

Meta-Analysis of Nonpharmacological Interventions for Neuropsychiatric Symptoms of Dementia

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Objective: Behavioral and psychological symptoms are common in dementia, and they are especially stressful for family caregivers. Nonpharmacological (or psychosocial) interventions have been shown to be effective in managing behavioral and psychological symptoms, but mainly in institutional settings. The authors reviewed the effectiveness of community-based nonpharmacological interventions delivered through family caregivers.

Method: Of 1,665 articles identified in a literature search, 23 included unique randomized or pseudorandomized nonpharmacological interventions with family caregivers and outcomes related to the frequency or severity of behavioral and psychological symptoms of dementia, caregiver reactions to these symptoms, or caregiver distress attributed to these symptoms. Studies were rated according to an evidence hierarchy for intervention research.

Results: Nonpharmacological interventions were effective in reducing behavioral and psychological symptoms, with an overall effect size of 0.34 (95% CI=0.20–0.48; $z=4.87$; $p<0.01$), as well as in ameliorating caregiver reactions to these behaviors, with an overall effect size of 0.15 (95% CI=0.04–0.26; $z=2.76$; $p=0.006$).

Conclusions: Nonpharmacological interventions delivered by family caregivers have the potential to reduce the frequency and severity of behavioral and psychological symptoms of dementia, with effect sizes at least equaling those of pharmacotherapy, as well as to reduce caregivers' adverse reactions. The successful interventions identified included approximately nine to 12 sessions tailored to the needs of the person with dementia and the caregiver and were delivered individually in the home using multiple components over 3–6 months with periodic follow-up.

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It is projected that by 2050 there will be over 115 million people with dementia worldwide (1). The management of dementia may be complicated by the presence of behavioral and psychological symptoms (also known as neuropsychiatric symptoms), which include screaming, physical aggression, personality clashes (arguments between patients and caregivers), wandering, depression, resistance to help with activities of daily living (e.g., dressing, washing, toileting, and eating), suspiciousness, accusations, and not sleeping at night. Estimated rates of behavioral and psychological symptoms of dementia in community settings range from 61% to 88% (2–4). Behavioral and psychological symptoms rather than cognitive dysfunction, physical dependence, or functional impairment have been found to impose the greatest burden on family caregivers (5, 6) and to predict caregiver decisions to institutionalize persons with dementia (7, 8). Because of the significant role of family care in providing independence for people with dementia as well as relief for institutional care facilities, finding effective methods for managing behavioral and psychological symptoms of dementia in home care is both a public health and an economic priority.

Pharmacological treatments for behavioral and psychological symptoms of dementia have limited efficacy and can have adverse effects (9). Antipsychotic drugs in particular have been associated with an increased risk of stroke and death (9–12), and the performance of antidepressants has been disappointing (13, 14). Systematic reviews have demonstrated the effectiveness of nonpharmacological or psychosocial treatments for behavioral and psychological symptoms (15–17) as well as the lack of adverse effects (18). The terms “nonpharmacological” and “psychosocial” are commonly used interchangeably to describe interventions used to treat behavioral and psychological symptoms of dementia (16–18). In this review, we use “nonpharmacological,” which includes interventions addressing aspects of social and psychological behaviors and symptoms of dementia that do not involve drugs. Most nonpharmacological interventions have been tested in residential care, which does not address care in the community, where the majority of persons with dementia live. Our aim in this study was to review the effectiveness of family caregiver interventions in the management of behavioral and psychological symptoms occurring in people with dementia living in the community.

This article is featured in this month's AJP **Audio**, is discussed in an **Editorial** by Dr. Gitlin (p. 894), is an article that provides **Clinical Guidance** (p. A32), and is the subject of a **CME** course (p. 1005)

Method

Search Procedure

Searches were carried out in MEDLINE, Embase, PubMed, PsycINFO, and Scopus to identify experimental and clinical trials and single-case studies published from 1985 through July 2010. The search criteria combined condition (dementia or Alzheimer*), care provider (caregiver* or carer*), intervention (treatment*, therap*, counsel*, intervention*, support, support group*, psychosocial, or nonpharmacologic*), and symptoms (behavioral and psychological symptoms of dementia, BPSD, neuropsychiatric symptoms, aberrant motor behavior, aggression, agitation, anxiety, apathy, delusion*, depressi*, disinhibition, disturbing behavior, dysphori*, euphoria, hallucination*, irritab*, lability, screaming, sleep, or vocalization), using variations to include Commonwealth spellings. Terms were searched in titles and abstracts.

