




Cognitive Behavioral Therapy for People with Chronic Obstructive Pulmonary Disease: Rapid Review

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Abstract: Cognitive behavioral therapy (CBT) is increasingly recommended in the management of people living with chronic obstructive pulmonary disease (COPD). This rapid review presents the evidence base for CBT for people with COPD and describes 1) the nature of CBT interventions and comparators in controlled trials (high or low resource intensity); and 2) factors influencing intervention effects on health outcomes (anxiety, depression, breathlessness, quality of life and exercise capacity). Primary studies reporting CBT interventions in adults with COPD were identified with data extracted by a single reviewer (20% of studies checked for data accuracy). Studies were synthesized descriptively with meta-analyses (random effects models) of controlled trials undertaken to report mean standardized effect sizes (95% CI) for health outcomes. Random effects meta-regression models explored whether CBT target, intervention dosage, intensity, facilitator profession, delivery mode, clinically significant anxiety/depression, trial design/quality and sample size predicted effect size. The search identified 33 primary studies published between 1996 and 2019 (controlled trials n=24, single group cohort n=6, case exemplars n=2, phenomenological n=1). Controlled trials frequently compared high-intensity CBT interventions against enhanced/usual care (n=12) or high-intensity CBT interventions against high-intensity comparators (n=11). When all controlled studies were included, small, significant improvements favoring CBT were evident across all health outcomes (SMD ranged from -0.27 to 0.35, p<0.05). When intensity dyads were considered, significant improvements were evident only when high-intensity CBT interventions were compared to enhanced usual care/usual care (SMDs ranged from -0.45 to 0.54, p <0.05). No other variable consistently predicted intervention effect sizes across all health outcomes. Overall, the evidence base supports the use of CBT for a range of health outcomes in people with COPD. Consistent benefits were evident when high-resource-intensive CBT interventions were compared to usual care. Low-resource-intensity CBT warrants further investigation in settings where cost of comprehensive care is prohibitive.

Keywords: cognitive behavioral therapy, chronic obstructive pulmonary disease, rapid review

Introduction

Cognitive behavioral therapy (CBT) is the broad term used to describe a range of therapies arising from cognitive behavioral models of anxiety disorders.¹ Within these therapeutic approaches, the person and therapist work collaboratively to 1) identify maladaptive thoughts, beliefs and impact of current symptoms or feelings; 2) develop skills to identify, monitor and counteract problematic cognitions related

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to the specific symptom; and 3) build a repertoire of coping skills appropriate to the target thoughts, beliefs, and behaviors.¹ In adults with generalized anxiety, panic disorders, and depression, high level evidence underpins recommendations within clinical guidelines for the use of CBT as part of management,^{1,2} where CBT interventions should 1) be based on treatment manuals used in clinical trials; 2) be delivered by trained and competent practitioners; and 3) usually consist of 12–15 weekly sessions (each lasting an hour) with duration of therapy adjusted pending responsiveness.¹

For generalized anxiety and depressive disorders, a stepped approach to management is recommended where the least intrusive and most effective intervention (non-pharmacological with or without pharmacotherapy) is devised in collaboration with the patient based on severity of the disorder, previous response to management, availability and patient preference.^{1,3} In general, stepped approaches move from least intrusive options (education about the disorder and active monitoring) to low-resource-intensive interventions (individual self-help such as written or electronic self-help materials (bibliotherapy) with no or minimal therapist involvement and psychoeducational groups). Where there is minimal response or symptoms are more severe, high-resource-intensive interventions are considered (therapist facilitated individual CBT, applied relaxation, psychodynamic therapy, non-directive therapies and counselling, or more specialized and complex psychological treatments) with or without pharmacotherapy.^{1,3}

In people living with COPD, anxiety and depression are comorbidities associated with poorer prognosis.⁴ In this population, a range of systematic reviews have been published specific to the impact of psychological interventions on psychological (anxiety, depression, quality of life)^{5–10} or psychological and physical health outcomes.^{11,12} Pending the intent, eligibility criteria, and publication dates, a number of studies denoted as including a CBT intervention recur throughout these reviews.^{13–22} These studies delivered CBT as either the sole intervention^{1,9,20–22,81} or in combination with pulmonary rehabilitation^{13,15,16} with comparators ranging from usual care^{13,18–20,22} to other active high resource interventions.^{13–17,21} Of the reviews that include meta-analysis or subgroup analysis of randomized controlled trials (RCTs) specific to CBT interventions, findings are inconsistent, concluding both in favor of CBT against comparators for psychological outcomes (depressive symptoms: $n=12$;⁶ $n=10$;¹² anxiety symptoms $n=3$,¹¹ $n=3$ ⁹) or alternatively reporting no significant difference between CBT intervention and comparators ($n=7$;⁷ $n=4$;⁸ $n=11$ ¹⁰). Consequently,

clinical practice guidelines for management of COPD offer a range of recommendations concerning the role or potential role of CBT for anxiety, depression, breathlessness, quality of life, or functional exercise capacity.^{4,23}

Unlike the stepped approach recommended for management of anxiety and depression in the general population, CBT interventions for people with COPD are rarely classified in terms of resource intensity of the intervention. It is also unclear whether the inclusion of CBT within high resource interventions such as pulmonary rehabilitation, produces a greater health benefit compared to the CBT alone, other high-resource interventions, low-resource interventions, or usual care.

In this rapid review we were interested to describe the evidence base of primary studies, irrespective of research approach, concerning use of CBT in people living with COPD. For controlled trials we aimed to:

1. describe the nature of CBT intervention and comparators (low vs high intensity) and
2. explore factors influencing intervention effect (effect sizes) for health outcome domains of anxiety, depression, breathlessness, quality of life, and exercise capacity.

For trials comparing CBT with usual care, we hypothesized that effect sizes would vary as a function of intervention: comparator intensity, with the largest between-group effects sizes likely to be present with the greatest contrasts in intensity between intervention and comparator (eg, high-intensity CBT interventions vs usual care comparators) and the smallest effect sizes between CBT interventions and comparators of similar intensity (eg, high-intensity CBT vs high-intensity comparator).

Methods

This rapid review used a range of approaches to identify primary studies of CBT interventions in people with COPD. We reviewed 1) articles excluded as CBT interventions as part of a prior systematic review of health counselling interventions for people with COPD (PROSPERO 2016: CRD42016046415²⁴); 2) prior systematic/critical reviews concerning psychological interventions for people living with COPD to identify studies where the intervention was described as CBT; 3) citations of studies identified as including a CBT intervention to identify more recent publications. In addition, we undertook a limited search of publicly available databases (October 2019, Medline,

Medline: epub ahead of print and Scopus; title and abstract including the terms CBT and COPD). Reference lists of included studies and systematic reviews identified during the search were reviewed to identify additional potentially relevant studies.

Studies were eligible for inclusion in this review if: 1) the original primary study was available as full text and published in English; 2) participants included adults with a physician or spirometric diagnosis of COPD, irrespective of disease severity or comorbidities; 3) the term “cognitive behavioural therapy” was used when describing the intervention either as a component of a multifaceted intervention or as a single stand-alone intervention irrespective of mode of delivery (individual vs group, home vs health setting, face to face, phone or electronic delivery). All study designs (experimental, observational or qualitative frameworks) were eligible for inclusion.

Studies were excluded where: 1) participants exclusively had a primary pulmonary condition other than COPD (asthma, interstitial lung disease, idiopathic fibrosis); 2) COPD data were not reported separately to other chronic conditions; 3) studies concerned additional or sub-analysis of primary study data (to avoid data duplication); and 4) records were conference abstracts, study protocols, commentaries or narrative reviews (reviews, editorials, letters).

Full text versions of each eligible study were screened by a single reviewer (MTW) against a priori eligibility criteria. Where studies could not be confidently included/excluded, independent review and advice was sought (CP, KNJ) and/or authors contacted for clarification. Where full text papers reported secondary analysis of an RCT the original parent study was sought. A data extraction template was developed prospectively, data were extracted by a single reviewer (MTW) with 20% of eligible studies, randomly checked for data accuracy (CP).

