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STATE OF THE ART REVIEW

Assessment and management of behavioral and psychological symptoms of dementia

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ABSTRACT

Behavioral and psychological symptoms of dementia include agitation, depression, apathy, repetitive questioning, psychosis, aggression, sleep problems, wandering, and a variety of inappropriate behaviors. One or more of these symptoms will affect nearly all people with dementia over the course of their illness. These symptoms are among the most complex, stressful, and costly aspects of care, and they lead to a myriad of poor patient health outcomes, healthcare problems, and income loss for family care givers. The causes include neurobiologically related disease factors; unmet needs; care giver factors; environmental triggers; and interactions of individual, care giver, and environmental factors. The complexity of these symptoms means that there is no "one size fits all solution," and approaches tailored to the patient and the care giver are needed. Non-pharmacologic approaches should be used first line, although several exceptions are discussed. Non-pharmacologic approaches with the strongest evidence base involve family care giver interventions. Regarding pharmacologic treatments, antipsychotics have the strongest evidence base, although the risk to benefit ratio is a concern. An approach to integrating non-pharmacologic and pharmacologic treatments is described. Finally, the paradigm shift needed to fully institute tailored treatments for people and families dealing with these symptoms in the community is discussed.

Introduction

Behavioral and psychological symptoms of dementia are defined as signs and symptoms of disturbed perception, thought content, mood, or behavior.[1] They include agitation, depression, apathy, repetitive questioning, psychosis, aggression, sleep problems, wandering, and a variety of socially inappropriate behaviors.[2] One or more symptoms will affect nearly all people with dementia over the course of their illness.[2] These symptoms are among the most complex, stressful, and costly aspects of care, and they lead to a myriad of poor patient health outcomes, including excess morbidity, mortality, hospital stays, and early placement in a nursing home.[3-5] Most people with dementia are cared for in the home by family care givers, and these symptoms are strongly associated with stress and depression in carers, as well as reduced income from employment and lower quality of life.[6-8]

This review covers the prevalence, types, outcomes, and causes of behavioral and psychological symptoms of dementia. It also describes a conceptual model that integrates factors related to neurobiology, the person with dementia, the care giver, and the environment. It details the evidence base for non-pharmacologic and pharmacologic treatments, as well as an approach to assessing behaviors and deriving treatment plans. The approach draws on our conceptual model and existing treatment plans informed by evidence. Finally, the article discusses a paradigm shift that will be needed to fully integrate tailored treatments into routine clinical care for people with dementia and families dealing with these symptoms. We realize that long term care facilities have more people in later stages of dementia with troubling behavioral and psychological symptoms. However, this review focuses on community dwelling patients with dementia because these symptoms often precipitate admission to long term care, are associated with higher use of healthcare facilities, and are often the most distressing aspect of providing family care.

Sources and selection criteria

We identified articles for this review through searches of publications listed by PubMed from January 1992 to 1 June 2014 (a period judged to capture the most important work on dementia care, care giving, and behavioral and psychological symptoms of dementia (BPSD)). We used the search terms "behavioral and psychological symptoms of dementia", "BPSD", "neuropsychiatric symptoms of dementia", "behavioral symptoms of dementia", "disruptive behaviors", "nonpharmacologic interventions/strategies/treatment", "psychosocial interventions/strategies/treatment", "pharmacologic treatment", "medications", and "adverse effects". We focused on community dwelling patients with dementia. We also searched for recent published systematic reviews, meta-analyses,

Types of behavioral and psychological symptoms of dementia*

- Delusions (distressing beliefs)
- Hallucinations
- Agitation:
  - Easily upset
  - Repeating questions
  - Arguing or complaining
  - Hoarding
  - Pacing
  - Inappropriate screaming, crying out, disruptive sounds
  - Rejection of care (for example, bathing, dressing, grooming)
  - Leaving home
- Aggression (physical or verbal)
- Depression or dysphoria
- Anxiety:
  - Worrying
  - Shadowing (following care giver)
- Apathy or indifference
- Disinhibition:
  - Socially inappropriate behavior
  - Sexually inappropriate behavior
- Irritability or lability
- Motor disturbance (repetitive activities without purpose):
  - Wandering
  - Rummaging
- Night-time behaviors (waking and getting up at night)

*Based on modified neuropsychiatric inventory-Q categories. Some behaviors under agitation need more research to determine whether they are part of agitation or their own entity (for example, rejection of care).

Cochrane reviews, and community based randomized controlled trials (RCTs) of non-pharmacologic or pharmacologic treatments from January 2001 to 1 June 2014 with behavioral and psychological symptoms of dementia as an outcome. We reviewed only articles published in English and also excluded those published in non-peer reviewed journals. In addition, we searched PubMed and websites of medical organizations for published guidelines on dementia care that included treatment for behavioral and psychological symptoms of dementia. The final reference list was based on highest relevance to the topics covered in the review. We included publications of AHRQ (Agency for Healthcare Research and Quality) classes I-IV (I: well designed RCTs or meta-analysis or multiple well designed RCTs; II: well designed non-randomized controlled trials; III: observational studies with controls; IV: observational studies without controls) because of the limited evidence base on the treatment of these symptoms. Our data synthesis and recommendations were developed using existing evidence and our clinical experience.

Prevalence

Dementia was estimated to affect 44 million people worldwide in 2013. This number is expected to reach 76 million in 2030 and 135 million by 2050.[9] Families are profoundly affected because over 75% of people are cared for by family or friends at home.[10] In the United States in 2013, 15.5 million family members and friends provided 17.7 billion hours of unpaid care to people with Alzheimer's disease and other dementias.[11] The Cache County study found that the five year prevalence of behavioral and psychological symptoms of dementia (at least one symptom) was 97%, with the most common symptoms being apathy, depression, and anxiety.[12] Many other studies have replicated the finding that nearly all people with dementia experience one or more of these symptoms at some point during their illness.[2 12-16] Symptoms often co-occur (for example, depression and anxiety; and wandering and sleep problems), increasing their impact even more.[17] Thus, the number of people with dementia and behavioral symptoms is huge and the impact on families is profound and far reaching.

