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Closing the treatment gap in low-income countries: outlining a culturally sensitive digital self-guided intervention for adolescents with anxiety disorder.

HOVEDOPPGAVE

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Forord

Bakgrunnen for oppgaven kommer fra et langvarig engasjement for en bistandsorganisasjon (Streetlight) som arbeider på Filippinene for å gi gatebarn og barn fra fattige familier en tryggere fremtid. Etter flere perioder med frivillighetsarbeid for denne organisasjonen, vokste det frem et stort ønske om å bidra mot å bedre disse barnas psykiske helse. Jeg ønsker først og fremst å rette en stor takk til min fantastiske veileder, Tine Nordgreen, for uvurderlig god hjelp gjennom hele prosessen. Hennes kunnskap, positivitet, tålmodighet og umiddelbare tilgjengelighet for alt av spørsmål har vært berikende bidrag, og svært betydningsfullt for resultatet. Jeg ønsker også å rette en takk til familien min som har hatt troen på meg og støttet meg. Videre er det mange i klassen min som fortjener en stor takk for positive stunder gjennom et langt semester, de har vært verdifulle for meg. Særlig vil jeg rette en takk til Christoffer og Julie som har bidratt med ekstra støtte og behjelpelighet i en krevende og travel innspurt. Sist, men ikke minst, ønsker jeg å takke organisasjonen Streetlight og alle barna jeg har vært så heldig å få bli kjent med under mine besøk der, for opplevelser som har formet meg som medmenneske.

Sammendrag

Angstlidelser er utbredt og starter ofte i ungdomsårene. På grunn av begrenset tilgang til effektiv behandling, spesielt i lav- og mellominntektsland, forblir mange ungdommer ubehandlet. For å lukke dette behandlingsgapet har digitale intervensjoner blitt prøvd ut og viser lovende effekter. Imidlertid eksisterer det få digitale intervensjoner som er kulturelt sensitive. I denne artikkelen vil jeg skissere en fremtidig kulturelt sensitiv, digital intervensjon for behandling av ungdom med angstlidelser i lavinntektsland. I første fase ble intervensjonsstudier som undersøkte effekten av digitale intervensjoner for ungdom med angstlidelse og symptomer identifisert og gjennomgått. I fase to de viktigste terapeutiske elementene i de inkluderte intervensjonene identifisert. I fase tre ble elementer fra kulturelle tilpasningsrammer identifisert. I fase fire, i henhold til et rammeverk for å utvikle komplekse intervensjoner fra Medical Research Council, ble en ny intervensjon skissert. Totalt 22 relevante artikler ble inkludert, og disse viste effekt til fordel for digitalt levert kognitiv atferdsterapi. De identifiserte effektive kjerneelementene var kognitive komponenter (som blant annet psykoedukasjon, kognitive restrukturering og problem-løsning) og atferdskomponenter (som blant annet eksponering, atferdseksperiment og avslapningsøvelser). Tre ramme for kulturell tilpasning av psykologisk behandling ble identifiser, og felleselementer ble avdekket (som blant annet å samarbeide med eksperter for å kunne tilpasse språk, eksempler, objekter, metode og kontekst). Basert på disse funnene ble en kulturell, digital intervensjon for behandling av angst hos ungdom i utviklingsland skissert.

Abstract

Anxiety is a common disorder, often with an onset during adolescence. Because of limited access to effective treatment, especially in low- and middle-income countries, many adolescents remain untreated. To bridge this treatment gap, digital delivered psychological therapy has shown promising effects. However, the existence of culturally sensitive digital delivered psychological treatment is scarce. In this paper I will map out a future culturally sensitive digital intervention for treating adolescents with anxiety disorder in a low-income country. Step one was to review clinical effects of digital interventions for adolescents with anxiety disorder and symptoms. Step two was to identify main therapeutic elements of the included interventions. The third step was to incorporate elements from cultural adaptation frameworks. Finally, according to a framework for developing complex interventions from Medical Research Council, a new intervention was outlined. A total of 22 relevant articles were identified, showing large effects for digitally delivered cognitive behavioral therapy. The core elements included in the effective interventions were identified as cognitive components (i.e. psychoeducation, cognitive restructuring and problem solving) and behavioral components (i.e. exposure, relaxation and behavioral experiments). Three cultural frameworks were included, and common elements for adaptation were identified (i.e. collaborating with experts, culturally welcoming environment, language, method, examples). Based on these findings, a future culturally sensitive digital intervention for treating adolescents with anxiety disorder in a low-income country was outlined.

Closing the treatment gap in low-income countries: outlining a culturally sensitive digital self-guided intervention for adolescents with anxiety disorder.

Mental health disorders and symptoms are major contributors to the burden of disease worldwide (Murray et al., 2012; Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015; World Health Organization, 2017). Mental health disorders and symptoms can occur after traumatic life experiences, bullying, neglect, abuse, loss of close relationships, loss of job or financial difficulties. It can as well occur as a result of underlying reasons less obvious, for instance temperament, learnt behavior, brain abnormalities, or genetic factors (Grøholt, Garløv, Weidle, & Sommerschild, 2015), or a combination of the two. Mental health disorders and symptoms often begins in childhood and adolescence (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Kessler et al., 2005; Merikangas, Nakamura, & Kessler, 2009; WHO, 2019), with potential long-term negative effects on the development going from childhood to adulthood (Copeland, Angold, Shanahan, & Costello, 2014; Essau, Conradt, & Petermann, 2002; Essau, Lewinsohn, Olaya, & Seeley, 2014; Rutter, Kim-Cohen, & Maughan, 2006). Therefore, it is a worldwide need for developing scalable, effective and culturally relevant interventions for coping with mental health disorders and symptoms in childhood and adolescence across the globe.

Mental health in adolescence

According to the World Health Organization (WHO), one in four people will experience mental health issues during their lifetime (WHO, 2001). As much as 14% of the global burden of disease can be accounted to mental health disorders (S. L. James et al., 2018). Mental health issues are consequently counted as one of the world's leading challenges and a major cause of non-fatal burden (Hay et al., 2017). Among all mental health issues,

depression and anxiety are the most prevalent mental health disorders (Baxter, Scott, Vos, & Whiteford, 2013; WHO, 2017).

According to WHO half of all mental disorders begin before the age of 14 (WHO, 2019). Large scale population studies from Norway shows that even though children experience good living conditions, with over 90% reporting being satisfied or very satisfied with their lives (Bakken, 2017; Samdal et al., 2016), 7% of children still had symptoms compatible with a psychiatric disorder (Heiervang et al., 2007; Wichstrøm et al., 2012). The most common disorders acquired by children and adolescents have been identified as anxiety, depression, ADHD, disruptive disorder, autism spectrum disorder (Kessler et al., 2012; Polanczyk et al., 2015; Roberts, Roberts, & Xing, 2007).

Anxiety. Prevalence studies report different estimates of anxiety in children and adolescents, ranging from 6-32% (Kessler et al., 2012; Leikanger & Larsson, 2012; Merikangas et al., 2010; Merikangas et al., 2009; Polanczyk et al., 2015; Roberts et al., 2007). Many of the anxiety disorders which develops in adolescence tend to persist if not treated (American Psychological Association, 2013), and furthermore might increase the risk for unemployment, maladjustment, poor coping skills and more chronic stress into adulthood (Essau et al., 2014). Early interventions and treatment for adolescent's mental health issues is therefore very important, and there is a great global need for effective, easily accessible interventions targeting youth anxiety worldwide.

Anxiety disorders are referred to as a state of turmoil and tension, with an anticipation of future threat (Skre, 2019). The underlying mechanisms are composed of three factors - physical symptoms (i.e. increased heart rate, shaking and muscle tension, blushing, sweating and difficulties breathing), cognitions on perceived threats accompanied by negative emotions like fear, and lastly behavioral components such as avoidance or safety strategies

(Abramowitz, Deacon, & Whiteside, 2011). Taken together, these symptoms might lead to impairment of daily functioning (Berge, 2012).

The variation in feared stimuli, or cognitions, is what separates different anxiety disorders roughly speaking. (American Psychiatric Association, 2013; WHO, 1992). The most common anxiety disorders that exists are separation anxiety disorder, general anxiety disorder, social phobia, specific phobias, panic disorder and obsessive-compulsive disorder (Anthony, Frederici, & Stein, 2012).

Treatment for adolescents with anxiety disorders

The most extensively studied and best supported treatment intervention for anxiety is cognitive behavioral therapy (CBT) (Butler, Chapman, Forman, & Beck, 2006; Fenn & Byrne, 2013; Nathan & Gorman, 2015; Reynolds, Wilson, Austin, & Hooper, 2012). Albert Ellis and Aaron Beck have been referred to as the founders and pioneers of CBT (Beck, 1967; Beck & Alford, 2009; Ellis, 1962). They proposed that people interpret and react differently to the same unpleasant events, suggesting that perceptions and appraisals play a big part in mental health (Beck, 1967; Ellis, 1962).

After years of development and research, CBT treatment manuals have been designed to encourage the client to explore the link between thoughts, emotions and behaviors (Abramowitz et al., 2011). In such way, it has been suggested that CBT can provide insight and techniques to impact own mental health, thus many states that CBT teaches the patient to become its own therapists (Fenn & Byrne, 2013). So, by reconstructing maladaptive cognitions and challenging maladaptive behaviors, the individual develops new adaptive strategies to deal with anxiety symptoms that may recur in the future. A key part of this is to expose the client to their fears, in a controlled and systematic manner (Fenn & Byrne, 2013).

One review looked at the effect of CBT on remission of all anxiety disorders. When comparing CBT with both waitlist controls and active controls, they found an overall remission rate of 60,7% for participants receiving CBT (Warwick et al., 2017). Another review found that individual-based CBT and group-based CBT was superior to waitlist controls, non-CBT active controls (attention control) and treatment as usual (Sigurvinsdóttir, Jensínudóttir, Baldvinsdóttir, Smárason, & Skarphedinsson, 2020). Ewing, Monsen, Thompson, Cartwright-Hatton, and Field (2015) looked at the effects of a transdiagnostic CBT intervention compared to a control group and found that CBT provided significant more chance for remission than the control group did. They found that the children in the treatment condition had a 9.15 times bigger chance for recovery.

Several other reviews have also found clear benefits for CBT as an effective treatment for anxiety disorders in childhood and adolescence (Ishikawa, Okajima, Matsuoka, & Sakano, 2007; A. C. James, James, Cowdrey, Soler, & Choke, 2015). Some also found that CBT provided great improvements on general functioning and secondary outcomes (Chu & Harrison, 2007; Kreuze, Pijnenborg, de Jonge, & Nauta, 2018; Scaini, Belotti, Ogliari, & Battaglia, 2016).

Psychological therapies with other theoretical foundations have been extensively researched as well (Bandelow, Michaelis, & Wedekind, 2017). Most notably psychodynamic therapy, interpersonal therapy, emotion-focused therapy and third-generation CBTs (i.e. meta-cognitive therapy, mindfulness therapy, acceptance and commitment therapy) (Anxiety and depression association of America, 2020).Several of these therapies have shown acceptable effectiveness in treating anxiety, however, CBT is recommended as a first treatment for anxiety disorders because of its substantially larger research base (Bandelow et al., 2017).

Worldwide access to CBT for adolescents. Even though effective treatment for anxiety do exist, only a small proportion receive adequate and effective help (Demyttenaere et

al., 2004; Kohn, Saxena, Levav, & Saraceno, 2004). This can be explained by the following barriers;

First, there is a lack of governmental prioritization of mental health, and this is a worldwide problem. Only 1% of the global health workforce works in mental health, and of these only 7% are psychologists (WHO, 2015). This makes treatment for mental health unavailable for many adolescents. Additionally, WHO reports that only 2 out of 3 member states have a stand-alone policy plan for mental health (WHO, 2015). Whereas WHO (2015) reports the median public expenditure on mental health per person as 50 US$ in high-income countries, it was only 2 US$ in low-income countries. Further, the reported median number of mental health beds per 100 000 population was 50 in high-income countries, compared to only 5 in low-income countries.

Second, there is a lack of therapists. Statistics and data from WHO shows that 45% of the world's population lives in a country with less than one psychiatrist per 100 000 people (WHO, 2015). A comparable number is one psychiatrist per every 4000 inhabitants in Norway (Holte, Siem, & Vartdal, 2014).

Third, low mental health literacy hinders adolescents from seeking help, and has been reported in several studies. This includes the lack of ability to recognize, describe and manage emotional experiences and mental health symptoms. The lack of knowledge about risks associated with mental illness, as well as a lack of knowledge on effective treatment and where to seek help, were also reported as barriers (Gulliver, Griffiths, & Christensen, 2010; Rickwood, Deane, & Wilson, 2007; Rickwood, Deane, Wilson, & Ciarrochi, 2005)

Fourth, adolescents seem reluctant to seek help for mental health problems. Several studies report that only one third (or less) of adolescents with severe mental health issues have sought help for their problems (Essau, 2005; Sawyer et al., 2001). A large-scale study from Norway found that among youths with mental symptom-load above 99th percentile, only 34%

had sought help in the past 12 months (Zachrisson, Rödje, & Mykletun, 2006). In Norway, mental health services are easily accessible and free of charge, nevertheless many adolescents stay untreated. One reason why adolescent appear to be reluctant to seek help have been identified as past negative experiences with mental health services, leading to mistrust of such services (Rickwood et al., 2007; Rickwood et al., 2005). Another reason has been identified as the existence of negative attitudes and beliefs (i.e. fear of stigma, confidentiality breach and discrimination, as well as negative appraisal of the problem as incomprehensible or untreatable) (Gulliver et al., 2010; Rickwood et al., 2007; Rickwood et al., 2005).

Taken together, these barriers explain the limited access to treatment for adolescents with anxiety disorders in low- and middle-income countries. Some are general across the globe, some are specific for low-income settings, and some are specific for non-western cultures. One proposed way to increase the access to effective psychological interventions worldwide is by using digital technology, well integrated to most adolescents' lives.

Adolescents' digital habits. Digital health interventions are likely to appeal to young people, as being online seems to be ubiquitous for adolescents in large parts of the world (Pew Research Centre, 2018). Low-income countries follow right behind, with smartphone ownership and internet usage increasing at high speed in developing parts of the world. Pew Research Centre (2016) did a large, global survey both in 2013 and 2015 – with participants from 40 different countries, several of whom were low-income countries. Data from these surveys show that the number of people owning a smartphone in low-income countries rose from 21% in 2013 to 37% in 2015. The same was true for internet usage, rising at an extraordinary rate from 45% in 2013 to 54% in 2015. Many large emerging economies have at least 60% of their population using the internet and within almost every country participating, millennials (18-34) were much more likely to own a smartphone and use the internet than the older population (Pew Research Centre, 2016).

