

Internet- and Mobile-Based Interventions for Mental and Somatic Conditions in Children and Adolescents

A Systematic Review of Meta-analyses

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Abstract: This meta-review integrates the current meta-analysis literature on the efficacy of internet- and mobile-based interventions (IMIs) for mental disorders and somatic diseases in children and adolescents. Further, it summarizes the moderators of treatment effects in this age group. Using a systematic literature search of PsycINFO and MEDLINE/PubMed, we identified eight meta-analyses (N = 8,417) that met all inclusion criteria. Current meta-analytical evidence of IMIs exists for depression (range of standardized mean differences, SMDs = .16 to .76; 95% CI: -.12 to 1.12; k = 3 meta-analyses), anxiety (SMDs = .30 to 1.4; 95% CI: -.53 to 2.44; k = 5) and chronic pain (SMD = .41; 95% CI: .07 to .74; k = 1) with predominantly nonactive control conditions (waiting-list; placebo). The effect size for IMIs across mental disorders reported in one meta-analysis is SMD = 1.27 (95% CI: .96 to 1.59; k = 1), the effect size of IMIs for different somatic conditions is SMD = .49 (95% CI: .33 to .64; k = 1). Moderators of treatment effects are age (k = 3), symptom severity (k = 1), and source of outcome assessment (k = 1). Quality ratings with the AMSTAR-2-checklist indicate acceptable methodological rigor of meta-analyses included. Taken together, this meta-review suggests that IMIs are efficacious in some health conditions in youths, with evidence existing primarily for depression and anxiety so far. The findings point to the potential of IMIs to augment evidence based mental healthcare for children and adolescents.

Keywords: eHealth, mHealth, psychotherapy, youth, meta-review

Internet- und mobilebasierte Interventionen psychischer Störungen und körperlicher Erkrankungen im Kindes- und Jugendalter: eine systematische Übersicht der meta-analytischen Evidenz

Zusammenfassung: Die vorliegende Übersichtsarbeit fasst die aktuelle meta-analytische Evidenz zur Wirksamkeit internet- und mobilebasierter Interventionen (IMIs) für psychische Störungen und körperliche Erkrankungen im Kindes- und Jugendalter zusammen. Darüber hinaus soll der derzeitige Wissensstand über mögliche Moderatoren dieser vergleichsweise neuen Interventionsform zusammengetragen werden. Mittels einer systematischen Literaturrecherche in den Datenbanken PsycINFO und MEDLINE/PubMed konnten acht Meta-Analysen (N = 8.417) identifiziert werden, die sämtliche Einschlusskriterien erfüllen. Effektstärken von IMIs im Vergleich zu vorwiegend inaktiven Kontrollgruppen (Warteliste; Placebo) liegen vor für die Bereiche Depression (Bandbreite standardisierter Mittelwertsdifferenzen, SMD = .16 bis .76; 95 %-KI: -.12 bis 1.12; k = 3 Meta-Analysen), Angststörungen (SMD = .30 bis 1.4; 95 %-KI: -.53 bis 2.44; k = 5) und chronischem Schmerz (SMD = .41; 95 %-KI: .07 bis .74; k = 1). Die Effektstärke für IMIs über verschiedene psychische Störungen hinweg beträgt SMD = 1.27 (95 %-KI: .96 bis 1.59; k = 1); die Effektstärke für IMIs bei verschiedenen somatischen Erkrankungen liegt bei SMD = .49 (95 %-KI: .33 bis .64; k = 1). Als signifikante Moderatoren konnten das Alter (k = 3), der Symptomschweregrad (k = 1) und die Art der Ergebnisevaluation (k = 1) identifiziert werden. Die Bewertung der methodischen Qualität der eingeschlossenen Meta-Analysen anhand der AMSTAR-2-Checkliste ergab insgesamt eine akzeptable methodische Güte. Zusammenfassend deutet diese Übersichtsarbeit auf die Wirksamkeit von IMIs bei verschiedenen Erkrankungen hin, wobei bislang aktuell überwiegend Evidenz zu depressiven Störungen und Angststörungen existiert. Dabei weisen die Ergebnisse auf das Potenzial dieser neuen Behandlungsform für eine mögliche Erweiterung der evidenzbasierten Gesundheitsversorgung für Kinder und Jugendliche mit psychischen Störungen hin.

Schlüsselwörter: eHealth, mHealth, Psychotherapie, Adoleszenz, Review

Introduction

The internet and its applications on mobile devices are today omnipresent in many peoples' daily life. This is especially true for many children and adolescents, who from their very beginning are familiar with an increasingly digitalized world. The fluency with, and the attractiveness of, the internet and its digital opportunities might prove to be such a key asset as to resort to these new media also in pediatric healthcare. Innovative treatment options and the ex-

tensions of existing practices for common mental disorders and somatic diseases are urgently needed, as uptake rates and service utilization of conventional evidence based psychological treatments are low in children and adolescents (Chavira, Stein, Bailey, & Stein, 2004; Costello, He, Sampson, Kessler, & Merikangas, 2014; Essau, 2005; Merikangas et al., 2011; Zachrisson, Rödje, & Mykletun, 2006). Structural barriers to the uptake of face-to-face treatments lie, for example, in the shortage of healthcare services, long waiting times, and high treatment costs (Andrade et al., 2014; Gulliver, Griffiths, & Christensen, 2010; Mohr et al., 2010); individual barriers comprise limitations in mobility and time, prejudices about therapists and treatments, and fear of stigmatization (Andrade et al., 2014; Gulliver et al., 2010; Mohr et al., 2010).

