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How are guide profession and routine care setting related to adherence and symptom change in iCBT for depression? - an explorative log-data analysis

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ABSTRACT

Background: While the antidepressant efficacy of guided digital interventions has been proven in randomized controlled trials, findings from routine care are less clear. Low adherence rates are common and limit the potential effectiveness. Adherence has been linked to sociodemographic variables and the amount of guidance, but the role of the guide's profession and their work setting has not yet been studied for routine care.
Methods: Routinely collected log data from a digital intervention for depressed patients (iFightDepression tool) were analyzed in an exploratory manner. The sample is a convenience sample from routine care, where guidance is provided by general practitioners (GP), certified psychotherapists (PT) or medical doctors specialized in mental health. Log data from 2184 patients were analyzed and five usage parameters were extracted to measure adherence (first-to-last login, time on tool, number of sessions, workshops completed and minimal dose). Multiple logistic regression was used to analyze relations between the guide's profession and clinical context as well as other covariates and adherence and symptom change on a brief depression questionnaire (PHQ-9).
Results: The analyses showed a significant relation of guide profession and adherence. Guidance by PT was associated to the highest adherence scores (reference category). The odds ratios (ORs) of scoring above the median in each usage parameter for patients guided by GPs were 0.50–0.63 (all ps < 0.002) and 0.61–0.80 ($p = .002$–0.197) for MH. Higher age, initial PHQ-9 score and self-reported diagnosis of depression were also significantly associated with higher adherence scores. In a subsample providing enough data on the PHQ-9 ($n = 347$), no association of guide profession with symptom reduction was found. Instead, a greater reduction was observed for patients with a higher baseline PHQ-9 ($\beta = -0.39$, $t(341.75) = -8.814$, $p < .001$) and for those who had achieved minimal dose ($\beta = -2.42$, $t(340.34) = -4.174$, $P < .001$) and those who had achieved minimal dose and scored high on time on tool ($\beta = 0.22$, $t(341.75) = 1.965$, $P = .050$).
Conclusion: Being guided by PT was associated with the highest adherence. The lowest adherence was observed in patients who were guided by GP. While no association of guide profession and symptom reduction was found in a subsample, greater adherence was associated with symptom reduction.

1. Introduction

The antidepressant effect of digital interventions in patients with mild and moderate forms of depression has been shown in a large number of randomized controlled studies (Karyotaki et al., 2021; Wright et al., 2019). Meta-analyses based mainly on studies testing against wait-list controls or treatment as usual report moderate to large effects of digital interventions (Karyotaki et al., 2021). First reviews on trials that compare guided digital interventions to face-to-face (group) therapy found no differences with respect to symptom reduction (Andersson et al., 2016).This is further supported by a large network meta-analysis including data from 15,191 participants, that did not find significant

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differences between different delivery formats of CBT such as guided digital, telephone or in person therapy (Cuijpers et al., 2019).

However, studies trying to translate these effects into routine care yield mixed results that vary widely. While Kivi et al. (2014) and Gilbody et al. (2015) reported no additional benefit of treatment as usual (TAU) plus minimally guided iCBT over TAU alone, Williams and Andrews (2013) reported significant medium to large pre-post effect sizes of a 10 week iCBT intervention prescribed by clinicians, in a quality assurance study that used data routinely collected from patients in routine care. A meta-analysis on trials on iCBT under routine care conditions for depression and anxiety reported a clinically relevant pooled effect size of 1.78 for depression, but again with high heterogeneity (Etzelmueller et al., 2020).This raises questions concerning the conditions responsible for the difference in effectiveness between different studies and routine care settings.

One key feature for the successful (or unsuccessful) use of digital interventions in routine care seems to be adherence to the intervention. This is especially visible in the study of Gilbody et al. (2015) where less than 20% of the participants completed the interventions and around 20% did not start the treatment at all, resulting in no additional benefits for the participants in the intervention group compared to the control condition. Since adherence is a predictor of efficacy (Donkin et al., 2011; Hilvert-Bruce et al., 2012), an understanding of how to best encourage patients to sufficiently use the digital intervention is crucial for a successful implementation into routine care.

Adherence, on the other hand, has been linked to the amount of guidance that users received. While the optimal amount of guidance has not yet been determined, first estimates describe a wide range. A systematic review did not find an association of profession of the guide and outcome (Baumeister et al., 2014). However, these results stem from a study setting and the heterogeneity might be much bigger in routine care where different professions work in different settings and deal with differing time resources allocated to each patient. It is not unlikely that, depending on the setting of data collection (study vs. routine care), as well as on the profession of the guide (e.g. certified psychotherapists vs. general practitioners), the amount and content of guidance will differ and, thus, might have an influence on both adherence and other factors relevant for effectiveness. Furthermore, guidance might also have antidepressant effects via other mechanisms than adherence, such as increased hope induction, activation or commitment, when working through the program. It also seem to be especially important to support patients with higher baseline severity (Karyotaki et al., 2021). To understand these differences and their impact on the use of digital interventions might help to optimize guidance and, thereby, adherence and ultimately antidepressant efficacy.

