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A Systematic Review of Interventions for Health Anxiety Presentations Across Diverse Chronic Illnesses

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Abstract

Purpose Health anxiety (HA) is associated with reduced quality of life among individuals with chronic illnesses. However, little is known about effective interventions for reducing HA in this context. This study aimed to comprehensively review the literature on interventions for the treatment of HA in chronic illness.

Methods This study was conducted as part of a larger systematic review on HA among individuals diagnosed with a chronic illness, using literature published between January 1996 and October 2017. A total of 51 articles were selected as they reported on interventions with pre-post measures and described the impact of the intervention on HA.

Results The data on psychotherapy (CBT, third-wave CBT, and mindfulness), patient education, and rehabilitation programs demonstrated effectiveness in cancer and cardiac patients. Exercise interventions demonstrated effectiveness in patients with Parkinson's disease, and medical interventions showed limited effectiveness in reducing HA in diabetes and epilepsy. Most interventions yielding significant outcomes were at least 6 to 8 weeks long.

Conclusions The literature supports that a variety of interventions may be effective in reducing HA in individuals with chronic illness. Future research should test single interventions across several illnesses, as well as several interventions within a single illness to better understand how HA can be managed across chronic illnesses.

Keywords Health anxiety · Chronic illness · Interventions · Systematic review · Treatments

Introduction

Health anxiety (HA) is a specific type of anxiety that arises when bodily sensations or changes are believed to be indicative of serious illness [1]. HA involves affective, cognitive, behavioral, and perceptual features [2]. More specifically, HA consists of distressing emotions (e.g., fear), thoughts of danger, and physiological arousal [3]. The experience of HA varies across individuals, and has therefore been conceptualized on a continuum ranging from mild and transient to severe and chronic [3]

In the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), the concepts of HA and hypochondriasis were used interchangeably: characterized by excessive fear or worry about ill health, which is believed to result from a preoccupation with the *incorrect* belief that one has, or is in danger of developing, a serious disease or a medical condition [4]. With the introduction of the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) in 2013, hypochondriasis was redefined and replaced with two new concepts: somatic symptom disorder and illness anxiety disorder [5]. Somatic symptom disorder is characterized by somatic symptoms, whether medically explained or not, that are either very distressing, or result in noteworthy disruption of functioning. Somatic symptom disorder is also characterized by excessive and disproportionate thoughts, feelings, and behaviors relative to those specific symptoms [5]. Illness anxiety disorder entails a preoccupation with having or acquiring a serious medical illness, where somatic symptoms are either absent or mild [5]. The introduction of these new diagnostic labels in DSM-5

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allows for the possibility of applying such diagnoses in chronically ill individuals.

Chronic illness is defined as a long-term disease that develops slowly over time, often progresses in severity, and can often be controlled but rarely cured [6]. While somatic symptom disorder and illness anxiety disorder may better capture the symptoms of HA in chronically ill individuals than the term hypochondriasis, disease-specific anxiety is frequently considered to be a realistic [7–9], non-neurotic [10] fear in the presence of severe physical symptoms [11]. It is therefore possible that existing interventions that aim to reduce HA in individuals with a chronic illness may have a different focus and theoretical underpinnings than recommended interventions for those without a medical condition (e.g., [3, 12]).

Among recommended interventions, cognitive behavioral therapy (CBT) has received the most empirical support. Barsky and Ahern [13] have proposed and tested CBT for the treatment of hypochondriasis by targeting self-perpetuating bodily perceptions and cognitions of the disorder. They suggest that life-threatening events may cause individuals to believe they have developed an illness, leading them to attend only to health information and bodily sensations in line with their beliefs. These individuals will also dismiss evidence against their beliefs. Their CBT intervention therefore targets these misinterpretations and misattributions of sensations, and targets behaviors that bolster their conviction of having the disease. This is done by correcting these misinterpretations and misattributions through cognitive restructuring, eliminating maladaptive behaviors, and redirecting attention [13]. Two recent systematic reviews [14, 15] have confirmed the efficacy of CBT for the treatment of HA. Furthermore, a recent Cochrane systematic review of somatoform disorders and medically unexplained physical symptoms reported CBT as having the most positive intervention trial results for these disorders [16]. This was in comparison to usual care or waitlist conditions and effects were durable within and after 1 year of follow-up.

CBT can also be used to limit reassurance seeking, which reduces the number of times patients are exposed to and reminded of the threat of illness. Patients who avoid can learn to expose themselves to triggers, which over time is effective in reducing anxiety [17]. Indeed, exposure therapy seems to be as effective as cognitive therapy to reduce HA in the general population [18, 19]. Exposure may thus be particularly effective among patients with chronic illness, where avoidance coping is correlated with HA [20]. Other tools such as attribution modification training can be employed to reduce cognitive processes that trigger HA [21].

While there are evidence-based treatments for HA in general and psychiatric populations, there is limited knowledge of how to apply them to individuals with chronic medical conditions. As described by Taylor and Asmundson, "Little is known about how treatment protocols need to be adapted or modified for special populations of health-anxious people, such as particular age groups, cultural groups, or groups with severe general medical conditions" [3]. However, a recent study found that CBT was effective in reducing HA in cardiology, endocrine, gastroenterology, and respiratory medicine clinics medical clinic outpatients [22], up to the 1-year follow-up.

Other forms of interventions that may be effective in decreasing HA in people with chronic conditions include exercise interventions. Among elderly populations (ages 68 to 85), exercise interventions have been found to show a small to moderate effect on the reduction of fear of falling (a form of HA that is common among patients with Parkinson's disease) immediately after the intervention, according to a Cochrane review of the evidence [23]. The interventions included strength, resistance, and balance training, and Thai Chi and yoga [23].