Effect of digital interventions for adolescents with anxiety disorders

Extensive research has been conducted, mainly in high-income countries, on digital mental health interventions for adults, adolescents and children, all showing promising results (Lattie et al., 2019; Lau, Smit, Fleming, & Riper, 2016; Peñate & Fumero, 2016). In the case of adolescents with anxiety, several reviews have provided results indicating that internet-delivered cognitive behavioral therapy (iCBT) are especially effective (Calear & Christensen, 2010; Clarke, Kuosmanen, & Barry, 2015; Ebert et al., 2015; Vigerland et al., 2016).

One meta-review analyzed 21 reviews, and found support of iCBT in treating anxiety and depression in adolescence, with significantly lower rates of anxiety post-intervention and at follow-up (Hollis et al., 2017). Grist, Croker, Denne, and Stallard (2018) reviewed 34 randomized controlled studies of digitally delivered treatment for children and adolescents with anxiety and depression. Their review yielded significant results on the effect of digitally delivered interventions in general, with a medium effect size in favor of iCBT interventions. In addition, another review found that parents and youth reported high satisfaction after completing iCBT for the treatment of adolescents with anxiety (Rooksby, Elouafkaoui, Humphris, Clarkson, & Freeman, 2015). This shows potential to the development of digital interventions targeting youth mental health, and this contribute to resolve issues of low accessibility of mental health services in low-resource settings in different parts of the world.

Review of digital interventions in low- and middle-income countries. Naslund et al. (2017) reviewed the use of technology in treating and preventing mental disorders in low- and middle-income countries. Mainly, their included studies examined the use of technology for promoting adherence in clinical treatment (i.e. text messaging and telephone support), to support mental health care delivery (i.e. videoconferencing for diagnostic consultation or follow-up care), or for digital training of mental health professionals. Although they identified

studies which examined the effect of digital interventions, only four of the total of 49 studies investigated the effect of iCBT for anxiety.

Another review which included 19 studies from different low- and middle-income countries from around the world, also found that the most frequently studied technological modality was videoconferencing. In this review, they only identified two studies which examined digital self-help program, whereas only one of these investigated the efficacy of the intervention. (Acharibasam & Wynn, 2018).

Nevertheless, a third review investigating the use of digital interventions for prevention, treatment and follow-up in Latin America, identified several studies on guided and unguided digital self-help programs. Only three of the identified studies were randomized controlled trials (RCT studies). Mainly these identified interventions targeted depression or substance abuse, and limited studies actually investigated effect (Jiménez-Molina et al., 2019).

These findings suggest that few studies examining the effect of digital self-help intervention programs for treating mental disorders have been conducted in low- and middle-income countries. This leaves the question of whether such programs will be effective in treating anxiety, especially for adolescents, unanswered. The field of research on this topic is seemingly still an early stage, nevertheless it shows promising growth.

Given that mental health services are down prioritized and poorly accessible in low- and middle-income countries, digital self-help interventions for treating mental health disorders can be a promising solution in bridging the treatment gap in these areas.

Culturally sensitive mental health interventions.

Culture may be seen as a key component in human development, influencing both perception, thoughts, feelings and behaviors. In this way, culture also can influence our

beliefs about health and illness, and thus it might have an impact on our pathways into treatment (Angel & Thoits, 1987; Jimenez, Bartels, Cardenas, Dhaliwal, & Alegría, 2012). Cultural influence on psychological treatment have nevertheless been debated. One side states that unique culturally specific treatments needs to be developed, and the opposition stating that change mechanisms are universal, and consequently, treatment should be as well (Bernal, Chafey, & Domenech Rodríguez, 2009). A middle ground unites these extremes by proposing frameworks and models on adaptation of well-established effective treatment manuals to fit with specific cultures, without conflicting the fidelity of the core mechanisms (Bernal, Bonilla, & Bellido, 1995; Hays, 2009; Kreuter, Lukwago, Bucholtz, Clark, & Sanders-Thompson, 2003; Leong, 2011; Rathod, Phiri, & Naeem, 2019; Resnicow et al., 2000). These frameworks have been used to develop culturally adapted psychotherapy (Salamanca-Sanabria, Richards, & Timulak, 2019), which have been found effective in several studies (Benish, Quintana, & Wampold, 2011; Chowdhary et al., 2014; Salamanca-Sanabria et al., 2020; van Loon, van Schaik, Dekker, & Beekman, 2013; Zhang et al., 2002).

When developing psychological interventions for adolescents in low-income countries, whether the interventions being digitally delivered or not, culture can therefore be considered as one important aspect to include. However, it is only in the recent years that the importance of cultural relevance in health interventions has been acknowledged (Griner & Smith, 2006; Salamanca-Sanabria et al., 2019).

Bernal et al. (2009) called attention to the importance of culture in psychotherapy by defining cultural adaptation as a systematic adjustment of evidence-based treatment protocols to be compatible with the client's culture by modifying specific elements in the treatment protocol. Previous to this, the American Psychological Association (APA) suggested guidelines for the multicultural context in psychology highlighting the importance of

including culture in psychological treatment, training, research, education, practice and organizational change (Manese et al., 2003).

Rathod et al. (2018) conducted the first review of meta-analyses of culturally adapted interventions. They found that the majority of meta-analyses provided a moderate to large effect for culturally adapted interventions. However, these results were limited by several factors. One limitation was heterogeneity among the included studies in several of the meta-analysis in regard to design and context (diversity in study design, population characteristics and methods to calculate effect size). Because of this over inclusiveness, little is known about the specificity of adapted interventions targeting specific diagnoses or ethnic populations. Rathod et al. (2018) also found that only one review compared culturally adapted treatment to non-adapted treatments (Benish et al., 2011) which leaves the question of relative effect rather unanswered. In addition, several meta-analyses did include the same studies, which might reflect the low number of studies that have been published on this topic. Additionally, Rathod et al. (2018) found that categorization of cultural adapted interventions seemed to vary widely, highlighting a lack of a systematic approach to cultural adaptation.

As most of the studies investigating effect of culturally adapted treatments have compered the cultural intervention to a wait-list control group, consequently it is not possible to conclude whether the effect of such adapted treatments is better than treatment as usual. Nevertheless, the review conducted by Benish et al. (2011) which did examine the relative effect of adapted psychotherapy to non-adapted provided support to the effectiveness of adapted treatments.

The complex intervention framework

In order to map out a culturally sensitive digital intervention for adolescents with anxiety in a low-income country, a “complex intervention” framework will be used (Craig et

al., 2013). Complex interventions are normally defined as interventions which contains several different interacting components. The complexity of an intervention may vary on several dimensions; range of possible outcomes, degree of flexibility, number of interactive components, number of targeted groups by the intervention. There are no clear boundaries between a simple and complex intervention, and in reality, few interventions are truly simple.

The framework of Craig et al. (2013) includes work in four stages; 1) Development, 2) Piloting, 3) Evaluation, 4) Implementation. These stages might interact in different ways, resulting in a great variety of possible outcomes of the development process.

The stage of development is about identifying the evidence base, identifying or developing appropriate theory, and modelling process and outcomes. Is the aim of the project clear, what are the desired outcomes, is there a coherent theoretical basis, can a proper description of the intervention be provided – these are helpful questions to ask oneself during the development process. Piloting is about calculating further procedures to be able to test the intervention properly. Estimates of necessary recruitment of subjects, and knowing what sample size is appropriate, will further lead to the opportunity to evaluate the intervention. Evaluation is about conducting studies investigating efficacy, feasibility and acceptability. Choosing your study design should be based on specific characteristics of the study, such as likelihood of selection and what effect size you would expect. Randomized controlled trials (RCT) are considered the most robust way of assessing effectiveness. Implementation is about making your project or findings available and translated into practice. Publication can be one way of achieving implementation and is stressed as essential (Craig et al., 2013).

This paper will present work from the first stage of developing a complex intervention, while piloting, evaluation and implementation remains as future projects.

Research questions

This article will strive to identify effective and culturally sensitive elements for a digital self-guided intervention for adolescents with anxiety disorder in a low-income country. The objectives for this article are therefor:

Research question one: Review existing research literature on the clinical effects of digital intervention for adolescents with anxiety disorder and symptoms.

Research question two: Review the effective therapeutic elements of interventions reported in research question one.

Research question three: Review frameworks for the cultural adaptation of psychological interventions and treatments.

Research question four: Based on research question one to three, what are the key effective elements of a future culturally sensitive digital self-guided intervention for adolescents with anxiety disorder in a low-income country.

Method

Research question one: Review existing research literature on the clinical effects of digital intervention for adolescents with anxiety disorder and symptoms.

A literature search was conducted on February 5th, 2020. An electronic search was conducted in PsycInfo and Medline to identify all relevant articles on the subject "computer-based anxiety treatment for adolescents". A combination of search terms was used, including computerized intervention ((Technolog* or computer or internet or digital or online or web) adj3 (intervention* or program or treatment or therap*)), and population (youth or teen* or adolescen* or juvenile or young*) and outcome (anxi* or GAD or worr* or fear). Mesh (abstract, title, headings, keywords, table of contents, original title, tests & measures) were

searched. Duplicates were resolved in each search, yielding a total of 532 articles in PsycInfo and 640 articles in Medline for further screening.

Paper titles and abstracts were initially scanned to determine eligibility, and then articles were read in full text to further determine eligibility. Included studies met the following inclusion criteria a) youngest participant between 12-16 years of age (no upper age limit), b) targeting anxiety symptoms or anxiety disorders (Specific phobias, OCD, panic disorder, GAD, Social anxiety, separation anxiety), c) intervention delivered digitally (online or offline computer based) d) prevention studies if targeted secondary or tertiary e) journal articles and doctoral theses, f) published in Norwegian or English. Comorbid anxiety will also be included when the other inclusion criteria are fulfilled (e.g. anxiety and depression).

Exclusion criteria were a) follow-up after clinical treatment b) intervention only targeting parents or health professionals, c) primary prevention interventions, d) studies investigating effect of intervention on post-traumatic stress disorder.

Research question two: Review the effective therapeutic elements of interventions reported in research question one.

After identifying all relevant articles who met inclusion criteria, each intervention where thoroughly investigated to find effective therapeutic elements, looking at design objectives and key elements. The therapeutic elements which were found to be effective in treating anxiety symptoms in most of the interventions analyzed, and which can be integrated with a cultural framework, will be adopted into a new culturally sensitive intervention targeting adolescents in low-middle income and low-resource settings.

Research question three: Review frameworks for the cultural adaptation of psychological interventions and treatments.

Cultural frameworks for adapting treatment interventions were identified through a search in Google Scholar. Two searches were done, one by combining “cultural adaption*” and “psychological intervention*”, and the other by combining “cultural adaption*” and “psychological intervention*” and “adolescent*”. Most cited articles, as well as other articles with relevant title and abstract, were screened for eligibility. This was not a systematic search, because it was only relevant to include a few cultural frameworks for adaptation of therapeutic elements to be culturally sensitive. The search led to inclusion of xx cultural frameworks, based on pragmatic relevance and recognition in the field.

Research question four: Based on research question one to three, what are the key effective elements of a future culturally sensitive digital self-guided intervention for adolescents with anxiety disorder in a low-income country.

The core elements of a new, culturally sensitive digital self-guided intervention for adolescents with anxiety symptoms and diagnosis will be mapped out using a framework by Medical Research Council for developing complex interventions (Craig et al., 2013), including guiding principles and a logic model (W.K. Kellogg Foundation, 2004). This will be based on the three prior steps, including the literature review of effective therapeutic elements in digital interventions for anxiety treatment for adolescents, and the pragmatic review of cultural adaptation frameworks. Through the guiding principles I will outline the intervention design objectives and key features addressing each objective. Through the logic model I will provide description of the core intervention elements (specific and common factors), mechanisms of change and desired outcomes.

Results

Research question one: Review existing research literature on the clinical effects of digital intervention for adolescents with anxiety disorders and symptoms.

A description of the inclusion of articles for research question/table one and two are shown in figure 1.

Insert figure 1 here

A total of 18 studies reporting effect size for adolescents with anxiety disorders and symptoms were included in the review. The articles were rated for sample size and design, anxiety disorder and symptoms, recruitment method, effect (effect sizes and significance) and adherence (Table 1).

Insert table 1 here

Sample size and design. A distinction was made between studies with more or less than 20 participants, to clarify robust findings. Only four studies had less than 20 participants (Chapman et al., 2016; Cunningham et al., 2009; Tillfors et al., 2011; Wahlund et al., 2020). Of these four, two studies were case studies (Chapman et al., 2016; Cunningham et al., 2009), one was an RCT (Tillfors et al., 2011) and one was an open pre-post study (non- concurrent, multiple baseline design study analysis) (Wahlund et al., 2020). Of the studies with more than >20 participants (n=14), eight were RCT studies (Calear, Christensen, Brewer, Mackinnon, &

Griffiths, 2016; Calear, Christensen, Mackinnon, Griffiths, & O'Kearney, 2009; Hoek, Schuurmans, Koot, & Cuijpers, 2012; Spence et al., 2011; Stjerneklar, Hougaard, McLellan, & Thastum, 2019; Topper, Emmelkamp, Watkins, & Ehring, 2017; Waite, Marshall, & Creswell, 2019; Wuthrich et al., 2012), five were open pre-post studies (Anstiss & Davies, 2015; Gunn et al., 2019; Mewton, Wong, & Andrews, 2012; Nordh et al., 2017; Rees, Anderson, Kane, & Finlay-Jones, 2016), and one was a quasi-experimental mixed design (Putwain, Chamberlain, Daly, & Sadreddini, 2014).

Seven of the included RCT studies compared one interventions group (internet-based treatment group) with a wait-list control group (Calear et al., 2016; Calear et al., 2009; Hoek et al., 2012; Stjerneklar et al., 2019; Tillfors et al., 2011; Waite et al., 2019; Wuthrich et al., 2012), whilst two RCT studies compared a second intervention group (i.e. face-to-face clinical CBT treatment) next to the first intervention group (i.e. internet delivered CBT treatment) and control group (i.e. wait-list) (Spence et al., 2011; Topper et al., 2017). The number of participants in the included studies ranged from five to 3225.