Besides guidance, other factors have been linked to adherence in the past. Previous research has shown that better adherence to digital interventions was predicted by age, symptom severity and gender, among others, but the presence and direction of these effects varied widely between studies (Batterham et al., 2008; Beatty and Binnion, 2016). For example, in their systematic review of 36 studies, Beatty and Binnion (2016) reported conflicting results concerning the relationship between age and adherence as well as the association of baseline symptom severity and adherence. Results concerning gender seem equally heterogeneous. While being female seems to be a predictor of higher adherence in some studies, other studies included in the reviews did not find this. A large trial on 509 participants published after these meta-analyses reported a connection of older age as well as higher baseline symptomatology to higher adherence scores (Fuhr et al., 2018) and further analyses on potentially relevant predictors of adherence could strengthen the evidence base.

The iFightDepression tool (iFD), a free guided web-based intervention, has been used in routine care in Germany since October 2016 by general practitioners (GP), certified psychotherapists (PT) and medical doctors specialized in mental health (e.g. psychiatrists, MH). The current paper aims to report an explorative analysis on factors connected to adherence in different routine care settings in the German healthcare system. The following research approaches were taken:

1) The relationship between the profession of the guides (GP vs. PT vs. MH) and the adherence of patients using iFD in routine care was explored taking into account other covariates like age, gender, baseline symptom severity and self-reported diagnosed depression.
2) The association of antidepressant effects measured with the PHQ-9 with adherence, guide settings and sociodemographic variables was tested in a subsample.

2. Method

2.1. Data extraction

The current analysis used routinely collected data from the users of a web-based intervention for patients suffering from depression. The sample was a convenience sample from routine care in Germany and was not part of a trial. For the analysis, anonymized data from all accounts of the German version of the iFD tool were used (excluding known test accounts and accounts (not) meeting the inclusion and exclusion criteria). The data were extracted from the system on July 10, 2020.

The protocol for the concomitant evaluation of iFD was reviewed and approved by the ethics committee of the Medical Faculty, University of Leipzig on March 18, 2015.

2.2. In−/exclusion criteria

Only data from accounts fulfilling the following requirements were included in the current analysis. Patients had to be at least 18 years old and were guided by a professional registered in the German healthcare system. Only patients invited by GP, PT or MH were included. All included patients gave informed consent to participate in an ongoing evaluation of the tool during their registration. All patient accounts that were created more than six weeks before data extraction, were included in the analysis so that users had had some time to work with the material.

2.3. Intervention

The iFD tool is a guided web-based intervention incorporating techniques from cognitive behavioral therapy (CBT) that has been described in more detail elsewhere (Oehler et al., 2019). It consists of six core workshops that include psychoeducation and interactive worksheets to support patients to incorporate the techniques they learned into their everyday lives. Each workshop focuses on a specific topic (e.g. activity documentation, sleep and depression, behavioral activation, problem solving and cognitive restructuring). Since iFD is a guided intervention, access for patients can only be gained through an iFD guide. GP, PT or MH working in routine care in Germany can become iFD guides by taking part in an online training and can then invite patients to use the tool free of charge. Access is not limited, so each patient who has received access can re-read all materials at any time and worksheets can be filled in as often and as long as needed, even if the initial treatment by the GP, PT or MH has been paused or already been completed.

2.4. Guidance

The current analysis focused on the effects of guide profession and clinical context on usage and effectiveness of iFD in routine care. It is important to highlight that guide profession as visible here does not only include different educational backgrounds of the guides, but also the settings in which these professions usually work. All described settings are part of routine care in Germany that is covered by health insurance companies and includes no additional cost for the patients. Patients can

choose where they seek treatment (taking into account local capacities). The classification of the guides into the different professional groups is based on self-report data. During the registration as an iFightDepression Guide, the membership of an occupational group is queried. In the following, we seek to describe the typical setting and working mode for each profession.

2.4.1. Medical doctor: general practitioner (GP)

GP are usually the first point of contact for medical questions and, thus, serve as guides in the health care system. Waiting times are moderate and visits can occur without appointments in case of acute symptoms. They know the personal situation of patients and have their trust. Therefore, general practitioners can sometimes have good access to patients with psychological problems or conflicts and often deliver psychological basic care. Since general practitioners see a large number of patients each day, their schedules usually only allow for short visits to check in on the patients. They may prescribe medication and issue certificates of incapacity to work.

