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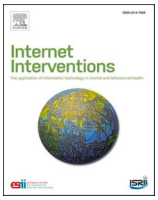

Who benefits from guided internet-based interventions? A systematic review of predictors and moderators of treatment outcome

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ABSTRACT

To our knowledge, no systematic review has been conducted on predictors or moderators of treatment outcome across diagnoses in guided internet-based interventions (IBIs) for adults. To identify who benefits from this specific format and therein inform future research on improving patient-treatment fit, we aimed to aggregate results of relevant studies. 2100 articles, identified by searching the databases PsycInfo, Ovid Medline, and Pubmed and through snowballing, were screened in April/May 2021 and October 2022. Risk of bias and intra- and interrater reliability were assessed. Variables were grouped by predictor category, then synthesized using vote counting based on direction of effect. $N = 60$ articles were included in the review. Grouping resulted in 88 predictors/moderators, of which adherence, baseline symptoms, education, age, and gender were most frequently assessed. Better adherence, treatment credibility, and working alliance emerged as conclusive predictors/moderators for better outcome, whereas higher baseline scores predicted more reliable change but higher post-treatment symptoms. Results of all other predictors/moderators were inconclusive or lacked data. Our review highlights that it is currently difficult to predict, across diagnoses, who will benefit from guided IBIs. Further rigorous research is needed to identify predictors and moderators based on a sufficient number of studies. PROSPERO registration: CRD42021242305.

1. Introduction

Internet-based interventions (IBIs) comprise a heterogenous group of interventions, varying in addressed outcomes, contents, formats, and theoretical basis. They can be delivered via a computer, tablet, or smartphone, are usually either accessed on a website or via an app (Andersson, 2018; Andersson et al., 2019) and can be unguided or guided.

Results of meta-analyses show that IBIs are effective for a variety of mental (e.g. Andrews et al., 2018; Kuester et al., 2016) and somatic health (e.g. Buhrman et al., 2016) outcomes and that transdiagnostic IBIs are also effective (e.g. Păsărelu et al., 2017). Overall, IBIs seem to provide equivalent effects than face-to-face interventions (e.g. Hedman-Lagerlöf et al., 2023), results can endure long-term (Andersson et al., 2018), and they are effective in routine care for anxiety and depressive symptoms (Etzelmueller et al., 2020).

However, knowing that IBIs are effective does not answer the question for whom IBIs work best. A proportion of participants deteriorate during (Rozental et al., 2017), do not respond to (Rozental et al., 2019), or drop-out of (predictors of drop-out see e.g. Karyotaki et al., 2015) IBIs, thus not reaping their potential benefits. Considering this the question on who does benefit from IBIs becomes especially prevalent.

Analyzing predictors – variables which influence treatment outcome regardless of treatment – and moderators – variables which influence the direction or strength of the relationship between the intervention and treatment outcome – offers insights into what works best, for whom, and under which circumstances (Baron and Kenny, 1986; Kazdin, 2007, 2009; Kraemer, 2016). Based on such analyses, interventions can be tailored towards those who benefit from it or aid in adapting it or finding better interventions for those who do not benefit (Kraemer et al., 2002, 2008), thus improving patient-treatment fit.

Previous IBI meta-analyses or systematic reviews have focused on predictors or moderators of e.g. adherence (Beatty and Binnion, 2016), deterioration (Ebert et al., 2016), drop-out (Karyotaki et al., 2015), or non-response (Rozental et al., 2019), have assessed the association of a single predictor/moderator with treatment outcome (e.g. adherence:

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Donkin et al., 2011; baseline symptom severity: Bower et al., 2013; working alliance: Flückiger et al., 2018; Kaiser et al., 2021) or as in a recent component network meta-analysis has focused on prognostic factors for a specific disorder (depression; Furukawa et al., 2021). To our knowledge, no review has been conducted on all predictors/moderators of treatment outcome across diagnoses in guided IBIs.

In a transdiagnostic framework, emotional disorders (which are studied most frequently in IBI research) have more in common than in distinction and specific disorders can be viewed as "trivial variations from a broader syndrome" (Farchione et al., 2012). Plus, cognitive behavioral therapy (CBT) protocols for different disorders show considerable overlap, the large majority including psychoeducation, cognitive interventions, behavioral interventions, and relapse prevention. Most guided IBIs also follow a similar path, including sequential self-help modules with information and exercises and weekly written feedback. From this perspective, the similarities between different IBIs (that largely target emotional disorders with cognitive-behavioral means) outweigh their differences. It therefore seems reasonable to assume that the same predictors might be relevant for different disorders and in different treatment protocols. A review of potential predictors might contribute to a proactive investigation of predictors, e.g. by developing and routinely administering instruments assessing the most important predictors. Also, novel machine learning approaches that show potential to advance the field of precision psychotherapy (e.g. Friedl et al., 2020; Schwartz et al., 2020) highly depend on a sound knowledge of reliable predictors.

Thus, this review addresses the following research questions: Which variables, if any, predict or moderate treatment outcome in guided, psychological IBIs for adults, across mental health diagnoses?

2. Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). It has been registered in the PROSPERO registry: CRD42021242305. The review protocol may be obtained from the first author.

2.1. Search strategy

Using the following, peer-reviewed search terms, with year limit set to 1995 to 2021: web OR online OR internet OR digital* OR digital OR computer* OR computer OR emental OR e-mental OR e-health OR ehealth OR m-health OR mhealth OR technolog* OR mobile OR smartphone OR app OR distance OR tele* OR virtual OR cyber OR cyber* [TITLE]ANDtherap* OR treatment OR self-help OR intervention OR psychotherap* OR counsel* OR approach [TITLE]ANDpredic* OR moder* [ABSTRACT]

ANDguid* OR support* OR self-help [ABSTRACT].

The electronic databases PsycInfo, Ovid Medline, and Pubmed were searched in April 2021 and updated in September 2022. Further potentially relevant studies were identified using the snowballing technique (Greenhalgh and Peacock, 2005), specifically: (a) the references of included articles were screened, and (b) the personal, (expert) knowledge of the subject area was utilized.

2.2. Study selection

Electronic database results were exported into Zotero (2021) for data management and into Rayyan (Ouzzani et al., 2016), where duplicates were removed. Titles and abstracts were screened by one reviewer (KH). Snowballing was conducted by one reviewer (KH). Full texts were screened in terms of the eligibility criteria by two reviewers independently (KH, PB). Disagreements were solved via discussion and by consulting a third reviewer (JB). Study screening took place in April and May 2021, as well as in October 2022.

2.3. Inclusion and exclusion criteria

In- and exclusion criteria were determined by following the participants, interventions, comparators, and outcomes (PICO) process and considering study and report characteristics. The following inclusion criteria had to be met: (a) participants must be over 18 years of age; the intervention (b) must be defined as internet-based, online, web-based, computerized, cyber, virtual, digital, mobile- or smartphone-based, (c) must be a stand-alone intervention (not blended), (d) must be guided, and (e) must be a psychological intervention; (f) at least one predictor or moderator must be analyzed in relation to at least one treatment outcome; (g) primary treatment outcomes must focus on (symptoms of) mental disorders as defined by and diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD); (h) studies must be published, between 1995 and 2021; and (i) full texts must be available in English or German. Studies were excluded if: (a) no predictor/moderator analyses were used (e.g. correlations only) or were not separated by group (e.g. guided and unguided samples analyzed together); and (b) studies were meta-analyses, systematic reviews, qualitative studies, or case reports.

The restriction on guided interventions was chosen as guidance is frequently identified as a very important distinctive ingredient that impacts outcome and adherence (e.g. Furukawa et al., 2021) and might therefore also impact the relevance of predictors. During the second search, we encountered studies using machine learning approaches. As machine learning analyses do not provide data on single predictors but rather on the accuracy of algorithms combining multiple predictors, these were not included in the current review.

2.4. Data extraction

The following data were extracted in May and June 2021, as well as November 2022: citation, sample size, study design, measurement time points, nationality, mean age of participants and, if available, standard deviation, number/percentage of gender of participants, primary diagnosis, duration of IBI, number of modules of IBI, theoretical approach of IBI, all predictors/moderators assessed in relation to the primary outcome and if applicable, how they were measured, all primary treatment outcomes analyzed in relation to predictors/moderators and if applicable, how they were measured, statistical analyses used, and results of predictor/moderator analysis. It was noted if relevant data were missing, but due to time restraints authors were not contacted to obtain such data. Data were extracted by one reviewer (KH). While single extraction does not substantially affect outcome (Shamseer et al., 2015), vote counting results were checked for accuracy by a second reviewer (PB).