Data extracted from eligible studies included publication demographics (year of publication, country of data source, study design) and participants (group mean and standard deviation (SD) for age, sex ratio, presence and nature of threshold criterion for anxiety or depression, sample size included in analysis). Details of the CBT intervention and comparator included CBT target/intent, sole or part of a complex intervention (exercise/pulmonary rehabilitation, health education), format (individual, group, face-to-face, telephone, computer-based), supporting resources (phone, print/audio materials); nature of the comparator (eg usual care, wait-listed, social group control, education), number of sessions (maximum possible), attendance,

duration of sessions (minutes), duration of intervention program (weeks), professional discipline of facilitator [Objective 1].

The primary health outcomes of interest in this review spanned five health domains: anxiety, depression, breathlessness, quality of life and exercise capacity. Where authors reported both a total and subdomain scores for an outcome measure, the subdomain score was used in preference to the total score where appropriate (eg Hospital Anxiety and Depression scale (HADS)– subdomain scores for HADS-Anxiety or HADS-Depression used rather than HADS-total score). Wherever possible, the ATS guideline for dyspnea was used to guide domain choice for breathlessness outcomes.²⁵ Where a breathlessness instrument assessed sensory-perceptual (intensity or quality) or affective distress (discomfort), the outcome was allocated to the breathlessness domain (eg, Chronic Respiratory Questionnaire – Dyspnea subscore,²⁵ Interpretation of Breathing Problems Questionnaire²⁶). Where the breathlessness instrument combined breathlessness with other symptoms (cough, wheeze, secretions) and assessed impact on functional performance/activity or health-related quality of life, the outcome was allocated to the quality-of-life domain (eg, COPD Assessment Test (CAT),²⁵ St George Respiratory Questionnaire,²⁵ COPD Self-Efficacy scale²⁷). Quality-of-life subdomain scores related to mental wellbeing (SF-36 Mental Component Score (MCS), CRQ-Mastery) and physical (SF-36 Physical Component Score (PCS), CRQ-Fatigue) health were used where available. Otherwise, total quality-of-life scores were used.

Where reported, data were extracted at baseline and after intervention with post-intervention follow-up assessments categorized as immediate (within 1 week to 1 month), short-term (2 to 6 months) and longer-term (>6 to 12 months). The analysis reported in this review considers only immediate post intervention outcomes. Where studies reported two time points within the post-intervention follow-up assessment categories, we chose the assessment at the most distant follow-up point. Within- and between-group differences (effect sizes) for primary outcomes – where reported – were extracted from the study or calculated if sufficient data were reported. Where outcome data were presented predominately in figures, online software (Digiplot²⁸) was used.

Data Management and Synthesis

Descriptive summaries of data extracted from each study were created. CBT interventions (and comparators) were

categorized into one of three categories; 1) high-intensity; 2) low-intensity; and 3) usual care (UC) or enhanced usual care (EUC). There is no universally agreed definition for low- and high-intensity psychological interventions.¹ The general principle of these categorizations concern resource implications rather than time required by an individual to complete the intervention. In this review we used the following definitions for both the active CBT intervention and comparators (where appropriate):

Low intensity = minimal (or no) involvement of a health professional. Where a health professional was involved these reflected psychological disciplines or other health professional discipline trained in the provision of CBT. These self-help interventions could include individual written or electronic self-help materials (bibliotherapy) and psychoeducational groups. Unless otherwise reported, it was assumed that low-intensity interventions (or comparators) represented additional activities provided on a background of usual care.

High intensity = majority of sessions (individual or group) were facilitated by a health professional from a psychological discipline or other health professional discipline trained in the provision of CBT. The CBT intervention included a direct intent to target and facilitate change in an individual's maladaptive cognitions/beliefs and related behaviors as a key focus or component within the CBT intervention. Unless otherwise reported, it was assumed that high-intensity interventions (or comparators) represented additional activities provided on a background of usual care.

Usual care or enhanced usual care = In trial comparator groups consisting of usual care or enhanced usual care, we acknowledged that all interactions with health-care professionals or services have the potential to modify, maintain or extinguish an individual's beliefs and related behaviors but there was no reported intentional strategy described to facilitate this change. Therefore, UC was defined as the health care expected or recommended for people living with COPD (with or without reporting of participation in pulmonary rehabilitation and pharmacotherapies and including wait list control). In contrast, EUC included reporting of activities specifically designed for the study to balance researcher contact with participants in the active intervention. These could include scheduling of appointments or phone calls for additional health or wellbeing assessments.

Meta-analysis was undertaken for controlled clinical trials (CCT/RCTs) that reported sufficient data to calculate

effect sizes within each outcome domain (anxiety, depression, breathlessness, quality of life and exercise capacity). Controlled studies were appraised for methodological quality using the Physiotherapy Evidence Database scale for RCTs (11 items, score range 0 to 10 with higher scores indicating higher quality).^{29,30} Where data were not reported or unable to be calculated, the study was excluded from further analysis (ie, missing data were not imputed or estimated). When the control/comparator group was used for multiple interventions, the sample size of the control/comparator group was divided by two to avoid double counting. Meta-analyses using random effects model were performed using the `admetan` function in STATA v.15.1 (StataCorp, College Station, TX, USA)³¹ and displayed as Forest plots. Heterogeneity was assessed using I^2 index and the Q statistic. Heterogeneity for I^2 was interpreted as; 0–40% might not be important, 30–60% may represent moderate heterogeneity, 50–90% may represent substantial heterogeneity, 75–100% considerable heterogeneity.³²

To explore factors influencing intervention effect (effect sizes) for health outcomes (Objective 2), random-effects meta-regression models estimated effect sizes for specific predictor variables (moderators) using the `MetaReg` command in STATA.³¹ In selecting our predictor variables, we were guided by prior meta-regression of CBT interventions specific to people with COPD¹² or older adults.^{33,34} Given the variability in the way CBT has been delivered, our primary interest was to explore predictors of effect size reflecting resource intensity dyads, and protocol components of both the CBT intervention and comparator, rather than participant characteristics.^{12,33,34} Models were run separately for each outcome category, unless the number of studies was too low (<10).³² Analyses were done separately for quality-of-life mental wellbeing and physical domains, with overall scores being used in both analyses for studies for which subdomain scores were not available. Separate models were estimated for the following list of predictor variables, which were defined a priori: intervention dosage in absolute terms (number of intervention sessions) and relative to comparator (ratio of intervention sessions/comparison sessions); CBT proportional dosage (CBT sessions as proportion of total intervention sessions); intensity of comparison (low or high with UC/EUC as reference group), facilitator (psychology professional only or not), inclusion threshold for anxiety/depression (yes, no), CBT mode (individual + group or group with individual as reference group), sample size included in analysis (continuous and as categories: 31–60, or ≥ 60 with ≤ 30 as reference

group), CBT intervention target (specific psychological focus (SPF) on symptoms (anxiety, depression, breathlessness) or self-management (SM) which included anxiety, depression, symptoms as part of a broader cognitive/behavior skill set). Two additional predictors were included following appraisal of CCT/RCT quality; study design (CCT with RCT as comparator) and quality appraisal score (PEDro score as a continuous variable). Alpha was set at 0.05.

