 0.5)	-	-	-
	Most of the time	7.78 (6.97 to 8.6)	3.69 (2.86 to 4.52)	0.54 (0.48 to 0.6)	-	-	-
	All of the time	9.81 (8.61 to 11.02)	2.97 (1.73 to 4.22)	0.56 (0.47 to 0.65)	-	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.051$	p = 0.696 $R^2 = 0.001$	<i>p</i> < 0.001 AUC 0.58 (0.56, 0.60)			

 $^{\circ}$ Cox and Snell R squared. Significance set at p < 0.001, significant values in bold.

association of each of the listed predictors to DOR at assessment can be evaluated both in the table, as a total effect, as well as graphically, as a classification tree "node", describing subgroups that are characterised by more than one predictor. A visualisation of the assessment DOR classification algorithm is presented in Appendix Figs. 1, 2, and 3.

Regarding post-treatment DOR, the strongest predictors from the list of all possible predictors were age, relationship status, education, employment status, GAD7 severity, and the total number of psychosocial difficulties ($R^2 = 2.6$ %). A visualisation of the post-treatment DOR classification algorithm is presented in Appendix Fig. 4.

The multivariate analyses of functional improvement events, as defined by a >50 % reduction in DOR scores, resulted in a model where employment status, being Aboriginal or Torres Strait Islander, education status, baseline PHQ9 severity, experiencing difficulties with grief and physical health as well as the total number of endorsed psychosocial difficulties were the greatest predictors of significant DOR improvement events (AUC, 69.9 %). A visualisation of the symptom improvement classification algorithm is presented in Appendix Fig. 5.

3.4. Relationship between changes to functional impairment (DOR) with changes to symptoms (K10, PHQ9 and GAD7)

Results from the three bootstrap serial mediation models are presented in Table 6, detailing indirect effects (noting a mediation effect), symptom change pathway (causal pathway), and symptom baseline pathway (reverse pathway). These results demonstrate that the pre-post change in depression, anxiety, and psychological distress symptom scores did not fully mediate the time-related change in DOR. Similarly, the three causal pathways were not statistically significant. These results suggest no clear causal link between change scores in symptoms and change in DOR. In contrast to these non-significant results, a reverse pathway between baseline anxiety, psychological distress and DOR was identified, suggesting that baseline severity of anxiety and distress is associated with a change in function with treatment.

4. Discussion

Mental disorders are associated with significant functional impairment, resulting in large loss of productivity to society (Whiteford et al., 2013; Vos et al., 2017; Productivity Commission, 2020). Mental health services, including DMHS, can play a significant role in reducing the burden of mental health symptoms through effective evidence-based care. However, the impact of treatment on functioning is not as well studied. The current study was to our knowledge the first to report on the degree of functional impairment in a large sample of patients accessing a national DMHS, and the first to report on the effect of treatment on functional recovery and the relationship between symptom and functional improvement in a sample that was large enough to analyse a range of predictors simultaneously, as well as test the relative effect of demographic and symptom patterns on functional impairment and on functional improvement from iCBT provided as part of routine care.

The level of functional impairment defined by self-reported DOR in this large help-seeking sample was similar to levels of impairment seen in other large scale community studies (Slade et al., 2009; McCallum et al., 2019), in which the presence of mental disorder and the DOR were established using semi-structured interviews. The current patient sample reported an average of 5.49 DOR, which is higher than the DOR of 3.9 reported by Slade et al. (2009) but slightly lower than the DOR of 6.0 reported by McCallum et al. (2019).

The factors associated with greater levels of functional impairment at assessment included older age, being separated, being unemployed or on disability payments, longer duration of depressive or anxiety symptoms, the severity of symptoms, and the presence of a higher number of concurrent psychosocial difficulties. Combined, these factors accounted for 32.7 % of the total variance explained. Of interest, the factors found to

Univariate and multivariate estimates of DOR at assessment, treatment completion and significant improvement for psychosocial predictors.