Internet- and mobile-based interventions (IMIs) offer several advantages over conventional approaches and might contribute to overcoming these treatment barriers, leading to a more comprehensive evidence based healthcare for children and adolescents (Andersson & Titov, 2014; Emmelkamp et al., 2014). This review defines IMIs as predominantly self-guided psychosocial interventions implemented by means of a prescriptive online program or mobile-based app, used by individuals seeking health-related support (Barak, Klein, & Proudfoot, 2009; Domhardt, Ebert, & Baumeister, 2018). These interventions aim to create positive behavior and symptom change, improve knowledge, awareness, and understanding by means of the delivery of health-related material, use of (inter)active components, and deployment of internet- and mobile-based therapeutic techniques (Barak et al., 2009; Domhardt et al., 2018). IMIs can be implemented as stand-alone interventions (Ebert et al., 2018), as part of a blended-therapy approach (Erbe, Eichert, Riper, & Ebert, 2017), or as low-intensity intervention in a stepped-care model (Domhardt & Baumeister, 2018), partly also called a sequential stepping-up blended therapy approach (Ebert et al., 2018; Erbe et al., 2017).

A major advantage of IMIs compared to conventional psychosocial interventions is their ability to be integrated flexibly into the daily life of the user, irrespective of the constraints of space and time. They may decrease time for travel and administration, reduce stigma threat by preserving anonymity, and allow individuals to work at their own pace with automated feedback on personal progress consecutively. Furthermore, IMIs might be particularly attractive from a public-health perspective, given their presumed potential with regard to scalability and cost-effectiveness (Andersson & Titov, 2014; Emmelkamp et al., 2014).

The evidence base of IMIs for most common-mental and some somatic disorders in adulthood has been firmly established. Solid and further growing evidence indicates that IMIs are efficacious in the treatment of depression (e.g., Königbauer, Letsch, Doebler, Ebert, & Baumeister,

2017; Richards & Richardson, 2012) and anxiety disorders (e.g., Arnberg, Linton, Hultcrantz, Heintz, & Jonsson, 2014; Olthuis, Watt, Bailey, Hayden, & Stewart, 2016), with comparable effect sizes to conventional face-to-face therapies at posttreatment (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014). Further meta-analytic evidence for the efficacy of IMIs was found for a range of other mental disorders such as posttraumatic stress disorder (Kuester, Niemeyer, & Knaevelsrud, 2016), obsessivecompulsive disorder (Dèttore, Pozza, & Andersson, 2015), and eating disorders (Melioli et al., 2016). There is also evidence from randomized controlled trials that IMIs work in the (co)treatment for some somatic conditions with significant psychosocial aspects (Andersson, 2016; Bendig et al., 2018). Among these somatic diseases are chronic pain (Baumeister et al., 2015; Lin et al., 2017), diabetes (Ebert et al., 2017; Nobis et al., 2015), and tinnitus (Andersson, 2015; Andersson, Strömgren, Ström, & Lyttkens, 2002) - to name only a few.

Compared to the empirical foundation of IMIs in numerous conditions for adults, the evidence base of IMIs for mental disorders and somatic diseases in children and adolescents is rather narrow, but evolving, given a range of recent randomized controlled trials (e.g., Spence, Donovan, March, Kenardy, & Hearn, 2017; Stjerneklar, Hougaard, Nielsen, Gaardsvig, & Thastum, 2018; Yap et al., 2018) and the particular dynamics in this research domain. Still, comprehensive and integrated meta-analytic knowledge on the efficacy of IMIs for children and adolescents in various health conditions is pending, as the only review of meta-analyses (i.e., meta-review) published so far is confined to mental disorders (Hollis et al., 2017) and characterized by the simultaneous consideration of diverse on- and offline-based technology-delivered interventions. Moreover, important research questions about the specific factors, design features, and developmentally necessary adaptations of IMIs for this young target group are largely unsettled to date, and the generalizability of findings from adult populations is questionable. Most prominently, information about the required intensity and amount of human support ("guidance") provided by e-coaches and caregivers in these online-based self-help interventions for children is essential (Baumeister, Reichler, Munzinger, & Lin, 2014). Scientifically informed knowledge about this and other issues is central to maximizing treatment outcomes and warranting the safety of internet-based interventions for children and adolescents.

In this systematic review, we aim 1) to provide a comprehensive overview of meta-analyses on the efficacy of IMIs for common mental disorders and somatic diseases in children and adolescents. By critically evaluating the existing meta-analyses in this field, we also intend 2) to identify specific (design) features, intervention components

and factors that are associated with the efficacy of IMIs in this younger age group (i.e., moderators of treatment effects) as well as 3) to highlight key areas for future research. The meta-review approach was chosen in order to provide readers with a comprehensive overview on the broad scope of IMIs for mental disorders and somatic diseases in children and adolescents.

Methods

Inclusion Criteria

Meta-analyses were eligible for inclusion if they met all of the following criteria:

Population: (1) Meta-analyses focused on studies with children and adolescents (aged O-18 years). (2) Participants met diagnostic criteria according to a classification system (e.g., ICD-10, DSM-IV, or DSM-5) for at least one mental disorder or somatic disease, or indicated significant symptom burden assessed by means of self- or observer- report data.