2.5. Risk of Bias assessment

To evaluate the quality of the included studies, the Quality in Prognosis Studies Tool (QUIPS; Hayden et al., 2013) was used. The six domains – (1) study participation, (2) study attrition, (3) prognostic factor measurement, (4) outcome measurement, (5) study confounding, and (6) statistical analysis and reporting – were judged to be of low, moderate, or high risk of bias as described in the tool's guidelines. We did not include an "unsure" category – if relevant information was missing it was considered as not present and thereby the bias risk was downgraded. Following Grooten et al. (2019) overall risk of bias was determined as follows: A study has low risk of bias if all domains are rated as low or up to one as moderate. A study has high risk of bias if one or more domain is rated as high or if three or more domains are rated as moderate. All other studies are considered moderate risk of bias.

Ten studies were pilot-rated and discussed by two reviewers (KH, PB). The remaining articles were assessed independently. Disagreements were resolved via discussion including a third reviewer (JB).

2.6. Certainty of evidence

The certainty of the evidence was assessed from the risk of bias ratings, the number of studies/analyses conducted on a predictor, and the significance of the findings.

2.7. Intra- and interrater reliability

Intra- and interrater reliability was calculated. For intrarater reliability of the title/abstract screening, 10 % of the database articles were re-screened ($n = 208$). Interrater reliability for full text screening was assessed after the first round of screening and after discussion between the two reviewers, as assessing it at different stages of coding is recommended (Belur et al., 2018). Interrater reliability for risk of bias assessments was calculated after initial screening, using quadratic weighted Cohen's Kappa.

2.8. Data synthesis

Results were synthesized narratively. All studies were included in the synthesis regardless of their risk of bias rating, though we report the frequency of high risk studies within each section. Multiple reports on the same study were not collated, as, upon inspection, they either assessed different predictors/moderators or were on different (sub-) samples of the study. We included all variables that were assessed in predictor/moderator analyses, even if they may conceptually be considered mediators/mechanisms of change, because the line between predictors or moderators and mediators can be ambiguous (Kraemer et al., 2001, 2002).

2.8.1. Grouping and frequency assessment

Due to the vast amount and variability of predictors/moderators assessed in the original studies we created groups based on overarching concepts. For example, variables such as “number of logins” and “time in program” were categorized as “adherence/treatment engagement”; specific medication use was summarized under “medication use (concurrent)” or “medication use (history)”. Based on these larger groupings, frequencies on how often a specific predictor was assessed across included studies were calculated.

2.8.2. Vote counting based on direction of effect

We used vote counting based on direction of effect for the synthesis of results, as recommended in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2019). Due to the inconsistencies and large heterogeneity of studies included, the analyses used, and results reported, other methods, such as summarizing effect estimates, were not feasible.

We considered three outcome measurements: Post/follow-up scores, change scores/rates of change, and remission/abstinence/clinically significant improvement. For change scores/rates of change reverse scoring, if not already done by the original authors, was conducted, so that a positive association indicates greater change/more improvement. We separated the results based on these measurements due to the difference in interpretation (e.g. a variable which positively predicts post-scores indicates that the participant has higher post scores, thus benefitting less, whereas a positive prediction of change score indicates that the participant improved more, thus benefitting more). The directions of effect can be derived in the vote counting table. For ease of readability in text, however, we summarize results based on whether a variable predicted either worse outcome or better outcome. Better outcome indicating that the participants had lower post-test scores, a higher rate of change, and/or a higher likelihood of being in remission.

Only predictors/moderators that have been assessed by at least three studies were included in vote counting. If a study assessed a variable in various ways (e.g. adherence: text read, time spent, etc.) only one mark for each direction of effect was set in the vote counting table and for highlighting significance we provided the lowest found for this association. Exception: when varying direction of effects were found, then it was marked in each relevant column. For example, if a study assessed text read and time spent, and one association was positive whereas the other was negative, a mark was set for each. If a study conducted more than one analysis (e.g. uni-, and multivariate), all results were included, but only one mark was set for each direction. A study was coded under no relationship if, e.g. the regression weight, was equal to 0.000.

We included all results, regardless of significance, but focus on significant findings in our evaluation of results. We also included all results regardless of their risk of bias rating, but report and highlight the bias ratings to help with interpretability regarding the trustworthiness of our results.

3. Results

All decisions made during the screening process of both searches are displayed in a PRISMA flow diagram (Fig. 1). A total of $n = 60$ studies were included into the review. Supplementary Material A includes a table of characteristics of excluded studies.

3.1. Intra- and interrater reliability

Results for intra- and interrater reliability are presented in Table 1. Shortly, interrater reliability for title/abstract as well as initial full text screening was substantial and for post discussion full text screening almost perfect. There were fifteen (out of 222) articles during screening for which a third reviewer was consulted to reach consensus. Interrater reliability for overall risk of bias was moderate. 100 % agreement was reached during discussion.

3.2. Characteristics of included studies

All characteristics of included studies are presented in Table 2. Of the 60 included, 32 studies used data from randomized controlled trials. Three used pooled data, partly from randomized trials and partly from other research designs. All others analyzed data from quasi-experimental designs. Sample sizes ranged from $n = 22$ to $n = 11{,}143$. The majority of interventions ($n = 53/66$) were based on CBT or a modification. The minimum duration of an intervention was 30 days. Some interventions did not provide a time-limit for the use of the intervention, however, most studies ($n = 49$) limited intervention use to between 5 and 16 weeks. Most interventions were structured into modules, phases, steps, lessons, or comparable concepts. Six delivered the intervention via smartphone app, one had a website and optional smartphone app usage, all others were delivered via website. Mean age of participants ranged from 23.2 to 71.2 years and in all but three studies the majority (>50 %) of participants were female.

3.3. Risk of bias assessment

Of the 60 studies included, 25 were rated to be of low, 9 of moderate, and 26 of high overall risk of bias. When inspecting each domain, domain 2 (attrition) and domain 5 (study confounding) were often rated to be of high ($n = 15$, 8 respectively) or of moderate risk ($n = 31$, 23 respectively), whereas domain 1 (study participation; $n = 57$), domain 3 (prognostic factor measurement; $n = 51$), domain 4 (outcome measurement; $n = 59$), and domain 6 (statistical analysis and reporting; $n = 49$) were most frequently rated as of low risk. The ratings for each study are presented in the Supplementary Material B.

3.4. Predictors/moderators

Of all variables analyzed in the 60 studies, 88 predictor/moderator variable groups were generated based on collating variables according to overarching concepts. An overview of analyzed predictors/