Variable	Variable sub-group	Univariate estima	ites		Multivariate estimates		
		Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement* (N = 2358)	Assessment DOR (N $=$ 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement (N = 2358)
	Total sample estimate	5.49 (5.36 to 5.61)	3.79 (3.5 to 4.09)	41 % (39 to 43.1)	5.49 (5.42 to 5.56)	3.79 (3.74 to 3.83)	45.9 % (45.3 to 46.4)
Relationship difficulty	Not endorsed	4.15 (3.75 to 4.56)	3.52 (3.11 to 3.93)	0.41 (0.39 to 0.43)	-	-	-
	Relationships with friends/family	5.34 (4.93 to 5.76)	4.08 (3.66 to 4.49)	0.5 (0.48 to 0.52)	-	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.014$	p = 0.062 $R^2 = 0.002$	p < 0.001 AUC 0.54 (0.52, 0.56)			
Vocational difficulty	Not endorsed	4.08 (3.69 to 4.48)	3.39 (3 to 3.79)	0.4 (0.38 to 0.43)	-	-	-
	Work/study/ vocational activities	5.53 (5.1 to 5.96)	4.27 (3.84 to 4.7)	0.52 (0.49 to 0.54)	-	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.021$	p = 0.003 $R^2 = 0.004$	p < 0.001 AUC 0.54 (0.52, 0.56)			
Grief difficulty	Not endorsed	4.62 (4.32 to 4.91)	3.75 (3.45 to 4.04)	0.45 (0.44 to 0.47)	-	-	45.3 (44.7 to 45.8
	Grief	8.09 (6.53 to 9.64)	5.16 (3.59 to 6.73)	0.58 (0.5 to 0.66)	-	-	59.9 (56.9 to 63)
	<i>p</i> -Value	p < 0.001 $R^2 = 0.007$	p = 0.082 $R^2 = 0.001$	p = 0.003 AUC 0.51 (0.50, 0.52)			
Financial difficulty	Not endorsed	3.96 (3.63 to 4.28)	3.68 (3.35 to 4.01)	0.41 (0.39 to 0.43)	-	-	-
	Finances	7.57 (6.96 to 8.19)	4.21 (3.58 to 4.83)	0.59 (0.56 to 0.62)	-	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.045$	p = 0.146 $R^2 = 0.001$	p < 0.001 AUC 0.55 (0.54, 0.57)			
Housing difficulty	Not endorsed	4.56 (4.26 to 4.86)	3.75 (3.45 to 4.05)	0.44 (0.43 to 0.46)	-	-	-
	Indicated	7.57 (6.39 to 8.74)	4.44 (3.26 to 5.62)	0.63 (0.57 to 0.68)	-	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.032$	p = 0.266 $R^2 = 0.001$	p < 0.001 AUC 0.52 (0.51, 0.53)			
Physical difficulty	Not endorsed	3.34 (2.98 to 3.71)	3.78 (3.41 to 4.15)	0.38 (0.36 to 0.4)	-	-	40.2 (39.5 to 41)
	Physical health	6.92 (6.47 to 7.38)	3.82 (3.36 to 4.28)	0.57 (0.54 to 0.59)	-	-	53.8 (53.1 to 54.5
	<i>p</i> -Value	p < 0.001 $R^2 = 0.055$	p = 0.898 $R^2 = 0.000$	<i>p</i> < 0.001 AUC 0.58 (0.56, 0.60)			
Alcohol difficulty	Not endorsed	4.59 (4.29 to 4.89)	3.82 (3.52 to 4.13)	0.45 (0.43 to 0.47)	-	-	-
	Alcohol use	6.54 (5.49 to 7.58)	3.45 (2.42 to 4.48)	0.56 (0.5 to 0.61)	-	-	-
	p-Value	p < 0.001 $R^2 = 0.001$	p = 0.498 $R^2 = 0.000$	p < 0.001 AUC 0.52 (0.50, 0.53)			
Religion difficulty	Not marked	4.67 (4.37 to 4.96)	3.78 (3.49 to 4.08)	0.45 (0.44 to 0.47)	-	-	-
	Religion/ spirituality	7.03 (5.35 to 8.7)	4.23 (2.5 to 5.96)	0.56 (0.48 to 0.65)	-	-	-
	<i>p</i> -Value	p = 0.007 $R^2 = 0.003$	p = 0.617 $R^2 = 0.000$	p = 0.017 AUC 0.51 (0.50, 0.51)			
Drug difficulty	Not endorsed	4.59 (4.3 to 4.88)	3.78 (3.49 to 4.08)	0.45 (0.43 to 0.46)	-	_	-
	Drug or substance use n-Value	10.09 (8.34 to 11.85)	4.16 (2.44 to 5.89) p = 0.671	0.71 (0.64 to 0.78)	-	-	-
	p-Value	p < 0.001 $R^2 = 0.026$	p = 0.671 $R^2 = 0.000$	p < 0.001 AUC 0.51 (0.51, 0.52)			
Sexual difficulty	Not endorsed	4.71 (4.41 to 5)	3.8 (3.51 to 4.1)	0.45 (0.44 to 0.47)	-	-	-
	Sexual identity or orientation	5.93 (4.11 to 7.76)	3.51 (1.69 to 5.33)	0.59 (0.49 to 0.68)	-	_	-
				<i>p</i> = 0.007	-	_	_