Intervention: (3) Meta-analyses investigated psychosocial interventions that are internet or mobile based (e.g., through webpages, e-mail, chat, videoconference, mobile app, or instant messaging). These IMIs could have been complemented with an initial face-to-face contact or regular phone calls if the main part (i.e., more than half of the time invested per participant) of the intervention was carried out online. Computerized or technology-delivered psychosocial interventions eligible for inclusion had at least one intervention component provided via the internet. (4) Furthermore, IMIs had a psychotherapeutic orientation and were based on an established psychotherapeutic approach, as defined by Kampling and colleagues (2014). Health behavior modification approaches had to be in a direct relation to a present somatic condition. Meta-analyses on IMIs with a prevention or rehabilitation focus were not included, because we wanted to specifically concentrate on psychosocial interventions delivered in an online setting addressing clinically relevant symptoms of common mental disorders or somatic diseases.

Control group: (5) Meta-analyses had to include studies with an active (e.g., face-to-face intervention, other IMI) or passive control group (e.g., placebo, treatment as usual/usual care, waiting-list control). Only meta-analysis reporting between-group effect sizes were included.

Outcomes: (6) Systematic reviews had to report at least one meta-analytical result on (a) the efficacy on symptom seve-

rity or (b) treatment adherence (i.e., the degree to which a person's behavior matches with medical or health advice given by a healthcare professional or self-management treatment regime) as outcomes in children and adolescents. Furthermore, meta-regression or moderator analyses on design features and factors that are associated with the efficacy of IMIs were eligible for inclusion as well as meta-analytical comparisons of intervention components. Of note, the secondary outcome of treatment adherence was chosen, because there is some evidence that this outcome is especially important in several chronic somatic diseases (Bendig et al., 2018); other possible relevant outcomes, like level of functioning or quality of life, were not considered because of the limited space for this meta-review.

Study design: (7) Meta-analyses were based on at least three randomized controlled trials (RCTs). The majority of primary studies included in a meta-analytical comparison had to be internet based.

Publication type: (8) Eligible meta-analyses had to be written in English or German and published in a peer-reviewed journal. Narrative reviews, scoping reviews, systematic reviews without a meta-analytical quantification of effect sizes, commentaries, dissertations, or other publication types were not included.

Search Strategy, Study Selection and Data Extraction

Relevant meta-analyses were identified in March 2018 by means of a systematic literature search in the electronic databases PsycINFO and MEDLINE/PubMed with no restriction on dates of inception. The search strategy employed a combination of search terms including the target population (i.e., children or adolescents), treatment delivery (internet, online, web, digital, etc.), and type of treatment (e.g., exposure, intervention, etc.). The full list of search strings can be found in the electronic supplementary material to this article (ESM). Additionally, we scanned the reference lists of included articles. Two reviewers (MD and LS) independently reviewed the studies for inclusion or exclusion and extracted the data of eligible meta-analyses.

Quality Assessment

In order to assess the methodological quality of meta-analyses included, we applied the AMSTAR-2 checklist (Shea et al., 2017). Each included meta-analysis was assessed independently by two reviewers (MD and LS) with regard to all 16 items of the AMSTAR-2 checklist, with any disagree-

ments discussed to reach consensus. The rating options for every item in this checklist are "Yes" and "No" as well as "Partially yes" (for items 2, 4, 7, 8, and 9), with "Yes" indicating the highest quality with regard to the respective item (Shea et al., 2017).

Results

Study Selection

The systematic literature search revealed a total of 897 records after the removal of duplicates. By screening the titles and abstracts, we identified 13 meta-analyses as potentially eligible and examined in full text review. In the end, eight meta-analyses were found to be eligible and included in this review (Ebert et al., 2015; Pai & McGrady, 2014; Pennant et al., 2015; Podina, Mogoase, David, Szentagotai, & Dobrean, 2016; Rooksby, Elouafkaoui, Humphris, Clarkson, & Freeman, 2015; Velleman, Stallard, & Richardson, 2010; Vigerland et al., 2016; Ye et al., 2014). Further details of the search process and inclusion of meta-analyses can be found in the PRISMA Flow Chart (Figure 1).

Characteristics of Meta-Analyses Included

The main characteristics of the meta-analyses included are summarized in Table 1. The meta-analyses were published between 2010 and 2016, with the last search dating back from March 2016 (Vigerland et al., 2016). They included 8,417 children and adolescents in total. Because most meta-analyses (k = 5) included studies not only limited to children and adolescents, but also incorporated studies with young adults, the age of included participants ranges between 2 and 29 years. Target diagnoses were depression (k = 3), anxiety (k = 5), chronic pain (k = 1), or unspecified health conditions (k = 2). Control conditions were nonactive (k = 5), face-to-face therapy (k = 2), a nontherapeutic control or active intervention (k = 1), a waiting-list control or computerized educational program (k = 1), and unspecified conditions like treatment as usual or education groups (k = 1).