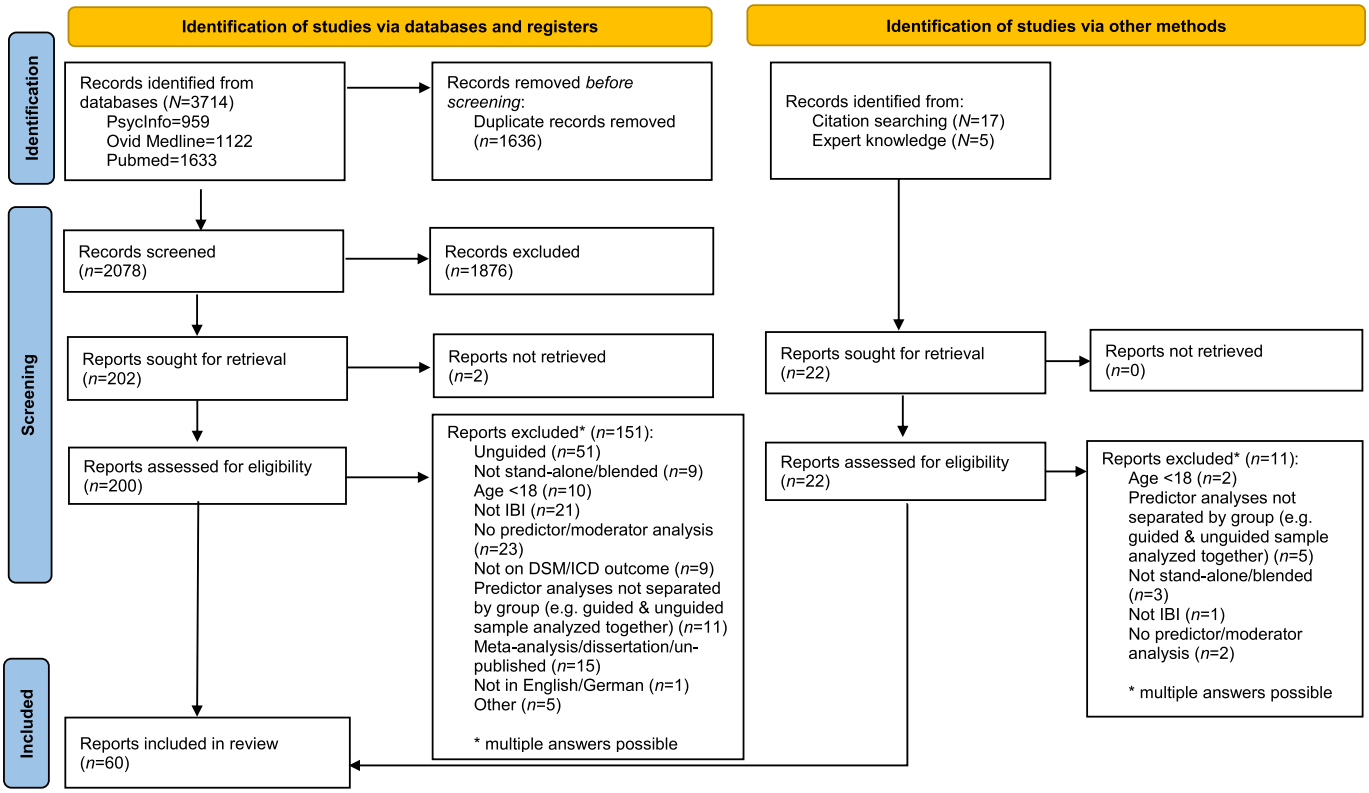

Fig. 1. PRISMA 2020 flow diagram.

Table 1
Intra- and interrater reliability.

	Cohen's Kappa
Title/abstract screening[a]	0.713
Initial full text screening	0.625
Post discussion full text screening	0.848
Risk of bias[b]	
Domain 1[c]	0.629
Domain 2[d]	0.612
Domain 3[e]	0.410
Domain 4[f]	0.249
Domain 5[g]	0.390
Domain 6[h]	0.110
Overall RoB[i]	0.551

Note. RoB = risk of bias.
[a] Intrarater reliability.
[b] Using quadratic weighed Cohen's Kappa.
[c] $n = 58$.
[d] $n = 50$.
[e] $n = 56$.
[f] $n = 59$.
[g] $n = 56$.
[h] $n = 55$.
[i] $n = 49$.

moderators by study is available in the Supplementary Material C. A table of the original variable names and how they were grouped is available in Supplementary Material D. Figs. 2 and 3 visualize the frequencies with which predictors/moderators were assessed across studies. Since only six studies applied moderation analyses that could be counted in this synthesis, their results are not reported separately, but incorporated in the following results section.

3.4.1. *Vote counting based on direction of effect*

Thirty-seven of 88 variables were assessed by at least three studies and thus included in vote counting. In 24 studies relevant information, e.g. the direction of effect for non-significant associations, were not or incompletely reported, and thus these results were not included in vote counting (see Supplementary Materials E for a table regarding missing information). Vote counting results are summarized in Table 3.

3.4.1.1. *Demographic predictors/moderators*

3.4.1.1.1. Education. Fifteen predictor/moderator analyses were conducted, of which seven were significant. Out of the seven significant analyses, four found higher education to predict worse outcome (one from a high risk study), whereas three found higher education to predict better outcome (two from high risk studies).

3.4.1.1.2. Age. Sixteen analyses were conducted, of which eight were significant. In four of the eight analyses older age predicted worse outcome (two from high risk studies), whereas in the other two older age predicted better outcome (four from high risk studies).

3.4.1.1.3. Gender. Five studies did not provide information regarding which gender was their reference category, thus they were excluded from vote counting. Nine analyses were conducted, only one was significant (low risk study), finding that being female predicted better outcome.

3.4.1.1.4. Employment. Thirteen predictor/moderator analyses were conducted, of which seven found significant results. Five out of the seven significant analyses found that being employed predicted better outcome (three from high risk studies), two found being employed to predict worse outcome (one from a high risk study).

3.4.1.1.5. Marital status. Thirteen analyses were conducted on the association between being married and outcome. Of those analyses five were significant: Three found being married to predict better outcome (one from a high risk study), two found being married to predict worse outcome (one from a high risk study).

3.4.1.1.6. Children. Six analyses focused on the association between having children and outcome, only one finding significant results: Having children predicted better outcome (low risk study).

Table 2
Characteristics of included studies.

	Author (year)	Sample size[a]	Study design	Measurement time points[b]	Country	Participants' age in years Mean (SD)	Participants' gender Female/male Number (percent)[c]	Primary diagnosis	Duration of IBI in weeks	Number of modules of IBI	Theoretical approach of IBI	Implemented via
1	Allende et al. (2022)	290	Longitudinal observational study	Pre, every 2 weeks during intervention, post	USA, Finland	39.64 (10.25)	229/61 (79/21)	Depression anxiety	12 weeks	12	CBT	Smartphone app
2	Andersson et al. (2004)	71	RCT	Pre, 6mFU	Sweden	37 (11)	56/15 (79/21)	Depression	7–10	5	CBT	Website
3	Andersson et al. (2008)	25	RCT	Pre, post, 12mFU	Sweden	34.2 (6.0)	17/8 (68/32)	Panic	10	10	CBT	Website
4	Andersson et al. (2015)	96 post 87 24mFU	Pooled: 1) RCT 2) Cohort, long-term study	Pre, post, 24 m FU	Sweden	34.93 (12.72)[d]	67/34 (66/34)[d]	OCD	10	10	CBT	Website
5	Bergman Nordgren et al. (2013)	27 pre 25 mid 58 post	RCT	Pre, post, 3 week mid treatment	Sweden	39.3 (11.2)	18/27 (67/33)	Anxiety	10	16 prescribed 6–10	Tailored CBT	Website
6	Böttche et al. (2016)	58	RCT	Pre, post, 6mFU	Germany	71.2 (4.6)	42/16 (69/31)	PTSD	6	3 + 11 essays	CBWT	Website
7	Brog et al. (2022)	107	RCT	Pre, post	Germany	40.36 (14.59)	87/20 (81.3/18.7)	Depression/ Covid-related distress	3 weeks	6 + introduction/ conclusion	CBT	Website
8	Carlbring et al. (2012)	284 total 218 post 196 36mFU	Non-comparative, single group study	Pre, post, 36mFU	Sweden	32.2 (8.8)	54/230 (19/81)	Pathological gambling	8	8	CBT	Website
9	Carrard et al. (2011)	95 post	Pooled: Multi-site evaluation, uncontrolled	Pre, post	Switzerland Spain Sweden Germany	24.7 (5.1)	95/0 (100/0)	Bulimia nervosa, (non-) purging type eating disorder, not otherwise specified	16 (4 months)	7	CBT	Website
10	Diefenbach et al. (2015)	26	Open trial	Pre, post	USA	37.08 (12.57)	17/26 (65/35)	OCD	15	9	Exposure & response prevention	Website
11	Edmonds et al. (2018)	837	Open trial + from continued offering of program	Pre, before lessons 2,3,4,5, post	Canada	37.92 (12.84)	592/245 (71/29)	Depression Anxiety	8	5	Transdiagnostic CBT	Website
12	Edmonds et al. (2020)	1201 total 836 post[e]	Exploratory study	Pre, post	Canada	37.92 (12.84)	852/1201 (29/71)	Depression Anxiety	8	5	Transdiagnostic CBT	Website
13	El Alaoui et al. (2013)	44 post 43 FU	RCT	Pre, 6mFU	Sweden	33.8 (9.7)[d]	32/18 (64/36)[d]	Panic (with/ without agoraphobia)	10	10	CBT	Website
14	El Alaoui et al. (2015a)	446	Longitudinal study	Pre, post, 6mFU, long-term FU (between 1.2 and 4.1 years from pre, M = 2.66, SD = 0.80)	Sweden	32.67 (9.71)	245/201 (55/45)	Social anxiety	12	9	CBT	Website
15	El Alaoui et al. (2015b)	764	Retrospective cohort study	Pre, treatment program factors: during, post; social	Sweden	32.51 (8.98)	351/413 (46/54)	Social anxiety	10	9 or 10[f]	CBT	Website

(*continued on next page*)

Table 2 (*continued*)

