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Mindfulness-Based Intervention for Stress Reduction of Family Caregivers of People with Dementia: A Systematic Review and Meta-Analysis

Abstract: Caring for people with dementia (PWD) poses a lot of challenges to family caregivers. Mindfulness based intervention (MBI) is a newly adopted psychosocial intervention through an integration of the mind and body to reduce stress of the participants (caregivers). This study aims to determine whether and to what extent MBI for family caregivers of PWD can reduce their stress. Electronic databases including MEDLINE, CINAHL, Cochrane Library, PsycINFO, EMBASE, and the Web of Science were searched for relevant studies published between 1990 and 2016. All randomized controlled trials (RCTs) and quasi-experimental studies evaluating the effects of MBI on reducing stress in family caregivers of PWD were eligible for inclusion in this review. Five studies were included. Of these, three trials involving 144 participants were eligible for the meta analysis. The analysis showed that stress levels dropped significantly after the MBI. The findings showed a significantly more favorable effect of MBI with the standardized mean difference with a moderate aggregated effect size of 0.57 (95% CI [0.23, 0.92], overall effect Z = 3.25 at p = 0.001). This effect was only found immediately after the MBI but not in the follow-up sessions. In conclusion, the available evidence suggests that MBI seems to be effective at reducing stress among family caregivers of PWD. However, it should be noted that the number of studies involved was small (n = 5), as were the sample sizes, and no sustained effect was found. Multi-center RCTs of the effects of MBI involving larger and more diverse samples of family caregivers of PWD are recommended before any clear conclusion can be reached.

Introduction

The prevalence of dementia keeps rising exponentially with the aging population worldwide. With the declined cognitive ability as the disease progresses, people with dementia (PWD) will gradually lose their ability to carry out simple daily activities. Family caregivers play an important role in caring for PWD. They are often required to provide a wide variety of caregiving tasks in extensive years for their loved one and must adapt to continuously changing and increasingly demanding circumstance with the advancement of the disease. This challenging role may cause chronic stress among many family caregivers of PWD (Waldemar et al. 2007). A study showed that about 70% of caregivers of PWD have experienced psychological distress and 56% have suffered from disturbed moods due to chronic stress (Chan et al. 2010). The triggers of caregiver stress can be categorized as those with primary or secondary causes (Schulz and Martire 2004). Primary stressors are related to the need to deal with the results of cognitive impairment, including the need to perform caregiving tasks (e.g., assistance in bathing, dressing, and shopping), and also to handle the behavioral and psychological symptoms of dementia (BPSD) (e.g., agitation, wandering, and delusions). BPSD is always reported to be the major cause of stress in these family caregivers (Chan et al. 2010). Indeed, the stress experienced by those caring for individuals exhibiting BPSD has been found to be much higher than that experienced by those caring for older adults with physical disabilities (Tremont 2011). The secondary stressors are regarded as the consequence of the demands arising from performing caregiving tasks, such as family conflict, loss of freedom, and difficulties at work. Some caregivers may need to quit their jobs in order to take up the caregiving role.

Various non-pharmacological interventions have been designed for such caregivers, including respite care, psychotherapy, and support groups. Several systematic reviews found that support groups and respite care cannot significantly alleviate the stress level of caregivers, although they can provide caregivers with skills and knowledge on dementia care (Maayan et al. 2014; Sörensen et al. 2002). Compared with other non-pharmacological interventions, Cognitive Behavioral Therapy (CBT) may be more likely to reduce their stress levels (Wilz and Kalytta 2012), but the effects have been found to be relatively small which only lasted for a short period of time, such as immediately post-intervention (Hofmann et al. 2012; Lynch et al. 2010; Salzer et al. 2011). Thus, there is a need to provide caregivers with an intervention that is sustainable and cost-effective for releasing their stress. In the past few decades, a number of studies have investigated the effects of MBI on reducing stress in different populations, but only a few examined its effectiveness on family caregivers of PWD.

MBI is regarded as a third wave of CBT (Churchill et al. 2010), with an aim to increase self-awareness at the present moment and foster inner calmness and a non-judgmental mind, so that people can observe their thoughts and feelings from a distance, without judging them to be good or bad, but simply accepting what they are (Kabat-Zinn 1990). The most commonly used MBI are the BMindfulness-Based Stress Reduction (MBSR) program^a (Kabat-Zinn 1990) and BMindfulness-based cognitive therapy (MBCT)^a (Segal et al. 2002). MBSR is a group-based intervention program primarily designed for patients with chronic pain. In its integration of cognitive-behavioral techniques, MBCT is based on the concept of MBSR and has primarily been used to treat people with recurrent depression (Segal et al. 2002).

MBI has been found to be effective at improving a few main psychological symptoms, including anxiety, depression, cognitive function, psychotic symptoms, and

stress (Chen et al. 2013; Chien and Thompson 2014; Chiesa et al. 2011; Jimenez et al. 2010; Paller et al. 2015; Stratford et al. 2014). Also, the positive effects were found in people with physical illness such as chronic pain (Morone et al. 2008), cancer (Carlson et al. 2007), people with mental illness such as schizophrenia (Chien and Thompson 2014), depression (Churchill et al. 2010) and also family caregivers of people with different chronic diseases such as cancer (Birnie et al. 2010) and developmental disabilities (Bazzano et al. 2015). The studies adopted different MBI protocols including MBCT, MBSR, and also some modified versions of MBSR or MBCT. Several systematic reviews have been conducted to determine the effectiveness of mindfulness interventions, but so far, no systematic reviews have focused specifically on the effectiveness of such an intervention on caregivers of PWD. Indeed, the available evidence supporting psychological interventions that are currently used to reduce stress in family caregivers of PWD is inconsistent and weak (Adelman et al. 2014). There is a need to explore possible alternative interventions for these family caregivers. Therefore, the aim of this systematic review and meta-analysis was to evaluate the effects of MBI on reducing stress for the family caregivers of PWD. It was hypothesized that MBI could significantly reduce caregiving stress in family caregivers of PWD.

