

# Assessment and Treatment of Nursing Home Residents with Depression or Behavioral Symptoms Associated with Dementia: A Review of the Literature

Mark Snowden, MD, MPH, Kersten Sato, and Peter Roy-Byrne, MD

Depression and the behavioral symptoms associated with dementia remain two of the most significant mental health issues for nursing home residents. The extensive literature on these conditions in nursing homes was reviewed to provide an expert panel with an evidence base for making recommendations on the assessment and treatment of these problems.

Numerous assessment instruments have been validated for depression and for behavioral symptoms. The Minimum Data Set, as routinely collected, appears to be of limited utility as a screening instrument for depression but is useful for assessing some behavioral symptoms. Laboratory evaluations are often recommended, but no systematic study of the outcomes of these evaluations could be found. Studies of nonpharmacological interventions outnumber those of pharmacological interventions, and randomized, controlled trials document the efficacy of many interventions. Antidepressants are effective for major depression, but data for minor depressive syndromes are limited. Recreational activities are effective for major and minor depression categories. Neither pharmacological nor nonpharmacological interventions totally eliminate behavioral symptoms, but both types of interventions decrease the severity of symptoms. In the absence of comparison studies, it is unclear whether one approach is more effective than another. Despite federal regulations limiting their use, antipsychotics are effective and remain the most studied medications for treating behavioral symptoms, whereas benzodiazepines and antidepressants have less support. Structured activities are effective, but training interventions for behavioral symptoms had limited results. There are sufficient data to formulate an evidenced-based approach to treatment of depression and behavioral symptoms, but more research is needed to prioritize treatments. *J Am Geriatr Soc* 51:1305–1317, 2003.

From the Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, Washington.

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Address correspondence to Mark Snowden, MD, MPH, Harborview Medical Center, Box 359911, 325 9th Avenue, Seattle, WA 98104. E-mail: snowden@u.washington.edu

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The American Geriatrics Society and the American Association for Geriatric Psychiatry organized an expert panel to make recommendations for improving the quality of mental health care in U.S. nursing homes and to write a consensus statement presenting the recommendations.<sup>1</sup> The expert panel requested a literature review for use in formulating its recommendations. The focus of the panel was on the nursing home setting, because it is unique in patient characteristics and systems issues, and on the assessment and treatment of depression and dementia-related behavioral symptoms, because these are the most common mental health problems of nursing home residents. Many guidelines and opinion articles on these conditions have been published, but this review includes only those studies providing outcome data on the assessment and management of depression or behavioral symptoms. Pharmacological and nonpharmacological interventions are reviewed. For each condition, the review presents data first on assessment and then on treatment. This is followed by comments on the strengths and weaknesses of the data and suggestions for future research. Studies are presented in the order of strength of design rather than by positive or negative findings.

## METHOD

Peer-reviewed journal articles were located using computerized searches of four databases: MEDLINE back to 1970; PsychINFO; Drugs and Pharmacology EMBASE (Excerpta Medica Database); and CINAHL (Cumulative Index to Nursing and Allied Health Literature). Review articles and consensus statements known to the panel's writer-researcher or suggested by expert panel members were also selected, and bibliographies of articles were reviewed to identify additional studies.<sup>2–14</sup> Articles submitted by panelists were also reviewed, including articles authored by panelists that were still in press. Studies presented as letters to the editor and individual case reports were excluded. Articles published before 1970 were excluded because diagnoses at that

time did not employ current common diagnostic criteria. Studies including both nursing homes and other settings were included if nursing home subjects clearly constituted half or more of the study sample. In cases where exact numbers of nursing home subjects were not indicated, studies were included as long as it was clear that some of the subjects were nursing home residents.

## RESEARCH ON DEPRESSION

### Assessment

Several screening and assessment scales developed in outpatient settings have been validated in nursing homes. In one study, across all subjects, the 30-item Geriatric Depression Scale (GDS) was found to have sensitivity and specificity of 63% and 83%, respectively.<sup>15</sup> These values increased to 84% sensitivity and 91% specificity for residents with Mini-Mental State Examination (MMSE) scores of 15 or greater. In another study, the GDS (30 items) and the Brief Carrol Depression Rating Scale were found to have the best criterion validity when used in residents with greater than 50% prorated MMSE scores, and the GDS (15 items) and the Center for Epidemiologic Studies—Depression scale were rated as having fair validity.<sup>16</sup> The Beck Depression Inventory was found to be unfeasible for most study participants, possibly because of the combined effect of its length and four-point rating for each item. One study found that nursing home staff use of instruments such as the Cornell Scale for Depression in Dementia or the Hamilton Depression Rating Scale (HAMD) increased sensitivity of depression diagnoses by staff from approximately 32% to 50%.<sup>17</sup>

Implementation of the Minimum Data Set (MDS) has prompted several studies comparing the validity of the MDS with that of other routinely used research instruments. The six such studies located included more than 400 subjects in more than 20 nursing homes.<sup>18–23</sup> These studies found that the MDS, as routinely collected by nursing home staff, has limited criterion validity, with correlation coefficients ranging from 0.15 to 0.44. In a study of 85 subjects,<sup>21</sup> it was found that the MDS identified only 24% of residents with a GDS score greater than 10. The study also found that, with a variation of the original MDS in which the seven items of the Sad or Anxious Mood section were summed and completed by research staff who also completed HAMD and Cornell Scale ratings, the MDS scale scores were statistically significantly associated with treatment response status as determined by other research instruments. Similarly, the MDS-based depression rating scale created by another study,<sup>22</sup> consisting of seven items of the MDS, when completed by nursing home staff observing the research nurse complete a HAMD, was found to have sensitivity and specificity of 91% and 69%, respectively, in comparison with the criterion standard of psychiatric diagnosis.