Outcomes

For persons with dementia, behavioral and psychological symptoms were rated on a variety of instruments measuring frequency (e.g., the Revised Memory and Behavior Problem Checklist) or severity (e.g., the Behavioral Pathology in Alzheimer's Disease Rating Scale) or both (e.g., the Neuropsychiatry Inventory) (for the full list, see Table S1 in the data supplement that accompanies the online edition of this article). For caregivers, outcomes were their reactions to these behavioral and psychological symptoms, usually rated on subsidiary scales embedded within those used for rating the symptoms (e.g., the Neuropsychiatry Inventory, the Revised Memory and Behavior Problem Checklist). Improvement for persons with dementia could be reduction in the frequency and/or severity of symptoms, and for caregivers, reductions in the severity of their reactions to the symptoms.

Selection Criteria for Review

We searched peer-reviewed journals with English-language studies that tested nonpharmacological interventions involving family caregivers. Studies were selected if they reported outcomes relevant to the frequency or severity of behavioral and psychological symptoms of dementia or caregiver reactions or distress attributed to these symptoms. Respite care interventions, drug trials for the treatment of behavioral and psychological symptoms of dementia, and review articles were excluded. Databases were searched for published or in-press articles that reported empirical research findings. Studies met criteria if they included more than five participants with a diagnosis related to dementia. The primary caregiver had to be a family member living with the person with dementia.

When two or more articles based on the same data and outcomes or similar studies by the same authors were available, the better or best study was selected for inclusion—that is, the most recent, the most relevant to behavioral and psychological symptoms of dementia, or the most complete study, or the one with the greater number of participants. Articles were excluded if the study included five or fewer participants, if care recipients had schizophrenia or bipolar disorder, or if outcomes relevant to behavioral and psychological symptoms of dementia were not assessed separately or quantitatively.

Methodological Quality Assessment

To establish interrater reliability, a second reviewer independently rated the methodological quality of 15 studies according to the National Health and Medical Research Council criteria for rating studies to assess the effectiveness of interventions (19, 20). Level I evidence, the highest level, is produced by a systematic review of level II studies; a level II study is a randomized

controlled trial. Level III-1 is a pseudorandomized controlled trial, level III-2 a comparative study with concurrent controls, and level III-3 a comparative study without concurrent controls. Level IV, the lowest level, is a case series with either posttest or pretest-posttest outcomes. Design characteristics, such as the use of randomization and control groups, were considered when rating studies. Because our analysis included only articles with original data and excluded systematic reviews, the highest level of evidence for an intervention in this review was level II. Only high-quality randomized (level II) or pseudorandomized (level III-1) studies were included.

Meta-Analysis

Meta-analysis was performed using Review Manager, version 5 (Cochrane Collaboration, Oxford, England). Effect sizes for continuous data were calculated as the standardized mean difference (Cohen's *d*) between treatment and control groups or between pre- and posttreatment assessments. Effect sizes were calculated for the most current follow-up assessment.

Results for random-effects models are displayed because tests for homogeneity and heterogeneity of studies under examination in terms of methods, type of intervention, sample characteristics, and outcome measures support the use of a random-effects model for most of the pooled estimates (21–23). Funnel plots, constructed for effects of interventions on behavioral and psychological symptoms of dementia and on caregivers, were symmetrical, indicating lack of publication bias (data not shown).

For studies that contained more than one control group with no post hoc differences, the control groups' scores were pooled. When there were differences in sample sizes, control scores were averaged using weighted mean difference scores. When studies provided difference scores and no posttest scores, these were used to calculate effect sizes.

Interventions were categorized according to the schema shown in Figure 1, by consensus. Studies generally used multiple types of intervention (see Table S1 in the online data supplement).