Ebert et al. (2015) included interventions delivered via computer, internet, or mobile applications based on cognitive behavioral therapy (CBT) principles, whereas delivery via an internet platform was the most common type. Pennant et al. (2015) incorporated any form of computerized therapies which varied between conventional CBT approaches and dynamic gaming-type interventions. The inclusion criteria of Podina et al. (2016) covered diverse multimedia platforms (e.g., computerized or internet-delivered virtual reality [VR] environments, web confe-

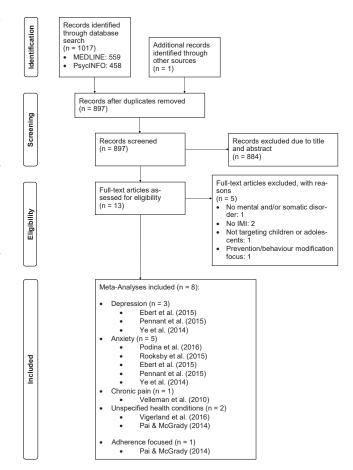


Figure 1. PRISMA Flow Chart

rences). Rooksby et al. (2015) summarized the results of several online and computer-assisted CBT programs. The included interventions in the meta-analysis of Velleman et al. (2010) covered CD-ROM-based and internet-based (self-help) interventions. The iCBT (internet-based cognitive behavioral therapy) definition of Vigerland et al. (2016) covered therapist-guided self-help interventions, in which a website provided content in form of texts, audio files, or videos. All interventions included in the meta-analysis of Ye et al. (2014) adhered to CBT principles and were internet and/or mobile based. In contrast to the seven symptom-focused meta-analyses mentioned above, the meta-analysis of Pai and McGrady (2014) evaluated the efficacy of online-based and conventional psychosocial interventions to promote treatment adherence.

Overall, the meta-analyses included considered a wide range of internet- and mobile-based psychosocial interventions, target diagnoses, age ranges, and control conditions; thereof, clinical heterogeneity can be considered as substantial, and we abstained from further meta-analyzing and integrating the effect sizes of the meta-analyses included.

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Table 1. Meta-analyses included concerning internet- and mobile-based interventions for mental and somatic disorders in children and adolescents.

Meta-analyses	Age range	Target diagnosis	Control conditions	No. of RCTs	Participants included	Effect size/SMD ^a	[95 % CI]
Symptom focused	ō						
Ebert et al. (2015)	6-25 years	Depression, anxiety or both	Nonactive control condition	13 7 4	796	Overall: g = .72 Anxiety: g = .68 Depression: g = .76	.55 to .90 .45 to .92 .41 to 1.12
Pennant et al. (2015)	11-25 years	Risk of/diagnosed anxiety disorders or depression	Nontherapeutic control or active intervention	9 /	220 279	Anxiety: .77 ^b Depression: .62 ^b	.09 to 1.45
Podina et al. (2016)	7-18 years	Anxiety	Waiting-list control or face-to-face treatment	ω ∞	404	vs. Waitlist-control: g = 1.4 vs. Face-to-face: g = .30	.38 to 2.44 53 to 1.12
Rooksby et al. (2015)	7-16 years	Anxiety	Waiting-list control	വ	219	۹69°.	.44 to .94
Velleman et al. (2010)	7-18 years	Chronic Pain	Waiting-list control or computerized educational program	4	150	.41 ^b	.07 to .74
Vigerland et al. (2016)	3-21 years	Identified psychiatric or somatic condition (or problem)	Waiting-list control Active control Face-to-face	7	1882	Overall: g = .62 Psychiatric: g = 1.27 Somatic: g = .49 vs. Active control: g = .10	.41 to .84 .96 to 1.59 .33 to .64 32 to .52
Ye et al. (2014)	7-25 years	Anxiety and depression	Waiting-list control or face-to face	0	9 2 2 2 3	vs. Waiting-list control: • Anxiety: .52 ^b • Depression: .16 ^b vs. Face-to-face: • Anxiety:08 ^b • Depression: 1.32 ^b	.14 to .90 12 to .44 50 to .35 26 to 2.90
Adherence focused	pe						
Pai & McGrady (2014)	2-29 years	Chronic health condition	Usual care conditions, education groups and other	23 23 6	3898	Adherence:° • Posttreatment: d = .20 • Follow-up: d = .29 Only web-based: d = .25	.08 to .31 .15 to .43 .10 to .40

Note. = positive effect sizes indicate treatment effects in favor of the internet- or mobile-based intervention at posttreatment. = specific method used to compute SMD was not provided. = only 26.1% of the ncluded studies were classified as web-based.

Quality Assessment

The methodological quality of the meta-analyses included was assessed deploying the AMSTAR-2 rating scale (Shea et al., 2017). The initial accordance between the two independent reviewers (MD and LS) was close to 90% across all meta-analyses, with discrepancies solved by discussion. The results of the quality assessment on each item can be found in Table 2. The overall quality of the meta-analyses included can be appraised as acceptable. At least half of the meta-analyses included were rated with partial to good quality ("Partial yes" or "Yes") with regard to information about PICO (participant, intervention, control condition, outcome; item 1), comprehensive literature search strategy (item 4), study selection in duplicate (item 5), data extraction in duplicate (item 6), list of excluded studies (item 7), study description in detail (item 8), risk of bias (RoB) assessment (item 9), appropriate methods for statistical combination of results (item 11), explanation and discussion of heterogeneity (item 14), and report of any potential sources of conflict of interest (item 16). The remaining items were rated as low in quality ("No") in the majority of meta-analyses included, with items 2, 3, and 10 being the least met (study protocol, explanation for the selection of study design, and report on the sources of funding for the studies included in the review).

Efficacy of IMIs for Children and Adolescents

Between-group effect sizes for IMIs in different mental disorders and somatic diseases range from SMD = .16 to 1.4 when compared to active- and nonactive controls. Most effect sizes can be classified as moderate, with effect sizes for mental disorders tending to be higher than those for somatic conditions. Cohen's d and Hedges' g were both applied in the meta-analyses included. Both statistics are denoted consistently as standardized mean differences (SMDs) in the following paragraphs; information of the actual effect size formula deployed in the respective meta-analysis can be found in Table 1.