(continued on next page)

Table 5 (continued)

Variable	Variable sub-group	Univariate estim	nates		Multivariate estimates		
		Assessment DOR (N = 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement* (N = 2358)	Assessment DOR (N $=$ 13,825)	Post-treatment DOR (N = 3988)	DOR 50 % improvement (N = 2358)
		$R^2 = 0.003$	$R^2 = 0.000$	AUC 0.51 (0.450, 0.51)			
Cultural difficulty	Not endorsed	4.71 (4.42 to 5.01)	3.77 (3.47 to 4.06)	0.46 (0.44 to 0.47)	-	-	-
	Cultural identity	6.18 (3.92 to 8.44)	5.5 (3.25 to 7.75)	0.5 (0.38 to 0.62)	-	-	-
	<i>p</i> -Value	p = 0.208 $R^2 = 0.002$	p = 0.134 $R^2 = 0.001$	p = 0.49 AUC 0.50 (0.496, 0.51)			
Carer difficulty	Not endorsed	4.72 (4.43 to 5.02)	3.79 (3.5 to 4.09)	0.46 (0.44 to 0.47)	-	-	-
	Carer responsibilities	5.97 (3.43 to 8.51)	3.93 (1.38 to 6.48)	0.58 (0.46 to 0.7)	-	_	-
	<i>p</i> -Value	p = 0.34 $R^2 = 0.001$	p = 0.918 $R^2 = 0.000$	p = 0.054 AUC 0.50 (0.497, 0.51)			
Parenting difficulty	Not endorsed	4.75 (4.44 to 5.06)	3.8 (3.49 to 4.11)	0.46 (0.44 to 0.48)	-	-	-
	Parenting/ childcare responsibilities	4.66 (3.82 to 5.51)	3.77 (2.92 to 4.62)	0.46 (0.42 to 0.5)	-	-	_
	<i>p</i> -Value	p = 0.846 $R^2 = 0.001$	p = 0.952 $R^2 = 0.000$	<i>p</i> = 0.901 AUC 0.50 (0.49, 0.52)			
No difficulty	Not endorsed	5.16 (4.84 to 5.48)	3.88 (3.56 to 4.2)	0.49 (0.47 to 0.5)	-	-	-
	None of these	2.76 (2.07 to 3.45)	3.39 (2.69 to 4.1)	0.31 (0.27 to 0.35)	-	-	-
	<i>p</i> -Value	p < 0.001 $R^2 = 0.019$	p = 0.222 $R^2 = 0.001$	<i>p</i> < 0.001 AUC 0.53 (0.52, 0.55)			
Total number of difficulties	0	2.76 (2.08 to 3.44)	3.39 (2.69 to 4.1)	0.31 (0.27 to 0.35)	3.69 (3.54 to 3.84)	3.21 (3.11 to 3.31)	32.3 (31 to 33.5)
	1	3.96 (3.39 to 4.54)	3.77 (3.19 to 4.36)	0.41 (0.38 to 0.44)	4.11 (3.99 to 4.23)	3.74 (3.67 to 3.81)	43.1 (41.9 to 44.3)
	2	4.3 (3.71 to 4.89)	3.74 (3.13 to 4.34)	0.43 (0.39 to 0.46)	5.04 (4.91 to 5.17)	3.83 (3.75 to 3.91)	43.7 (42.8 to 44.5)
	3	5.63 (4.93 to 6.34)	3.58 (2.87 to 4.29)	0.51 (0.47 to 0.54)	5.63 (5.49 to 5.77)	3.81 (3.72 to 3.91)	48.3 (47.3 to 49.4)
	4	7.56 (6.59 to 8.54)	4.11 (3.13 to 5.09)	0.61 (0.56 to 0.66)	6.85 (6.65 to 7.05)	4.26 (4.09 to 4.44)	58.5 (56.9 to 60)
	5	8.46 (7.14 to 9.78)	5.42 (4.07 to 6.77)	0.63 (0.56 to 0.69)	8.19 (7.84 to 8.53)	4.4 (4.12 to 4.68)	62.7 (60.7 to 64.8)
	6+	9.64 (7.99 to 11.29)	4.93 (3.16 to 6.7)	0.7 (0.62 to 0.77)	9.82 (9.41 to 10.23)	4.59 (4.24 to 4.94)	62 (60 to 63.9)
	<i>p</i> -Value	p < 0.001 $R^2 = 0.083$	p = 0.164 $R^2 = 0.004$	<i>p</i> < 0.001 AUC 0.60 (0.58, 0.62)			
Multivariate model diagnostics					R^2	R^2	AUC
(including all three demographic, clinical and psychosocial predictors)					32.7 % (31.4 to 34)	2.6 % (1.4 to 4)	69.9 % (68.2 to 71.6)