Results

Following the search and screening strategy, 33 studies published as full text between 1996 and 2019 were identified which reported outcomes for a CBT intervention for people with COPD. Across all included studies there were 3,215 participants (61% male) with a mean age 67 years (range 40 to 86). Details of study characteristics are presented in Supplemental materials [Table S1](#). The majority of studies were controlled trials (ie, CCT or RCT $n=24$).^{13–22,35–48} In addition, there were six single group cohort designs,^{49–54} two papers reported case exemplars^{55,56} and one a phenomenological study.⁵⁷ Eight studies were not included as they reported the sub-analysis of a parent study.^{58–65}

The majority of studies exclusively recruited people with COPD (78.7%, $n=26$). With the exception of Blumenthal et al⁴⁸ where 42% of participants had COPD, in the remaining seven studies, at least half the sample analyzed were categorized as COPD (Cully et al (75%),⁴¹ Pumar et al (75%),³⁸ Cully et al (74%),⁵² Cully et al (66%),⁵⁶ Jonker et al (51%),⁴⁵ Malpass et al (50%)⁵⁷). In studies reporting threshold criteria as an eligibility requirement ($n=15$, 45%), these ranged between including people with at least mild-to-moderate anxiety or depression (HADS-A ≥ 8 , Beck Anxiety Inventory (BAI) scores 10–18, Beck Depression Inventory (BDI) ≥ 13) or clinically significant symptoms (State-Trait Anxiety Inventory STAI-STAIT ≥ 39 , Patient Health Questionnaire PHQ-9 ≥ 10). The majority of studies reported an outcome for anxiety ($n=30$, 91%, commonest instrument: HADS-A $n=7$ studies with one study reporting HADS-Total), depression ($n=29$, 88%, commonest instruments: HADS-D $n=8$ studies) and health-related quality of life ($n=27$, 82%, commonest instrument: SGRQ $n=8$ studies). Outcome measures for breathlessness and exercise capacity were reported by just over a third of the studies (both $n=12$ 36%) with the CRQ-dyspnea sub domain scores (5 studies) and 6-minute walk distance (9 studies) the most frequent assessments reported.

Details of CBT interventions and comparators for experimental study designs is presented in Supplemental materials [Table S2](#) (studies $n=30$; two studies included two interventions against a comparator; active comparator data sets $n=32$ ^{13,16}). Study quality scores ranged between 3 and 8 (mean 6 ± 1) with CCTs scoring consistently lower than RCTS (mean 3 ± 1 vs 6 ± 1) (details presented in Supplemental materials, [Table S3](#)). The majority of CBT interventions ($n=22$, 68%) had a specific psychological focus (anxiety, depression or symptom) with the remaining interventions including CBT as part of, or to facilitate chronic condition self-management. Interventions in eight studies provided 12 or more sessions of CBT in line with recommendations for generalized anxiety disorders (12–15 sessions¹), with 22 studies providing ≤ 10 sessions of CBT (which could potentially be defined as a brief CBT). While there was variation between studies, where reported, CBT interventions were more commonly provided by psychology professionals alone or in concert with other professionals (21 studies), to individuals rather than groups (19 vs 10 studies), with direct face-to-face contact rather than phone/telemedicine (24 vs 2 studies), weekly rather than less frequently (19 vs 9 studies) and for ≥ 60 minutes rather than shorter durations (19 vs 7 studies). CBT interventions were commonly delivered as the sole intervention (17 studies) or in combination with exercise/pulmonary rehabilitation with or without additional education (10 and 8 studies respectively).

Within CCT/RCTs, high-intensity CBT interventions predominated within active intervention groups (23/32 groups) with comparator groups reflecting a range of intensities (EUC/UC $n=12$, high-intensity $n=9$, low-intensity $n=3$). The most common comparator was EUC/UC (12 studies including two studies where pulmonary rehabilitation was available as part of UC^{19,43}) followed by exercise/pulmonary rehabilitation with or without additional education (6 and 2 studies respectively [Table S2](#)). For CCT/RCTs, it was more common to compare high-intensity CBT interventions against EUC/UC ($n=12$) and high-intensity interventions against high-intensity comparators ($n=11$). Single studies reflected comparisons of high-intensity interventions against low-intensity comparators, low-intensity interventions against low-intensity comparators or low-intensity interventions against EUC/UC ([Table S2](#)).

[Figure 1](#) presents meta-analyses outcomes for each health domain for the immediate post-intervention follow-up. In studies which included a threshold criterion for anxiety or depression ([Table S1](#) and [Table S2](#)), participants allocated to CBT intervention or comparator

groups did not differ significantly at baseline for anxiety/depression scores with the exception of Eiser et al³⁷ where, by design, the treatment group had significantly higher anxiety than the comparator group (HADS-A 12 ± 4 vs 7 ± 3 , $p < 0.01$). See sensitivity analysis for the impact of excluding Eiser et al³⁷ as one of the two CCTS's^{36,37} included within the original meta-analysis models.

Data for anxiety was available for 20 studies with two studies reporting two active interventions.^{13,16} While considerable heterogeneity existed across studies, overall, CBT interventions were associated with small, significant improvements in anxiety (SMD -0.25 , 95% confidence intervals -0.41 , -0.09 , $p = 0.002$, $I^2 = 70.5\%$). With respect

to intensity dyads (excluding categories where a single study was represented), significant improvements for anxiety were noted only when high-intensity CBT interventions were compared to EUC/UC (10 studies; SMD -0.25 , 95% CI -0.44 , -0.06 , $p = 0.011$, $I^2 = 62.9\%$).

A similar pattern was seen across all health outcomes. When all studies were included, overall small, significant improvements favoring CBT were evident (Depression $n = 18$ studies, SMD -0.27 , 95% CI -0.38 , -0.17 , $p < 0.0001$, $I^2 = 24.1\%$; Breathlessness $n = 7$ studies, SMD -0.24 , 95% CI -0.47 , 0.00 , $p = 0.045$, $I^2 = 70.7\%$; Quality of life–Mental Wellbeing $n = 16$ studies SMD 0.28 , 95% CI 0.15 , 0.42 , $p < 0.0001$, $I^2 = 44.8\%$; Quality of life–Physical