Types of behavioral and psychological symptoms of dementia

These symptoms (also known as neuropsychiatric symptoms of dementia) occur in clusters or syndromes identified as psychosis (delusions and hallucinations), agitation, aggression, depression, anxiety, apathy, disinhibition (socially and sexually inappropriate behaviors),[18 19] motor disturbance, night-time behaviors, and appetite and eating problems (box).[20 21]

Although these symptoms are seen almost universally in dementia, regardless of the underlying cause, some types of dementia are associated with certain behaviors. For example, depression is more common in vascular dementia and hallucinations are seen more often in Lewy body dementia than in Alzheimer's disease. People with frontotemporal dementia often exhibit behaviors typical of executive control loss, such as disinhibition, wandering, social inappropriateness, and apathy.[22-24]

These symptoms occur across all stages of dementia, although their type and prominence depend on the stage. For example, anxiety and depression are common in early stage Alzheimer's disease and may worsen with progression. Agitation (a broad category that includes excessive psychomotor activity such as pacing, trailing, restlessness, dressing and undressing, and emotional distress) is common, persistent, and may increase with disease severity.[12 25-28] Apathy is commonly reported by family members across all stages of dementia and tends to worsen over time, whereas delusions, hallucinations, and aggression are more episodic and more common in moderate to severe stages of the disease.[2]

Outcomes of behavioral and psychological symptoms of dementia

Although cognitive symptoms are the hallmark of dementia, behavioral and psychological symptoms often dominate both the presentation[29 30] and course of disease,[3-5 31] creating the most difficulties for people with dementia, their carers, and providers. Unlike cognitive and functional deficits, for which there is a downward trajectory of decline, these symptoms tend to fluctuate episodically but may last for six months or more. Their episodic nature contributes to the complexity of their prevention and management.

Behavioral and psychological symptoms of dementia commonly lead to early placement in a nursing home,[3 4]

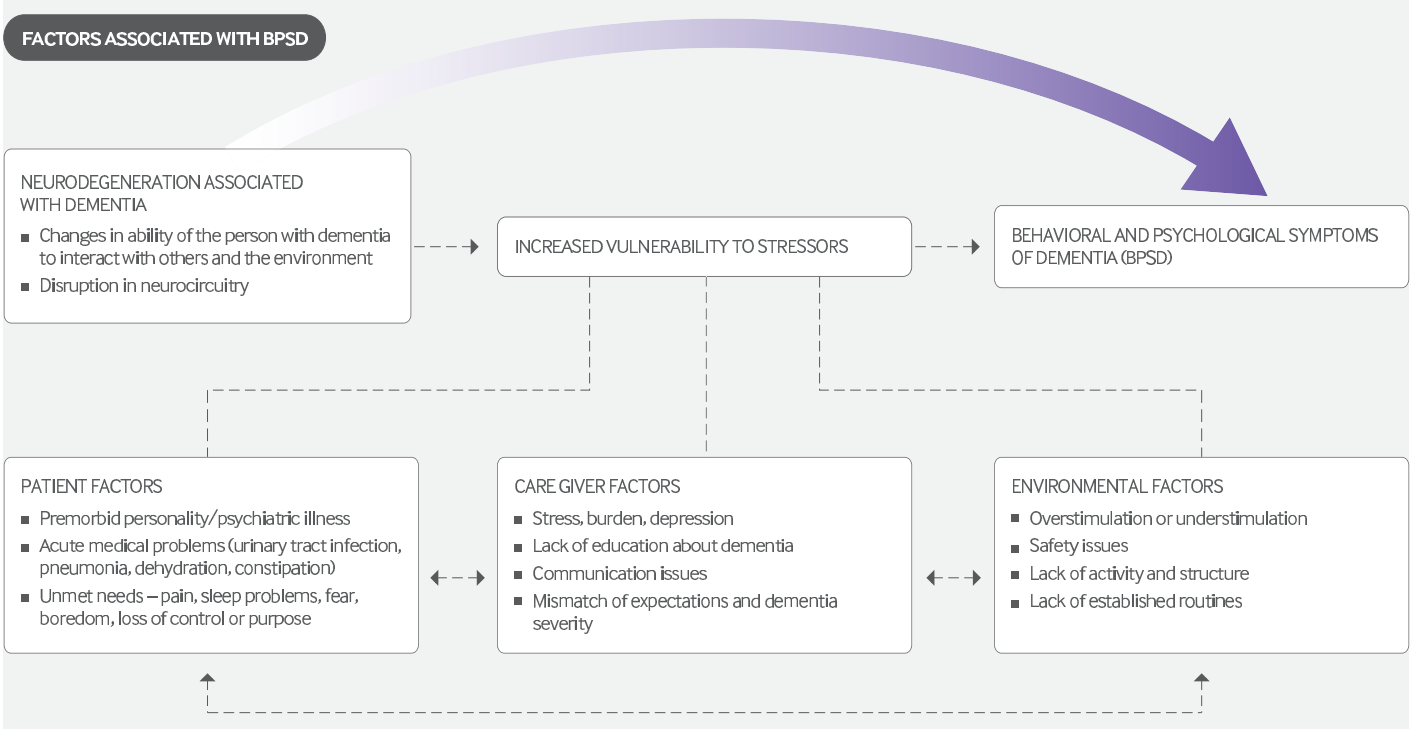

Fig 1 | Conceptual model describing how interactions between the person with dementia, care giver, and environmental factors cause behavioral and psychological symptoms of dementia (BPSD)

as well as excess morbidity, mortality, and hospital admissions.[5] A third of dementia care costs have been attributed to the management of these symptoms owing to greater use of health services, direct care costs, and family time spent in daily oversight.[32 33] Although patients with untreated behavioral and psychological symptoms have faster disease progression than those without such symptoms,[31] it is not yet clear whether treating these symptoms slows decline.

Behavioral and psychological symptoms of dementia are also associated with poor care giver outcomes, including reduced quality of life, worse health, and reduced income from employment.[6-8] Care givers managing such symptoms are more distressed or depressed (or both) than carers of people with dementia alone or with other chronic diseases.[34] Managing wandering, repetitive vocalizations, sleep disturbances, and other symptoms such as resisting or refusing care and restlessness are among the most problematic and distressing aspects of care provision.[2 8 35 36]

Causes of behavioral and psychological symptoms of dementia

Because cognitive decline alone cannot explain these symptoms, various contributory factors have been identified, which can be categorized as factors related to the person with dementia (neurobiologically related disease factors, acute medical illness, unmet needs, and pre-existing personality and psychiatric illness factors), care giver factors, and environmental factors. Figure 1 is a conceptual model that depicts how degeneration caused by dementia changes the ability of people with dementia to interact with others (especially their care givers) and the environment. Dementia may also directly cause symptoms by disrupting brain circuitry involved in behavior and emotion. Care giver and environmental effects can also trigger behaviors independently or in interaction with the circuit disruptions seen in brain degeneration. All of this suggests a need for approaches that are tailored to the patient and care giver to assess behaviors and the context in which they occur, derive and help families implement a treatment plan, and evaluate its effectiveness.