^{*} Cox and Snell R squared. Significance set at p < 0.001, significant values in bold.

be significant at baseline did not predict post-treatment levels of impairment. While age, relationship status, employment status, anxiety severity, and culminative psychosocial factors remained significant in the multivariate model, they only accounted for 2.6 % of the total variance in DOR after treatment. Treatment, therefore, appears to reduce the influence of these factors on functioning.

Nearly half the sample who completed treatment (45.9 %) experienced a 50 % or more reduction in DOR following treatment. This is comparable to the 42.2 % who experienced a 50 % or more symptom reduction in the K10 previously reported in a similar patient sample from the same service (Cross et al., 2022). The greatest gains in functional improvement came from those who reported the highest levels of functional and symptomatic impairment at initial assessment, and those who were unemployed or on disability payments reported significant functional improvement after treatment (65.1 % and 64 % respectively), as did those with severe levels of depression on the PHQ9 (61.4 %) and those with four or more psychosocial difficulties (>58.5 %). These results suggest that the greatest functional gains may be made from psychological treatment in those with significant levels of impairment at service entry. On average, 8.5 DORs for those on disability payments and 5.6 DORs for those unemployed were returned to patients after treatment. The results add support to the recommendation from the Australian Government's Productivity Commission inquiry into mental health, that further investment in online supported psychological treatment would result in a 'net benefit' in terms of cost savings and productivity gains (Productivity Commission, 2020).

The study also found that changes in function were independent of changes in psychological symptoms, consistent with findings published elsewhere (Becker et al., 2011; Sheehan et al., 2011; Sheehan et al., 2017) which suggests that symptom improvement and measures of

Indirect (mediation) effect sizes associated with the serial mediation of each symptom outcome on DOR.