Results

Of 1,665 articles identified, 23 met all review criteria (24–46) (Figure 2). These studies, which collectively included 3,279 dyads in their intent-to-treat analyses, used a variety of techniques, often in combination. Results were largely positive or partially positive, with only three studies reporting neutral findings for all behavioral and psychological symptom outcomes (25, 28, 29) and one reporting negative results (26). No study reported adverse effects. Durations of interventions ranged from 6 weeks to 24 months. Sustainability of symptom outcomes was reported in 10 studies (29, 35, 37–39, 41–44, 46), with follow-ups ranging from 3 to 24 months after trial entry. Participant numbers were characteristically moderate, with 14 studies recruiting at least 80 caregivers or dyads. All but three studies had interventions delivered individually to caregivers or dyads (28, 36, 46). Two studies were telephone-based interventions with no face-to-face contact (37, 45).

Sixteen of the 23 studies met criteria for a randomized controlled trial (19, 20). Another seven that reported randomization but for which the method was not stated,

FIGURE 1. Categories and Elements of Interventions Included in the Review

- 1. Skills training for caregivers**
 - Managing behavioral and psychological symptoms of dementia
 - Communicating better with care recipient
 - Using role play, videos modeling behavior management strategies, cognitive-behavioral interventions, vignettes, live interviews
 - Enhancing care recipients quality of life, e.g., improving daily activities, increasing pleasant events
- 2. Education for caregivers**
 - Psychoeducation
 - Improving home care
 - Tailored advice and recommendations
 - Problem-solving methods
 - Improving support network
 - Computer-mediated automated interactive voice response
 - Planning: emergencies, legal, financial
- 3. Activity planning and environmental redesign**
 - Planning activities with caregiver for care recipient
 - Modifying care recipient's physical and social environment
- 4. Enhancing support for caregivers**
 - Social support
 - Web or telephone support
 - Strategies on how to access support
 - Family counseling
- 5. Self-care techniques for caregivers**
 - Health management
 - Stress management
 - Coping with change as a result of caregiving
 - Music therapy
 - Counseling
- 6. Miscellaneous**
 - Collaborative care with a health professional or care manager
 - Exercise for care recipient

was not obtained by correspondence with the author, was unclear, or was inadequate to conceal group allocation were classified as pseudorandomized.

Effect sizes for symptom outcomes for studies ranked level II and level III-1 are listed in Figure 3. The medium pooled-estimate effect size for these 17 studies, 0.34 (95% CI=0.20–0.48, $z=4.87$; $p<0.01$), suggests a positive overall effect of caregiver interventions on behavioral and psychological symptoms in persons with dementia.

Effect sizes for caregiver outcomes related to behavioral and psychological symptoms of dementia for studies ranked levels II and III-1 are listed in Figure 4. The low but significant pooled-estimate effect size for these 13 interventions, 0.15 (95% CI=0.04–0.26, $z=2.76$; $p=0.006$), suggests that caregiver interventions were effective in improving caregivers' reactions to these symptoms.