Ebert et al. (2015) investigated the efficacy of computer- and internet-based cognitive-behavioral treatments (cCBT) for treating depression and anxiety symptoms in youth. The overall mean effect size posttest was SMD = .72 (95% CI: .55 to .90; s = 13 studies), whereas cCBT was superior over nonactive controls for interventions targeting specifically anxiety (SMD = .68; 95% CI: .45 to .92; s = 7) and depression (SMD = .76; 95% CI: .41 to 1.12; s = 4) as well as for transdiagnostic treatments (SMD = .94; 95% CI: .23 to 1.66; s = 2); of note, the latter meta-analyti-

cal comparison is based only on two studies. Pennant et al. (2015) also focused on anxiety and depression and found positive effects of cCBT on symptoms in young people aged between 12 and 25 years that are at risk of, or diagnosed with, anxiety disorders (SMD = .77; 95% CI: .09 to 1.45; s = 6) or depression (SMD = .62; 95% CI: .11 to 1.13; s = 7) when compared to active interventions or nontherapeutic control conditions. In this meta-analysis, there was no clear evidence with regard to the efficacy of IMIs in children (5-11 years) (Pennant et al., 2015). Studies investigating exclusively anxiety disorders were included in the meta-analyses of Podina et al. (2016) and Rooksby et al. (2015). Podina et al. (2016) found evidence that cognitive-behavioral therapy via electronic and technological devices or applications (eCBT) might be equally efficacious as standard cognitive-behavioral therapy (SMD = .30; 95 % CI: -.53 to 1.12; s = 8) and more efficacious than a waiting-list control (SMD = 1.4; 95 % CI: .38 to 2.44; s = 6) in children and adolescents (7–18 years). Rooksby et al. (2015) investigated the efficacy of internetdelivered CBT for pediatric anxiety disorder, and their results suggest that the programs are both comparably efficacious to clinic-based CBT when compared to waiting-list control (SMD = .69; 95% CI: .44 to .94; s = 5). Velleman et al. (2010) focused on four studies on chronic pain and found evidence that children and adolescents completing a cCBT treatment are more likely to experience a posttreatment symptom reduction than those in the waiting-list control or computerized educational program control group (SMD = .41; 95 % CI: .07 to .74; s = 4). Vigerland et al. (2016) summarized studies investigating the efficacy of internet- and mobile-based interventions (iCBT) for identified mental or somatic conditions and found that iCBT showed superior effects when compared to waiting-list (SMD = .62; 95 % CI: .41 to .84; s = 24). For mental-health conditions, the effect size was SMD = 1.27(95% CI: .96 to 1.59; s = 11), with anxiety disorders being the most common mental disorder included (six studies); for somatic conditions the effect size was SMD = .49 (95% CI: .33 to .64; s = 13), with pain being the most common somatic condition (five studies). When iCBT-interventions were compared to active controls in a subgroup analysis, no significant differences emerged (SMD = .10; 95% CI: -.32 to .52; s = 3). However, at the same time, iCBT was not inferior when compared to conventional face-to-face CBT (SMD = .22; 95% CI: -.07 to .50; s = 3). Ye et al. (2014) again concentrated on anxiety and depression. Their results showed both reduced anxiety symptom severity (SMD = .52; 95% CI: .14 to .90; s = 6) and increased remission rate (pooled remission rate ratio = 3.63; 95% CI: 1.59 to 8.27; s = 3) for internet-based interventions compared to waiting-list control. They found no statistically significant effect size of IMIs for

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Item 14 Item 13 Item 12 Item 11 Item 10 Item 9 Item 8 Item 7 Item 6 Item 5 Item 4 Item 3 Item 2 Item 1 Meta-analyses

Meta-analyses	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16
Symptom focused	р															
Ebert et al. (2015)	Yes	Partial yes	o N	Partial yes	Yes	Yes	Yes	Partial yes	Partial yes	o N	Yes	Yes	Yes	Yes	Yes	Yes
Pennant et al. (2015)	Yes	o Z	o Z	Partial yes	Kes	Yes	Yes	Partial yes	Yes	Yes	Yes	o Z	°Z	Yes	o Z	Yes
Podina et al. (2016)	Yes	°Z	°Z	Partial yes	Kes	° Z	Partial yes	Partial yes	0 Z	°Z	o Z	°Z	o Z	Yes	Xes	Yes
Rooksby et al. (2015)	°Z	°Z	°Z	Partial yes	°Z	° Z	o Z	o Z	Partial yes	°Z	Yes	°Z	Yes	Yes	o Z	o Z
Velleman et al. (2010)	Yes	°Z	°Z	Partial yes	Yes	° Z	o Z	Yes	0 Z	°Z	Yes	o Z	°Z	Yes	o Z	o Z
Vigerland et al. (2016)	Yes	°Z	Yes	Partial yes	Yes	° Z	Yes	o Z	* N	°Z	**	o Z	°Z	Yes	Yes	Yes
Ye et al. (2014)	Yes	Partial yes	o N	Partial yes	Yes	Yes	o Z	Yes	Yes	o N	Yes	Yes	Yes	o N	o N	Yes
Adherence focused	pə															
Pai & McGrady (2014)	Kes	o Z	Yes	Partial yes	o N	Yes	Partial yes	o Z	Yes	o N	Kes	Kes	Xes.	o N	o Z	Yes