Anxiety disorder and symptoms. Included studies differed in whether they investigated a pure clinical sample of participants with an anxiety diagnosis or not.

Half of all included studies investigated effect of the intervention on a purely clinical sample (n=9) (Chapman et al., 2016; Cunningham et al., 2009; Nordh et al., 2017; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012). Participants included in these studies had an anxiety diagnosis according to DSM-IV or DSM-V. Some studies investigated transdiagnostic treatment (n=6), including generalized anxiety disorder, separation anxiety disorder, social phobia, specific phobia, panic disorder with or without agoraphobia or agoraphobia without panic disorder, obsessive-compulsive disorder and anxiety disorder not otherwise specified (Chapman et al., 2016; Cunningham et al., 2009; Spence et al., 2011; Stjerneklar et al., 2019; Waite et al.,

2019; Wuthrich et al., 2012). Other studies looked at disorder specific treatment, such as separation anxiety disorder (n=1) (Nordh et al., 2017), generalized anxiety disorder (n=1) (Wahlund et al., 2020), and social phobia (n=1) (Tillfors et al., 2011).

The remaining studies had no clinical criteria for eligibility and therefore included both participants with and without a probable anxiety diagnosis (n=9) (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Gunn et al., 2019; Hoek et al., 2012; Mewton et al., 2012; Putwain et al., 2014; Rees et al., 2016; Topper et al., 2017). Of these, some studies provided clinical cut-of scores for- or estimates of the number of participants with a proper or probable diagnosis (n=6) (Calear et al., 2016; Calear et al., 2009; Gunn et al., 2019; Hoek et al., 2012; Mewton et al., 2012; Rees et al., 2016). These studies are categorized as a mixed sample.

The remaining studies did not report any estimates of participants with probable diagnosis (n=3) (Anstiss & Davies, 2015; Putwain et al., 2014; Topper et al., 2017)

Recruitment method. Recruitment methods in the included studies differed between community samples, clinical samples and a mix of the two. Community samples recruited participants through TV and radio commercials, ads on the internet, schools, secondary referrals (i.e. parents, teachers). Clinical samples recruited participants through referrals from health professionals. Among the included studies, community sampling was mostly used (n=12) (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Cunningham et al., 2009; Gunn et al., 2019; Putwain et al., 2014; Rees et al., 2016; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017). Clinical sampling (n=3) (Chapman et al., 2016; Mewton et al., 2012; Waite et al., 2019) and mixed method (n=4) (Hoek et al., 2012; Nordh et al., 2017; Wahlund et al., 2020; Wuthrich et al., 2012) was sometimes used.

Effects (effect sizes and significance). Mostly, studies reported effect size by using cohen's d (n=12) (Calear et al., 2016; Calear et al., 2009; Mewton et al., 2012; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2016; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Wahlund et al., 2020; Wuthrich et al., 2012). Of these, eleven studies reported significant reduction in anxiety symptoms after intervention (Calear et al., 2009; Mewton et al., 2012; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2016; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Wahlund et al., 2020; Wuthrich et al., 2012), whereas eight showed large effect size (Mewton et al., 2012; Nordh et al., 2017; Rees et al., 2016; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Wahlund et al., 2020; Wuthrich et al., 2012), two showed medium effect size (Putwain et al., 2014; Topper et al., 2017) and one showed small effect size (Calear et al., 2009).

Some studies did not report any effect size (n=6) (Anstiss & Davies, 2015; Chapman et al., 2016; Cunningham et al., 2009; Gunn et al., 2019; Hoek et al., 2012; Waite et al., 2019). Of these, one study nevertheless reported significant improved outcome measures from pre-treatment to post-treatment (Anstiss & Davies, 2015), three studies showed non-significant results (Gunn et al., 2019; Hoek et al., 2012; Waite et al., 2019) and the two case studies did not report anything about statistical analysis of the results although they reported improvement in anxiety ratings for almost all participants with some reporting subclinical levels on post-measures (Chapman et al., 2016; Cunningham et al., 2009).

Among the studies which reported significant results (N=12), half where RCT studies (n=6) (Calear et al., 2009; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Wuthrich et al., 2012) and the remaining were pre-post assessment studies (n=5) (Anstiss & Davies, 2015; Mewton et al., 2012; Nordh et al., 2017; Rees et al.,

2016; Wahlund et al., 2020) and quasi-experimental design studies (n=1) (Putwain et al., 2014).

Adherence. The reviewed studies differed in how they defined completers. The variety of definitions range from participants who finished intervention and follow-up questionnaire (n=2) (Anstiss & Davies, 2015; Wuthrich et al., 2012), participants who finished all existing modules (n=9) (Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Gunn et al., 2019; Hoek et al., 2012; Mewton et al., 2012; Putwain et al., 2014; Spence et al., 2011; Waite et al., 2019), participants who completed some modules (n=3) (Cunningham et al., 2009; Nordh et al., 2017; Wahlund et al., 2020), and in one study participants were defined as completers regardless of the number or amount of completed modules (Stjerneklar et al., 2019).

Additionally, only six out of 18 reviewed studies reported mean number of completed modules (Calear et al., 2009; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Wahlund et al., 2020). One study did not report any adherence estimates because it was an ongoing study at the time the article was written (Rees et al., 2016). Differences in defining adherence affects the reported number of completers. Thus, the adherence estimates cannot be compiled in a way that provides a good estimate of general adherence. However, a total of eleven studies reported adherence in terms of completing the entire program (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Gunn et al., 2019; Hoek et al., 2012; Mewton et al., 2012; Putwain et al., 2014; Spence et al., 2011; Waite et al., 2019; Wuthrich et al., 2012). The adherence rates ranged from 13,7% to 100%. No impact of guidance on adherence rates were found.

Research question two: Review the effective therapeutic elements of interventions reported in research question one.

A total of 16 interventions were identified after reviewing a total of 22 included studies. The interventions were reviewed for theoretical background, anxiety disorder and symptoms, guidance, caregiver involvement, number and length of modules, key therapeutic elements (cognitive and behavioral) and layout (Table 2).

Insert table 2 here

Theoretical background. In large part the intervention's theoretical background was in line with the golden standard for anxiety treatment, with 15 out of 16 interventions based on CBT. Of these, some interventions (n=9) were reported to be entirely based on CBT elements (Cunningham, Rapee, & Lyneham, 2006; Cunningham et al., 2009; Gunn et al., 2019; Mewton et al., 2012; Nordh et al., 2017; Rees, Anderson, & Finlay-Jones, 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012), whilst some interventions (n=6) used a combination of CBT and elements from other therapies, such as meta-cognitive therapy, mindfulness therapy, interpersonal therapy and rational-emotive therapy (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Putwain et al., 2014; Topper et al., 2017).

Only one intervention was not based on classic CBT theory, instead it was based on a problem-solving therapy (Hoek, Schuurmans, Koot, & Cuijpers, 2009; Hoek et al., 2012). Problem solving therapy contains some of CBT's key elements but differs in its large emphasis on concrete problem solving, which constitutes the majority of treatment. Problem

solving elements are also common in classical CBT, however they are secondary to the primary emphasis on exposure and cognitive restructuring.

Anxiety disorders or symptoms. Identified interventions were either transdiagnostic- or disorder specific treatments, or they were secondary prevention interventions targeting participants with elevated levels of anxiety.

The transdiagnostic treatment interventions (n=4) targeted participants with clinical levels of any anxiety diagnosis, i.e. generalized anxiety disorder, separation anxiety disorder, social phobia, specific phobia, panic disorder with or without agoraphobia or agoraphobia without panic disorder, obsessive-compulsive disorder and anxiety disorder not otherwise specified (Chapman et al., 2016; Cunningham et al., 2009; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Waite et al., 2019; Wuthrich et al., 2012). Other interventions were disorder specific (n=3) and targeted treatment towards populations with separation anxiety disorder (Nordh et al., 2017), generalized anxiety disorder (Wahlund et al., 2020), and social phobia (Tillfors et al., 2011).

Some interventions seemed to be secondary preventions, targeting participants with elevated levels of anxiety. Mostly, these interventions (n=7) targeted populations with both clinical- and subclinical levels of anxiety (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Gunn et al., 2019; Hoek et al., 2009, 2012; Mewton et al., 2012; Rees et al., 2016), while other interventions (n=2) targeted participants with sub-clinical levels of anxiety (Putwain et al., 2014; Topper et al., 2017).

Guidance. Whether the interventions are guided by therapists or mental health care professionals through phone calls or email feedback is of interest because it has an impact on the required resources for implementing an intervention. Of the interventions investigated in this review, mostly were categorized as guided interventions (n=10) (Anstiss & Davies, 2015; Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Hoek et al., 2009,

2012; Nordh et al., 2017; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012), and some were categorized as unguided interventions (n=5) (Calear et al., 2016; Calear et al., 2009; Gunn et al., 2019; Mewton et al., 2012; Rees et al., 2015; Rees et al., 2016). Only one study did not report on whether the intervention they investigated was guided or not (Putwain et al., 2014).

Caregiver involvement. Several of the review interventions involved caregivers in different ways (n=7), (Cunningham et al., 2006; Cunningham et al., 2009; Hoek et al., 2009, 2012; Nordh et al., 2017; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012). Some includes a parallel caregiver program (n=3) (Nordh et al., 2017; Spence et al., 2008; Spence et al., 2011; Wahlund et al., 2020; Waite et al., 2019), whilst others provided information leaflets on core elements of anxiety and treatment and advice on how to support their teenager through therapy (n=4) (Cunningham et al., 2006; Cunningham et al., 2009; Hoek et al., 2009, 2012; Rees et al., 2015; Rees et al., 2016; Stjerneklar et al., 2019; Wuthrich et al., 2012)

Mostly, studies included in this review did not mention anything about whether the intervention promoted or required caregiver involvement in the treatment procedure (n=9) (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Gunn et al., 2019; Mewton et al., 2012; Putwain et al., 2014; Tillfors et al., 2011; Topper et al., 2017).

Number and length of modules. Number of modules and length of each session varied amongst the different interventions. Number of modules stretched from 5-10, while the weight of interventions included between 5-8 modules (n=11) (Calear et al., 2009; Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Gunn et al., 2019; Hoek et

al., 2012; Mewton et al., 2012; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Stjerneklar et al., 2019; Topper et al., 2017; Wuthrich et al., 2012). In regard to the length of each session, several studies (n=11) did not report this. For those who did mention length, session stretched from 15 minutes to 60 minutes. Mostly, the length of an intervention module stretched from 20 minutes to 40 minutes (n=5) (Calear et al., 2016; Calear et al., 2009; Cunningham et al., 2006; Cunningham et al., 2009; Putwain et al., 2014; Stjerneklar et al., 2019; Wuthrich et al., 2012).

Key therapeutic elements. When analyzing the main therapeutic elements, they were separated into two categories; cognitive elements (which influence thought processes such as perception, recognition and reasoning, and challenges the appraisal of these) and behavioral elements (which influence actual behavior that strengthens and maintain anxiety symptoms such as avoidance and safety behaviors).

Cognitive elements. Psychoeducation was explicitly mentioned as a key element in 15 out of 16 interventions (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Gunn et al., 2019; Mewton et al., 2012; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012). The problem-solving intervention was the only one which did not mention anything explicit about psychoeducation (Hoek et al., 2009, 2012).

In addition to the problem-solving intervention which clearly focused on problem solving, several other interventions also included some kind of problem-solving tasks (n=9) (Calear et al., 2016; Calear et al., 2009; Cunningham et al., 2006; Cunningham et al., 2009; Hoek et al., 2009, 2012; Mewton et al., 2012; Nordh et al., 2017; Spence et al., 2008; Spence

et al., 2011; Stjerneklar et al., 2019; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012).

Many interventions included cognitive restructuring (n=13) (Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Gunn et al., 2019; Mewton et al., 2012; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Waite et al., 2019; Wuthrich et al., 2012). Some explicitly referred to it as cognitive restructuring, whilst others framed it in different ways, i.e. negative core belief reappraisal, or challenging dysfunctional beliefs via the provision of corrective psychoeducational information.

Other key cognitive elements identified in the reviewed studies were; goal setting (n=9) (Anstiss & Davies, 2015; Calear et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Stjerneklar et al., 2019; Tillfors et al., 2011; Wahlund et al., 2020; Wuthrich et al., 2012), symptom or thought detection and monitoring exercises (n=7) i.e. thought records, assessment of thoughts, or worry awareness training (Anstiss & Davies, 2015; Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Gunn et al., 2019; Tillfors et al., 2011; Wahlund et al., 2020), assertiveness training (n=4) (Cunningham et al., 2006; Cunningham et al., 2009; Nordh et al., 2017; Stjerneklar et al., 2019; Tillfors et al., 2011; Wuthrich et al., 2012), attention shift exercises (n=4) (Gunn et al., 2019; Nordh et al., 2017; Tillfors et al., 2011; Topper et al., 2017), rewards and motivation (n=3) (Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Stjerneklar et al., 2019), guided imagery and visualization tasks (n=3), i.e. to promote relaxation or as in-vitro exposure (Calear et al., 2016; Putwain et al., 2014; Spence et al., 2008; Spence et al., 2011; Waite et al., 2019), functional analysis (n=1) (Nordh et al.,

2017), realistic thinking (n=1) (Stjerneklar et al., 2019), and social skill training (n=1) (Nordh et al., 2017).

Some interventions explicitly mentioned including a focus on relapse prevention, nevertheless we also categorized reviewing previously learned material and generalizing techniques to everyday situations as relapse prevention (n=7) (Cunningham et al., 2006; Cunningham et al., 2009; Gunn et al., 2019; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Stjerneklar et al., 2019; Wahlund et al., 2020; Wuthrich et al., 2012).

***Behavioral elements*.** Different types of exposure exercise were reported in several of our included studies (n=9). One intervention implemented exposure as a group exercise in addition to the digital intervention (Nordh et al., 2017), another intervention included in vitro exposure (i.e. thought exposure) in addition to in vivo exposure (i.e. exposure to situations associated with uncertainty) (Wahlund et al., 2020). The rest included graded exposure (Cunningham et al., 2006; Cunningham et al., 2009; Mewton et al., 2012; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Waite et al., 2019; Wuthrich et al., 2012), of these some explicitly mentioned including an exposure hierarchy, whereas other did not.