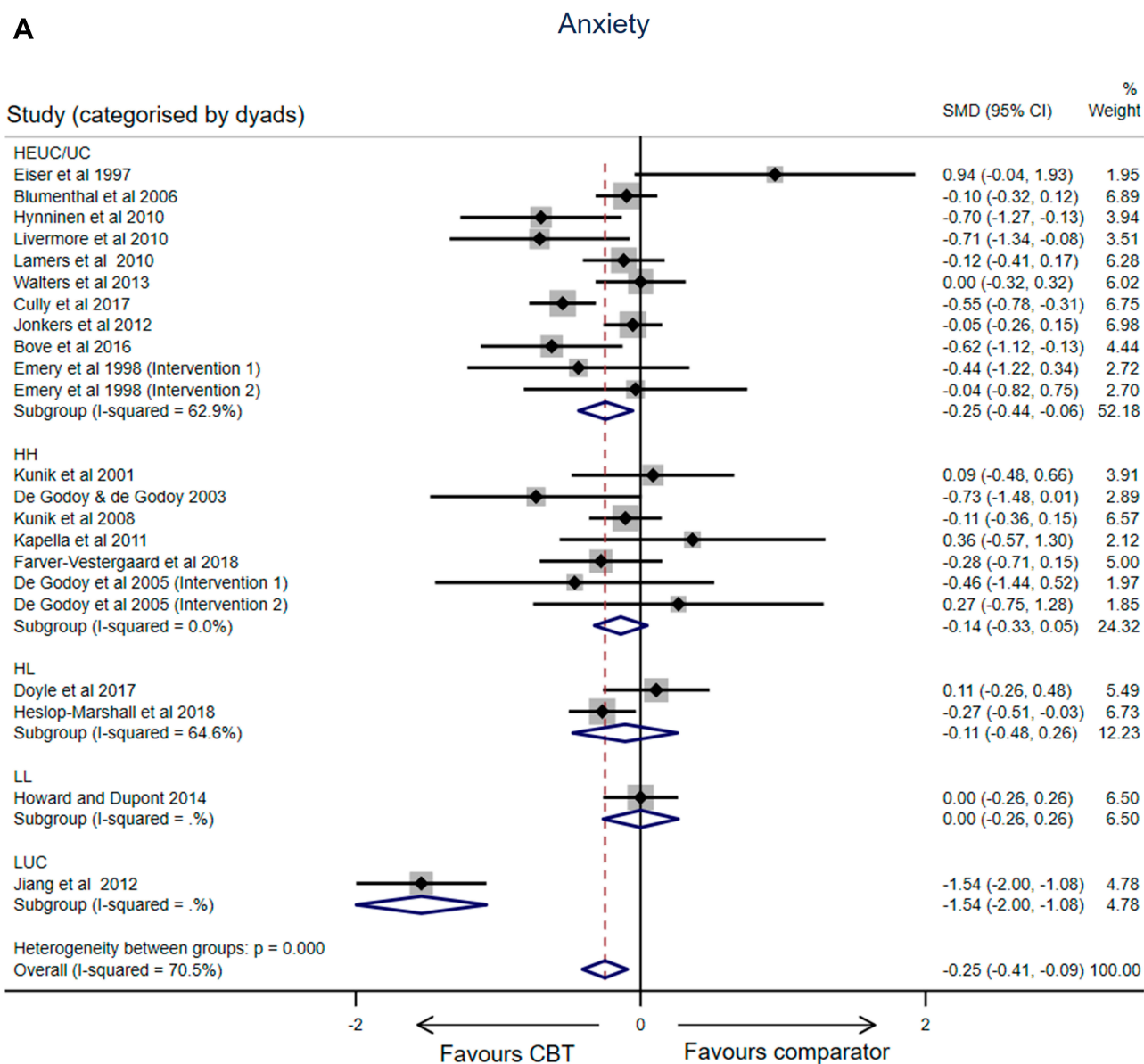


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B

Depression

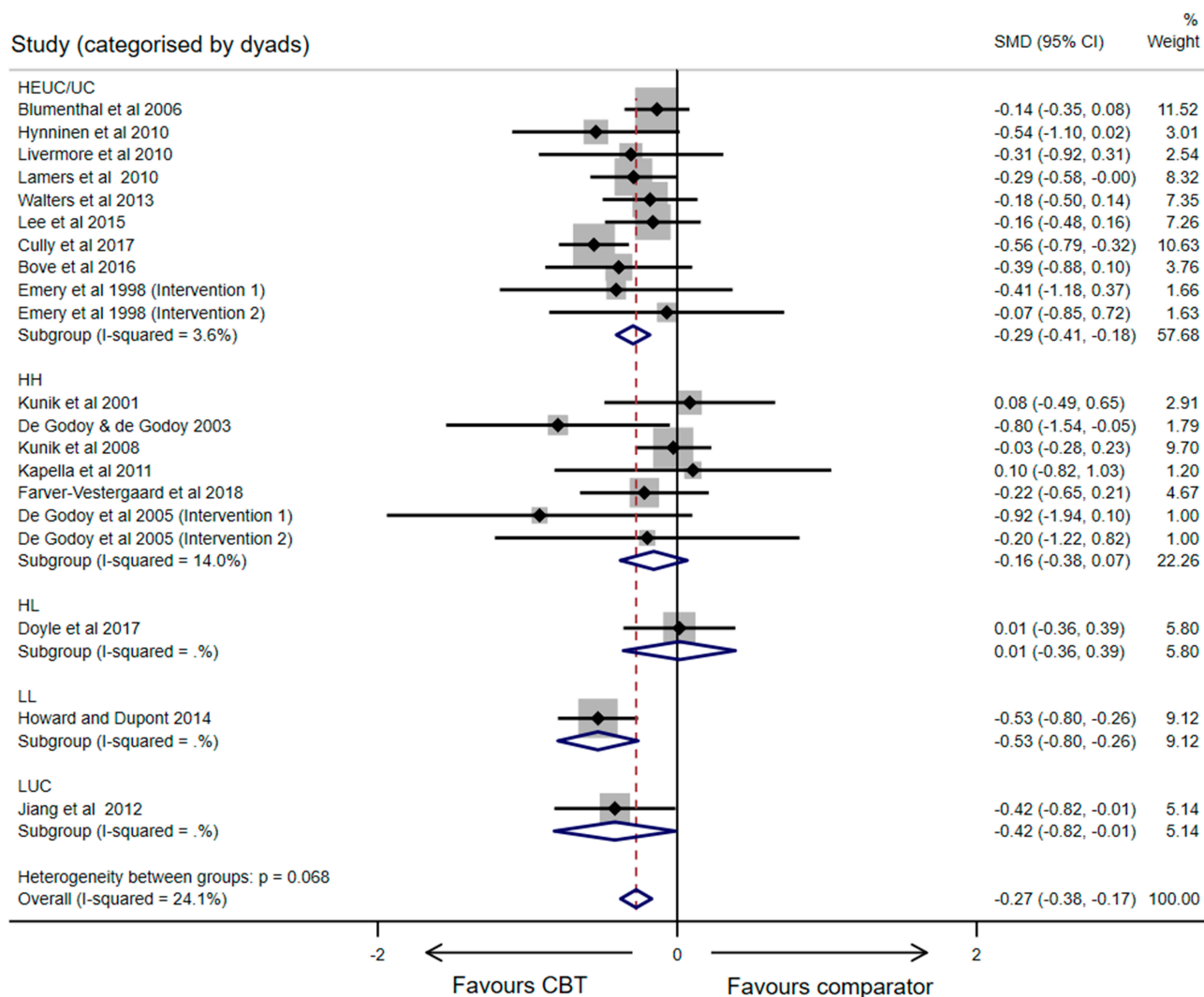


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n=17 studies SMD 0.35, 95% CI 0.02, 0.69, p=0.037, $I^2=91.6%$). Our conservative approach to avoid double counting (halving sample sizes where studies included more than a single active intervention) might explain the findings for exercise capacity which favored CBT but did not reach significance (n=7 studies SMD 0.16, 95% CI -0.02, 0.35, p=0.089, $I^2=0.0%$).

When intensity dyads were considered (and excluding categories where a single study was represented), significant improvements were evident only when high-intensity CBT interventions were compared to EUC/UC (Depression SMD -0.29, 95% CI -0.41, -0.18, p<0.0001, $I^2=3.6%$; Breathlessness SMD -0.45, 95% CI -0.86, -0.05, p=0.028, $I^2=77.7%$; Exercise capacity SMD

0.54, 95% CI 0.06, 1.03, p=0.028, $I^2=0.0%$; Quality of life-Mental Wellbeing SMD 0.40, 95% CI 0.20, 0.61, p=0.001, $I^2=57.0%$; Quality of life-Physical SMD 0.31, 95% CI 0.11, 0.51, p=0.002, $I^2=54.6%$).

Meta-Regression

Table 1 presents a summary of the findings from the meta-regression (not attempted for breathlessness or exercise capacity as <10 studies³²). With the exception of two variables, no other factors significantly predicted intervention effect. The ratio of intervention to comparator sessions was a significant predictor of intervention effect for Anxiety (-0.11, 95% CI -0.18, -0.04, p=0.005) and Quality of Life-Mental Wellbeing (0.11, 95% CI 0.04,