Discussion

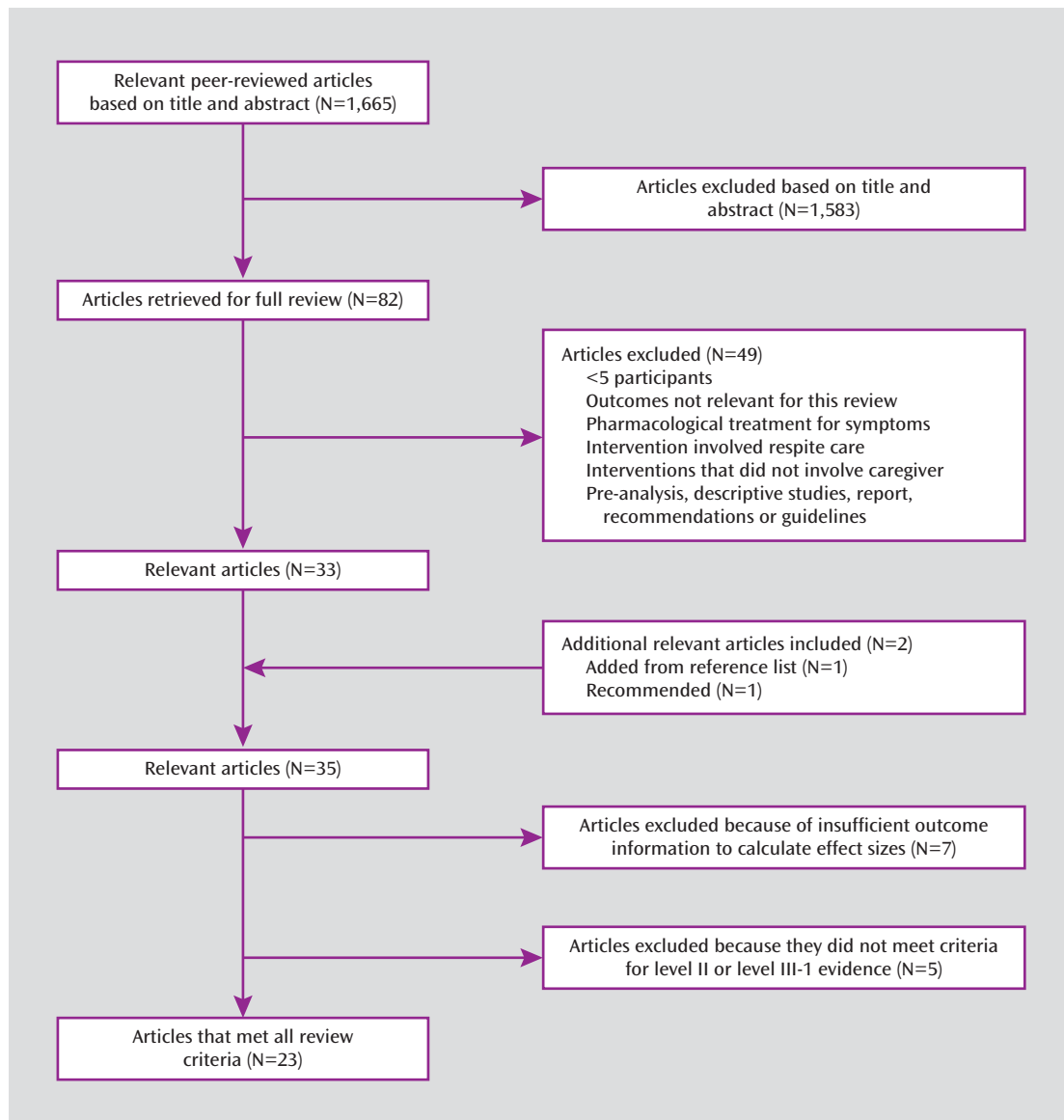
While the negative effects of behavioral and psychological symptoms of dementia on caregivers are well documented,

there is little appreciation of caregivers' ability to influence the occurrence and severity of these symptoms. This meta-analysis reveals that caregiver interventions can significantly reduce behavioral and psychological symptoms in the person with dementia as well as the caregiver's negative reactions to these symptoms. Ayalon and colleagues (18) reported that nonpharmacological interventions that addressed behavioral issues and included caregivers were more likely to be efficacious for managing behavioral and psychological symptoms of dementia, but the authors stressed the need for confirmatory studies. The present review found significant benefits for behavioral and psychological symptoms of dementia from high-research-quality interventions that targeted these symptoms and included the family caregiver. The availability of 23 high-quality trials from just the past two decades effectively delivering a wide range of interventions in the community indicates how the field has advanced. These effects are at least comparable to those of antipsychotics. From a report by Yury and Fisher (47) on behavioral and psychological symptoms of dementia treatment, a net effect size of 0.13 can be calculated from their findings of 0.45 (95% CI=0.16–0.74) for atypical antipsychotics and 0.32 (95% CI=0.10–0.53) for placebo. Similarly, Schneider and colleagues (48) reported an effect size of 0.18 ($z=3.43$; $p=0.0006$) in favor of antipsychotics in the treatment of behavioral and psychological symptoms of dementia. Unlike with antipsychotics, however, caregiver interventions had no adverse effects on caregivers or persons with dementia. In the only study with negative effects, behavior deteriorated over time but to similar degrees in the intervention and control groups (26). The three studies with no treatment effects on symptoms still had other positive outcomes for caregivers, namely, a reduction in caregiver depressive symptoms (28), a decrease in caregiver burden (29), and an increase in caregiver general well-being (25). Of these three studies, one (25) had a behavior management component in both the intervention and control groups and found improvements in both groups in the measure "bother associated with care recipient behaviors."