data extraction in duplicate? Item 7: Did the review authors provide a list of excluded studies and justify the exclusions? Item 8: Did the review authors describe the included studies in adequate detail? Item 9: Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? Item 10: Did the review authors report on the sources were established prior to the conduct of the review, and did the report justify any significant deviations from the protocol? *Item 3*: Did the review authors explain their selection of the study designs for inclu-5. Did the review authors perform study selection in duplicate? Item 6: Did the review authors perform **Note. Item 1:** Did the research questions and inclusion criteria for the review include the components of PICO? Item 2: Did the report of the review contain an explicit statement that the review methods sion in the review? Item 4: Did the review authors use a comprehensive literature search strategy? Item of funding for the studies included in the review? *Item 11:* If meta-analysis was performed, did the re-

was performed, did the review authors assess the potential impact of RoB in individual studies on the view authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? Item 15: If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact view authors use appropriate methods for statistical combination of results? Item 12: If meta-analysis results of the meta-analysis or other evidence synthesis? Item 13: Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review? Item 14: Did the reon the results of the review? Item 16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?; * = NRSIs (nonrandomized studies of interventions) also investigated; ** = No meta-analysis included for NRSIs (nonrandomized studies of interventions).

Table 2. AMSTAR-2 Rating of included meta-analyses.

anxiety when compared to face-to-face therapy (SMD = .08; 95% CI: -.35 to .50; s = 2); of note, this comparison was based only on two studies. For depression, no significant effect for symptom severity when compared to waiting-list control was found (SMD = .16; 95% CI: -.12 to .44; s = 7). Again, the comparison of IMIs vs. face-to-face therapy was based only on two studies and was nonsignificant (SMD = -1.32; 95% CI: -2.90 to .26; s = 2). Lastly, Pai and McGrady (2014) investigated the efficacy of online- and nononline adherence-promoting interventions for children and adolescents with chronic health conditions and found small effect sizes both at posttreatment (SMD = .20; 95% CI: .08 to .31; s = 23) and at follow-up (SMD = .29; 95% CI: .15 to .43; s = 9). The authors did not find differences between the type of intervention deliveries: Online-based interventions were as efficacious as well (SMD = .25; 95 % CI: .10 to .40; s = 6).

Moderators and Intervention Components

Four of the eight meta-analyses included also conducted subgroup analyses to investigate sources of heterogeneity and to provide information about possible moderators. In this context, all four studies investigated the possible moderator variable age. Ebert and colleagues (2015) showed that studies aimed at adolescents achieved better results compared to those in children and mixed samples, which mirrors findings of Podina et al. (2016), who also found that older participants benefited more from IMIs for anxiety. In contrast, Vigerland et al. (2016) found no significant moderating effects of age in diverse conditions. Pennant et al. (2015) also found no moderating effects of age in studies for depression, whereas studies for anxiety showed significant moderating effects of age, in that the intervention effect was greater in studies in participants aged 18-25 years compared to those aged 12-17 years.

Participants with elevated symptom scores (undiagnosed population) showed greater effects than those with a diagnosed disorder in studies for anxiety but not in those for depression (Pennant et al., 2015).

With regard to human support, Podina et al. (2016) showed that therapist involvement (conceptualized after Newman, Szkodny, Llera, & Przeworski, 2011) significantly moderated the effect size with minimal therapist involvement yielding higher effect sizes compared to the significant therapist involvement group (e.g., additional face-to-face meetings or online patient-therapist interactions during the online intervention), whereas Pennant et al. (2015) found no moderating effect of therapist input (divided into "minimal" and "some" input) in studies for depression. Ebert et al. (2015) found no effect for parental involvement.

Vigerland et al. (2016) found moderating effects of different types of outcome ratings, with clinician ratings resulting in the highest effect sizes, whereas Pennant et al. (2015) found no effect for source of outcome assessment. Ebert et al. (2015) found no significant moderating effect of target condition or diagnosis, and Vigerland et al. (2016) found no significant effects for treatment duration.

Discussion

In this review we provided an overview of meta-analyses of internet- and mobile-based interventions for children and adolescents in various health conditions. By means of a systematic literature search, we included eight meta-analyses on different mental-health and somatic conditions in youth. Overall, we found meta-analytical evidence that IMIs achieve moderate to large effect sizes in depression and anxiety (Ebert et al., 2015; Pennant et al., 2015; Podina et al., 2016; Rooksby et al., 2015; Vigerland et al., 2016; Ye et al., 2014) and moderate effect sizes in the cotreatment of some somatic disorders (Velleman et al., 2010; Vigerland et al., 2016) when compared to nonactive controls. A finding that mirrors the meta-analytic evidence in adults (Andersson, 2016; Bendig et al., 2018), although effect sizes generally tend to be higher in adult populations. The most comprehensive meta-analytical evidence base of IMIs for children and adolescents can be found for anxiety disorders, with medium to large effect sizes, following depression with medium effect sizes, substantiated by several meta-analyses. The moderate effect size of IMIs for chronic pain is based on only one meta-analysis.