C

Dyspnea

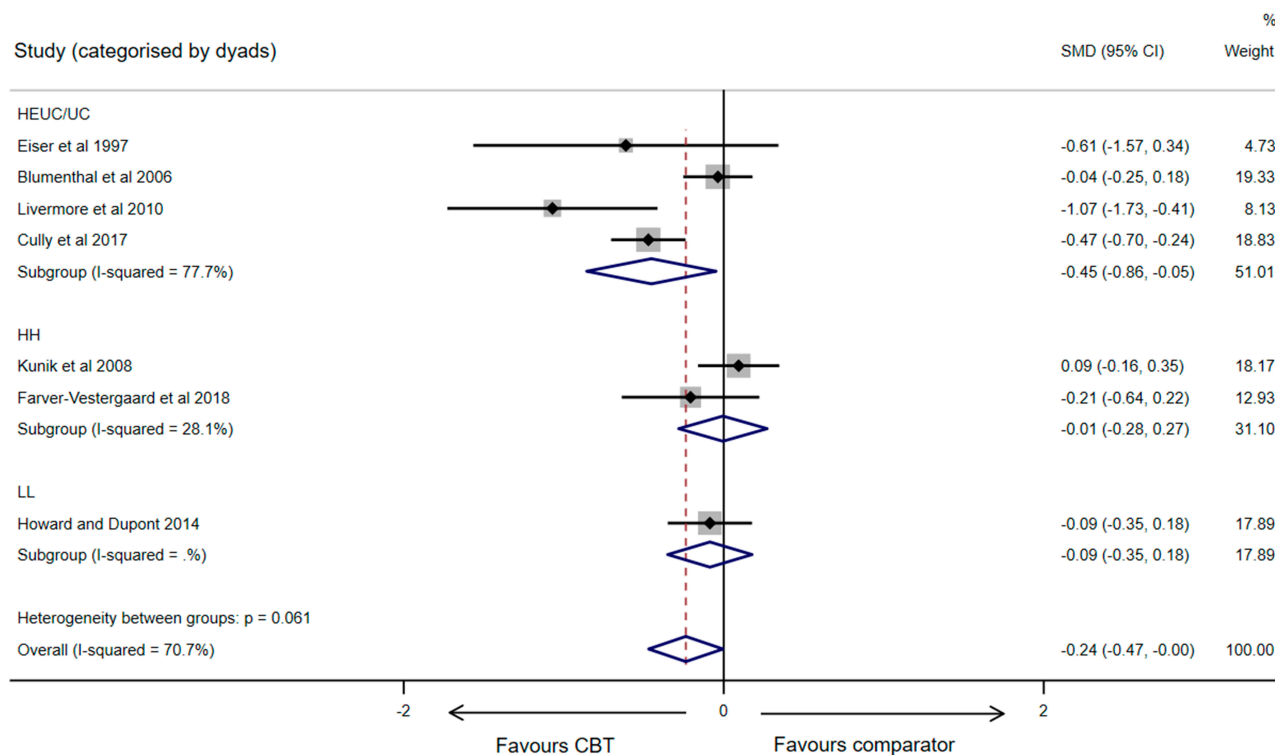


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0.19), $p=0.005$). For these two health domains, effect size and direction of effect were the same; stronger effects when the ratio of intervention to comparator sessions was higher. For Quality of Life–Physical, the intervention effect size was stronger for low-intensity comparators compared to EUC/UC (1.07, 95% CI 0.09, 2.06, $p=0.03$).

Sensitivity Analysis

Of the three CCTs included within the review, one³⁵ did not contribute data to meta-analysis/regression models. The two remaining CCTs reflected different resource dyads (high intensity resource vs high intensity resource³⁶ and high-intensity resource vs enhanced/usual care³⁷) with neither contributing data for Depression. Revised models were run for Anxiety and Breathlessness (excluding Eiser et al³⁷), and Exercise Capacity, Quality of life–Mental Wellbeing and Quality of life–Physical, (excluding both Eiser et al³⁷ and Williams et al³⁶).

When these CCTs were excluded, standardized mean differences (Effect size) and heterogeneity (I^2) were essentially unchanged across health outcomes (Dyad and Overall) (see [Table S4](#)). Significant differences

in between-group effects were no longer present for the high-intensity resource vs enhanced/usual care dyad for breathlessness (SMD -0.44 , 95% CI -0.89 , 0.02) or Exercise capacity (SMD 0.59 , 95% CI -0.02 , 1.20). The significant overall between-group effects (pooled) were no longer present for breathlessness (Overall SMD -0.22 , 95% CI -0.46 , 0.02) or Quality of Life–Physical (Overall SMD 0.33 , 95% CI -0.02 , 0.69). For the three health domains where CCTs contributed data, meta-regression indicated that compared to RCTs, CCTs did not significantly predict effect sizes ([Table 1](#)).

Discussion

The most recent GOLD guidelines⁴ propose that there is “... no evidence that anxiety and depression should be treated differently in the presence of COPD.” There is a consistent evidence base supporting the positive impact of CBT on anxiety and/or depressive symptoms in both people with generalized anxiety and depressive disorders, and people living with COPD. In this review, there were small significant intervention effects favoring CBT across CCT/RCTs for all five health domains. When compared to usual care, high-intensity

D

Exercise Capacity

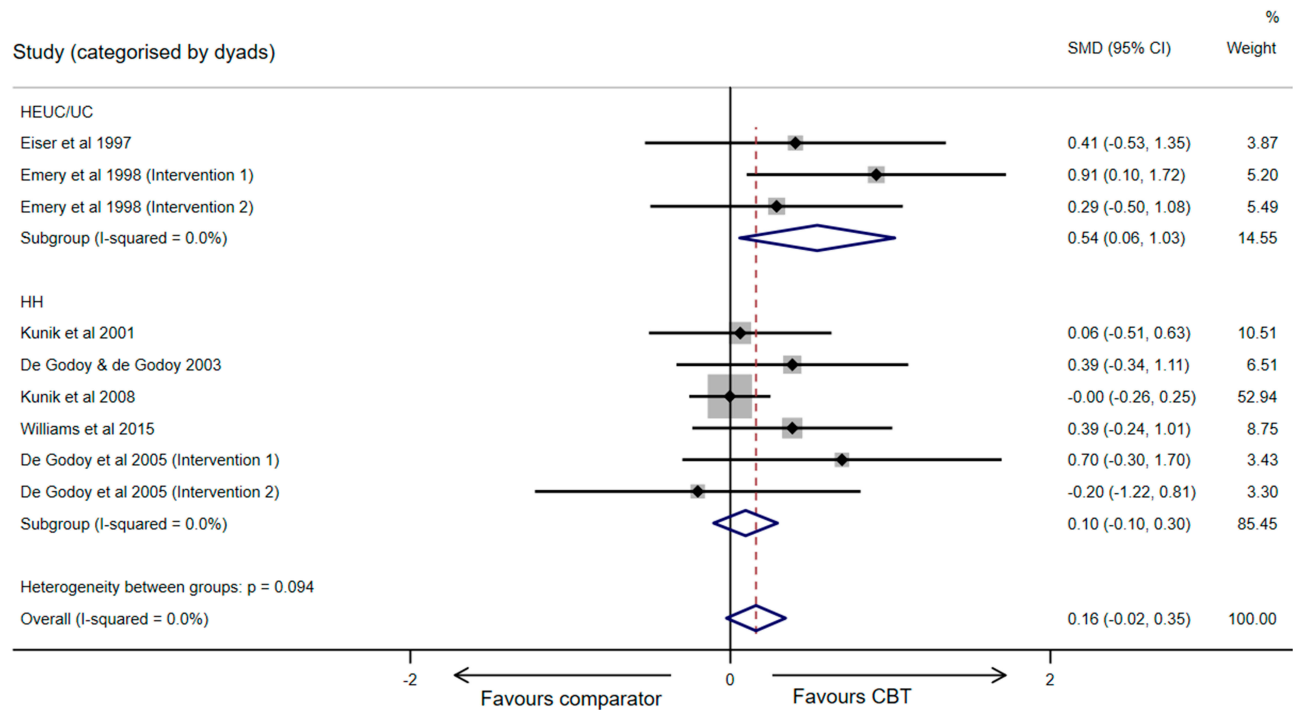


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CBT interventions consistently resulted in significant improvements in symptoms (anxiety, depression, breathlessness), quality of life and exercise capacity. However, when CBT interventions and comparators were of equally high resource intensity, there was less compelling evidence of benefit for CBT. Overall, there was negligible evidence that the specific focus of the CBT intervention, number of intervention sessions, facilitator profession, delivery mode, presence of co-morbid clinical anxiety/depression or sample size/study quality were associated with the effect sizes of health outcomes.

In our meta-analysis, heterogeneity varied across analyses for health outcomes where heterogeneity was considerable ($I^2=75-100\%$) for Quality of Life-Physical (91.6%, $n=17$ studies), substantial ($I^2=50-90\%$) for Anxiety (70.5% $n=20$ studies) and Dyspnea (70.7%, $n=7$ studies), moderate ($I^2=30-60\%$) for Quality of life-Mental Wellbeing (44.8%, $n=16$ studies) and may have been unimportant ($I^2=0-40\%$) for Depression (24.1% $n=18$ studies) or Exercise capacity (0.0%, $n=7$ studies). While noting that the I^2 does not inherently depend upon the number of studies included in the analysis, this metric will be influenced by the combination of specific studies, composition of outcome measures and grouping of

psychological interventions included in each analysis and hence will be “unique” to each analysis.