Method

Search Strategy

Systematic searches were made using six main electronic databases, namely, the MEDLINE, CINAHL, Cochrane Library, PsycINFO, EMBASE, and Web of Science, for works published from January 1990 to March 2016. The keywords BM i n d f u 1 * , ^ BM B S R , ^ BM B C T, ^ BD e m e n t i a , ^

BAlzheimer*,^ BCognit*,^ BCaregiv*,^ and BCarer*^ were used in a free-text search, as well as different combinations of these words. We also searched clinical trial registries (clinicaltrials.gov and International Clinical Trials Registry Platform [ICTRP]), ProQuest Dissertation & Thesis, and Conference Proceedings Citation Index (CPCI) for gray literature. Additional methods of searching included hand searches by reviewing the reference lists of all of the relevant articles that were identified from the electronic databases, Google Scholar, and hard copies in university libraries to identify any articles missed by the database search.

Eligibility Criteria

Types of Studies

This review considered any randomized controlled trials (RCTs) and quasiexperimental studies (e.g., pre-test, posttest, and non-equivalent comparison group studies) that evaluated the effectiveness of MBI and were written in English.

Studies with usual care (TAU) or active controls as the control group were also included.

Types of Participants

The study population consisted of family caregivers aged 18 or above who were blood relatives or relatives by marriage (e.g., spouses, siblings, children, and grandchildren) of people who had been clinically diagnosed with dementia, regardless of the type of dementia. Studies focusing on the family caregivers of relatives diagnosed with a chronic disease other than dementia were included for a qualitative synthesis, provided that more than 75% of the cases in the studies were dementia cases. We

excluded professional caregivers such as nurses and domestic helpers. Studies focusing on the outcomes of people with dementia, but not their caregivers, were excluded.

Types of Interventions

Interventions for caregivers that adopted mindfulness as a major component were included in this review. There are many kinds of MBI. In our review, we considered MBSR, MBCT, and those defined by the author as mindfulness interventions where the core components of mindfulness were breathing awareness, body awareness, mindful movement, and mindful eating. MBI combined with other elements such as emotional coping strategies (e.g., capitalizing on positive events, gratitude, and focusing on personal strengths) were excluded because the aim of the review was to investigate the main effects of MBI. Interventions using mindfulness as an adjunct component or a component mixed with other interventions could mask the effects of the MBI or their outcomes, making it difficult to draw a meaningful conclusion about the effectiveness of MBI for family caregivers of PWD.

Types of Outcome Measurements

The primary outcome of this review was perceived stress. We also reviewed changes in other important secondary outcomes, including depression, anxiety, and caregiver burden.

Data Extraction

The titles and abstracts of all of the retrieved articles were screened. Potentially relevant articles were assessed in full text against the inclusion and exclusion criteria by two investigators working independently. The reviewers came to a consensus on the

eligibility of the articles by discussing the results of their assessment. The extracted data included information on the design of the studies, the sample sizes, the sociodemographic characteristics of the caregivers, the main characteristics of MBI used, the types of control group, the outcome measurements, the main findings, and the suggested or identified limitations.

Risk of Bias

The risk of bias in the trials of the reviewed studies was assessed using Cochrane Collaborations' risk of bias assessment tool (Higgins et al. 2011) by two authors working independently. Seven items of the assessment tool potentially related to bias included sequence generation, allocation concealment, the blinding of the participants and personnel, the blinding of the assessment of outcomes, incomplete data on outcomes, selective reporting of outcomes, and others. Each item was rated as Bhigh risk, or Bunclear risk. The final score was discussed by the authors, and any disagreements about the rating were solved by having the research team come to a consensus. The aim of this assessment of the risk of bias was to determine the level of evidence or quality of a study; the risk of bias itself was not used as a criterion for the inclusion of a study in this review.

Data Analysis

Statistical analyses were conducted using the computer software program Review Manager 5.1 (RevMan). The standardized mean differences (SMD) and their 95% confidence intervals were calculated by using a random effects model. The heterogeneity of the studies was assessed using Chi-squared and I-squared statistics. The Chi-squared statistic of a p value < 0.05 was taken as suggestive of heterogeneity

(Higgins et al. 2003), whereas an 1^2 value $\le 50\%$ was considered to indicate low heterogeneity. We calculated overall effect sizes and their 95% confidence intervals to estimate their pooled treatment effects.

Results

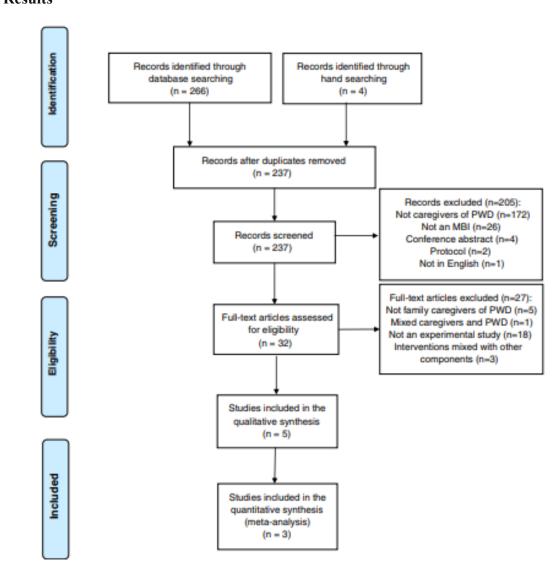


Fig.1 Literature research

Our search strategy initially identified 270 publications (Fig. 1). Gray literature such as abstracts, protocols, and theses/dissertations were traced as unpublished data; however, no additional articles were found. After removing duplicates, 237 abstracts were screened. Conference abstracts, study protocols of some published studies, non-