	Author (year)	Sample size[a]	Study design	Measurement time points[b]	Country	Participants' age in years Mean (SD)	Participants' gender Female/male Number (percent)[c]	Primary diagnosis	Duration of IBI in weeks	Number of modules of IBI	Theoretical approach of IBI	Implemented via
				anxiety: weekly week 1–10, post								
16	El Alaoui et al. (2016)	1738	Longitudinal, retrospective cohort study	Pre, weekly from week 1–10, post	Sweden	37.73 (12.08)	1164/574 (67/33)	Depression	12	10	CBT	Website
17	Ezawa et al. (2020)	31	Pooled: 1) Study with two conditions 2) Open trial	Pre, post, every 2 weeks for 1 year	USA	32 (10.7)	20/11 (64/36)	Depression	8	8	CBT	Website
18	Fernández-Aranda et al. (2009)	62[g]	Non-randomized controlled trial	Pre, post, food diary throughout	Spain	23.7 (3.6)	62/0 (100/0)	Bulimia nervosa, purging subtype	16 (4 months) WL: posttest = 12	7 steps	CBT	Website
19	Flygare et al. (2020)	88	RCT	Pre, post, 3mFU, 12mFU, 24mFU	Sweden	32.48 (11.62)	74/14 (84/16)	Body dysmorphic	12	8	CBT	Website
20	Fuhr et al. (2018)[k]	382	RCT	Pre, post	Germany	42.81 (11.04)	350/32 (69/31)	Depression Dysthymia	12	10	CBT	Website
21	Goldin et al. (2019)	22 study 1 95 study 2	Pilot studies	Pre, post	Finland	23.2 (1.1) study 1 32.0 (9.85) study 2	22/0 (100/0) study 1 76/19 (80/20) study 2	Depression	8	8	MBSR & MBCT & CBT & BA	Smartphone app
22	Gómez Penedo et al. (2020)[k]	223	RCT	Pre, post, 3mFU, 9mFU	Germany	44.48 (10.68)	157/66 (70/30)	Depression	12	10 + intro/summary	CBT	Website
23	Graham et al. (2015)	675 total 391 FU[e]	RCT	Pre, 3m FU, 6mFU	USA	36.2 (10.9)[h]	680/556 (55/45)[h]	Nicotine dependence	6 months free access	0 website	Evidence-based tobacco dependence treatment	Website
24	Hadjistavropoulos et al. (2014)	195 total 83 depression 112 anxiety	Exploratory study	Pre, mid, after module 6, before final module (post)	Canada	39.99 (12.54)	134/61 (69/31)	Depression Anxiety	18–19 mean 12 encouraged	12	Both CBT	Website
25	Hedman et al. (2013)[l]	81	RCT	Pre, 6mFU	Sweden	39 (9.7)	60/21 (74/26)	Severe health anxiety	12	12	CBT	Website
26	Hedman et al. (2015)[l]	158	RCT	Pre, post	Sweden	41.7 (13.6) ICBT 41.4 (13.2) IBSM	64/15 (81/19) ICBT 61/18 (77/23) IBSM	Severe health anxiety	12	12	CBT, IBSM	Website
27	Knaevelsrud and Maercker (2006)	48	RCT	Pre, post	Germany	35	44/48 (92/8)	PTSD	5	3 phases + 10 essays	CBT	Website
28	Kraepelien et al. (2019)[o]	207 total subgroups: 106 worry 39 panic 34 social anxiety 131 stress 97 insomnia	RCT	Pre, post	Sweden	44.2 (12.1)	159/48 (77/23)	Depression comorbid conditions	12	30 4 mandatory	Tailored CBT	Website

(*continued on next page*)

Table 2 (*continued*)

	Author (year)	Sample size[a]	Study design	Measurement time points[b]	Country	Participants' age in years Mean (SD)	Participants' gender Female/male Number (percent)[c]	Primary diagnosis	Duration of IBI in weeks	Number of modules of IBI	Theoretical approach of IBI	Implemented via
		39 pain[i]										
29	Kraepelien et al. (2021)	67	RCT	Pre, post	Sweden	47 (15.2)[d]	59/14 (81/19)[d]	Insomnia	8	8	CBT	Website
30	Levallius et al. (2020)	79	RCT	Pre, post	Sweden	27.3 (7.3)[h]	79/0 (100/0)	Bulimia nervosa	24 max.	7	CBT	Website
31	Lindner et al. (2016)[m]	115	RCT	Pre (after attention training), post	Sweden	34.09 (10.53)	70/45 (61/39)	Social anxiety	9 + 2 attention training	9	CBT	Website
32	Lüdtke et al. (2021)	100	RCT	Pre, post	Germany Switzerland	40.15 (9.58)	59/41 (59/41)	Psychosis	8 weeks	11	CBT	Website, optional smartphone app
33	Månsson et al. (2015)	26	Cross over study	Pre, 1yFU	Sweden	32.3 (9.6)	22/26 (85/15)	Social anxiety	9 ICBT 4 ABM	9 ICBT 8 ABM	CBT, ABM	Website
34	Mathiasen et al. (2018)	60 depression 143 anxiety	Uncontrolled retrospective cohort study	Pre, post	Denmark	36.03 (10.97) depression 36.80 (13.55) anxiety	47/13 (78/22) depression 94/52 (66/34) anxiety	Depression anxiety	Flexible encouraged weekly, could take longer	6 +2 optional depression 9 anxiety	CBT	Website
35	Mohr et al. (2021)	401 cumulative Study 1: 105 Study 2: 150 Study 3: 146	Cumulative of 3 studies: RCT, single arm, factorial design	Pre, post	USA	Study 1: 38.9 (14.1) Study 2: 37.3 (12.2) Study 3: 42.3 (13.8)	Study 1: 80/25 (76/24) Study 2: 121/29 (81/19) Study 3: 121/25 (83/17)	Depression Anxiety	8 weeks	Study 1 & 2: 12 apps, study 3: 5 apps	CBT	Smartphone apps
36	Niles et al. (2021)	370	Prospective cohort study	Pre, post	Sweden	41.4 (15.1)	240/130 (65/35)	Depression Social anxiety panic	10 weeks	8	CBT	Website
37	Nissen et al. (2021)	82	RCT	Pre, post, 6mFU	Denmark	54.47 (10.10)	75/7 (92/8)	Depression anxiety	8	8	Mindfulness CBT	Website
38	Nordgreen et al. (2010)	27	Pilot study	Pre, post, 6mFU	Norway	40.5 (12.4)	19/8 (70/30)	Panic	10	10	CBT	Website
39	Nordgreen et al. (2012)[n]	149	Pooled: 1) RCT 2) Open study	Pre, post, 6mFU, 12mFU	Sweden	34.42 (9.43)	100/149 (67/33)	Social anxiety	9	9	CBT	Website
40	O'Mahen et al. (2017)	32	RCT	Pre, post	United Kingdom	None given also not in original study	32/0 (100/0)	Postpartum depression	Flexible could take as many weeks as want	12 Up to	BA	Website
41	Palacios et al. (2022)	89	RCT	Pre, post, 9mFU	England	34.83 (13.39)	69/20 (77.5/22.5)	Depression anxiety	8 weeks	7	CBT	Website
42	Peters et al. (2017)	112 ICBT 114 PPT	RCT	Pre, post, 6mFU	Netherlands, Belgium	48.7 (11.5) ICBT 47.5 (13.2) PPI	95/17 (85/15) ICBT 95/19 (83/17) PPI	Depression in fibromyalgia patients	8	8	CBT, PPI	Website
43	Rahman et al. (2017)[o]	480	RCT	Pre, post	Sweden	43.55 (12.26) Val group	271/106 (72/28) Val group	Depression	12	13	CBT	Website

(*continued on next page*)

Table 2 (*continued*)