Consequently, compared to previous meta-analyses of similar health outcomes reported for CBT/psychological interventions in people with COPD, heterogeneity in our meta-analysis was similar to that reported for Anxiety (substantial heterogeneity $I^2: 74.1\%$, $n=13$ studies,¹² 80%, $n=4$ studies,⁸ 62%, $n=3$ studies⁹), Depression (unimportant heterogeneity $I^2: 10.1\%$, $n=12$ studies,¹² 10.1%, $n=7$ studies,⁷ 0.00, $n=6$ studies¹⁰) and Dyspnea (substantial heterogeneity $I^2=59.5\%$, $n=9$ studies¹²). Heterogeneity in our meta-analysis differed to that reported for Anxiety (moderate heterogeneity $I^2=34.5\%$, $n=7$ studies⁷), Depression (substantial heterogeneity $I^2=74\%$ $n=4$ studies⁸), Quality of Life ($I^2=56.3\%$, $n=16$ studies¹²) and Exercise capacity ($I^2=64.4\%$, $n=10$ studies¹²).

In line with current health service strategies to provide the greatest availability of psychological interventions to people living with generalized anxiety, panic or depressive disorders,^{1,3} we opted to explore CBT interventions and comparators categorized as low- or high-resource intensity. In prior systematic reviews of psychological interventions for people with COPD, where sub-group meta-analyses are reported, these consider intervention type (CBT, mind-body, self-management,^{7,12} inclusion of exercise training^{7,11} or

E

Quality of Life - Mental Wellbeing

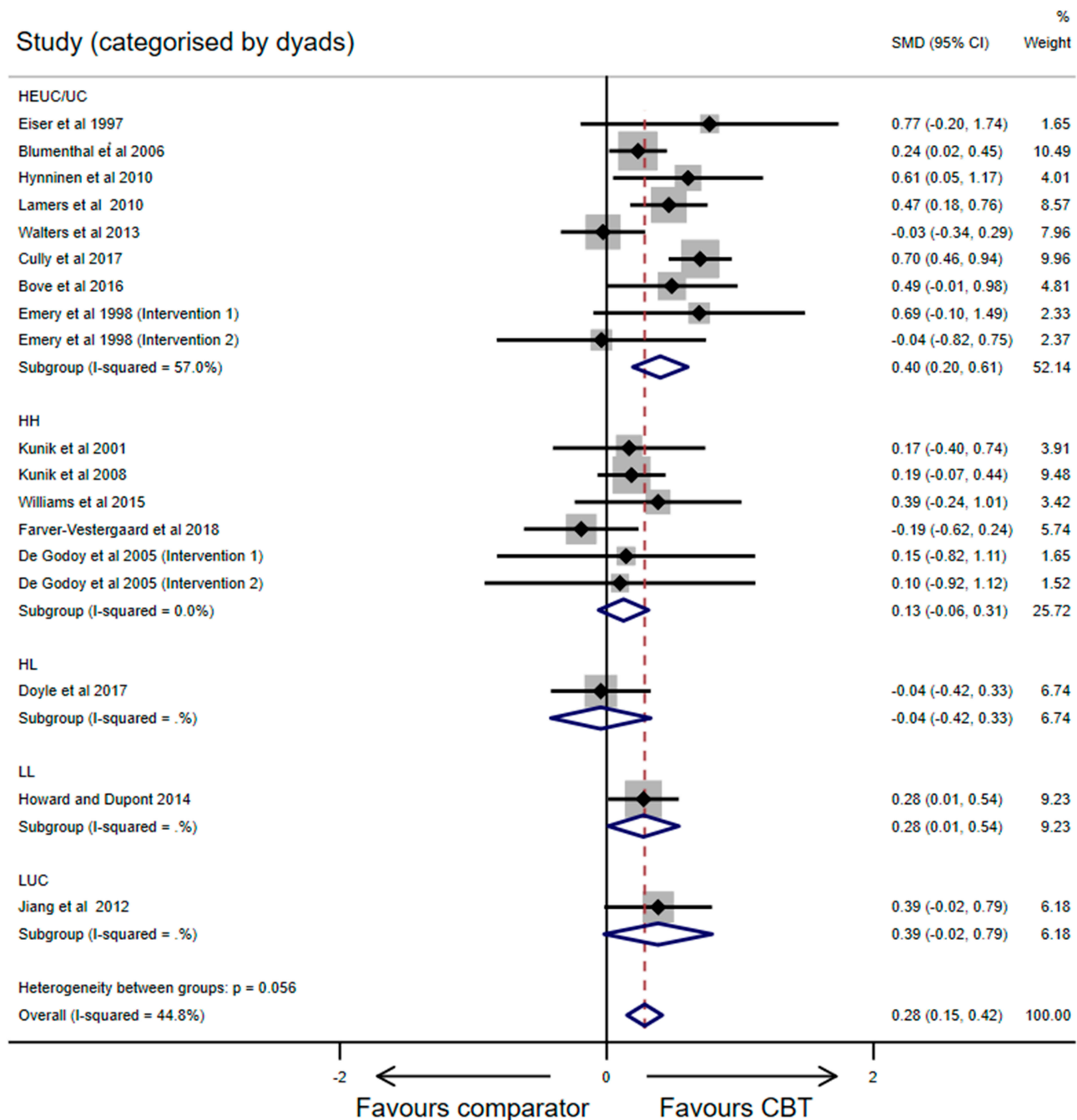


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severity of anxiety or depressive symptoms⁷). Few prior reviews provide sub-group meta-analysis concerning the nature of intervention-comparator dyads or predictors of intervention effect. Where such sub analyses have been reported in previous systematic reviews of people with COPD, our findings are consistent in that 1) CBT consistently produces a

significant effect when compared to usual care;¹⁰⁻¹² 2) where active interventions are compared to active comparators, size and significance of the between-groups effect are diminished;¹² 3) the number of CBT sessions did not significantly predict effect size;¹² and 4) CBT interventions showed similar benefit in those with confirmed or above-criterion