Factors related to the person with dementia

Neurobiological underpinnings

Advances in neuroscience have shown that there are extensive and reciprocal connections between brain centers that govern emotion and cognition.[37] Over the past three decades, structural and functional neuroimaging and biomarker investigations have provided a greater understanding of the neurobiological basis of behavioral and psychological symptoms of dementia. The circuit model theorizes that three or more frontal-subcortical circuits have frontal, basal ganglia, and thalamic components that affect human behavior. These circuits comprise the dorsolateral circuit (which mediates planning, organization, and executive function), the prefrontal-basal ganglia circuits (which mediate motivated behavior),[38] and the orbitofrontal circuit (which mediates inhibitory control and conformity with social norms).[39] Behavioral and psychological symptoms of dementia could result from synaptic or circuit disconnections in these networks. There are also five large scale overlapping and reciprocal "cortico-cortical" networks involved in emotion and cognition.[37 40-42] The ascending monoaminergic system

also plays a role—cell bodies of neurons primarily located in the brain stem that produce serotonin, norepinephrine (noradrenaline), and dopamine widely project to virtually all brain regions to mediate behavior.[39] Lastly, glutamate mediated excitatory neurotoxicity may also play a role.

Neuroimaging and biomarker investigations have increased our understanding of these symptoms and identified defects that are associated with certain symptoms.[43] For example:

- Depression: decreased monoaminergic neurotransmitter function and decreased frontoparietal metabolism
- Apathy: structural atrophy and functional deficits in medial and frontal regions (associated with motivation and reward mechanisms)
- Agitation and aggression: cortical dysfunction in the anterior cingulate, insula, lateral frontal, and lateral temporal regions; deficits in cholinergic transmission (over and above that seen in dementia itself); and increased D2/D3 receptor availability in the striatum.

Acute medical conditions

Undiagnosed medical conditions are also important contributors. People with dementia may be disproportionately affected by pain and undiagnosed illnesses compared with those without cognitive impairment.[16 44-46] In a study of community dwelling older adults with dementia, 36% had undetected illness that was associated with behavioral and psychological symptoms, including agitation, repeated questioning, crying out, delusions, and hallucinations.[44] Pain is associated with aggressive behavior in patients with dementia,[16] and pain management can reduce such behaviors.[47 48] Finally, side effects of drugs or drug-drug interactions can give rise to these symptoms.

Unmet needs

In the need-driven dementia-compromised behavior (NDB) model,[49] behavioral and psychological symptoms of dementia are viewed as an expression of unmet needs or goals (physical, psychological, emotional, or social). The loss of ability to express needs or goals verbally leads the person with dementia to communicate and express needs through various behaviors. This model emphasizes the interaction between individual characteristics and fluctuating environmental factors that may cause stress or discomfort. The model also recognizes that lack of meaningful activity may develop into unmet needs.[50]

Pre-existing personality and psychiatric illnesses

Clinical experience suggests that longstanding personality patterns and characteristics may affect the development of behavioral and psychological symptoms of dementia—the loss of inhibitory control may accentuate premorbid personality traits.[51] More studies are needed to understand this association. Lifelong psychiatric disorders (such as major depression, anxiety, bipolar disorder, and schizophrenia) and their management (for example, treatment with antidepressants, anxiolytics, mood stabilizers, and antipsychotics) may also affect the development of these symptoms.

Factors related to care givers

One of the complexities of dementia relates to the special role of family care givers. Levels of psychological distress and stress are higher, whereas self-efficacy, subjective wellbeing, and physical health are significantly lower in those who care for people with dementia than in other care givers.[52] When compared with non-care givers, these differences are even greater.[53] Various studies show that rates of depression range from 23% to 85% in people caring for patients with dementia,[54 55] and from 16% to 45% in those caring for patients with anxiety.[35 56-58]

Stress and depression among care givers increase when managing behavioral and psychological symptoms of dementia.[59] In turn, such symptoms may be triggered or exacerbated when a care giver is stress or depressed.[34] In addition, factors related to the care giver, such as negative communication styles (anger, screaming, or negative affect), coping abilities and strategies, and the mismatch between care giver expectations and the stage of illness can also trigger or worsen symptoms.[60]

Assessments of these symptoms also depend on a proxy report; however, care giver stress, burden, depression, culture, and other factors may influence how carers report symptoms.[61] Both pharmacologic and non-pharmacologic treatments for symptoms depend on others to carry them out. The extent to which care givers are "ready" and able to implement strategies is important, particularly with non-pharmacologic strategies that may not be fully understood, require changes in care giver behavior that are challenging to achieve, or are judged too stressful or complicated to be implemented by care givers.[62] Finally, providers are also dependent on the care giver to evaluate the impact of interventions.

Environmental triggers

The progressively lowered stress threshold model provides a framework with which to understand and reduce challenging behaviors by reducing internal and external stressors.[63] Because people with dementia have progressive difficulty processing and responding to environmental stimuli, behaviors vary with disease stage and environmental stimuli. With decreased ability to process stimuli, the stress threshold of the person with dementia becomes lower and the potential for higher levels of frustration increases; if unabated, serious anxiety and severe agitation can develop. Stress may be caused by changes in routine, too many competing or misleading stimuli, lack of stimuli, physical and social environmental changes, and demands that exceed functional ability.[64] In another model, behaviors are viewed as occurring within an environmental context conceptualized as consisting of four hierarchically arranged, interacting layers:

- Objects (physical tools or items in the home)
- Tasks that compose daily life routines (dressing, bathing, toileting)
- Social groups and their organizations (household composition and other social resources)
- Culture (values and beliefs that shape the provision of care in the home).[65 66]

Each layer may be difficult for a person with dementia to respond to or negotiate and will need to be modified

to balance the demands imposed by that aspect of the environment as the person's level of competency or abilities decline.

Prevention

To our knowledge, no studies have examined the impact of prevention on the development of behavioral and psychological symptoms of dementia. Future research should assess:

- How often mild symptoms progress to more severe ones
- Whether screening and monitoring for behavioral symptoms can identify behaviors at an early stage and alter their course
- Whether screening for risk factors for behavioral symptoms and then modifying them can prevent occurrences.

Treatment

Because of the complex causes of behavioral and psychological symptoms of dementia, a "one size fits all" solution does not exist. Furthermore, given the role of care givers (family and professional care givers), management involves thinking beyond patient centered care and considering the special role of carers. Care of behavioral and psychological symptoms of dementia in community dwelling people with dementia requires a care giver and patient centered focus. Here we present the current evidence for non-pharmacologic and pharmacologic treatments. We also describe an approach that integrates treatment modalities of both types in an approach tailored to the patient and care giver (again focusing on community dwelling people with dementia). The quality and strength of evidence supporting the treatments is described throughout.