Some guideline and opinion articles recommend routine laboratory testing for anemia, thyroid disease, infection, or metabolic disturbances, but this review found no studies of the systematic physical or laboratory evaluation of depressed nursing home residents. Thus, the clinical utility or cost-effectiveness of these practices cannot be determined.

## Treatment

### Nonpharmacological Interventions

Nonpharmacological treatment trials of depression in nursing home residents typically use validated scales for determining outcomes but inconsistently use a diagnosis of major depression as an inclusion criterion. This review includes studies of six nonpharmacological interventions for the management of depression (Table 1).<sup>21,24–30</sup> In five of the six, entry was based on a depression scale score without clinical diagnosis of major depression. Four of these studies were randomized controlled trials (RCTs); all four demonstrated statistically significant improvement in depression. One study<sup>21</sup> used a peer volunteer intervention with peers supervised by a social worker to treat 85 residents with entry MMSE scores of greater than 19 in three nursing homes, all entering with GDS scores above 10. Depression scale change scores were statistically significantly improved in the intervention group (40% reduction in GDS vs 1% increase in controls) even after adjusting for the greater use of antidepressants in intervention than in control subjects (50% vs 17%). Another study<sup>24</sup> compared the results of group cognitive therapy and music therapy in 60 residents included on the basis of Beck Depression Inventory scores and found group cognitive therapy to be superior (30% reduction in Beck scores with cognitive therapy vs 3% with music therapy). One investigator<sup>25</sup> instituted therapeutic recreation activity (staff taking depressed residents around the facility grounds with the resident seated in a wheelchair attached in tandem to the front of a bicycle for 1 hour daily 5 days a week). GDS short-form scores improved significantly (45% reduction vs 8% increase in controls). A study using a variety of recreational therapy activities, documented statistically significant HAMD score improvement in 22 residents with major and minor depression.<sup>26</sup> A crossover, double-blind, controlled trial comparing bright light (10,000 lux) therapy with a control condition of lower light found significant improvement in GDS scores (24% lower) after bright-light exposure versus worsening in controls.<sup>27</sup>

### Health Service Models

This review includes two studies of health services models for the delivery of depression treatment to long-term care residents. One study<sup>29</sup> used a psychiatric registered nurse, working in consultation with a psychiatrist who did not see the subjects, to provide consultation to a nursing home. In chart review follow-up of 100 residents, 68 were rated “improved.” An Australian study of residential care subjects<sup>30</sup> used a multifaceted intervention consisting of group activities, staff education, and limited psychiatric consultation to demonstrate small but statistically significant improvements (12% intervention vs 4% controls) as measured by the GDS, which was used for entry criteria and outcome measurement.

### Antidepressants

Of seven antidepressant studies, three were randomized, double-blind, placebo-controlled trials (Table 2).<sup>31–37</sup> Investigators<sup>31</sup> studied the use of nortriptyline at an average dose of 65 mg/day in residents with major depression and HAMD scores of 18. HAMD totals and Clinical Global Impression (CGI) scores significantly improved in the

**Table 1. Nonpharmacological Treatments for Depression in Nursing Home Residents**

Author, Year	Treatment	Design	N	Length	Results
McCurren et al. 1999 <sup>21</sup>	Supervised peer volunteer program	RCT, usual-care	85	24 wk	Statistically significant 40% decrease in GDS scores versus 1% in controls
Zerhusen et al. 1991 <sup>24</sup>	Group cognitive versus music therapy versus usual care	RCT, usual-care control	60	10 wk	Statistically significant 30% decrease in depression scale score with cognitive versus 3% with music versus worsening with usual care
Fitzsimmons et al. 2001 <sup>25</sup>	Therapeutic recreation: wheelchair-biking in tandem	RCT	40	2 wk	Statistically significant 45% decrease in GDS scores versus 8% increase in controls
Rosen et al. 1997 <sup>26</sup>	Recreation therapy activity	RCT	22	6 mo	36% response rate with intervention versus 0% control
Sumaya et al. 2001 <sup>27</sup>	Bright-light therapy	Crossover, double blind, control	11	3 wk	24% improvement in GDS score versus worsening in controls
Kaas et al. 1999 <sup>28</sup>	Group cognitive behavioral therapy	Qualitative	11	8 wk	No ratings of depression severity outcome
Santmyer et al. 1991 <sup>29</sup>	Psychiatric nurse consultation	Chart review	100	40 mo	68% of patients improved via chart review
Llewellyn-Jones et al. 1999 <sup>30</sup>	Multifaceted	Observational	220	9.5 mo	Statistically significant 11.3% change in GDS with intervention versus 5% with control