F

Quality of Life - Physical

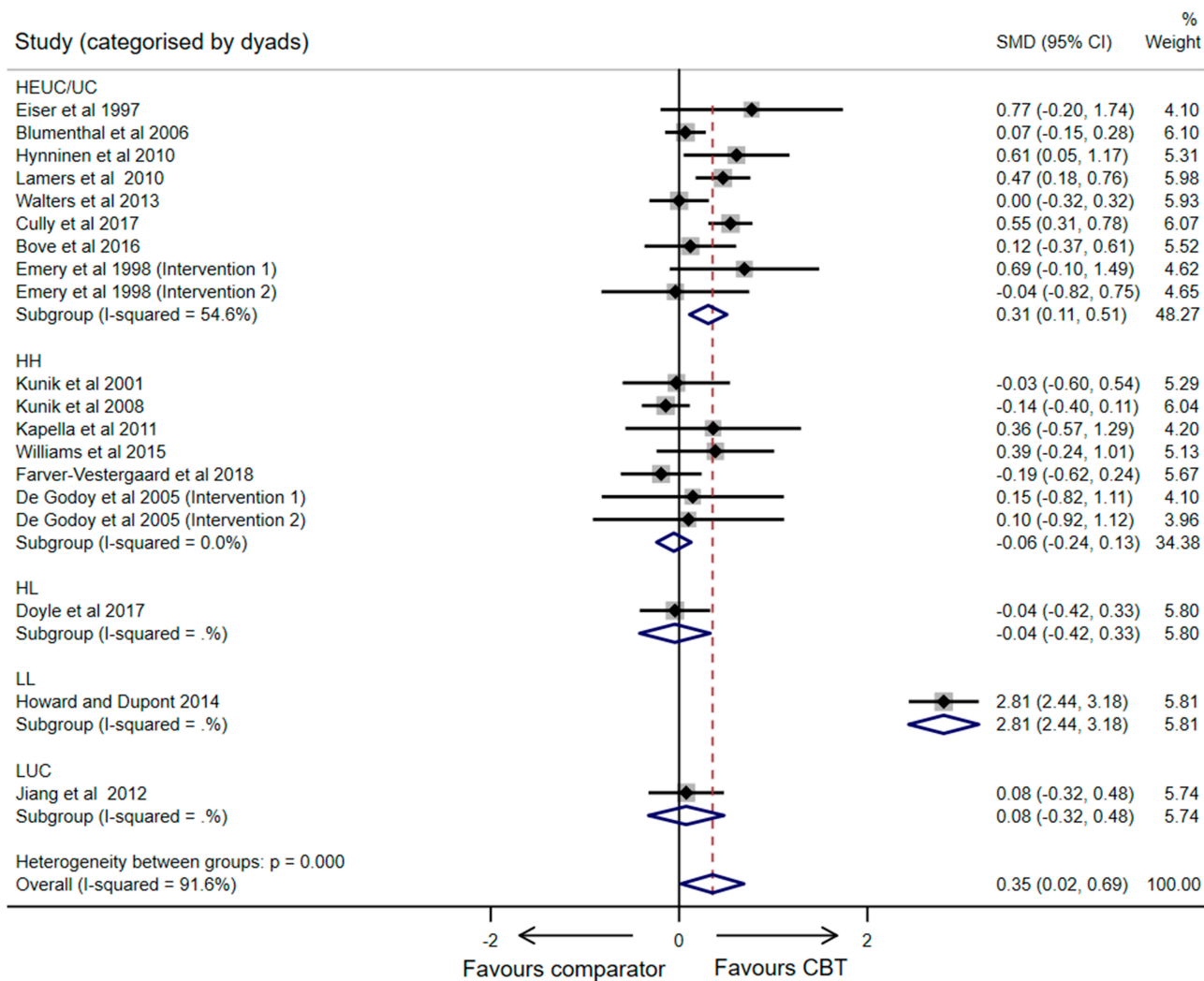


Figure 1 Effects of cognitive behavior therapy (CBT) interventions (random effects models) presenting overall effect and subgroup analysis for intensity dyads (A) Anxiety. (B) Depression. (C) Dyspnea (Breathlessness). (D) Exercise capacity. (E) Quality of Life (Mental Wellbeing). (F) Quality of Life (Physical).

Abbreviations: HEUC/EC, High intensity intervention compared to Enhance Usual Care/Usual care; HH, High-intensity intervention compared to High-intensity comparator; HL, High-intensity intervention compared to Low-intensity comparator; LL, Low-intensity intervention compared to Low-intensity comparator; LUC, Low-intensity intervention compared to Usual care (including Enhanced Usual Care where appropriate).

threshold scores and without co-existing anxiety and/or depression.⁷ These findings are not unique to CBT use in people living with COPD. Similar findings have been reported for CBT use in the older population with and without generalized anxiety or depressive disorders.^{33,34,66}

Previous systematic reviews reporting meta-regression for CBT interventions in older people with and without COPD have included combinations of variables reflecting characteristics of the CBT intervention (ie, number of sessions, duration of program, individual or group),^{12,33,34,66} the comparator (passive or active),^{33,34} study quality (sample size, appraisal scores)^{12,33,34} and/or participants (age,

sex, presence of anxiety/depression symptoms).^{12,33,34} Few variables have been identified which significantly predict effect sizes for CBT interventions (treatment duration—longer duration, smaller effect sizes³⁴), type of control group (non-active vs active³³), sessions per week (>1 per week⁶⁶) and complexity of the CBT intervention (CBT augmented by motivational interviewing vs CBT alone³³).

In people with COPD, the prevalence of psychological comorbidities, such as anxiety and depression and associations with poorer health outcomes are well recognized. Rationales for CBT interventions within this population are often based on the exertional breathlessness—breathing discomfort—anxiety—

Table 1 Summary of Meta-Regression Findings (K = Number of Studies, B = Regression Estimate, 95% CI = 95 Percent Confidence Limits)

Predictor Variable	Anxiety			Depression			QOL (Physical)			QOL (Mental Wellbeing)						
	K	B	95% CI	P	K	B	95% CI	P	K	B	95% CI	P				
Threshold for anxiety/depression	22	0.15	(-0.26, 0.55)	0.46	20	-0.10	(-0.34, 0.13)	0.37	19	0.51	(-0.17, 1.18)	0.13	18	0.22	(-0.05, 0.50)	0.11
Number of intervention sessions	21	0.00	(-0.01, 0.01)	0.45	19	-0.00	(-0.01, 0.01)	0.40	18	-0.01	(-0.03, 0.01)	0.50	17	-0.00	(-0.01, 0.01)	0.47
Ratio intervention/comparison sessions	13	-0.11	(-0.18, -0.04)	0.005	12	-0.07	(-0.17, 0.03)	0.14	13	0.02	(-0.36, 0.41)	0.90	12	0.11	(0.04, 0.19)	0.005
Proportion of sessions CBT-focused	21	0.16	(-0.31, 0.63)	0.48	19	0.04	(-0.38, 0.47)	0.83	18	0.53	(-0.49, 1.54)	0.29	17	0.18	(-0.30, 0.66)	0.44
Intervention target (SM vs SPF)	22	0.17	(-0.36, 0.69)	0.51	20	0.15	(-0.10, 0.41)	0.22	19	-0.25	(-1.11, 0.62)	0.55	18	-0.16	(-0.50, 0.18)	0.35
Facilitator psychology professional	22	0.22	(-0.18, 0.62)	0.26	20	0.07	(-0.17, 0.31)	0.56	19	0.20	(-0.52, 0.93)	0.56	18	-0.17	(-0.45, 0.11)	0.21
Delivery (vs individual)	22	0.02	(-0.95, 0.94)	0.97	20	0.09	(-0.46, 0.64)	0.72	19	-0.63	(-2.22, 0.95)	0.41	18	-0.50	(-1.12, 0.13)	0.11
Group		0.19	(-0.31, 0.69)	0.44		0.18	(-0.12, 0.48)	0.22		0.15	(-0.92, 0.62)	0.69		0.02	(-0.30, 0.35)	0.87
Comparison sample size	22	0.06	(-0.39, 0.52)	0.78	20	0.05	(-0.27, 0.37)	0.75	19	0.29	(-0.55, 1.12)	0.48	18	-0.05	(-0.45, 0.35)	0.81
≥60		-0.35	(-0.91, 0.22)	0.22		0.08	(-0.31, 0.48)	0.65		-0.26	(-1.15, 0.63)	0.54		-0.18	(-0.64, 0.27)	0.40
30-60		0.001	(-0.002, 0.005)	0.53	20	0.003	(-0.002, 0.003)	0.77	19	0.003	(-0.005, 0.011)	0.48	18	0.000	(-0.002, 0.003)	0.77
N (continuous)	22	0.22	(-0.27, 0.70)	0.36	20	0.14	(-0.14, 0.43)	0.31	19	-0.25	(-0.92, 0.43)	0.45	18	-0.28	(-0.61, 0.06)	0.10
High		0.30	(-0.25, 0.85)	0.27		-0.00	(-0.35, 0.34)	0.98		1.07	(0.09, 2.06)	0.03		-0.26	(-0.65, 0.14)	0.19
Low		1.22	(-0.05, 2.49)	0.06		-	-	-		0.22	(-1.01, 1.45)	0.71	18	0.24	(-0.42, 0.90)	0.45
Controlled clinical trial (vs randomized)	22	-0.12	(-0.32, 0.09)	0.25	20	-0.02	(-0.15, 0.12)	0.80	19	-0.11	(-0.46, 0.24)	0.52	18	-0.06	(-0.23, 0.10)	0.43
Study quality (PEDRO score)																

Notes: Dyspnoea and exercise capacity not included in meta-regression (less than 10 studies).