The purpose of the present review was thus to identify interventions that have been investigated in the context of HA in chronic illness and, where sufficient data exists, to examine their effectiveness across illnesses. This is an urgent matter of research attention given that HA is associated with increased psychological and physical impairments and healthcare utilization [24, 25] and reduced quality of life [20] in individuals with chronic illness.

Method

Database Search

This study was conducted as part of a larger systematic review that aimed to exhaust the literature on HA constructs among patients living with chronic illness. The literature search was performed in two phases. During phase I, the following databases were used in September and October 2014: (a) PsycINFO, (b) PubMED, (c) CINAHL, (d) Web of Science, and (e) SCOPUS. To guide the search, HA was conceptualized as *concerns or worry or fear that one's illness or an aspect of or a symptom of one's illness* (i.e., *hypoglycemia*, *falling*) *may worsen*, *progress*, *or recur*. The keyword formula was developed based on the targeted chronic illnesses and the respective HA constructs (e.g., for searches on diabetes the HA construct of fear of hypoglycemia was used), as well as general constructs (e.g., fear of illness progression, HA, health concerns). For a complete list of keywords by illness type, please see supplementary Table 1 (available online).

In addition, to identify German-language articles not covered by the included databases, a literature search was conducted using the German database PSYNDEX in July 2015. This database includes literature published in German-speaking countries. Reference lists of relevant German-language publications were also searched. All duplicates were

removed once the searches were complete. The total number of publications found at this stage was 1660. A second phase of literature search was performed to update the literature until October 2017 using the same search terms, yielding an additional 1116 publications.

Inclusion and Exclusion Criteria

Once all searches were performed, all titles and abstracts were divided into four alphabetical sections and first screened by pairs of reviewers (with the exception of those written in German which were screened by one reviewer, AD) based on the following inclusion criteria: (a) be published in a peer-reviewed journal between January 1996 to October 2017, except for articles pertaining to cancer for which the search was limited to 2011 to October 2017 (given the recent literature reviews on fear of cancer recurrence by Simard and colleagues [20] and Crist and Grunfeld [26] that did not include articles published between 2011 and 2017); (b) written in English, French, or German; (c) include an adult population; (d) report quantitative results on HA-related constructs; and (e) include individuals with a chronic illness.

Exclusion criteria consisted of (a) pediatric studies; (b) studies with healthy individuals only; (c) studies that did not separate data between healthy and chronically ill patients; (d) no quantitative data; (e) case reports; (f) review articles; (g) not a peer-reviewed article (books, chapters, poster abstracts, conference proceedings, or dissertations); (h) editorials; (i) irrelevant publications; (j) language other than English, French, or German; and (k) duplicate publications. Inter-rater agreement was obtained based upon consensus between paired reviewers and discrepancies were resolved through discussion. During the screening process, the research team met on a regular basis to refine the inclusion criteria (e.g., exclusion of medically ambiguous diagnoses like non-cardiac chest pain). Upon consensus, all articles pertaining to pain conditions were eliminated ($n = 112$), as these often do not result from a clear medically explained condition [27] and were thus considered to be different from chronic illnesses. Moreover, if the fear reported in the article was not related to progression of the disease, symptom worsening, or fear of death, the articles were excluded (e.g., fear of shock in cardio-defibrillator patients, which was considered as fear of treatment). A total of 927 articles and abstracts were retained after this phase. A second screening was performed, in which all retained articles were divided into four alphabetical sections and were read by pairs of reviewers (with the exception of articles written in German which were extracted by one reviewer, AD). The same inclusion and exclusion criteria were applied to this phase of screening. Articles were retained based upon consensus between paired reviewers. The references in identified papers were reviewed for additional relevant articles ($n = 48$). After this stage, a total of 408 articles and abstracts were retained for data extraction.

For this study, all articles reporting a pre and post measure of the HA construct with an intervention between the measures were selected ($n = 53$; see Fig. 1 for the PRISMA flow diagram of the article selection process). Any independent variable introduced to participants following the baseline measure was considered as an intervention for our purposes (e.g., medical intervention, psychotherapy, exercise, peer support). From the 53 articles selected, two were excluded [28, 29] as they reported results on an intervention already included in the study [10]. The 51 final articles are presented in Table 1.

Data Extraction

A standardized data spreadsheet was designed to extract data. This spreadsheet was used to collect the following information from articles when available: (1) details of the publication, (2) research design, (3) HA construct, (4) chronic illness studied and sample size, (5) location of the study, (6) type of intervention, (7) description of intervention, (8) theoretical model of the intervention, (9) outcomes, (10) effect sizes, and (11) primary and secondary outcomes of the studies. Inter-reviewer agreement was also achieved by comparing data extracted by paired reviewers. For articles not reporting effect sizes, authors were contacted to provide their ratings. For those who did not respond, Cohen's d was calculated if there was sufficient data provided on means, standard deviations, and sample sizes. Quality assessments were conducted on these interventions in order to improve the interpretation of our results and conclusions drawn around interventions. The Downs and Black checklist [80] was used for this purpose. Question 27, measuring power, was adapted so a value of 1 was given if the study was adequately powered, and a value of 0 was given if power was not reported (see [81]). Therefore, the modified version of the checklist had a maximum of 28 points, where the higher the rating, the higher the quality of the study [81].