Table 1 Characteristics of clinical trials and their main findings

Study and	Design	Country	Country Sample	Demographic	Intervention		Comparison	Measures	Main findings	Attrition
E SE				CRES	Treatment protocol	Self- practice arrangement	O INCIDENCE (S)			2
Okon et al. (2010)	3-arm RCT	SO	Family categivers of PWD; providing at least 12 h per work of assistance (//=28)	Gender Femnale (30.678) Moam age 64.5 (SD=9.1) Care recipions relationship Spouse (74.278) Parent (25.8%) Behnschy White (20.2%) African Amorican Anoxican (3.2%) Asian (3.2%)	Group inservention (ve 10) One oducation assists on demonstria and a weekly 90-min MB-CT session for 6-woods Contours (1) dislactic insertuction and discussion concerning stress, reductation, and mind-body interaction; and mind-body interaction; (2) instruction and part-tice in meditations and part-tice in meditations and practice in meditations and discussion and problem solving regarding successes and difficulties in practicing the exercises; (3) group discussion and problem solving regarding successes and difficulties in practicing the exercises and applying the principles in the child applying the principles in the child applying the principles in the child applying the principles	Required regular daily punctice	A. 7-week group-based education program about caring for P.WD (well I). B. 3h of respite care once per week for 7-weeks (we 10).	PSS RMBMC CESD SF-36 Farigue MAAAS HFNJ GPS E FFNJ GPS	Both mindfalness and obnomions interventions decreased the self-mind caregiver stress compared to the respite-only control (no significance befreen group differences).	12.9%
Epotein-Lultow et al. (2011)	Protest post-test one-group design	ns	Family categivers of PWD (v=7) or functional impairment; providing at least 20th per work of assistance (N=9)	Gender Fernale (100%) Mean ags 56.2 (SD7.7) Care recipional relationship Parent (77.8%) Spouse (22.2%) Eleminishy Casca siens Casca siens African African African	Group indexvention (re-9) Workly 75-min MBSR session for 8wordss Confusion for 8wordss Confusion for 8wordss Confusion for 8wordss Confusion for using mindfulness exercises, (2) gaided through specific techniques designed to promote and foster the experience of mindfulness in drifty life, and (3) encouraged daily homework exercises prior to returning to class the following words.	Roquired regular daily pen crico	₹	PSS CIS-D ZBI STAI ITG ITG SF-6a SF-6a	Self-reported deperession and burden decreased during the 8-week interactions with further reductions demonstrated after a 1-meetin follow-up on burden, while depensive symptoms returned to the baseline level. No significant difference was found in the self-reponded stress and the PSS scores only trended toward a statistical significance (p=0.058)	ğ

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Study and	Design	Country	Country Sample	Demographic	Intervention		Comparison	Measures	Main findings	Attrition
ug man				or o	Treatment protocol	Self- practice arrangement	condition(s)			3 2
O'Doensell (2013)		SI	Family caregivess of PWD (N=24)		Group intervention (v=11) Weekly 150-min MIBS R session for 8weeks plus a 7.54 retteral. Contents (1) Focused on body scan mediantion, siting mediantion, mindful huttu yoga, and walking mediantion, (2) Information about srees and its impact on health in addition to working with the dynamic aspects of the group. Each class included opportunities for questions and the sharing of experiences with the practices.	Required regular daily practice	Weekly progressive muscle reluxation program for Sweeks plus a 1-day retreat (n=13); focus on aut ogenic training.		The MISSR group showed greater significant reductions in self-re ported levels of depression and isolation from pre- to post-intervention, and those changes remained significant at 8 weeks post-intervention. Both groups showed similar decrease in the stress level.	
(2013)	2-am RCT		Family caregivess of people with dementia (78)	Gender Fernale (88.5%) Mean age 56.8 (SD=9.8) Care recipient relationship Adult child (74.4%) Spouse, sibling friend (25.6%) Ethnic ity White (98.7%) Amorican Indam (1.3%)	Group intervention (v=38) Weekly 150-min MBS R session for 8works plus a 5-h retreat. Contemts (1) Concepts of mindfulness, (2) practiced meditarion, sitting and walking modification, body scan modification, gontle Hatha yoga and staretching evertises each week, (3) CDs and written mod entit week (3) CDs and written not encounting engagement in home	Required regular daily practice	Caregiver education & support (m-40). Weekly 150-min seesion for 8weeks plus a 5-h wellness dry. Focus on issues a filecting family caregivers and group social and emotional support.	PSS CCES-D STA1 MCS-12 MGCSS MOSS SS	MBS R was more effective at improving overall membel health, reducing stress, and decreasing depression than CCES. Both interventions improved caregiver mental health and were similarly effective at improving anxiety, social support, and burden.	95 O

Table 1 (continued)

Study and	Design	Country Sample	Sample	Demographic	Intervention		Comparison	Measures	Main findings	Attrition
udiceo				CERTIFIE	Treatment protocol	Self- practice arrangement	CONTROL (S)			54 121
Bown et al. (2015)	2-am RCT	SI	Family care give is of people with demonstra (N=38)	Gender Fennale (84.2%) Mean age 61.1 (SD=10.4) Care recipient relationship Parant (47.8%) Spouse (47.8%) Spouse (47.8%) Spouse (47.8%) Spouse (47.8%) African American (75.7%) African American (75.7%) Hispanic/Lat- ino (2.7%)	Gooup intervention (v=23) N/A Weekly 90–120-min MIBSR se seion for 8/weeks plus a day-long intensive mindfulness practice and docussion session Contents (1) Increasing avaranteess of experiences and sensoiness related to physical symptoms, emotions, thoughts, and behaviors during interactions with care recipients. (2) Mindfulness practice following the MSR memad (3) Discussion of care giving and minor adjustments to some mindfulness exercises to a commodate physical limitations common among older individuals.	NA VA	Social support with education element for 8weeks (v=15); leader facilizated discussion of group-ge mented to coming for their ADide mentia care recipient.	PSS AAQ POMS SR-36 ZBI FCL-MS Coefisol	MBSR participants beyonded significantly lower levels of pence ived store a and mood disturbance at post-intervention relative to SS participants. At the 3-month follow-up, participants in both tour month conditions apported improvements in several post-broockial cutcomes. At follow-up, there were no condition differences on the se cutcomes, nor did NBSR and SS participants differ in durant changes in contion response over the source of the study.	10.5%