	Author (year)	Sample size[a]	Study design	Measurement time points[b]	Country	Participants' age in years Mean (SD)	Participants' gender Female/male Number (percent)[c]	Primary diagnosis	Duration of IBI in weeks	Number of modules of IBI	Theoretical approach of IBI	Implemented via
44	Ruwaard et al. (2009)	36 post 39 FU	RCT	Pre, post, 18mFU	Netherlands	45.42 (12.35) Met group 42 (10)[d]	117/53 (69/31) Met group 37/17 (69/31)[d]	Depression	11 could take longer Median: 16	8	CT & BA	Website
45	Schlicker et al. (2019)	253 total 127 IG	RCT	Pre, post, 6mFU	Germany	50.7 (11.7) total 50.16 (11.68) IC	159/94 (63/37) total 80/47 (63/37)	Depression in people with diabetes	6	6 +2 optional +1 booster	Systemic BA & problem solving	Website
46	Schlosser et al. (2017)	30 post 36 total[e]	Evaluation Uncontrolled, open label	Week 1, 2, 3, 4, 8, post	USA	31.33 (12.4)	28/8 (78/22)	Depression	8	0 app	CBT & mindfulness & psychoeducation & BA	Smartphone app
47	Schmidt et al. (2022)	49	RCT	Pre, post	Germany	No info found	42/7 (86/14)	Prolonged grief	5 weeks	No info found	CBT	Website
48	Schønning and Nordgreen (2021)	575 total, PD: 280, SAD: 306	Open study	Pre, after each module, post, 6mFU	Norway	31.8 (10.9)	351/224 (61.4/38.6)	Panic Social anxiety	14 weeks	9	CBT	Website
49	Tillfors et al. (2015)[n]	167	Pooled: RCT	Pre, post	Sweden	34 (9.22)	115/52 (69/31)	Social anxiety	9	9	CBT	Website
50	van Luenen et al. (2020)	97	RCT	Pre, post, 5mAfterPretest	Netherlands	45.53 (10.32)	12/85 (12/88)	Depression in HIV patients	8	8 in 4 components	CBT & stress management	Website
51	Varga et al. (2022)	143	Pilot study	Pre, post	Hungary	37.8 (10.05)	101/42 (70.6/29.4)	Depression	6 weeks	6	CBT	Website
52	Venkatesan et al. (2020)	139 depression 143 anxiety	Retrospective observational study	Automated assessments every 2 weeks, pre, post, 1yFU, 3mFU, 6mFU, 9 m FU	USA	36.42 (9.22) depression 36.10 (9.03) anxiety	95/42 (68/30) 2 (1.4) did not specify, depression 104/41 (71/28) 1 (0.7) did not specify, anxiety	Depression Anxiety	12 could use longer	0 app	CBT	Smartphone app
53	Venkatesan et al. (2022)	1512	Retrospective single arm study	Pre, week 6, post (12 weeks), every 3 months up till 1 year	USA	47.5 (11.9)	1267/240 (83.8/15.9), not disclosed 5 (0.3)	depression anxiety	12 weeks	No information	CBT	Smartphone app
54	Wagner et al. (2012)	47	RCT	Pre, mid, post	Arabic speaking, 70 % Iraqi nationality	27.7 (7.0)	38/9 (81/19)	PTSD	Flexible 14 mean 5–37 range	3 +10 essays	CBT	Website
55	Walderhaug et al. (2019)	143	Open pre-post effectiveness study	Pre, weekly during treatment modules 2–9, 6mFU	Norway	34.9 (11.5)	84/59 (59/41)	Panic	14 Up to	9	CBT	Website
56	Weise et al. (2019)	174 total 86 IG	RCT	Pre, post, 6mFU	Germany	33.49 (6.32)	174/0 (100/0)	Premenstrual dysphoric	8	14	CBT	Website
57	Wheaton et al. (2021)	40 total 30 post[e]	Open trial	Pre, post	USA	36.61 (11.13)[d]	23/17 (58/42)[d]	OCD	12	10	CBT	Website

(*continued on next page*)

Table 2 (*continued*)

	Author (year)	Sample size[a]	Study design	Measurement time points[b]	Country	Participants' age in years Mean (SD)	Participants' gender Female/male Number (percent)[c]	Primary diagnosis	Duration of IBI in weeks	Number of modules of IBI	Theoretical approach of IBI	Implemented via
58	Zagorscak et al. (2020)	1089	RCT	Pre, at the beginning of M3, M5, M7, post, 3mFU,6mFU,12mFU	Germany	45.7 (11.3)	714/375 (66/34)	Depression	6–8	7	CBT	Website
59	Zbikowski et al. (2008)	11,143[j]	Evaluation of a real-world service	Pre, 6mFU	USA	43.0 (10.8)	6017/5126 (54/46)	Nicotine dependence	0 website	4 "areas" of interaction 7 key features	SCT	Website
60	Zbikowski et al. (2011)	399	RCT	Pre, 6mFU (after individually set "to quit date")	USA	47[h]	802/396 (67/33)[h]	Nicotine dependence	Tied to quit date usually 30 days from pre	4 "areas" of interaction 7 key features	SCT	Website

Note. IBI = internet-based Intervention. FU = follow-up. RCT = randomized controlled trial. OCD = obsessive compulsive disorder. PTSD = post-traumatic stress disorder. CBT = cognitive behavioral therapy. CBWT = Cognitive Behavioral Writing Therapy. MBSR = mindfulness-based stress reduction. MBCT = mindfulness-based cognitive therapy. BA = behavior(al) activation. IBSM = internet-delivered behavioral stress management. ABM = attention bias modification. PPI = internet-delivered positive psychology program. CT = cognitive therapy. SCT = social cognitive theory. SD=Standard deviation. m = month. IG=Internet group.

[a] Those used for predictor analysis, e.g. if no imputation was used.
[b] Only those that were assessed in predictor analyses.
[c] If a publication did not provide information on both it was calculated, however, this does not consider that some answers may have been missing/participants may not have specified.
[d] Total sample size without attrition.
[e] Unclear if ITT or completer analysis.
[f] Exact number of modules unclear.
[g] Unclear if predictor analysis is on all after waitlist received treatment or only on half.
[h] Total sample of all groups (e.g. not just IBI group).
[i] Subgroups may overlap.
[j] Number varies for analyses due to missing values.
[k] Both on same trial, but 20 uses only subsample.
[l] Both on same trial, but different measurement times used in analyses.
[m] Only social anxiety sample included in review.
[n] Pooled data overlaps, but not completely.
[o] Both on same trial, but different predictors/moderators.

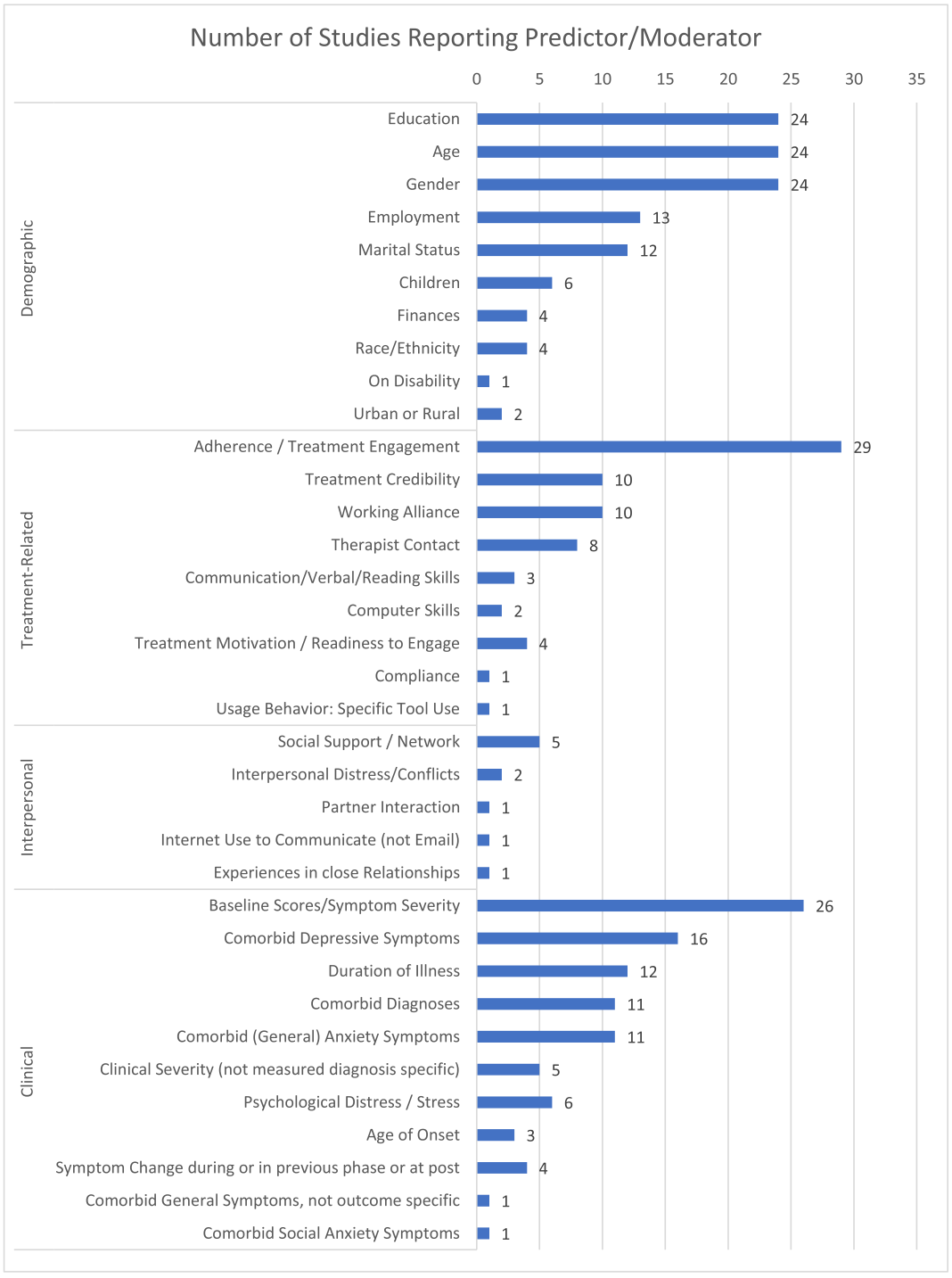

Fig. 2. Frequencies of predictors/moderators.