RCT = randomized controlled trial; wk = weeks; GDS = Geriatric Depression Scale; mo = months.

nortriptyline group (58% at least “much improved” on CGI scores vs 8% in controls), but because of side effects, 34% of subjects randomized to nortriptyline were discontinued. A study<sup>32</sup> found that, in demented subjects, low-dose

nortriptyline (9 mg) is more effective (42% responders) than regular doses of nortriptyline (14% responders). A randomized, double-blind trial comparing sertraline with placebo restricted to severely demented nursing home

**Table 2. Pharmacological Treatments for Depression in Nursing Home Residents**

Author, Year	Treatment	Design	N	Length	Results
Katz et al. 1990 <sup>31</sup>	Nortriptyline	RCT, placebo control	30	7 wk	Statistically significant 40% change in HAMD scores with nortriptyline versus 11% with placebo
Streim et al. 2000 <sup>32</sup>	Nortriptyline: regular (49 mg) versus low (9 mg)	RCT, placebo control	69	8 wk	Responders: 38% with regular versus 36% with low dose; statistically significant 42% HAMD improvement in cognitively impaired with lower dose
Magai et al. 2000 <sup>33</sup>	Sertraline for severely demented	RCT, placebo control	31	8 wk	No significant difference between sertraline and placebo
Trappler et al. 1996 <sup>34</sup>	Fluoxetine	Open label	29	12 wk	41% decrease in HAMD scores
Trappler et al. 1998 <sup>35</sup>	Fluoxetine, sertraline, paroxetine	Open label	50	12 wk	42% response rate across all treatment groups; 93% in cognitively intact versus 7% responders in demented subjects
Oslin et al. 2000 <sup>36</sup>	Sertraline versus nortriptyline	Open label, parallel	97	8 wk average	Statistically significant 35% improvement in HAMD scores with nortriptyline versus 13% with sertraline
Rosen et al. 2000 <sup>37</sup>	Sertraline	Open label	12	6 wk	Statistically significant improvement in HAMD scores

RCT = randomized controlled trial; wk = weeks; HAMD = Hamilton Depression Rating Scale.

residents,<sup>33</sup> found no significant improvement in depression severity using the Cornell Scale for Depression in Dementia. Three additional open-label trials also reported decreased efficacy of selective serotonin-reuptake inhibitor (SSRI) agents in demented subjects, and results of two of the trials suggest improvement in nondemented residents.<sup>34–36</sup> A single open-label study of the use of antidepressants in residents with minor depression found an SSRI to be effective in improving eight of the 12 subjects to a point of remission from minor depression.<sup>37</sup>

### **Depression Summary**

Several depression scales have been validated for use in nursing homes. Self-report scales such as the GDS are better than routine completion of the MDS for identifying depressed residents but have decreased utility in identifying depression in severely demented residents. Interviewer-rated instruments such as the Cornell Scale for Depression in Dementia and the HAMD function well for residents with or without significant cognitive impairment but may require some training for use by nursing home staff. Significant resource limitations make the routine use of instruments beyond the MDS difficult, but no other effective screening strategies have been developed. Alternative methods of performing and quantifying the MDS performed well with trained research personnel but need to be tested under routine nursing home conditions. Effective nonpharmacological interventions include various types of structured recreational activities and more specialized psychotherapy, particularly cognitive psychotherapy, but specialized psychotherapy may not be readily available in most nursing homes. Controlled trials of antidepressants are limited, but data suggest the efficacy of nortriptyline, albeit with significant side effects. Several studies suggest efficacy of SSRIs in cognitively intact residents but possibly limited efficacy in those who are severely demented. No studies were found that systematically combined antidepressants with nonpharmacological interventions to investigate the possible added benefit of a combined approach. These types of studies, along with placebo-controlled trials of newer antidepressants for major and minor depression, are needed.

## **Research on Dementia-Related Behavioral Symptoms**

### **Assessment**

Numerous instruments for assessing and documenting behavioral symptoms are available, but there is little agreement about their routine use by nursing home staff. Behavioral symptoms are identified without the use of screens and, unlike depression, are not likely to go unrecognized by staff, but valid quantitative data from behavioral instruments can help to determine when and how to intervene. Some studies investigating interventions for symptoms such as agitation rely on staff identification and referral but require a threshold severity from a quantitative instrument to determine whether subjects are eligible for the study and intervention. The MDS is routinely used to assess behavior problems. Three studies comparing the MDS with research instruments<sup>18,19,38</sup> were found to demonstrate good interrater reliability coefficients (0.63)<sup>18</sup> and concurrent validity correlations of 0.51 to 0.58.<sup>19,38</sup> Only one study using nurse aide ratings of

positive and negative affect found poor correlations with MDS items ( $-0.02$  and  $-0.03$ , respectively).<sup>20</sup>

Reviews of the assessment and management of dementia-related behavioral symptoms often recommend evaluation of social, environmental, and acute medical problems, yet few systematic evaluations of the contributions of these factors exist.<sup>39–41</sup> In a chart review study of 408 residents, investigators<sup>41</sup> found physically aggressive behaviors to be more associated with cognitive impairment and activity of daily living dysfunction than with other factors; they also found that physically aggressive residents were not likely to have acute physical illness or pain problems, but residents with verbal agitation were found to have statistically significant associations of pain and physical illness diagnoses. Using MDS data,<sup>40</sup> in a retrospective review of more than 8,500 residents across three states, investigators examined variables associated with wandering behavior and found several items to be associated with an increased odds ratio (OR) for wandering: constipation (OR = 1.82), dementia diagnosis (OR = 19.4), pneumonia (OR = 3.15), and antipsychotic use (OR = 1.70).

