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**A systematic review of digital and face-to-face cognitive  
behavioral therapy for depression**

**Ein systematischer Review der digitalen und Face-to-Face  
kognitiven Verhaltenstherapie bei Depressionen**

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# Table of Content

<b>GLOSSARY</b>	<b>7</b>
<b>1. SUMMARY</b>	<b>8</b>
1.1. Summary in English	8
1.2. Zusammenfassung auf Deutsch	9
<b>2. INTRODUCTION</b>	<b>11</b>
2.1. Depression	12
2.2. CBT	13
2.2.1. Barriers to therapy	14
2.3. Digital CBT for depression	15
2.3.1. Examples	16
2.3.2. Effectiveness of digital CBT	17
2.4. Comparing face-to-face and digital CBT for depression	18
2.5. Aims	19
<b>3. PUBLICATION</b>	<b>20</b>
<b>4. DISCUSSION</b>	<b>29</b>
4.1. Clinical outcome	29
4.2. Moderator analysis	30
4.3. Challenges and opportunities of digital CBT	32
4.4. Limitations	33
4.5. Conclusion	34
<b>5. REFERENCES</b>	<b>35</b>

## Glossary

ADM	Antidepressant Medication
BDI	Beck Depression Inventory
CBT	Cognitive Behavioral Therapy
GP	General Practitioner
HDRS	Hamilton Depression Rating Score
PHQ-9	Patient Health Questionnaire-9
RCT	Randomized Controlled Trial
SSRI	Selective Serotonin Reuptake Inhibitor
TAU	Treatment As Usual
TCA	Tricyclic Antidepressants



## 1. Summary

### 1.1. Summary in English

Depression is a common mental disorder with a great impact on individual and societal level. Among the psychotherapeutic options, cognitive behavioral therapy (CBT) has the strongest evidence. However, access to traditional face-to-face CBT for depressed people is difficult due to barriers such as limited health service resources. Digital interventions are therefore gaining relevance and have proven to be effective in the treatment of depression. But so far, research on the equivalence of digital and face-to-face CBT is limited and shows weaknesses.

The present review compared the effectiveness of both approaches for the treatment of depressive disorders with regard to depressive and comorbid anxiety symptoms as well as psychosocial functioning. For this purpose, a systematic literature search for randomized controlled trials was conducted. The mean difference standardized by raw scores (SMCR) from pre- to post-intervention was used in random-effects meta-analytic models.

In total, 106 studies on 161 samples with 11854 participants (face-to-face CBT: 81 samples with 3257 participants, digital CBT: 80 samples with 8697 participants) were included in this review.

On average, treatment in the digital studies was shorter and included more participants. These showed significantly lower depression scores at baseline, took antidepressants more often and discontinued treatment more often than participants in the face-to-face studies.

For depression severity, face-to-face CBT showed superior effectiveness compared to digital CBT ( $p < 0.001$ , face-to-face CBT: SMCR = 1.97, 95%-CI: 1.74–2.13, digital CBT: SMCR = 1.20, 95%-CI: 1.08–1.32). Similarly, psychosocial functioning improved significantly better in face-to-face studies ( $p < 0.001$ , face-to-face CBT: SMCR = 1.29, 95%-CI: 0.87–1.71, digital CBT: SMCR = 0.49, 95%-CI: 0.39–0.58). No significant differences in efficacy were found for comorbid anxiety.

We applied propensity score matching and moderator analysis to control for differences between face-to-face and digital CBT. The results suggested that clinical effectiveness was more comparable between the two approaches when differences in patient and study characteristics were taken into account. Relevant variables that moderated the effects were baseline depression severity, treatment adherence, number of therapy sessions and intensity of treatment as well as human support in digital CBT.

Overall, digital approaches showed more comparable effectiveness to face-to-face CBT than initially assumed. Based on these findings, further research efforts are needed to identify and investigate the role of moderators in the future personalisation of digital treatment.

## 1.2. Zusammenfassung auf Deutsch

Depressionen sind eine häufige psychische Störung mit schwerwiegenden Auswirkungen auf den Einzelnen und die Gesellschaft. Den höchsten Evidenzgrad unter den psychotherapeutischen Optionen hat die kognitive Verhaltenstherapie (KVT). In der Praxis ist jedoch der Zugang zu traditioneller KVT von Angesicht zu Angesicht, im Folgenden Face-to-Face genannt, oft schwierig, z.B. aufgrund mangelnder Ressourcen im Gesundheitssystem. Digitale Interventionen gewinnen daher zunehmend an Bedeutung und stellen eine wirksame Alternative zur Behandlung von Depressionen dar. Bislang gibt es jedoch nur begrenzte Belege für die klinische Gleichwertigkeit von digitaler und Face-to-Face KVT.

In der vorliegenden Metaanalyse wurde die Wirksamkeit beider Ansätze für die Behandlung der Depression im Hinblick auf depressive und komorbide Angstsymptome sowie auf die psychosoziale Funktionsfähigkeit verglichen. Zu diesem Zweck wurde eine systematische Literaturrecherche nach randomisierten kontrollierten Studien durchgeführt. In den meta-analytischen Modellen wurde die durch Rohwerte standardisierte mittlere Differenz (SMCR) von vor und nach der Intervention verwendet. Um potenzielle Verzerrungen durch Störfaktoren zu berücksichtigen, wurden im Rahmen eines Propensity-Score-Matchings möglichst ähnliche Studien miteinander verglichen. Zudem wurde eine Moderatorenanalyse durchgeführt, um den Einfluss von Patienten- und Studienvariablen auf die klinische Wirksamkeit zu untersuchen.

Es wurden insgesamt 106 Studien an 161 Stichproben mit 11854 Teilnehmern eingeschlossen (Face-to-Face KVT: 81 Stichproben mit 3257 Teilnehmern, digitale KVT: 80 Stichproben mit 8697 Teilnehmern). Die digitalen Studien wiesen im Schnitt eine kürzere Behandlungsdauer auf und schlossen mehr Teilnehmer ein. Im Vergleich zu den Teilnehmern der Face-to-Face Studien wiesen die der digitalen Studien bei Studienbeginn eine leichtere Depression auf, nahmen häufiger Antidepressiva ein und brachen die Behandlung häufiger ab.

Die Face-to-Face Studien zeigten eine signifikant höhere Reduktion der depressiven Symptome als die digitalen Studien ( $p < 0,001$ , Face-to-Face KVT: SMCR = 1,97, 95%-KI: 1,74-2,13, digitale KVT: SMCR = 1,20, 95%-KI: 1,08-1,32). Auch hinsichtlich der Verbesserung der psychosozialen Funktionsfähigkeit wiesen die Face-to-Face Studien eine Überlegenheit auf ( $p < 0,001$ , Face-to-Face KVT: SMCR = 1,29, 95%-KI: 0,87-1,71, digitale

KVT: SMCR = 0,49, 95%-KI: 0,39-0,58). Lediglich für die komorbiden Angstsymptome wurden keine signifikanten Unterschiede in der Wirksamkeit festgestellt.

Zusätzliche Analysen deuteten darauf hin, dass die klinische Wirksamkeit zwischen den beiden Ansätzen vergleichbarer war, wenn Unterschiede bei den Patienten- und Studienmerkmalen berücksichtigt wurden. Relevante Faktoren, die die Effekte moderierten, waren der Ausgangsschweregrad der Depression, die Therapietreue, die Anzahl der Therapiesitzungen und die Behandlungsintensität sowie die Begleitung bei der digitalen KVT.

Insgesamt zeigten beide Ansätze eine ähnlichere Wirksamkeit als zunächst angenommen. Auf der Grundlage dieser Ergebnisse bedarf es weiterer Forschungsanstrengungen, um die Rolle der Moderatoren für die künftige Personalisierung der digitalen Behandlung zu untersuchen.

## 2. Introduction

Major depression is a leading global mental health issue affecting individual's quality of life and belongs to the major contributors to disability worldwide<sup>1</sup>. Considering the impact, the demand for easily accessible and efficient treatment is high. Although there is a recent increase in the promotion of mental health awareness, most of the people affected with major depression are not seeking or receiving therapy<sup>2,3</sup>. Pharmacotherapy and psychotherapy are established treatments for depression and their effectiveness has been confirmed in numerous research studies so far, with cognitive behavioral therapy (CBT) being the most evidence based form of psychotherapy<sup>4-7</sup>. CBT stands for a set of interventions involving cognitive, behavioral and emotion-centered approaches aiming to detect maladaptive cognitive and behavioral patterns and replace them with more adaptive ones<sup>8,9</sup>. However, limited resources of health care services and long waiting lists, financial barriers as well as difficult access to psychotherapy for individuals from rural areas are some of the common obstacles to enter psychotherapeutic treatment. Moreover, patients' concern about stigma and lack of motivation lead to undertreatment<sup>2,10,11</sup>. Due to the COVID-19 pandemic, there are further challenges to face<sup>12,13</sup>. Digital therapies can contribute to fill the demand-supply gap in the treatment of depressive disorders, help to decrease stigma and boost patients' motivation.

Digital interventions based on CBT have proven to be effective for the treatment of depressive disorders<sup>14,15</sup>. It is suggested that guided as well as unguided digital interventions outperform the control conditions which usually include waiting list participants or patients that receive treatment as usual such as pharmacotherapy, different face-to-face therapeutic approaches or a combination of both in a non-experimental setting<sup>14-18</sup>. However, guided digital treatments involving human support show a superiority in reducing symptom severity compared to unguided ones<sup>14,15,19</sup>.

Given these promising results, the question evolves whether digital interventions are as effective as common face-to-face CBT in ameliorating depressive symptoms and comorbid anxiety. Majority of meta-analyses and reviews have mostly dealt with effectiveness of different digital CBT formats<sup>14-16,20,21</sup>. Those that directly compared face-to-face and digital CBT are scarce, include few studies<sup>22,23</sup> and include other mental disorders than depression<sup>24-27</sup>. However, all studies show equal effectiveness between face-to-face and guided digital formats in reducing depressive symptom severity<sup>22,23,25-27</sup>.