3.4.1.1.7. Finances. Eight analyses were conducted, of which one was significant: Higher income predicted worse outcome (high risk study).

Taken together, prediction based on demographic variables remains inconclusive due to similar frequency counts of associations to worse and better outcome, few significant findings, and inclusion of high risk studies.

3.4.1.2. Treatment-related predictors/moderators

3.4.1.2.1. Adherence. Thirty-three analyses were conducted, of which 22 were significant and all of which found that higher adherence predicted better outcome (eight from high risk studies).

3.4.1.2.2. Treatment credibility. Twenty analyses were conducted, of which eight were significant and all eight found higher treatment credibility to predict better outcome (two from high risk studies).

3.4.1.2.3. Working alliance. Fourteen analyses were conducted, of which nine were significant. In eight out of the nine analyses stronger working alliance predicted better outcome (one from a high risk study), in one stronger working alliance predicted worse outcome (low risk study).

3.4.1.2.4. Therapist contact. Seven analyses were conducted, five of which were significant. In four of the five significant analyses more

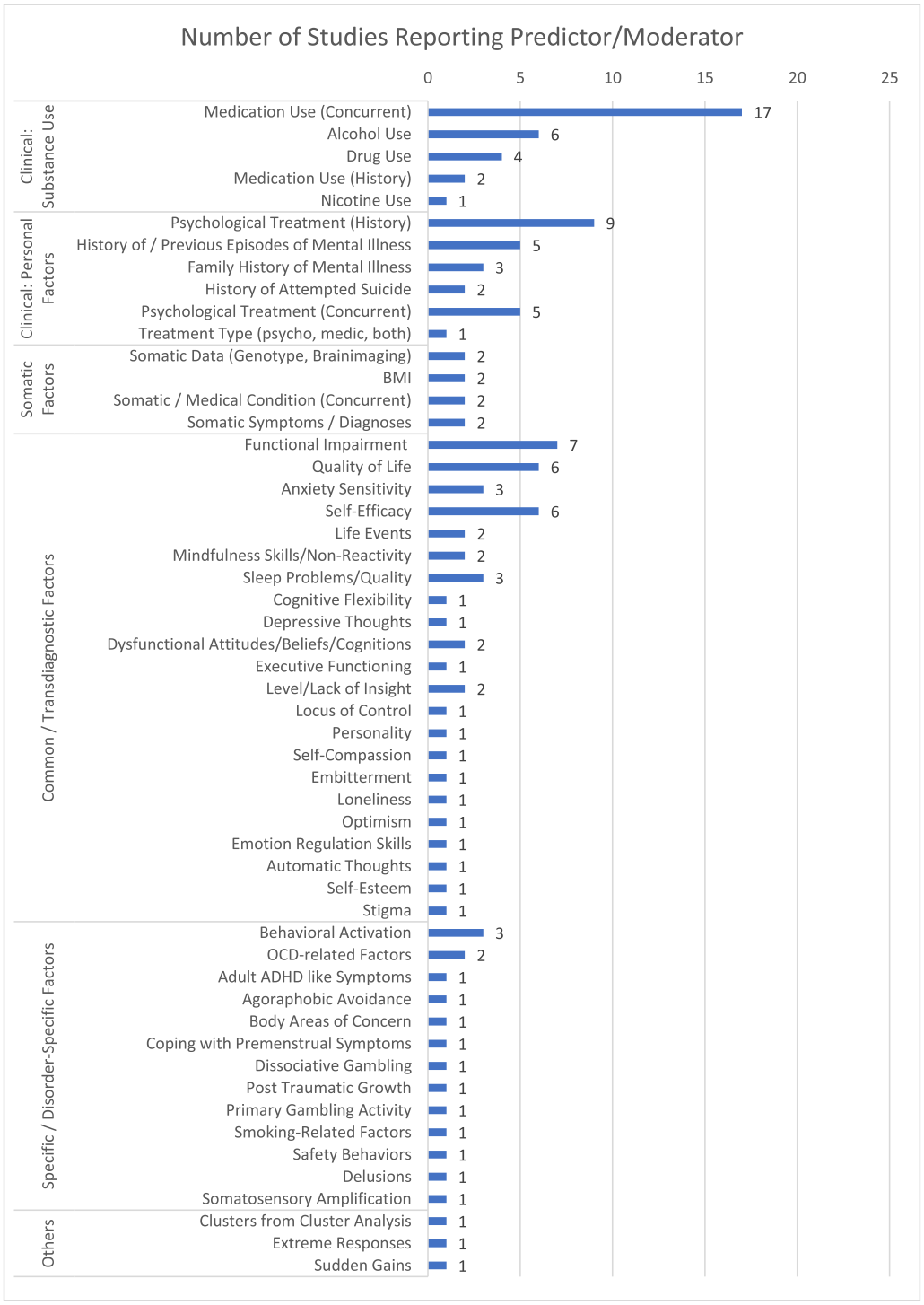

Fig. 3. Frequencies of predictors/moderators contin.

therapist contact predicted better outcome (three from high risk studies), in one it predicted worse outcome (low risk study).

In summary, higher adherence, treatment credibility, and working alliance were predictors of better outcome. More therapist contact displayed a tendency to predict better outcome, but most results came from high risk studies. Results from all other variables were inconclusive or lacked data.

3.4.1.3. Interpersonal predictors/moderators. Few studies assessed interpersonal factors and only social support was reported by at least three studies, all of which were rated as high risk of bias. Of those, one found more social support to significantly predict better outcome.

3.4.1.4. Clinical predictors/moderators

3.4.1.4.1. Baseline scores. Thirty-one analyses included baseline scores as predictor/moderator, of which 24 were significant. Nine of the 24 significant analyses found higher baseline scores to predict worse outcome (two from high risk studies), 15 found higher baseline scores to predict better outcome (three from high risk studies).

3.4.1.4.2. Comorbid depressive symptoms. Nineteen analyses were

conducted, of which eight found significant results. In five of the eight significant analyses, comorbid depressive symptoms predicted worse outcome (one from a high risk study), in three comorbid depressive symptoms predicted better outcome (two from high risk studies).

3.4.1.4.3. Comorbid anxiety symptoms. Of the twelve analyses in total, seven were significant. In six of the seven significant analyses, comorbid anxiety predicted worse outcome (four from high risk studies), in one comorbid anxiety predicted better outcome (low risk study).

3.4.1.4.4. Comorbid diagnoses. Eleven analyses were conducted, of which three were significant: Two found comorbid diagnoses to significantly predict worse outcome (one moderate risk study), one found comorbid diagnoses to significantly predict better outcome (low risk study).