Non-pharmacologic treatments

Non-pharmacologic treatments encompass a vast array of behavioral, environmental, and care giver supportive interventions. Numerous guidelines, medical organizations, and expert groups recommend non-pharmacologic strategies as the preferred first line treatment approach (except in emergency situations where there is imminent danger or safety concerns).[67-70] However, these strategies have largely not been translated into real world clinical management and standard care.[71]

Drugs are preferred over non-pharmacologic strategies for several reasons: lack of provider training in the use of non-pharmacologic strategies,[72] time needed and lack of reimbursement for such approaches; lack of clear guidelines on dosing and timing of these strategies; and perceived lack of efficacy compared with drugs. Concerns about efficacy may be secondary to the heterogeneity of behavioral interventions encompassing everything from aromatherapy and massage to supportive interventions for care givers. Providers may be unclear about which non-pharmacologic approaches are effective and how to choose and implement them. Lack of efficacy in previous trials may have been due to small sample sizes, a lack of methodological rigor, and a focus on patients with more severe dementia and those living in residential settings.[73-75]

There is a lack of clear agreement in the field about how to categorize non-pharmacologic interventions, but to link them to our model (fig 1) we group them into three categories: those targeting the person with dementia, those targeting the care giver, and those targeting the environment.

Approaches targeting the person with dementia

The evidence for the following non-pharmacologic strategies for reducing symptoms is heterogeneous, and no positive or negative conclusions can be made for this group of interventions overall:

- Reminiscence therapy (discussion of past experiences)
- Validation therapy (working through unresolved conflicts)
- Simulated presence therapy (use of audiotaped recordings of family members' voices)
- Aromatherapy (use of fragrant plant oils)
- Snoezelen (placing the person with dementia in a soothing and stimulating environment known as a "snoezelen room")
- Cognitive training and rehabilitation
- Acupuncture
- Light therapy.[76-82]

Studies of interventions for specific behaviors (such as wandering and agitation) are even more limited than the studies looking at behavioral and psychological symptoms of dementia in general. Four systematic reviews of non-pharmacologic strategies found no evidence of benefit for physical activity or walking programs for wandering in randomized trials.[76] Several randomized trials have found that engagement in physical activity and pleasant events reduced depression in persons with dementia living at home.[83-85] A recent systematic review found that exercise had no impact on mood,[86] although it may improve night-time sleep.[87] There is some evidence from a few RCTs that specific symptoms of aggression, agitation, and wandering were reduced with use of music therapy. Although these results are promising, more high quality RCTs are needed.[78-82 88] Strategies such as distraction, backing away, and leaving the room have been reported to be helpful for symptoms of aggression, but more high quality data are needed.[12 89] There is some evidence (based on two RCTs) that hand massage reduces agitation in the short term and that touch can encourage eating, but more RCTs are needed.[90] Studies in nursing home residents have suggested that agitation and aggression during bathing may be reduced by personalizing the bathing experience (for example, offering choices, creating a spa-like atmosphere),[91] but again more high quality studies are needed.

Interventions for family care givers

In this type of approach, problem solving with a family care giver to identify precipitating and modifiable causes of symptoms is followed by efforts to modify these causes with selected non-pharmacologic strategies. Although the Resources for Enhancing Alzheimer's Caregiver Health (REACH II) initiative and REACH-VA involved generalized approaches that incorporated good dementia care and

support programs for carers, they also integrated a tailored problem solving approach for working with care givers with regard to behaviors.[92 93] Both trials showed significant reductions in the frequency of behavioral symptoms.

The Tailored Activity Program (TAP) used eight sessions with occupational therapists to train care givers in customized activity based on the person with dementia's current and previous interests and cognitive and physical abilities.[94] It showed significant reductions at four months in the frequency of problem behaviors (P=0.14, Cohen's d=0.75) and care givers' appraisal of time they are "on duty" (P=0.001, Cohen's d=0.74).

The Care of Persons with Dementia in their Environments (COPE) study involved up to 12 contacts by health professionals to assess underlying medical problems and train care givers to identify care recipients' strengths and weaknesses to problem solve interventions.[95] Results at four months included significant improvements in patients' functional dependence (adjusted mean difference 0.24, 95% confidence interval 0.03 to 0.44) and wellbeing of care givers (adjusted mean difference 0.22, 0.08 to 0.36).

The Advancing Caregiver Training (ACT) study used 11 visits by health professionals working with care givers to identify potential triggers of problem behaviors (including underlying medical causes) and train care givers to modify them.[36] At four months' follow-up, improvement in target behaviors was significantly greater in the intervention group (67.5% *v* 45.8% for controls, x^2=8.7; P=0.002). The study also found significant reductions in care giver upset (adjusted mean difference −0.93, −1.76 to −0.10) and negative communications with people with dementia (−0.93, −1.69 to −0.17), as well as enhanced care giver confidence in managing behaviors (0.33, 0.08 to 0.58). Similar outcomes were found at 24 weeks, as well as a significant difference between the intervention and controls in improved ability to keep patients at home (46.5% *v* 17.6%; x^2=22.0; P=0.001).

A meta-analysis of 23 randomized clinical trials, involving almost 3300 community dwelling patients and their care givers, looked at interventions aimed at family care givers. It confirmed that such interventions significantly reduced behavioral symptoms (effect size 0.34, 0.20 to 0.48).[96] Although the effect size was small, it is greater than that found in trials of antipsychotics for behavioral symptoms, as well as cholinesterase inhibitors for memory symptoms.[97 98]

Although this article focuses on community dwelling people with dementia, it should be noted that similar training approaches for staff caring for long term care patients have also been shown to be efficacious.

Environmental approaches

These include tackling factors in the person's environment including:

- Being overstimulated (for example, excess noise, people, or clutter in the home) or understimulated (for example, lack of anything of interest to look at)
- Safety problems (for example, access to household chemicals or sharp objects or easy ability to exit the home)
- Lack of activity and structure (for example, no regular exercise or activities that match interests and capabilities)
- Lack of established routines (for example, frequent changes in the time, location, or sequence of daily activities).

A qualitative synthesis of 63 research studies on the effects of environmental interventions provided evidence for its role in preventing and reducing behavioral symptoms, such as wandering or agitation.[99] Although 90% of the studies reviewed showed positive effects, most studies did not use randomized trials. Of 11 studies, six were conducted in long term care, two in dementia special care units, two in home environments, and one in different settings. All but one reported improvements in a wide range of outcomes, including behavioral symptoms, overall wellbeing, activity engagement, elopement behavior (attempting to leave the facility, nursing home, or living residence), and acceptance of care.

A wide range of environmental strategies have been tested, including reduction of clutter, use of color contrasts, and signage. Two RCTs that included training families in the use of these strategies at home also had positive outcomes.[100 101] Because these strategies are often used in combination it is difficult to pinpoint one preferred approach; rather, a combination of adjustments to the environment seems to yield behavioral changes.