## 2.1. Depression

The risk of developing a depressive disease in the course of life is 16-20%<sup>28,29</sup>. Globally, depression is thus one of the most common and at the same time one of the most underestimated diseases<sup>30</sup>. The burden of disease on an individual and societal level is high, with depression being one of the leading causes of disability worldwide<sup>1,31</sup>.

There is big interindividual variability in the disease course. Typically, a depressive disorder is characterized by temporally limited episodes, that can remit completely or incompletely with residual symptoms. A course of subsyndromal symptoms longer than two years is called dysthymia, whereas a depressive episode on top of a dysthymic phase is called „double depression“. A more chronic course, the so-called „persistent depressive disorder“, is characterized by a depressive episode which lasts longer than two years<sup>32</sup>.

About one fifth of the patients affected develop a bipolar depressive disease with hypomanic, manic or mixed episodes<sup>33</sup>. In this thesis, however, the focus will be on unipolar depression.

Main symptoms of a depressive disorder according to ICD-10 are a depressed mood, loss of interest and joy as well as increased fatigability with a reduction of drive and restriction of activities. Following additional symptoms are possible: decreased concentration, a decrease in self-confidence and self-esteem, a pessimistic outlook on the future, feelings of guilt and worthlessness, possible thoughts of self-harm or suicidal acts, sleep disturbances as well as a reduced appetite<sup>34</sup>.

For the diagnosis of depression according to ICD-10, at least two of the main symptoms must be present for the duration of minimum two weeks, for a severe depressive episode all three must be fulfilled. For further determination of the severity ranging from mild to moderate to severe, the additional ICD-10 criteria mentioned above are applied<sup>34</sup>.

The goal in the treatment of depression is symptom improvement on the one hand, at best the achievement of remission, and on the other hand the restoration of occupational as well as psychosocial functioning and participation. In the long term, a relapse and recurrence should be avoided<sup>34</sup>.

When choosing suitable therapy, clinical factors such as symptom severity and the course of disease so far as well as patient preferences must be considered<sup>34</sup>.

In addition to antidepressants such as selective serotonin reuptake inhibitors (SSRI), tricyclic antidepressants (TCA) and many others, there is a number of psychotherapeutic options for treating depression. Combined treatment is indicated in case of a severe depressive episode or recurrent, chronic as well as double depression<sup>35,36</sup>, especially since compliance with pharmacotherapy is higher when psychotherapy is provided at the same time<sup>37</sup>. Vice versa, acceptability of psychotherapy measured in the drop-out rate is better in combination with

antidepressants. Also for patients with moderate depression, combined therapy seems to provide the best effects<sup>38</sup>.

Established psychotherapeutic practices include cognitive behavioral, psychodynamic and –analytic, systemic as well as interpersonal approaches<sup>34</sup>. Low-intensive therapies can consist of psychoeducation with or without guidance by a therapist, counseling as well as problem solving strategies<sup>34</sup>. More alternative methods include among others sleep deprivation therapy, light therapy, ergotherapy or artistic and movement-related therapy<sup>34</sup>.

## 2.2. CBT

Cognitive behavioral theories form the basis of most psychological interventions<sup>6</sup>. As gold standard for the treatment of depression, CBT is the most examined psychotherapy for depression and shows well-founded results in improvement of depression and anxiety symptoms and of social functioning<sup>39–41</sup>.

The theoretical basis of CBT was developed in the 1970s by Aaron T. Beck and Albert Ellis<sup>8</sup>. The therapy is grounded in the assumption that information processing is based on genetic, biological, developmental and interpersonal influences. Experiences are thus organized and interpreted differently and individual cognitive structures lead to specific behavioral patterns.

According to Beck, stressful life events seem to play a decisive role in the development of a depressive disease<sup>42</sup>. They can trigger changes in our set of thoughts and beliefs which can cause negative and irrational thinking of the self, the environment and the future, the so-called „cognitive triad“<sup>43</sup>. In the long term, behavior and psychosocial functioning are negatively affected as well<sup>43</sup>.

CBT aims to address these maladaptive cognitive patterns and to change them towards a more rational thinking, leading to positive changes in emotional state and behavior<sup>8,43</sup>. Initial steps of CBT involve joint goal setting and psychoeducation at an early stage, followed by individual treatment planning according to the patients' current situation and needs.

A core strategy is to uncover and question negative beliefs and associations, which should give rise to cognitive restructuring<sup>43</sup>.

Another essential component is behavioral activation through the (re-)establishment of pleasurable activities into daily life<sup>44</sup>. As a means to counteract avoiding and withdrawing behavior typical for depression, behavioral change is supposed to lead to positive mood changes<sup>43</sup>.

One key of successful implementation of the learned skills is “homework“, assigning tailored tasks to practice outside the therapy session for better internalization of the content, which has also proven to prevent patients from relapsing<sup>45</sup>.

The following are proposed as general factors for the effectiveness of psychotherapy, regardless of the psychotherapeutic orientation: the therapeutic relationship between patient and therapist, the activation of individual resources of the patient, addressing relevant problems and visualizing them, motivational clarification to explore the conscious and unconscious determinants behind the problems, and active help to solve problems<sup>46,47</sup>.

CBT is usually delivered in individual format, however, there are several different established formats including group therapy, self-help strategies, remote treatment by telephone or video as well as therapy delivered through the internet<sup>48</sup>. Compared to the more intensive individual face-to-face interventions, these formats have in common that they are resource-saving and therefore easier to implement<sup>38</sup>.

### 2.2.1. **Barriers to therapy**

Finding solutions to facilitate access to therapy is of great importance given the fact that depression is substantially undertreated: only 16.5% of the people affected around the globe receive adequate therapy each year<sup>11,49</sup>. 57% of the patients diagnosed with depression acknowledge the need for therapy, whereas 71% of these initiate treatment visiting at least one therapy session. Of those, 41% receive minimum standards of therapy<sup>49</sup>.

Barriers to care are manifold including practical and psychological factors<sup>50</sup>. Practical barriers emerging both from caregivers’ and patients’ side can be of financial nature due to the lack of funding or since patients cannot afford therapy and do not possess sufficient insurance coverage<sup>51</sup>. Apart from that, lack of time because of the job or child care, long waits due to the lack of services<sup>17,51</sup> or transport problems for patients from remote areas<sup>52</sup> pose obstacles to successfully enter or complete therapy.

Psychological barriers include the lack of insight in the existing problem<sup>53</sup>, stigma concerns, lack of motivation or the perception of therapy to be inefficient<sup>10,11,54</sup>.

In the COVID-19 pandemic, social isolation and the fear of losing job and one’s existence on the one hand, with a higher need for professional help and reduced availability of psychiatric care services on the other hand have resulted in a sharpening of the pre-existing treatment gap<sup>12,13</sup>. At the same time, the pandemic is perceived as a “catalyst“ and a “turning point“ for the acceptance and implementation of digital health technologies<sup>13,55</sup>.

### 2.3. Digital CBT for depression

Slowly emerging in the 1990s, digital interventions for mental disorders have been expanding over the past two decades<sup>13,56</sup>. At the same time, doubts have been put forward preventing digital therapy formats from being implemented in routine health care<sup>57</sup>. The health professionals' caution was mainly rooted in assumptions about the healthcare system being unprepared for digital changes. A main aspect was the assumed inability of building a therapeutic alliance via the internet due to the lack of face-to-face interaction<sup>13,58</sup>. The definition of alliance is a relationship between the therapist and patient that is built on collaboration and joint beliefs in the methods and goals of the treatment<sup>59,60</sup>. The therapeutic relationship is one of the general efficacy factors of psychotherapy that has the greatest impact on therapy outcomes, both in face-to-face and digital approaches<sup>61</sup>. Contrary to the expectations so far, there are indications that from the clients' perspective, the establishment and quality of therapeutic alliance in digital formats is similar to face-to-face, provided the digital format is therapist-guided<sup>62,63</sup>.

The pandemic situation in 2020 has launched a process of rethinking among mental health professionals and patients, leading to a rapid increase of internet-based interventions and its acceptance. Due to the advantages of digital technology such as agility, resilience as well as time- and cost effectiveness, the tendencies may be not only temporary<sup>13</sup>.

"Internet-based intervention" is a generic term describing a broad range of therapeutic activities delivered via the internet<sup>64</sup>. Following subgroups have been suggested to categorize internet-based interventions: (1) web-based internet interventions with or without human guidance, (2) online counseling including videoconferencing and communication via chat or email, (3) internet-operated therapeutic software (e.g. gaming, robotic simulation or virtual reality) and (4) other online activities such as online support groups<sup>64,65</sup>. More recent studies show that smartphones play an increasingly important role in delivering therapeutic content<sup>51</sup>. In this meta-analysis, the focus will be on web- and app-based interventions.

For the treatment of depression, there are numerous digital offers and the majority of them are based on CBT<sup>27</sup>. The interventions show a great diversity regarding the type of administration and the extent of human support. While some treatments are completely unguided and based solely on self-help, others contain regular therapist involvement. The nature of communication in case of therapist guidance is mainly text-based and asynchronous<sup>62</sup>.



### 2.3.1. Examples

In the following, two programs out of many CBT-based digital interventions are presented as examples, both of which have existed across countries for about two decades. They are used in clinical settings, but have been repeatedly addressed and further developed in experimental contexts as well.

