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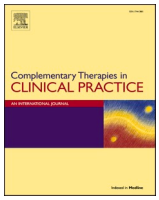

Efficacy of laughter-inducing interventions in patients with somatic or mental health problems: A systematic review and meta-analysis of randomized-controlled trials

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ABSTRACT

Background and purpose: Laughter-inducing interventions hold promise as affordable and easy to implement treatments for a range of ailments. The aim of this study was to build on meta-analytic evidence for the efficacy of such interventions in treating somatic or mental health patients.

Methods: Studies eligible for the meta-analysis were identified by a comprehensive literature search in MEDLINE, CENTRAL, Web of Science, and PsycINFO and by a manual search (date of last search 22/06/2021). All randomized controlled trials comparing spontaneous laughter or simulated laughter to treatment as usual, no treatment/waitlist, or attention control groups were included. There were no language or date restrictions. Separate random-effects meta-analyses were conducted for mental health, physiological, and physical health outcomes. Hedges' g is reported as the standardized mean difference estimate. The study was registered on PROSPERO (#CRD42019139299).

Results: Forty-five studies comprising 2,547 randomized participants were included. Laughter-inducing interventions showed significant positive effects on mental health (31 studies, 1,543 patients, g = 0.74, 95% CI [0.48; 1.00], I^2 = 81%), physiological (14 studies, 761 patients, g = 0.61 [0.20; 1.03], I^2 = 86%), and physical health outcomes (21 studies, 1,105 patients, g = 0.59 [0.30; 0.88], I^2 = 80%). Only one study reported adverse events, which were mild in nature.

Conclusion: Laughter-inducing interventions can have beneficial effects on a variety of health-related outcomes including mental health, physical health, and physiological parameters. Future research should focus on examining differential intervention effects and mechanisms of action.

1. Introduction

Always laugh when you can. It is cheap medicine. — Lord Byron [1].

Laughter is a natural and universal human behavior. Clinically, laughter has been successfully used to positively influence stress, immune function, and health [2]. The clinical use of laughter for health-related purposes does not require large amounts of time or effort [2]. Thus, laughter-related therapies could provide a reliable treatment option and considerable savings for health-care systems globally. Despite these appealing qualities, such therapies are generally understudied. The present report is a meta-analysis of laughter-related interventions for patients with mental or somatic health problems.

In the context of this report, laughter is defined as 'a psychophysiological response to either humor or any other favourable external or internal stimuli (positive emotions, pleasant thoughts, self-induced laughter or by their spreading, etc.)' (p. 1) [3]. Although often associated, humor and laughter are distinct and do not necessarily appear together [3]. There are several kinds of laughter. *Spontaneous laughter* is triggered by external, often humorous stimuli and positive emotions while *simulated laughter* is self-induced, purposeful, and not elicited by external stimuli or positive emotions. *Stimulated laughter* occurs as a reaction to external stimulation like tickling. *Induced laughter* is a result of the use of specific drugs or substances (e.g., alcohol or 'laughing gas'). *Pathological laughter* may appear as a symptom of certain neurological or psychiatric disorders [3].

Spontaneous laughter and simulated laughter have been studied most frequently in the context of health interventions [4]. Interventions using spontaneous laughter typically include humor-related exercises

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such as watching funny videos or interacting with clowns. Laughter-related interventions that do not employ humor include things like clapping, dancing, and vocalizing sounds like growling, howling, or laughter-like sounds. Those interventions are usually embedded in a broader set of exercises that can also include, e.g., breathing and relaxation exercises or facial and body gymnastics [4]. One of the most frequently applied interventions is laughter yoga, which combines breathing techniques with real or fake laughter and humor [3,5,6]. Table 1 contains a detailed description of the different laughter interventions.

Research of the past decades has shown that laughter has beneficial effects but could potentially also cause harm, albeit at low risk [7–10]. Among the positive effects, physiological benefits have been observed involving the muscular, cardiovascular, respiratory, endocrine, immune, and central nervous systems. Psychological benefits in terms of cognitive, and social functioning, mental health, and quality of life have been described in various reviews [3,7–14]. In the past few years, several meta-analyses have summarized the evidence on the effectiveness of humor and laughter interventions in various patient populations and healthy participants using different psychological and physiological outcomes. In a meta-analysis with four randomized-controlled trials consisting of 157 participants, laughter therapy was found to decrease anxiety levels [15]. Small, non-significant effects of laughter therapy on quality of life were shown in another meta-analysis of seven studies including 421 participants [15]. Further meta-analytic findings of ten studies with 814 participants revealed that laughter and humor interventions significantly decreased depression and anxiety while improving sleep quality [16]. Therapy duration has shown to be important, with long-term laughter interventions having a stronger effect on depression than shorter therapies [6]. The most comprehensive meta-analytic evaluation to date looked at the efficacy of laughter-induced therapies for different populations and outcomes and included nine randomized and 20 quasi-randomized studies [5]. In that study, laughter-inducing therapies showed significant positive effects on depression and anxiety. Interestingly, simulated, non-humorous laughter also proved to be more effective than spontaneous, humorous laughter.

Table 1
Description of included types of laughter interventions.

Laughter Yoga	Laughter therapy	Clown	Passive stimuli
• Commonly following a manual by Dr. Kataria • Laughter exercises (e.g., greeting laughter, lion laughter, milkshake laughter, cell phone laughter, closed mouth laughter) • Laughter meditation (focusing on the experience of laughter and the associated bodily sensations) • Handclapping or body movement with chanting ("hoho, hahaha") • Breathing exercises • Relaxation exercises • Positive affirmations (e.g., "I am the happiest person in the world!")	• Usually consisting of 3 phases with varying content (e.g.): 1) Warm-up • Information about benefits of laughter • Simultaneously singing • Humming, hugging, clapping 2) Main activities • Practicing various forms of simulated laughter • Reciting funny poetry and prose or playing funny games to foster spontaneous laughter 3) Cool-down • Sharing of feelings • Relaxation/ meditation with music • Stretching exercises	• Clown with costumes and make up • Interaction with patients using various methods (e.g., balloons, puppets, word games, magic tricks, dice tricks, jokes etc.) • Combination of humor (bringing fun to people and making people laugh) and love (treating patients with compassion and generosity, getting close to patients)	• Watching funny videos • Watching comedian live-performances • Listening to an humorous audiotape

While the existing meta-analytic reviews on the efficacy of laughter-inducing interventions are encouraging, many research questions remained unanswered. Past research has mainly focused on the meta-analytic summary of psychological outcomes, e.g., anxiety and depression. There has been much less work, and no meta-analyses, involving the physiological outcomes of laughter-related interventions. Moreover, important moderators of treatment effects have not been sufficiently explored. For example, what works for whom and under which circumstances? Finally, albeit only anecdotally reported in the past, it remains completely unclear if, and to what extent, also negative effects of laughter-inducing interventions exist.

Hence, the aims of this study were to provide a comprehensive overview of laughter-inducing interventions using both spontaneous laughter and simulated laughter and to evaluate their influence on mental health, physiological, and physical health outcomes. The clinical samples included patients with somatic or mental health problems. In an attempt to enhance methodological and clinical homogeneity, and in comparison to the meta-analyses referenced above, we restricted study inclusion to randomized-controlled trials and patients with mental/somatic health problems. A further novel aspect of our analysis was the examination of physiological outcome measures. Our study further aimed at exploring the impact of various patient and intervention characteristics, which might provide valuable information in how to refine such interventions. Lastly, to provide a comprehensive and complete picture of the benefits and harms of laughter-related interventions [17,18], we provide an initial assessment of the reporting of adverse events.

2. Methods

2.1. Protocol and registration

This review was registered in the international prospective register of systematic reviews (PROSPERO) under the registration number CRD42019139299.

2.2. Eligibility criteria

We included randomized-controlled trials without restrictions of publication date and language, given an English abstract was available. Eligible studies involved patients with somatic or mental disorders, patients with somatic or mental symptoms, or patients undergoing medical procedures. Interventions targeting spontaneous or simulated laughter were considered eligible, while trials on other types of laughter (i.e., stimulated, induced, or pathological laughter) were excluded [3]. Eligible interventions could have been conducted individually or in groups, as 'stand-alone' treatments or as treatments added to standard care.

We considered 'no treatment', 'waitlist control groups', 'attention-control', or 'treatment as usual' as eligible control groups. Attention-control groups were defined as those delivering a comparable amount of time and attention but without specific therapeutic components. Primary outcomes were mental health and physiological outcomes. Mental health outcomes included measures of mental distress, e.g., depression, anxiety, wellbeing, and relaxation. Physiological outcomes comprised e.g., cortisol, blood pressure, and C-reactive protein. In addition to the outcomes pre-specified in the review protocol, we also considered physical health measures as eligible as these were frequently reported in the primary studies. Physical health outcomes included self-reported somatic symptoms, e.g., pain, fatigue, and physical functioning, and was regarded as a secondary outcome. Adverse events, as defined by the authors of the included primary studies, were also

considered secondary outcomes.

2.3. Information sources and search

We performed a systematic literature search in the electronic databases MEDLINE, Web of Science, CENTRAL, and PsycINFO using a search strategy that specified terms referring to the intervention (e.g., laughter, humor, mirth), patient population (e.g., medical procedure, diagnostic, treatment), and study design (e.g., randomized controlled trial, random*; see Supplementary Material Appendices 1-4 for details of the search strategy). Date of last search was 22 June 2021. References of recent reviews, meta-analyses, and included primary studies were checked to identify additional studies. We further searched the ProQuest Dissertations and Theses Full Text database in order to detect unpublished studies. In case of identified conference abstracts, we contacted study authors to provide further information.

2.4. Study selection

First, one author (KS) screened the titles and abstracts of studies identified in the literature search for eligibility. In a second step, full texts of the preselected studies were examined in detail for eligibility independently by two authors (KS, JR). Disagreements were resolved by consensus discussion.

2.5. Data extraction

One author (KS) extracted descriptive data from the studies, including information on publication (e.g., authors, publication year, country of origin), sample characteristics (e.g., sample size, gender, age, type of health problem), characteristics of the intervention (e.g., treatment format, treatment modality, number of sessions, length of sessions, total duration), and characteristics of the control condition (e.g., type of control group). Information on outcomes (e.g., type of outcome, measure, timepoint) and statistical data needed for effect size estimation were extracted independently by two authors (KS, JR). Any disagreements were resolved by consensus discussion. In cases of uncertainty, we contacted study authors to provide further information. Supplementary Table S1 contains an overview of all data items.

2.6. Risk of bias in individual studies

We evaluated various indicators of bias according to assignment to intervention (the 'intention-to-treat' effect) by using the current version of the Cochrane Risk of Bias Tool for Randomized Trials (ROB2 – revised version from August 2019) [19]. Risk of bias was assessed according to five distinct domains independently by the two authors (KS, JR). In order to achieve risk of bias ratings within each domain, one or more signaling questions were answered. For each domain, judgments of 'low risk of bias', 'some concerns', or 'high risk of bias' were proposed based on defined algorithms. Finally, the judgments within each domain resulted in an overall risk-of-bias judgment per study.

2.7. Summary measures

For each comparison and outcome of interest, between-group effect sizes (Hedges' g) were computed. Hedges' g represents the standardized mean difference calculated by subtracting the post-treatment mean of the intervention group from the post-treatment mean of the control group, dividing the result by the pooled standard deviation, and multiplying by a small-sample bias correction factor [20]. If means and standard deviations were not reported, we used other statistics (F, t, or p-value) to calculate effect sizes. For dichotomous outcomes, Log Odds Ratios were calculated and converted to Hedges' g in order to pool across different effect size formats [21]. Hedges' g can be interpreted as Cohen's d, with an effect size of $\geq$ 0.20 representing a small, $\geq$ 0.50 a medium and $\geq$ 0.80 a large difference between two groups [22]. Positive effect sizes indicated that the intervention was superior to the respective control treatment, whereas negative effect sizes suggested superiority of the control treatment. All summary measures are reported with a 95% confidence interval (CI). We used the software Comprehensive Meta-Analysis (CMA, Biostat. Inc. Version 3) for computing effect sizes and performing data analyses.