Knowledge of moderators of treatment effects in IMIs for children and adolescents is still scarce and inconsistent. In sum, three meta-analyses found evidence for the moderating effect of age (Ebert et al., 2015; Pennant et al., 2015; Podina et al., 2016), one for symptom severity (Pennant et al., 2015), and one for type of outcome assessment (Vigerland et al., 2016). Moderator analyses for age indicated that older participants achieve better results in IMIs for anxiety disorders (Ebert et al., 2015; Pennant et al., 2015; Podina et al., 2016). This is in line with previous results on IMIs (Hollis et al., 2017) and on conventional face-to-face-psychotherapy for anxiety disorders in youth (Reynolds, Wilson, Austin, & Hooper, 2012), but stands in contrast with the results of the meta-analysis of Vigerland et al. (2016), where age as moderator was nonsignificant in IMIs for various health conditions. Additionally, Pennant et al. (2015) did not find a moderating effect of age in studies for depression.

The moderating effect of disorder severity was previously shown in conventional psychotherapy (Weisz et al., 2013), which echoes the findings of Pennant et al. (2015),

who revealed greater effects for participants with only elevated scores than for those with a diagnosed disorder in IMIs for anxiety, but not in those for depression. The previously proposed importance of parental involvement (Barrett, Dadds, & Rapee, 1996) could not be substantiated in one meta-analysis on IMIs (Ebert et al., 2015), which found no association between the inclusion of parents and better treatment outcomes. Still, in a recent meta-analysis on mobile-based apps for health behavior change in youth, Fedele and colleagues (2017) found evidence that the interventions that included caregivers produced larger effect sizes than those that did not include caregivers. As such, further research is needed to enlarge the limited evidence base and to explore the role of parental support in IMIs in more detail.

The same applies for the role of therapist support (i.e., guidance). Studies with a focus on children tended to have a higher degree of guidance than studies directed to older participants (Pennant et al., 2015; Rooksby et al., 2015). Nevertheless, all moderator analyses of therapist support were nonsignificant, despite the findings from Podina et al. (2016), where the minimal therapist involvement group revealed better outcomes than the significant therapist involvement group for anxious children and adolescents. Still, there is a large evidence base in IMIs for adults in different common mental disorders, suggesting that guided IMIs are more beneficial than completely unguided selfhelp interventions (Baumeister et al., 2014; von Rezori, Geßlein, Baumeister, & Domhardt, submitted). It is possible that in some anxiety disorders minimal therapist input might be sufficient to achieve clinically relevant effects, and that additional intensive guidance might be beneficial especially in patients with lower levels of motivation (Domhardt, Geßlein, von Rezori & Baumeister (in press); Newman, Erickson, Przeworski, & Dzus, 2003). The nonsignificant findings with regard to the role of guidance in most meta-analyses included in this review are probably due to the fact that the majority of examined IMIs had some degree of therapist support, which is why differentiated analyses were not possible. Furthermore, missing data on the actual therapist time invested precluded fine-grained analyses in some meta-analyses (e.g., Vigerland et al., 2016). Therefore, a standardization with regard to the degree of therapist support (e.g., Newman et al., 2011) as well as the investigation of the impact of guidance on intervention adherence in future research are worthwhile, as high attrition and drop-out rates are a common problem in IMIs.

At the moment, evidence-based knowledge on design features and intervention components for IMIs in children and adolescents is rather limited. Thus, recommendations on how to best design and adapt IMIs for youth are largely intuitive and based on practical experiences to date. This applies to the role of parental support and guidance by e-

coaches, which ought to be provided in IMIs especially for children and younger adolescents. Guidance by e-coaches might be central to warranting the safety of interventions and secure, that nonresponding youth are referred to service supplies of higher intensities. The design, content, and presentation of material of IMIs should be all adapted to the age and developmental needs of the respective target group (Stasiak et al., 2016). Qualitative research designs (e.g., focus groups or think-aloud interviews) might help to detect the specific needs of children and adolescents, which could be later complemented by specific methods for the formative development of intervention packages of IMIs (e.g., Collins, Murphy, & Strecher, 2007). Furthermore, the Persuasive System Design (PSD) framework might highlight intervention components that are associated with greater user satisfaction and engagement with IMIs (such as "credibility," "dialogue support," "liking and similarity," "reduction and tunneling of therapeutic content" or "use of self-monitoring"), all contributing to improved functioning (Wozney et al., 2017). In consideration of relatively high drop-out rates, potential further acceptance- and adherence-facilitating features (such as interactive quizzes, videos, or cartoons) should be integrated in the intervention, although comprehensive empirical proof for a gamification approach and the other recommendations listed above has yet to be brought forward.

Limitations

When interpreting the findings of this meta-review, several limitations pertaining to the review itself, the meta-analyses included as well as their respective primary studies should be considered. The present systematic review of meta-analyses itself might be limited by the small number and heterogeneity of meta-analyses included as well as the omission of an a priori published study protocol. Because of the clinical heterogeneity of eligible meta-analyses, no meta-analytical integration of effect sizes of the meta-analyses was carried out. Moreover, because of the limited and inconsistent evidence base, no robust conclusions can be drawn on the critical (design) features and intervention components for this age group up to now.