Limitations

Our findings are subject to several limitations. First, the use of multicomponent strategies and omnibus behavior rating scales prevented identification of which specific elements of interventions were effective for which behaviors. Second, not all interventions targeted behaviors; for example, Chang (26) focused on care generally. Third, the choice of instruments may have mitigated demonstration of effects. For example, about a third of the items in the Revised Memory and Behavior Problem Checklist concern activities of daily living, a third depressive symptoms, and a third other behaviors. Even if interventions had significant benefits for nondepressive behaviors, these effects would have been diluted by the nonbehavioral items. Fourth, caregivers' variability in knowledge, skills, and supports prior to intervention affect their capacity for improvement.

FIGURE 2. Summary of Study Selection



Where outcomes were adjusted for caregivers' scores on these variables at baseline, those with the lowest scores benefited the most (37). For example, in phase 2 of the Resources for Enhancing Alzheimer's Caregiver Health study of three different ethnic groups, the Latino-Hispanic group may have benefited significantly more because the intervention was provided in Spanish and may have been the first time participants had received such assistance (24).

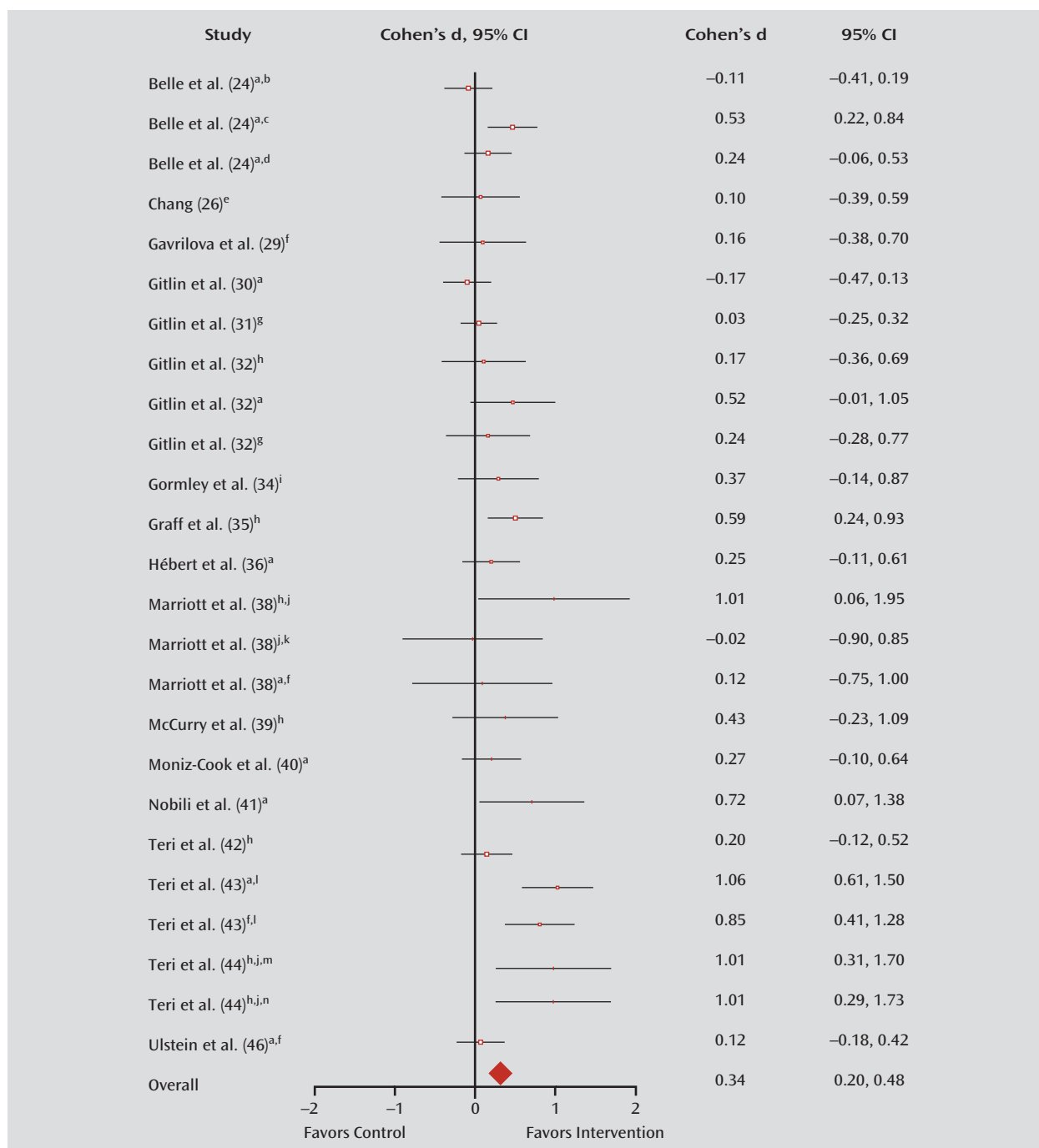
Fifth, the quality of research and sample sizes varied. While there is clearly room for improvement, the cost of such trials and the difficulty in recruitment of representative samples of caregivers and people with dementia are considerable. Sixth, nonpharmacological intervention studies appear to recruit patients with less severe behavioral disturbances than do drug trials and usually exclude