Several interventions included elements of relaxation strategies (n=7). Mostly, this regarded breathing exercises or progressive muscle relaxation exercises (Anstiss & Davies, 2015; Calear et al., 2016; Chapman et al., 2016; Putwain et al., 2014; Spence et al., 2008; Spence et al., 2011; Waite et al., 2019). One intervention did not provide any description of the type of relaxation strategy being included (Calear et al., 2009). Another intervention framed it as “calming activities” with no more description (Stjerneklar et al., 2019).

Other key behavioral elements identified in the reviewed studies were; behavioral activation (n=5) i.e. physical activity or promoting trying new activities (Anstiss & Davies,

2015; Calear et al., 2016; Chapman et al., 2016; Mewton et al., 2012; Topper et al., 2017), mindfulness (n=3) (Anstiss & Davies, 2015; Calear et al., 2016; Chapman et al., 2016), behavioural experiments (n=3) (Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017), focus on self-esteem or resilience building (n=3) i.e. promoting self-care, including self-appreciation exercises or including strategies to increase self-esteem (Anstiss & Davies, 2015; Calear et al., 2009; Rees et al., 2015; Rees et al., 2016), promoting participants to share information about their disorder (n=1) (Rees et al., 2015; Rees et al., 2016), to "let go of control behaviors" (n=1) (Wahlund et al., 2020), and consolidation of ERP principles (n=1) (Rees et al., 2015; Rees et al., 2016).

Layout. Also, layout elements were reviewed to see if there were any trends emerging amongst the included interventions;

Several interventions specifically mentioned vivid graphics and sound (n=11) as important factors to promote engagement and adherence amongst youths (Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Gunn et al., 2019; Nordh et al., 2017; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Wahlund et al., 2020; Waite et al., 2019; Wuthrich et al., 2012).

Further, peer modelling was often included (n=10) to demonstrate how peers have struggled with similar problems and how they have had good use of the techniques thought in the interventions (Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Mewton et al., 2012; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Topper et al., 2017; Waite et al., 2019; Wuthrich et al., 2012). Also, some interventions mentioned including comments by a graphically rendered expert (n=4) to guide the adolescent through the intervention, and to increase credibility of the content (Chapman et al., 2016;

Gunn et al., 2019; Mewton et al., 2012; Spence et al., 2008; Spence et al., 2011; Waite et al., 2019).

The ‘Pesky gNATs’ intervention was the only intervention entirely framed as a game (Chapman et al., 2016), although several other interventions also included elements of interactive exercises and gamifications, such as quizzes and puzzles to promote repetition of learnt material in a fun way (n=9) (Calear et al., 2009; Cunningham et al., 2006; Cunningham et al., 2009; Hoek et al., 2009, 2012; Putwain et al., 2014; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Tillfors et al., 2011; Topper et al., 2017; Waite et al., 2019; Wuthrich et al., 2012).

Implementation of homework between sessions (n=9) to promote learning of techniques and to encourage use of these in everyday life, were too reported in several interventions (Chapman et al., 2016; Cunningham et al., 2006; Cunningham et al., 2009; Gunn et al., 2019; Mewton et al., 2012; Putwain et al., 2014; Spence et al., 2008; Spence et al., 2011; Stjerneklar et al., 2019; Tillfors et al., 2011; Topper et al., 2017; Waite et al., 2019; Wuthrich et al., 2012).

Other layout elements identified in the included interventions were as following; use of tunneled intervention design where one module must be finished before starting the next (n=7) (Calear et al., 2016; Calear et al., 2009; Chapman et al., 2016; Nordh et al., 2017; Rees et al., 2015; Rees et al., 2016; Spence et al., 2008; Spence et al., 2011; Tillfors et al., 2011; Waite et al., 2019), use of menu intervention design where participants can choose where to start and proceed (n=2) (Cunningham et al., 2006; Cunningham et al., 2009; Stjerneklar et al., 2019; Wuthrich et al., 2012), including summary of module content (n=2) (Calear et al., 2009; Wahlund et al., 2020), incorporating a workbook (n=3) (Calear et al., 2016; Calear et al., 2009; Putwain et al., 2014), using a progress chart (n=2) (Calear et al., 2009; Stjerneklar et al., 2019), providing material for printing or downloading (n=2) (Calear et al., 2016; Tillfors

et al., 2011), adapting content and language to the target age group, i.e. using youthful abbreviations and slang (n=3) (Anstiss & Davies, 2015; Spence et al., 2008; Spence et al., 2011; Tillfors et al., 2011; Waite et al., 2019), providing contact info to mental health services in case of aggravated symptoms or suicidal thoughts (n=2) (Calear et al., 2016; Calear et al., 2009), including a relaxation CD (n=1) (Spence et al., 2008; Spence et al., 2011; Waite et al., 2019) intervention delivered via text message (n=1) (Anstiss & Davies, 2015), use of humor (n=1) (Gunn et al., 2019), use of metaphors (n=1) (Rees et al., 2015; Rees et al., 2016), and individualizing treatment content (n=1) (Gunn et al., 2019).

Research question three: Review frameworks for the cultural adaptation of psychological interventions and treatments.

Several methods and frameworks have been proposed to help clinicians adapt treatment to better fit with a specific culture, but no authority has offered common guidelines or a golden standard on how to do so. This leads to subjective and individual decisions on whether to adapt and how to adapt treatment. Thus, it also affects the decision on which framework to include. I have focused on pragmatic utility making adaptations of key elements in the intervention as easy, but still thorough, as possible. This has led to the inclusion of three frameworks which will be further explained in this section.

Ecological Validity Framework (EVF). Bernal et al. (1995) proposed a framework which was designed to achieve cultural sensitivity in treatment research and adaptation of interventions. The framework, called Ecological Validity Framework (EVF), is based on findings from a review of 20 years of research on treatment of Hispanic with focus on cultural sensitivity and ecological valid interventions. Bernal et al. (1995) suggested that this framework would serve as a guide for developing new culturally sensitive treatments, or to adapting existing psychosocial treatments to specific ethnic minority groups. The framework

consists of 8 dimensions with associated culturally sensitive elements - with recommendations to what elements that should be culturally specific in an intervention.

The eight dimensions are; 1) language should be culturally suited. This counts for more than just the mechanical translation of an intervention to the relevant language and applies for both written and spoken language. This will involve using culturally important and relevant words and phrases and avoid using words with negative associations or that are foreign in the specific culture.

2) Persons, referring to the variables in both the client and therapist which influences the therapeutic relationship. E.g. ethnic and racial similarities and differences between client and therapist might influence alliance. Both therapist and treatment program need to have the flexibility to consider such similarities and differences, and to embrace the clients cultural background and worldview.

3) metaphors, stating that use of symbols and concepts should align with culturally constant ideas, refrains and images. E.g. objects or symbols of importance for the specific culture should be represented. This also applies to sayings, idioms and metaphors, and overlaps with the first dimension of adapting language.

4) content; knowledge about the cultural values, traditions and costumes as factors influencing the uniqueness of groups are important when adapting any intervention program. Content also regards social, economic, historical and political factors in which the culture has developed and unfolds, and which influences the individual. E.g. Gender roles, personal space, collectivism vs. individualism, importance of family, time orientation - are all culturally specific factors that should shape content of an intervention.

5) concepts; treatment conceptualization are normally traditional constructs used within a theoretical psychosocial model, which impacts the framing of the problem. Such conceptualization should consider culture, and the conceptualization of a problem needs to

consider the cultural belief system and core beliefs - e.g the normality or abnormality of dependence vs interdependence vs independence in different cultures.

6) Goals need to be worked out in agreement between the therapist and client to maintain a good alliance. To do so, culture needs to be acknowledged. Therefore, this dimension also requires cultural knowledge, as it is desirable to frame goals of treatment in line with values, customs and tradition within the culture. E.g. transmission of positive and adaptive cultural values into goal formation is important.

7) methods; the procedures used for achieving goals needs to be culturally acceptable. E.g. The importance of family in some cultures might make it acceptable and necessary to include family in the treatment process.

8) context; this dimension overlaps with the content dimension. The therapeutic content should be sensitive to the clients social, economic, political and historical context. Consideration of changing contexts in assessment during treatment or intervention is important. E.g. acculturative stress, phase of migration, developmental stages, social support, relationship to country of origin are all context in which can influence members of a culture. Taking these eight dimensions into account, Bernal et al. (1995) believed that any interventions could be made to fit with specific cultures.

Cultural sensitivity framework. Resnicow et al. (2000) proposed a cultural sensitivity framework stating that cultural sensitivity is defined by the two dimensions of surface structure (the more general characteristics and values of the target population) and deep structure (the more profound forces that affects the individual's development). This was a product of their work on culturally adapting interventions for substance abuse in 2000, but these two dimensions are also stated to be applicable in the adaption of any intervention.

Surface structure concerns matching the material and messages of the intervention to the characteristics of a target population. This would involve adapting language, presenting

acceptable role models, using relevant examples, places, music, food, brands and clothing preferred by the target population. The dimension of surface structure refers to how well the intervention fits the specific target culture. Surface structure also includes identifying what channels (e.g., media) and settings (e.g., churches, schools) are most appropriate for delivery of messages and programs. To fit the intervention in such a way would require cultural expertise and involvement of the target population, to ensure understanding of the characteristics of the behavior in question.

Deep structure concerns cultural, social, historical, environmental and psychological forces that influences health behaviors in the target population and in the individual itself. Such forces would influence health behaviors differently across racial or ethnic populations, but also would influence each individual differently. Deep structure should therefore include an understanding of how the specific target population perceives the cause and course of illness and treatment, but at the same time keep in mind the heterogeneity of the target population. Also, an appreciation for how multiple factors such as religion, family, society, economics and government - both in perception and in fact - influences the target behavior, needs to be incorporated into the therapeutic intervention.

Resnicow et al. (2000) stated that whereas surface structure most likely will increase acceptance and understanding of the message, deep structure communicates salience. Surface structure establishes feasibility, whereas deep structure determines program impact.

Evidence based framework for adapting CBT. Rathod et al. (2019) developed a framework for cultural adaptation of CBT, inspired by the work of Tseng, Chang, and Nishjzono (2005). Rathod et al. (2019) stated that “every individual has a unique culture that is influenced by their wider culture, sub-culture and further developed through unique life experiences.” (Rathod et al., 2019, p. 5). This indicates that even within a specific culture, individual differences will exist, and therapies are therefore likely to benefit from flexible

properties. The framework proposed by Rathod et al. (2019) includes three principles referred to as the 'Triple-A' (Awareness of relevant cultural issues and preparation for therapy, Assessment and engagement, Adjustments in therapy), which all are encompassed in the frameworks four aspects in focus; (i) Philosophical orientation, (ii) Practical considerations of societal and health system-related factors, (iii) Technical adjustments of methods and skills and (iv) Theoretical adaptations of concepts.

The triple-A. The triple-A's are referred to as the fundamental areas of delivery. First is awareness of relevant cultural issues and preparation for therapy. This is the pre-engagement phase, with focus on access to therapy, delivery of therapy and availability for a given culture. Here, Rathod et al. (2019) suggested a further sub-division including 1) culture-related issues such as religion and spirituality, family and community, language and communication, 2) system and environmental aspects such as individual capacity, circumstances, system of support, services and help seeking pathways into care, 3) cognitive biases and unhelpful beliefs that can be directly related to the problem and its treatment. According to Rathod et al. (2019) this is as important as adaption of intervention. The next A, "Assessment and engagement" highlights the importance of using culturally sensitive screening tools for anxiety disorders and symptoms. The last A "Adjustments in therapy" concerns among others verbal and body language, cultural norms and courtesy, and to create a culturally welcoming environment by including culturally relevant objects, words and examples.

The four aspects. (i) Philosophical orientation; Rathod et al. (2019) state that philosophical orientation can affect perception on health and illness, relationship with services and professionals, and treatment and goals. Therefore, they also pointed out this aspect as important to consider when adapting interventions to fit diverse cultural contexts. Further they stated that life views can be affected by experiences acquired during lifetime, so that original

cultural beliefs can change and thus make up a diversity of attitudes that individuals in the same culture can have. Understanding the level of such acculturation in an individual might help understanding how to engage with them and explain therapy content based on their value system. Beliefs and attitudes in an individual can affect pathways into care, e.g. some individuals from cultures with high spirituality and religious beliefs might prefer traditional healing as treatments instead of psychopharmaca or conventional services. Cultural orientation towards psychotherapy and beliefs about interventions might also influence an individual's engagement with different therapies, e.g. for an individual religiously oriented towards Buddhism, mindfulness-based CBT might fit better with this individual's core beliefs rather than classical CBT. Therefore, understanding the individuals background in relation to culture might be helpful when considering adaptation of intervention content.

(ii) Practical considerations of societal and health system-related factors; here the authors points to the influence of both social factors and politics on mental health services. First, mental health policies will influence how services are structured and what type of help is offered to who. E.g. whether culturally adapted therapies would be available, or whether adapting therapy is a priority. Secondly, Rathod et al. (2019) here mention the power of the system of privilege and oppression in which the client lives. They state that racism and discrimination do occur across all cultures, and even within several cultural groups. Further they point out that racial differences between clinician and patient might influence whether the issue of experienced discrimination is addressed. E.g. The way in which the system of privilege and oppression have affected the clinician and the client differently, might further affect the ability to empathize with patients and recognize potential significant impact experiences with racism will have on mental health.

(iii) Technical adjustments of methods and skills; regards the specific adaptation of therapeutic content and focus, to better suit the individual. This involves an understanding

that 1) the setting and environment of therapy should be culturally welcoming, information should be available in appropriate language, and that individual adjustments in lengths and numbers of sessions need to be made based on distance and transportation issues for the client. 2) Therapeutic relationship or alliance is a well-known factor contributing to the outcome of psychotherapy and therefore therapists need to strive to build alliance at all stages of therapy. A warm and trustworthy personal style of therapist in the first sessions is suggested by the authors as a promoting factor, and appropriate self-disclosure might lead to gaining trust. 3) Therapeutic style can mismatch with cultural values, and therefore therapists must strive to come up with suitable techniques adapted to the individual's cultural values. 4) Family structure and emphasis on family involvement should be examined together with the client. In some cultures, families are strongly tied together, thus family can work as a strength helping the client reach their goals. 5) the role of religion is also important to consider in therapy. According to Rathod et al. (2019) many clinicians describe feeling disempowered when touching upon the subject of religious and spiritual beliefs. However, by avoiding discussing this topic in therapy the client might feel that important aspects of their personality and core beliefs are overlooked, and thus it might have negative impact on alliance, engagement and outcome.