### **Treatment**

In the nursing home setting, studies of nonpharmacological interventions outnumbered studies of medication. In nearly all of the intervention studies, multiple types of dementia were included. The most commonly studied symptom, agitation, can be subdivided according to types (e.g., physically aggressive, nonaggressively physical, verbally disruptive, wandering, hiding, and hoarding), but most intervention studies do not target a specific type. Reports of several nonpharmacological trials indicate that subjects continued to take psychotropic drugs and that dosing was occasionally adjusted during the trial. Nearly all the reviewed studies used direct observation of behaviors, validated scales, or both to assess the outcomes. Therapies using sensory stimulation and activities outnumbered those using more classical behavior modification, training, and environmental enhancement techniques.

### **Activities-Based Interventions**

Most of the studies of nonpharmacological interventions employ an observational design. Three of the 10 activities-based interventions were RCTs, all using direct observation of behaviors, validated scale ratings, or both for outcome assessment. (See Table 3 for a summary of all the nonpharmacological studies reviewed.)<sup>42–87</sup> In one study,<sup>42</sup> group activities by a researcher-hired group therapist were combined with guidelines for the use of thioridazine in the management of psychotic and behaviorally dangerous subjects, along with a staff education component. Blinded observational ratings by a research psychiatrist and nonblinded ratings by registered nursing staff revealed a 71% drop in categorically determined prevalence of agitation in the intervention group versus 49% in the control group (OR = 0.38,  $P = .037$ ). In the physical activity-based intervention study<sup>43</sup> age-appropriate exercises and walking activity were compared with a control condition of sleep hygiene improvement in 29 residents. Observations of agitation decreased 22% in the 15 intervention subjects but increased 150% in the control

**Table 3. Nonpharmacological Interventions for Behavioral Symptoms Associated with Dementia in Nursing Home Residents**

Author, Year	Treatment	Design	N	Length	Results
<b>Activities</b>					
Rovner et al. 1996 <sup>42</sup>	Activities	RCT	89	6 mo	Statistically significant 71% reduction in agitation with intervention versus 49% with control
Alessi et al. 1999 <sup>43</sup>	Exercises versus sleep hygiene	RCT	29	15 wk	Statistically significant 22% decrease in agitation with exercise versus 150% increase with control
Camberg et al. 1999 <sup>44</sup>	Simulated presence—audio	RCT	54	71 d	No significant differences on agitation scale
Woods et al. 1995 <sup>45</sup>	Simulated presence	Observational	9	2 mo	Statistically significant 60% decrease in disruptive behavior
Holmberg, 1997 <sup>46</sup>	Walking program	Observational	11	1 year	Statistically significant 30% decrease in staff incident reports of aggression
Cohen-Mansfield et al. 1997 <sup>47</sup>	1:1 socialization versus family video versus music listening	Observational	32	12 wk	Significant decrease in verbal disruption per observation; no significant decrease in nurse-rated agitation scale
Buettner et al. 1996 <sup>48</sup>	Recreational therapy	Observational	34	8 wk	50% fewer agitation incidents
Hall et al. 1997 <sup>49</sup>	Video activity	Observational	36	63 min	No significant decrease in agitation
Aronstein et al. 1996 <sup>50</sup>	Recreational activities	Qualitative	15	6 wk	73% of staff report recreational activities helped “somewhat”
Churchill et al. 1999 <sup>51</sup>	Pet therapy	Observational	28	1 hr	No quantitative analysis; reported decreased agitation
<b>Training</b>					
McCallion et al. 1999 <sup>52</sup>	Nurse aide training	RCT	105	6 mo	Statistically significant 20% decline in verbal agitation; no significant change in physically aggressive and nonaggressive behaviors
Proctor et al. 1999 <sup>53</sup>	Training and education	RCT, facility level	120	6 mo	No difference in behavior change score
Beck et al. 2002 <sup>54</sup>	ADL therapy versus psychosocial versus combined ADL therapy and psychosocial	RCT, placebo control	179	20 wk	No reduction in disruptive behavior scores
Williams et al. 1994 <sup>55</sup>	Inservice training	Observational	2	Not reported	Statistically significant decrease in incident reports per chart review
Cohen-Mansfield et al. 1997 <sup>56</sup>	Inservice training	Observational	NA	1 mo	No change in observed behavior, increased restraint use
Werner et al. 1994 <sup>57</sup>	Restraint reduction	Observational	142	2 mo	Decreased restraint and decreased agitation scores
Mentes et al. 1989 <sup>58</sup>	Nurse aide training	Observational	342 beds	Not reported	Decrease in incident reports; no statistical analysis
<b>Sensory therapy</b>					

*continued*

Table 3. (continued)