AAQ Acceptance and Action Questionnaire II, ANT Attentional Network Test, CCES Community Caregiver Education and Support, CEQ Credibility Expectancy Questionnaire, CES-D Center for Epidemiological Studies—Depressions cale, CRI Coping Responses Inventory, ESS Epworth Sleepiness Scale, FCLMS Family Care Inventory—Mutuality Scale, FFVJ measure of being non-judgmental adapted from factor five, GDS The Geriatric Depression Scale, GPSE General Perceived Self-Efficacy, ITG Inventory of Complicated Grief, InCRP High-Senatury C-Reactive Protein, IL-6 interleukin-6, AMAS The Mindful Attention Awareness Scale, ABCEBS Montgomery Borgatta Caregiv or Burden Scale, ABCT Mindfulness-Based Cognitive Therapy, ABSR Mindfulness-Based Stress Reduction, ARCS Mental Component Summary Scale, MOSSSS Medical Outcomes Study Social Support Survey, PCS Physical Component Summary score, SS Social Support, KMS Kentucky of Mindfulness Skills, NPI Narropsychiatric Inventory, PMP Progressive Muscle Relaxation, POAS Profile of Mood States, PSQI Pittsburgh Skep Quality Index, PSS Perceived Stress Scale, RMBPC Revised Memory and Behavior Problems Checklist, SCS The Self-Compassion Scale, SF Short-Form Health Survey, SF-12 Short-Form 12 Health Survey, SF-36 Medical Outcomes Study Short-Form Health Survey, STAL Short-Form Study Short-Form Health Survey, STAL State—Trait Anxiety Inventory, TAF-a Tumor Necrosis-a, ZBI Zurit Burden Interview English papers, and trials that did not focus on dementia caregivers and/or the MBI were excluded (n = 205). The remaining 32 articles were selected for further assessment. Twenty-seven articles were excluded for the following reasons: (a) the caregivers were not family caregivers of people with dementia (n = 5); (b) the intervention was mixed with other components (n = 3); (c) the study population was a mixture of caregivers and people with dementia (n = 1); and (d) the study was a nonexperimental one (n = 18). A list of excluded studies that were included in full text review (n = 27) was prepared as Supplementary Materials. In the end, five studies with total 179 subjects that fulfilled the selection criteria were analyzed. We conducted the meta-analysis of caregiver stress with three studies involving a total of 144 subjects, as there were insufficient outcome data in the remaining two studies to conduct a statistical analysis (Epstein-Lubow et al. 2011; O'Donnell 2013).

Characteristics of the Studies

Design

The five reviewed studies were those by Brown et al. (2015), Epstein-Lubow et al. (2011), O'Donnell (2013), Oken et al. (2010), and Whitebird et al. (2013). The studies of Brown et al. (2015) and Oken et al. (2010) were both pilot RCTs, with 38 and 31 caregiver subjects, respectively; whereas the RCTs of Whitebird et al. (2013) and O'Donnell (2013) involved 78 and 24 participants, respectively. Only Epstein-Lubow et al.'s (2011) studyusedasingle-group,pre-testandpost-testdesign,withonlya small sample of 11 caregivers. Oken et al.'s (2010) study was a three-arm design and the subjects were assigned to two comparison intervention groups (mindfulness and education) and respite care as the control group, while the studies by Brown et al. (2015)

and Whitebird et al. (2013) were two-arm design studies (i.e., a mindfulness group and an active control group (social support)). O'Donnell (2013) compared a mindfulness-based intervention with muscle relaxation training in an RCTas her master's thesis. The Characteristics of Family Caregivers

The characteristics of the participants are shown in Table 1. In the five studies, most of the subjects were women (ranging from 80 to 100%). The mean age range was from 56.2 to 71.3 years (SD 6.7 to 10.4). A confirmed clinical diagnosis of dementia in the care recipients was not required in the study conducted by Brown et al. (2015) and Whitebird et al. (2013). Instead, caregiver reports of the cognitive symptoms and functional decline of the care recipients were used to identify appropriate PWD participants, and in this way, appropriate caregivers were recruited as subjects of the study. Epstein-Lubow et al.'s (2011) study included caregivers of frail elderly people with chronic diseases, and about 78% of the care recipients in the study had been diagnosed with dementia. The caregivers' relationship with the PWD in the reviewed trials included the spouse (20 to 74%) and parents (50 to 74.4%) of the PWD, while this information was not reported in the study by O'Donnell (2013). The mean figures on the duration of the caregiving ranged from 46.6 to 48.8 months (SD 32.0 to 39.3) in the trials by Whitebird et al. (2013) and Brown et al. (2015); however, this information was not reported in the studies by Oken et al. (2010), O'Donnell (2013), and Epstein-Lubow et al. (2011). The duration of caregiving is usually related to the stress level of the caregiver (Zainuddin et al. 2003).

Intervention

In all five studies, the experimental intervention was either MBSR or MBCT, and most of these interventions were modified from the original design in terms of length and duration. The original MBSR consists of eight 2.5-h, weekly sessions plus a day retreat. Oken et al. (2010) used six weekly 90-min MBCT sessions plus an education session on dementia, while O'Donnell (2013) and Whitebird et al. (2013) adopted the entire original design of MBSR (Kabat-Zinn 1990). EpsteinLubow et al. (2011), Brown et al. (2015), and Oken et al. (2010) reduced the duration of each weekly session to 1.25–2 h, in an attempt to enhance participant adherence to the intervention protocol. In all five studies, the intervention was delivered by certified and experienced MBI teachers; information was provided about the intervention protocol, but the contents of each session were not provided in detail in the papers. In each study, all of the subjects were encouraged to practice mindfulness daily after class. Weekly telephone follow-ups were provided only in Whitebird et al.'s (2013) study, and the participants' rate of adherence to practicing mindfulness at home was recorded only in O'Donnell's (2013) study. Both Whitebird et al. (2013) and Brown et al. (2015) adopted social support as the control condition, which included education and discussions about caring skills; whereas O'Donnell (2013) used muscle relaxation as an active component of the intervention in the control group. In addition, Oken et al. (2010) compared the mindfulness-based intervention with respite care as the control condition. A summary of the interventions used in the five reviewed studies is presented in Table 1.

Outcomes Measurement

The primary outcome of this review was the carers' perceived stress level and the secondary outcomes were their psychological symptoms such as depression and anxiety. The perceived stress level in all five studies was measured using the Perceived Stress Scale (PSS) (Cohen et al. 1983). To assess the stress levels of participants after completing the interventions, Oken et al. (2010), O'Donnell (2013), and Brown et al.

(2015) also measured the carers' salivary cortisol levels at different times of the day, for example, at bedtime and/or after awakening. To measure the sustainability of the intervention effects, Brown et al. (2015), O'Donnell (2013), and Whitebird et al. (2013) further measured the stress levels at 4, 8, and 16 weeks after the interventions.