2.8. Data synthesis

Outcome data were meta-analyzed using a random-effects approach. We applied the generic inverse variance method with heterogeneity estimated using the DerSimonian-Laird method [23]. In case of multiple comparisons within one study (two control groups were compared against one shared intervention group), we combined groups to create a single pair-wise comparison [24]. If applicable, comparisons were considered individually in subgroup analyses (e.g., one comparison in the treatment as usual subgroup, one in the attention control subgroup).

If multiple outcomes were reported within one outcome domain (e.g., two measures of mental health), effect sizes were aggregated within domains for each unit of analysis. Statistical heterogeneity across studies was assessed with χ^2 heterogeneity tests (Cochrane's Q) and the I^2 statistic [25]. I^2 describes the percentage of the variability in effect estimates that is due to heterogeneity rather than chance. Following a rough guide for interpretation [26], values from 0 to 40% indicate no important heterogeneity, 30%–60% moderate, 50%–90% substantial, and 75%–100% considerable heterogeneity. In case of considerable heterogeneity, analyses were rerun with exclusion of statistical outliers (defined as effect sizes with confidence intervals not overlapping with the confidence interval of the pooled effect) [27]. Additionally, we computed 95% prediction intervals representing the possible underlying effect in a new study that is similar to the studies in the meta-analysis. It can be also interpreted as a summary of the spread of underlying effects in the studies included in the random-effects meta-analysis [26,28]. Finally, we assessed the quality of the evidence (also known as certainty in evidence) for each outcome category by using Grading of Recommendations, Assessment, Development and Evaluations (GRADE). GRADE uses five considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) for assessment, and has four levels of evidence, i.e., very low, low, moderate, and high [29].

2.9. Risk of bias across studies

For each outcome category, we visually inspected funnel plots and performed Egger's regression tests for funnel plot asymmetry to address potential publication bias [30]. Additionally, we used Duval and Tweedie's trim and fill procedure to determine whether small studies with non-significant effects were underrepresented in the meta-analysis [31]. Possible missing studies were imputed, and the effect size estimate was recalculated. Additionally, we computed Rosenthal's Fail Safe N [32].

2.10. Additional analyses

Pre-specified moderator analyses were conducted using meta-regression models for continuous moderators (year of publication, age, proportion of women, treatment dosage) and subgroup analyses for categorical moderators (type, format, and modality of the intervention, type of control group, type of health problem, region of study conduct). Sensitivity analyses were performed to test the robustness of effect size estimates, by excluding approximated effect sizes, effect sizes set to zero, and studies with high risk of bias in any domain.

3. Results

3.1. Study selection

We screened a total of 5,792 records and finally included n = 47 studies in the qualitative analysis and n = 45 in the meta-analysis (Fig. 1). Two of the eligible studies [33,34] could not be considered for meta-analysis, because no adequate statistical data required for effect size estimation were reported.

3.2. Study characteristics

Characteristics of the included studies are shown in Table 2. Included studies were published between 1991 and 2021. Among the eligible studies, there were two doctoral dissertations [48,65] and three conference abstracts or posters [40,49,73]. All studies were published in English language, except two that were published in Farsi and one published in Korean, all with English abstracts [36,51,69]. Altogether, the trials randomized 2,547 participants to either laughter-inducing interventions (i = 48) or control groups (j = 51), with sample sizes ranging from eight to 211 participants. Mean age of the participants was 46.8 years and 66% were female. Eleven studies were from Iran, seven came from each of Japan and the USA, six were Korean, three came from each of Israel and Turkey, India and Canada each had two, and one study came from each of Egypt, Brazil, Switzerland, China, Slovenia, and St. Lucia. Study participants suffered from mental disorders/problems (n = 10), somatic disorders/problems (n = 32), or they were undergoing medical procedures (n = 5). In the majority of studies (n = 30), participants were recruited in hospitals. In 22 intervention groups spontaneous laughter was used, while 23 intervention groups applied simulated laughter, and three intervention groups used a combination of both. Passive stimuli were applied in 19 intervention groups (i = 17 using video and i = 2 using audio recordings). Laughter yoga was applied in 14 intervention groups, laughter therapy in seven intervention groups, and another six used a combination of laughter interventions. Two studies (of which one was included in the qualitative review only) used clowns [33,66]. The effects of laughter-inducing interventions were compared to either treatment as usual (j = 30), attention control groups (j = 17), no treatment control groups (j = 3), or waitlist control groups (j = 1). Thirty-one studies reported outcomes on

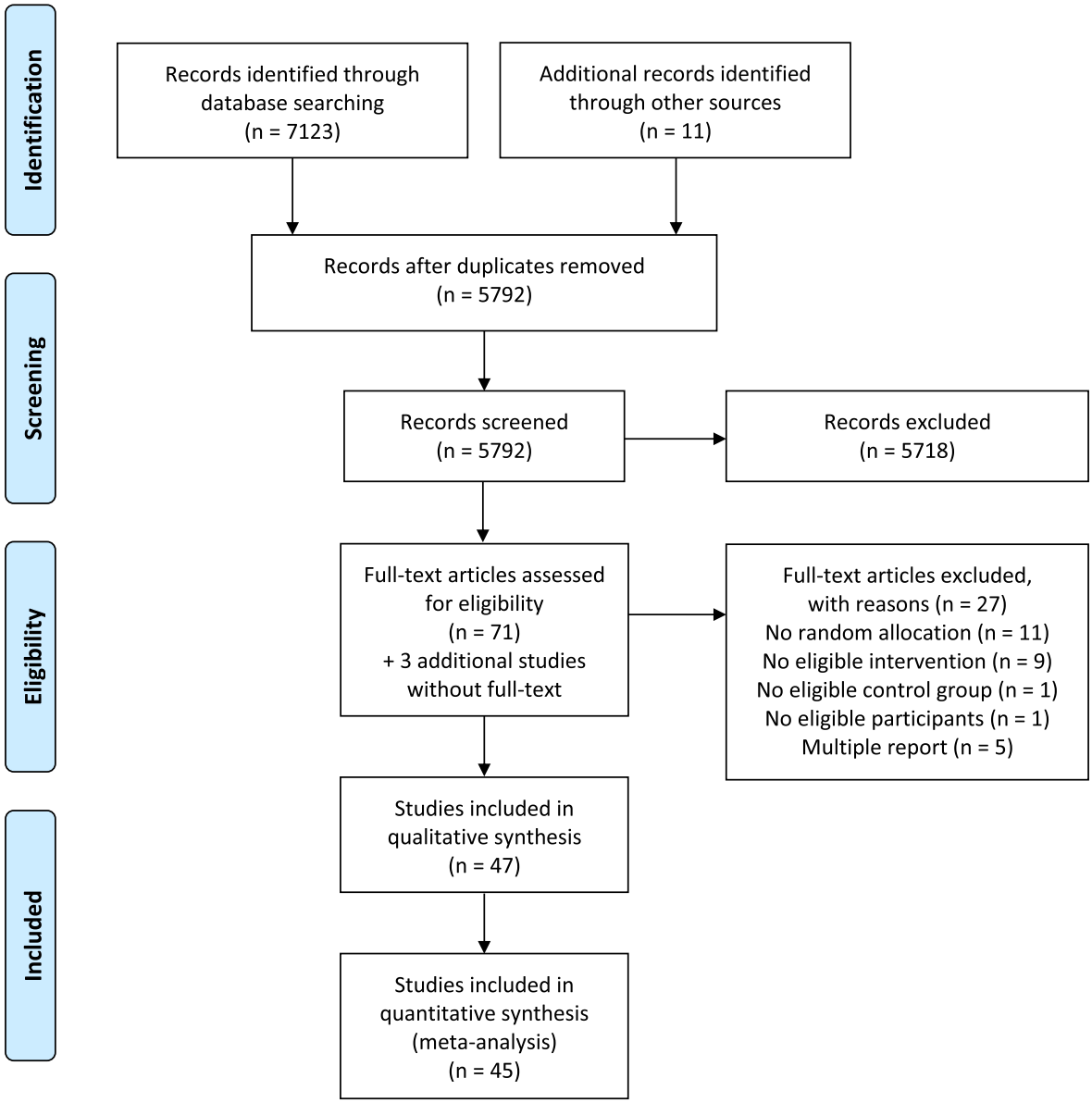

Fig. 1. Flow chart of study inclusion.

Table 2
Characteristics of the included studies.

Study	Sample				Intervention				Control group	Outcomes
	N	Age in years (mean, median or range)	% female	Patient population	Type of intervention	Total duration (min)	Modality	Intervention format		
Auerbach et al. (2016)[a] [33]	IG: 44 CG: 44	45.4	19	Patients of a physical rehabilitation center	Clown	6.6	Live	Group	AttCG	n.r.
Armat et al. (2020) [35]	IG: 31 CG: 31	58.3	100	Retired women with mild to moderate depression or anxiety	Laughter yoga	1440	Live	Group	TAU	Anxiety, depression
Behrouz et al. (2017) [36]	IG: 31 CG 32	73.9	71	Elderly living in nursing homes suffering from chronic pain	Laughter therapy, passive stimuli + humor games	360	Live	Group	TAU	Pain
Bressington et al. (2019) [37]	IG: 23 CG: 27	IG: 46.3 CG: 49.4	70	Community-dwelling people with depressive disorder	Laughter yoga	360	Live	Group	TAU	Anxiety, depression, mental quality of life, stress, physical quality of life
Choi et al. (2016) [38]	IG: 30 CG: 12	20.3	66.7	Students with smartphone addiction or high risk for smartphone addiction	Laughter therapy	720	n.r.	n.r.	NT	Stress
Cokolic et al. (2013) [39]	IG: 110 CG: 101	n.r.	n.r.	Patients with type 2 diabetes mellitus not receiving insulin therapy	Laughter yoga	30	Live	Group	AttCG	Blood glucose level
Donelli da Silveira et al. (2019) [40]	IG: 11 CG: 11	62	36.4	Patients with stable coronary heart disease	Passive stimuli	30	Recorded	Individual	AttCG	Cardiopulmonary parameters
Elmali & Akpinar (2017) [41]	IG: 30 CG1: 30 CG2: 30	37.4	31.1	Patients with postoperative pain after orthopedic surgery	Passive stimuli	20	Recorded	Individual	CG1: AttCG CG2: WL	Pain
Farifteh et al. (2014) [42]	IG: 25 CG: 25	n.r.	62.7	Cancer patients hospitalized for chemotherapy	Laughter yoga	25	Live	n.r.	TAU	Stress
Fukuoka et al. (2016) [43]	IG: 5 CG: 3	IG: 74.6 CG: 77	12.5	Stable outpatients with COPD participating in pulmonary rehabilitation program	Laughter yoga	10	Live	Group	TAU	Anxiety, depression, emotional (role) functioning, general/ global health, mental quality of life, social functioning, pain,p hysical (role) functioning, physical quality of life, vitality, cardiopulmonary parameters
Gaberson (1991) [44]	IG: 5 CG1: 5 CG2: 5	20 to 79	60	Patients scheduled for elective surgery	Passive stimuli	20	Recorded	Individual	CG1: TAU CG2: AttCG	Anxiety
Gaberson (1995) [45]	IG: 15 CG1: 15 CG2: 16	IG: 42.9 CG1: 47.1 CG2: 51.8	58.7	Patients scheduled for elective, nondiagnostic surgery	Passive stimuli	20	Recorded	Individual	CG1: TAU CG2: AttCG	Anxiety
Gelkopf et al. (1993) [46]	IG:17 CG: 17	IG: 43.8 CG: 45.1	17.6	Chronic schizophrenic inpatients	Passive stimuli	n.r.	Recorded	Group	AttCG	Anxiety, depression, symptoms of mental disorder, cardiopulmonary parameters
Gelkopf et al. (2006) [47]	IG: 15 CG: 14	IG: 42.5 CG:46.1	62.1	Chronic residual schizophrenia inpatients	Passive stimuli	n.r.	Recorded	Group	AttCG	Anxiety, depression, symptoms of mental disorder