3.4.1.4.5. Substance use. Concurrent medication use was assessed in 17 studies, however, only 10 reported data to be used for vote counting. In these studies, 13 analyses were conducted, but only two found

Table 3
Vote counting based on direction of effect.
Vote Counting Based on Direction of Effect

	Outcome:	Post/FU Score			Change Score, (linear) Rate of Change			Remission, Responder Status, Abstinence, Clinical. Sign. Improvement (Binary)			Total Number of Studies[c]
Category	Predictor	Association			Association			Association			
		+	–	0	+	–	0	+	–	0	
Demographic	Higher Education	57, 42*, 7, 32	15***, 42*, 32		24, 34*	11**, 15, 24, 34, 38**, 35***					10
	Older Age	7*, 32*	15**, 26, 1		34, 38*	15*, 24, 11**, 51, 35	34, 11	23*, 41**[c]			12
	Gender										7
	Being Female	16	7, 32*		16	35					
	Being Male				11, 24	11, 51					
	Being Employed		15***, 16***, 25		11[a], 16**, 34**, 35	11[a]**, 15*, 24, 34, 35		23**			8
	Being Married		15, 57, 16[b]***		11*, 15, 24, 34*, 16[b], 35	11*, 24, 34*, 35					7
	Having Children		15		15, 24	24		19*, 25			4
	Finances										4
	Having Debts							8	8		
	High Income		40			35		8	8, 23*	8	
	Race/Ethnicity	57				35					2
	White										
	Black				35						
	Other										
Treatment-Related	Adherence / Treatment Engagement		15***, 16***, 21***, 25*, 26**, 29**, 46*, 7, 32, 35***		14, 15***, 16***, 20, 24**, 25*, 26**, 34*, 39*, 52***, 58***, 53**, 35***		11, 34	19**, 39*, 59***, 60, 41	19, 41	60	25
	Treatment Credibility	32	15**, 16***, 26**, 32		14, 15***, 16***, 26*, 39, 58, 3	39, 58, 3	39, 58	19**, 26*, 39			9
	Working Alliance	22	4*, 22***, 26		4*, 22, 26*, 54**, 5*, 58**	4*	58	19*			8
	Therapist Contact	15	15**, 46		11*, 15, 24	11, 15, 24**		59***, 60*	60		6
	Communication/ Verbal/Reading Skills				24*						1
	Treatment Motivation/Readiness to Engage	7	1					8			3
Interpersonal	Social Support / Network	40						8, 23**			3
Clinical	Baseline Scores/Symptom Severity	4***, 16***, 25***, 26***, 28***, 29, 40*, 57***, 13***			4***, 6***, 9*, 16***, 24*, 25***, 26*, 39*, 45***, 52***, 37*, 51***, 35***, 47*	39	39	18, 30***, 39	19, 25***, 39		24
	Comorbid Depressive Symptoms	15, 25***, 26, 55**, 57	55**		34**, 38, 39*	15, 25***, 38, 39, 35		39, 41[c]	19*, 25***	19	11
	Duration of Illness		15, 57		15	38**			41*[c]		4

	Comorbid Diagnoses	25, 26, 57	15, 35*[f]	15, 24, 35***	24, 3*		41[e]		8
	Comorbid (General) Anxiety Symptoms	2*, 25*, 7*, 32	32	25*, 26, 24	34*		25*, 19, 41*[c]		9
	Clinical Severity (not measured diagnosis specific)	15***		12***, 38	15, 38*				3
	Psychological Distress / Stress	56***, 7*		11***, 45, 58*	45	45			6
	Age of Onset		15, 57		15				2
	Symptom Change during a previous phase or at post	1***	1	25, 58***					3
Clinical: Substance Use	Medication Use (Concurrent)	12***, 15, 1, 32	57, 7	24	15, 24, 35		60*, 41	41		10
	Alcohol Use		15	15			8*		8	2
	Drug Use	16	15	15	16					2
Clinical: Personal Factors	Psychological Treatment (History)	57*, 32*	15, 7*	11***, 15	11, 36*[d]					6
	History of / Previous Episodes of Mental Illness	15	7*		2*, 15					3
	Family History of Mental Illness	15	15	15	14*, 15					2
	Psychological Treatment (Concurrent)		7**	35**	36, 24**					4
Common/ Transdiagnostic Factors	Functional Impairment	40, 57, 13**	15***	11***	15***				19	6
	Quality of Life	7	2*, 57, 7				8, 19	8	8	5
	Anxiety Sensitivity	25*	13*	25*, 26*						3
	Self-Efficacy		15, 7, 48***	15, 47**						4
	Sleep Problems/Quality	16***		16***	38*					2
Specific/Disorder-specific Factors	Behavioral Activation	40*								1

Note. Numbers refer to individual studies, see study characteristics table. Colors refer to risk of bias rating: green = low, orange = moderate, red = high. FU = follow-up. Negative association in the Post/FU score reflects lower post/FU scores = better outcome. Positive associations in the Change score/rate of change indicates more change/larger improvement = better outcome; studies were reverse coded if necessary. Positive associations in the Remission/abstinence/responder status category indicates higher chance of remission/abstinence/being a responder = better outcome.

*$p < .05$.

**$p < .01$.

***$p < .001$.

[a]Reverse scored as used unemployed as reference category.

[b]Reverse scored as used single as reference category.

[c]Of those which provided data for vote counting.

[d]Reverse scored as those without history achieved more change.

[e]Reverse scored as in paper articulated as more likely to relapse/risk of relapse.

[f]Comorbidity moderates association between adherence and postscores.

significant results: Concurrent medication significantly predicted worse outcome in one analysis (moderate risk study) and significantly predicted better outcome in the other analysis (high risk study).

3.4.1.4.6. Psychological distress/stress. Seven analyses were conducted, four yielding significant results: In two analyses more stress predicted worse outcome (one high risk study) and in the other two it predicted better outcome.

3.4.1.4.7. History of previous treatments. Eight analyses were conducted on the association between history of previous treatments and outcome, five of which were significant. Of the five significant analyses, three found that previous treatment predicted better outcome (one from a high risk study), whereas in two previous treatment predicted worse outcome.

3.4.1.4.8. Previous episodes of mental illness. Two high risk studies provided significant data: One found that a previous episode of mental illness predicted better outcome, one that it predicted worse outcome.

3.4.1.4.9. Concurrent treatment. Four analyses were conducted, three of which yielded significant results. In two of the three significant analyses concurrent treatment predicted better outcome (one from a high risk study), whereas in the other analysis concurrent treatment predicted worse outcome.

In sum, higher baseline symptoms predicted better, but also worse

outcome. Comorbid depressive or anxiety symptoms displayed a tendency to predict worse outcome, although some results remain inconclusive and data from high risk studies was included. The results for all other clinical variables were inconsistent or data was too limited to draw conclusions.

3.4.1.5. Common/transdiagnostic factors

3.4.1.5.1. Functional impairment. Seven analyses were conducted, four finding significant associations: Two found more functional impairment to predict worse outcome, the other two found functional impairment to predict better outcome (one from a high risk study each).

3.4.1.5.2. Quality of life. Eight analyses were conducted, of which one was significant and found quality of life to predict better outcome (high risk study).

3.4.1.5.3. Anxiety sensitivity. Four significant predictor/moderator analyses were conducted, of which three found anxiety sensitivity to predict better outcome and one analyses found it to predict worse outcome.

In summary, only few analyses were conducted on these variables with few significant results. Additionally, results were inconsistent, finding both prediction of better and worse outcome. It is thus difficult to draw conclusion.

3.5. Certainty of evidence

We consider the evidence to be of moderate to high certainty regarding the four predictors, which we found conclusive results for – namely adherence, treatment credibility, working alliance, and baseline scores. While their analyses include a few studies rated to be of high risk of bias, the majority of studies that have found the association between these predictors and treatment outcome have been rated as low risk. For all other variables we consider certainty of evidence to be low due to lack of data, too few studies which have assessed these variables, non-significant findings, and/or data stemming mainly high risk of bias studies.

4. Discussion

A variety of predictors and moderators of treatment outcome in guided IBIs for adults have been assessed so far. In our systematic review, adherence, treatment credibility, working alliance, and baseline scores emerged as the most conclusive predictors/moderators. Small tendencies for comorbid depressive or anxiety symptoms could be noted.

Adherence was the most frequently assessed variable across studies and provided the most conclusive results: Better adherence predicted better outcome in almost all studies. It should be noted, however, that even though adherence and outcome are associated we do not yet understand the mechanisms. Adherence is usually operationalized as a measure of treatment use across treatment length and it might well be that improvement precedes adherence, or that another factor, such as credibility, influences both. A causal relation cannot be derived from our current operationalization and we recommend investigating adherence more thoroughly in future studies.

Furthermore, it is still unclear how to promote adherence in IBI: While it has been suggested that more attractive userfaces, tailored contents, or personalized levels of therapeutic support could improve adherence (e.g. Beatty and Binnion, 2016; Hentati et al., 2021), there is still a lack of research to solidify these suggestions.

The fact that better working alliance predicted better treatment outcome in almost all studies included in our review is not surprising. Working alliance and its association to treatment outcome is one of the most frequently studied variables in psychotherapy research (Flückiger et al., 2018). Associations between working alliance and treatment outcome of IBIs have already been discovered (meta-analyses: Flückiger et al., 2018; Kaiser et al., 2021).