Author, Year	Treatment	Design	N	Length	Results
Gerdner, 2000 <sup>59</sup>	Music therapy	Crossover	39	18 wk	Statistically significant 65% decrease in observed agitation
Groene, 1993 <sup>60</sup>	Music therapy versus reading	Parallel group	30	15 wk	No significant change in wandering
Goddaer et al. 1994 <sup>61</sup>	Music during meal	Observational	29	4 wk	On average, agitation decreased 63% ( $P < .0001$ )
Brottons et al. 1996 <sup>62</sup>	Live music therapy	Observational	20	2.5 wk	Statistically significant 30% decrease in mean agitation scale scores
Tabloski et al. 1995 <sup>63</sup>	Music	Observational	20	30 min	Significant decrease in mean agitation score (24 before vs 18 during vs 20 after)
Clark et al. 1998 <sup>64</sup>	Music during bath	Observational	18	4 wk	Statistically significant 46% decrease in observed agitation
Thomas et al. 1997 <sup>65</sup>	Music during bath	Observational	14	9 baths	Statistically significant 46% decrease in aggressive behavior scale scores
Casby et al. 1994 <sup>66</sup>	Music	Observational	3	16 d	Statistically significant decrease in observed verbal disruption in two residents
Snyder et al. 1996 <sup>67</sup>	Music and hand massage	Observational	5	5 wk	Trend level decrease in aggression ( $P = .09$ )
Kim et al. 1999 <sup>68</sup>	Hand massage	Observational	30	25 d	Statistically significant 42% decrease in agitation scale scores
Thorpe et al. 2000 <sup>69</sup>	Bright-light therapy	Observational	16	2 wk	Statistically significant 9% improvement in agitation scale scores
Lovell et al. 1995 <sup>70</sup>	Bright-light therapy	Observational	6	4 wk	Statistically significant 50% decrease in mean agitation scores
Brooker et al. 1997 <sup>71</sup>	Massage and aroma	Observational	4	3 mo	One subject with significant improvement
Burgio et al. 1996 <sup>72</sup>	White noise	Observational	13	32 d	Nine of 13 were responders
Snyder et al. 1995 <sup>73</sup>	Hand massage	Crossover	26	35 d	No consistent change in number of observed agitation behaviors
Denney, 1997 <sup>74</sup>	Music during meal	Observational	9	4 wk	No statistical analysis; reported 37% decrease in mean agitation scores
Gerdner et al. 1993 <sup>75</sup>	Music (individualized)	Observational	5	2 wk	No statistical analysis; 47% to 80% decrease in agitation
Behavior therapy Matteson et al. 1997 <sup>76</sup>	Piaget-based therapy planning	Facility-level group parallel study	93	18 mo	39% attrition; report decrease in intervention versus control group behavior problem scores.
Rogers et al. 1999 <sup>77</sup>	Behavior rehabilitation	Observational	84	25 d	Statistically significant decrease in behaviors
Doyle et al. 1997 <sup>78</sup>	Behavior modification	Observational	12	3 wk	29% to 43% responders

continued

Table 3. (continued)

Author, Year	Treatment	Design	N	Length	Results
Hussian, 1988 <sup>79</sup>	Stimulus enhancement	Observational	5	Not reported	85% reduction in frequency of observed agitated behaviors
Heard et al. 1999 <sup>80</sup>	Differential reinforcement	Observational	4	Not reported	No statistical analysis; reports 50% to 80% reduction in wandering
Boehm et al. 1995 <sup>81</sup>	Behavior modification	Observational	2	16 wk	Decrease in frequency of agitation; no statistical analysis
Environmental					
Cohen-Mansfield et al. 1998 <sup>82</sup>	Enhanced environment	Observational	27	8 wk	No significant change in exit-seeking or other behavioral symptoms
Chafetz, 1990 <sup>83</sup>	Tape grid on floor	Observational	30	6 wk	No significant benefit from intervention
Whall et al. 1997 <sup>84</sup>	Natural sights and sounds	2-group parallel	31	2 baths	Statistically significant decrease in observed agitation
Namazi et al. 1992 <sup>85</sup>	Unlocked door	Observational	22	100 hr	Decrease in observed behavior counts
Cleary et al. 1988 <sup>86</sup>	Special care unit	Observational	11	6 mo	Reported 53% decrease in agitation level
Middleton et al. 1997 <sup>87</sup>	Individualized environmental change	Observational	4	14 wk	Reported 3 patients improved

RCT = randomized controlled trial; mo = months; wk = weeks; d = days; min = minutes; hr = hours; ADL = activity of daily living; NA = not applicable.

group. The third RCT found no differences when comparing an audio tape-simulated presence of family members to usual care in 54 agitated residents.<sup>44</sup> All the remaining observational studies of activities therapy suggest some degree of improvement (12% to 60%); three of the remaining seven studies achieved statistical significance,<sup>45-47</sup> and one reached a trend level of statistical significance ( $P < .1$ ).<sup>48</sup>