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Table 2 (*continued*)

Study	Sample				Intervention				Control group	Outcomes
	N	Age in years (mean, median or range)	% female	Patient population	Type of intervention	Total duration (min)	Modality	Intervention format		
Hashemi (2015)/ Yekta et al., 2015 [48, 49]	IG: 45 CG: 45	n.r.	n.r.	Cancer patients undergoing chemotherapy	Passive stimuli	240	Recorded	n.r.	TAU	Depression, fatigue
Hayashi et al. (2007)[a] [34]	IG: 10 CG: 10	55.3	40	Patients with type 2 diabetes mellitus	Passive stimuli	60	Recorded	Group	TAU	n.r.
Heo et al. (2018) [50]	IG: 20 CG: 20	IG: 54.1 CG: 53	42.5	Hemodialysis patients	Laughter therapy	982	Live	Group and individual	TAU	Mental quality of life, mood, physical quality of life, hormones and regulatory proteins
Keykhaho-seinpoor et al. (2013) [51]	IG: 12 CG: 12	IG: 52.6 CG: 55.5	100	Patients with Parkinson's disease	Laughter yoga	1080	Live	Group	TAU	Balance, flexibility, motor function
Kheirandish et al. (2015) [52]	IG: 15 CG: 15	n.r.	100	Patients with multiple sclerosis	Laughter yoga	300	Live	Group	TAU	Depression, stress
Kim, Kim et al. (2015) [53]	IG: 31 CG: 31	>40 to <60	100	Breast cancer patients receiving postoperative radiation therapy	Laughter therapy	240	Live	Group	TAU	Anxiety, depression, stress
Kim, Kook et al. (2015) [54]	IG: 33 CG: 31	30 to <70	68.8	Cancer patients undergoing radiation therapy	Laughter therapy	180	Live	Group	TAU	Mood
Kimata (2004a) [55]	IG: 12 CG: 12	14	50	Patients with moderate atopic dermatitis	Passive stimuli	87	Recorded	n.r.	AttCG	Neurotrophins
Kimata (2004b) [56]	IG: 20 CG: 20[b]	27	50	Patients with mild atopic dermatitis	Passive stimuli	73	Recorded	n.r.	AttCG	Cytokines, immunoglobulin
Kimata (2008) [57]	IG: 36 CG: 36[b]	35	0	Patients with atopic dermatitis suffering from erectile dysfunction	Passive stimuli	278	Recorded	Group	AttCG	Erectile function, hormones and regulatory proteins
Kimata (2010) [58]	IG: 24 CG: 24[b]	28	50	Patients with mild atopic dermatitis	Passive stimuli	657	Recorded	n.r.	AttCG	Mood, polyamines
Kumar & Patra (2018) [59]	IG: 30 CG: 30	n.r.	n.r.	Senior citizens in old age homes suffering from depression	Laughter therapy	375	n.r.	n.r.	TAU	Depression
Lebowitz et al. (2011) [60]	IG: 12 CG: 10	IG: 68.8 CG: 66.5	63.6	Patients with COPD	Passive stimuli	80	Recorded	Individual	AttCG	Mood, dyspnea, cardiopulmonary parameters
Lee et al. (2020) [61]	IG: 20 CG: 20	20 to <60	100	Gynaecological cancer patients	Laughter therapy + music-related activities	495	Live	Group	TAU	Depression, mental quality of life, stress, physical quality of life
Memarian et al. (2017) [62]	IG: 15 CG: 15	55 to 75	33.3	Patients with Parkinson's disease	Laughter yoga	720	n.r.	n.r.	TAU	Anxiety, sleep quality
Morishima et al. (2019) [63]	IG: 30 CG: 31	IG: 55 CG: 56	75.4	Patients receiving active treatment or follow-up for cancer	Laughter yoga + passive stimuli	240	Live	Group	TAU	Cognitive functioning, emotional (role) functioning, general/ global health, appetite loss, constipation, diarrhea, dyspnea, fatigue, insomnia, nausea and vomiting, pain, physical (role) functioning, social functioning
Moura et al. (2015) [64]	IG: 32 CG: 26	IG: 47.7 CG: 42	100	Patients with systemic lupus erythematosus	Passive stimuli	120	Recorded	Individual	AttCG	Hormones and regulatory proteins

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Table 2 (*continued*)

Study	Sample				Intervention				Control group	Outcomes
	N	Age in years (mean, median or range)	% female	Patient population	Type of intervention	Total duration (min)	Modality	Intervention format		
Nelson (2017) [65]	IG: 30 CG: 33	54.5	69	Patients with multiple sclerosis	Laughter therapy + Laughter yoga	113	Live	Group	TAU	Mood, well-being
Newman et al. (2019) [66]	IG: 23 CG: 22	IG: 5.7 CG: 5.9	42.2	Children undergoing elective hernia repair surgery	Clown	60	Live	Individual	TAU	Pain, serum cortisol
Nia et al. (2019) [67]	IG: 39 CG: 39	IG: 49 CG: 45.2	68.2	Cancer patients undergoing chemotherapy	Laughter yoga	100	Live	Group	TAU	Well-being
Özer et al. (2021) [68]	IG: 34 CG: 34	IG: 62.7 CG: 60.3	53	Patient receiving hemodialysis treatment	Laughter yoga	480	Group	Live	TAU	Neuropeptides, pain, sleep quality
Park et al. (2019) [69]	IG: 40 CG: 39	IG: 59.5 CG: 57	61.5	Patients with gastrointestinal cancer	Laughter therapy	480	Group	Live	TAU	Anxiety, depression, fatigue, sleep quality
Rad et al. (2015) [70]	IG: 33 CG: 34	IG: 43.8 CG: 51.9	100	Breast cancer patients receiving radiation therapy	Passive stimuli, jokes + fun competitions	480	Recorded + Live	Group	TAU	Fatigue
Rotton & Shats (1996) [71]	IG: 40 CG: 40	43	50	Patients after orthopedic surgery	Passive stimuli	445	Recorded	Individual	AttCG	Pain
Rudnick et al. (2014) [72]	IG: 12 CG: 12	n.r.	n.r.	Patients with diagnosed mental illness	Passive stimuli	1080	Recorded + Live	Group	TAU	Life satisfaction, mood, stress, symptoms of mental disorder
Sahai-Srivastava et al. (2014) [73]	IG: 14 CG: 8	41	100	Patients with chronic migraine	Laughter yoga	480	Live	Group and individual	TAU	Depression, emotional (role) functioning, fatigue, pain
Saritas et al. (2019) [74]	IG: 47 CG: 47	IG: 58.7 CG: 51.9	54.3	Postsurgical cancer patients	Passive stimuli	10	Recorded	Individual	TAU	Anxiety, pain
Sayed & Gandham (2018) [75]	IG: 37 CG: 39	56 to <75	48.7	Residents of old age institutions suffering from anxiety and depression	Laughter therapy, Laughter yoga + passive stimuli	3762	n.r.	n.r.	TAU	Anxiety, depression
Shahidi et al. (2011) [76]	IG: 23 CG1: 23 CG2: 24	IG: 65.5 CG1: 65.7 CG2: 68.4]	100	Depressed old women	Laughter yoga	n.r.	n.r.	n.r.	CG1: AttCG CG2: NT	Depression, life satisfaction
Shattla et al. (2019) [77]	IG: 32 CG: 32	<30 to >40	65.6	Psychiatric nurses with burnout syndrome	Laughter yoga	420	Live	Group	NT	Symptoms of mental disorder
Spencer et al. (2020) [78]	IG: 33 CG: 33	62	100	Patients receiving chemotherapy for recurrent gynecologic cancer	Passive stimuli	96	Recorded	Group	AttCG	Fatigue, mood
Tavakoli et al. (2017) [79]	IG: 20 CG: 20	IG: 33.1 CG: 31.7	73.3	Patients with irritable bowel syndrome	Laughter yoga	425	Live	Group	TAU	Anxiety, irritable bowel syndrome severity
Walter Jaisingh et al. (2019) [80]	IG1: 50 IG2: 50 CG: 50	n.r.	n.r.	Patients with type 2 diabetes mellitus	IG1: Laughter therapy IG2: Passive stimuli	IG1: 280 IG2: n.r.	IG1: n.r. IG2: Recorded	n.r.	TAU	Blood glucose level

AttCG = attention control group; CG = Control group; IG = Intervention group; NT = No treatment; TAU = Treatment as usual; n.r. = not (sufficiently) reported.
[a] Study not included in quantitative analysis.
[b] Crossover design with the same patients allocated to intervention and control group.

mental health, 21 studies on physical health, and 14 trials on physiological outcomes (see Supplementary Table S2 for a detailed description of considered outcomes). We contacted authors of 17 studies to clarify questions regarding statistical data or to provide additional data required for effect size estimation. Seven authors replied, three proving the requested data and four without a useable response. In nine studies, effect sizes had to be approximated using different estimation methods.

3.3. Risk of bias within studies

An overview of the risk of bias judgements for the included studies (randomization processes, deviations from intended interventions,

missing outcome data, measurement of outcome, selective outcome reporting) is provided in Figs. 2 and 3. More than half of the studies (53%) were judged as having a high overall risk of bias, the remaining studies were rated with 'some concerns'. In both categories, most ratings were due to missing or insufficiently reported information.

3.4. Results of individual studies and synthesis of results

Laughter-inducing interventions revealed significant positive, medium-sized effects in comparison to control groups on the primary outcomes mental health (n = 31, 1,543 patients, g = 0.74, 95% CI [0.48; 1.00], p < 0.001) and physiological outcomes (n = 14, 761 patients, g = 0.61, 95% CI [0.20; 1.03], p < 0.001), and on the secondary outcome physical health (n = 21, 1,105 patients, g = 0.59, 95% CI [0.30; 0.88], p < 0.001). Individual study results are shown in Table 3. Heterogeneity was substantial in all analyses, with I^2 ranging from 80% to 86%, p < 0.001. According to the GRADE approach, the quality of evidence for mental health was rated as moderate due to limitations in consistency. For physiological and physical health outcomes, we judged the evidence as very low-quality due to risk of bias, inconsistency, and imprecision. The 95% prediction intervals included the null effect for all outcome categories (Table 4).

In a second step, we excluded statistical outliers (effect sizes with confidence intervals not overlapping with the confidence interval of the pooled effect) to reduce heterogeneity. Adjusted effects were smaller, but heterogeneity only dropped considerably for mental outcomes. Accordingly, the 95% prediction interval without outliers still included the null effect for physiological and physical health outcomes (Table 4). Figs. 4–6 show the results of the included studies, together with the mean overall effect with statistical outliers set to zero weight.

When different outcomes were considered separately (when n > 5 studies reported the outcome), significant positive effects were found for depression, anxiety, mood, stress, and pain with largest effects for anxiety (n = 13, g = 0.98, 95% CI [0.45; 1.52], p < 0.001). Effects for fatigue and cardiopulmonary outcomes did not reach statistical significance (Table 5).

With respect to the secondary outcome adverse events, only one study reported such an occurrence [37]. Specifically, three participants in a laughter yoga group described experiencing some discomfort relating to an increased heart rate, developing a dry mouth and feeling breathless. However, none of these issues required any medical/nursing intervention. Substantial negative effect sizes were found for physiological outcomes in two studies [43,66], though the effect was significant only in one investigation (laughter intervention produced higher serum cortisol levels than standard care) [66].

3.5. Risk of bias across studies

For all outcomes, the visual inspection of funnel plots provided a relatively symmetrical distribution of studies (Fig. 7). Trim and fill analysis revealed no missing studies indicating no risk for publication bias. Egger's regression test also did not indicate a risk for publication bias (mental health: β = 2.43; t(29) = 1.50; p = 0.143; physiological outcomes: β = −0.29; t(12) = 0.15; p = 0.885; physical health: β = 2.44; t(19) = 1.27; p = 0.221). Fail-safe N analysis showed that the results are robust as for mental health 1,164, for physiological outcomes 203, and for physical health 362 new studies would be needed to bring the p-value above 0.05, i.e., to a non-significant level.