Summary

The non-pharmacologic approaches with the strongest evidence base are those based on family care giver interventions, which have been shown to have greater effect than antipsychotics. These approaches typically provide the care giver with education and support, training in stress reduction or cognitive reframing techniques (or both), and specific skills in problem solving to manage behavioral symptoms. They include increasing the activity of the person with dementia; enhancing communication with the person with dementia; reducing the complexity of the physical environment; and simplifying tasks for the person with dementia. Individual non-pharmacologic approaches (such as music and physical activity) may be used within such approaches as tailored activities.

Adverse events

Although non-pharmacologic strategies do not carry the level of risk associated with drugs, the potential for adverse effects should not be ignored. Several studies have reported increased agitation with cognitive or emotion oriented interventions, and increased agitation and physical aggression have also been reported for sensory approaches such as music therapy, massage and touch therapies, and aromatherapy.[76 102]

Drug treatments

No drugs have been approved by the Food and Drug Administration for behavioral and psychological symptoms of dementia in the US, so all drugs are used off label. In Canada, however, risperidone is approved for symptomatic management of behavior in severe dementia.

Antipsychotics

A systematic review of two meta-analyses (12 RCTs) and two additional RCTs found no clear evidence for efficacy of conventional antipsychotic agents.[103-107] Sample sizes were small and follow-up for a maximum of 12 weeks in most trials. Haloperidol may have a slight benefit for aggression (at doses of 1.2-3.5 mg/day; effect size −0.31, −0.49 to −0.13), but it is unclear whether this benefit outweighs the adverse effects of this agent (including extrapyramidal symptoms and sedation).[103 104]

There have been at least 15 RCTs of atypical antipsychotics for behavioral and psychological symptoms of dementia, but several of these are not in the public domain. Taken together, more than 5000 patients were involved and treated for 8-12 weeks in general. A meta-analysis found evidence for symptomatic efficacy of aripiprazole (three trials; standardized mean difference (SMD) −0.22, −0.36 to 0.08; Z=3.08; P=0.002) and risperidone (five trials; SMD −0.18, −0.29 to −0.08; Z=3.43; P=0.0006) but not olanzapine (five trials).[108] There was insufficient evidence for quetiapine because the three trials used different selection criteria and outcomes and could not be statistically combined. Notably, most of the aripiprazole and risperidone trials were in nursing home patients. There was evidence that less severe cognitive impairment, the presence of psychosis, and being an outpatient were each associated with lower efficacy. A second meta-analysis found similar results with the exception that olanzapine was also found to be efficacious for agitation and aggression (dose 5-10 mg: weighted mean difference 0.77, −1.44 to −0.10; P=0.03), but not psychosis.[109] The efficacy of risperidone appeared to be higher in a third meta-analysis in patients with more severe psychosis (effect size 0.29, 0.120 to 0.469).[110] The overall effect size (total effect size minus placebo effect size) for atypical antipsychotics ranged from 0.16 (Z=3.89; P=0.0001) in one meta-analysis[105] to 0.13 in another.[111]

The Clinical Antipsychotic Trial of Intervention Effectiveness-Alzheimer's Disease (CATIE-AD) was a 42 site double blind placebo controlled trial of 421 subjects with behavioral and psychological symptoms of dementia including psychosis, aggression, or agitation, which was followed for up to 36 weeks.[97] The main outcome was time to discontinuation. No significant differences were found in overall time to discontinuation or in clinical improvement between treatment with antipsychotics and placebo. However, time to discontinuation for lack of efficacy favored risperidone (odds ratio 0.61, 0.41 to 0.89; P=0.01) and olanzapine (0.51, 0.35 to 0.74; P>0.001) over placebo, whereas time to discontinuation for adverse events favored placebo over drug treatments (olanzapine: hazard ratio 4.32, 1.84 to 10.12; P<0.001; risperidone: hazard ratio 3.62, 1.45 to 9.04; P=0.006). In the group of patients who received quetiapine, time to discontinuation for lack of efficacy was no different from that in the placebo group, and time to discontinuation for adverse events favored placebo (quetiapine: hazard ratio 3.58, 1.44 to 8.91; P=0.006). A sub-analysis of CATIE-AD data indicated that atypical antipsychotics may be more effective for particular symptoms such as anger, aggression, and paranoid ideas.[112]

Adverse events with antipsychotics

Adverse events associated with typical antipsychotics include all of those associated with atypical agents (below) as well as a greater risk of anticholinergic effects, hyperprolactinemia, postural hypotension, prolonged QT, sexual dysfunction, and extrapyramidal symptoms (including parkinsonism, dystonia, and tardive dyskinesia).[108 113 114]

Atypical antipsychotics are associated with weight gain, diabetes, and the metabolic syndrome[115]; cognitive worsening; seizures (clozapine); somnolence (clozapine, olanzapine, and quetiapine); extrapyramidal symptoms (risperidone)[109]; and abnormal gait (risperidone and olanzapine).[108] Although limited data suggest that conventional antipsychotics may be associated with an increased risk of stroke, the risk is more established with atypical antipsychotics and may be even higher than that with conventional antipsychotics.[116] Pooled data from risperidone trials indicate that it is associated with a threefold increased risk of cerebrovascular events, which may be a class effect for all antipsychotics (a meta-analysis showed that stroke occurred in 1.9% of the drug group versus 0.9% of the placebo group, with an odds ratio of 2.13, 1.20 to 3.75; Z=2.60; P=0.009).[108 109]

Finally, patients with Lewy body dementia are at increased risk of having adverse effects with antipsychotics and the effects are worse than in other patients with dementia, so extra caution should be used if prescribing these drugs for these patients.

In 2005, the FDA announced that, based on a re-analysis of 17 placebo controlled trials (several of which were unpublished), atypical antipsychotics were associated with a 1.7-fold increase in mortality compared with placebo.[117 118] As a result, it announced a black box warning for the use of atypical antipsychotics for behavioral and psychological symptoms of dementia. A meta-analysis found an odds ratio for mortality with these drugs of 1.54 (1.06 to 2.23; Z=2.28; P=0.02), with pooled events of 3.5% mortality for the drug versus 2.3% for placebo. A similar black box warning for conventional antipsychotics, based on two observational studies that showed increased risk of mortality in older adults using conventional versus atypical antipsychotics, was announced in 2008.[117-119]

The meta-analysis also used combined data from two RCTs (risperidone-placebo and quetiapine-placebo) that had haloperidol arms (243 patients received haloperidol and 239 received placebo). It found 15 deaths (6.2%) with haloperidol and nine (3.8%) with placebo, resulting in an odds ratio of 1.68 (0.72 to 3.92; P=0.23).[120]