Results

Of the 51 articles that reported an intervention, targeted disease populations included cancer ($n = 19$), diabetes ($n = 12$), Parkinson's disease (PD; $n = 11$), cardiac disease ($n = 5$), epilepsy ($n = 2$), high level gait and balance disorder ($n = 1$), and one had arthritis and cancer patients ($n = 1$). In terms of the study design, most studies employed a randomized control trial design (RCT; $n = 30$), next was quasi-experimental ($n = 7$), pilot studies ($n = 9$), and single-arm observational studies ($n = 5$). Studies were conducted in the following locations: USA ($n = 17$), UK ($n = 5$), Australia ($n = 5$), Germany ($n = 4$), Canada ($n = 3$), Israel ($n = 2$), Italy ($n = 2$), Spain ($n = 2$), Netherlands ($n = 3$), Hong Kong ($n = 1$),

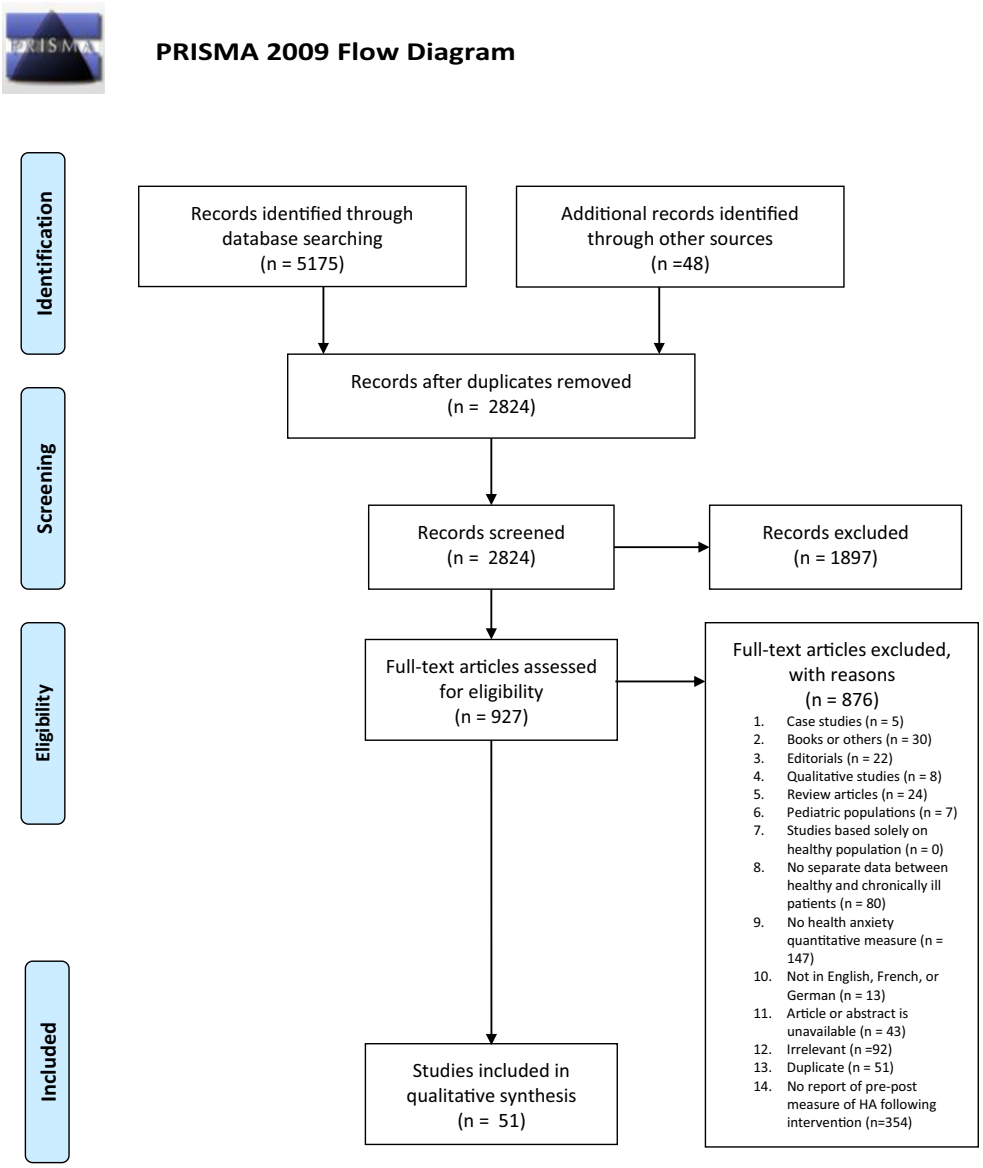

Fig. 1 PRISMA flow diagram of the article selection process

Belgium ($n = 1$), Turkey ($n = 1$), Japan ($n = 1$), Korea ($n = 1$), New Zealand ($n = 1$), Sweden ($n = 1$), and both in European countries and in Israel ($n = 1$). Number of participants ranged from 10 to 1281 participants: less than 50 participants ($n = 25$), 51 to 100 participants ($n = 9$), 101 to 150 participants ($n = 6$), 151 to 200 participants ($n = 2$), 201 to 300 participants ($n = 6$), 301 to 400 participants ($n = 2$), and one study had 1281 participants. Eleven studies had the health anxiety construct as the primary outcome and 40 studies measured it as a secondary outcome.

Using the adapted version of the Downs and Black checklist developed by Trac and colleagues [81], the average score was 17.37 out of 28 (range 11–23), demonstrating adequate quality overall but few studies obtaining very high scores. As stated above, 37 of the 51 articles employed a randomized control design or a quasi-experimental design, which obtained the highest scores. The lowest score was of 11, in a feasibility study (single group, pre-test post-test) for one mindfulness-based therapy [53]. The tool used was designed to evaluate intervention studies, so these articles lost points due to lack of randomization, absence of a control group, unrepresentative and small samples, and lack of follow-up outcomes. Areas where most articles lost quality points were in generalizability of the sample, a lack of acknowledgment of possible adverse events, professionals delivering interventions were not representative of usual care for the sampled population, a lack of blinding (or inability to blind) from measurement as well as randomization, and many articles did not adjust their analyses to account for confounding variables. Of note, 40 interventions were designed to target symptoms other than HA, such as balance in PD or glycemic control in diabetes. The average quality of these articles was of 16.85, which is similar to the