3.6. Additional analyses

We did not find significant differences in intervention effects between different control groups (Supplementary Table S3). Further subgroup analyses also did not demonstrate differences in effect sizes for a number of moderator variables (Supplementary Table S4). Of note, simulated laughter produced significantly larger effects on mental health (n = 19, g = 0.93, 95% CI [0.57; 1.29], p < 0.001) than spontaneous laughter (n = 10, g = 0.34, 95% CI [0.07; 0.22], p = 0.056; p for difference = 0.011). Studies conducted in Asian countries revealed larger effects on physiological outcomes (n = 7, g = 1.17, 95% CI [0.58; 1.76], p < 0.001) than studies conducted in countries outside Asia (n = 7, g = 0.10, 95% CI [−0.33; 0.54], p < 0.001, p for difference = 0.004). Interventions applied in groups were more efficacious in improving physical health outcomes (n = 12, g = 0.83, 95% CI [0.35; 1.31], p = 0.001) compared to interventions in an individual setting (n = 5, g = 0.24, 95% CI [0.01; 0.46], p = 0.041, p for difference = 0.029).

Results of meta-regression analyses revealed a significant impact of dosage on effect size (β = 0.0005, SE = 0.0002, p = 0.013, R^2 = 0.20) for mental health (but not for the other outcomes), indicating an increasing effect of laughter-inducing interventions with increasing total duration of the intervention. Year of publication, age and proportion of women were not associated with effect size.

Sensitivity analyses largely proved the robustness of our results, i.e., findings and conclusions did not change for mental health and physical health outcomes when excluding effect sizes that were approximated or set to zero and studies with high risk of bias judgements in single bias domains or in the overall rating. However, results on physiological outcomes dropped to small, non-significant effect sizes when excluding effects that were approximated or set to zero and studies with high risk of bias judgements in single bias domains or in the overall rating (Supplementary Table S5).

4. Discussion

4.1. Summary of the evidence

The aim of this study was to evaluate the efficacy of laughter-inducing interventions to impact mental health, physiological, and physical health outcomes in patients with mental or somatic disorders or health problems. We included 47 randomized-controlled trials, of which 45 provided sufficient data for meta-analysis. Results revealed considerable heterogeneity across studies and therefore statistical outliers with extreme effect sizes were excluded. For each outcome category we found significant positive effects of laughter-inducing interventions. However, due to the remaining heterogeneity, the 95% prediction intervals for all pooled estimates were quite broad and included the null effect. This suggests that future studies, which are similar to those in this meta-analysis, would be expected to fall within this range. Hence, the intervention effects in a new study could also be null or even negative. The quality of the evidence was moderate for mental health, i.e., we believe that the true effect is probably close to the estimated effect. For physiological and physical health outcomes, the quality of evidence was very low, i.e., we have very little confidence in the effect estimate and the true effect is probably markedly different from the estimated effect.

Our results are in line with current meta-analytic findings [5,6,15] showing significantly positive, at least medium sized effects of laughter-inducing interventions on mental health, e.g., anxiety, depression, and stress. Additionally, we provided meta-analytic estimates on physiological outcomes and, in addition to our review protocol, also considered physical health as it was frequently measured. Effects found in this meta-analysis were in line with findings of current reviews based on narrative summaries only [3,9–11].

In order to make a balanced decision about any intervention it is essential to comprehensively estimate both the benefits and adverse effects [17,18]. However, only one study mentioned adverse events in their report [37]. In that study, adverse events were minor in nature (e.g., discomfort from being out of breath) and did not require any further intervention. Although the current standards for the reporting of randomized-controlled trials point to the importance of addressing harm [81], negative effects and adverse events were not considered in the nearly all of the included studies. Therefore, it remains unclear whether laughter-inducing therapies indeed have few and very minor negative

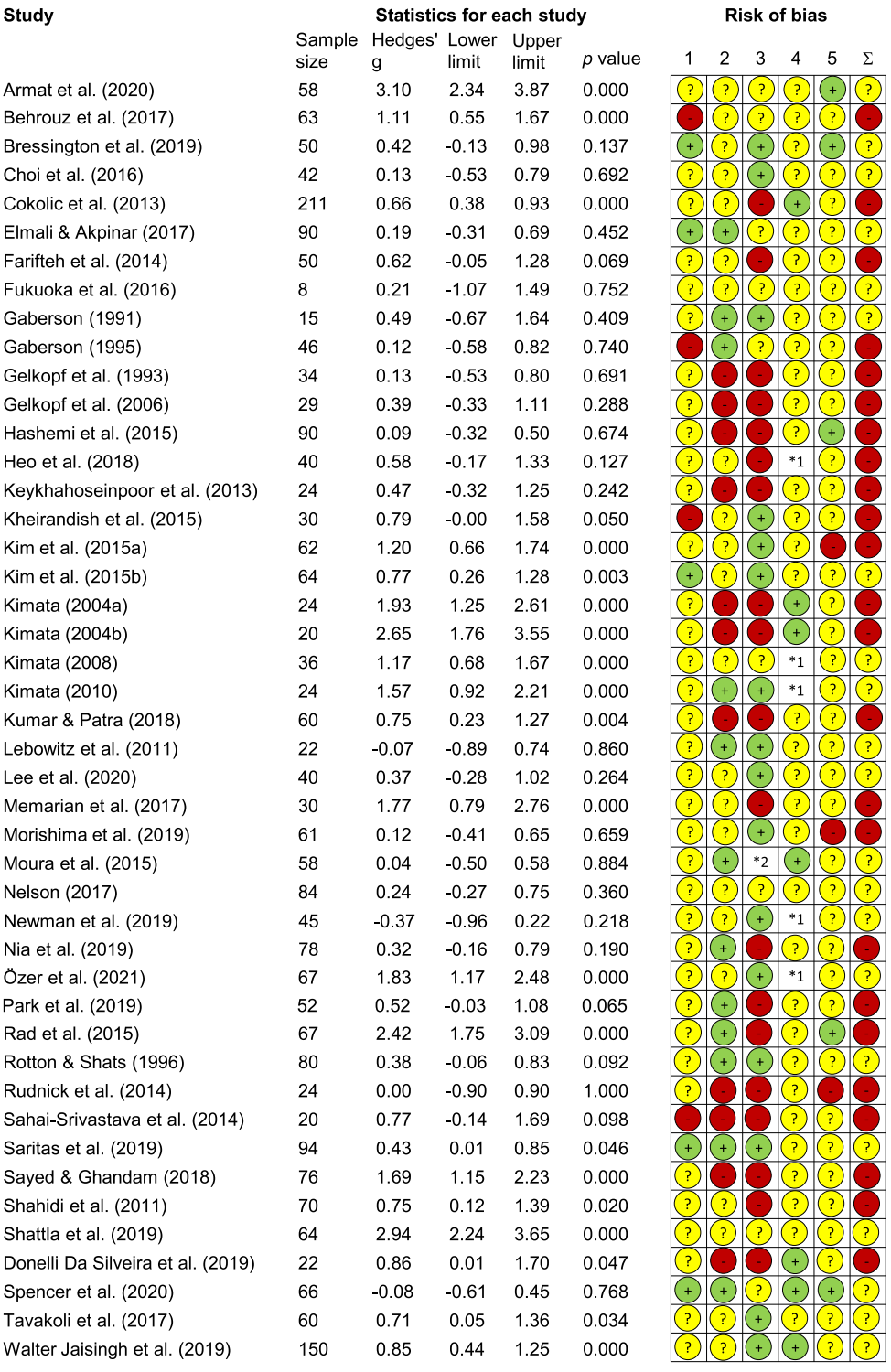

Fig. 2. Risk of bias summary: review authors' judgements about each risk of bias domain for each included study.

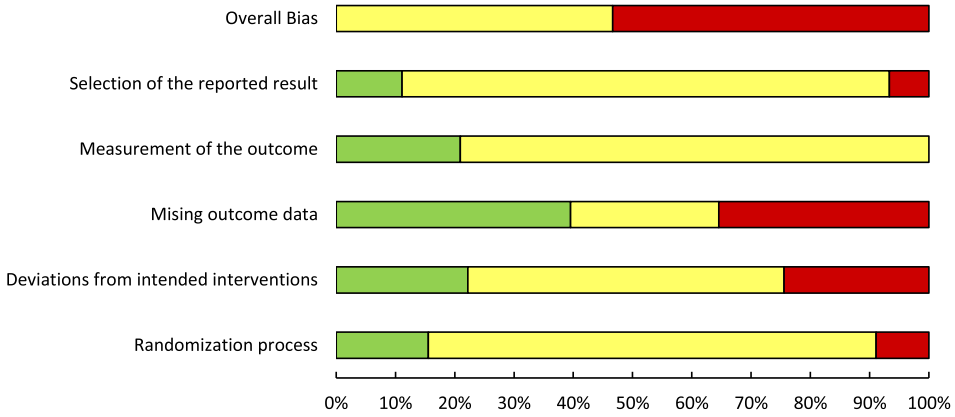

Fig. 3. Risk of bias summary: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Table 3
Effect sizes per study.

Study	Mental health		Physiological outcomes		Physical health	
	Hedges' g	95% CI	Hedges' g	95% CI	Hedges' g	95% CI
Armat et al. (2020)	3.10	2.34; 3.87				
Behrouz et al. (2017)					1.11	0.55; 1.67
Bressington et al. (2019)	0.51	−0.05; 1.07			0.06	−0.49; 0.61
Choi et al. (2016)	0.13	−0.53; 0.79				
Cokolic et al. (2013)			0.66	0.38; 0.93		
Donelli da Silveira et al. (2019)			0.86	0.01; 1.70		
Elmali & Akpinar (2017)					0.19	−0.31; 0.69
Farifteh et al. (2014)	0.62	−0.05; 1.28				
Fukuoka et al. (2016)	0.02	−1.23; 1.27	−0.96	−2.35; 0.44	0.45	−0.83; 1.73
Gaberson (1991)	0.49	−0.67; 1.64				
Garberson (1995)	0.12	−0.58; 0.82				
Gelkopf et al. (1993)	0.31	−0.36; 0.97	−0.09	−0.76; 0.57		
Gelkopf et al. (2006)	0.39	−0.33; 1.11				
Hashemi et al. (2015)	0.10	−0.31; 0.51			0.08	−0.33; 0.49
Heo et al. (2018)	0.96	0.19; 1.73	0.37	−0.37; 1.10	0.32	−0.42; 1.05
Keykhahoseinpoor et al. (2013)					0.47	−0.32; 1.25
Kheirandish et al. (2015)	0.79	0.00; 1.58				
Kim, Kim et al. (2015)	1.20	0.66; 1.74				
Kim, Kook et al. (2015)	0.77	0.26; 1.28				
Kimata (2004a)			1.93	1.25; 2.61		
Kimata (2004b)			2.65	1.76; 3.55		
Kimata (2008)			1.14	0.64; 1.64	1.25	0.74; 1.75
Kimata (2010)	1.37	0.74; 1.99	1.62	0.97; 2.27		
Kumar & Patra (2018)	0.75	0.23; 1.27				
Lebowitz et al. (2011)	0.23	−0.59; 1.05	−0.34	−1.16; 0.47	−0.11	−0.91; 0.70
Lee et al. (2020)	0.46	−0.19; 1.11			0.10	−0.54; 0.74
Memarian et al. (2017)	2.99	1.85; 4.14			0.56	−0.23; 1.34
Morishima et al. (2019)	0.14	−0.39; 0.67			0.11	−0.42; 0.64
Moura et al. (2015)			0.04	−0.50; 0.58		
Nelson (2017)	0.24	−0.27; 0.75				
Newman et al. (2019)			0.11	−0.47; 0.68		
Nia et al. (2019)	0.32	−0.16; 0.79				
Özer et al. (2021)			2.56	1.83; 3.29	0.35	−0.13; 0.83
Park et al. (2019)			0.65	0.09; 1.21	−0.85	−1.45; −0.24
Rad et al. (2015)					2.42	1.75; 3.09
Rotton & Shats (1996)					0.38	−0.06; 0.83
Rudnick et al. (2014)	0.00	−0.90; 0.90				
Sahai-Srivastava et al. (2014)	0.73	−0.17; 1.63			0.82	−0.12; 1.76
Saritas et al. (2019)	0.55	0.13; 0.98			0.30	−0.12; 0.72
Sayed & Ghandam (2018)	1.69	1.15; 2.23				
Shahidi et al. (2011)	0.75	0.12; 1.39				
Shattla et al. (2019)	2.94	2.24; 3.65				
Spencer et al. (2020)	−0.11	−0.64; 0.42			−0.05	−0.58; 0.48
Tavakoli et al. (2017)	0.56	−0.09; 1.20			0.85	0.19; 1.51
Walter Jaisingh et al. (2019)			0.85	0.44; 1.25		