Study	Tools	Effect si	ze (d)		
		Post- MBI	I month post-MBI	3 months post-MBI	4 months post-MBI
Oken et al. (2010)	PSS	0.00			
	CES-D	0.30			
Epstein-Lubow	PSS	0.15	0.60		
et al. (2011)*	CES-D	0.29^	-0.05		
	STAI	0.01	0.22		
	ZBI	0.33^	0.64^		
Whitebird et al.	PSS	0.61^			0.47
(2013)	CES-D	0.66^			0.39
	STAI	0.59^			0.52
	MBCBS Objective	0.11			0.11
	MBCBS Subjective Stress Burden	-0.24			0.13
	MBCBS Subjective Demand Burden	0.83			
Brown et al. (2015)	PSS	-0.51^		0.05	
	POMS-depression	-0.73^		-0.20	
	ZBI	0.05^		0.39	

PSS Perceived Stress Scale, CES-D Center for Epidemiological Studies—Depression scale, STAI State—Trait Anxiety Inventory, MBCBS Montgomery Borgatta Caregiver Burden Scale, POMS Profile of Mood States

Table 2 Effect size of MBI on different psychological outcomes used

The secondary outcomes of this review included depression, anxiety, and caregivers' burden. Anxiety was measured by Epstein-Lubow et al. (2011) and Whitebird et al. (2013) using the State-Trait Anxiety Inventory (Spielberger and Gorsuch 1983). Depression was measured in all studies by using different assessment tools, namely the Center for Epidemiological Studies depression scale (McDowell 2006) in the study of Whitebird et al. (2013), Oken et al. (2010), and Epstein-Lubow et al. (2011); the Geriatric Depression Scale (Yesavage and Sheikh 1986) in O'Donnell's

^{*}Pre-test post-test single-group design (within-group effect size)

 $^{^{}n}p < 0.05$

(2013) study; and the Profile of Mood States—Depression (McNair et al. 1971) in Brown et al.'s (2015) study. Caregiver burden was measured by the Zarit Burden Interview (Zarit et al. 1980) in the studies of Epstein-Lubow et al. (2011) and Brown et al. (2015); and by the Montgomery Borgatta Caregiver Burden Scale (Montgomery et al. 2000) in the study of Whitebird et al. (2013). The between-group effect sizes (d) of MBI for the psychological outcomes of four out of the five reviewed studies are summarized in Table 2. The effect sizes on the four outcomes varied among the five studies; whereas, the effect sizes on perceived stress ranged from 0 to 0.61 and on depression (CES-D) ranged from 0.29 to 0.66. The data reported by O'Donnell (2013) were insufficient for calculating effect size. Epstein-Lubow et al.'s (2011) study used a single-group, pretest and post-test design, thus reporting the within-group effect sizes only.

Risk of Bias Across the Included Studies

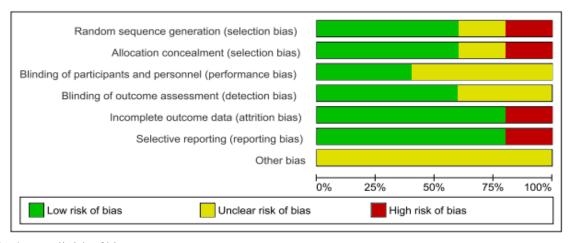


Fig. 2 Overall risk of bias

In all of the reviewed RCTs, the risk of bias was assessed through the Cochrane Collaborations' risk of bias assessment tool (Higgins et al. 2011). The assessment adopted an objective approach based on documentary evidence rather on personal

reports from the authors. The overall risk of bias is reported in Fig. 2, and an assessment of the bias in individual studies is given in Fig. 3.

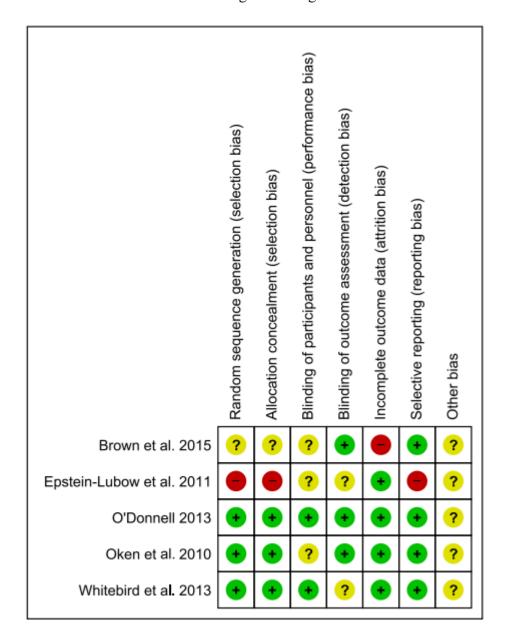


Fig. 3 Assessment of the bias of individual studies

The study with the highest risk of bias was the one by Epstein-Lubow et al. (2011), which was a single-group, pretest and post-test design; thus, the items of sequence generation and allocation concealment were irrelevant to the assessment of its risk of bias. The procedures of blinding subjects and measuring outcomes were not mentioned, so with regard to bias, we regarded them as unknown risks.

There were no dropouts from the group, which may relate to the small sample (n = 9), so the study was regarded as being at a low risk of Battrition bias.^ Epstein-Lubow et al. (2011) provided the effective size for some outcomes and information such as significance. The p value was not reported, so the study was judged as being at a high risk of Breporting bias.^ We concluded that O'Donnell's (2013) study had the lowest risk of bias because all of the procedures, such as blinding, allocation, and the management of missing data, were reported in sufficient detail.

In all of the reviewed RCTs, the randomization procedure (i.e., using a computerized algorithm) and the allocation concealment method (i.e., central allocation) were well reported, except in the study of Brown et al. (2015). Therefore, most of the studies were deemed to be at a low risk of bias in terms of Brandom sequence generation^a and Ballocation concealment. MBI is an interventional study, so blinding the subjects to the intervention is challenging. Comparing the nature of the active control with the MBI in all studies, we found that the structure and nature of the intervention are similar in the studies of O'Donnell (2013) and Whitebird et al. (2013). Therefore, the participants may not know if they are in the active control or intervention group, so we regarded their studies as being at a low risk of bias with respect to the Bblinding of participants^a and judged the other studies to be at an Bunknown risk of bias. Objective data such as the salivary cortisol was collected in the studies of Brown et al. (2015), O'Donnell (2013), and Oken et al. (2010), and the blinding of assessors was also mentioned in the studies. Therefore, they were determined to be at a low risk of bias in terms of detection bias. The risk of attrition bias was judged to be low in all studies, with the exception of the study of Brown et al. (2015) due to the uneven sample recruited/assigned and dropouts between the two study groups. Brown et al. (2015) reported that 23 subjects were randomized in the MBI group and 15 subjects to the