Table 1 Interventions ($n = 51$) on HA presentations among patients with chronic illnesses

Article	Study design	HA construct	Disease	Intervention	HA primary outcome?	Results of intervention on HA construct	Effect size	Quality rating scores
Allen et al. 2010 [30]	RCT	FoF	PD	Exercise	No	Trend towards a statistically significant improvement in FoF	$d = 0.48$ calculated based on data provided	22
Asbury et al. 2011 [31]	RCT	HA	Cardiac	Support group meetings	Yes	No improvement over the 12 months of the intervention	Insufficient data	21
Asbury et al. 2012 [32]	RCT	HA	Cardiac	Cardiac rehabilitation and symptom monitoring	No	8-week follow-up scores showed significant improved scores of HA for the intervention group; 16-week demonstrated reduced HA for the control group (symptom monitoring only)	Insufficient data	21
Bajaj et al. 2016 [33]	Pilot	FH	Diabetes	Titration measure	No	12-week follow-up showed intervention group had a significant improvement in FH	Insufficient data	21
Balash et al. 2007 [34]	Q-E	FoF	HLGD	Walking	Yes	Walking with walker, guarding, and handholding all reduced FoF compared to walking without intervention; largest effect found with the handholding	Insufficient data	15
Bergey et al. 2015 [35]	RCT	Seizure worry	Epilepsy	Medical (VNS stimulator)	No	Improvement in seizure worry	$d = 0.52$ calculated based on data provided	15
Cakit et al. 2007 [36]	RCT	FoF	PD	Exercise	No	FoF scores improved significantly after the 8-week training program	Insufficient data	17
Canning et al. 2015 [37]	RCT	FoF	PD	Exercise	No	At 6-month follow-up, exercise group reported lower FoF than control group	$d = 0.32$ calculated based on data provided	22
Chambers et al. 2012 [38]	SAPP	FCR	Cancer	Mindfulness-based cognitive therapy group	No	Trend in improvements in FCR after completion of the 8-week program	Authors reported partial $\eta^2 = 0.28$	15
Chomiak et al. 2017 [39]	Pilot	FoF	PD	Exercise	No	At 4-week follow-up, no improvement in FoF	Authors reported $d = 0.15$	16
Cramer 2001 [40]	Q-E	Seizure worry	Epilepsy	Vagus nerve stimulation pulse generator	No	Improvement for fear of seizures	$d = 0.37$ calculated based on data provided	14
Crane-Okada et al. 2012 [41]	RCT	FCR	Cancer	Mindful movement sessions	No	FCR was reduced in intervention group after the 12-week sessions	Authors reported $d = 0.73$	15
Davey et al. 2012 [42]	Q-E	FH	Diabetes	Glucose monitoring with and without alarm	Yes	No significant difference between baseline FH scores and following the alarm and no alarm conditions	Authors reported $d = 0.18$	14
Dodds et al. 2015 [43]	Pilot	FCR	Cancer	Cognitive-based compassion training	No	After the 8-week program, FCR was reduced but not significant at the 1-month follow-up	Authors reported $d = 0.50$	20
Galasso et al. 2016 [44]	SAPP	FH	Diabetes	Change in medication	No	From baseline to 12-week follow-up FH was significantly reduced	Insufficient data	15
Griffin et al. 2011 [45]	Q-E	FoF	PD	Walking	No	No decrease in FoF with virtual reality visual cues introduced	Insufficient data	14
Hackney et al. 2007 [46]	RCT	FoF	PD	Exercise or tango	No	Improvement in HA in the PD tango group; decline in exercise group	Insufficient data	18

Table 1 (continued)

Article	Study design	HA construct	Disease	Intervention	HA primary outcome?	Results of intervention on HA construct	Effect size	Quality rating scores
Hayes et al. 2007 [47]	RCT	FH	Diabetes	Human insulin inhalation powder	No	A significant increase in FH was detected from baseline to endpoint. No difference between groups	$d = 0.69$ calculated based on data provided	17
Herschbach et al. 2010 [10]	RCT	FoP	Arthritis and cancer	CBT and SET group therapies	Yes	Both interventions associated with a decrease in FoP at 12-month follow-up, but only among cancer patients; no difference between interventions on FoP	Authors reported Cohen's d for Cancer: CBT = 0.54 SET = 0.50 control = 0.14 Arthritis: CBT = 0.40 SET = 0.28 control = 0.47	23
Hershman et al. 2013 [48]	RCT	Cancer or health worry	Cancer	Education	No	Significant difference between experimental and control groups at 3 months but not 6 months	$d = 0.08$ calculated based on data provided	22
Ismail et al. 2008 [49]	RCT	FH	Diabetes	MET and CBT	No	No evidence indicated that the interventions affected FH	Insufficient data	22
Jones et al. 2016 [50]	RCT	CA	Cardiac	Education	No	At 7-week follow-up, control group was more avoidant of CA, no significant difference in heart focused attention	Authors reported partial $\eta^2 = 0.08$ for avoidance subscale and for attention subscale partial $\eta^2 = 0.00$	19
Kubiak et al. 2006 [51]	Q-E	FH	Diabetes	Self-management education	No	FH only decreased in control	$d = 0.26$ calculated based on data provided	16
Lebel et al. 2014 [52]	Pilot	FCR	Cancer	Cognitive-existential group therapy	Yes	Decreased FCR immediately after intervention and at 3-month follow-up	Authors reported partial $\eta^2 = 0.73$	17
Lengacher et al. 2011 [53]	Q-E	FCR	Cancer	Mindfulness-based stress reduction	Yes	FCR significantly reduced post-intervention	Insufficient data	11
Lengacher et al. 2014 [54]	RCT	FCR	Cancer	Mindfulness-based stress reduction	No	From baseline to 6 weeks, the MBSR(BC) group experienced more favorable changes than the usual care group for FCR	$d = 0.658$ for FCR concerns $d = 0.601$ for FCR problems calculated based on data provided	19
Lengacher et al. 2016 [55]	RCT	FCR	Cancer	Mindfulness-based stress reduction	No	At 12-week follow-up, intervention group showed significantly reduced FCR	Authors reported $d = 0.35$	20
Lengacher et al. 2018 [56]	Pilot	FCR	Cancer	Mindfulness-based stress reduction	No	At 12-week follow-up, intervention group showed significantly reduced FCR	Authors reported $d = 0.60$–0.85	16
Lichtenthal et al. 2017 [57]	RCT	FCR	Cancer	Attention and interpretation modification intervention	Yes	At post-intervention, a trend in the reduction of FCR; at 3-month follow-up, there was a significant reduction in FCR in the intervention group	Authors reported Hedges G = 0.61	19
Little et al. 2014 [58]	RCT	FH	Diabetes	Four conditions of glucose monitoring	No	FH reduced in all four conditions	MDI vs. CII $d = 0.04$ SMBG vs. real-time monitoring $d = 0$ calculated with data provided	20
Lundgren et al. 2016 [59]	RCT	CA	Cardiac	Internet-based CBT	No	At 9-week follow-up, the intervention group had significantly lower CA	Authors reported d = 0.31	21
Manne et al. 2017 [60]	RCT	FCR	Cancer		No		Insufficient data	19