Table 4
Efficacy of laughter-inducing interventions on mental health, physiological outcomes and physical health.

	n	Hedges' g	95% CI	p (g)	Q	p (Q)	I^2	95% PI
All studies included								
Mental health	31	0.74	0.48; 1.00	<0.001	155.84	<0.001	81%	−0.68; 2.15
Physiological outcomes	14	0.61	0.20; 1.03	0.004	92.47	<0.001	86%	−0.98; 2.20
Physical health	21	0.59	0.30; 0.88	<0.001	97.66	<0.001	80%	−0.72; 1.89
Outliers excluded								
Mental health	26	0.50	0.37; 0.64	<0.001	30.83	0.195	19%	0.15; 0.86
Physiological outcomes	11	0.51	0.18; 0.83	0.002	35.49	<0.001	72%	−0.50; 1.52
Physical health	19	0.39	0.20; 0.57	<0.001	32.53	0.019	45%	−0.21; 0.99

n = number of studies, 95% CI = 95% confidence interval; 95% PI = 95% prediction interval.

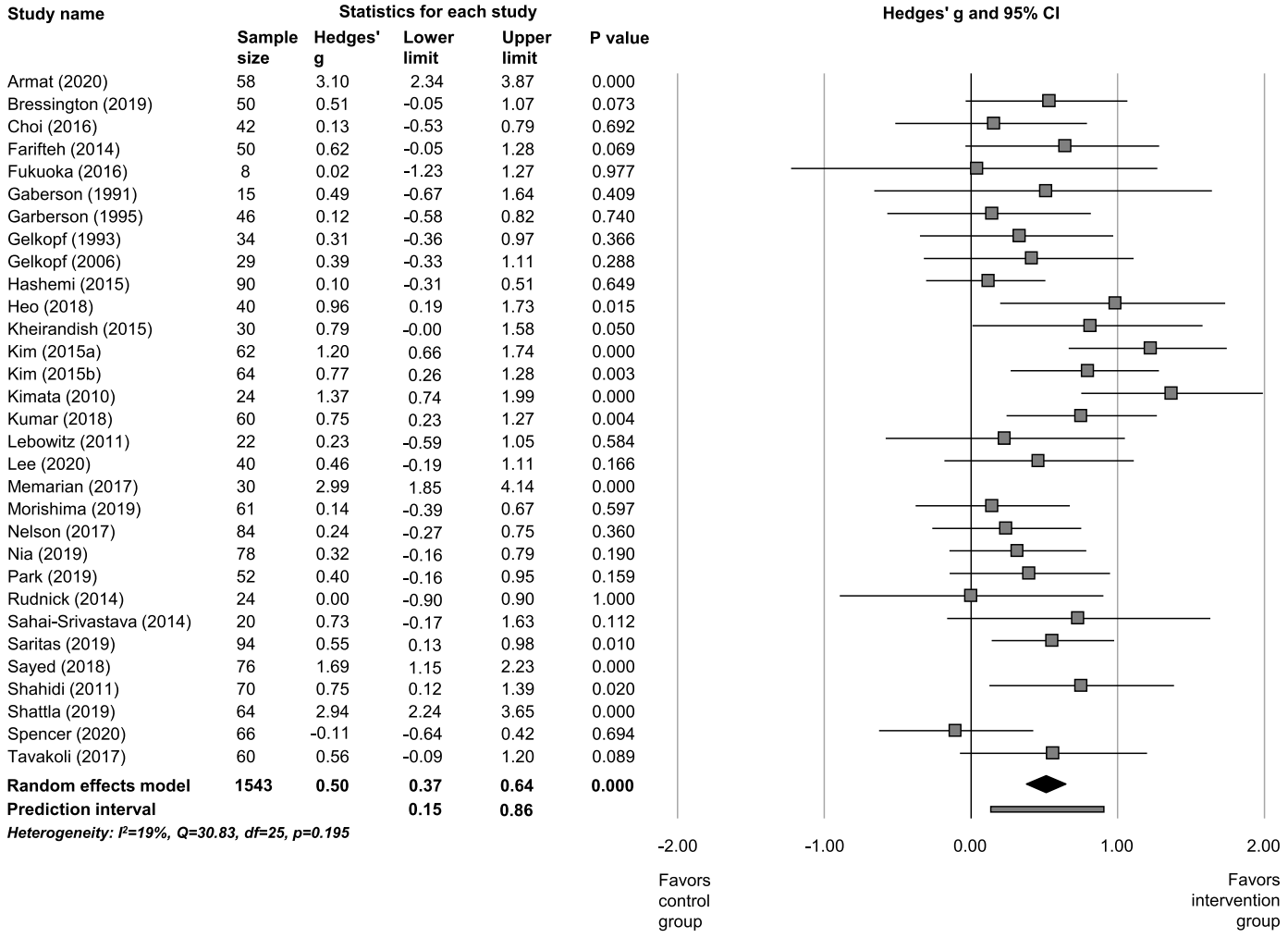

Fig. 4. Forest plot for mental health outcomes. *Note.* Studies with statistically outlying effect sizes are presented, but these studies were not included in the estimation of the total effect (weight = 0%).

effects, or, whether such effects occurred but were not noticed and/or reported.

We also conducted various moderator analyses to help explain the statistical heterogeneity between single study results. In line with previous findings [6], we found an association between total duration of the intervention and effect size for mental health. More specifically, an increasing effect of laughter-inducing interventions was found with increasing intervention dosage (i.e. duration). Similar to recent research [5], our results further show that simulated laughter has larger effects on mental health than spontaneous (humorous) laughter. Theoretical models might also support this finding [82]. Laughter, even of the simulated sort, leads to physiological changes in the body. These include changes in musculoskeletal, cardiovascular, endocrine, immunological, and neural systems that are positive and conducive to health [83,84]. Another potential explanation is that it remains unclear, if and to what extent passive stimuli made the participants laugh since this information was not controlled for in the primary studies.

We further found that laughter-inducing interventions were more effective when applied in groups (though the effect was significant only for physical health). One common explanation for this finding refers to behavioral mimicry and emotional contagion. Laughing in groups might activate somatic and autonomic responses resulting in mimicry facilitating physiological and motor feedback that could induce or enhance particular emotions in the respective observer (emotional contagion)

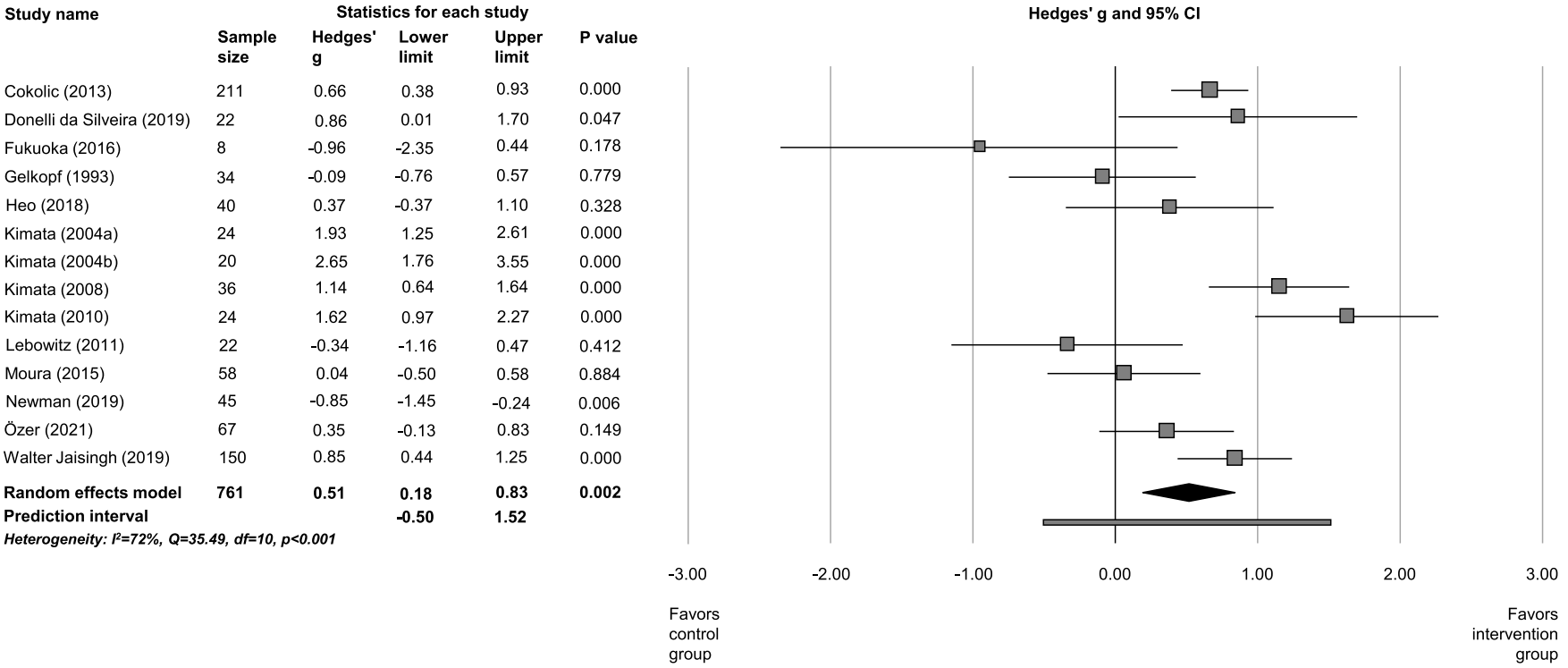

Fig. 5. Forest plot for physiological outcomes. *Note.* Studies with statistically outlying effect sizes are presented, but these studies were not included in the estimation of the total effect (weight = 0%).