### Training Interventions

Seven nursing home training interventions were identified, including three RCTs, all with negative or mixed results. The study of nurse aide training<sup>52</sup> found statistically significant lowering of verbal agitation (20% decrease) but no significant lowering of physically aggressive or nonaggressive behaviors. A study<sup>53</sup> using seven 1-hour training and education seminars for staff coupled with weekly visits by a research registered nurse for treatment plan development found no significant differences in behavior change scores between the intervention and the usual-care control nursing homes. Yet another study<sup>54</sup> compared two interventions in which research nurse aides were trained to implement interventions for care in activities of daily living, in psychosocial activities, and in a combination of both. The investigator compared these interventions with usual care and a placebo condition in which research staff had regular visits with residents. This elegant RCT, using 179 subjects in seven nursing homes, found no reduction in disruptive behaviors for any of the

three intervention groups. One prepost study of nurse aide training found a statistically significant 79% decline after the training in the number of incident reports of aggressive behaviors for 2 residents.<sup>55</sup> Another study found no change in agitated behaviors and an unexpected increased use of physical restraints after the training.<sup>56</sup>

### Sensory Modulation

The majority of the 20 sensory modulation studies reviewed were music listening activities. No RCTs were found, but one study<sup>59</sup> used a crossover design to demonstrate significantly decreased agitation in 39 subjects provided with music individualized to family-indicated musical preferences (65% decrease in observed agitation) as opposed to standard classical music (29% decrease). One study<sup>60</sup> targeted wandering behavior with a music-listening intervention in 30 subjects via a parallel group design and found no significant difference in wandering behavior. The majority of the music-listening interventions show some degree of improvement (25-54% reductions in agitation) during the activity; six observational design studies reached statistical significance,<sup>61-66</sup> and one showed a trend-level statistical significance.<sup>67</sup> One of three hand massage or touch studies found a statistically significant 42% decrease in agitation during, but not after, the time of hand massage in 30 subjects.<sup>68</sup> Two bright-light therapy studies using observational designs in a total of 22 subjects each found statistically significant reductions (9-50%) in agitation measured with standardized agitation scales.<sup>69,70</sup>

### **Behavioral Modification**

Two of the six behavioral modification studies were relatively large, having sample sizes of 93 and 84. One study<sup>76</sup> used Piagetian theory to categorize demented agitated residents by developmental stages and design stage-based treatment plans. Only 61% of subjects completed this 18-month intervention. At 3 months, there were no significant improvements, but at 12 and 18 months, there were significantly lower scores for problem behavior in the intervention than in the parallel control group. Another study<sup>77</sup> used a behavior rehabilitation approach to improve behaviors during morning care routines in 84 subjects. There was a small but statistically significant decrease from 0.05 agitated behaviors per minute baseline to 0.02 per minute after the intervention. Each of the remaining four studies reported improvements but averaged fewer than 15 subjects per study and varied greatly in quantitative analysis.<sup>78–81</sup>

### **Environmental Enhancements**

Six of the studies reviewed used environmental enhancements and manipulation.<sup>82–87</sup> Two of these were observational studies that targeted exit-seeking and wandering behaviors. Neither found statistically significant improvements, with sample sizes of 27 and 30, respectively.<sup>82,83</sup> A study targeting bath-related agitation used pictures of birds, recordings of bird songs, and sounds of babbling streams with 31 subjects divided into two parallel groups and found that the intervention group had 6.7 fewer agitated behaviors per bath than the control group ( $P = .004$ ).<sup>84</sup>

### **Pharmacological Interventions**

In pharmacological interventions for behavioral symptoms (Table 4), trials of antipsychotic medications outnumber trials of other agents, such as antidepressants or anticonvulsants.<sup>88–118</sup> Most of the studies controlled the use of other psychotropic drugs during the trials, but their reports do not indicate whether nonpharmacological interventions were being used before or during the trials. The trials typically included behaviorally disturbed residents meeting an entry threshold of agitation usually defined using a validated scale. Several studies included subjects who were simultaneously psychotic and agitated.

Seven randomized, placebo-controlled, double-blind trials of antipsychotics were reviewed. In the four larger trials, each having at least 200 subjects, a modest statistically significant effect was found.<sup>88–90,92</sup> In one trial,<sup>88</sup> lower-dose risperidone (0.5 mg/day) was found to be no more effective than placebo, and doses of 1 mg and 2 mg were found to be significantly superior to placebo (45% and 50% response, respectively, vs 33% for placebo). This effect was not diminished after adjusting for the presence of or improvement in psychotic symptoms, which suggests that improvement in behavioral symptoms were due to more than the reduction in psychotic symptoms. Two randomized, placebo-controlled, double-blind trials of olanzapine and thiothixene in 206 and 33 subjects, respectively, also found statistically significant improvement in subjects receiving the active drug (43–53% responder rate for olanzapine vs 25% for placebo, and

69% responder rate for thiothixene vs 19% for placebo).<sup>92,93</sup> The single negative RCT of 60 subjects used two different drug groups in addition to the placebo group and used antipsychotic doses lower than those generally found to be effective in large antipsychotic trials.<sup>94</sup> Three studies compared different types of antipsychotics, comparing a more-potent antipsychotic with a less-potent, more-sedating agent. No major differences in Brief Psychiatric Rating Scale scores were found between antipsychotics.<sup>94–96</sup> In the three double-blind randomized trials comparing antipsychotics with benzodiazepines, antipsychotic agents were found to be modestly superior to benzodiazepines; detailed analyses indicated even less anxiety with antipsychotic agents than with benzodiazepines.<sup>89,98,99</sup>

Several reviews report the use of selective serotonergic agents in nondepressed, agitated dementia outpatients,<sup>2,5,10</sup> but only two studies involving nursing home residents were located.<sup>102,103</sup> The only randomized, placebo-controlled study<sup>102</sup> found that citalopram reduced irritability and depressed mood but not restlessness, anxiety, fear, or confusion. They did not study more-typical agitated behaviors (e.g., aggression).