		Bootstrapped ES (with 95 % confidence interval)	Conclusion implied
Indirect DOR to symptom (meditation)	PHQ9 (depression) symptoms	0.06 (-0.002 to 0.014)	No identified mediation
pathways ($a1 * b1$; X \rightarrow M2 \rightarrow Y)	GAD7 (anxiety) symptoms K10 (psychological distress)	0.002 (-0.05 to 0.01) 0.001 (-0.007 to 0.008)	No identified mediation No identified mediation
Direct DOR to symptom change pathway (b2; M2)	symptoms PHQ9 (depression) symptoms	0.058 (-0.007 to 0.123)	No identified pathway over baseline
$M1 \rightarrow Y$)	GAD7 (anxiety) symptoms	0.025 (-0.046 to 0.097)	No identified pathway over baseline
	K10 (psychological distress) symptoms	0.006 (-0.038 to 0.049)	No identified pathway over baseline
Symptom-baseline (reverse) to DOR pathway (<i>adj</i> 2;	PHQ9 (depression) symptoms	0.028 (-0.035 to 0.092)	Non- significant pathway
$M1 \rightarrow Y$)	GAD7 (anxiety) symptoms	0.088 (0.022 to 0.153)*	Association to baseline severity
	K10 (psychological distress) symptoms	0.063 (0.010 to 0.116)*	Association to baseline severity

Note. GAD-7 = Generalized Anxiety Disorder-7; PHQ-9 = Patient Health Questionnaire-9; K10 = Kessler 10 Psychological Distress Questionnaire; 95%CI of the effect size estimates are shown in rounded parentheses; all estimates were derived from models that resampled 5000 cases from the treatment samples to create bootstrapped estimates of the effects. * p < 0.01

functional recovery should be reported as independent outcomes, especially given the increased interest in the role of mental health care in improving productivity.

4.1. Limitations and strengths

A key strength of this study is the use of a large community-based sample of patients accessing a DMHS as part of routine care, and consequently the relationships and findings are likely to reflect those in real-world clinical care. However, the absence of a control group means the observed changes in DORs should be interpreted with caution. The examination of variables at baseline and during and after treatment enabled us to identify and examine factors associated with impairment across the service 'flow' or 'journey'. This resulted in 'missing cases' between the groups as a result of the natural service flow, which was partly overcome by a high sample number, and statistical methods that were powerful enough to detect differences within sample groups of different sizes. Further, we set the rate of functional improvement at 50 %, which is comparatively high, and which may have underestimated the degree of functional improvement for the whole sample. An additional limitation was use of a single measure of functional impairment. Other measures such as the World Health Organization Disability Assessment Schedule (WHODAS) (Üstün et al., 2010) could be used to replicate these findings. Further, there is no commonly accepted statistical approach to report on change in the days out of role, and further psychometric research is required to understand the strengths and weaknesses of the approach taken in the current paper. Replication of these findings in both face to face and DMHS, using other measures of disability, and incorporating health economic analyses is recommended.

5. Conclusions

This study shows that the patients who access a high volume national DMHS providing effective treatment for high prevalence mental disorders have significant levels of functional impairment, and achieve significant functional gains from treatment. However, changes in symptom scores did not fully match the changes in DOR, which suggests that treatment related changes in symptoms and function are independent. Further research linking measures of symptomatic recovery with functional recovery could help confirm the results of this study. Linking subjective outcomes to objective measures of function, such as physical activity, sleep, welfare, income, health care usage and educational outcomes might provide a more complete account of the effect of psychological treatment on the lives of the patients under our care.

Funding

Investigator-initiated.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: N. Titov and B. Dear are authors and developers of the treatment courses used at the MindSpot Clinic but derive no personal or financial benefit from them. All other authors declare they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.invent.2023.100603.

References

Aafjes-van Doorn, K., Kamsteeg, C., Bate, J., Aafjes, M., 2021. A scoping review of machine learning in psychotherapy research. Psychother. Res. 31 (1), 92–116.