The eight reviewed meta-analyses themselves are based on a limited number of primary studies (Ebert et al., 2015; Pai & McGrady, 2014; Pennant et al., 2015; Velleman et al., 2010; Vigerland et al., 2016). Furthermore, most of the meta-analyses on mental disorders were limited to anxiety and depression, and the effect sizes of IMIs were most often calculated in comparison to nonactive control groups. So far, only three meta-analyses included in the current meta-review report effect sizes for IMIs in

comparison to face-to-face therapy based on a very low number of primary studies (Podina et al., 2016; Vigerland et al., 2016; Ye et al., 2014). Additionally, the findings have to be interpreted in the light of the heterogeneity of included primary studies regarding treatment format (Ebert et al., 2015), outcome assessment (Pennant et al., 2015; Vigerland et al., 2016), design and sample sizes (Rooksby et al., 2015), intervention duration, outcome follow-up length and baseline differences (Ye et al., 2014), and the diversity of populations and adherence targets (Pai & McGrady, 2014). Likewise, the generalizability is limited because included primary studies were most often conducted in high-income countries (e.g., Ebert et al., 2015) and participants referred themselves to the intervention or where nonsystematically selected (e.g., Rooksby et al., 2015). Overall, the quality rating of the eight meta-analyses indicated some methodological weaknesses and a comprehensive examination of different intervention components is still unresolved, in order to determine the active ingredients of IMIs.

Future Directions

We identified several important gaps in the literature that represent key areas for future research on IMIs for children and adolescents. First of all, because the meta-analyses included could only resort to a rather narrow number of primary studies, it is central to conduct further RCTs in order to enlarge the evidence base for the efficacy of IMIs, especially with regard to children and younger adolescents (≤12–14 years). Additionally, it is also central to further determine the long-term treatment effects of IMIs in this younger age group as well as to conduct direct comparisons of IMIs against face-to-face therapies, since only few studies provided such information. Second, integrated and meta-analytical knowledge on the cost-effectiveness of IMIs for children and adolescents is imminent and urgently needed, so that the often presumed advantage of IMIs with regard to health economic costs, scalability, and reduced therapist time can be validated and corroborated (Boydell et al., 2014; Hollis et al., 2017). Third, despite the overall importance of information on possible adverse events of IMIs, the evidence base for children and adolescents lags behind the field in adults, where comprehensive knowledge on the safety of these interventions already exists (Ebert et al., 2016; Karyotaki et al., 2018). Future studies should routinely capture the safety of IMIs and address this issue in corresponding publications, providing the opportunity to integrate knowledge in specific systematic reviews and meta-analyses. Fourth, more research on moderators is necessary to answer the question for whom IMIs work and for whom they work best. Besides the identified moderators in this review (Table 3), research on the active intervention components of IMIs in direct comparisons (i.e., dismantling or additive design studies; e.g., Borkovec & Castonguay, 1998) is worthwhile. In a similar vein, future studies on the mediators and mechanisms of change in IMIs for children and adolescents is valuable, in order to guarantee the efficacy of newly developed interventions and maximize treatment packages. Fifth, considering that most meta-analyses included are based on primary studies with clinical samples, important future directions lie in considering efficacy studies in nonclinical and general populations as well as determining the efficacy in specific populations of children and adolescents with chronic medical conditions. Finally, beside the possible advantages of IMIs outlined above, these interventions might also be prone to several constraints and special challenges, which should all be considered in future research. Among the possible limitations of IMIs are different issues such as data-safety concerns, appropriate diagnostic procedures, restricted capabilities in crises intervention, high dropout rates, and the limited knowledge on possible negative effects or contraindications to this point (for an in-depth review of the pros and cons of IMIs see Andersson & Titov, 2014).

Conclusion

This meta-review suggests that internet- and mobile-based interventions are efficacious in some (mental)-health conditions for youths, with moderate effect sizes on average. At present, the evidence base is substantiated for anxiety disorders, depression, and chronic pain – at least for the short-term, in older participants (adolescents) and when compared to waiting-list. However, because the current evidence is restricted to a rather small sample of meta-analyses based on a limited number of primary studies, and several important research questions are not (sufficiently) answered up to now, future and ongoing high-quality research is needed to comprehensively assess the potential of IMIs to improve access to evidence-based (mental) healthcare for children and adolescents.

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 Table 3.
 Moderators and intervention components of included meta-analyses.

Meta-analyses	Significant moderators	Nonsignificant moderators	Intervention components
Symptom focused	P		
Ebert et al. (2015)	 Age: better results in studies aimed at older participants (adolescents) 	Target conditionConfirmation of disorderParental involvementRisk of bias	ı
Pennant et al. (2015)	 Age (for studies for anxiety): greater effect for older participants (same subgroups of studies as for severity) Severity (for studies for anxiety): greater effects for studies in young people with only elevated symptom scores compared with studies of young people with diagnosed anxiety disorders 	 Age (for studies for depression) Severity (for studies for depression) 	Comparisons of ABM, CBM-1, cPST, and a mobile-phone application with nontherapeutic controls showed inconclusive findings Therapist involvement/guidance: for studies for depression there was no conclusive difference between subgroups
Podina et al. (2016)	Age: older participants show greater clinical benefits	Source of anxiety assessment	 Therapist involvement/guidance: minimal therapist involvement condition most efficacious
Rooksby et al. (2015)		ı	
Velleman et al. (2010)		ı	
Vigerland et al. (2016)	Outcome measurement: highest effect size with clinician ratings (significant higher than child self-report ratings and physiological measures); no significant difference between parent ratings and clinician ratings	Sample sizeTreatment durationAgeStudy quality	
Ye et al. (2014)		ı	
Adherence focused	pə		
Pai & McGrady (2014)		1	1

Note. ABM = Attention bias modification. CBM-I = Cognitive bias modification of interpretations. cPST = Computerized problem-solving therapy.

Electronic Supplementary Material

The electronic supplementary material (ESM) is available with the online version of the article at doi 10.1024/1422-4917/a000625.

ESM 1. Table.

Search strings for PsycINFO and MEDLINE/Pubmed in Ovid.

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