Table 1 (continued)

Article	Study design	HA construct	Disease	Intervention	HA primary outcome?	Results of intervention on HA construct	Effect size	Quality rating scores
				Coping and communication-enhancing intervention, and supportive counseling		No change in FCR in either intervention		
Mehnert et al. 2013 [61]	SAPP	FCR	Cancer	Cancer rehabilitation	Yes	Patients improved significantly overtime in FCR	Authors reported partial $\eta^2 = 0.10$	15
Merckaert et al. 2017 [62]	RCT	FCR	Cancer	Single component group intervention, and multiple component group intervention	No	Multiple-component group intervention showed greater reduction in FCR	Authors reported $d = 0.38$	18
Montesinos et al. 2016 [63]	RCT	FCR	Cancer	Acceptance and commitment therapy	No	At 3-month follow-up, FCR significantly reduced in intervention group	Authors reported interference $d = 1.75$ and anxious preoccupation $d = 0.82$	12
Nakae et al. (2014) [64]	SAPP	FoF	PD	Exercise	No	At 2-month follow-up, FoF reduced	Insufficient data	15
Nørgaard et al. 2013 [65]	SAPP	FH	Diabetes	Individual recommendations	No	Total FH score significantly improved after 12 months of treatment	Insufficient data	14
Otto et al. 2016 [66]	RCT	FCR	Cancer	Online gratitude intervention	No	At 6-week follow-up, death worry significantly reduced in comparison to control group	Authors reported $d = 0.45$	19
Park 2014 [67]	RCT	FoF	PD	Exercise: communal and individual	No	At 10-week follow-up, FoF was lower in communal exercise group compared to the individual exercise condition and a control group	Insufficient data	15
Parker et al. 2012 [68]	Q-E	FCR	Cancer	Surgery	No	No effect of surgery type on FCR	Insufficient data	15
Pilleri et al. 2015 [69]	SAPP	FoF	PD	Exercise: over-ground robot-assisted gait training	No	At 3-week follow-up, FoF reduced	Insufficient data	15
Rudolph et al. 2018 [70]	SAPP	FCR	Cancer	CBT group	Yes	Reduction in FoP measured immediately after the 6-week intervention	Authors reported Cohen's $d = 0.9$	12
Shen and Mak 2014 [71]	RCT	FoF	PD	Balance training	Yes	Balance training decreased FoF past intervention and at a 12-month follow-up	Insufficient data	20
Shiloh et al. 2014 [72]	RCT	CA	Cardiac	View screen and ask questions during angiography	No	Intervention group had less CA than the controls at a 1-month follow-up	Authors reported partial η^2: fear and worry scale $\eta^2 = 0.00$; avoidance scale $\eta^2 = 0.29$; attention scale $\eta^2 = 0.09$; General $\eta^2 = 0.02$	19
Snoek et al. 2001 [73]	SAPP	FH	Diabetes	CBT	No	No change in FH from baseline to 6-month follow-up	Insufficient data	15
Sparrow et al. 2016 [74]	RCT	FoF	PD	Exercise	No	At 3-month follow-up, there was trend in decreased FoF for the experimental group	Authors reported Hedge's $G = -0.77$	20
Vallejo-Mora et al. 2017 [75]	RCT	FH	Diabetes	Insulin bolus calculator	No	At 4-month follow-up, there was no change in FH	Insufficient data	15
	RCT	FH	Diabetes		No		Insufficient data	16

Table 1 (continued)

Article	Study design	HA construct	Disease	Intervention	HA primary outcome?	Results of intervention on HA construct	Effect size	Quality rating scores
van Beers et al. 2017 [76]				Continuous glucose monitoring and self-monitoring		No significant differences between groups		
van de Wal et al. 2017 [77]	RCT	FCR	Cancer	Blended cognitive behavior therapy	Yes	Intervention group had significantly less FCR	Authors reported $d = 0.76$	22
Walker et al. 2014 [78]	Q-E	FH	Diabetes	Continuous glucose monitoring	No	Reduction in FH in both groups, no significant difference between groups	$d = 0.69$ calculated based on data provided	17
Wootten et al. 2015 [79]	RCT	HA	Cancer	Self-guided psychological intervention to facilitate emotional wellbeing, peer forum, and combination of both	No	All three groups showed a significant reduction in HA	Authors reported partial $\eta^2 = 0.05$	16

CA, cardiac-related anxiety; *CBT*, cognitive behavioral therapy; *FCR*, fear of cancer recurrence; *FH*, fear of hypoglycemia; *FoF*, fear of falling; *FoP*, fear of progression; *HA*, health anxiety; *HLGD*, higher-level gait disorder; *PD*, Parkinson's disease; *Q-E*, quasi-experimental designs (i.e., non-randomized trials with experimental and control); *RCT*, randomized control trials; groups); *SAPP*, single-arm pre-post (i.e., longitudinal prospective studies with assessments before and after the intervention); *SET*, supportive-experiential group therapy; *VNS*, vagus nerve system stimulation

overall average and the average of all other articles that intended to target HA.