- Alonso, J., Petukhova, M., Vilagut, G., Chatterji, S., Heeringa, S., Üstün, T.B., Bromet, E., 2011. Days out of role due to common physical and mental conditions: results from the WHO world mental health surveys. Mol. Psychiatry 16 (12), 1234–1246.
- Becker, K.D., Chorpita, B.F., Daleiden, E.L., 2011. Improvement in symptoms versus functioning: how do our best treatments measure up? Adm. Policy Ment. Health Ment. Health Serv. Res. 38 (6), 440–458.
- Bi, Q., Goodman, K.E., Kaminsky, J., Lessler, J., 2019. What is machine learning? A primer for the epidemiologist. Am. J. Epidemiol. 188 (12), 2222–2239.
- Productivity Commission, 2020. Mental health. (95). Canberra. Retrieved from. http s://www.pc.gov.au/inquiries/completed/mental-health/report.
- Cross, S.P., Karin, E., Staples, L.G., Bisby, M.A., Ryan, K., Duke, G., Titov, N., 2022. Factors associated with treatment uptake, completion, and subsequent symptom improvement in a national digital mental health service. Internet Interv. 27, 100506 https://doi.org/10.1016/j.invent.2022.100506.
- de Groot, M., Laceulle, O.M., Cissen, H., Tiemens, B., van der Heijden, P.T., 2022. Symptom distress and disability: different sides of the same coin? An investigation of the relationship between symptom distress and disability over time in patients receiving treatment for internalizing disorders. J. Clin. Psychol. 78 (12), 2446–2455.
- Dear, B., Staples, L., Terides, M., Fogliati, V., Sheehan, J., Johnston, L., Titov, N., 2016. Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for social anxiety disorder and comorbid disorders: a randomized controlled trial. J. Anxiety Disord. 42, 30–44.
- Dear, B.F., Fogliati, V.J., Fogliati, R., Johnson, B., Boyle, O., Karin, E., Titov, N., 2018. Treating anxiety and depression in young adults: a randomised controlled trial comparing clinician-guided versus self-guided internet-delivered cognitive behavioural therapy. Aust. N. Z. J. Psychiatry 52 (7), 668–679.
- Erik von Elm, M., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., Vandenbroucke, J.P., 2007. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann. Intern. Med. 147 (8), 573e577.
- Etzelmueller, A., Vis, C., Karyotaki, E., Baumeister, H., Titov, N., Berking, M., Ebert, D.D., 2020. Effects of internet-based cognitive behavioral therapy in routine care for adults in treatment for depression and anxiety: systematic review and meta-analysis. J. Med. Internet Res. 22 (8), e18100.
- IsHak, W.W., Greenberg, J.M., Cohen, R.M., 2013. Predicting relapse in major depressive disorder using patient-reported outcomes of depressive symptom severity, functioning, and quality of life in the individual burden of illness index for depression (IBI-D). J. Affect. Disord. 151 (1), 59–65.
- Kessler, R.C., Ames, M., Hymel, P.A., Loeppke, R., McKenas, D.K., Richling, D.E., Ustun, T.B., 2004. Using the World Health Organization health and work

S.P. Cross et al.

Internet Interventions 31 (2023) 100603

performance questionnaire (HPQ) to evaluate the indirect workplace costs of illness. J. Occup. Environ. Med. 46 (6), \$23–\$37.

Kessler, R.C., Andrews, G., Colpe, L.J., Hiripi, E., Mroczek, D.K., Normand, S.L.T., Zaslavsky, A.M., 2002. Short screening scales to monitor population prevalences and

- trends in non-specific psychological distress. Psychol. Med. 32 (6), 959–976. Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression
- severity measure. J. Gen. Intern. Med. 16 (9), 606–613. Lam, R.W., Filteau, M.-J., Milev, R., 2011. Clinical effectiveness: the importance of

psychosocial functioning outcomes. J. Affect. Disord. 132, S9-S13.

Lee, Y.-C., Gao, L., Dear, B.F., Titov, N., Mihalopoulos, C., 2017. The cost-effectiveness of the online MindSpot clinic for the treatment of depression and anxiety in Australia. J. Ment. Health Policy Econ. 20 (4), 155–166.

McCallum, S.M., Batterham, P.J., Calear, A.L., Sunderland, M., Carragher, N., 2019. Reductions in quality of life and increased economic burden associated with mental disorders in an australian adult sample. Aust. Health Rev. 43 (6), 644–652. https:// doi.org/10.1071/AH16276.

Montoya, A.K., Hayes, A.F., 2017. Two-condition within-participant statistical mediation analysis: a path-analytic framework. Psych.Methods 22 (1), 6.

Revicki, D.A., Irwin, D., Reblando, J., Simon, G.E., 1994. The accuracy of self-reported disability days. Med. Care 32 (4), 401–404.