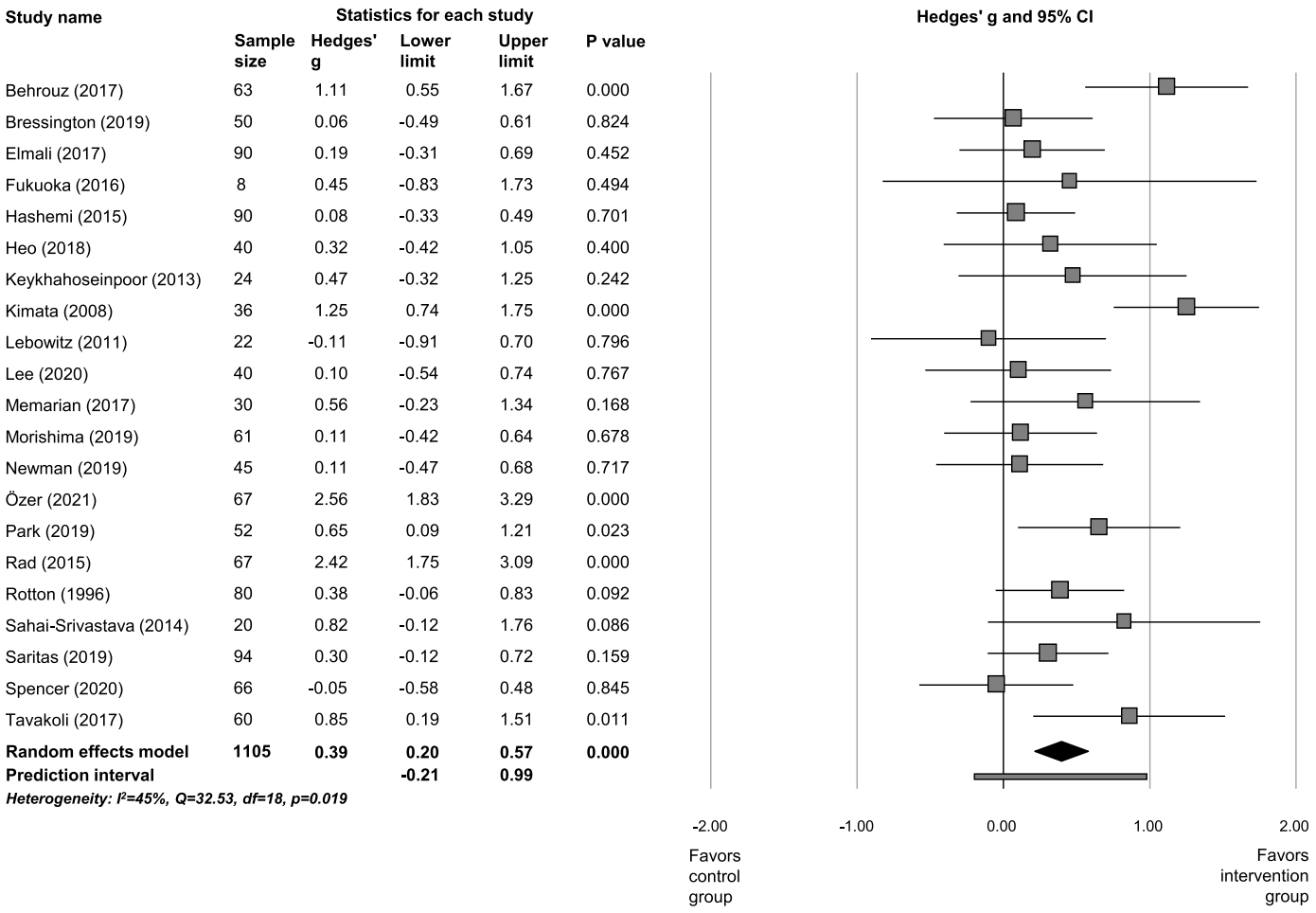

Fig. 6. Forest plot for physical health outcomes. *Note.* Studies with statistically outlying effect sizes are presented, but these studies were not included in the estimation of the total effect (weight = 0%).

Table 5
Efficacy of laughter-inducing interventions on specific outcomes.

	n	Hedges' g	95% CI	p (g)	Q	p (Q)	I^2
Depression	14	0.79	0.41; 1.17	<0.001	66.67	<0.001	81%
Anxiety	13	0.98	0.45; 1.52	<0.001	99.31	<0.001	88%
Pain	9	0.44	0.18; 0.70	0.001	15.19	0.055	47%
Mood	7	0.50	0.06; 0.95	0.026	20.20	0.003	70%
Stress	7	0.45	0.00; 0.89	0.049	19.13	0.004	69%
Fatigue	6	0.56	−0.12; 1.22	0.110	41.99	<0.001	88%
Cardiopulmonary outcomes[a]	5	0.14	−0.19; 0.47	0.397	4.06	0.398	1%

n = number of studies; 95% CI = 95% confidence interval.
[a] Cardiopulmonary outcomes include self-reported dyspnea and various cardiopulmonary parameters (e.g., heart rate, blood pressure, vital capacity, inspiratory/expiratory volume).

[85].

With our review, we were able to extend the evidence base of previous meta-analytic summaries by applying the current standards of systematic reviews. While the most comprehensive meta-analysis until now [5] included nine randomized and 20 quasi-randomized studies, we included 45 trials of which were five overlapping (i.e., also included in [5]) and 40 additional studies. Further strengths of this study are the pre-registration of our review, and the evaluation of the internal validity of the included studies by using the most current version of the Cochrane risk of bias tool (ROB2) [19]. Moreover, we extended our outcomes to negative effects, provided meta-analytic estimates for physical health and physiological outcomes in addition to mental health [5], and provided 95% prediction intervals to estimate the possible underlying effect in similar future studies [26].

4.2. Limitations

Our study has several noteworthy limitations. One weakness of this meta-analysis, as with many reviews, is that the patient populations, the settings, the applied interventions and control conditions, and the outcome definitions are not the same across studies. This clinical diversity might have led to the unexplained heterogeneity and resulting uncertainty about the true effect of laughter-inducing interventions. There is a longstanding debate about how much diversity across the included studies should be allowed to retain external validity, with two opposite lines of argument. The 'narrow' approach suggests that studies

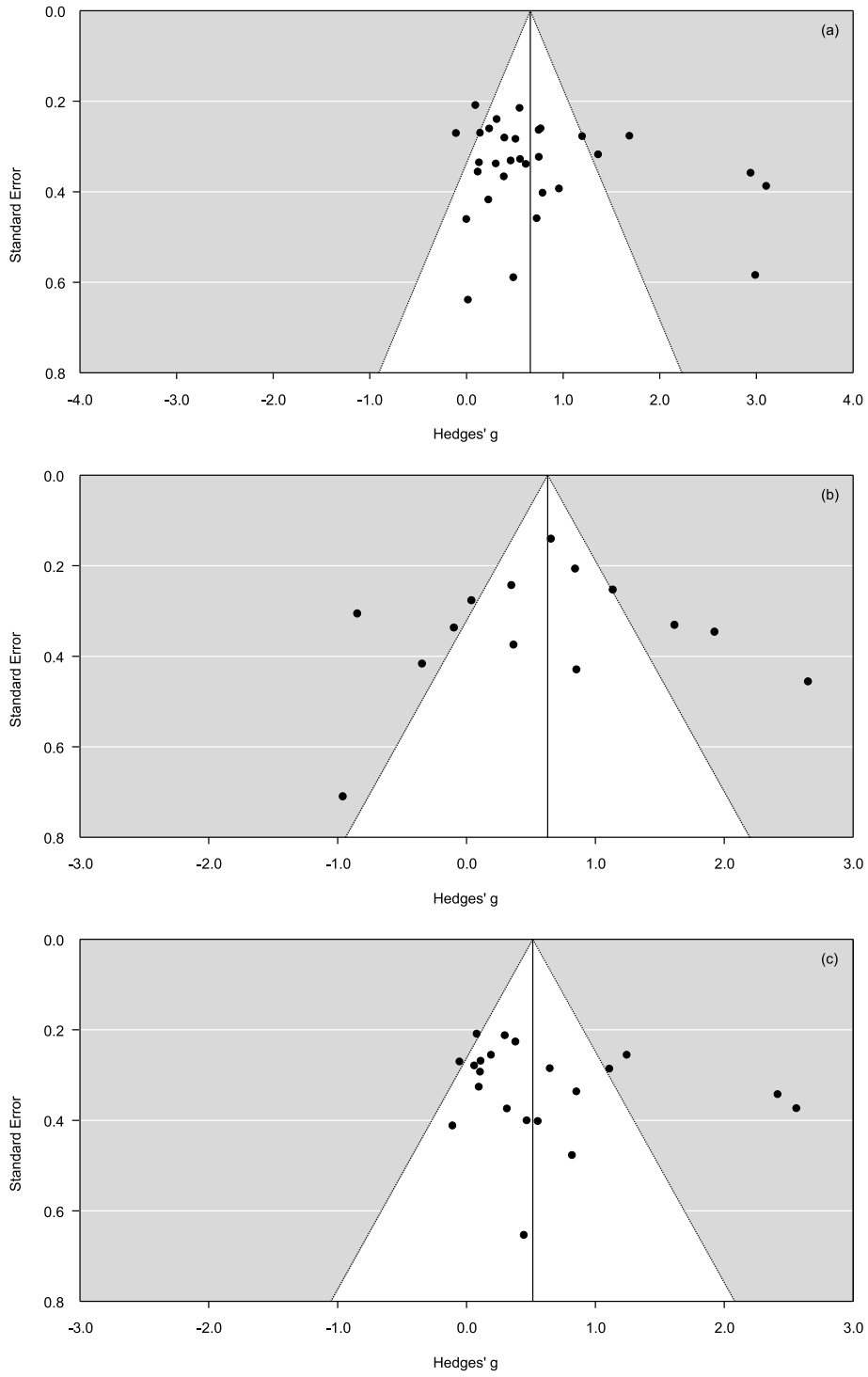

Fig. 7. Funnel plots for (a) mental health, (b) physiological outcomes, and (c) physical health.

should be sufficiently similar to be included in the same analysis. On the contrary, within the 'broad' approach it has been argued that the generalizability and usefulness of meta-analyses are increased considerably if there is some diversity in study characteristics such as patient populations, settings, and intervention properties [86]. In our review, we followed the 'broad' approach, which increases power, reduces the risk of erroneous conclusions, and facilitates exploratory analyses for generating hypotheses for future research.

We did not search Embase for eligible trials, since access to this database was not available for the review team. It has been suggested that searching Medline but not Embase could overestimate effects, but this risk is likely slight, provided the rest of the search is comprehensive [87].

One of our initial aims – to provide a comprehensive and complete picture of the evidence including benefits and harms – could not be achieved. While our analyses on positive effects are based on broad evidence, reporting of adverse events was limited to one study. Future randomized-controlled trials should provide a balanced report on both, the beneficial effects and possible adverse events.

Although we included a large sample of studies in our review and the moderator analyses were based on larger samples than in the existing reviews, statistical power of the moderator analyses might still pose a

problem [88]. For that reason, non-significant findings should not be interpreted as evidence for a non-existent effect [21,89]. In addition to low statistical power, findings of moderator analyses are only observational and do not imply causal relationships [90]. Taken together, caution is warranted when interpreting the results of our moderator analyses.

The majority of laughter-inducing interventions were applied in groups, so patients shared a common environment (e.g., same therapist, same group members), which results in a dependency of data [91]. This dependency among observations within groups should be properly accounted for in statistical tests to avoid a predictable inflation of type I error (i.e., findings are falsely considered as significant) [92]. Since all of the included studies examining group interventions ignored data dependency, this might have resulted in false-positive effects. Hence, adequate statistical methods accounting for data dependency should be used in future research.

5. Conclusion

Laughter-inducing interventions could have a positive impact on health in patients with somatic or mental health problems. Patients might benefit from those interventions through improved mood, well-being, or quality of life, or alternatively through reduced anxiety, depression, stress, pain or fatigue. Adverse events were reported very rarely and only one study found significant negative effects of laughter interventions. Laughter-inducing interventions using simulated laughter produced the largest positive effects on mental health. Moreover, it seems to be more beneficial when laughter is applied in groups. However, internal validity of the included trials was limited and there was substantial heterogeneity in the study pool, which could be reduced only in part, by excluding statistical outliers. We suggest future research apply methods leading to low risk of bias and to aim at a balanced reporting of benefits and harms of laughter-inducing interventions. Open research questions are related to differential effects of laughter (Who benefits most under which circumstances?) and mechanisms of action (Why does it work?).

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author statement

Katharina Stiwi: Investigation, Data curation, Writing - review & editing. **Jenny Rosendahl:** Conceptualization, Methodology, Validation, Formal analysis, Visualization, Writing - original draft, Project administration, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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List of Abbreviations

CI	Confidence interval
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
ROB2	Cochrane Risk of Bias Tool for Randomized Trials, revised version

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctcp.2022.101552.