Description of the Interventions

Most interventions consisted of psychotherapies ($n = 19$), followed by exercise interventions ($n = 13$), medical interventions ($n = 12$), providing information/education to patients ($n = 4$), rehabilitation programs ($n = 2$), and support groups ($n = 1$).

Psychotherapy Psychotherapy interventions demonstrated effectiveness in reducing HA, mostly in studies with cancer patients (see Table 1 for study outcomes). The psychotherapy interventions included CBT-based ($n = 8$) or third-wave CBT (e.g., acceptance commitment therapy, attention and interpretation modification training; cognitively based compassion training; $n = 3$), mindfulness-based interventions ($n = 5$), motivational enhancement therapy (MET) + CBT ($n = 1$), a coping and communication-enhancing intervention ($n = 1$), and an online gratitude intervention ($n = 1$). Interventions were administered through groups ($n = 10$), individual therapies ($n = 4$), and the internet or iPads ($n = 4$), and one was a combination of individual and online consultation. Control conditions included supportive expressive therapy or an in-person support group or online discussion forum ($n = 5$), waitlist ($n = 2$), usual care ($n = 5$), and placebo conditions ($n = 2$). The duration of the sessions ranged from 15 min to 2 h and the number of sessions ranged from three to fifteen sessions. Fifteen studies found significant improvements in HA or components of HA, and four found non-significant results.

Fifteen studies targeted patients with cancer, two those with diabetes, one patient with cardiac conditions, and one patient with cancer and arthritis. Among the studies with cancer patients, CBT-based ($n = 5$), third-wave CBT ($n = 3$), mindfulness-based ($n = 4$), and an online gratitude intervention all demonstrated a significant reduction in some element of HA, with the majority of effect sizes reported in the moderate range. Of note, many of these studies were small pilot studies [43, 53, 56, 63, 70] and had short-term follow-ups (i.e., up to 3 months [43, 52–57, 63, 66, 70], or while they found a reduction in HA, they were not more effective than an online discussion forum [79].

Internet-based CBT was found to reduce one HA component among cardiac patients, while other elements did not decrease [59]. However, the intervention was only marginally better than the control condition, an online discussion forum, and reported effect sizes were small. Neither group-based CBT and supportive expressive therapy was found to be effective in arthritis patients but was found to be effective in cancer patients with a moderate effect size at 12-month follow-up [10]. Among diabetes patients, neither individual MET and CBT nor group CBT were found to reduce fear of hypoglycemia [49, 73].

While several authors speculated about the mechanisms by which their interventions reduced HA, only three tested these putative effective ingredients. Reported daily practice of mindfulness-compassion exercises was a predictor of changes in HA post-intervention [43]. Changes in attentional bias to threatening HA stimuli were found to correlate with improvements in HA in an online attention and interpretation modification training intervention [57]. Last, spending more time planning for future goals explained 22% of the change in one aspect of HA, death worry, in an online gratitude intervention [66].

Exercise Overall, studies on exercise interventions demonstrated effectiveness in reducing HA with small to moderate effect sizes. All 13 studies on exercise interventions were conducted in PD or high-level gait and balance disorders except one in cancer, which had a mindfulness component. Exercise interventions included walking under certain conditions ($n = 2$), tango dancing ($n = 1$), and balance exercises and training ($n = 9$) in PD patients and high-level gait and balance disorders, and mindfulness-movement group training ($n = 1$) in cancer patients. Nine interventions, totaling eight RCTs, were found to improve HA, with one study finding maintenance of gain 12 months after completion of a 4-week balance training intervention [71]. Another two studies found a trend towards significance, and two did not find a significant change in HA. Walking while holding an aid's hand [34], home-based daily self-exercise [64], a smart application for communal exercise [67], over-ground robot assistant gait training [69], and incremental treadmill training [36] significantly reduced fear of falling (FoF) in PD. Significant reductions in FoF were found in balance and strength training exercises [37, 71]; however, two smaller RCT (< 50 participants) only reported a trend towards significance [30, 74]. Finally, tango dance lessons were reported to improve FoF compared to a chair exercise program [46]. The mindfulness-movement sessions were found to significantly reduce fear of cancer recurrence [41]. Walking with the help of virtual cues delivered via virtual reality glasses [45] and training with a wearable device with music did not decrease FoF [39].

In order to understand how the exercise interventions may reduce HA, information was pulled on mechanisms of action when they were described in the article. Only one article formally tested potential mechanisms and found that an improvement in performance and ability to balance was correlated with changes in HA in patients with PD who completed a 4-week balance training intervention [71].

Medical Interventions Medical interventions demonstrated effectiveness in reducing HA in less than half of the studied interventions ($n = 5$ out of 12) with a moderate effect size reported by only three studies, and only two having a control condition. Effects were typically reported at a 3-month follow-up but also included studies with 12-month and 5.4-year follow-ups. Out of these five interventions, sensory-augmented pump therapy for insulin therapy [65], an insulin titration web tool [33], and switching from twice-daily to once-daily insulin administration [44] were shown to significantly reduce HA among patients with diabetes. Vagus nerve stimulation (an implanted device that prevents seizures) was found to significantly reduce HA in patients with epilepsy [35, 40]. All other interventions showed no effect or increased HA. In fact, in diabetic patients, glucose monitoring with an alarm was not effective in reducing fear of hypoglycemia [42], inhalation powder was shown to increase fear of hypoglycemia [47], and the use of laparoscopic vs. open surgery was not found to reduce fear of recurrence in cancer patients [68].