social support (control) group. Eventually, there were no dropouts in the control group and four dropouts in the MBI group at the end point of the study due to time scheduling and health problems. However, they did not test any differences between the participants from the MBI and control group at baseline, and any exposure-outcome association such as health condition. As there is limited information to understand the homogeneity of study groups and higher sample recruitment and dropouts in the MBI group, we regarded high risk of attrition bias in Brown et al.'s (2015) study. All of the RCTs (Brown et al. 2015; O'Donnell 2013; Oken et al. 2010; Whitebird et al. 2013) were reported as being of low risk in terms of reporting bias. Although some of these studies did not mention whether there was a study protocol with prespecified outcomes, most expected outcomes related to caregiver stress, such as perceived stress level, were measured in all of the studies.

All studies were considered to have different types of unknown bias, which resulted from insufficient information about the calculation of sample sizes, the rate of adherence to the intervention, the imbalance of male and female subjects, the stage of the dementia, and the duration of caregiving.

Results of Individual Studies

The main findings of the five studies reviewed are summarized in Table 1. Compared with the control group, stress levels decreased significantly after the MBI in the studies of Whitebird et al. (2013) and Brown et al. (2015), but no significant between-group differences were noted in the studies of Oken et al. (2010) and O'Donnell (2013). Of these four RCTs, the levels of depression in the MBI group decreased significantly in the studies of Brown et al. (2015), O'Donnell (2013), and Whitebird et al. (2013), when compared with those in the control group. In all of the

RCTs measuring caregiver burden, no significant changes were found between the MBI and control groups. Likewise, in the pre-test and post-test study of Epstein-Lubow et al. (2011), significant within-group differences in depression, anxiety, and caregiver burden were noted immediately after the MBI with further reductions demonstrated after a 1-month follow-up in caregiving burden but depressive symptoms returned to the baseline level. No significant differences were found in self-reported stress and PSS scores only inclined toward statistical significance (F(1,7) = 5.11, p = 0.058).

Effects of MBI

We performed the meta-analysis to compare the effects of MBI on the intervention groups versus the control groups on two main outcomes, namely stress and depression, among the studies of Brown et al. (2015), Oken et al. (2010), and Whitebird et al. (2013). O'Donnell's (2013) and EpsteinLubow et al.'s (2011) studies were excluded due to insufficient data (i.e., mean values and standard deviations at individual times of measurement) for statistical analysis. Oken et al.'s (2010) study was a three-arm design consisting of the MBI, education, and control (respite care) groups. Regarding the contents of program for the education group, we found that it was similar to that of the active control (social support) group in Brown et al.'s (2015) and Whitebird et al.'s (2013) studies, which provided training and discussion about skills in dementia care. Therefore, we selected the MBI and education (control) groups from Oken et al.'s (2010) study to perform the meta-analysis. As there were only three RCTs on the MBI identified in this review for meta-analysis, the validity of the pooled results or their findings could be reduced and thus be treated with caution.

Effect of MBI on Stress Reduction

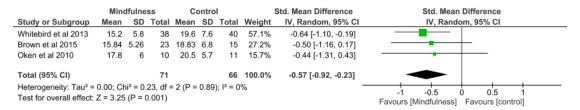


Fig. 4 Comparison of the effects of MBI and social support on stress

The pooled effects of MBI on perceived stress for the three reviewed studies are summarized in Fig. 4, which compares the MBI groups with the control groups in the immediate posttest period. The total number of subjects was 137. The MBI had a significant positive effect on the perceived stress of the caregivers, and the standard mean difference (Hedges' adjusted g) was 0.57 (95% CI [0.23, 0.92], overall effect Z = 3.25 at p = 0.001). There was non-significant heterogeneity among the studies ($I^2 = 0\%$, p = 0.23), and the overall result from the three studies demonstrated that the MBI had a moderately favorable effect on reducing the stress level of caregivers of PWD.

Effect of MBI on Depressive Symptoms

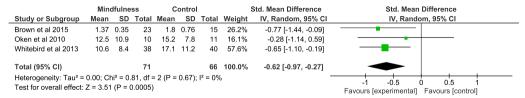


Fig 5. Comparison of the effects of MBI and social support on depression

The pooled effects of MBI on depression for the three reviewed studies are summarized in Fig. 5, which compares the MBI with the controls in the immediate posttest period. The MBI had a significant positive effect on the depressive symptoms of the caregivers, and the standard mean difference (Hedges' adjusted g) was 0.62 (95% CI [0.97, 0.27], overall effect Z = 3.51 at p = 0.0005). There was non-significant heterogeneity among the studies ($I^2 = 0\%$, p = 0.67), and the overall result from the three

studies demonstrated that the MBI had a moderately favorable effect on improving the depressive symptoms of caregivers.

Discussion

This systematic review with a meta-analysis showed that the MBI had a moderate effect on both stress and depression in family caregivers of PWD. In comparison with the control groups that were provided with social support, the MBI produced a significantly greater reduction in the stress and depression levels of the caregivers. The effects of MBI on other psychosocial outcomes, such as anxiety and caregiving burden, were inconclusive because of the inconsistent results or insufficient data reported in the studies. The effects of MBI on stress reduction have been widely studied in family caregivers of cancer patients (Birnie et al. 2010), children with chronic diseases (Minor et al. 2006), and people with developmental disabilities (Bazzano et al. 2015). Significant and positive effects on stress reduction were found in those studies, although most of them adopted a short-term, pretest and post-test design. Our meta-analysis has further demonstrated that MBI is effective at reducing the stress levels of caregivers of PWD.

Besides stress, depression was also a common problem among caregivers of PWD (Ferrara et al. 2008). The stressful tasks and wide range of uncertainties involved in caregiving can expose caregivers to a high risk of depression. Rumination (repetitive thoughts about distress and stressors) is regarded as a common cause of depression. The caregivers may repeatedly think about the uncertainties related to caregiving, resulting in depression. It is believed that MBI can help these caregivers be more accepting to their negative thoughts without judging them, thus minimizing their ruminations and depressive symptoms.