Subsequent observational studies have confirmed concerns about increased mortality in patients with dementia with conventional antipsychotics versus atypical antipsychotics,[121] and atypical antipsychotics versus other psychotropic drugs.[122] The three studies that found no increase in mortality with antipsychotics in patients with dementia had several methodological problems. These included examining prevalent users not new users,[123 124] not controlling for exposure,[123-125] problems with statistical power,[124 125] not controlling for other psychiatric drugs,[125] and varying lengths of follow-up.[125]

Most recently, a large retrospective cohort study examined the mortality risk associated with individual antipsychotics using various methods to control for confounding.[126] It looked at a national sample of more than 33 000 older veterans with dementia newly started on haloperidol, risperidone, olanzapine, quetiapine, or valproic acid and derivatives (as a non-antipsychotic comparator). Mortality was highest in those receiving haloperidol (relative risk 1.54, 1.38 to 1.73), followed by risperidone (reference, relative risk 1) and olanzapine (0.99, 0.89 to 1.10), then valproic acid (0.91, 0.78 to 1.06), and lastly quetiapine (0.73, 0.67 to 0.80).[126] These results were found across all analyses (intention to treat, exposure, dose adjusted, propensity adjusted).

Antidepressants

Tricyclic antidepressants have been shown to have limited benefit and potential risks in the treatment of depression in dementia. An earlier meta-analysis (four RCTs) suggested that selective serotonin reuptake inhibitors (SSRIs) had good tolerability and a favorable treatment response (effect size −0.93, −3.27 to 1.41),[127] with a methodologically sound study indicating a good treatment response to sertraline (depression improvement effect size 0.68, F(1,41) 10.9; P=0.002).[128] However, a recent meta-analysis of five studies on SSRIs reported a lack of clear benefit for depression.[128-134] It reported that studies differed in terms of depression diagnostic criteria, drug tested, and outcome measures, which could have accounted for overall lack of clear benefit for depression.

Antidepressants have also been used to target agitation and psychosis in dementia. A review of such trials found evidence for a reduction in agitation with sertraline and citalopram compared with placebo (mean difference −0.89, −1.22 to −0.57).[135] Most recently, the Citalopram for Agitation in Alzheimer Disease (CITAD) study randomized 186 people with clinically significant agitation to receive a psychosocial intervention plus citalopram (target dose of 30 mg) or placebo for nine weeks.[136] People taking citalopram showed significant improvement over placebo on several clinical measures (including clinical global impression of change (odds ratio 2.13, 1.23 to 3.69; P=0.01) and lower care giver distress (−2.70, −4.94 to −-0.47; P=0.02).

More trials are needed to examine the dosing of citalopram in these patients (given concern about potential QT prolongation at 30 mg) and to compare efficacy between citalopram and atypical antipsychotics (an earlier study suggested that SSRIs may be as efficacious as atypical antipsychotics for treating agitation with no difference found on follow-up scores of symptoms).[137]

Adverse events with antidepressants

Tricyclic antidepressants are associated with orthostatic hypotension, seizures, glucose dysregulation, anticholinergic effects (dry mouth, urinary retention, constipation, and confusion), prolonged QT, weight changes, sexual dysfunction, and falls.[138] Although safety considerations and current evidence favor SSRIs, adverse events do occur. These include nausea and vomiting; headaches; sleep changes; diarrhea; tremor; sexual dysfunction; hyponatremia, owing to the syndrome of inappropriate antidiuretic hormone secretion (in about 10% of patients),[139] and gastrointestinal bleeding. In CITAD, worsening of cognition and QT prolongation were also seen in the citalopram group,[136] although only a small number of patients met the gender specific threshold of QTc (three in the drug group and one in the placebo group).[140] Although the FDA has issued a warning for QT prolongation and torsade de pointes with only citalopram (doses >20 mg) among the SSRIs, QT prolongation has been associated with SSRIs as a class. However, QT prolongation is associated with hundreds of drugs, and the literature on the association between QT prolongation and arrhythmias such as torsade de pointes is mixed. A subsequent observational study found no increased risk of ventricular arrhythmia or cardiac mortality with citalopram or sertraline.[141]

Mood stabilizers

Studies of valproic acid and derivatives have not shown treatment benefits for patients with behavioral and psychological symptoms of dementia.[142] Two small trials of carbamazepine (n=51 and n=21) of less than six weeks' duration showed some benefit for agitation and global clinical outcomes.[143 144] Data for other antiepileptic drugs are limited.

Adverse events with mood stabilizers

Side effects of valproic acid and derivatives include sedation, gait disturbances, and tremor. Other risks include alopecia, thrombocytopenia, hyperammonemia, pancreatitis, liver injury, cognitive changes, and mortality.[126 145] Carbamazepine has been associated with hepatitis, serious blood dyscrasias, and cognitive changes.[145]

Cholinesterase inhibitors and memantine

Although a meta-analysis showed a small but significant improvement in behavioral and psychological symptoms of dementia with cholinesterase inhibitors over placebo during six months of treatment, the improvement may not be clinically significant (summary estimate 1.72 point improvement *v* placebo on the 120 point neuropsychiatric inventory (NPI) scale, 0.87 to 2.57).[146] Furthermore, the treatment effect was driven by two studies of metrifonate, which has never been approved by the FDA in the US owing to concerns about toxicity.[103] In addition, donepezil showed no benefit for clinically significant agitation over 12 weeks in a large RCT,[147] or for overall change in neuropsychiatric inventory scores in a longer term trial with up to four years' follow-up.[98]

It has been suggested that cholinesterase inhibitors improve psychotic symptoms in Lewy body dementia. However, an RCT found no difference between rivastigmine and placebo on overall NPI scores or on a "Lewy body cluster" of symptoms (delusions, hallucinations, apathy, and depression).[148] Although one RCT in Parkinson's disease dementia found no significant improvement in behavior with donepezil over placebo,[149] a recent systematic review found that the use of cholinesterase inhibitors in this disease had a positive impact on behavioral and psychological symptoms of dementia (SMD −0.20,

−0.36 to −0.06; P=0.01). However, use of cholinesterase inhibitors was associated with an increased risk of parkinsonian symptoms, such as tremor.[150]

Although data from RCTs of memantine in patients with moderate to severe dementia had indicated that it might also confer benefit,[151-153] a recent trial specifically examining the efficacy of this agent for Alzheimer's dementia with agitation found no benefit over placebo.[154]

Adverse events with cholinesterase inhibitors and memantine

Cholinesterase inhibitors are associated with diarrhea, nausea, and vomiting, and less commonly with symptomatic bradycardia and syncope.[153 155] These drugs should therefore be used with caution in people with low resting heart rates. Memantine has been associated with dizziness, headache, confusion, and constipation.[156]

Benzodiazepines

RCTs comparing benzodiazepines with placebo for behavioral and psychological symptoms of dementia are lacking. Given serious concerns about adverse events, such agents are not recommended except for management of an acute crisis.