Patient Education Three out of the four interventions were found to reduce HA [48, 50, 72], at least in the short-term, and one showed non-significant results in a diabetes population [51]. The three effective interventions were tested through RCTs and the non-significant one was tried in a controlled pre-post trial without randomization. Education programs included education lessons, meetings with nurse practitioners, and information given during a medical procedure. In cancer patients, one 1-h meeting with a nurse practitioner to receive information was found to decrease cancer worry at 3 months post-intervention with a small effect size; however, no difference was found at 6 months from the control group [48]. The act of viewing and being told to ask questions about an angiography procedure was found to significantly reduce cardiac anxiety in cardiac patients 1-month post-angiography [72], as was a psychoeducational video on acute coronary syndrome and heart-influencing health behaviors after 7 weeks [50]. Both of these interventions achieved a moderate effect. Comparatively, in diabetes patients, six 45-min sessions focusing on coping with hypoglycemia in everyday situations, mechanisms of hypoglycemia perception, causes of impaired hypoglycemia awareness, individual health beliefs, and self-care behavior offered by a psychologist were not found to significantly reduce fear of hypoglycemia over a 6-month period in comparison to two 45-min education sessions without self-management [51].

Rehabilitation Programs Evidence suggested that rehabilitation programs were somewhat effective in reducing HA in cancer and cardiac samples, but they were only evaluated in two studies with some methodological limitations. Rehabilitation studies included a large single-arm observational study of a 3-week cancer rehabilitation program in Germany comprised of patient education, relaxation, exercise, and psychosocial support [61] and a small RCT of an 8-week cardiac rehabilitation program that included symptom monitoring, exercise, and education [32]. Both interventions showed a significant reduction in HA overtime to 12 months [61] and 8 weeks post-rehabilitation program [32], with a moderate and no-effect size reported,

respectively. However, while the cardiac rehabilitation program demonstrated a significant reduction in one aspect of HA (reassurance seeking) overtime, the control group, which consisted of daily symptom monitoring, demonstrated improvements in another aspect (health worries) [32].

Support Groups There was one RCT of a support group intervention that included 90-min monthly meetings over a 12-month period compared to usual care in cardiac patients. The topics covered included medication, diet advice, relaxation, and exercise. Results showed no difference between both conditions by the end of the 12-month program [31]. Of note, the article describes the group facilitators as informed conveners, and do not specify the type or level of training received.

Intervention Characteristics

Most effective interventions involved approximately six to eight weekly sessions, including for mindfulness [53–56], psychotherapy [43, 48, 52, 66, 70, 77], and exercise or rehabilitation programs [32, 36, 64]. Overall, 15 interventions were not effective in reducing health anxiety, six lasting 12 sessions or weeks or longer [30, 31, 49, 74–76], three lasting six to eight sessions or weeks [38, 51, 60], and six lasting less than four sessions or weeks [39, 42, 45, 47, 68, 73].

Among interventions that had HA as the primary outcome, nine demonstrated effectiveness and two did not. Those that were effective included psychotherapy ($n = 6$), exercise ($n = 2$), and rehabilitation ($n = 1$). The two that were not effective included a diabetes medical intervention [42] and a support group in cardiac populations [31]. Among those designed for other treatment targets, 28 effectively reduced HA and 12 did not, mostly in patients with diabetes [42, 47, 49, 51, 73, 75, 76]. Thus, it appears that HA being the primary vs. secondary focus of the intervention had limited impact on its effectiveness in reducing HA.

Twenty-three articles specified theoretical models in their description of their interventions. Among these, 11 used a CBT or third-wave CBT framework [10, 49, 52, 57, 59, 62, 63, 70, 73, 77, 79] and six referred to a mindfulness framework [38, 41, 53–56]. Finally, Bandura's self-Efficacy theory was described in a balance training intervention for FoF among patients with PD [71].

Discussion

The results of the present literature review demonstrate that psychotherapy interventions consisting of CBT, third-wave CBT, and mindfulness may be effective, especially in cancer and cardiac patients, compared to diabetes and arthritis patients. Moreover, the data suggest that walking and balance training seems to be an effective intervention for PD patients who express FoF. The data also suggests that patient education was effective in decreasing HA in the short term in cancer and cardiac patients but long-term effects were not demonstrated. Rehabilitation programs show tentative effectiveness in both cardiac and cancer patients, but were evaluated in only two studies. The data on effectiveness of medical interventions yielded mixed results. Medical interventions that reduced HA included sensory automatic pump (SAP) insulin administration in patients with diabetes [65], and vagus nerve stimulation (VNS) in patients with epilepsy [35, 40]. However, one VNS study evaluated a database retrospectively [35], and in the other, groups were not randomly assigned as the VNS was assigned to the group of participants who did not respond to medication treatment [40]. Further, the SAP study comments that the sample seemed to report fewer episodes of severe hypoglycemia when compared to previous studies on glycemic control devices [65], and there was no control group or randomization as this was an observational study. Thus, given the quality of studies reporting on medical interventions, conclusions must be seen as tentative. Last, support groups were infrequently studied but showed no evidence of effectiveness in reducing HA in people with chronic illness when they were the experimental condition [31]. Other studies that used some form of supportive interventions (e.g., supportive expressive therapy, online discussion forum) as a control group found they were comparable to the experimental condition in reducing HA [10, 79] or that they improved some aspect of HA [59].