2.4.2. Certified psychotherapist (PT)

PT are required to hold a master's degree or diploma in psychology with additional psychotherapeutic education training lasting a minimum of three years. It includes around 600 h of theoretical education and 2400 h of practical training. The work of this professional group includes identification, healing or alleviation of disorders for which psychotherapy is indicated. Psychotherapy can be based on different methods, such as behavioral therapy or psychoanalysis. The beginning of psychotherapeutic treatment can be delayed by waiting times up to several months. It usually takes place in weekly or biweekly sessions of 50 min. PT are not authorized to prescribe medication or give certificates of incapacity to work.

Medical doctor: specialized in mental health, e.g. “psychiatry and psychotherapy” or “psychosomatic medicine and psychotherapy” (MH) MH are physicians, e.g. psychiatrists or specialists for psychosomatics. Their field of expertise can include psychotherapeutic treatment approaches and recommendations. The MH may prescribe medication and issue certificates of incapacity to work. Appointments with MH usually take place in larger intervals and are usually shorter than psychotherapy sessions. Initial visits can be associated with waiting times up to several months. While most MHs prescribe medication, some work as psychotherapists only. The training in psychotherapeutic techniques encompasses around 120 h of theory and 220 h of practical training. In this study, this category mainly consists of psychiatrists.

2.5. Measures

Since the data stem from a convenience sample of routine care users of iFD, only a small number of measures were collected. During the registration process, patients completed a questionnaire that provided some sociodemographic information (age, gender, current and past treatment, self-reported presence of depression diagnosis made by a healthcare professional). At the start of the intervention as well as every seven days, users were prompted to fill in the PHQ-9 (Löwe et al., 2004; Martin et al., 2006), a brief measure to assess symptoms of depression. Between the prompts, patients were able to fill in the PHQ-9 at any time.

For the investigation of adherence, anonymized log data of the iFD platform were used. These included timestamped logs of all activities within the iFD tool undertaken by the patients. Adherence was operationalized by several parameters of usage that were generated from the log data for each patient:

2.5.1. First-to-last login

This parameter gives the time span in days between the first and the last login to the iFD tool for each patient.

2.5.2. Time on tool

As an estimator of the time users spent engaged with the iFD tool, the sum of minutes spent on the tool was calculated. Patients on the iFD tool are automatically logged off after 30 min of inactivity. Therefore, if the time span between two logged activities was greater than 30 min, it was not included in the time on tool parameter.

2.5.3. Number of sessions

This parameter counts the number of sessions patients have engaged online with the iFD tool. A new session was counted every time two activities were more than 30 min apart.

2.5.4. Workshops completed

Completion of a workshop was defined as having accessed at least 70% of the material for each workshop. This parameter gives the sum of completed workshops (possible: zero to nine, six core workshops + three additional workshops).

2.5.5. Minimal dose

Users who completed at least two core workshops within six weeks after starting the iFD tool were regarded as having received a minimal dose that might have been effective (dichotomous variable). This definition was chosen based on the findings that even the usage of single components of CBT can lead to a reduction in symptoms of depression (Bell and D'Zurilla, 2009; Cuijpers et al., 2007, 2018).

2.6. Statistical analysis

Baseline differences in sociodemographic variables were tested for statistical significance using Chi-squared tests for categorical variables, Analysis of Variance (ANOVA) for normally distributed numeric data and Kruskal-Wallis rank sum tests in case of non-normally distributed data (extension of Wilcoxon test for more than two groups, nonparametric since the user data were not normally distributed, McKight and Najab, 2010). All p-values of the comparisons were corrected for multiple testing using an FDR correction (False Discovery Rate, Jafari and Ansari-Pour, 2019).

To assess the first question and compare usage parameters between different guide settings, pairwise Wilcoxon tests with Benjamini-Hochberg correction were calculated with the usage parameters as dependent variables to compare the groups among themselves.

To test if potential differences between guide settings remained significant after taking into account sociodemographic variables as covariates, generalized linear models with a log link function were calculated. This decision was made because usage parameters entered as dependent variables were extremely right-skewed and parametric models either did not yield an acceptable fit or would have made the transformation of the data necessary. In order to avoid the latter and to thereby receive model parameters that can be interpreted and yield meaningful conclusions, a median-split was performed for the dependent variables to dichotomize them into equal groups.