The two largest randomized, double-blind, placebo-controlled trials of anticonvulsants were reviewed. One used carbamazepine<sup>104</sup> and the other, divalproex sodium.<sup>105</sup> Carbamazepine at a modal dose of 300 mg demonstrated superiority over placebo, according to CGI improvement ratings (77% for carbamazepine vs 21% for placebo) and Brief Psychiatric Rating Scale scores, as well as decreasing staff-reported care taking time. The degree of change seen in the valproate study was similar, but valproate demonstrated only trend-level ( $P = .08$ ) improvements in unadjusted analyses because of a higher placebo response rate than that seen in the carbamazepine study. Three additional studies of valproate involving a total of 48 subjects (one open label and two retrospective chart reviews) found mixed results for valproate.<sup>106–108</sup> A study comparing valproate with lorazepam in 146 subjects found that 57% of valproate subjects had improved, versus 31% of lorazepam-treated residents ( $P < .05$ ).<sup>109</sup> A single RCT in which buspirone was compared with haloperidol in 26 subjects found greater reductions in tension and anxiety with buspirone (10%), with no ratings for agitation.<sup>115</sup>

Other drug studies include a randomized, placebo-controlled trial of donepezil in nursing homes in which residents were selected based on being demented as opposed to having agitation.<sup>113</sup> In the 208 subjects, there were no differences in Neuro-Psychiatric Inventory total ratings, the primary outcome measure of a number of noncognitive domains. In an open-label study of 10 residents, melatonin was found to decrease agitation in residents believed to have sundowning agitation.<sup>116</sup> Case-report data on four men given estrogen preparations demonstrated some instances of dramatically reduced sexually aggressive behaviors.<sup>117,118</sup>

### **Behavioral Symptoms Summary**

The MDS is comparable with other research instruments as an indicator of some behavioral symptoms, although its responsiveness to change over time is less clear. Studies employing a severity score threshold for entry are more

**Table 4. Pharmacological Treatment of Behavioral Symptoms Associated with Dementia in Nursing Home Residents**

Author, Year	Treatment	Design	N	Length	Results
<b>Antipsychotics</b>					
Katz et al. 1999 <sup>88</sup>	Risperidone	RCT	625	12 wk	Statistically significant greater response with 1 mg (45%) and 2 mg (50%) versus placebo (33%)
Stotsky, 1984 <sup>89</sup>	Thioridazine	RCT	358	4 wk	Statistically significant 74% improved anxiety scale scores versus 42% with placebo
Stotsky, 1984 <sup>89</sup>	Thioridazine, diazepam	RCT, no placebo	252	4 wk	Statistically significant improvement in anxiety scale scores; thioridazine 77% versus diazepam 65%
De Deyn et al. 1999 <sup>90</sup>	Risperidone, haloperidol	RCT	344	12 wk	2% lower BEHAVE-AD scores versus placebo; 5% lower CMAI scores versus placebo; no difference in responder status
Clark et al. 2001 <sup>91</sup>	Olanzapine	RCT	165	6 wk	Trend decrease in emergence of psychosis (8.3% vs 25% with placebo)
Street et al. 2000 <sup>92</sup>	Olanzapine	RCT	206	6 wk	Statistically significant 43% to 53% improvement versus 25% with placebo
Finkel et al. 1995 <sup>93</sup>	Thiothixene	RCT	33	11 wk	Statistically significant decrease in agitation scores (69% responders vs 19% with placebo)
Barnes et al. 1982 <sup>94</sup>	Thioridazine, loxapine	RCT	60	6 wk	No significant behavior scale change or global improvement
Lovett et al. 1987 <sup>95</sup>	Haloperidol, trifluoperazine	RCT, no placebo	54	6 wk	No significant behavior scale differences between the two drugs
Smith et al. 1974 <sup>96</sup>	Haloperidol, thioridazine	RCT, no placebo	46	6 wk	No significant difference between the two drugs
Goldberg et al. 1997 <sup>97</sup>	Risperidone	Observational	109	1-6 mo	Rated helpful in 38%
Coccaro et al. 1990 <sup>98</sup>	Haloperidol, oxazepam, diphenhydramine	RCT, no placebo	59	8 wk	Equal efficacy of all drugs
Covington, 1975 <sup>99</sup>	Thioridazine, diazepam	RCT, no placebo	40	4 wk	Statistically significant 45% response rate with thioridazine versus 30% with diazepam
Goldstein et al. 1976 <sup>100</sup>	Thioridazine, piperacetazine	Crossover, no placebo	50	30 d	Reported improvement with both drugs; no statistical analysis