(iv) Theoretical adaptations of concepts; to best fit the individual and their cultural strengths, some change in theoretical concepts need to be made to align with such strengths. E.g. when explaining the relationship between physical symptoms and mental illness, the therapist should keep in mind the cultural differences of the body-mind-assumption. Or when embarking upon the subject of feelings with a client coming from a culture or context where feelings are hardly ever discussed, the therapist must explain content in a way that aligns with the client's prerequisites and stay sensitive to the client's signals. Rathod et al. (2019) also

points out the importance of keeping in mind the cultural differences in regard to individualism versus collectivism when setting treatment goals, focusing on cultural strengths.

Comparing these three frameworks

Although these included frameworks for cultural adaptation of psychological interventions all are structured in different ways, they include several common elements. First, common for all frameworks appears to be a focus on the importance of acquiring a thorough and correct cultural understanding before the process of adapting an intervention begins. To achieve this, collaborating with an expert on the specific culture and representatives of the target population might be good ways of ensuring correct knowledge in the work of culturally adapting interventions.

Second, all three frameworks highlight the importance of adapting language. Resnicow et al. (2000) only mention it briefly although stating its importance, whilst the two other frameworks (Bernal et al., 1995; Rathod et al., 2019) provides more detailed information on different aspects of adapting language. They mention the specific translation into the mother tongue of the target population, as well as more semantic adaptation of the language to fit the cultural perception e.g. by reframing some words to be more cultural appropriate, and by avoiding using foreign words or words with negative associations. Also, adaptation of theoretical concepts in order to be more understandable and suitable with the audience receiving the intervention, is mentioned as another aspect in regards of adapting language. Language can have great power, and by using culturally significant and salient words the therapeutic content might be more accepted and understood by the target population.

Third, all three frameworks (Bernal et al., 1995; Rathod et al., 2019; Resnicow et al., 2000) mentioned in some way how different variables amongst the involved persons (therapist, role models and client) might influence the therapeutic relationship, and thus might

affect the outcome of therapy. Some variables mentioned in the different frameworks are ethnic and racial similarities and differences, orientation towards psychotherapy, religious belief system, theoretical preference and communication style. Bernal et al. (1995) points this out in a separate dimension (persons) focusing on differences and similarities between therapist and client. The same goes for Rathod et al. (2019) framework, where the importance of the therapeutic relationship is a recurring theme. E.g. they point out that racial difference, or a discrepancy between therapeutic style and cultural values both can affect the therapeutic relationship. Resnicow et al. (2000) included a focus on the influence of role model similarities and differences. They stated that racial differences in role models might impact how much the audience identifies themselves with these role models - which further might impact the role models influence on credibility and adherence of the intervention. Taken together, it appears that all three frameworks highlight the importance of resolving factors that can create a distance between the intervention and the target population, such as suppression and alienation, to increase efficacy of an intervention. One possible way of achieving this might be to communicate an open and non-judgmental attitude in the intervention content.

Fourth, creating a culturally welcoming environment may also appear to be a common element in all three frameworks (Bernal et al., 1995; Rathod et al., 2019; Resnicow et al., 2000). This involves including cultural important objects, such as food, music, brands and colors (Resnicow et al., 2000), cultural symbols, idioms and relevant examples (Bernal et al., 1995) and by including an emphasize on cultural values such as family involvement and religious beliefs (Rathod et al., 2019). By doing this, both respect and acknowledgement for the specific culture is communicated, and suppression is avoided. Also, cultural pride might increase, which in turn can facilitate the use of cultural strengths in reaching therapeutic goals.

Fifth, adapting the method to be culturally acceptable seems to have been acknowledged by all three frameworks. Resnicow et al. (2000) highlights that delivery of intervention in regards to channels (e.g., media) and settings (e.g., churches, schools) needs to be culturally appropriate, Rathod et al. (2019) mentions that therapeutic techniques needs to be congruent with cultural values and beliefs, and Bernal et al. (1995) points out that procedures used for achieving goals, as well as the goals themselves, needs to be culturally acceptable. If methods used in the intervention aligns with the specific culture, the chance that assignments and exercises are completed and successful might increase.

Finally, Resnicow et al. (2000) proposed a deeper structural aspect of adaptation to be included. According to them, forces that can influence health behaviors also needs to be taken into account when adapting interventions. E.g. that the intervention must build upon an understanding of the target population's perception of health and illness. Rathod et al. (2019) also suggested in their framework that philosophical orientation can affect perception on health and illness, which may seem to fit with the deep structure proposed by Resnicow et al. (2000).

Many elements mentioned in these three frameworks may seem to overlap with each other. By integrating these frameworks through comparing them, a pragmatic approach to cultural adaptation of the new intervention is the desired outcome. At the very least, it appears to be a consensus revolving several important elements of adaptation that should be considered when mapping out a new culturally sensitive digital self-guided intervention for adolescents with anxiety disorder in a low-income country.

Research question four: Based on research question one to three, what are the key elements of a future culturally sensitive digital self-guided intervention for adolescents with anxiety disorder in a low-income country.

According to a framework for developing complex interventions from The Medical Research Council (Craig et al., 2013), and by using a logic model and guiding principles (W.K. Kellogg Foundation, 2004), elements for a future culturally sensitive digital self-guided intervention for adolescents with anxiety symptoms and diagnosis are outlined in figure 2.

Insert figure 2 here

First, what makes our intervention complex is the number of interacting components, number and variability of outcomes, and degree of flexibility or tailoring of the intervention. In this final phase, findings from research question one, two and three will be incorporated.

The key intervention objective provides information about the core motivation for developing this intervention. Second, an understanding of the needs and characteristics of the individuals who will be using the intervention is necessary for further developing the guiding principles. Key issues that the intervention must address to be successful and achieve intervention objectives, are also listed. To address these key issues, intervention design objectives and key intervention features are outlined. Finally, ingredients and mechanisms for change are presented in a logic model.

Key intervention objective. Motivation behind this key intervention objective was based on the knowledge of an exciting treatment gap for adolescents in low- and middle-income countries, both in regards of low accessibility of mental health services and the low existence of culturally sensitive treatment for adolescents from diverse cultures.

Patient characteristics and key issues needs and challenges. Based on research and statistics, key issues in the target population were identified. These key issues were identified on both an individual level and a societal level, both equally important to target for our intervention to be successful.

Guiding principles. With the guiding principles I provide a description of several intervention design objectives that were developed to address key issues identified in the target population. Each design objective is provided with key features that are intended to achieve the design objective. E.g., to address the issue of physical, cognitive and behavioral anxiety symptoms in the target population, one design objective is therefore to reduce these anxiety symptoms. Consequently, providing evidence-based treatment for anxiety (i.e. CBT) will be one important key feature in achieving this design objective. Other key features target the specific aspects of each anxiety symptom, and included elements will therefore be psychoeducation, cognitive restructuring, mindfulness exercise, exposure and behavioral experiments.

Logic Model. To address the identified problem, being anxiety symptoms and disorders in adolescents, I want to provide a culturally sensitive digital self-guided psychological treatment as a resource, based on findings from research question one, two and three. This Logic model provides a visual description of the core elements of which I intend to implement into the intervention. The mechanisms of change and the desired outcomes are further elaborated. Common elements were included in order to increase hope, credibility, normalization, self-efficacy, expectancies and knowledge. Other ingredients were incorporated (based on results from research question one and two) in order to increase approach behavior, realistic thinking, neutral focus of attention, coping strategies, and the understanding of psychological mechanisms. The aim is further to decrease avoidance, safety behaviors, worry, cognitive biases, and attention towards feared stimuli with the same

ingredients. Culturally sensitive elements (based on research question three) were also included in order to increase cultural specificity and relevance of the intervention, cultural pride and strengths in the population, as well as to decrease culturally specific stigma and shame. Lastly, desired short– and long–term outcomes were mapped out in the logic model.

Discussion

The aim of this study was to identify effective and culturally sensitive elements for a digital self-guided intervention for adolescents with anxiety disorders in a low-income country.

The effect of digital interventions for adolescents with anxiety disorders and symptoms

A review was done on existing research literature on the clinical effects of digital interventions for adolescents with anxiety disorders and symptoms. Overall, 18 articles were included in this review and found that most studies reported significant reduction in anxiety symptoms and diagnosis post intervention, with a total of eight studies reporting large effect size. The interventions reviewed were mainly effective in treating both subclinical levels of anxiety as well as clinical levels of several different anxiety disorders (i.e. generalized anxiety disorder, separation anxiety disorder, social phobia, specific phobia, panic disorder with or without agoraphobia or agoraphobia without panic disorder and obsessive-compulsive disorder).

The quality of the evidence is mixed. Ten RCT studies were included, with nine of these including more than 20 participants. Two of these even included an active control group (i.e. face-to-face clinical CBT treatment) compared to the internet delivered CBT treatment, as well as a wait-list control group (Spence et al., 2011; Topper et al., 2017). Two case studies

did not report statistical data (Chapman et al., 2016; Cunningham et al., 2009), and thus these were not able to provide acceptable evidence of the effects of iCBT on anxiety symptoms.

Adherence is an important factor predicting treatment effects. In this study large differences in how to define adherence was identified (from completing some modules to completing all modules). This inconsistency makes it difficult to compare adherence across studies, and thus, conclusions are hard to draw. This has two consequences. Firstly, adherence and response rates directly affect the validity of the treatment effects, for instance the finale completers could be the ones who experienced improvement while the dropouts may be the ones who do not experience any improvements. Thereby skewing the results in a favorable way. Secondly, comparing and/or compiling the evidence for treatment effects are difficult, and thus establishing robust evidence across studies is challenging.

Key therapeutic elements in the digital interventions

A review was conducted on the main therapeutic elements of the digital interventions reported in research question one. A total of 16 digital interventions for treating adolescents with anxiety were identified. Of the reviewed digital interventions, all except one were based on CBT. The review provides support to prior findings suggesting CBT as a golden standard when anxiety is treated digitally (Rooksby et al., 2015; Vigerland et al., 2016)

Specific elements identified in more than half of the reviewed intervention programs were psychoeducation, cognitive restructuring, problem solving, exposure and relapse prevention. Additionally, the main emphasis of interventions ranged from 5 to 8 modules, each lasting for 20 to 40 minutes. However, differences in providing description of the investigated interventions were identified. Some studies provided vague or no definition of reported elements. This led to difficulties in reviewing key elements for two reasons. Firstly, it was challenging to determine whether the elements reported in the included interventions

belonged in the same category. For instance, one intervention reported including "preventing future problems by making techniques easier to use in everyday situations" (Cunningham et al., 2009), which may be interpreted as a relapse prevention element, and thus this intervention can be grouped together with those who do report including relapse prevention. Or, "increasing approach behavior" which was mentioned by another intervention (Topper et al., 2017) can either be categorized as an exposure exercise or an behavioral experiment, and thus be grouped together with other interventions also including similar elements.

Secondly, because of shallow descriptions and few definitions, information might have been omitted. For instance, "detecting and monitoring symptoms" which was identified as a key element in some interventions, might too have been included in other interventions without being specifically described. Sometimes exercises to detect and monitor symptoms may be considered a part of the psychoeducation or cognitive restructuring, and thus I may not have identified all interventions including elements of detecting and monitoring symptoms. Goal setting is another example, which too may be considered a part of the psychoeducation and therefor may not be explicitly mentioned as a separate element in some interventions. Based on these findings, it is important for future studies to report the key elements in the intervention in order to further develop this field of research and clinical practice.

Cultural adaptation

Existing frameworks for cultural adaptation of psychological interventions and treatments was conducted. Three frameworks were included in this paper in order to identify state-of-the art approaches on how to best adapt digital interventions for adolescents with anxiety. Common elements across the three frameworks were; 1) the importance of collaborating with cultural experts and representatives of the specific culture, 2) adaptation of

language in regards to several aspects, 3) inclusion of culturally relevant people that positively affects the therapeutic relationship (such as role models being from the same culture), 4) inclusion of cultural objects, symbols, sayings, examples and values, 5) incorporating culturally accepted methods, and 6) consider deeper structural forces that might influence perception of health and illness as well as health behaviors.

A systematic framework acknowledged by any global authority such as WHO was not identified, which probably have contributed to the development of the several different existing frameworks. Ideally, a common and general framework for tailoring interventions to specific cultures is desirable, nevertheless this may be considered difficult to accomplish due to the high heterogeneity of both the available interventions intended to be adapted, and in the cultures targeted.

The frameworks reviewed in this study can be considered general in that they help to identify culturally sensitive elements that should be adapted. In order to actually adapt the intervention for a specific culture, correct and thorough knowledge of one target culture needs to be acquired. To do so, collaborating with experts, stakeholders and representatives from the target population would be absolutely necessary, and have been highlighted in other frameworks focusing on the adaptation process (Hwang, 2009). This is not within the scope of this particular paper.

Whether culturally adapted interventions are superior to non-adapted interventions have still not been established. A meta-review by Rathod et al. (2018) concluded that few empirical studies have been published, as well as only one review examining the relative effect of culturally adapted interventions (Benish et al., 2011). More quality research is needed on this topic, in addition to the need of developing more culturally adapted intervention in order to examine their effects.

Outlining a culturally sensitive digital self-guided intervention for adolescents with anxiety disorder in a low-income country

Based on these reported findings, a culturally sensitive digital self-guided intervention for adolescents with anxiety disorder in a low-income country was outlined. By using guiding principles and a logic model, key ingredients, mechanisms of change and desired outcomes were formed. This new intervention includes common elements, specific elements and culturally sensitive elements.

Findings reported in this paper provides a clear guidance in choices of therapy direction, with CBT being extensively supported as effective in treating anxiety online. Thus, a choice to build the intervention on CBT principles was taken.

No association between guidance and adherence were found after conducting a comparison across Table 1 and Table 2, although prior research have found guided online interventions to have higher compliance rates compared to non-guided online interventions (Clarke et al., 2015; Peñate & Fumero, 2016). Thus, our findings did not provide us with a clear answer to whether our intervention should be guided or unguided. Nevertheless, taking into account that 1) low-income countries have few resources available, both in terms of therapist capacity and finances, and 2) that digitally delivered unguided interventions both are very cost-effective and demands limited to no use of therapist resources – a choice to provide an unguided intervention was therefore made.