The following covariates were entered into the model and then excluded in a stepwise process: guide setting (GP, PT or MH), gender (female vs. male), age (years), currently taking antidepressants (yes vs. no), had psychotherapy in the past (yes vs. no), took antidepressants in the past (yes vs. no), diagnosed depression (yes vs. no), baseline PHQ and the interaction of diagnosed depression and baseline PHQ. Current psychotherapy (yes vs. no) was excluded as a predictor, since the risk of collinearity with the variable “guide setting” was very high. A covariate was excluded if its model parameter was not statistically significant and its exclusion did not lower the model fit (AIC = Aikaike Information Criterion). A nested-random intercept was added for guide ID to account for shared variance that was caused by several patients that were guided by the same healthcare practitioner. The reference category for guide setting was set to be PT. For the reporting of the final model, the model estimates were transformed to odds ratios (OR) for better interpretation.

2.6.1. PHQ analysis

To get an estimate for real world effectiveness, the routinely collected PHQ-9 data were used. As an estimate of symptom change, the mean difference of PHQ-9 values after six to nine weeks and PHQ-9 at registration was calculated for all patients with values available in the category after six to nine weeks. This time span was used based on our experience from a different study, during which the effects of the intervention were found to be largest after six or more weeks (Oehler et al., 2020). If patients had completed more than one PHQ-9 after six to nine weeks past registration, a mean value was used. Since this difference score fulfilled the criteria of normal distribution, it was used as dependent variable for a linear mixed effects model with guide setting as predictor and a random intercept for guide ID. To further explore a possible connection, all usage parameters and sociodemographic variables mentioned above were entered as predictors. An interaction term for guide setting and the minimal dose indicator variable was added for exploratory purposes. Variables for the final model were selected as described above. This analysis was designed to test whether changes in symptoms of depression were dependent on the guide's profession, the usage of iFD or an interaction of both.

All statistical analyses were performed with $\alpha = 0.05$ and using the software R (R Core Team, 2013). For the mixed model calculations, the packages lme4 and lmerTest were used to estimate the model coefficients and corresponding p-values. Models were fitted using restricted maximum likelihood (REML) estimation and the Kenward-Roger approximation to calculate the denominator degrees of freedom for the *t*-statistics as this has been reported to be the most robust way to determine statistical significance of parameters in mixed models (Luke, 2017).

3. Results

3.1. Sample

Inclusion criteria were met by 2184 of the 2875 patients, who had received access to the iFD tool by June 29, 2020. Of these, 1306 (59.8%) reported to be female, and the mean age was 38.69 years (SD = 13.57, range: 18–79).

Patients included in the analyses were invited by 440 guides, each of whom included a mean of 5.08 patients (median = 3, SD = 8.48). As expected, some of the baseline variables were not equally distributed across guide profession since treatment variables correlate with the profession of the guide who is also the treating healthcare professional (for details please see Table 1).

3.2. Usage variables by guide profession with covariates

Overall, the distribution of usage parameters was strongly right-skewed. In Table 2, the key variables are listed, split up for the guiding professional, and results on significant differences are reported.

Table 3 shows the results of the logistic regression analyses with usage parameters as dependent variables. The model coefficients are given as ORs, with values greater than one indicating that higher values of the dependent variables are associated with the predictor, ORs smaller than one indicate a negative association of dependent variable and predictor. Patients guided by a GP were more likely to score below the median on all usage parameters compared to those guided by a PT. Patients with diagnosed depression and higher baseline PHQ-9 values had a higher chance to reach a score above the median. Being older was also associated with higher usage parameters and male gender was connected to a longer interval between first and last login but lower rates of completed workshops and a lower chance to achieve minimal dose.

Table 1
Baseline characteristics by guide profession.

Variables	Total (n = 2184)	GP (n = 838)	PT (n = 834)	MH (n = 512)	p (adjusted p) with FDR method
Female (%)	1306 (59.8%)	512 (61.1%)	492 (59.0%)	302 (59.0%)	0.620 (0.620)
Age in years (SD)	38.69 (13.6)	38.90 (13.5)	37.86 (13.51)	39.68 (13.74)	0.055 (0.065)
Diagnosis MD (% yes)	1559 (71.4%)	576 (68.7%)	641 (76.9%)	346 (67.6%)	<0.001 (0.001)
Baseline PHQ-9 (SD)	13.98 (5.57)	14.50 (5.35)	13.20 (5.61)	14.52 (5.69)	<0.001 (<0.001)
Currently receiving PsyT (% yes)	1025 (46.9%)	197 (23.5%)	637 (76.4%)	218 (42.6%)	<0.001 (<0.001)
Currently receiving AD (% yes)	853 (39.1%)	322 (38.4%)	296 (35.5%)	235 (45.9%)	<0.001 (0.001)
PsyT in the past (% yes)	627 (28.7%)	203 (24.2%)	260 (31.2%)	164 (32.0%)	0.001 (0.002)
AD in the past (% yes)	526 (24.1%)	179 (21.4%)	212 (25.4%)	135 (26.4%)	0.057 (0.065)

GP: medical doctor - general practitioner, PT: licensed psychotherapist, MH: medical doctor - specialized in mental health, FDR: False Discovery Rate, SD: standard deviation, MD: Major Depression, AD: antidepressants, PsyT: psychotherapy, AD: antidepressants.