One example is the program “MoodGYM“, which was developed in the year 2002 by Australian researchers<sup>66</sup>. Christensen and co-authors initially designed a cost-free, self-paced and unguided program for the prevention and treatment of depression and anxiety. The intervention was aimed at young people and consisted of 5 training modules based on cognitive behavioral theories and a workbook with exercises to engage in parallelly. In addition, participants were instructed to fill out online depression assessments. Based on these results, the modules were modified<sup>67</sup>. In later randomized controlled trials (RCTs) to test the efficacy of the program, the modules were complemented by human guidance, e.g. by telephone support of technical or therapeutic nature<sup>68,69</sup> or consultation by the general practitioner (GP)<sup>70</sup>. In Germany, the national health insurance AOK offers MoodGYM for prevention and treatment of mild depressive symptoms in addition to guidance by the GP<sup>71</sup>. In a meta-analysis testing the effectiveness of MoodGYM in 11 studies, a small effect size from pre- to post-intervention for depression symptoms ( $g = 0.36$ , 95%-CI: 0.17-0.56) and a medium effect size for anxiety symptoms ( $g = 0.57$ , 95%-CI: 0.20-0.94) was demonstrated. However, the effect was among others strongly confounded by the amount of therapist guidance and the adherence to the trial<sup>72</sup>.

“Beating the Blues“ is another CBT-based program having been developed in the UK<sup>73</sup>. The original intervention consisted of eight computerized modules disseminated weekly with homework after every session. No direct therapist guidance was included, however, the sessions originally took place at the general practice with supervision and technical support by a study nurse without any therapeutic content. At the end of each module, a progress report for the patient and the GP was printed out. In a non-randomized trial, a moderate pre-post effect size (0.50) was reported<sup>74</sup>.

In a large RCT evaluating the effectiveness and acceptability of both MoodGYM and Beating the Blues compared to usual care by the GP (REEACT trial), no significant differences between control and both intervention groups were found<sup>68</sup>. Again, dropout rates were high with 24%<sup>75</sup>. For the intervention conditions, technical telephone support of non-therapeutic nature was provided. However, contrary to the original concept, Beating the Blues was not set in primary care offices but at home. From the patients` perspective, a higher therapeutic involvement and guidance would have been desirable to boost the motivation for continuation and greater benefit<sup>68</sup>. As a response to that, in the REEACT-2 trial MoodGYM was offered

with additional therapeutic support by telephone on a weekly basis. Compared to the control condition, which received only technical, non-regular telephone support on demand, the intervention group showed significantly better improvement in depression and in anxiety scores. Pre-to-post effect size in the more guided group was small to moderate. Dropout rate was 25% in the intervention and 30% in the control group<sup>69</sup>.

In 2018, a modernized version of Beating the Blues in America without the binding to primary care offices and services was tested. A few of the other changes included the possibility to interrupt a session and continue later and a stronger focus on stress and anxiety next to depression. „TeleCoach“ was part of the intervention and included telephone and email contact with a fixed contact person aiming to discuss the expectations, provide feedback and support and improve adherence<sup>76</sup>. The combination of MoodGYM and Telecoach showed superior results compared to the waitlist control group with large pre-to-post effect sizes (Hedge`s g = 1.45) and a dropout rate of 29%<sup>76</sup>.

In a previous study, the addition of “TeleCoach“ helped to achieve higher adherence, but not better therapeutic outcome compared to an unguided digital intervention. However, both intervention groups showed significant improvement compared to the waitlist control<sup>77</sup>.

### **2.3.2. Effectiveness of digital CBT**

The vast majority of meta-analyses and reviews suggest robust evidence of the effectiveness of digital CBT for the improvement of depression and anxiety symptoms in adults with a depressive disorder<sup>78</sup>. An improvement of work and social functioning is reported as well<sup>79</sup>. There seems to be a variance in the reported between-group effect sizes at post-intervention from small to large (0.24-1.0), but all meta-analyses show superior results for depression and anxiety compared to control conditions including mainly waitlist or treatment as usual (TAU) by the GP<sup>14,15,21,80-83</sup>. A persistence of the effects over the longer-term is reported as well<sup>16,18,82,84</sup>.

Overall acceptability among patients has proven to be good<sup>81,85</sup>, although there is also evidence that despite similar effectiveness of individual, group and telephone CBT as well as guided self-help (via book or internet), the latter might be less favored by patients<sup>7</sup>.

Regarding the aspect of guidance, there seems to be a consensus that therapists' support has a positive influence on the adherence to therapy<sup>77,86</sup> and its effectiveness<sup>14-16,20,83,87</sup>. While guided digital interventions for depression show a moderate to large effect size (0.61-0.67) compared to control groups, digital CBT without guidance renders a smaller effect size (0.24-0.25) in comparison to the control conditions<sup>14,15,19</sup>.

A methodological weakness of most studies examining the effectiveness of digital CBT is the passivity of the control conditions consisting primarily of waitlist or TAU. For making solid statements about the effectiveness of digital interventions, there is high demand for noninferiority trials with active control groups, especially with common individual face-to-face CBT<sup>17</sup>.

#### **2.4. Comparing face-to-face and digital CBT for depression**

Overall, meta-analyses and reviews comparing CBT for depression delivered in digital and face-to-face format reveal equal effectiveness. One of the earlier comprehensive meta-analyses juxtaposing digital and face-to-face therapy showed no difference in 14 included studies (effect size 0.39 in digital vs. 0.34 in face-to-face studies)<sup>80</sup>. However, most of these studies included other disorders than depression (e.g. body image and eating disorders) and other therapeutic approaches than CBT. In 2010, a meta-analysis on guided internet interventions including groups of patients with depression and anxiety only was published. Over the short and long-term, both guided digital as well as face-to-face approaches showed equal results and no differences on drop-out rates<sup>25</sup>. Importantly, out of 21 included studies, six addressed depressive disorder and two of them applied internet-based therapies, whereas the rest delivered therapy mainly via telephone.

Similar results were presented in a review comparing guided digital and face-to-face CBT in 13 studies. However, psychiatric as well as somatic conditions were included, so that only two studies investigated depression, one of them only late-life-depression. Besides, seven studies included face-to-face group therapy instead of individual therapy<sup>26</sup>. In 2016, a meta-analysis was published including five studies investigating depression only. Again, face-to-face CBT showed no superiority compared to digital interventions<sup>22</sup>.

A recent meta-analysis even showed digital CBT to be more effective in reducing depressive symptoms compared to face-to-face CBT in 14 included studies. For global functioning, no significant differences between the two formats were found<sup>23</sup>.

In anxiety disorders, digital approaches showed to be equally effective in reducing symptoms as compared to face-to-face CBT<sup>24,83,88,89</sup>.

Although existing studies report consistent results, the evidence regarding RCTs that compare CBT for depression in digital and face-to-face format in a comparable setting is scarce. Furthermore, most reviews and meta-analyses are not restricted to cognitive behavioral approaches or a depression diagnosis. The delivery format often including group therapy or telephone therapy alongside the choice of participants which involves adolescents or elderly patients only contribute to heterogeneity.

## 2.5. **Aims**

The purpose of the current study is to conduct a comprehensive, multi-outcome meta-analysis by comparing symptom improvement and functional outcome in digital and face-to-face CBT formats for depressive disorders. The primary outcome of interest is the depression symptom severity, secondary outcomes are symptoms of anxiety and multiple levels of functioning including general, social, work and health dimensions as well as quality of life. In addition to that, this comprehensive investigation of digital and face-to-face CBT is complemented by moderator effects analyses using patient characteristics and therapy administration particularities.

### 3. **Publication**

## REVIEW ARTICLE OPEN



# A systematic review of digital and face-to-face cognitive behavioral therapy for depression

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Cognitive behavioral therapy (CBT) represents one of the major treatment options for depressive disorders besides pharmacological interventions. While newly developed digital CBT approaches hold important advantages due to higher accessibility, their relative effectiveness compared to traditional CBT remains unclear. We conducted a systematic literature search to identify all studies that conducted a CBT-based intervention (face-to-face or digital) in patients with major depression. Random-effects meta-analytic models of the standardized mean change using raw score standardization (SMCR) were computed. In 106 studies including  $n = 11854$  patients face-to-face CBT shows superior clinical effectiveness compared to digital CBT when investigating depressive symptoms ( $p < 0.001$ , face-to-face CBT: SMCR = 1.97, 95%-CI: 1.74–2.13, digital CBT: SMCR = 1.20, 95%-CI: 1.08–1.32) and adherence ( $p = 0.014$ , face-to-face CBT: 82.4%, digital CBT: 72.9%). However, after accounting for differences between face-to-face and digital CBT studies, both approaches indicate similar effectiveness. Important variables with significant moderation effects include duration of the intervention, baseline severity, adherence and the level of human guidance in digital CBT interventions. After accounting for potential confounders our analysis indicates comparable effectiveness of face-to-face and digital CBT approaches. These findings underline the importance of moderators of clinical effects and provide a basis for the future personalization of CBT treatment in depression.

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## INTRODUCTION

Cognitive behavioral therapy (CBT) is the gold-standard intervention for major depression besides pharmacotherapy<sup>1</sup>. Since its emergence nearly fifty years ago, a large number of studies has underlined the effectiveness of CBT in improving depressive symptoms, anxiety symptoms and psychosocial functioning<sup>2,3</sup>. In order to increase accessibility to CBT, recent digital CBT approaches have been developed by incorporating technological tools such as emails, smartphone apps or internet-guided therapy<sup>4</sup>. These approaches hold a number of potential advantages such as cost effectiveness, improved accessibility to evidence-based care for patients living in remote areas, patients living abroad or patients with immobility and - most recently - to face the challenge of providing CBT during the COVID-19 pandemic<sup>5</sup>.

A number of studies suggest that CBT can effectively reduce depressive symptoms, anxiety or psychosocial functioning<sup>6–13</sup>. In line with these promising aspects, healthcare professionals<sup>14</sup> and especially young patients report to be open towards the adoption of digital treatments<sup>15</sup>. For patients and clinicians there is a strong preference for blended approaches which combine face-to-face CBT with digital interventions<sup>16,17</sup>. However, the majority of patients with depression seem to prefer face-to-face CBT<sup>18</sup> and adherence to digital interventions is often low<sup>19,20</sup>.