These results suggest that specific treatment modalities may be more effective in the treatment of HA in certain illnesses compared to others. When the risk of the feared health consequences can be reduced medically, problem-solving interventions seem to be most effective, such as devices that effectively reduce hypoglycemic episodes in diabetes, VNS which reduces chances of seizure in epilepsy, and balance training in PD which reduces the risk of falling. One of the only interventions that was effective in diabetes was SAP, which is reported to effectively monitor and reduce glycated hemoglobin levels without increasing the risk of hypoglycemia. This problem-solving quality may explain why no other interventions demonstrated effectiveness (such as psychotherapies and education programs or increased monitoring) in patients with diabetes. Of note, the psychotherapy interventions with diabetes patients had limitations: the CBT group intervention had only four sessions which were targeted to help with glycemic control, which may be too few for there to be change in HA [73]. Additionally, the CBT-MET group involved 4 MET sessions of 15 min, and 8 CBT sessions [49], which also may be too few to result in a change in HA. These findings however are tentative given the few interventions that have been done and the moderate quality of most articles on diabetes samples (14 to 22 out of a possible 28).

When medical solutions to limit chances of recurrence or progression are not available, such as in cancer or cardiac diseases, psychotherapies targeting maladaptive cognitions and behaviors, or acceptance of reality through third-wave interventions, may be most effective. However, it is important to note that the long-term efficacy of these therapies was seldom demonstrated and that adverse events were usually not reported. This would be important in future studies given a recent study that found that a mindfulness intervention was associated with negative outcomes in the short term in patients with cancer undergoing active treatment [82]. Our findings on the effectiveness of CBT on HA is consistent with a meta-analysis by Cooper and colleagues [14] that found a large mean effect size in randomized control trials of CBT in treatment of HA, in both healthy populations and populations with medical conditions. This effect was found at 6- and 12-month follow-up in the studies reviewed [14].

The current literature is limited by a lack of studies that have compared the efficacy of their intervention in more than one disease population. The only study to do so compared the efficacy of CBT and supportive expressive therapy in patients with cancer and arthritis and found both interventions to be effective in reducing HA in patients with cancer but not arthritis [10]. The authors suggested that disease-specific differences may override common factors in the experience of HA but further studies are needed to draw this conclusion. There is also a paucity of studies that have compared different types of interventions within the same populations. For example, addressing self-efficacy directly through psychotherapy could improve outcomes of exercise interventions for patients with PD [71] but no intervention has used psychotherapy or psychoeducation in combination with exercise in this population despite effectiveness of such a multicomponent intervention in reducing FoF in older adults [83]. On the other hand, rehabilitation programs integrate several types of interventions and showed tentative effectiveness in reducing HA in cardiac and cancer patients [32, 61]. These programs, however, may be quite resource intensive and require a large time commitment from implicated patients.

Several mechanisms of action were hypothesized to explain the efficacy of the interventions, but few were formally tested. CBT directly targets avoidance coping behaviors by presenting new, more effective methods that can target anxiety and increase self-efficacy [10]. Mindfulness-based interventions may promote interoceptive exposure, as well as acceptance of previously feared internal experiences [84]. Last, exercise and patient education interventions may have increased activities which may have otherwise been avoided by exposing them directly or by eliminating myths about exposure and risks leading patients to avoid these activities [36].

Limitations

Not all interventions were investigated in all chronic illness (i.e., CBT was not tested in PD; exercise was not tested in diabetes or cardiac disease), which limits the ability to generalize the effectiveness of specific interventions across illness type. Only a small number of studies were investigated by treatment modality, for example, only one study described a support group intervention. The results should therefore be interpreted with caution. As this review included studies that were not necessarily designed to test the intervention (e.g., observational and pilot studies), the quality of the findings is limited as evidenced by the quality ratings. Most articles that were reviewed were of moderate quality (highest being 23 out of a possible 28). Most interventions were not designed specifically for HA, which may explain their limited impact on HA. Further, the overall lack of generalizability of samples, ecological validity, and control groups suggests that our results should be interpreted with caution.

Future Directions

In order to gain a better understanding of interventions that could be used across diseases, protocols and research need to be conducted in multiple disease populations. It would be important to consider the effectiveness of conducting similar interventions in populations that seem to respond to different modalities, such as diabetes and cancer. It may also be beneficial to have interventions that theoretically can be applied to diseases where problem-solving and risk-reduction interventions may be beneficial, as well as behavioral and acceptance-based therapies where this is appropriate. Of note, most interventions did not describe their theoretical framework, but that among those who did, CBT was most often cited. However, no intervention used CBT models specific to HA, despite their proven usefulness in guiding efficacious treatments [14, 15], including among medical outpatients [22]. Future studies should consider using these HA-specific models when designing interventions to decrease HA. Additionally, more research is needed on the different types of interventions within specific illnesses in order to compare the effectiveness of these different interventions. The effectiveness of group vs. individual interventions has also yet to be evaluated in this population and will be an important consideration for future studies. Additional studies are needed to examine the mechanisms underlying effective interventions in certain diseases, so that they may potentially be modified for other illnesses with similar HA characteristics (i.e., around problem solving, behavioral, or acceptance-based therapies). Resources and practicality of interventions also need to be considered, as this systematic review found that interventions seemed to be most effective when they involved at least six to eight sessions, or were conducted over several weeks.

Conclusion

Few interventions have been designed specifically for the treatment of HA among individuals living with chronic illness. Data suggest that psychotherapy, exercise, patient education, and rehabilitation programs appear to be effective in helping the management of HA, and it seems certain types of interventions are more effective in certain chronic illnesses, as compared to others. Future research is necessary in order to establish guidelines for interventions for HA in patients with chronic illnesses. Research should compare interventions across several illnesses and different interventions within a single illness in order to determine best practices.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants performed by any of the authors.

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