psychotic patients. Seventh, a limitation of nearly all pharmacological and nonpharmacological studies is the reliance on reports of behaviors, which may be biased, rather than on direct observation. Finally, for many of the interventions, we were unable to calculate the effect size or the sustainability of outcomes. Of the 10 studies that reported follow-up (29, 35, 37–39, 41–44, 46), symptomatic and/or related caregiver improvements were maintained in eight studies (35, 37, 39, 41–44, 46).

Implications

Fine-grained questions regarding which elements of interventions are effective for which behavioral and psychological symptoms of dementia delivered by which caregivers to which persons with dementia require further attention. Questions about the optimal duration, frequency,

FIGURE 3. Efficacy of Interventions for Behavioral and Psychological Symptoms of Dementia



^a Frequency of behavioral symptoms in dementia.

^b Black/African American group.

^c Hispanic/Latino group.

^d White/Caucasian group.

^e Severity of deterioration of behavioral symptoms in dementia.

^f Severity of behavioral symptoms in dementia.

^g Presence or absence of behavioral symptoms in dementia.

^h Depressive symptoms.

ⁱ Symptomatology and severity of behavioral symptoms in Alzheimer's disease.

^j Effect size calculated as pooled estimates from two control group scores that had no significant between-group differences.

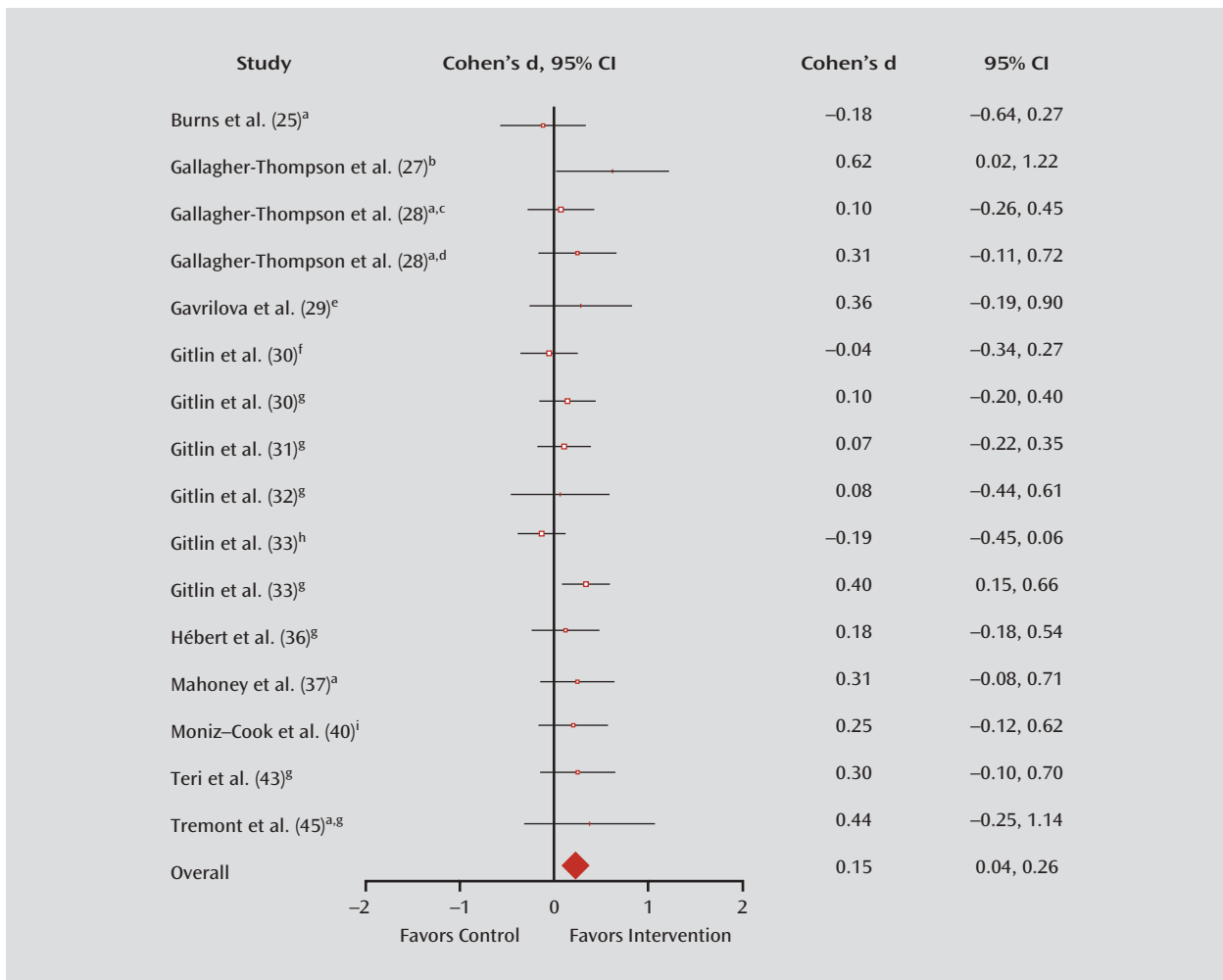
^k Frequency and severity of psychiatric symptoms in dementia.