Table 2
Pairwise Wilcoxon comparisons for usage parameters by guide profession.

Guide profession	First-to-last login (in days)	Time on tool (in hours)	Number of sessions	Workshops completed	Minimal dose
GP	54.33 (SD = 119.77)	1:35 (SD = 7:38)	8.01 (SD = 40.88)	1.25 (SD = 1.53)	227 (27.1%)
PT	63.04 (SD = 119.77)	1:58 (SD = 3:32)	10.34 (SD = 18.39)	1.72 (SD = 1.81)	305 (36.6%)
MH	65.28 (SD = 127.59)	1:27 (SD = 3:17)	7.31 (SD = 14.63)	1.28 (SD = 1.65)	123 (24.0%)
GP vs. PT	Z = 4.826, p < .001***	Z = 4.921, p < .001***	Z = 5.28, p < .001***	Z = 5.412, p < .001***	Z = 4.161, p < .001***
GP vs. MH	Z = 2.206, p = .041*	Z = 1.534, p = .12	Z = 0.620, p = .54	Z = 0.420, p = .67	Z = 1.246, p = .21
MH vs. PT	Z = 1.776, p = .076	Z = 5.520, p < .001***	Z = 5.086, p < .001***	Z = 4.940, p < .001***	Z = 4.797, p < .001***

GP: medical doctor - general practitioner, PT: licensed psychotherapist, MH: medical doctor – specialized in mental health, SD: standard deviation.

3.3. Effectiveness by guide profession

At least one entry in the PHQ-9 after six to nine weeks was available for 347 patients of which 224 (64.55%) fulfilled the criteria for minimal dose (see also Fig. 1). An initial analysis without covariates did not show a significant association of symptom change and guide profession (MH vs. PT ($\beta = -0.7996$, $t(344) = -8.814$, $p = .260$), GP vs.PT ($\beta = -0.2491$, $t(344) = -0.417$, $p = .677$).

During the variable selection process for the final model, most usage parameters and sociodemographic variables were excluded. The sum of all completed workshops and the minimal dose variable were highly correlated, therefore only minimal dose was kept in the model to avoid collinearity. The same was true for diagnosis and baseline PHQ. Yet,

Table 3
Results of the logistic regression analyses with usage parameters as dependent variables.

	First- to-last login (OR, Z, P)	Time on tool (OR, Z, P)	Number of sessions (OR, Z, P)	Workshops completed (OR, Z, P)	Minimal dose (OR, Z, P)
Intercept	0.474 (Z = −2.263, p = .024)	0.359 (Z = −3.063, p = .002)	0.310 (Z = −3.452, p < .001)	0.714(Z = −1.576, p = .115)	0.510 (Z = −3.091, p = .002)
Group [GP]	0.623 (Z = −3.526, p < .001)	0.589 (Z = −3.929, p < .001)	0.502 (Z = −5.186, p < .001)	0.579 (Z = −4.407, p < .001)	0.625 (Z = −3.832, p = .001)
Group [MH]	0.802 (Z = −1.291, p = .197)	0.637 (Z = −2.645, p = .008)	0.642 (Z = −2.624, p = .009)	0.693 (Z = −2.350, p = .019)	0.611 (Z = −3.162, p = .002)
Diagnose [yes]	2.042 (Z = 2.188, p = .029)	2.438 (Z = 2.701, p = .007)	2.441 (Z = 2.659, p = .008)	–	–
Initial PHQ	1.047 (Z = 2.040, p = .041)	1.084 (Z = 3.468, p < .001)	1.085 (Z = 3.497, p < .001)	1.010 (Z = 1.148, p = .251)	1.014 (Z = 1.486, p = .137)
Diagnose x initial PHQ*	0.956 (Z = −1.848, p = .065)	0.931 (Z = -2.809, p = .005)	0.933 (Z = −2.769), p = .006)	–	–
Gender [male]	1.179 (Z = 1.604, p = .109)	–	–	0.841 (Z = −1.705, p = .089)	0.833 (Z = −1.752, p = .080)
Age	1.010 (Z = 2.589, p = .010)	1.020 (Z = 5.046, p < .001)	1.014 (Z = 3.551, p < .001)	1.007 (Z = 1.755, p = .079)	1.007 (Z = 1.769, p = .077)
AIC	2468.5	2383.9	2441.7	2439.7	2340.8
R^2m (variance explained through fixed effects)	0.023	0.042	0.041	0.021	0.020
R^2c (variance explained through fixed and random effects)	0.083	0.095	0.096	0.054	0.044