References

[1] G.G. Byron, The Island or, Christian and His Comrades, Deadtree Publishing, London, 2015.
[2] M.P. Bennett, C.A. Lengacher, Humor and laughter may influence health. I. History and background, Evid. Based Complement, Alternative Med. 3 (2006) 61–63, https://doi.org/10.1093/ecam/nek015.
[3] R. Mora-Ripoll, Potential health benefits of simulated laughter: a narrative review of the literature and recommendations for future research, Complement, Ther. Med. 19 (2011) 170–177, https://doi.org/10.1016/j.ctim.2011.05.003.
[4] R. Mora-Ripoll, Laughter techniques for therapeutic use in medicine, OA Altern. Med. 1 (2013) 25.
[5] C.N. van der Wal, R.N. Kok, Laughter-inducing therapies: systematic review and meta-analysis, Soc. Sci. Med. 232 (2019) 473–488, https://doi.org/10.1016/j.socscimed.2019.02.018.
[6] J. Zhao, H. Yin, G. Zhang, G. Li, B. Shang, C. Wang, et al., A meta-analysis of randomized controlled trials of laughter and humour interventions on depression, anxiety and sleep quality in adults, J. Adv. Nurs. 75 (2019) 2435–2448, https://doi.org/10.1111/jan.14000.
[7] M.P. Bennett, C.A. Lengacher, Humor and laughter may influence health: II. Complementary therapies and humor in a clinical population, Evid. Based Complement, Alternative Med. 3 (2006) 187–190, https://doi.org/10.1093/ecam/nel014.
[8] M.P. Bennett, C.A. Lengacher, Humor and laughter may influence health: III. Laughter and health outcomes, Evid. Based Complement, Alternative Med. 5 (2008) 37–40, https://doi.org/10.1093/ecam/nem041.
[9] M.P. Bennett, C.A. Lengacher, Humor and laughter may influence health IV. Humor and immune function, Evid. Based Complement, Alternative Med. 6 (2009) 159–164, https://doi.org/10.1093/ecam/nem149.
[10] R.E. Ferner, J.K. Aronson, Laughter and MIRTH (methodical investigation of risibility, therapeutic and harmful): narrative synthesis, BMJ 347 (2013) f7274, https://doi.org/10.1136/bmj.f727.
[11] R. Mora-Ripoll, The therapeutic value of laughter in medicine, Alternative Ther. Health Med. 16 (2010) 56–64.
[12] M. Demir, Effects of laughter therapy on anxiety, stress, depression and quality of life in cancer patients, J. Cancer Sci. Ther. 7 (2015) 272–273, https://doi.org/10.4172/1948-5956.1000362.
[13] F.N. Gonot-Schoupinsky, G. Garip, Laughter and humour interventions for well-being in older adults: a systematic review and intervention classification, Complement, Ther. Med. 38 (2018) 85–91, https://doi.org/10.1016/j.ctim.2018.04.009.
[14] J. Yim, Therapeutic benefits of laughter in mental health: a theoretical review, Tohoku J. Exp. Med. 239 (2016) 243–249, https://doi.org/10.1620/tjem.239.243.
[15] M. Demir Doğan, The effect of laughter therapy on anxiety: a meta-analysis, Holist. Nurs. Pract. 34 (2020) 35–39, https://doi.org/10.1097/HNP.0000000000000363.
[16] S.H. Hwang, H.C. Jeong, J.W. Hwang, Effect of laughter therapy on healthy life: a meta-analysis, J. Korea Converg. Soc. 10 (2019) 291–299, https://doi.org/10.15207/JKCS.2019.10.9.291.
[17] Y.K. Loke, D. Price, A. Herxheimer, Cochrane Adverse Effects Methods Group, Systematic reviews of adverse effects: framework for a structured approach, BMC Med. Res. Methodol. 7 (2007) 32, https://doi.org/10.1186/1471-2288-7-32.
[18] H.M. McIntosh, N.F. Woolacott, A.M. Bagnall, Assessing harmful effects in systematic reviews, BMC Med. Res. Methodol. 4 (2004) 19, https://doi.org/10.1186/1471-2288-4-19.
[19] J. Sterne, J. Savović, M.J. Page, R.G. Elbers, N.S. Blencowe, I. Boutron, et al., RoB 2: a revised tool for assessing risk of bias in randomised trials, BMJ 366 (2019) l4898, https://doi.org/10.1136/bmj.l4898.
[20] L.V. Hedges, I. Olkin, Statistical Methods for Meta-Analysis, Academic Press, Orlando, 1985.
[21] M. Borenstein, L.V. Hedges, J.P.T. Higgins, H.R. Rothstein, Introduction to Meta-Analysis, Wiley & Sons, New York, 2009.
[22] J. Cohen, A power primer, Psychol. Bull. 112 (1992) 155–159, https://doi.org/10.1037//0033-2909.112.1.155.
[23] R. DerSimonian, N. Laird, Meta-analysis in clinical trials, Control, Clin. Trials 7 (1986) 177–188, https://doi.org/10.1016/0197-2456(86)90046-2.
[24] J.P.T. Higgins, S. Eldridge, T. Li, Chapter 23: including variants on randomized trials, in: J.P.T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M.J. Page, et al. (Eds.), Cochrane Handbook for Systematic Reviews of Interventions (Version 6.1 [updated September 2020]). Cochrane, 2020. Available from, https://www.training.cochrane.org/handbook.