^l Effect size calculated as change from pretest to posttest mean scores within the intervention group.

^m BT-PE=behavior therapy with pleasant events.

ⁿ BT-PS=behavior therapy with problem solving.

FIGURE 4. Efficacy of Interventions for Caregiver Outcomes Related to Behavioral and Psychological Symptoms of Dementia



^a Bother associated with behavioral symptoms of dementia.

^b Stress associated with troublesome behavioral symptoms of dementia.

^c Anglo group.

^d Latino group.

^e Distress associated with behavioral and psychological symptoms in dementia.

^f Self-efficacy in managing behavioral symptoms of dementia.

^g Upset associated with behavioral symptoms of dementia.

^h Confidence managing most distressing behavioral symptom of dementia.

ⁱ Management of behavioral symptoms of dementia.

and setting of interventions cannot be answered empirically from these data. Successful interventions included approximately nine to 12 sessions tailored to the needs of the person with dementia and the caregiver and were delivered individually in the home using multiple components over 3–6 months interspersed with telephone sessions and subsequent individual or group telephone follow-ups. Behaviors more likely to respond to such interventions appear to be agitation, aggression, disruption, shadowing, depression, and repetitive behaviors rather than psychosis. From the emerging pattern for success, we recommend adopting interventions that are multicomponent, tailored to the needs of the caregiver and the person with dementia, and delivered at home with periodic follow-ups.

The implications from this meta-analysis are extensive. For policy makers, our findings suggest that supporting programs to work with caregivers would be an efficient and potentially sustainable model. For clinicians, caregivers, and persons with dementia, there is a preference for trying nonpharmacological approaches first and avoiding or delaying the use of medications, which have the potential for serious adverse effects and high attrition (9). Despite the onus assumed by caregivers in these interventions, caregivers reported significant benefits to their own psychological health (24–28, 30–33, 35, 37, 38, 40, 43, 44), general health (35, 38), general well-being (25, 31, 33), overall quality of life (24, 35), caregiving burden (29, 33, 43, 45), and caregiving skills (30–32, 40, 41). For researchers, our

findings suggest numerous questions that require investigation; in addition to those outlined above, information about cost-benefit and delay in institutionalization will be persuasive in advocating for funding for such interventions. Systematic reporting of sufficient data to allow comparative analysis should be complemented by at least one follow-up to test sustainability.

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