GP: medical doctor - general practitioner, MH: medical doctor – specialized in mental health, OR: Odds Ratio; AIC: Aikaike Information Criterion, *interaction terms are reported in a ratio of Odds Ratios, in this case, the significant interactions indicate that patients with a self-reported diagnosis and higher PHQ-9 values were more likely to achieve higher usage in the respective variable.

while diagnosis had great predictive value for user behavior, the change in PHQ-9 was more accurately predicted by baseline PHQ.

The final model only included baseline PHQ (β = −0. 39,478, t(341.75) = −8.814, P < .001), time on tool (β = −0.16643, t(341.76) = −1.541, P = .124), and minimal dose (β = −2.41929, t(340.34) = −4.174, P < .001) and the interaction of time on tool and minimal dose (β = 0.21548, t(341.75) = 1.965, P = .050) as significant fixed effects. This means that in the current analysis greater reduction in symptoms of depression was associated with a higher baseline PHQ, longer time on tool and achieving minimal dose. The significant interaction term indicates that the greatest symptom reduction was reported by patients who achieved minimal dose and spent more time on the iFD tool (for visualization, see Fig. 2). Both the guidance variable and its interaction with minimal dose were not significant and therefore excluded from the model.

The final model yielded a conditional R^2 of 0.251 and a marginal R^2 of 0.217, indicating that 25.1% of the variance in the dependent variable was described by the model and 21.7% of variance can be explained by the fixed effects alone.

4. Discussion

The current log data analysis explored the association of guide profession and the setting of care as well as other sociodemographic variables to adherence. In the current data set, differences in adherence to iCBT for depression were connected to the guide's profession. Patients who were guided by PT also spent significantly more time logged into the intervention (1:58 h vs. 1:35 h and 1:27 h) during more sessions (10 sessions vs. 8 and 7), completed more workshops (1.72 vs. 1.25 and 1.28) and had a higher chance of receiving a minimal dose of the treatment (36.6% vs 27.1% and 24%) compared to both other groups (guided by GP or MH respectively). While guidance by MH was associated to the longest mean time span between first and last login (65 days vs. 63 for PT and 54 for GP), other adherence variables did not differ statistically significantly between MHs and GPs.. This might be due to the typically longer intervals between appointments at MH compared to the other professions, especially PT. PT have a background in psychotherapy and can usually offer high frequency appointments with more time spent with the patients. Therefore, patients undergoing psychotherapy communicate very frequently with their guides and reminders of iFD are likely to occur at greater intervals compared to the other professions, leading to greater adherence. On the other hand, patient preference might play a role as well. If patients undertake psychotherapy, their motivation to work on their own behavior might be greater compared to the other groups. In contrast, patients guided by GP or MH might have benefited more from pharmacologic treatment of their depression than from psychosocial interventions. But, based on the current data, these interpretations are hypothetical.

Further comment is required about the overall low adherence to the intervention. Only a third to a quarter of the participant achieved minimal dose. This is a known problem of interventions and specifically visible when interventions are implemented in routine care outside of the scope of controlled trials (Baumel et al., 2019; Gilbody et al., 2015).

The differences in adherence related to guide profession remained significant when sociodemographic variables, that were suspected to have an influence on user behavior, were included in the logistic regression model. As has been reported repeatedly, the baseline severity was positively associated to higher adherence for three out of five usage parameters in the current analysis and interacted significantly with self-reported diagnose of depression. That means, higher adherence was found for patients who reported both a higher baseline severity and a diagnosis. It is noteworthy that only two-thirds of patients reported having been diagnosed with depression despite being in treatment, and it is both possible, that diagnoses are missing because of lacking assessment by the healthcare professional or that patients did not report their diagnosis for some reason. The additional explanatory value of diagnosed depression suggests, that it is not only a proxy for symptom severity, but might also be connected to a better understanding or acceptance of one's depression or to a higher perceived need for treatment. On the other hand, patients who did not report a diagnosis of depression might not have felt understood or addressed appropriately by the intervention. “Feeling not taken seriously” is a known unwanted effect of digital interventions (Görges et al., 2018; Oehler et al., 2021) that might emerge especially if there is no perceived correspondence between the problem that the intervention addresses and one's own diagnosis.