The effect sizes (Cohen's d) of the MBI in the reviewed RCTs ranged from 0.05 to 0.83 on different psychological outcomes such as stress, burden, and depression. Compared with the effect sizes of current psychosocial interventions for caregivers of PWD such as Hedge's g of 0.44 in the metaanalysis of support groups by Chien et al. (2011) and Cohen's d between 0.09 and 0.23 in psychoeducation intervention by Adelman et al.'s (2014) systematic review, MBI indicates a larger effect on improving psychological stress and well-being of these family caregivers. Since mindfulness is not only an intervention but an attitude of daily living, it is of our interest that MBI will have a larger sustainable effect than other psychosocial interventions. For the long-term effect, our study found the effect sizes of MBI on these psychological outcomes ranged from 0.05 to 0.52. Compared with support group intervention (pooled effect sizes Hedge's g 0.49; Chien et al. 2011) and various psychosocial interventions (Cohen's d of 0.10-0.17; Pinquart and Sörensen 2006), there is no strong evidence supporting the MBI has better sustainable effects than the other psychosocial interventions. We may need more information about participants' adherence to daily mindfulness practices during and after the intervention in order to better understand its sustainable effects.

MBI was found not only to be a relaxation exercise but to also involve modifications to participants' cognitive and emotional coping process (Jain et al. 2007). However, this coping process can only be sustained if the participants can extend the mindful practices from the training sessions to their daily life activities. Therefore, all the five reviewed studies encouraged their participants to practice mindfulness daily. However, only O'Donnell's (2013) study provided information about the participants' adherence to daily mindfulness practice; and a moderate negative correlation was found between the self-reported 16-week daily practice rate and the PSS score immediately post-MBI (r(21) = -0.49, p = 0.025). This supports the view that the effect of MBI on

stress reduction can be related to the sustainability of one's home practices. Therefore, the future studies are recommended to assess the effects and contributions of the participants' level of adherence to daily mindful practices to their psychosocial wellbeing at different followup periods. In this review, the effect of MBI on stress reduction was only found immediately after the intervention. Two studies (Brown et al. 2015; Whitebird et al. 2013) measured stress levels after the completion of the MBI at 24 and 12 weeks, respectively; however, there were no significant differences between the MBI and control groups at both follow-ups. The insignificant results in the follow-ups might relate to the discontinuation of the practices of mindfulness after the MBI. A recent RCT targeting at mental health of caregivers of people with chronic disease found that only about 50% of the caregivers continuously practiced mindfulness after an 8-week MBSR program (Hou et al. 2014). The study did not follow up why several caregivers had given up the practice; and this could be related to different reasons such as their busy caregiving tasks. It is suggested that the outcomes at follow-ups and adherence to home practices after intervention should be measured for better understanding of the sustainable effect of MBI in caregivers of PWD, as well as how it relates to participants' adherence to mindfulness practice.

The aims of MBI are to help people (caregivers) learn and apply mindful exercises into their daily life in an attempt to be aware of, understand, and accept their stressors. It is important to investigate any obstacles that caregivers might face to practice such exercises in their everyday life, resulting in rebound of their stress level after the MBI program. In order to enhance the participants' adherence to home practice, Brown et al.'s (2015) study reduced the duration of each of the MBI sessions to 1.5 h (from the original 2.5 h) weekly. To improve rates of adherence, consideration can be given in a future study to modifying the mode of delivering the MBI, the content, and/

or the duration according to the needs, convenience, and preferences of the caregivers, without sacrificing sufficient training in mindfulness and between-session practices.

Mindfulness originated from Buddhism; its philosophy and concepts are considered to be abstract and may be difficult to define and conceptualize (Chiesa 2012). One widely adopted definition of mindfulness refers to Bpaying attention in a particular way; on purpose, in the present moment, and nonjudgmentally (Kabat-Zinn 1990). In the past decades, several self-reporting questionnaires have been developed to measure mindfulness, such as the Mindfulness Attention Awareness Scale (MAAS) (Brown and Ryan 2003), the Kentucky

Inventory of Mindfulness Skills (KIMS) (Baer et al. 2004), the Toronto Mindfulness Scale (Lau et al. 2006), the State

Mindfulness Scale (Tanay and Bernstein 2013), and the Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al. 2008). Of the five reviewed studies, three (Epstein-Lubow et al. 2011; Oken et al. 2010; O'Donnell 2013) measured the level of mindfulness by using the MAAS, FFMQ, or KIMS, while the level of mindfulness was not measured in the other two studies (Brown et al. 2015; Whitebird et al. 2013). Measuring the level of mindfulness obtained by the participants after they have received the intervention can provide researchers information about the progress and extent to which participants master the skills. Thus, researchers can understand and explain the relationship between the practice of mindfulness and the psychological outcomes, as well as the presence of any active ingredients and other mediators of the intervention (or its effects). In future trials, the levels of mindfulness achieved by each participant can be measured and used to predict their psychological health outcomes including perceived stress and emotional regulation.

There have been an increased number of multi-component interventions for addressing various needs of the caregivers of PWD in recent years. For example, Livingston et al. (2013) designed an 8-week intervention, which consisted of psychoeducation about dementia and stress, assertive communication skills, changing unhelpful thoughts, and relaxation skills for caregivers of PWD. Gonzalez et al. (2014) designed a 6-week intervention consisting of cognitive behavioral intervention, coping strategy and problem solving skill, priority setting, and decision making. These two studies found a positive effect on a few psychological outcomes of the caregivers. A recent systematic review and meta-analysis compared the effects between the multicomponent interventions and usual care on psychological well-being of caregivers of PWD (Laver et al. 2016). The findings showed significantly more favorable effects of multi-component interventions. When compared with other single-component psychosocial interventions, MBI has its unique feature and stress reduction effect, helping family caregivers accept their thoughts and feelings in a non-judgmental manner. Since MBI has a positive effect in stress reduction among various populations, this review highlights that there is limited information about the applicability and the effect of incorporating MBI as an adjunct intervention in different multi-component dementia care programs, which can be considered in future research.