Previous meta-analyses compare face-to-face with digital CBT for different conditions<sup>21,22</sup> and report inconsistent results, possibly due to small samples of studies and heterogeneous

interventions. Despite robust evidence for the clinical effectiveness of face-to-face and digital CBT, the equivalence of these treatments remains an open question. This represents a critical challenge for mental health professionals that need to decide which intervention should be recommended to patients and which factors should be considered when making this decision.

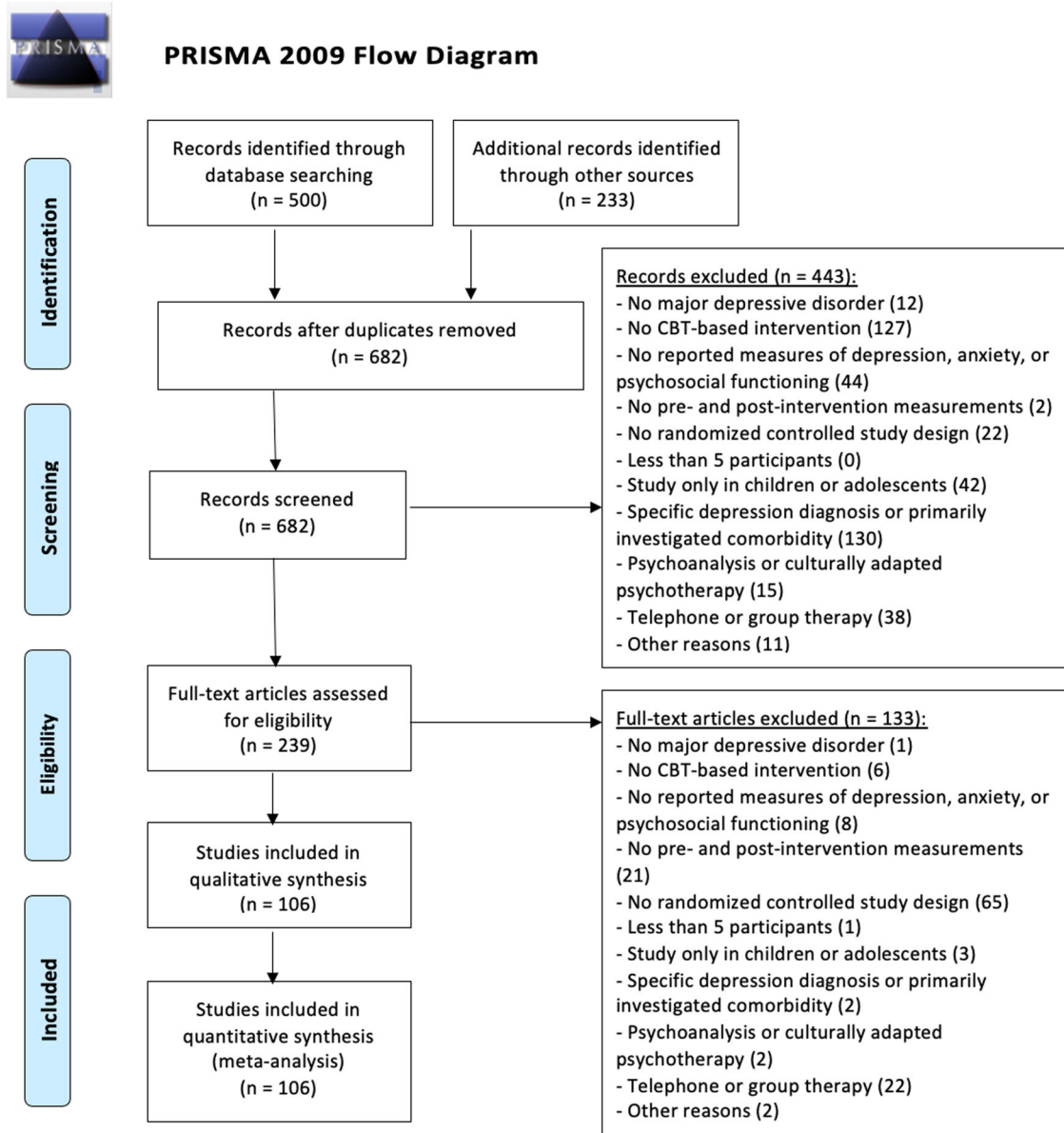
Our primary aim of this systematic review is to compare the effects of face-to-face vs. digital CBT interventions. The secondary aim is to investigate the moderating factors for these interventions. Overall our results indicate that after controlling for a number of potential confounders, face-to-face and digital CBT might be comparable in terms of clinical effectiveness for treating depression. We identify a number relevant factors that moderate the treatment response such as the duration of the intervention, baseline severity, adherence and the level of human guidance in digital CBT interventions.

## RESULTS

### Literature search

We identified 682 potential studies out of which 239 studies were retrieved and assessed in full-text according to our inclusion criteria. Of the included studies, 22 face-to-face studies and 63 digital CBT studies had more than one patient sample that was eligible for inclusion due to multiple study arms. For the face-to-face CBT studies, we identified a small number of studies with a very long treatment duration ( $n = 5$  studies between 1 and 6 years

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**Fig. 1** Flow-chart of the literature search according to the recommendation of the PRISMA guidelines.

of treatment duration). In order to make face-to-face and digital studies more comparable, we restricted all following analyses to studies that had a treatment duration of not more than 1 year. Thus, in total  $n = 106$  studies with a total of  $n = 161$  samples and  $n = 11854$  patients were included in the present meta-analysis (Supplementary Tables 5 and 6). This resulted in  $n = 81$  samples ( $n = 3257$  patients) receiving face-to-face CBT and  $n = 80$  samples ( $n = 8597$  patients) receiving digital CBT (see Fig. 1).

We observed significant differences between face-to-face and digital CBT samples with respect to multiple patient characteristics and other aspects of the intervention (see Table 1).

The assessment of risk of bias indicated an overall high risk of bias and comparable risk for studies investigating face-to-face CBT and studies investigating digital CBT approaches. For both interventions, the main risk of bias resulted from insufficient blinding of participants and insufficient blinding of the outcome assessment. A direct comparison indicated higher risk of selection bias (due to insufficient allocation concealment) in face-to-face CBT studies ( $p = 0.005$ ) whereas digital CBT studies showed higher potential detection bias (blinding of outcome

assessment,  $p = 0.017$ , Supplementary Figs. 2 and 3, Supplementary Table 4).

### Effectiveness of face-to-face vs. digital CBT

In the analysis of depressive symptoms, face-to-face interventions (SMCR = 1.97, 95%-CI: 1.74–2.13) showed significantly stronger reductions ( $p < 0.001$ ) as compared to digital interventions (SMCR = 1.20, 95%-CI: 1.08–1.32, Fig. 2). The difference between digital and face-to-face CBT studies remained significant after applying the trim-and-fill method to compensate for putatively missing studies ( $p < 0.001$ ) and after controlling for differences in study design by using number of sessions and duration of intervention as covariates in the meta-analytic models ( $p = 0.010$ ). However, there were no significant differences between digital and face-to-face CBT samples after controlling for differences in patient characteristics (mean age, gender ratio, antidepressant treatment, severity of depressive symptoms at baseline) using moderator analysis ( $p = 0.068$ ) or when employing propensity score matching to control for

**Table 1.** Characteristics of face-to-face and digital CBT studies as included in the analysis of depressive symptoms (see supplement for an overview of included studies investigating psychosocial functioning and anxiety symptoms).

	Face-to-face studies	Digital studies	Face-to-face vs. Digital studies <sup>a</sup>
Number of samples	81	80	–
Mean number of patients (SD)	40.21 (40.05)	107.46 (139.83)	W = 4911.5, $p < 0.001$
Mean age (SD)	37.82 (5.47)	40.58 (5.26)	W = 3864.5, $p = 0.001$
Mean ratio of male patients	30.46%	27.09%	W = 2199.5, $p = 0.012$
Mean baseline severity (SD) <sup>b</sup>	31.02 (6.36)	27.29 (5.68)	W = 1634.0, $p = 0.002$
Mean ratio of patients on antidepressants	16.70%	33.93%	W = 1677.0, $p < 0.001$
Mean ratio of patients completing intervention	81.86%	72.41%	W = 1997.5, $p = 0.001$
Mean treatment duration in weeks (SD)	14.65 (8.37)	8.54 (2.89)	W = 1059.0, $p < 0.001$
Mean number of sessions (SD)	14.48 (6.26)	8.23 (3.25)	W = 1201.0, $p < 0.001$
Ratio of studies with long-term follow-up	55.56%	80.00%	X <sup>2</sup> = 9.9, $p = 0.002$
Mean follow-up duration (months)	7.94 (6.38)	6.20 (4.69)	W = 1289, $p = 0.322$

<sup>a</sup>Based on two-sample Mann–Whitney-*U* test for continuous variables and on X<sup>2</sup>-test for categorical variables.

<sup>b</sup>Based on BDI-II scores when available or on scores converted to BDI-II with published conversion rules.

differences in study design and patient characteristics ( $p = 0.700$ , Supplement page 5 and 6). In a subanalysis of samples based on BDI-II scores ( $n = 102$  samples from 62 studies), depression scores were significantly higher in face-to-face studies as compared to digital studies at baseline ( $p = 0.048$ , independent *t*-test) but no differences after the intervention ( $p = 0.708$ , independent *t*-test) or at follow-up ( $p = 0.384$ , independent *t*-test) yielded significance (Fig. 2 and Table 1). The analysis of adherence indicated significantly fewer drop-outs in face-to-face (82.4%) as compared to digital CBT studies (72.9%,  $p = 0.014$ , Fig. 3, Supplement page 7 and 8). When accounting for these differences in adherence, face-to-face CBT showed stronger improvements of depressive symptoms as compared to digital CBT ( $p < 0.001$ ).