In the current data set, there was also a significant association of age and all usage parameters. Older patients were likely to spend more time logged into the tool and to do so during more sessions and over a longer period of time. They completed more workshops and had a higher chance to achieve minimal dose. This is in line with the results of another large RCT (Fuhr et al., 2018). While results on age as a predictor for adherence were mixed in a systematic review (Beatty and Binnion, 2016), e.g. for a large sample of Australian community users, the

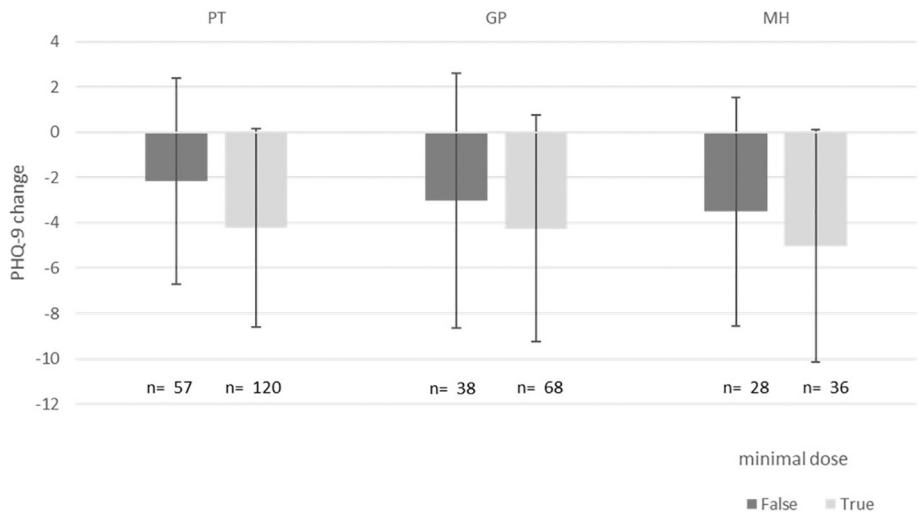

Fig. 1. Mean change in PHQ-9 by minimal dose and guide profession without correction for differences in covariates
PT: licensed psychotherapist, GP: medical doctors - general practitioner, MH: medical doctor – specialized in mental health, PHQ: Patient health questionnaire.

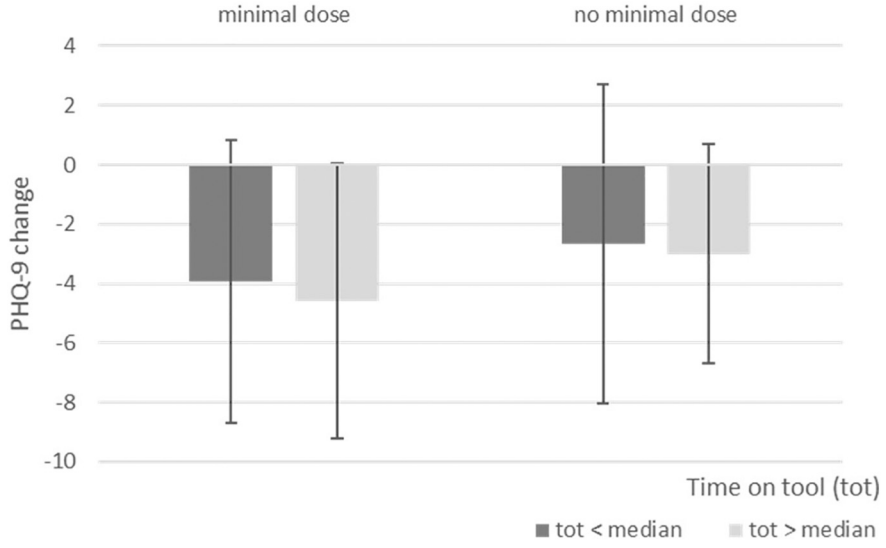

Fig. 2. Mean change in PHQ-9 by minimal dose and time on tool
PHQ: Patient health questionnaire.

opposite relationship was shown with younger users engaging more with the digital intervention (Batterham et al., 2008). The current study cannot inform on the reasons why this difference arose, but one possibility is that the intervention design appealed to different age groups or guides anticipated older patients to need more help and therefore offered more support in the current setting.

Concerning our second analysis approach, the current analysis on subgroups of participants providing PHQ-9 data after six to nine weeks, did not find a significant connection of guide profession to symptom reduction. The guidance variable could even be excluded from the model with symptom change as dependent variable. This is in accordance with earlier results, where no connection was found between the guide's profession and effectiveness (Baumeister et al., 2014). On the other hand, adherence was found to be connected to the effectiveness of digital interventions (Donkin et al., 2011) which could be replicated in the current paper.

The significant main effect of baseline PHQ in the prediction of symptom change indicates that a higher initial symptom score was associated with larger symptom reduction over time. This has been observed in several studies (Bower et al., 2013; Karyotaki et al., 2021) and can probably be at least partially explained by regression to the mean.