MBI can help caregivers to cultivate a non-judgmental attitude toward their caring tasks, role, and demands in an attempt to reduce the stress of caregiving. This attitude directly affects how the caregivers appraise and view stressful events in the caring process; and this interference may be one of the mechanisms of stress reduction. According to the Stress and Appraisal Theory by Lazarus and Folkman (1984), stress is a relationship between the person and the environment that is appraised by the person as exceeding his or her resources, and thus endangering his or her well-being. To

manage this stress in family caregivers of PWD, it is important to intervene and improve the caregivers' appraisal of demands (stressors) and adaptive capacities (Schulz and Martire 2004). The nonjudgmental attitude promoted in MBI may trigger the reappraisal process; and it is considered a therapeutic component of MBI to reduce one's stress level (Garland et al. 2009).

The mechanisms by which mindfulness improves physiological health and reduces stress levels have aroused much interest from researchers in the field of psychological health. In traditional cognitive therapy, the emphasis of interventions is on helping caregivers understand their life situations and encouraging them to develop alternative or positive thoughts and feelings (Beck and Dozois 2011). The concept of MBI is somewhat different, in that caregivers are facilitated to learn to recognize and accept their thoughts and feelings in a nonjudgmental manner (Shapiro and Carlson 2009). As was suggested in one recent systematic review and one critical discussion paper (Gu et al. 2015; Hölzel et al. 2011), the active ingredients of MBI can include attention control, body awareness, and emotional regulation; and its possible mediators to improving psychological health may involve repetitive negative thinking, selfcompassion, cognitive and emotional reactivity, and psychological flexibility. In addition, another similar model on mindful coping, put forward by Garland et al. (2011), also includes the concepts of Bdecentering[^] (i.e., seeing thoughts or feelings as objective events in the mind rather than personally identifying with them) and the positive reappraisal of stress in the MBI, to explain its stress reduction process and its effect on family caregivers of PWD. While there are a few models explaining the therapeutic effects of MBI, the five reviewed interventional studies have not yet examined any of the mechanisms of their actions. Therefore, further research on the

process and active components of MBI for caregivers of people with PWD is recommended.

Limitations of the Review

One of the main concerns of this review with small numbers of RCTs is the selection bias since a considerable number of recent systematic reviews and meta-analyses have used only a few RCTs. In addition, most of the studies identified were preliminary or pilot controlled trials and the sample sizes in the five reviewed studies varied greatly (n = 9–78). In which, only O'Donnell (2013) reported the sample size calculation. All of these affected the generalization of the findings of this review. The risk of bias in the studies was not taken into account when excluding studies from this review. Two studies were regarded as having a moderate to high risk of bias; however, they were included in this review. Therefore, the results should be treated with caution. This review was somewhat selective in study inclusion. It only focused on caregiving stress and depression outcomes but did not include quality of life and related outcomes of PWD (e.g., cognitive functioning). The studies in which the MBI mixed with other active components were also excluded.

Recommendations for Future Research

As only a few clinical trials (i.e., four RCTs and one quasiexperimental study) identified for this review, it signified that more research can be done to examine the effects of MBI for family caregivers of PWD. There are several recommendations for future research on this topic. First, there should be more valid and specific outcome measures adopted or developed for measuring the stress and related psychosocial wellbeing of family caregivers of PWD. In addition, several selfreporting

questionnaires were developed to measure level of mindfulness such as the Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al. 2008) during and after the MBI. This mindfulness assessment can provide data to understand the mediating effect or active components of MBI contributing to the significant benefits of the participants. However, in this review, two studies (Brown et al. 2015; Whitebird et al. 2013) did not measure the level of mindfulness practice/learning.

Second, the daily exercises or practices of mindfulness should be carefully monitored and recorded, together with reflective diary on their experiences and challenges/difficulties. These data would be useful to understand the participants' adherence to the MBI protocol and examine the relationship between the level of adherence and study outcomes (Garland et al. 2011).

Third, the caregivers of PWD often have high demands, duration, and volumes of caring tasks. The original MBSR program (weekly 150-min session for 8 weeks, plus a 7.5-h retreat) may not fit for them due to its high intensity and long duration. It may be difficult for most caregivers to put aside their caregiving tasks for a few hours of mindfulness sessions and daily practices, as well as attending a full-day mindfulness retreat. These may increase the attritions of the study or incompletion of the MBI. For instance, O'Donnell (2013) studied the effect of MBSR program and resulted in an attrition rate that was 17.2%; whereas, Brown et al.'s (2015) study reduced the duration of each MBI session to 1.5 h weekly resulting in an attrition rate of 10.5% and significantly reduced stress level after the intervention. The optimal dose, format, and content of MBI for these caregivers should be examined in order to maximize their attendance and adherence to and thus benefits from the program.

Lastly, the MBI in the included studies were based on different approaches although there were only five studies reviewed. Varied emphases or formats were found

in these programs, as well as different outcomes used in these studies, raised concerns about the homogeneity of the intervention protocols and findings of the studies. Therefore, there is a need for identifying the therapeutic components or a standardized intervention protocol of MBI for future research and subsequently for field practice. In addition, the comparison of the effectiveness between the two most common approaches to MBI (i.e., MBSR and MBCT) for caregivers of PWD on stress reduction and other psychosocial outcomes should also be made.

Conclusion

The findings of this review suggest that MBI can produce statistically significant reductions in stress and depression in family caregivers of PWD over a short-term follow-up, especially at immediately after the intervention. The findings of the five studies (four RCTs and one quasi-experimental study) reviewed suggest that MBI can be an effective approach to psychosocial intervention for family caregivers of PWD on stress and depression reduction, in adjunct/addition to the usual family supports and care. Compared with other psychosocial interventions, MBI indicates a larger effect on improving psychological stress and well-being of the family caregivers which may improve their quality of life or benefit the PWD. Although large effect of MBI were found, it is difficult for us to determine the magnitude of the improvement and how MBI impact the caregivers in this study. Moreover, the long-term effect of MBI was not found in this review and only four RCTs with relatively small sample sizes were reviewed. More controlled trials with larger and more diverse samples are needed before more definitive conclusions can be drawn. Future research should also measure the adherence to the MBI and the performance of practices of mindfulness, as well as the factors influencing the caregivers' learning of mindfulness, their

psychological outcomes, and the most appropriate dose of MBI. We would then be able to better understand its optimal and sustainable effects on these caregivers. Qualitative research can be conducted to understand the perceived difficulties or obstacles that caregivers face in practicing and maintaining mindfulness, especially after the completion of the intervention.

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