Adverse events with benzodiazepines

Benzodiazepines are associated with excessive sedation, lack of coordination, dizziness, falls, worsened cognition, respiratory depression, possible dependency and withdrawal, and occasionally paradoxical disinhibition.[157]

Agents under investigation

Several RCTs are investigating new compounds for agitation and aggression in dementia. Compounds include:

- Scyllo-inositol: speculated to ameliorate amyloid pathology
- Prazosin: an α1 adrenoceptor antagonist used for hypertension and benign prostatic hypertrophy[158]
- Brexpiprazole: an antipsychotic that is chemically similar to aripiprazole
- Dextromethorphan and quinidine[159]
- Melatonin agonists
- Δ9-tetrahydrocannabinol: the most biologically active isomer of tetrahydrocannabinol, a compound extracted from marijuana.[159]

Summary of drug treatments

Of all agents currently used for behavioral and psychological symptoms of dementia, atypical antipsychotics have the strongest evidence base, although their benefits are moderate at best (effect size 0.13-0.16). Any such benefits must be balanced against the risk of adverse events, including mortality. The mortality findings among individual antipsychotic agents seem to be consistent with the tolerability profile of individual atypical antipsychotics in the CATIE-AD trial, where olanzapine and risperidone were more efficacious than either quetiapine or placebo, but quetiapine and placebo were better tolerated.[126] Thus, although quetiapine (and valproic acid) may have a better safety profile than olanzapine and risperidone, this fact needs to be balanced against their reduced efficacy. This reflects the complex trade-offs that confront clinicians prescribing antipsychotics for these patients.

Antidepressants have shown limited benefit for depression in dementia. However, it has been theorized that because clinical trials often exclude severely depressed patients, the apparent treatment benefit may be reduced.[138] Recent evidence indicates that citalopram may hold promise for the treatment of agitation in dementia, but more research is needed to determine the optimal dose given concerns about possible QT prolongation at 30 mg.

Tailoring assessment and management

More effective assessment and management of the behavioral and psychological symptoms of dementia is needed. Although a variety of scales and tools are available to describe and document these symptoms (such as the Cohen-Mansfield agitation inventory,[160] behavioral pathology of Alzheimer's disease, and BEHAVE-AD),[161] they are rarely used in real world settings to guide management.[162] The short version of the NPI, the NPI-Q,[163] may strike the best balance between comprehensiveness and brevity.

If symptoms are not present, preventive measures can be put into place with care givers (counseling them about available resources, how to monitor for symptoms, the needs of the person with dementia—such as structured routines and activity—and the importance of self care).[164]

In terms of assessment, referring back to the conceptual model in fig 1, most of the contributory factors are potentially modifiable including:

- Factors related to the person with dementia (acute medical illness, underlying psychiatric illness, sensory deficits, and unmet needs)
- Factors related to the care giver (poor communication, emotional upset)
- Environmental factors (clutter, overstimulation, understimulation).

The provider should examine, exclude, and identify possible underlying and modifiable causes.

With regard to management, current evidence suggests that non-pharmacologic strategies, such as family care giver interventions, show greater effect than most drug treatments. However, drugs still have their place, especially for the management of acute situations where the safety of the person with dementia or family care giver may be at risk.

An evidence based standardized approach is needed that can detect and manage symptoms, carefully consider possible causes, and then integrate pharmacological and non-pharmacological treatments. We present an approach that we have developed in conjunction with a multidisciplinary national expert panel (composed of 12 US experts in dementia care from geriatric psychiatry, geriatric medicine, behavioral science, geriatric psychology, pharmacy, and nursing) to bridge this gap.[165] The panel was organized and sponsored by the University of Michigan Program for Positive Aging in collaboration with the Johns Hopkins Alzheimer's Disease Research Center and the Center for Innovative Care in Aging. The approach that the panel synthesized, referred to as DICE, stands for