Face-to-face studies (SMCR = 1.29, 95%-CI: 0.87–1.71) showed significantly stronger improvement in psychosocial functioning ( $p < 0.001$ ) as compared to digital studies (SMCR = 0.49, 95%-CI: 0.39–0.58, Fig. 2). This difference remained significant after controlling for potential publication bias ( $p < 0.001$ ) and after controlling for differences in study design by using number of sessions and duration of intervention as covariates ( $p = 0.013$ ). However, there were no significant differences between digital and face-to-face CBT samples after controlling for differences in patient characteristics (mean age, gender ratio, antidepressant treatment, severity of depressive symptoms at baseline) using moderator analysis ( $p = 0.091$ ) or when employing propensity score matching to control for differences in study design ( $p = 0.068$ , see supplement page 4 and 5).

In addition, face-to-face studies (SMCR = 1.30, 95%-CI: 0.65–1.95) showed no significant difference with regard to anxiety ( $p < 0.240$ ) as compared to digital studies (SMCR = 0.90, 95%-CI: 0.78–1.03, see Fig. 2). These results remained unchanged when accounting for potential publication bias ( $p < 0.240$ ). There were too few studies to conduct further analyses while controlling for additional potentially confounding variables.

All results were robust with respect to different estimates of the correlations between pre- and post-intervention assessments ( $r = 0$  to  $r = 1$  in steps of 0.1, Supplementary Fig. 1).

In the analysis of the long-term stability of treatment gains, face-to-face and digital interventions showed no statistical difference in depressive symptoms ( $p = 0.550$ ), psychosocial functioning ( $p = 0.078$ ) or anxiety symptoms ( $p = 0.820$ , Fig. 2, Table 1 and Supplement page 5 and 6).

### Moderator analysis

Face-to-face CBT treatments were superior to guided digital CBT treatments regarding improvement of depressive symptoms ( $p < 0.001$ ), improvement of psychosocial functioning ( $p < 0.001$ ) and in adherence ( $p < 0.001$ , see Fig. 3). At the same time, guided digital CBT was superior to unguided digital CBT regarding depressive symptoms ( $p < 0.001$ ) and psychosocial functioning ( $p = 0.043$ ) but there was no difference in adherence ( $p = 0.207$ ). No differences between face-to-face CBT, guided digital CBT and unguided digital CBT were found regarding anxiety symptoms (all  $p > 0.1$ ).

The effect of CBT on depressive symptoms was moderated by the number of sessions ( $p = 0.017$ ) and the treatment intensity ( $p < 0.001$ ) in face-to-face studies whereas in digital studies there was a moderation effect of the duration of the intervention ( $p = 0.034$ ). Baseline symptom severity moderated effects of CBT on depressive symptoms in face-to-face studies ( $p = 0.038$ ) and in digital studies ( $p = 0.029$ ).

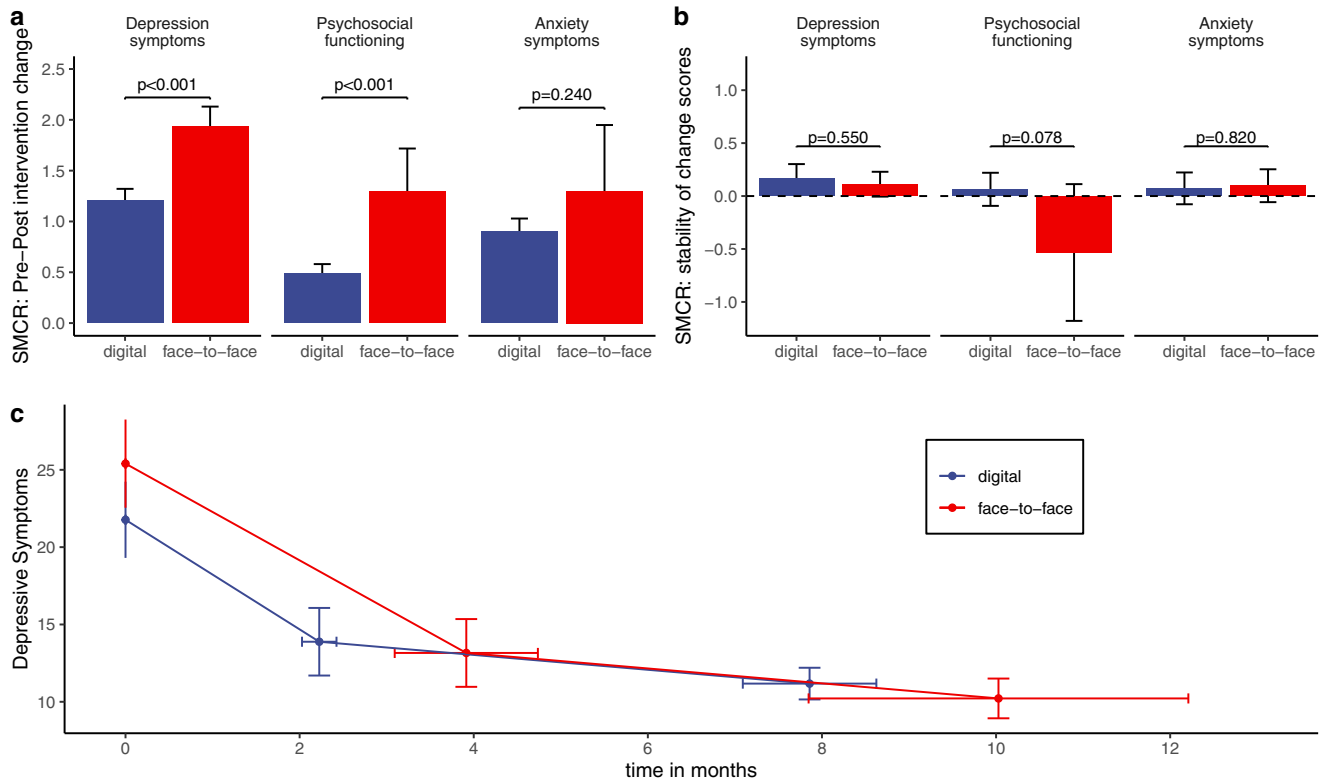
The effect of CBT on psychosocial functioning was moderated by age of onset of depression ( $p = 0.004$ ) but there were too few studies to investigate this effect in digital studies. Mean age was a significant moderator in face-to-face ( $p < 0.001$ ) but not in digital studies ( $p = 0.058$ ). Presence of antidepressant treatment and comorbid anxiety disorder were significant moderators in face-to-face studies ( $p < 0.001$  and  $p = 0.013$ , respectively) but not in digital studies ( $p > 0.05$ ).

In the analysis of anxiety symptoms, the effect of CBT was moderated by the baseline severity of depressive symptoms in digital studies ( $p = 0.001$ ) but not in face-to-face studies ( $p = 0.714$ ).

### DISCUSSION

Digital CBT interventions are becoming increasingly relevant for the treatment of depressive disorders. Despite the rapid proliferation of these approaches, a systematic assessment of the clinical effectiveness of CBT as compared to traditional (face-to-face) approaches, is still lacking. In the present meta-analysis we compared a total of 106 studies and over 11000 patients. To the best of our knowledge the current analysis represents the largest and most comprehensive analysis of the comparative clinical effectiveness of face-to-face and digital CBT interventions for depression. Overall, our results indicate that face-to-face approaches show superior clinical effectiveness in reducing depressive symptoms and psychosocial functioning but not in





**Fig. 2 Results of meta-analyses investigating the effect of digital and face-to-face CBT interventions.** **a** Effects of CBT on anxiety symptoms, depression symptoms and psychosocial functioning. **b** Results of the meta-analyses of long-term stability of treatment gains. **c** Subanalysis of samples based on depression severity based on BDI-II scores. *P* values indicate significance of differences between digital and face-to-face interventions tested by moderator analysis. Error bars indicate lower and upper limits of the 95% confidence interval. Effect sizes and *p* values are presented without correction for differences in patient samples or study design characteristics and without correction for potential publication bias.

reducing comorbid anxiety symptoms. In a supplementary analysis of BDI-II equivalent scores, we largely confirmed the findings of our main analysis. Importantly, face-to-face studies were associated with higher treatment adherence. However, there were significant differences in sample-characteristics and interventions between face-to-face and digital CBT studies. Informed by knowledge that multiple factors including age, gender or disease severity at baseline may moderate treatment response<sup>(23–26 but see<sup>27,28</sup>)</sup>, we employed covariate analysis and propensity score matching to control for these differences. These analyses revealed no significant differences between the face-to-face and digital interventions, suggesting that these approaches might have more comparable clinical effectiveness when accounting for moderators. Further controlled studies conducted in more comparable populations, interventions and study designs are needed to confirm these findings. Our results provide a strong foundation to initiate these efforts.