- Sheehan, D.V., Harnett-Sheehan, K., Spann, M.E., Thompson, H.F., Prakash, A., 2011. Assessing remission in major depressive disorder and generalized anxiety disorder clinical trials with the discan metric of the Sheehan disability scale. Int. Clin. Psychopharmacol. 26 (2), 75–83.
- Sheehan, D.V., Nakagome, K., Asami, Y., Pappadopulos, E.A., Boucher, M., 2017. Restoring function in major depressive disorder: a systematic review. J. Affect. Disord. 215, 299–313.
- Slade, T., Johnston, A., Oakley Browne, M.A., Andrews, G., Whiteford, H., 2009. 2007 National Survey of mental health and wellbeing: methods and key findings. Aust. N. Z. J. Psychiatry 43 (7), 594–605.

Spitzer, R.L., Kroenke, K., Williams, J.B., Löwe, B., 2006. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch. Intern. Med. 166 (10), 1092–1097.

Staples, L.G., Fogliati, V.J., Dear, B.F., Nielssen, O., Titov, N., 2016. Internet-delivered treatment for older adults with anxiety and depression: implementation of the wellbeing plus course in routine clinical care and comparison with research trial outcomes. BJPsych Open 2 (5), 307–313. Titov, N., Andersson, G., 2022. Using brief measures to identify depression and other mental disorders: a challenge for research and clinical practice. Internet Interv. 28.

- Titov, N., Dear, B., Nielssen, O., Staples, L., Hadjistavropoulos, H., Nugent, M., Hovland, A., 2018. ICBT in routine care: a descriptive analysis of successful clinics in five countries. Internet Interv. 13, 108–115.
- Titov, N., Dear, B.F., Nielssen, O., Wootton, B., Kayrouz, R., Karin, E., Staples, L.G., 2020. User characteristics and outcomes from a national digital mental health service: an observational study of registrants of the Australian MindSpot clinic. Lancet Digit. Health 2 (11), e582–e593. https://doi.org/10.1016/S2589-7500(20)30224-7.
- Titov, N., Dear, B.F., Staples, L.G., Bennett-Levy, J., Klein, B., Rapee, R.M., Nielssen, O.B., 2016. The first 30 months of the MindSpot clinic: evaluation of a national e-mental health service against project objectives. Aust. N. Z. J. Psychiatry. https://doi.org/ 10.1177/0004867416671598.

Titov, N., Schofield, C., Staples, L., Dear, B.F., Nielssen, O., 2019. A comparison of indigenous and non-indigenous users of MindSpot: an australian digital mental health service. Australas. Psychiatry 27 (4), 352–357.

Üstün, T.B., Chatterji, S., Kostanjsek, N., Rehm, J., Kennedy, C., Epping-Jordan, J., Pull, C., 2010. Developing the World Health Organization disability assessment schedule 2.0. Bull. World Health Organ. 88 (11), 815–823.

Valente, M.J., MacKinnon, D.P., 2017. Comparing models of change to estimate the mediated effect in the pretest–posttest control group design. Struct. Equ. Model. Multidiscip. J. 24 (3), 428–450.

- van Os, J., Guloksuz, S., Vijn, T.W., Hafkenscheid, A., Delespaul, P., 2019. The evidencebased group-level symptom-reduction model as the organizing principle for mental health care: time for change? World Psychiatry 18 (1), 88–96.
- Vos, T., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abera, S.F., 2017. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet 390 (10100), 1211–1259.
- Whiteford, H.A., Degenhardt, L., Rehm, J., Baxter, A.J., Ferrari, A.J., Erskine, H.E., Johns, N., 2013. Global burden of disease attributable to mental and substance use disorders: findings from the global burden of disease study 2010. Lancet 382 (9904), 1575–1586.
- Zimmerman, M., McGlinchey, J.B., Posternak, M.A., Friedman, M., Attiullah, N., Boerescu, D., 2006. How should remission from depression be defined? The depressed patient's perspective. Am. J. Psychiatry 163 (1), 148–150.