[25] J.P. Higgins, S.G. Thompson, J.J. Deeks, D.G. Altman, Measuring inconsistency in meta-analyses, BMJ 327 (2003) 557–560, https://doi.org/10.1136/bmj.327.7414.557.
[26] J.J. Deeks, J.P.T. Higgins, D.G. Altman, Chapter 10: analysing data and undertaking meta-analyses, in: J.P.T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M.J. Page, et al. (Eds.), Cochrane Handbook for Systematic Reviews of Interventions (Version 6.1 [updated September 2020]). Cochrane, 2020. Available from, https://www.training.cochrane.org/handbook.
[27] P. Cuijpers, M. Sijbrandij, S. Koole, M. Huibers, M. Berking, G. Andersson, Psychological treatment of generalized anxiety disorder: a meta-analysis, Clin. Psychol. Rev. 34 (2014) 130–140, https://doi.org/10.1016/j.cpr.2014.01.002.
[28] R.D. Riley, J.P. Higgins, J.J. Deeks, Interpretation of random effects meta-analyses, BMJ 342 (2011) d549, https://doi.org/10.1136/bmj.d549.
[29] G.H. Guyatt, A.D. Oxman, R. Kunz, G.E. Vist, Y. Falck-Ytter, H.J. Schünemann, et al., What is "quality of evidence" and why is it important to clinicians? BMJ 336 (2008) 995–998, https://doi.org/10.1136/bmj.39490.551019.BE.
[30] M. Egger, G. Davey Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, BMJ 315 (1997) 629–634, https://doi.org/10.1136/bmj.315.7109.629.
[31] S. Duval, R. Tweedie, Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis, Biometrics 56 (2000) 455–463, https://doi.org/10.1111/j.0006-341x.2000.00455.x.
[32] R. Rosenthal, The file drawer problem and tolerance for null results, Psychol. Bull. 86 (1979) 638–641, https://doi.org/10.1037/0033-2909.86.3.638.
[33] S. Auerbach, W. Ruch, A. Fehling, Positive emotions elicited by clowns and nurses: an experimental study in a hospital setting, Transl, Issues Psychol. Sci. 2 (2016) 14–24, https://doi.org/10.1037/tps0000055.
[34] T. Hayashi, S. Tsujii, T. Iburi, T. Tamanaha, K. Yamagami, R. Ishibashi, et al., Laughter up-regulates the genes related to NK cell activity in diabetes, Biomed. Res. 28 (2007) 281–285, https://doi.org/10.2220/biomedres.28.281.
[35] M.R. Armat, A. Emami Zeydi, H. Mokarami, A. Nakhlband, S.K. Hojjat, The impact of laughter yoga on depression and anxiety among retired women: a randomized controlled clinical trial, J. Women Aging (2020), https://doi.org/10.1080/08952841.2020.1774225.
[36] S. Behrouz, S.R. Mazloom, H. Kooshyar, N. Aghebati, N. Asgharipour, H.R. Behnam Vashani, Investigating the effect of humor therapy on chronic pain in the elderly living in nursing homes in Mashhad, Iran, J. Evid. Based Care 7 (2017) 27-37, https://doi.org/10.22038/ebcj.2017.24247.1529.
[37] D. Bressington, J. Mui, C. Yu, S.F. Leung, K. Cheung, C. Wu, et al., Feasibility of a group-based laughter yoga intervention as an adjunctive treatment for residual symptoms of depression, anxiety and stress in people with depression, J. Affect. Disord. 248 (2019) 42–51, https://doi.org/10.1016/j.jad.2019.01.030.
[38] W. Choi, S. Park, J. Park, H. Jung, J. Yim, S. Lee, et al., The effects of laughter therapy on autonomic nervous system activity and stress in smartphone addict, Adv. Sci. Technol. Lett. 132 (2016) 151–154. Healthcare and Nursing.
[39] M. Cokolic, S. Stangler Herodez, S. Sternad, S. Krebs, The inhibitory effect of laughter yoga on the increase in postprandial blood glucose in type 2 diabetic patients, Diabetol. Croat. 42 (2013) 54-58.
[40] A. Donelli Da Silveira, R. Petry Buhler, R. Cechet De Oliveira, T. Lima Horn, M. Zanini, R.M. Nery, et al., An isolated 30-minute comedy session increases systolic volume and cardiac output in patients with stable ischemic heart disease, Eur. J. Prev. Cardiol. 26 (2019) S47, https://doi.org/10.1177/2047487319860046.
[41] H. Elmali, R. Balci Akpinar, The effect of watching funny and unfunny videos on post-surgical pain levels, Complement, Ther. Clin. Pract. 26 (2017) 36–41, https://doi.org/10.1016/j.ctcp.2016.11.003.
[42] S. Farifteh, A. Mohammadi-Aria, A. Kiamanesh, B. Mofid, The impact of laughter yoga on the stress of cancer patients before chemotherapy, Iran, J. Cancer Prev. 7 (2014) 179–183.
[43] A. Fukuoka, M. Ueda, Y. Ariyama, K. Iwai, Y. Kai, M. Kunimatsu, et al., Effect of laughter yoga on pulmonary rehabilitation in patients with chronic obstructive pulmonary disease, J. Nara Med. Assoc. 67 (2016) 11-20.
[44] K.B. Gaberson, The effect of humorous distraction on preoperative anxiety. A pilot study, AORN J. 54 (1991) 1258–1264, https://doi.org/10.1016/s0001-2092(07)66875-6.
[45] K.B. Gaberson, The effect of humorous and musical distraction on preoperative anxiety, AORN J. 62 (1995) 784–791, https://doi.org/10.1016/s0001-2092(06)63531-x.
[46] M. Gelkopf, S. Kreitler, M. Sigal, Laughter in a psychiatric ward. Somatic, emotional, social, and clinical influences on schizophrenic patients, J. Nerv. Ment. Dis. 181 (1993) 283–289.
[47] M. Gelkopf, B. Gonen, R. Kurs, Y. Melamed, A. Bleich, The effect of humorous movies on inpatients with chronic schizophrenia, J. Nerv. Ment. Dis. 194 (2006) 880–883, https://doi.org/10.1097/01.nmd.0000243811.29997.f7.
[48] R. Hashemi, Effects of Laughter Therapy on Fatigue and Depression in Cancer Patients Undergoing Chemotherapy [Master Thesis in Medical Surgical in Nursing], Tehran University of Medical Sciences, 2015.
[49] Z.P. Yekta, R.H. Tazangi, M.S. Yekaninejad, Effects of laughter therapy on the treatment of fatigue in cancer patients undergoing chemotherapy, Avicenna J. Phytomed. 5 (2015) 14.
[50] E.H. Heo, S. Kim, H.J. Park, S.Y. Kil, The effects of a simulated laughter programme on mood, cortisol levels, and health-related quality of life among haemodialysis patients, Complement, Ther. Clin. Pract. 25 (2016) 1–7, https://doi.org/10.1016/j.ctcp.2016.07, 001.
[51] A. Keykhahoseinpoor, N. Rahnama, A. Chitsaz, Effects of eight weeks laughter yoga training on motor function, balance, and flexibility in subjects with Parkinson's disease, J. Res. Rehabil. Sci. 9 (2013) 39–47.
[52] A. Kheirandish, S. Hosseinian, E. Kheirandish, S. Ahmadi, Effectiveness of laughter yoga on stress (subscales of stress the frustration and aggressiveness) and depression patients with multiple sclerosis (MS), Indian J. Fund. Appl. Life Sci 5 (2015) 1483–1492. http://www.cibtech.org/sp.ed/jls/2015/04/jls.htm.
[53] S.H. Kim, Y.H. Kim, H.J. Kim, Laughter and stress relief in cancer patients: a pilot study, Evid. Based Complement, Alternative Med. (2015) 864739, https://doi.org/10.1155/2015/864739, 2015.
[54] S.H. Kim, J.R. Kook, M. Kwon, M.H. Son, S.D. Ahn, Y.H. Kim, The effects of laughter therapy on mood state and self-esteem in cancer patients undergoing radiation therapy: a randomized controlled trial, J. Alternative Compl. Med. 21 (2015) 217–222, https://doi.org/10.1089/acm.2014.0152.
[55] H. Kimata, Reduction of plasma levels of neurotrophins by laughter in patients with atopic dermatitis, Pediatr. Asthma Allergy Immunol. 17 (2004) 131–135, https://doi.org/10.1089/0883187041269869.
[56] H. Kimata, Reduction of allergen-specific IgE production by laughter, Eur. J. Clin. Invest. 34 (2004) 76–77, https://doi.org/10.1111/j.1365-2362.2004.01294.x.
[57] H. Kimata, Short-term improvement of erectile dysfunction by viewing humorous films in patients with atopic dermatitis, J. Sex. Med. 5 (2008) 2107–2110, https://doi.org/10.1111/j.1743-6109.2007.00767.x.
[58] H. Kimata, Modulation of fecal polyamines by viewing humorous films in patients with atopic dermatitis, Eur. J. Gastroenterol. Hepatol. 22 (2010) 724–728, https://doi.org/10.1097/MEG.0b013e32832e09f1.
[59] A. Kumar, S. Patra, Laughter therapy decreases depression among senior citizens residing in old age homes, Intervent. Gynecol. Women's Healthcare 2 (2018) 187–188, https://doi.org/10.32474/IGWHC.2018.02.000143.
[60] K.R. Lebowitz, S. Suh, P.T. Diaz, C.F. Emery, Effects of humor and laughter on psychological functioning, quality of life, health status, and pulmonary functioning among patients with chronic obstructive pulmonary disease: a preliminary investigation, Heart Lung 40 (2011) 310–319, https://doi.org/10.1016/j.hrtlng.2010.07.010.
[61] Y.J. Lee, M.A. Kim, H.J. Park, Effects of a laughter programme with entrainment music on stress, depression, and health-related quality of life among gynaecological cancer patients, Complement, Ther. Clin. Pract. 39 (2020) 101118, https://doi.org/10.1016/j.ctcp.2020.101118.
[62] A. Memarian, A. Sanatkaran, S.M. Bahari, The effect of laughter yoga exercises on anxiety and sleep quality in patients suffering from Parkinson's disease, Biomed. Res. Ther. 4 (2017) 1463–1479, https://doi.org/10.15419/bmrat.v4i07.200.
[63] T. Morishima, I. Miyashiro, N. Inoue, M. Kitasaka, T. Akazawa, A. Higeno, et al., Effects of laughter therapy on quality of life in patients with cancer: an open-label, randomized controlled trial, PLoS One 14 (6) (2019), e0219065, https://doi.org/10.1371/journal.pone.0219065.
[64] C.S. Moura, R. Li, S. Lawrie, A. Bar-Or, A.E. Clarke, D. Da Costa, et al., Humor in systemic lupus erythematosus, Eur. J. Rheumatol. 2 (2015) 5–9, https://doi.org/10.5152/eurjrheumatol.2015.0070.
[65] J.L. Nelson, The Efficacy of Laughter-Therapy for Supplementing Conventional Multiple Sclerosis Support Group Activities [Doctoral dissertation], Grand Canyon University, 2017.
[66] N. Newman, S. Kogan, M. Stavsky, S. Pintov, Y. Lior, The impact of medical clowns exposure over postoperative pain and anxiety in children and caregivers: an Israeli experience, Pediatr. Rep. 11 (3) (2019) 8165, https://doi.org/10.4081/pr.2019.8165.
[67] M.N. Nia, S. Mohajer, M. Ghahramanzadeh, S.R. Mazlom, Effect of laughter yoga on mental well-being in cancer patients undergoing chemotherapy, Evid. Based Care J. 9 (2019) 7–14, https://doi.org/10.22038/ebcj.2019.39928.2050.
[68] Z. Özer, S. Ateş, Effects of laughter yoga on hemodialysis patients' plasma-beta endorphin levels, pain levels and sleep quality: a randomized controlled trial, Complement, Ther. Clin. Pract. 43 (2021) 101382, https://doi.org/10.1016/j.ctcp.2021.101382.
[69] S. Park, Y. Lee, H.H. Chung, S. Choi-Kwon, Effects of a laughter therapy on depression, anxiety, fatigue and quality of sleep in gastrointestinal cancer patients post-treatment: a randomized controlled trial, J. Korean Biol. Nurs. Sci. 21 (2019) 188–198, https://doi.org/10.7586/jkbns.2019.21.3.188.
[70] M. Rad, F. Borzoee, S. Shahidsales, Y. Tabarraie, F. Varshoee-Tabrizi, The effects of humor therapy on the fatigue in breast cancer patients undergoing external radiotherapy, J. Babol Univ. Med. Sci. 16 (2015) 45-52.
[71] J. Rotton, M. Shats, Effects of state humor, expectancies, and choice on postsurgical mood and self-medication: a field experiment, J. Appl. Soc. Psychol. 26 (1996) 1775–1794, https://doi.org/10.1111/j.1559-1816.1996.tb00097.x.
[72] A. Rudnick, P.M. Kohn, K.R. Edwards, D. Podnar, S. Caird, R. Martin, Humour-related interventions for people with mental illness: a randomized controlled pilot study, Community Ment. Health J. 50 (2014) 737–742, https://doi.org/10.1007/s10597-013-9685-4.
[73] S. Sahai-Srivastava, A. Joyce, C.C. Christie, C. Ugurlu, C. Manh, H. Kimblin Licht, Pilot study of laughter yoga therapy in treatment of chronic migraine, Headache 54 (S1) (2014) 30.
[74] S. Sarıtaş, H. Genç, Ş. Okutan, R. İnci, A. Özdemir, G. Kizilkaya, The effect of comedy films on postoperative pain and anxiety in surgical oncology patients, Complement, Med. Res. 26 (2019) 231–239, https://doi.org/10.1159/000497234.
[75] M.A. Sayed, S.V. Gandham, Effectiveness of laughter therapy on the levels of anxiety and depression among inmates residing at an old age institution: an interventional research, Int. J. Sci. Res. 7 (2018) 57–60, https://doi.org/10.36106/ijsr.

[76] M. Shahidi, A. Mojtahed, A. Modabbernia, M. Mojtahed, A. Shafiabady, A. Delavar, et al., Laughter yoga versus group exercise program in elderly depressed women: a randomized controlled trial, Int. J. Geriatr. Psychiatr. 26 (2011) 322–327, https://doi.org/10.1002/gps.2545.
[77] S.I. Shattla, S.M. Mabrouk, G.A. Abed, Effectiveness of laughter yoga therapy on job burnout syndromes among psychiatric nurses, Int. J. Nurs. 6 (2019) 33–47, https://doi.org/10.15640/ijn.v6n1a5.
[78] R. Spencer, V. Alexander, J. Eickhoff, K. Woo, E. Costanzo, N. Marx, et al., A digital media attention diversion improves mood and fear in patients receiving chemotherapy for recurrent gynecologic malignancies: results of a randomized trial, Int. J. Gynecol. Cancer 30 (2020) 525–532, https://doi.org/10.1136/ijgc-2019-001185.
[79] T. Tavakoli, N. Davoodi, T.S. Jafar Tabatabaee, Z. Rostami, H. Mollaei, F. Salmani, et al., Comparison of laughter yoga and anti-anxiety medication on anxiety and gastrointestinal symptoms of patients with irritable bowel syndrome, Middle East, J. Dig. Dis. 11 (2019) 211–217, https://doi.org/10.15171/mejdd.2019.151.
[80] P. Walter Jaisingh, S. Vijayalakshmi, R. Vijayaraghavan, Effectiveness of laughter therapy versus humour therapy on blood glucose level among individuals diagnosed with type 2 diabetes mellitus, Int. J. Res. Ayurveda Pharm. 10 (2019) 67-71, https://doi.org/10.7897/2277-4343.1005107.
[81] J.P. Ioannidis, S.J. Evans, P.C. Gøtzsche, R.T. O'Neill, D.G. Altman, K. Schulz, et al., Better reporting of harms in randomized trials: an extension of the CONSORT statement, Ann. Intern. Med. 141 (2004) 781–788, https://doi.org/10.7326/0003-4819-141-10-200411160-00009.
[82] M. McCreaddie, S. Wiggins, The purpose and function of humour in health, health care and nursing: a narrative review, J. Adv. Nurs. 61 (2008) 584–595, https://doi.org/10.1111/j.1365-2648.2007.04548.x.
[83] R.A. Martin, Humor, laughter, and physical health: methodological issues and research findings, Psychol. Bull. 127 (2001) 504–519, https://doi.org/10.1037/0033-2909.127.4.504.
[84] R.A. Martin, Sense of humor and physical health: theoretical issues, recent findings, and future directions, Humor 17 (2004) 1–19, https://doi.org/10.1515/humr.2004.005.
[85] E. Prochazkova, M.E. Kret, Connecting minds and sharing emotions through mimicry: a neurocognitive model of emotional contagion, Neurosci. Biobehav. Rev. 80 (2017) 99–114, https://doi.org/10.1016/j.neubiorev.2017.05.013.
[86] P.C. Gøtzsche, Why we need a broad perspective on meta-analysis. It may be crucially important for patients, BMJ 321 (2000) 585–586, https://doi.org/10.1136/bmj.321.7261.585.
[87] M. Sampson, N.J. Barrowman, D. Moher, T.P. Klassen, B. Pham, R. Platt, et al., Should meta-analysts search Embase in addition to Medline? J. Clin. Epidemiol. 56 (2003) 943–955, https://doi.org/10.1016/s0895-4356(03)00110-0.
[88] J.A. López-López, F. Marín-Martínez, J. Sánchez-Meca, W. Van den Noortgate, W. Viechtbauer, Estimation of the predictive power of the model in mixed-effects meta-regression: a simulation study, Br. J. Math. Stat. Psychol. 67 (2014) 30–48, https://doi.org/10.1111/bmsp.12002.
[89] S. Hempel, J.N. Miles, M.J. Booth, Z. Wang, S.C. Morton, P.G. Shekelle, Risk of bias: a simulation study of power to detect study-level moderator effects in meta-analysis, Syst. Rev. 2 (2013) 107, https://doi.org/10.1186/2046-4053-2-107.
[90] L.V. Hedges, T.D. Pigott, The power of statistical tests for moderators in meta-analysis, Psychol. Methods 9 (2004) 426–445, https://doi.org/10.1037/1082-989X.9.4.426.
[91] S. Barkowski, D. Schwartze, B. Strauss, G.M. Burlingame, J. Rosendahl, Efficacy of group psychotherapy for anxiety disorders: a systematic review and meta-analysis, Psychother. Res. 30 (2020) 965–982, https://doi.org/10.1080/10503307.2020.1729440.
[92] S.A. Baldwin, D.M. Murray, W.R. Shadish, Empirically supported treatments or type I errors? Problems with the analysis of data from group-administered treatments, J. Consult. Clin. Psychol. 73 (2005) 924–935, https://doi.org/10.1037/0022-006X.73.5.924.