Research indicates that working alliance in IBIs can be established regardless of targeted symptoms/diagnoses (Kaiser et al., 2021), frequency of contact between therapist and patient (Kaiser et al., 2021), timing of contact (synchronous or asynchronous, Wehmann et al., 2020), or mode of contact (e.g. video, voice, or text-based, Kaiser et al., 2021; text-based, van Lotringen et al., 2021; with an avatar—an automated program that simulates human interaction – Heim et al., 2018). It is less clear how working alliance is best established in all these different formats and whether how it can be promoted differs between them. Probst et al. (2019) consult theories of computer-mediated communication (e.g. compensation of nonverbal communication by creating the other person in one's mind or the online disinhibition effect leading to higher levels of openness) to explain alliance development in IBIs. A qualitative analysis of an IBI for adolescents with depression identified three values most present in high-alliance cases: a sense of togetherness, agency, and hope (Mortimer et al., 2022). Furthermore, current research suggests that working alliance in IBIs could potentially be divided in two aspects: alliance with the therapist and alliance with the program (Zalaznik et al., 2021). These two aspects may be distinctively different from each other and their association to treatment outcome differs: Alliance to program was significantly associated with symptom improvement, whereas alliance with therapist was not (Zalaznik et al., 2021). The exact role and influence of these two aspects of working alliance in IBIs, however, still remains unclear. Tremain et al. (2020) hypothesize that alliance may not be directly, but rather indirectly associated with treatment outcome via engagement and adherence. Thus, as with adherence, a causal relationship between working alliance and treatment outcome cannot be derived.

The results of our review also show that higher treatment credibility predicted better outcome. This is in line with a meta-analysis on face-to-face treatment (Constantino et al., 2018). Higher treatment credibility was also associated with increased adherence in IBI (Beatty and Binnion, 2016). Further, Zalaznik et al. (2021) describe that a stronger belief in the program (by our definition treatment credibility) may follow from a stronger relationship between working alliance and symptom improvement. This again highlights that causal relationships cannot be established, and that mediation and moderation studies are needed to shed further light on these associations.

Finally, baseline symptom severity emerged as a strong predictor, which is in accord with a recent component network meta-analysis, in which baseline symptom severity emerged as the strongest prognostic factor of depression outcome in IBI (Furukawa et al., 2021). In our review there seems to be a pattern, in which participants who start IBIs with higher baseline scores continue to have higher scores at posttest/follow-up (worse outcome) but demonstrate more improvement over the course of IBI (better outcome). These results make sense, when considering that those who have initial higher symptoms are simply able to improve more as the range from their pre- to posttreatment scores is larger than for those with lower baseline scores. While this is consistent with the results of other studies – e.g. Bower et al. (2013).

Rozental et al. (2019) found higher baseline severity to be significantly associated with higher odds of non-response in IBIs and Karyotaki et al. (2018) found a moderation effect of baseline depressive severity on remission but could not firmly conclude on a moderation effect on treatment response. One explanation may be regression to the mean. Statistical regression describes the tendency for extreme values to move closer to the mean when measures are repeated over time, that is extreme outcomes are followed by more moderate ones. Regression to the mean likely accounts for some changes attributed to treatment effects, even though it is independent of any intervention and tends to characterize all measures (Finney, 2008; Morton and Torgerson, 2005). We cannot rule out that in some studies we included regression to the mean might also have been mistakenly attributed to the treatment effect.

Nevertheless, it remains a possibility, that highly impaired individuals can improve in IBIs and often do so more than only mildly

affected individuals. Symptom severity should thus not primarily be an exclusion criterion for those prescribing or recommending IBI in clinical practice. At the same time, those who experience the most severe difficulties before treatment may still experience substantial distress after treatment and may need additional support. Blended therapy approaches – combining face-to-face therapy with online modules – are currently under study (e.g. Schaeuffele et al., 2022; Titzler et al., 2019) and may provide a good solution for those individuals experiencing stronger symptoms.

We detected small tendencies for two other variables, although results need to be interpreted cautiously due to inconsistencies, results coming from high risk studies, and limited available data.

Comorbid depressive as well as comorbid anxiety symptoms mostly predicted worse outcome. Comorbidity is common in mental disorders, with almost 50 % of individuals in the European Union having at least two diagnoses (Wittchen and Jacobi, 2011). Tailored and/or transdiagnostic IBIs addressing comorbidity specifically are already available and well-studied, showing a tendency to be more effective than disorder-specific IBIs for some outcomes (e.g. Newby et al., 2016; Păsărelu et al., 2017). In this review, all interventions of the studies reporting on comorbid symptoms as predictors were disorder-specific. It is possible that participants with comorbid symptoms would benefit more from a transdiagnostic approach. Clinical decision makers should thus preferably prescribe a transdiagnostic IBI to a person with comorbid diagnoses.

For the remainder of predictors/moderators, results were mostly non-significant, inconsistent, stemmed from high risk studies, or lacked data to draw conclusions. This highlights that there is currently still a rather large gap in our knowledge regarding predictors of treatment outcome in IBIs.

5. Limitations

Several limitations need to be considered when interpreting the results of this study.

Interrater reliability was low in several domains in the risk of bias rating. However, the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2019) highlights that more emphasis should be laid on resolving disagreements than on reporting Kappa values. We always reached consensus after discussion.

A significant proportion of high-risk studies ($n = 26$) were included in our review. However, this may be over-estimated. We provided an overall bias rating, as it has been suggested as useful (Hayden et al., 2013), however, overall bias assumes that each domain weighs the same in importance, whereas some domains may be more relevant than others, depending on the study and topic of research (Grooten et al., 2019). Our criteria for assessing overall bias were relatively strict with a study only needing one high or three moderate ratings to be considered of high bias and not allowed to have more than one moderate rating to be of low bias. Moreover, lack of information regarding attrition or confounders was often the reason for a high-risk rating in these domains, as we did not include an "unclear" rating, assuming that, if the information was not reported, it was not considered. Finally, most of the included studies were not explicitly designed to analyze predictors/moderators. QUIPS, however, was developed to judge prognostic studies (Gilpin et al., 2017). While other IBI reviews have not used QUIPS or provided overall bias ratings, their bias assessments are mixed, some finding that only few studies meet their criteria (Beatty and Binnion, 2016) and others judging the included studies to be mostly of low bias/of high quality (Ebert et al., 2016; Karyotaki et al., 2015).

Another limitation is the use of vote counting based on direction of effect, which does not permit conclusions regarding the magnitude of effects and study size differences cannot be accounted for (Higgins et al., 2019).

Our findings are also mainly limited to guided IBIs that are delivered via computers. Only a small proportion of the included studies applied interventions via smartphones. We cannot deduce if predictors might affect outcomes differently in smartphone-based interventions.

6. Future research

A core finding of this report is that many predictors have been studied only once. This also applies to predictors that might be relevant across a broader range of disorders and treatments. In fact, most IBIs are based on CBT and its assumed mechanism of change in cognitions and (mostly avoidance) behaviors. It is therefore surprising that there are so few studies including variables such as cognitive flexibility or avoidance as predictors. It is true that instruments which measure, for example, avoidance behavior across disorders are still scarce. However, to enhance the comparability of results, future research should aim at including predictor variables that are relevant for all or at least a subset of disorders (Schaeuffele et al., 2021).

Another major finding of this report is that interpretability of results is aggravated by the use of similar yet slightly different constructs as predictors. For example, we found single studies on constructs such as 'depressive thoughts', 'negative automatic thoughts', 'dysfunctional attitudes', and 'anxiety sensitivity'. While acknowledging differences between these constructs, we would advocate the use of instruments depicting the essence of these constructs. Mechanism research in CBT is affected by the same problem and instruments have been put forward to promote a more general understanding of the impact of CBT interventions (e.g. the Cognitive-Behavioral Therapy Skills Questionnaire; Jacob et al., 2011).

Third, as discussed in the introduction section, most analyzed trials investigate predictors in secondary analyses. This means that these analyses mostly rely on predictors that have been assessed routinely. More thought should go into predictors that are theoretically relevant. To support this and to ensure and keep a high standard quality of research, prognostic study protocols and complete reporting of results are necessary.

7. Conclusion

Our results suggest that participants who adhere better, are convinced of the treatment's credibility, and form a working alliance benefit more from IBIs. Furthermore, results show that highly impaired participants can improve in IBIs, although they may still experience higher symptom levels after treatment. However, overall, results for most predictors/moderators studied so far are still inconclusive. This highlights that it is currently difficult to predict, across diagnoses, who will benefit from guided IBIs for adults. Consequently, deriving clinical decisions about whom to prescribe IBIs from the current literature is not yet straightforward. Additional, rigorous research is needed to identify predictors and moderators based on a sufficient number of studies.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.invent.2023.100635.

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