The statistically significant main effect of minimal dose could indicate that, in order to be effective, the intervention has to be used. Patients who completed at least two workshops during their first six weeks reported a greater reduction in symptoms of depression compared to those who did not complete workshops, but still logged into the intervention. The interaction with time on tool further underlines the effect, showing that patients with both more time on tool and at least two completed workshops reported the largest change in the PHQ-9. But, since causality cannot be inferred from this design, it is also possible that patients who experienced greater symptom reductions then showed grater adherence to the intervention.

Given the fact that PT guidance is associated with higher adherence and higher adherence in turn is linked to higher rates of symptom improvement, one might expect a direct link between PT guidance and PHQ-9 scores. However, no evidence could be found in the data supporting this assumption. In the subsample with PHQ-9 data available,

guide profession was not significantly associated with changes in PHQ-9 scores even when no other usage parameters were entered into the model. This apparent contradiction could have been caused by the reduced sample that was available for the PHQ-9 calculation. Only patients who logged into the iFD tool at least once after six to nine weeks and filled in the mood questionnaire were eligible for this analysis, reducing the variance in adherence. Proportionately, most patients in this subgroup were guided by PTs (see Fig. 1). Since the sample selection is confounded with the guides' profession, it is difficult to draw valid conclusions on the role of guide profession and future research might shed more light onto this connection. However, a large study on patients with mild to moderate symptoms of depression that compared automated feedback with individualized email-guidance by psychologists found a similar pattern where differences in guidance were not predictive of symptom change, but individualized feedback was associated with higher adherence (Zagorscak et al., 2018).

4.1. Limitations

As a convenience sample was used, there was no control condition available, the assignment to the different guide settings was not randomized and only limited knowledge on sociodemographics and accompanying treatment was available. For example, the level of education would have been a valuable predictor to test in a primary care sample, since study samples are usually not representative for all users and a lower level of education might be connected to a higher risk of experiencing negative effects (Ebert et al., 2016). Furthermore, the amount and quality of guidance could not be measured in this setting. It is quite possible, that the guidance varied widely between different guides. Our assumptions about differences between guide professions are based on knowledge of the German healthcare system and could not be assessed within this study.

A possible confounder in the current analysis is the treatment provided by the guide besides iFD. While PT will probably also provide psychotherapy and have regular contact with their patients, GP might provide guidance for iFD but usually do not have the capacity to stay in close contact with the patient and to support their learning of CBT skills. On the other hand, GP and MH can prescribe medication, which cannot be done by PT. Therefore, no direct prediction of efficacy by guide profession was reported or should be inferred from these data.

Another limitation concerning the PHQ-9 results is that, only a small subsample provided data to be included in this analysis and that adherence is connected to the availability of data. If users did not log into the intervention any more (= lower adherence), no data on symptom change were collected. This again limits the conclusions that can be drawn from the PHQ-9 analysis and prohibits the calculation of long-term effects.

Finally, the definition for “minimal dose” is based on experience and not on published empirical analyses since, to our knowledge, there is no known cut-off for how much of an intervention needs to be used to potentially alleviate symptoms of depression.

4.2. Conclusion

Although a well-designed intervention that is easy to use and incorporates interactive and engaging features is important for adequate adherence (Kelders et al., 2012), the current explorative analysis support the conclusion, that guidance for digital interventions seems necessary to make them effective in routine care. Greater adherence was found for patients that were guided by PTs, of higher age, reported to be diagnosed with depression and had more symptoms of depression at baseline. Greater adherence is in turn associated with larger symptom reduction. Therefore, it is plausible that healthcare systems will only fully benefit from digital interventions when they support guides, e.g. by providing sufficient time resources to support patients in online interventions. Interventions should be developed to also appeal to younger patients and might need to incorporate further measures to enhance adherence by this group.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

The iFD tool was developed by the European Alliance against Depression (EAAD), of which UH is chairman of the board. In Germany, iFD is operated, continuously developed and evaluated by the German Depression Foundation, a member organization of the EAAD. The German Depression Foundation is an independent non-profit foundation under civil law, financed primarily by donations, endowments, grants and third-party funding for projects and research. It also receives income from its business operations, but works independently of the pharmaceutical industry. CRK, FG, KS and CO work or have worked for the German Depression Foundation, implementing the iFightDepression tool in Germany. PD has worked for the EAAD, which is a registered non-profit association based in Germany, primarily funded by research grants, membership contributions and donations. CRK received lecture honoraria by Servier and is member of an advisory board for Recordati. Within the last two years, UH has been a member of the Advisory Board for Janssen and a speaker for Servier and Medice.

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