Variable definition and interpretation

- Threshold for anxiety/depression = inclusion criterion for anxiety or depression (yes/no)
- Number of intervention sessions = total number of intervention sessions (inclusive of CBT)
- Ratio of intervention sessions/comparator sessions = Ratio of total number of intervention to comparator sessions (includes only comparators that reported sessions)
- Proportion of sessions CBT focused = number of CBT sessions as a proportion of all sessions provided in an intervention.
- Intervention target = CBT focus where specific psychological focus (SPF) was symptoms and Self-management (SM) included CBT as part of broader behavioral skill set.
- Facilitator psychology professional = Psychologist alone vs all other professionals (including a psychology professional)
- Delivery = CBT mode with individual as reference group vs individual + group sessions or group sessions
- Comparison sample size = reference group is ≤30 for samples between 30 and 60 and ≥60. Sample size (N) as a continuous measure was run as a separate analysis.
- Intensity of comparator = reference group is Enhanced Usual Care/Usual care (EUC/UC) for high-intensity comparator and low-intensity comparator
- Controlled clinical trial = reference group is randomized controlled clinical trials (RCT)
- Study quality (PEDRO score) = continuous variable.

inactivity vicious cycle. Where people with COPD experience “breathlessness they find frightening” a cognitive behavioral component is recommended for inclusion within self-management plans to help reduce anxiety and distress.⁶⁷ Yet the aetiology and pathophysiology of these psychological comorbidities is complex and likely includes interactions between biological (eg, systemic inflammation, hypoxia,⁶⁸ cognitive/perceptual (eg, symptom distress, illness intrusiveness, self-efficacy, mastery, coping strategies, learning capacity^{69,70}) and sociodemographic factors⁷¹ (eg, income, access to health services, use of preventative health care, sex, high-risk health behaviors, comorbidities).

Of the CCT/RCTs included in this review (n=24), the most frequent comparator to CBT was EUC/UC (n=12). While strategies used to balance time spent with participants were explicitly reported (eg, laboratory visits,³⁷ phone calls,^{18,46} depression/anxiety assessments⁴¹), what constituted usual care was more opaque. In controlled trials within this review, UC was described as: standard care for COPD,¹⁸ the care usually received from their physicians,^{44,46} or medical center,^{19,41,48} according to relevant chronic disease clinical practice guidelines,^{20,43,47} or was not described.^{13,22,37} People with COPD receive less specialized medical care than people living with other chronic conditions⁷² and health professional knowledge of, and adherence to clinical practice guidelines specific to COPD have been estimated to be as low 6.7% for community-based people living with COPD⁷³ and range between 29.8%⁷³ and 36% for hospital-based registry data.^{74,75} The difficulty with interpreting comparisons between CBT and usual care lies in the absence of information concerning what constituted usual care, especially where key components of usual care might improve psychological outcomes.

Pulmonary rehabilitation (PR) is currently recommended as part of standard or usual care for people with COPD and has been confirmed to reduce symptoms of anxiety, depression, breathlessness and improve health-related quality of life and exercise capacity.^{4,23} Excluding direct comparisons of PR with and without CBT, four studies included explicit statements concerning the inclusion of PR as part of UC or a comparator^{19,40-43} with Bove et al,⁴³ Heslop-Marshall⁴⁰ and Doyle et al⁴² reporting the proportion of people within the CBT and comparator groups participating in PR (past 12 months, CBT group = 45% vs UC group=39%;⁴³ completed prior to entry to study in CBT group = 33% vs self-help leaflet group = 36% or completed by end of study, CBT group = 46% vs 44% self-help leaflet group;⁴⁰ past or current attendance at PR clinic in CBT group= 65% vs

Befriending group= 80%⁴²). The potential for PR participation to confound the key findings was expressed by Doyle et al.⁴² In these three studies it is worth noting that where PR participation rates were higher for the CBT group, significant between-group effects were reported for anxiety (favoring CBT) at each post intervention time point^{40,43} and where PR participation rates were higher in the comparator group (Befriending), both groups improved and no significant between-group effect was reported for anxiety or depression.⁴²

Participation in PR is influenced by a wide range of individual (consumer⁷⁶ and clinician⁷⁷) and socio-environmental factors.^{78,79} While PR is recommended as usual care, poor referral, access and uptake rates suggest that for many people living with COPD, it continues to be “best or recommended practice” or “not quite usual practice.”⁸⁰

The second most frequent intervention-comparator dyad in this review were high-intensity interventions vs high-intensity comparators (n=9), the most frequent of which concerned PR with or without CBT^{15,16,35,36,38} or mindfulness-based cognitive therapy (MBCT³⁹).

Anxiety and fear associated with physical exertion are common in people with COPD.⁸¹ PR results not only in a physiological training response but as an individual’s functional exercise capacity improves, provides opportunities for associative learning and reframing an individual’s expectations concerning anxiety associated with activity.⁸²

As PR includes exercise training under the direction of a health-care professional, this may address exertional breathlessness-related cognitive and emotional factors, even when CBT is not intentionally prescribed. There is significant overlap in components of CBT interventions listed in the included studies (eg, education on anxiety and COPD; education about depression and inactivity in COPD; distraction, relaxation, and breathing techniques; self-monitoring and goal setting) and common content of the education component of pulmonary rehabilitation (anxiety/depression and panic control management; symptom management including breathing strategies⁸³). In both center- or home-based PR programs,⁸⁴ individualized education and goal setting occurs during the supervised exercise sessions.⁸⁵

This combination of functional exercise exposure with cognitive behavioral strategies, or “functional cognitive therapy” is recognized in the rehabilitation of disabling low-back pain⁸⁶ and has resulted in greater therapeutic benefits (reduced pain and disability) than exercise and manual therapy alone.⁸⁷ These factors may explain why so few studies report significant changes in psychological health outcomes with the

addition of specific CBT to comparators that include PR. However, the degree to which cognitive and emotional factors are addressed in PR is highly variable as this is not yet a standardized component of program delivery.⁸⁸

The findings of this review support the value of CBT in targeting anxiety and depression for people with COPD but highlight that it may not be resource-wise to add when usual care includes high-intensity interventions, such as PR. Models such as integrated palliative and COPD care and breathlessness intervention services for people with advanced disease already incorporate CBT.⁸⁹ While these services provide alternative opportunities for delivery of improved health outcomes, these models are not yet widely available. Given the risk that PR (with its capacity to deliver aspects of CBT) may not be accessible to all with COPD in low-resource environments, further investment in targeting, development, delivery of low-intensity CBT is indicated. In our analysis, associations with effect sizes for Quality of Life–Physical (1.07, 95% CI 0.09, 2.06, $p=0.03$) were stronger for low intensity comparators compared to EUC/UC. No such difference was found for high intensity comparators. In both the education component of PR and in CBT, multiple factors including learning ability influence benefit gained or not from such interventions and needs to be assessed in potential participants.^{70,85}

Rapid reviews are not as methodologically stringent as systematic reviews and while we did not include a number of the standard methodological processes required for systematic reviews (comprehensive search of databases, appraisal of publication bias), we worked to an a priori protocol and where possible, we endeavored to strengthen and transparently report our process.⁹⁰ We used a pragmatic definition for CBT and included studies if they were self-described as CBT or based on CBT principles, rather than screen each intervention against a specific set of criteria. Our classification of interventions/comparators into high- or low-resource intensity, while in line with current psychological health services initiatives, is a very blunt approach with misclassification potential for a small number of studies. We included all data where available (reported or could be calculated) but both the meta-analysis and meta-regression are limited by small samples sizes and limited availability of health outcomes such as breathlessness and exercise capacity.

Conclusion

The intent of CBT is to assist individuals to identify and develop strategies to address problematic cognitions related to specific symptoms. The evidence base for use

of CBT in people living with COPD is modest but growing. The analysis presented in this review confirmed that 1) compared to usual care, high-resource intensive CBT consistently resulted in small but significant reductions in symptom burden (anxiety, depression, breathlessness) and improved exercise capacity and quality of life; 2) embedding CBT within high-resource intensive, complex interventions did not confer additional health benefits, potentially as these include forms of covert CBT as part of personalized education, behavioral goal setting with or without direct adverse symptoms exposure, and 3) in general, the presence of anxiety/depressive symptoms, delivery mode or dosage of the CBT intervention did not overtly influence the size of the intervention effect. Given the dearth of specific studies (qualitative and experimental) of low-resource CBT identified within this review and the implications for health-care resources, especially for people with COPD without access to or participating in recommended care, exploration of low-intensity CBT against similar intensity interventions and/or usual care warrants further investment.

Author Contributions

MTW initiated the original concept for this review; all authors contributed to the design and development of the final framework; data acquisition was completed by MTW and CP, data analysis was undertaken by CP with MTW and KNJ contributing to interpretation. All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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