Additionally, sensitive elements for cultural adaptation was identified (i.e. language, culturally meaningful or disrespectful words, objects, examples, as well as context). Nevertheless, this intervention has not yet been targeted towards a specific culture, as this was not within the scope of this particular paper, and thus the actual adaptation process remains for a future project.

It is important to maintain fidelity to the core concepts of the psychological theory base of the intervention (i.e. CBT in this case), while at same time recognizing the influence of cultural values and beliefs. Sometimes cultural traditions and beliefs may be incongruent with psychological theories and mechanisms of change - e.g. when some might believe that symptoms of anxiety are symptoms of a heart attack, a punishment from God, or signs that they are punished with bad karma from a previously lived life. For instance, in Filipino culture, when a negative event or sensation occurs it is typically attributed to will of God which is called "Kaloob ng Diyos" (*God's will*) (Abad et al., 2014).

To treat anxiety with evidence-based methods such as CBT, symptoms of anxiety must be understood within the very framework of this theory. Thus, a balance of focusing on increasing mental health literacy at the same time as acknowledging cultural influence on health behaviors, will be important in the further adaptation process for this intervention.

Limitations

First, this is a pragmatic review and the method it therefore is not strictly systematic. PsycInfo and Medline were considered to be the databases with most relevant hits in regard to internet delivered anxiety treatment for adolescents. Limitations can come from only conducting a search in two databases, and relevant studies may not have been identified.

Second, there are several regarding the search process. Although the search string used in this review included several different variations of words for the elements of interest, it might be that the choice of words also led to the failure of identifying all relevant articles. In addition, only one person reviewed abstract, title and full text of all hits from the search, and no cross-check was conducted. Thus, the results from this search is at risk of being subject to personal bias. Relevant literature might also have been published after the search for this review were conducted and have therefore not been included in this article.

Third, the present review did not conduct a thorough risk of bias assessment. A risk of bias assessment is commonly conducted in systematic reviews and would provide more confidence in the validity of the results by illuminating biases (Higgins, Savović, Page, Elbers, & Sterne, 2019). Since this was a pragmatic review, a risk of bias assessment was not conducted. Consequently, the quality of the evidence from the individual studies have not been perfectly addressed. However, based on a face value evaluation of the quality of the included studies, this review concludes that digitally delivered CBT for treating anxiety in adolescence may be effective.

In regard to cultural adaptation of psychological interventions, this article is written from a western scientific paradigm, and psychological interventions do not automatically translate into other cultural paradigms. The usefulness of developing a culturally sensitive digital intervention is assessed from a western perspective, where psychological therapies is recognized as the first-line treatment for anxiety disorders (National Institute for Health and Care Excellence, 2014). However, psychological therapy may not be the first choice of treatment in many other cultures. Even though a psychological intervention is culturally adapted, psychological therapy in general may not be acknowledged or endorsed as a treatment practice. Thus, the development of a culturally adapted psychological intervention may be of little use, if the culture itself does not endorse psychological therapy or interventions as a treatment practice for mental health issues.

Further recommendations

The trend of digitally delivered interventions are rising in low- and middle-income countries. Nevertheless there is still a great need for developing scalable interventions targeting mental health, as well as conducting more studies on the efficacy of digital interventions in these countries (Naslund et al., 2017).

A golden standard on how to measure and report adherence estimates is needed for future studies, in order to be able to compare adherence across studies. There is also a great need of more research on culturally adapted interventions, and the impact of culture on the effects of psychological treatments. Future research should focus on relative effect of culturally adapted therapies compared to non-adapted therapies, a question which now remains unanswered. A global, common adaptation framework for adjusting psychological treatments to fit with specific cultures is also needed to the extent that it is possible to develop such a general framework for all cultures.

In line with the framework for developing complex interventions (Craig et al., 2013), the next phases for this project will be to pilot, evaluate and implement the intervention. It would be desirable to use a community-oriented approach in order to identify the specific beliefs, values and traditions in the target culture. For instance, by collaborating with experts, stakeholders and representatives from the target population which will ultimately enable the adaptation of culturally sensitive content.

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Appendix

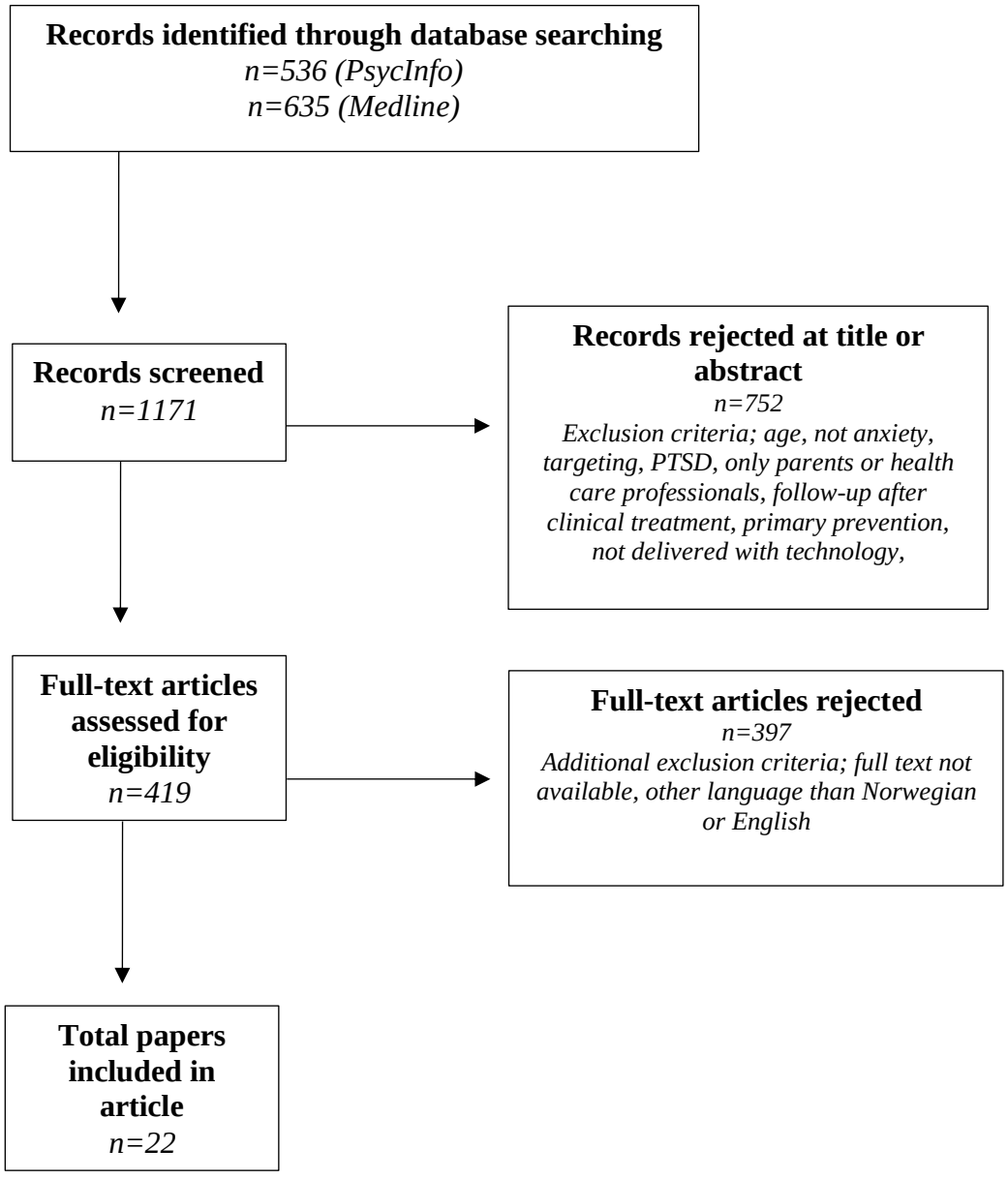


Figure 1. Flow chart

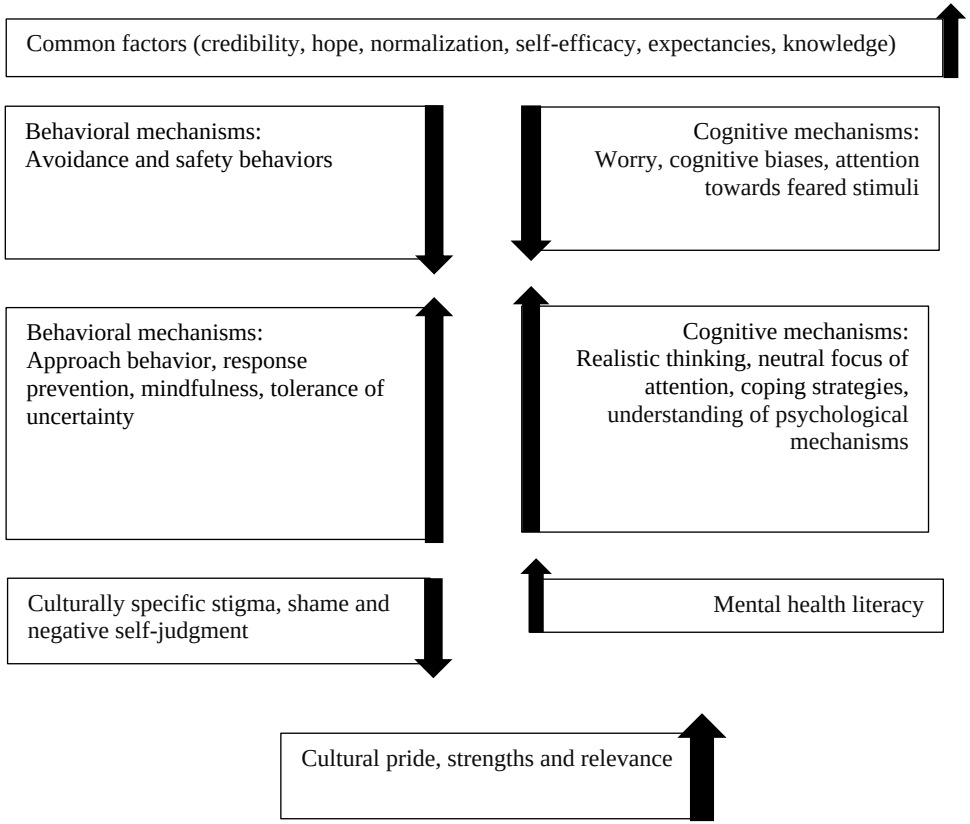
KEY INTERVENTION OBJECTIVES	PATIENT CHARACTERISTICS AND KEY ISSUES, NEEDS AND CHALLENGES
To provide an evidence based culturally sensitive digital self-help intervention for adolescents with anxiety in a low-income country	**INDIVIDUAL LEVEL** Adolescents with anxiety symptoms from diverse cultural backgrounds. **SOCIETAL LEVEL** (low-income country characteristics) Low socioeconomic status, low level of education, very limited access to mental health professionals, low mental health literacy, cultural influences **Key issues, needs and challenges:** 1. Physical symptoms of anxiety; heart rate increase, hard to breathe, tunnel vision 2. Cognitive symptoms of anxiety; focus on feared stimuli, thinking "worst case scenario", negative appraisal 3. Behavioral symptoms: avoidance and safety behaviors 4. Early onset of mental health disorders 5. Heterogeneity in target group and societal influences 6. Low adherence in digital interventions 7. Low mental health literacy and trust in mental health services 8. Few existing culturally sensitive digital interventions for treating anxiety in adolescents

GUIDING PRINCIPLES

Intervention design objective	Key intervention features relevant to each objective
To reduce physical and cognitive symptoms of anxiety in adolescents	• Offer an evidence-based rationale for anxiety treatment • Build intervention on a theoretical framework that has good support in research (CBT) • Implement effective elements to address cognitive symptoms such as; psychoeducation, goal setting, cognitive restructuring • Implement effective elements to address physical and behavioral symptoms such as; exposure, behavioral activation, behavioral experiments and mindfulness exercises. • Behavioral elements; exposure
To increase self-efficacy and resilience	• Foster autonomy through choice • Psychoeducation -> increasing mental health literacy -> increasing self-efficacy • Including elements of assertiveness training and self-care • Address locus of control (in a culturally sensitive way/with respect to cultural values and religious beliefs)

Intervention design objective	Key intervention features relevant to each objective
To be an easy to use resource, preventing users from becoming overwhelmed	• Provide a simple, attractive interface, with a focus on accessibility of content • Use videos and images rather than text • Simple layout with clear structure • Tunneled intervention design • Short length of modules • Possibility to complete modules and assignments at a time of choice.
To promote credibility of intervention and foster positive experiences with psychological treatment	• including supportive comments and guidance from an expert character • including other elements of trust - find out what already has credibility in the target group, can it be incorporated into the intervention without conflicting fidelity of the psychological theory. • Address concerns the patients may have from their previous experiences • Communicate empathy and acknowledgement of barriers to change • Address stigma with normalization and inclusion of culturally sensitive elements
To provide treatment in a manner that aligns with the preferences of our target group	• deliver intervention as an app or computer program • Include elements of gamification, e.g. framing modules as levels with rewards • Include vivid graphics and sounds • Offer a wide range of different coping strategies to choose from • Optional elements of caregiver support
To promote and maintain motivation to increase adherence	• Implement elements to increase motivation such as; goal setting and reward for achieved goals. • Self-tailoring of different coping strategies through a workbook • Promote relatedness through peer modeling; facilitating normalization of symptoms and provide success stories of using techniques • Include elements of gamification • Sub-goals followed by immediately positive reinforcements
Promote consolidation of learned material	• Providing immediately reinforcing feedback • Repetition through quizzes and summaries • Opportunity to go back to previous models for repetition • Workbook including self-tailored assignments and recap of core information
Include culturally sensitive elements	• Use culturally relevant examples and characters. • Include cultural symbols and objects • Use culturally appropriate language. • Communicate acknowledgement of cultural values and beliefs, e.g. family, community, religion, spirituality, independence, education etc.

OVERARCHING GOAL:	To provide an evidence based culturally sensitive digital self-help intervention for adolescents with anxiety in a low-income country, as a way of bridging the existing treatment gap	LOGIC MODEL DATE:	13.05.2020

PROBLEM	RESOURCES	INGREDIENTS	MECHANISM(S)	OUTCOMES
Anxiety symptoms and disorder	Digital self-help psychological treatment	General introduction Psychoeducation for both adolescents and caregiver Goal setting with focus on sub-goals Monitoring and assessing symptoms Therapeutic tools: Workbooks, quizzes, levels Culturally specific elements: i.e. language, examples, objects, values and beliefs.		Reduced anxiety Increased self-efficacy Increased mental health literacy

Note. Direction of arrows indicates whether the intervention aims to increase or decrease the prevalence of the recognized mechanisms.