*continued*

Table 4. (continued)

Author, Year	Treatment	Design	N	Length	Results
Christenson et al. 1998 <sup>101</sup>	Alprazolam 1 mg, haloperidol 0.64 mg	Crossover, no placebo	48	6 wk	Average number of episodes and agitation scores equal for the two drugs
SSRIs					
Nyth et al. 1990 <sup>102</sup>	Citalopram	RCT	89	4 wk	Statistically significant decrease in irritability and depressed mood
Ramadan et al. 2000 <sup>103</sup>	Paroxetine	Observational	8	3 mo	62% decrease in agitation scale scores; no statistical analysis
Anticonvulsants					
Tariot et al. 1998 <sup>104</sup>	Carbamazepine	RCT, double blind, placebo	51	6 wk	Statistically significant global improvement in agitation (21% placebo vs 77% with carbamazepine)
Porsteinsson et al. 2001 <sup>105</sup>	Divalproex	RCT, double blind, placebo	56	6 wk	Trend improvement in agitation scores (15.4% for placebo vs 30.8% for divalproex, $P = .08$ )
Lott et al. 1995 <sup>106</sup>	Valproate	Observational	10	4–34 wk	Eight patients subjectively rated as having >50% reduction in agitation
Marshall et al. 2001 <sup>107</sup>	Divalproex	Chart review	20	7 mo	No statistically significant improvement
Gardner et al. 2001 <sup>108</sup>	Adjunctive divalproex	Chart review	18	16 wk	Reduction in aggressive behaviors
Frenchman et al. 2000 <sup>109</sup>	Divalproex, lorazepam	Chart review	146	Not reported	Statistically significant 57% of divalproex patients improved versus 31% of lorazepam patients
Tariot et al. 1994 <sup>110</sup>	Carbamazepine	Crossover, placebo	25	12 wk	Statistically significant improvement in agitation scores
Hawkins et al. 2000 <sup>111</sup>	Gabapentin	Chart review	22	4–24 wk	77% patients rated as much improved
Herrmann et al. 2000 <sup>112</sup>	Gabapentin	Open label, observational	12	4–24 wk	No change in agitation scale scores
Other agents					
Tariot et al. 2001 <sup>113</sup>	Donepezil	RCT	208	24 wk	No total difference in behavior symptoms between groups
Cooper et al. 2001 <sup>114</sup>	Buspirone conversion	Open label	54	1 yr	Equal rates of agitation
Cantillon et al. 1996 <sup>115</sup>	Buspirone, haloperidol	RCT, no placebo	26	10 wk	Decrease in tension and anxiety scores; no statistical analysis
Cohen-Mansfield et al. 2000 <sup>116</sup>	Melatonin	Observational	10	4 wk	Statistically significant decrease in agitation, especially during evening shift
Cooper, 1987 <sup>117</sup>	Medroxyprogesterone	Observational	3	2 yr	Behaviors completely resolved within 2 wk
Kyomen et al. 1991 <sup>118</sup>	Diethylstilbestrol	Observational	1	3 wk	80% average reduction in aggression; verbal abusiveness continued

RCT = randomized controlled trial; wk = weeks; BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Rating Scale; CMAI = Cohen-Mansfield Agitation Inventory; SSRIs = selective serotonin-reuptake inhibitors; mo = months; d = days; yr = years.

often able to detect statistically significant differences in outcomes. Thus, screening for the sake of detecting agitation is not necessary, but screening for severity or duration may help indicate which residents need and will benefit from specialized interventions.

Numerous labels, such as agitation, disruptive behaviors, behavioral symptoms, and noncognitive symptoms, have come in and out of favor and have broadened the scope of symptoms being studied, but use of any of these vague terms complicates using the literature as a guide to treatment, because the symptoms they encompass are varied (e.g., apathy, physical aggression). Interventions effective for one behavioral symptom may not be effective for others. The primary targets of research interventions need to be clearer, especially as the range of targets and treatments expand.

Nonpharmacological interventions may not have had the financial support that has been available to industry-sponsored studies of medications, yet they easily outnumber published pharmacological studies. Some nonpharmacological interventions have employed large sample sizes and used elegant methodologies. Activities therapies have demonstrated efficacy in one well-done, rigorous study. Music listening, given the ease of implementation and ability to target specific times or activities, appears promising but needs more controlled trials to establish efficacy. Although often cited as a great need in nursing homes, training interventions have been found to be relatively ineffective. Rapid staff turnover may undermine this type of intervention, and it may be that training is a necessary but insufficient single component of an effective multifaceted approach.

Antipsychotics remain the most rigorously studied type of medication, with evidence of efficacy beyond that of reducing psychosis. SSRI antidepressants have not been rigorously targeted for typical physically aggressive behaviors but do show some benefit for emotional problems that would include depressive symptoms. Of the anticonvulsants, carbamazepine, despite concerns of greater side effects, currently has better supporting data than divalproex sodium. Medications and nonpharmacological interventions reduce severity of behavioral symptoms but rarely totally eliminate target behaviors. The current nursing home literature is insufficient for prioritizing a nonpharmacological versus a pharmacological approach for most behavioral symptoms, because comparison studies have not been done.

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