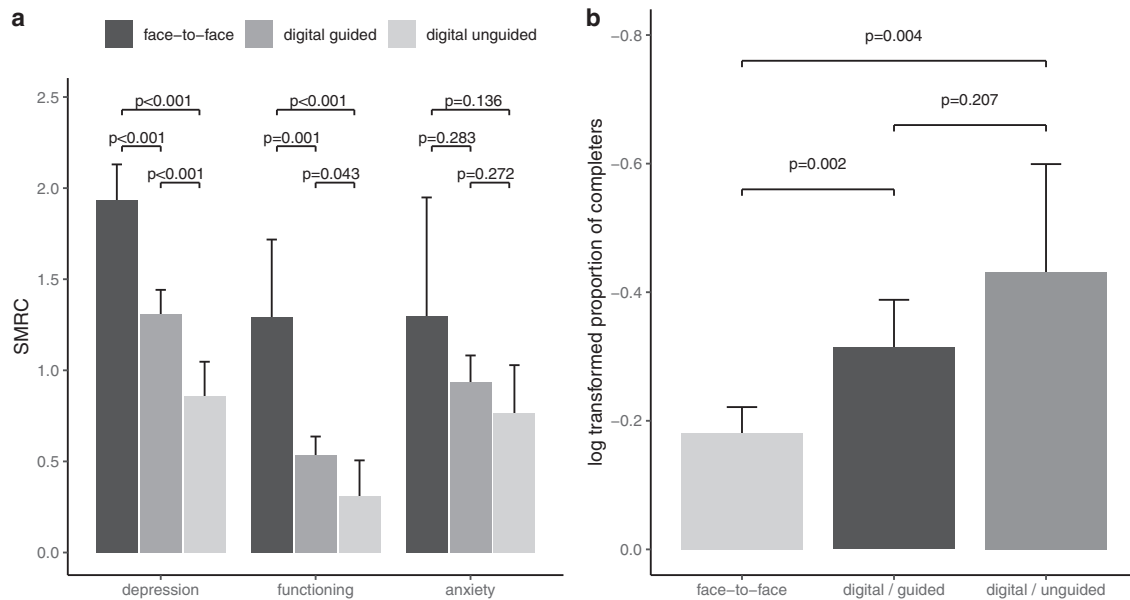
Motivated by the recent calls for precision psychiatry approaches, a number of studies have investigated potential moderators of clinical effects of face-to-face<sup>29,30</sup> and digital CBT treatments<sup>23,30,31</sup> with the aim to increase clinical effectiveness and to facilitate the adoption of digital tools for clinical scenarios or populations in which they are most successful.

For digital CBT, some studies indicated that high baseline severity of depressive symptoms predicts improvement of depressive symptoms<sup>24,31–35</sup> or psychological distress<sup>36</sup>. Conversely, other studies reported no such effect<sup>28,37,38</sup> or even a better response to a CBT intervention delivered by trained clinicians via internet in patients with lower baseline severity of symptoms<sup>39</sup>. Interestingly, our findings show a significant moderation effect of baseline severity on the improvement of depressive symptoms in

face-to-face CBT studies and a moderation effect of similar size in digital CBT studies (see Fig. 4). This suggests that both digital and face-to-face CBT may be suitable interventions for patients with more severe forms of depression.

In line with our findings, a recent study indicated that concurrent use of antidepressant medication is common in digital CBT trials of depression and anxiety<sup>40</sup>. In this analysis, digital CBT showed equivalent efficacy for patients with antidepressant medication and patients not using them<sup>40</sup>. Another study focused on psychological distress and found significantly higher improvements in patients on antidepressants after participating in a digital CBT programme<sup>36</sup>. Importantly, a high number of studies investigating face-to-face CBT, antidepressant medication was an exclusion criterion whereas this was not the case for most digital CBT studies. Thus, antidepressant medication represents a potential confound for the identified differences between digital and face-to-face CBT studies.

Treatment adherence is another important challenge for the successful implementation of digital mental health<sup>41,42</sup>. Previous studies investigated the role of adherence and identified adherence as a predictor of faster treatment response to digital CBT<sup>28,35</sup>. In the current analysis, patient characteristics and the design of the intervention were not related to adherence. However, face-to-face CBT was associated with higher adherence compared to digital CBT and no difference between guided and unguided digital CBT with respect to adherence was observed. Interestingly, our results indicate that adherence is related to the reduction of depressive symptoms in digital CBT interventions (but not in face-to-face interventions) whereas improvement of functioning was moderated by adherence in face-to-face interventions (but not in digital interventions).



**Fig. 3** Comparison of face-to-face, guided digital and unguided digital CBT treatments regarding. **a** Clinical outcomes following the CBT intervention. **b** Comparisons of adherence. *P* values indicate significance of differences between digital and face-to-face interventions tested by moderator analysis in the meta-analytic model. Error bars indicate lower and upper limits of the 95% confidence interval.

In line with these findings, a higher number of sessions is an important positive predictor of the success of digital CBT treatment<sup>39</sup>. Interestingly, previous meta-regression analysis on the effect of the duration of CBT on treatment outcome revealed only minor effects but this analysis underlined the importance of treatment intensity (e.g. the number of treatment sessions per week)<sup>43</sup>.

A number of potential limitations need to be considered in the interpretation of our current findings. First, the result that face-to-face and digital CBT show similar clinical effects after the statistical correction of potential confounds remains to be confirmed in trials designed specifically to test this hypothesis. Second, we acknowledge that in the present analysis the main outcome measures are pre-post difference scores which need to be interpreted carefully as they include other effects besides the intervention such as placebo effects or the natural course of the depressive disorder. However, our main results focus on the comparison of face-to-face and digital CBT which should not lead to confounded results. Lastly, our analysis of potential biases indicated several potential risks for the majority of the included studies. This was mainly a result of insufficient blinding of participants and raters.

Face-to-face and digital CBT are effective therapy approaches for the treatment of major depression. While currently available evidence suggests robust effectiveness of face-to-face approaches, digital CBT might show comparable effects when controlling for moderators. In particular, additional human support, longer interventions and high adherence were associated with favorable treatment effects of digital CBT. Our results emphasize the potential of digital CBT to be integrated as a valuable tool in specific clinical scenarios including more severe presentations of major depression. Finally, specific moderators might guide clinicians as well as future studies in the personalization of CBT treatment for patients with depression.

## METHODS

### Search strategy and selection criteria

We conducted a systematic literature search in the PubMed database to identify all relevant studies published until January 11th, 2021. In addition, primary studies in existing meta-analyses were checked for

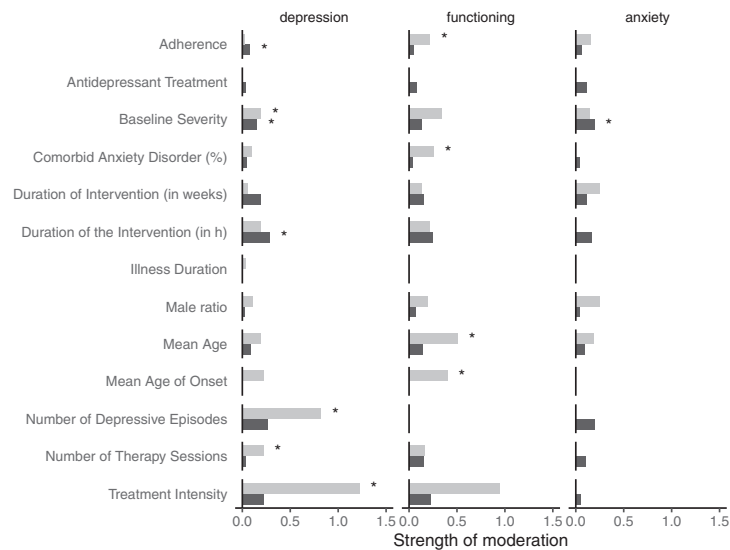
eligibility<sup>2,7,12,22,44</sup>. The search terms were: (“cognitive behavioral therapy”) OR (“digital psychotherapy” OR “psychotherapy app” OR “mobile” OR “internet”) AND (“major depression”) NOT (“bulimia” OR “anorexia” OR “psychosis” OR “bipolar” OR “OCD” OR “anxiety”) NOT (“review”[Publication Type]).

We included studies that: (1) investigated patients with Major Depressive Disorder as diagnosed by the Diagnostic Statistical Manual (DSM) or International Classification of Diseases ICD, (2) employed an individual, CBT-based intervention (including second- and third-wave CBT approaches such as schema therapy, mindfulness therapy and interpersonal psychotherapy), (3) reported measures of either depressive symptoms, anxiety symptoms or psychosocial functioning (4) before and after the intervention in a (5) randomized controlled study design. We included CBT interventions administered in a face-to-face manner and CBT in a digital setting. Digital CBT could be administered in a guided or unguided manner and we included computer-based approaches (internet-based, computerized CBT-modules or email-based) as well as smartphone-based approaches.

Studies were excluded if they: (1) included less than five participants, (2) included children or adolescents (<18 years), (3) focused exclusively on a more specific depression diagnosis (i.e. postpartum depression or late-life depression), or primarily investigated somatic (e.g. HIV, diabetes) or psychiatric main diagnose preceding depressive symptomatology (e.g. panic disorder), (4) employed a psychotherapeutic intervention based on psychoanalysis or culturally-adapted psychotherapy as well as therapy delivered by a telephone or group therapy of any therapy direction.

In case some relevant data was not reported in the published manuscripts of the studies identified during the literature search, we contacted authors via email in order to obtain the missing data. In some cases we did not receive any response or the needed data was not available. Studies were excluded from our meta-analysis, if data was not sufficient to calculate effect sizes as specified in the methods section.

The procedure for this meta-analysis has been publicly registered at <https://osf.io/z45xr>. We follow the PRISMA reporting guidelines<sup>45</sup> and additional details regarding the literature search are provided in the supplementary methods. Approval from the



**Fig. 4 Results of the moderating analysis on depression symptoms, psychosocial functioning and anxiety symptoms.** Strength of moderation was quantified by the beta-coefficient of the meta-analytic moderation model and moderation effects are plotted as absolute and sqrt values for better visualization. “\*” indicates significant moderation effects ( $p < 0.05$ ) in the meta-analytic model.

local ethics committee was waived as no original data was acquired in the context of this study.

#### Data extraction

Depressive and anxiety symptoms were assessed by self- or observer-rated clinical scales (e.g. Beck’s Depression Inventory, Hamilton Depression Scale, State Trait Anxiety Inventory-STAI, Hamilton Anxiety Scale). In order to compare depressive symptom severity at baseline across studies, reported symptom measures were converted to BDI-II using published conversion procedures<sup>46,47</sup>. Psychosocial functioning was assessed using measures of global functioning (e.g. Global Assessment of Functioning), work-related functioning (e.g. Well-Being Inventory), social functioning (e.g. Social and Occupational Functioning Assessment Scale), health-related functioning (e.g. World Health Organization Quality of Life) and life quality (e.g. Quality of life scale). Adherence was quantified for all samples by the ratio of patients that did not drop out of the study and underwent an assessment after the intervention.