Figure 2. Logic Model and Guiding Principles

Table 1

Main effects of interventions

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
A randomized controlled trial of internet-delivered cognitive behavior therapy for adolescent anxiety disorders in a routine clinical care setting with and without parent sessions	Waite, Marshall, and Creswell (2019)	n=60 *I=30* *C=30*	CLIN	RCT age 13-18	Remission of primary AD: internet-group= 40% wait list = 23.3% CSR: Internet group M 5.73 (sd 0.87) pre M 3.89 (sd 2.58) post Wait list M 5.77 (sd 1.01) pre M 4.86 (sd 2.19) post	NR	Non-significant difference between intervention group and wait-list	DSM-IV diagnostic criteria for GAD, SAD, SoP, SP, PD with or without AP, AP without PD	Completed all modules: 79.3%
A randomized controlled trial of online versus clinic-based CBT for adolescent anxiety.	Spence et al. (2011)	n=115 *I1=44* *I2=44* *C=27*	COM	RCT age 12-18	Remission of primary AD: internet-group = 36.6%, clinic-group = 32.5%, wait list = 4.2% CSR Internet-group M 5.91 (se 0.13) (pre) M 3.85 (se 0.26) (post) clinic-group M 6.30 (se 0.13) pre, M 4.08 (se 0.27) post wait list M 5.67 (se 0.16) pre M 5.50 (se 0.34) post	Internet CSR: d=2.12 Clinic CSR: d=3.42 wait list CSR: d=0.24	Significant change from pre- to post treatment for the two intervention groups Significant difference between groups (intervention group with significant more improvement compared to wait-list - but equal effect as clinic group)	DSM-IV diagnostic criteria for GAD, SAD, SoP, SP	Completed all modules: Adolescents 39% Parents 66% Mean completion rate by participants in internet group: 7.5 out of 10 modules for adolescents and 4.48 out of 5 for parents.

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
The Cool Teens CD-ROM for anxiety disorders in adolescents: A pilot case series.	Cunningham et al. (2009)	n = 5	COM	Open case study Age 14-16	Remission of primary AD= 40% (2 of 5) CSR: M 6 (pre) M 3,8 (post) Range from 2-6	NR	Significance not reported Participant 1) large improvement in anxiety ratings, but no changes in ADIS diagnosis or severity. Participant 2) ADIS-C rating for GAD was reduced from 6 to 4. Post-treatment social anxiety fears met criteria for SP. Participant 3) ADIS rating for SAD showed slight improvement post-treatment. Reduced severity ratings for secondary diagnoses. Participant 4) discontinuing treatment after week 4 (reported she no longer had anxiety). Participant 5) Improved to a subclinical level, ADIS-C anxiety rating reduction from 6 to 2.	GAD and SAD diagnosis (measured by ADIS).	Completed 6 out of 8 modules: (4/5) 80%
A Randomized Controlled Trial of the Cool Teens CD-ROM Computerized Program for Adolescent Anxiety.	Wuthrich et al. (2012)	n=43 *I=24* *C=19*	CLIN and COM	RCT Age 14-17	Remission of primary AD: internet-group 41%, Wait list 0% CSR: internet-group M 6.91 (se 0.25) pre M 4.75 (se 0.29) post wait list M 6.95 (se 0.29) pre M 6.58 (se 0.31) post	Internet ADIS: d=1.13 CSR d=1.69 Wait-list ADIS d=0.22 CSR d=0.33	Significant change from pre- to post treatment for intervention group. Significant difference between groups (intervention group with significant more improvement compared to waitlist). Significant reduction in the clinical severity and in the total number diagnoses over time.	DSM-IV diagnostic criteria for GAD, OCD, SAD, SoP, SP, PD and anxiety disorder not otherwise specified	Completed all modules and follow up: (19/24) 79,17%
The effectiveness of internet cognitive behavioral therapy for generalized anxiety disorder in clinical practice.	Mewton, Wong, and Andrews (2012)	n=588	CLIN	Open pre-post quality assurance study	Remission of primary AD: 61.7% GAD-7: M 11.56 (sd 5.33) pre	GAD-7: d=0.91	Significant change from pre- to post treatment. Completed all modules: (324/588) 55.1%	Subclinical- and clinical levels of GAD (measured by GAD-7)	Completed all modules: (324/588) 55.1%

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
				age 16-80	M 7.09 (sd 5.09) post				
Prevention of anxiety disorders and depression by targeting excessive worry and rumination in adolescents and young adults: A randomized controlled trial.	Topper, Emmelkamp, Watkins, Ehring (2017)	n=253 *I1=84* *I2=84* *C=85*	COM	RCT age 15-18	PSWQ: Internet-group M58.73 (sd 6.96) pre M 51.87 (sd 8.85) post clinic-group M 58.20 (sd 6.59) pre M 51.29 (sd 8.58) post wait-list M 59.15 (sd 6.78) pre M 57.80 (sd 8.54) post	Internet PSWQ d= 0.79 Clinic PSWQ: d=0.98 Wait list PSWQ: d= 0.24	Significant change from pre- to post treatment for both intervention groups. Significant difference between groups (intervention groups with significant more improvement compared to waitlist - but internet and group intervention showed equal effect)	Elevated levels of worry and rumination	Participants who had started the internet condition completed on average 3.96 modules
'Reach Out, Rise Up': The efficacy of text messaging in an intervention package for anxiety and depression severity in young people.	Anstiss and Davies (2015)	n=40	COM	Open pre-post efficacy study Age 12-24	GAD-7 M 8.1 (sd 3.2) pre M 4.9 (sd 3.7) post	NR	Significant change from pre- to post treatment.	Subclinical- and clinical levels of anxiety (measured by GAD-7).	Completed the full text package and follow-up: (21/40) 52,50%
Reducing test anxiety among school-aged adolescents: a field experiment	Putwain, Chamberlain, Daly, and Sadreddini (2014)	n=3225 I=1602 C=1623	COM	quasi-experimental mixed design Mean age 14.97	worry (and tension) scales from RTAS, for those with high test anxiety: Internet-group: Worry M 3.21 (sd 0.43) pre M 2.87 (sd 0.55) post Tension M 3.59 (sd 0.43) pre M 3.06 (sd 0.65) post Control-group: Worry	High test anxiety-group worry d=0.63 tension d=0.53	Significant change from pre- to post treatment for both worry and tension for those with high test anxiety. Significant difference between groups (intervention groups with significant more improvement compared to waitlist)	Low-, middle- and high test-anxiety (measured by RTAS, worry and tension scale).	Completed all modules: (217/1600) 13.7% Completed one or more modules: (407/1600) 25.5% Did not complete any part of the program: (965/1600) 60.8%

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
					M 3.26 (sd 0.41) pre M 3.20 (sd 0.50) post Tension M 3.59 (sd 0.43) pre M 3.41 (sd 0.66) post				
The YouthMood Project: A cluster randomized controlled trial of an online cognitive behavioral program with adolescents.	Calear, Christensen, Mackinnon, Griffiths, and O'Kearney (2009)	n=1477 *I=563* *C=914*	COM	Cluster RCT age 12-17	RCMAS Internet-group: M 8.88 (sd 6.41) pre M 7.86 (sd 6.99) post Wait-list group: M 8.83 (sd 6.42) pre M 8.90 (sd 7.03) post	RCMAS d=0.15	Significant difference between groups (intervention groups with significant more improvement compared to waitlist)	Subclinical- and clinical levels of anxiety (and depression)	Completed all modules: (183/559) 32.7% Completed three or more modules: (347/559) 62% Mean completion rate: 3.16 out of 5 modules
Effects of internet-based guided self-help problem-solving therapy for adolescents with depression and anxiety: A randomized controlled trial.	Hoek, Schuurmans, Koot, and Cuijpers (2012)	n=45 *I=22* *C=23*	CLIN and COM	RCT age 12-21	Remission of primary AD = 60% of the 31 participants with clinical levels at baseline HADS-A Internet-group: M 8.63 (sd 3.22) pre, M 7.17 (sd 3.04) post Wait-list group: M 9.04 (sd 3.99) pre M 7.56 (sd 4.70) post	NR	No significant time, group or group x time interaction effects were found. Recovery effects for those with clinical levels at baseline were not significantly different between intervention and waiting list groups. Depressive and anxiety symptoms declined in both groups.	Subclinical- and clinical levels of anxiety (based on self-reported measures).	Completed all modules: (6/22) 27% Completed three or more modules: (10/22) 45%
A randomized trial of internet-delivered treatment for social anxiety disorder in high school students.	Tillfors et al. (2011)	n=19 *I=10* *C=9*	COM	RCT age 15-21	Reliable change in social anxiety measures= 60% for SPSQ-C, 53% for LSAS-SR Internet-group:	SPSQ-C: Within d=1.06 Between d=1.28	Significant change from pre- to post treatment for SPSQ-C and LSAS-SR fear. Significant difference between groups for SPSQ-C and LSAS-SR fear (intervention group with significant more improvement compared to waitlist). Significant interaction effects	DSM-V diagnostic criteria for SoP	Mean completion rate: 2.9 out of 9 modules

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
					SPSQ-C M 14.8 (sd 2.2) pre, M 12.2 (sd 2.7) post LSAS-SR fear M 23.8 (sd 11.8) pre M 14.6 (sd 8.2) post LSAS-SR avoidance M 21.4 (sd 13.6) pre M 15.0 (sd 9.1) post Wait-list group: SPSQ-C M 15.7 (sd 2.8) pre M 16.0 (sd 3.2) post LSAS-SR fear M 27.3 (sd 13.8) pre M 31.0 (sd 13.4) post LSAS-SR avoidance M 23.4 (sd 14.9) pre M 30.0 (sd 16.4) post	LSAS-SR: Avoidance Within d=0.55 Between d=1.13 LSAS-SR: Fear Within d=0.91 Between d=1.48	(Group x Time) for SPSQ-C, LSAS-SR fear and LSAS-SR avoidance, supporting differential improvement in treated relative to untreated subjects. Non-significant change for LSAS-SR avoidance from pre- to post treatment, nor between intervention and wait list group.		
'Pesky gNATs': investigating the feasibility of a novel computerized CBT intervention for adolescents with anxiety and/or depression in a Tier 3 CAMHS setting.	Chapman et al. (2016)	n=11	CLIN	case study age 13-16	mean scores not reported	NR	At the end of the seven sessions it was found that 5/11 participants showed reliable reductions on at least one subscale. However, four participants showed reliable increases on subscale scores following the intervention.	Clinical levels of anxiety	Completed all modules: 100%
Online cognitive behavior therapy for adolescents with excessive worry: a multiple baseline design feasibility study	Wahlund et al. (2020)	n=13	CLIN and COM	non-concurrent, multiple baseline design study	Remission of primary AD = 50% PSWQ-C M 33.69 (sd 3.95) pre M 25.00 (sd 8.06) post	PSWQ-C d=1.38	Significant change from pre- to post treatment. Significant effects of time for the primary outcome variable (PSWQ-C/P).	DSM-V diagnostic criteria for GAD	Completed 6 of 10 modules: (12/13) 92,31%

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
				analysis age 13-17					Mean completion rate: 9.8 out of 10 modules
Phase I trial of a standalone internet social anxiety treatment for adolescents who stutter: iBroadway	Gunn et al. (2019)	n=27	COM	Open pre-post study age 12-17	Remission of primary AD: out of 10 participants with a primary anxiety disorder, only 4 showed remission post-treatment: RCMAS: M 12.33 pre M 11.00 post	NR	No significant change from pre- to post treatment were found. Remission of primary AD were non-significant. There was no evidence of any self-reported or parent-reported improvement with stuttering severity.	Subclinical- and clinical levels of anxiety (OCD, GAD, SoP, AP, SP, PD) Stuttering diagnosed by a speech-language pathologist.	Completed all modules: 52.4%
A randomized controlled trial examining the efficacy of an internet-based cognitive behavioral therapy program for adolescents with anxiety disorders	Stjerneklar, Hougaard, McLellan, and Thastum (2019)	n=70 *I=35* *C=35*	COM	RCT age 13-17	Remission of primary AD: Internet-group=40%, control group=16% CSR Internet-group: M 6.69 (sd 0.68) pre M 3.83 (sd 2.65) post Wait list control M 6.54 (sd 0.92) pre M 5.09 (sd 2.29) post	CSR Within Internet d=1.48 Wait list d=0.83 CSR Between d=0.65	Significant change from pre- to post treatment. Significant difference between groups (intervention group with significant more improvement compared to waitlist).	DSM-V diagnostic criteria for GAD, SAD, SoP, SP, PD with or without AP, AP without PD, OCD	Participants were considered completers regardless of their number of completed modules or amount of completed therapist calls: (33/35) 94,29% Mean completion rate: 5.4 out of 8 modules
Therapist-guided internet-delivered cognitive–behavioral therapy supplemented with group exposure sessions for adolescents with social anxiety disorder: a feasibility trial	Nordh et al. (2017)	n=30	CLIN and COM	Open pre-post feasibility study age 13-17	Remission of primary AD=47% CGI-S M 4.6 (sd 0.72) pre M 3.3 (sd 1.3) post	CGI-S d=1.17	Significant change from pre- to post treatment.	DSM-IV diagnostic criteria for SAD.	Completed 7–9 modules: (11/30) 37% Completed 4–6 modules: (13/30) 43%

Article	Reference	N = xx	Recruitment	study design (and age)	Main measure including pre and post score	Effect size	Main effects	Diagnose	Adherence
									Completed 2–3 modules: (6/30) 20% None completed fewer than two modules.
A pilot randomized controlled trial of the e-couch anxiety and worry program in schools	Calear, Christensen, Brewer, Mackinnon, and Griffiths (2016)	n=225 *I=127* *C=98*	COM	cluster RCT age 13-17	SCAS (GAD subscale) Internet-group: M 6.25 (sd 3.69) pre M 5.42 (sd 3.72) post Wait-list group: M 5.99 (sd 3.41) pre M 5.45 (sd 3.43) post	SCAS (GAD subscale) d=0.08	No significant differences were found between intervention group and wait list control.	Subclinical- and clinical levels of GAD (measured by GAD-7)	Completed all program: 45% Completed four out of six weeks: 68% Completed the first two out of six weeks: 98%
Online Obsessive-Compulsive Disorder Treatment: Preliminary Results of the "OCD? Not Me!" Self-Guided Internet-Based Cognitive Behavioral Therapy Program for Young People	Rees, Anderson, Kane, and Finaly-Jones (2016)	n=132	COM	open trial, within-group design age 12-18	C-FOCI severity M 11.56 (se 0.31) pre M 5.77 (se 0.97) post C-FOCI symptoms M 7.82 (se 0.34) pre M 3.87 (se 0.83) post	C-FOCI Severity d=0.89 Symptoms d=0.64	Significant change from pre- to post treatment for both symptoms and severity.	Subclinical- and clinical levels of OCD (measured with YODA)	NR