Literature search and data extraction were conducted independently by two researchers (L.V. and U.M.R.). Discrepancies were resolved in a consensus conference (L.K.I., L.V. and U.M.R.). All information was checked for potential extraction errors independently by two researchers (N.D., J.W.).

#### Outcome measures

We computed the standardized mean change using raw score standardization (SMCR) describing changes between measures before and after the intervention<sup>48</sup>.

$$SMCR = \frac{Mean_{Pre} - Mean_{Post}}{SD_{Pre}} \quad (1)$$

Here,  $Mean_{Pre}$  and  $Mean_{Post}$  refer to the mean of clinical measures before and after the intervention and  $SD_{Pre}$  refers to the standard deviation before the intervention. As compared to the widely used standardized mean difference (SMD), SMCR accounts for the dependence of groups in pre-post study designs in the calculation of the sampling variances.

SMCRs were computed separately for the three outcome dimensions (depressive symptoms, anxiety symptoms, psychosocial functioning). In case studies reported more than one measure for a specific outcome, these measures were averaged. Long-term

stability of treatment gains following CBT were analyzed by calculating changes between the post-intervention time point and the follow-up assessment. As the calculation of SMCRs requires the correlation between baseline and follow-up measures, we estimated a correlation of  $r = 0.65$  based on several previous studies<sup>49,50</sup>. We conducted sensitivity analyses using the entire spectrum of possible correlations (0–1 with steps of 0.05) to test whether the overall effects are robust to different correlation coefficients (supplementary materials).

#### Meta-analytic procedures

The main outcome was the difference in clinical effectiveness between face-to-face and digital CBT interventions. This was assessed by conducting a meta-analysis including all effect sizes (SMCR) and testing for the relevance of the factor “intervention” (face-to-face vs. digital CBT). Potential confounders including characteristics of the patient samples (mean age, gender ratio, severity of depressive symptoms at baseline, antidepressant treatment) or by differences in interventions (number of sessions, duration of intervention in weeks) was assessed by including these factors in our meta-analysis. Moreover, we investigated the moderating effect of treatment intensity which was defined as the number of CBT sessions divided by the duration of the intervention in weeks. In addition, we employed propensity score matching of face-to-face and digital CBT studies to control for differences in potentially confounding variables. In case studies did not report values for these factors, we employed median imputation. Lastly, moderator analysis was conducted to assess the role of additional factors for the clinical effectiveness of CBT interventions. Moderator analysis was conducted separately for face-to-face and digital CBT studies Table 2.

For all meta-analyses, heterogeneity was assessed using  $I^2$  statistics to describe the percentage of variation across studies<sup>51</sup>. Higher values indicate larger heterogeneity, with  $I^2$  values of 25%, 50% and 75% representing low, moderate and high heterogeneity respectively<sup>51</sup>. Publication bias was assessed by visual inspection of funnel plots and by employing Egger’s test for funnel plot asymmetry for each meta-analysis. In case of significant Egger’s test, we used the trim-and-fill method to estimate the number of missing studies and report corrected estimated effect sizes<sup>52</sup>. A significance level of  $p < 0.05$  (two-tailed) was used for all analyses. All reported  $p$  values describe summary effect sizes or moderation effects of meta-analytic models unless stated otherwise.

**Table 2.** Results of meta-analyses investigating pre/post effects and long-term stability of treatment gains for digital and face-to-face CBT interventions. *P* values indicate significance of meta-analytic summary effect sizes (SMCR) testing the difference between symptoms pre- vs. post-intervention. Effect sizes and *p* values are presented without correction for differences in patient samples or study design characteristics and without correction for potential publication bias.

Outcome	Face-to-face studies				Digital studies				Face-to-face vs. Digital	
	<i>k</i>	SMCR	95%-CI	<i>p</i> value	<i>k</i>	SMCR	95%-CI	<i>p</i> value	Direction	<i>p</i> value
Pre/Post analysis										
Depression symptoms	81	1.934	1.737–2.130	<i>p</i> < 0.001	80	1.204	1.086–1.321	<i>p</i> < 0.001	face-to-face > digital	<i>p</i> < 0.001
Psychosocial functioning	18	1.293	0.869–1.718	<i>p</i> < 0.001	53	0.489	0.398–0.580	<i>p</i> < 0.001	face-to-face > digital	<i>p</i> < 0.001
Anxiety symptoms	4	1.299	0.649–1.949	<i>p</i> < 0.001	44	0.902	0.775–1.029	<i>p</i> < 0.001	face-to-face > digital	<i>p</i> = 0.240
Follow-Up analysis										
Depression symptoms	45	0.112	−0.005–0.229	<i>p</i> = 0.061	64	0.167	0.031–0.302	<i>p</i> = 0.016	face-to-face < digital	<i>p</i> = 0.550
Psychosocial functioning	9	−0.533	−1.179–0.113	<i>p</i> = 0.106	45	0.064	−0.093–0.220	<i>p</i> = 0.426	face-to-face < digital	<i>p</i> = 0.078
Anxiety symptoms	3	0.098	−0.057–0.253	<i>p</i> = 0.217	36	0.073	−0.077–0.223	<i>p</i> = 0.343	face-to-face > digital	<i>p</i> = 0.820

### Quality assessment

Two independent authors (U.M.R. and L.K.I.) assessed risk of bias using the Cochrane Risk of Bias tool<sup>53</sup>. We used four previously established classification criteria to quantify the risk of bias each study (high, low or unclear risk of bias): (1) random sequence generation, (2) allocation concealment, (3) selective outcome reporting (4) incomplete outcome data (5) blinding of participants and study personnel (6) blinding of outcome assessment.

### Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this article.

### DATA AVAILABILITY

All data analyzed in this meta-analysis is available upon reasonable request from the corresponding author.

### CODE AVAILABILITY

All code for analysis is available upon reasonable request from the corresponding author. All analyses were performed using R version 4.1.1<sup>54</sup> and the package metafor<sup>55</sup>.

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## AUTHOR CONTRIBUTIONS

L.K.-I. and U.R. contributed equally to this work. L.K.-I. & J.K. designed the study. U.R., L.V., J.W. and J.W. contributed to literature search, data extraction and quality control. L.K.-I., J.K. and U.R. conducted the analysis. F.J., U.R., P.U. and M.A.-J. advised during data analysis. L.K.-I., J.K., U.R., F.J., U.R., P.U. and M.A.-J. contributed to the interpretation of the data and the writing of the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content and approved the final version of the manuscript. All authors are accountable for all aspects of the work.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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## 4. Discussion

In the treatment of depressive disorders, digital approaches are becoming increasingly important alongside pharmacotherapy and face-to-face treatment. Digital CBT has gained a reputation as a low-threshold, affordable and effective tool for treating depression. However, direct comparisons are too rare to evaluate whether digital CBT approaches are an equivalent alternative to traditional face-to-face CBT.

The present meta-analysis compared 80 samples with 8697 patients receiving digital CBT and 81 samples with 3257 patients receiving face-to-face CBT. A total of 106 studies with 161 samples and 11854 participants were included<sup>90</sup>.

### 4.1. Clinical outcome

Several significant differences were found between digital and face-to-face studies. In terms of study characteristics, CBT delivered in digital format was significantly shorter measured in weeks and contained a smaller number of sessions. In addition, adherence was found to be significantly lower in the digital CBT<sup>90</sup>. As for patient characteristics, significantly more patients and a higher proportion of females participated in the digital trials. Moreover, participants who received digital CBT were significantly older, had lower depression severity at baseline and were more likely to be taking antidepressants than those who received face-to-face CBT<sup>90</sup>.

Our overall findings showed significant differences in clinical effectiveness in favor of face-to-face therapy for depression symptom severity and psychosocial functioning. No significant differences were observed between digital and face-to-face CBT for comorbid anxiety symptoms<sup>90</sup>.

Considering several significant differences between digital and face-to-face CBT in terms of study and patient characteristics, we controlled for these differences by performing propensity score matching and moderator analysis. The moderator analysis found unchanged a stronger improvement in clinical effectiveness for face-to-face therapy after controlling for differences in study characteristics including the duration of intervention and the number of sessions as covariates<sup>90</sup>. However, clinical effectiveness for depression and functioning was not significantly different when controlling for differences in patient characteristics including baseline depression symptom severity, mean age, gender ratio and antidepressant treatment in moderator analysis, and when accounting for study and patient characteristics in propensity score matching<sup>90</sup>. These analyses suggest that digital and face-to-face CBT could yield more comparable effectiveness when controlling for potential confounders.

## 4.2. Moderator analysis

In a meta-analytic model, the moderating effects of study and clinical characteristics were separately analyzed. Among others, a significant association could be observed between depression baseline severity and treatment response in both digital and face-to-face CBT, indicating that patients with higher depression severity at baseline might benefit more from the CBT treatment<sup>90</sup>. In contrast to our findings, a few studies report that patients with lower pretreatment depression severity benefit more from digital CBT<sup>91,92</sup> or show no significant associations between initial depression severity and treatment response in both digital<sup>73,93–95</sup> and face-to-face CBT<sup>96</sup>. However, our observations are in line with the majority of studies suggesting a significant positive moderation effect of higher pretreatment depression severity on the outcome of digital and face-to-face therapy<sup>84,97–105</sup>.

Mixed research results also exist for the effect of concurrent treatment with antidepressants. Some studies report either greater symptom reduction in patients taking antidepressant medication (ADM)<sup>102</sup>, or no associations<sup>73,106</sup>, or even poorer response to therapy in digital as well as in face-to-face CBT<sup>35,103,107,108</sup>. Reasons for this could include lower treatment engagement when taking ADM due to emotional blunting or relevant side effects such as agitation or insomnia<sup>109,110</sup>. In the present meta-analysis, concomitant ADM use did not significantly moderate the improvement of depression symptoms during therapy<sup>90</sup>.