Note. N=number (of participants), CLIN=clinical referral, COM=community referral, RCT = Randomized controlled trial, pre = pretreatment, post = posttreatment, M=mean, sd = standard deviation, se = standard error, AD = anxiety disorder, CSR = Clinician Severity Rating, GAD-7=A seven item screening tool for Generalized Anxiety Disorder, PSWQ (C/P)= Penn State Worry Questionnaire (Children and Parent report versions), RTAS=Revised Test Anxiety Scale, RCMAS= Revised Children's Manifest Anxiety Scale, SPSQ-C=Social Phobia Screening Questionnaire for Children, LSAS-SR=Liebowitz Social Anxiety Scale self-report version, HADS-A=Hospital Anxiety and Depression Scale, CGI-S=Clinical Global Impression – Severity, SCAS= Spence Children's Anxiety Scale, C-FOCI= Children's Florida Obsessive-Compulsive Inventory, NR= not reported, ADIS=Anxiety Disorders Interview Schedule, GAD=Generalized anxiety disorder, SAD=Separation anxiety disorder, SoP=Social Phobia, SP=Specific Phobia, therapy, OCD=Obsessive-compulsive disorder, PD=Panic disorder, AP=Agoraphobia

Table 2

Key therapeutic elements

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout
A randomized controlled trial of internet-delivered cognitive behavior therapy for adolescent anxiety disorders in a routine clinical care setting with and without parent sessions	Waite, Marshall, and Creswell (2019)	CBT (Brave)	13-17	DSM-IV diagnostic criteria for GAD, SAD, SoP, SP, PD with or without AP, AP without PD	Therapist gives feedback via mail and phone	Parallel caregiver program; 5 modules á 60 minutes	10 weekly sessions á 60 minutes	Graded exposure, breathing exercises, and progressive muscle relaxation	Psychoeducation, cognitive restructuring, problem solving, guided imagery, self-talk strategies, cognitive distortions, and self-reinforcement of ‘‘brave’’ behavior	Graphics and sounds, interactive exercises, peer modeling, graphic expert guidance, homework, age-appropriate, relaxation CD, and tunneled intervention design
A randomized controlled trial of online versus clinic-based CBT for adolescent anxiety	Spence et al. (2011)	CBT (Brave)	12-18 (13-17)	DSM-IV diagnostic criteria for GAD, SAD, SoP, SP						
Online CBT in the Treatment of Child and Adolescent Anxiety Disorders: Issues in the development of BRAVE–ONLINE and Two Case Illustrations	Spence et al. (2008)	CBT (Brave)	10, 17 (13-17)	DSM-IV diagnostic criteria for SAD and SoP						
The Cool Teens CD-ROM for anxiety disorders in adolescents: A pilot case series.	Cunningham et al. (2009)	CBT (Cool Teens)	14-18 (13-17)	Clinical levels of GAD and SAD	Therapist gives feedback via phone	Caregivers receiving information about core elements	8 modules á 15-30 minutes	Graded exposure	Psychoeducation, goal setting, cognitive restructuring, problem solving, assertiveness training, and preventing future problems by making	Graphics and sounds, interactive exercises, peer modeling, homework, and menu intervention design

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout
									technique easier to use in everyday situations	
A Randomized Controlled Trial of the Cool Teens CD-ROM Computerized Program for Adolescent Anxiety.	Wuthrich et al. (2012)	CBT (Cool Teens)	7-17 (13-17)	DSM-IV criteria for GAD, OCD, SAD, SoP, SP, PD and anxiety disorder not otherwise specified						
The Cool Teens CD-Rom: A multimedia self-help program for adolescents with anxiety	Cunningham, Rapee, and Lyneham (2006)	CBT (Cool Teens)	7-17 (13-17)	No participants						
The effectiveness of internet cognitive behavioral therapy for generalized anxiety disorder in clinical practice.	Mewton, Wong, and Andrews (2012)	CBT	16-80	Subclinical- and clinical levels of GAD	Unguided	Not reported	6 lessons	Graded exposure and behavioral activation	Psychoeducation, cognitive restructuring, and problem solving	Peer modeling, graphic expert guidance, and homework
Prevention of anxiety disorders and depression by targeting excessive worry and rumination in adolescents and young adults: A randomized controlled trial.	Topper, Emmelkamp, Watkins, Ehring (2017)	Rumination focused CBT/ Metacognitive therapy	15-22	Elevated levels of worry and rumination	Therapist gives personalized, written feedback	Not reported	6 sessions	Increase approach behavior (exposure), behavioral activation, and behavioral experiments	Psychoeducation, cognitive restructuring, and attention shift	Interactive exercises (writing), peer modeling, and homework

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout
'Reach Out, Rise Up': The efficacy of text messaging in an intervention package for anxiety and depression severity in young people.	Anstiss and Davies (2015)	CBT + mindfulness therapy	12-24	Subclinical- and clinical levels of anxiety	Therapist gives feedback via phone each week	Not reported	10 weeks	Breathing exercise, mindfulness, trying new activities, mood journal, and self-care	Psychoeducation, goal setting, and thought record	Delivered via text message, age appropriate language
Reducing test anxiety among school-aged adolescents: a field experiment	Putwain, Chamberlain, Daly, and Sadreddini (2014)	CBT + rational-emotive therapy (STEPS)	Mean age 14.97	All levels of test anxiety	Not reported	Not reported	6 session á 30-40 minutes	Relaxation strategies (abdominal breathing and progressive muscle relaxation)	Psychoeducation, goal setting, cognitive restructuring, visualization, techniques to learn and apply test-taking skills, motivation, and reviewing previously learned material (relapse prevention)	Graphics and sounds, interactive exercises, peer modeling, homework, workbook, and reflection tasks
The YouthMood Project: A cluster randomized controlled trial of an online cognitive behavioral program with adolescents.	Calear, Christensen, Mackinnon, Griffiths, and O'Kearney (2009)	CBT + interpersonal therapy (Mood Gym)	12-17 (>16)	Subclinical- and clinical levels of anxiety (and depression)	Fully automated and self-directed	Not reported	5 modules, á 20-40 minutes	Relaxation strategies, strategies to increase self-esteem	Psychoeducation, cognitive restructuring, problem-solving strategies, and thought recognition and recordings	Graphics and sounds, interactive exercises (quizzes), peer modeling, summary, workbook, progress chart, provided with help seeking contacts, and tunneled intervention design
STUDY PROTOCOL: Prevention of depression and anxiety in adolescents: A randomized controlled trial testing the efficacy and mechanisms of Internet-based self-	Hoek, Schuurmans, Koot, and Cuijpers (2009)	Problem-solving Therapy (PST) *Based on SET*	12-18	Subclinical- and clinical levels of anxiety	Mental health professionals give feedback via mail	Caregivers receiving information about core elements	5 lessons, 1 each week	Divide problems into three categories: (a) unimportant problems, (b) important problems which can be solved, and (c) important problems which cannot be solved Metacognitive techniques to handle solvable and important problems, coping techniques for managing unsolvable and important problems (eliminate negative thoughts, enhance positive		Exercises

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout
help problem-solving therapy								thoughts, and reduce avoidance by writing or talking about difficult experiences related to negative emotions), work out long term goals		
Effects of internet-based guided self-help problem-solving therapy for adolescents with depression and anxiety: A randomized controlled trial.	Hoek, Schuurmans, Koot, and Cuijpers (2012)	Problem-solving Therapy (PST) *Based on SET*	12-21	Subclinical- and clinical levels of anxiety						
A randomized trial of internet-delivered treatment for social anxiety disorder in high school students.	Tillfors et al. (2011)	CBT	15-21	DSM-5 criteria for SoP	Therapist gives feedback, but not specified	Not reported	9 modules	Exposure and behavioral experiments	Psychoeducation, goal setting, cognitive restructuring, assertiveness training, attentions shift training, and identifying and registering NAT	Interactive exercises (quizzes and essay questions), homework, age-appropriate, printable materials, and tunneled intervention design
'Pesky gNATs': investigating the feasibility of a novel computerized CBT intervention for adolescents with anxiety and/or depression in a Tier 3 CAMHS setting.	Chapman et al. (2016)	Metacognitive therapy + Mindfulness therapy (Pesky gNATs)	13-18 (9-12)	Clinical levels of anxiety.	All sessions completed together with the therapist	Not reported	6-8 sessions	Muscle relaxation, breathing exercises, mindfulness exercises, and behavioral activation	Psychoeducation, negative core belief reappraisal, cognitive monitoring, and cognitive perspective exercise	Graphics and sounds, interactive exercises (games), peer modeling, graphic expert guidance, homework, and tunneled intervention design
Online cognitive behavior therapy for adolescents with excessive worry: a multiple baseline design feasibility study	Wahlund et al. (2020)	CBT (BIP worry) *Based on IU*	13-17	DSM-V diagnostic criteria for GAD	Therapist gives feedback via mail	Parallel caregiver program	10 modules	Exposure to thoughts, exposure to situations associated with uncertainty, and let go of control behaviors	Psychoeducation, goal setting, problem solving, worry awareness training, and relapse prevention.	Graphics, summaries

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout
Phase I trial of a standalone internet social anxiety treatment for adolescents who stutter: iBroadway	Gunn et al. (2019)	CBT (iBroadway)	12-17	Subclinical- and clinical levels of anxiety (OCD, GAD, SoP, AP, SP, PD), Stuttering diagnosed by a speech-language pathologist.	Unguided	Not reported	7 modules		Psychoeducation, cognitive restructuring, repair self-focused attention, assessment of thoughts and feared situations, and relapse prevention	Graphics and sounds, interactive exercises (scientific trivia and puzzles), graphic expert guidance, homework, individualized adjustments, and humor
A randomized controlled trial examining the efficacy of an internet-based cognitive behavioral therapy program for adolescents with anxiety disorders	Stjerneklar, Hougaard, McLellan, and Thastum (2019)	CBT (Chilled Out)	13-17	DSM-V diagnostic criteria for GAD, SAD, SoP, SP, PD with or without AP, AP without PD, OCD	Psychologist gives feedback via phone	Caregivers receiving information about core elements and advice on how to best support their teenager during treatment	8 modules á 30 minutes	Graded exposure, calming activities, and behavioral experiments	Psychoeducation, goal setting, cognitive restructuring, problem solving, assertiveness training, realistic thinking, reward for reached goals, and relapse prevention	Graphic and sounds, peer modelling, homework, progress chart, and menu intervention design with suggested order
Therapist-guided internet-delivered cognitive–behavioural therapy supplemented with group exposure sessions for adolescents with social anxiety disorder: a feasibility trial.	Nordh et al. (2017)	CBT (BiP SOFT)	13-17	DSM-IV diagnostic criteria for SAD	Group exposure together with a therapist online contact every week and via phone if necessary	Parallel caregiver program; 5 modules	9 modules and 3 group exposure sessions	Exposure in vivo	Psychoeducation, treatment goals, cognitive restructuring, problem solving, focus shift, self-assertive behaviors, social skill training, strategies to handle negative thoughts, coping strategies, functional analysis and relapse prevention	Graphics and sounds, and tunneled intervention design

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout
A pilot randomized controlled trial of the e-couch anxiety and worry program in schools	Calear, Christensen, Brewer, Mackinnon, and Griffiths (2016)	CBT + interpersonal therapy and mindfulness therapy (e-couch Anxiety and Worry program)	13-17	Subclinical- and clinical levels of GAD	Unguided	Not reported	2 main sections, 6 weeks á 30-40 minutes	Mindfulness, progressive muscular relaxation, and physical activity	Psychoeducation, goal setting for physical activity (using SMART model), cognitive restructuring, problem solving, learning how to detect worry, and using imagery together with relaxation	Graphics and sounds, peer modeling, workbook, audio and text-files for downloading, contact information if "feeling suicidal", and tunneled intervention design
OCD? Not Me! Protocol for the development and evaluation of a web-based self-guided treatment for youth with obsessive-compulsive disorder	Rees, Anderson, and Finlay-Jones (2015)	CBT (with a focus on ERP therapy) (OCD? Not Me!)	12-18	No participants	Unguided	Caregivers receive information; psychoeducation, tips for supporting teenagers, and strategies for reducing levels of family distress.	8 stage	Graded, prolonged and real-life exposure, self-appreciation exercise, talking with friends and family about OCD, and consolidating principles of ERP	Psychoeducation, goal setting, challenging dysfunctional beliefs via the provision of corrective psychoeducational information, rewards, and relapse prevention	Graphics and sounds, interactive exercises, peer modeling, graphs, using metaphors (climbing the OCD-mountain), and tunneled intervention design
Online Obsessive-Compulsive Disorder Treatment: Preliminary Results of the "OCD? Not Me!" Self-Guided Internet-Based Cognitive Behavioral Therapy Program for Young People	Rees, Anderson, Kane, and Finlay-Jones (2016)	CBT (with a focus on ERP therapy) (OCD? Not Me!)	12-18	Subclinical- and clinical levels of OCD						

Article	Reference	Theory (Name of intervention, if any)	Age range (program target)	Diagnosis or symptoms based on inclusion criteria	Guidance	Caregiver involvement	Number and length of modules	Behavioral elements	Cognitive elements	Layout

Note. CBT=Cognitive Behaviour Therapy, IU=Intolerance of uncertainty model pathological worry, SET=Self-Examination Therapy, DSM-V=The Diagnostic and Statistical Manual of Mental Disorders - fifth edition, ERP=exposure and response prevention, BIP=Cognitive-behavioral intervention, BiP=Barn Internet Prosjektet, GAD=Generalized anxiety disorder, SAD=Separation anxiety disorder, SoP=Social Phobia, SP=Specific Phobia, therapy, OCD=Obsessive-compulsive disorder, PD=Panic disorder, AP=Agoraphobia