Similarly, we found no moderation effects of age and gender ratio on therapy outcome, with the exception of younger age predicting higher improvement in psychosocial functioning in face-to-face CBT<sup>90</sup>. In the literature, results are rather inconsistent: some studies showed no moderating effects of age<sup>96,99</sup>, while others found that younger age increased the effectiveness of face-to-face CBT<sup>103,111</sup>. Interestingly, some studies associated older age with higher benefits in digital CBT<sup>84,92</sup>, although younger patients are known to be more technology-savvy. One explanation might be the greater patience and adherence of older patients, but further studies examining their engagement with new technology are needed to draw more precise conclusions. In terms of gender, studies have not shown significant moderating effects for face-to-face CBT<sup>96,103,105</sup>, but there is some evidence that female gender may be a positive predictor of response to digital CBT<sup>94,97</sup>.

Duration of illness did not moderate the outcome of face-to-face therapy in the present meta-analysis, but a greater number of depressive episodes seemed to predict a poorer response to face-to-face CBT<sup>90</sup>. Consistent with this finding, it is reported that chronic depression has a negative impact on the outcome of face-to-face therapy<sup>111</sup>. For digital CBT, the number of depressive episodes did not show a moderating effect in our analysis<sup>90</sup>.

With regard to the length of treatment, we found that the number of sessions and intensity of treatment (number of sessions per week), but not the duration of the intervention in weeks,

positively influenced therapy outcome in face-to-face CBT<sup>90</sup>. This finding is confirmed by Cuijpers et al., who reported that “concentrated therapy within a brief time frame might be best”<sup>112</sup>. Catarino et al. also observed that a higher number of sessions predicted a positive response to digital CBT<sup>92</sup>. In our analysis, however, length of therapy did not show a significant moderating effect on digital CBT in terms of number of sessions, duration of CBT in weeks or intensity of intervention<sup>90</sup>. Moreover, the duration of the intervention and the number of sessions were applied as covariates in our meta-analysis, showing that face-to-face CBT was still significantly more effective than digital CBT<sup>90</sup>.

It is suggested that adherence to therapy is a relevant moderator for the success of digital CBT. Our analyses suggest that lower dropout rates in digital CBT lead to a better treatment response<sup>90</sup>, which is in line with previous studies<sup>95,113</sup>. It is also confirmed that adherence and perceptions of therapy as credible lead to higher and faster reductions in depression symptoms<sup>108</sup>. Interestingly, our analysis revealed that adherence was not a significant moderator of treatment outcome in terms of improvement in depression symptom severity in face-to-face CBT<sup>90</sup>, which is consistent with findings in the existing literature<sup>103</sup>. However, unlike in digital interventions, higher adherence appeared to moderate improvement in psychosocial functioning in face-to-face CBT studies<sup>90</sup>.

Since patients' response to digital CBT is related to adherence, it is important to find ways to encourage and support their engagement. It is reported that ADM intake has no effect on adherence in digital CBT<sup>106</sup>. Human guidance of digital therapy, however, has been discussed as a moderator of higher adherence<sup>77,86</sup>. Regular automated or human support and reminders are considered essential for promoting adherence, although the therapeutic character may be of secondary importance<sup>104</sup>.

In the present meta-analysis, we found evidence that guided digital therapy is indeed more effective than unguided digital CBT in reducing depression symptom severity and improving psychosocial functioning<sup>90</sup>. This goes in line with previous findings<sup>14–16,20,83,87</sup>. In contrast to observations in existing research, we found no difference in adherence between guided and unguided digital CBT<sup>90</sup>.

Because guidance in digital CBT has been shown to be a key moderator of therapy outcomes, a more nuanced view should be taken. For example, the amount and nature of guidance has been subject of debate. There is evidence that the content might be secondary with no significant differences between therapist- and more practical, technician-assisted digital CBT<sup>114,115</sup>. However, in the REAACT-2 trial mentioned above, therapist-guidance showed significantly better results than guidance by a technician<sup>69</sup>.

Königbauer et al. further differentiated that therapeutic support might be more beneficial for individuals with moderate and severe depressive symptoms, but less so for patients with mild



depression<sup>16</sup>. Similarly, a recent meta-analysis indicated that symptom severity measured at baseline significantly moderated how helpful human guidance was perceived to be<sup>18</sup>. It was also observed that the availability of pre-treatment contacts moderates the effectiveness of guidance<sup>87</sup>.

#### **4.3. Challenges and opportunities of digital CBT**

As a rapidly evolving technology of increasing relevance, many studies have dealt with digital health and highlighted the barriers and chances associated with these developments.

One of the biggest concerns expressed is low engagement with therapy. This applies to interventions within the framework of clinical trials, as confirmed by our meta-analysis, but especially for digital tools outside of research settings<sup>116,117</sup>. For example, unsupervised mental health apps are estimated to have a dropout rate of approximately 90% within the first 10 days of use<sup>118</sup>. Although we could not confirm this in our meta-analysis<sup>90</sup>, there is solid evidence that human support is a major factor in improving adherence<sup>83</sup>. Another suggestion is to increase user participation in app development so that the needs of participants are better addressed<sup>119,120</sup>.

Another issue that needs to be addressed is the lack of evidence-based framework in smartphone apps<sup>117,121,122</sup>. For example, a study showed that all 25 of the most successful iPhone apps for treating anxiety lacked evidence-based content<sup>123</sup>.

Lax data security and privacy concerns are another issue that needs to be addressed in terms of the deficiencies of digital interventions<sup>116,124,125</sup>. On the other hand, the ability to passively and actively collect real-time data presents opportunities. In response to the data, timely and individually adapted interventions could be offered using artificial intelligence and machine learning<sup>126,127</sup>. This is not yet used in the vast majority of digital apps, but in the longer term has the potential to pave the way for precision psychiatry, a more individualized and real-time therapeutic response<sup>51</sup>.

It becomes obvious that most of the challenges addressed apply to digital health approaches outside the research and clinical sector. The current situation is described as “lawless wild west” with an overabundance of non evidence-based offers and loose privacy regulations<sup>51</sup>. As a result, acceptance and trust in digital health technologies among both patients and clinicians has been rather low in recent years<sup>115,128</sup>.

Given the clear benefits and proven effectiveness of digital CBT, it is certainly worthwhile to face existing challenges and skepticism. For a more successful implementation, further efforts are needed in research, clinics and politics. For example, stronger regulations for the responsible use of patient data are required<sup>51</sup>. Moreover, clinicians should be better educated

about the risks and benefits. There is even the idea of implementing “digital navigators“, professionals who integrate digitalisation of therapy into clinical routine care<sup>129</sup>. Digital interventions can be offered as stand-alone therapy with guidance, embedded in stepped care procedures or in combination with face-to-face therapy<sup>115</sup>. The latter showed promising results in a recent pilot study investigating interpersonal therapy in a blended setting for major depression<sup>130</sup>.

#### 4.4. Limitations

There are some limitations to the interpretation of our findings that need to be addressed.

First of all, the calculation of effect size in our meta-analysis was based on symptom change from pre- to post-intervention within a sample<sup>90</sup>. However, this approach could lead to biased outcomes, as the effect size is not only influenced by the intervention itself, but also by the natural course of disease and patient characteristics. Besides, the calculation of the pre-post standardized mean difference (SMD), which we also applied, requires a correlation coefficient (R) for the association between pre- and post-intervention measurements, as they are not independent of each other<sup>131</sup>. This value was not reported in most studies and therefore had to be estimated, which can be a source of error. We estimated an R of 0.65 in line with Rosenthal’s conservative estimate of 0.7<sup>132</sup>. In addition, we performed sensitivity analyses with other R values to check if the overall effect was robust to a number of imputed correlation coefficients. Estimates with R = 0, R = 0.2, R = 0.4, R = 0.6, R = 0.7, R = 0.8 and R = 1 did not change the direction of effect<sup>90</sup>. Furthermore, our focus was less on the pre-post changes within a study and more on comparing these effects between digital and face-to-face studies<sup>90</sup>.

Secondly, the risk of bias assessment revealed an overall high risk for both digital and face-to-face studies<sup>90</sup>. The domains blinding of participants and raters as well as blinding of outcome assessment were critical to this overall judgment<sup>90</sup>. However, in the context of mental health interventions, blinding of participants and staff is generally not possible. For self-assessed measures, which were prevalent in many of the included studies, blinding of outcome assessment was also not feasible.

Finally, we did not have many face-to-face studies (k=4) reporting comorbid anxiety symptoms, so these results should be interpreted with caution. Also, the moderating analysis of anxiety symptoms in face-to-face studies could not be applied to most potential moderators due to lack of data<sup>90</sup>.

#### 4.5. Conclusion

The current meta-analysis findings suggest that both face-to-face and digital CBT are effective interventions for the treatment of depression, with face-to-face CBT showing significantly higher effect sizes in ameliorating depressive symptoms and improving psychosocial functioning<sup>90</sup>. However, this could be attributed to numerous significant differences in study design and patient characteristics between face-to-face and digital CBT. After statistically correcting for these differences, the effects were comparable. Moderator effects analysis showed that depression symptom improvement in face-to-face CBT was influenced by initial depression severity, number of depressive episodes as well as by the number of sessions and intensity of treatment. Corresponding moderators in digital CBT were baseline depression severity and treatment adherence<sup>90</sup>.

A more profound understanding of moderating factors is crucial for optimizing treatment and offering more scalable interventions, especially in digital health. Tailoring treatment can help to meet patients' needs and lead to a better response to therapy<sup>94</sup>. However, given the paucity of evidence on moderators and predictors in the treatment of depression, further research is needed towards precision psychiatry<sup>103,105</sup>. In addition, further randomized controlled studies with a more comparable selection of patients and study settings, especially with regard to relevant moderators, are needed to confirm our findings and pave the way for a more personalized and successful implementation of digital CBT in the treatment of depressive disorders.

## 5. References

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