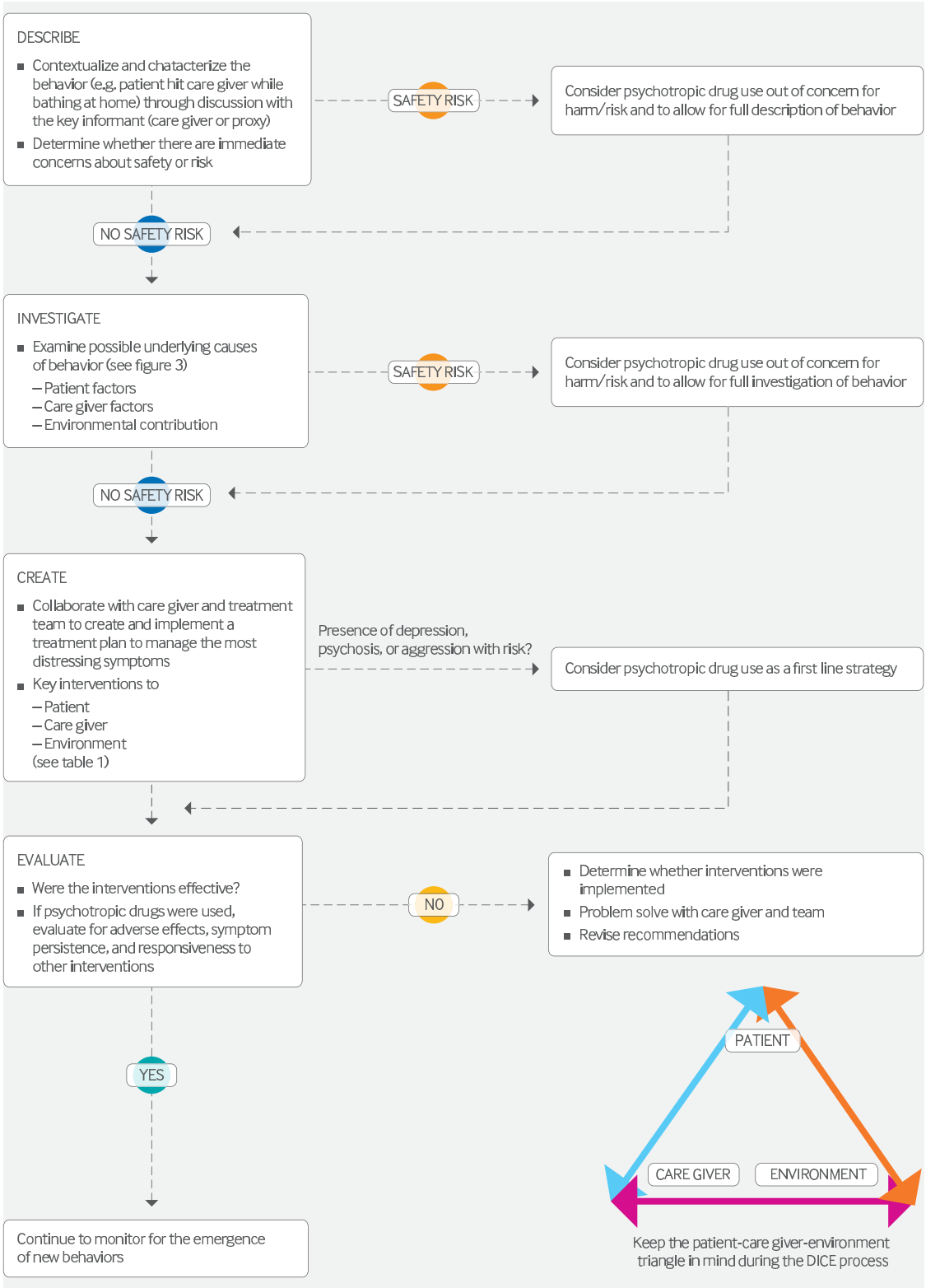

Fig 2| The DICE (describe, investigate, create, and evaluate) approach

"describe, investigate, create, and evaluate." The DICE approach assumes that a problem BPSD has been identified and brought to the provider's attention (fig 2). We have designed DICE to be used by any health professional and to work well within a team care setting that facilitates coordination among the implementation of medical, pharmacological, and non-pharmacologic strategies.

The DICE approach

Step 1: Describe

The first step is to elicit a thorough description of the symptoms by accurately characterizing the symptoms and the context in which they occur through discussion with the care giver and the person with dementia (if possible). This description should include consideration of possible

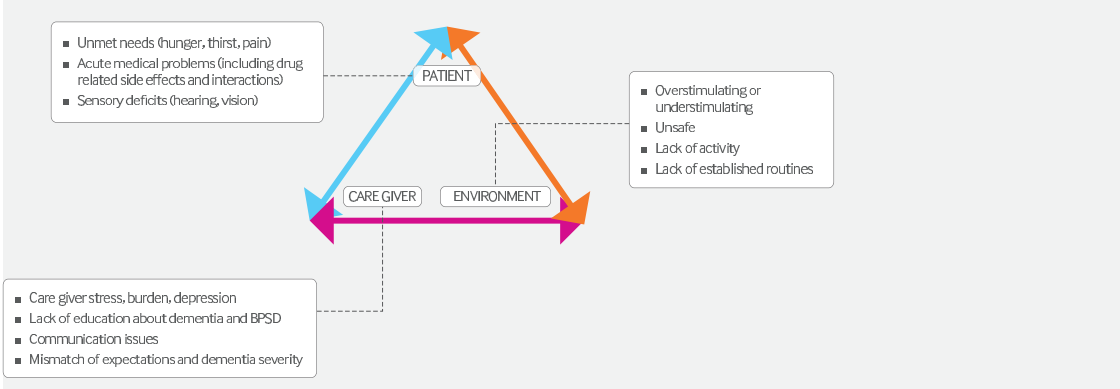

Fig 3| Modifiable causes of behavioral and psychological symptoms of dementia

antecedents or triggers of the behavior. It is important to understand which aspects of the symptoms are most distressing or problematic to the person with dementia and the care giver, as well as their treatment goal.

Step 2: Investigate

Once the symptoms are well characterized, the next step is for the provider to examine, exclude, and identify possible underlying and modifiable causes. Similar to the examination of delirium, the key to managing these symptoms is a thorough assessment of the underlying causes. Figure 3 depicts underlying causes that are potentially modifiable through intervention; we find it useful to think of the patient, care giver, and environment as an interacting triangle.

Undiagnosed medical conditions are important contributors. People with dementia may have disproportionately more pain and undiagnosed illnesses (such as urinary tract infection or anemia) than those without dementia.[44 166] An assessment of underlying causes also includes examining the current medication profile. It is crucial to investigate medical conditions such as urinary tract infection and other infections, constipation, dehydration, and pain. It may be helpful to perform blood tests, such as blood glucose and electrolytes, complete blood count with differential, and urine analysis. Other important considerations include previous psychiatric comorbidity, limitations in functional abilities, severity of cognitive impairment, poor sleep hygiene, unmet needs, sensory deficits (hearing or vision), and boredom.

The care giver's historical relationship with the person with dementia, communication styles, expectations, overestimation and underestimation of the patient's abilities, and their own stress and depression may inadvertently exacerbate behaviors. An environment that is overstimulating or understimulating, or that is difficult for patients to find their way around, can also contribute to symptoms, as can a lack of predictable routines and pleasurable activities.

Step 3: Create

In this step, the provider, care giver, person with dementia (if possible), and team collaborate to create and implement a treatment plan. Treatments can be categorized as medical, non-pharmacologic (referred to as "behavioral and environmental modifications" which target the patient, care giver, or environment (or a combination)) or pharmacologic. Figure 4 shows examples of various "create" interventions; although the examples depicted are general, there are many other possible interventions for specific symptoms.

In terms of medical treatments, the provider should prioritize responding to physical problems detected in the "investigate" step (such as prescribing antibiotics for a urinary tract infection, giving fluids for dehydration, or managing constipation). The treatment plan may also include stopping drugs that can have behavioral side effects if possible and evaluating whether other drug related side effects may be contributing to the symptoms. Effective pain management also has an important role and can reduce unnecessary psychotropic prescriptions.[48] Good sleep hygiene measures should be instituted. Sensory impairments (hearing and vision) should be investigated and corrected—for example, by changing glasses prescriptions and providing hearing aids.

Providers should brainstorm behavioral and environmental approaches with the care giver, person with dementia (when possible), and other team members (such as visiting nurse, social worker, and occupational therapist). Care givers are crucial team members because they will be carrying out and evaluating the effects of the recommended interventions. Modeling a problem solving approach and involving carers in decision making is key (for example, teaching them how to identify problem symptoms and brain storm effective solutions) to long term success. Although there are many potentially effective strategies, depending on the person with dementia, the care giver, and the environment, five domains of generalized strategies represent "low-hanging fruit":

- Providing education for the care giver
- Enhancing effective communication between the care giver and the person with dementia
- Creating meaningful activities for the person with dementia
- Simplifying tasks and establishing structured routines
- Ensuring safety and simplifying and enhancing the environment.[36 44 93 95 96 167 168]

Figure 4 lists examples of "create" strategies, including the five types of generalized strategy.

Because of the limited evidence base for psychotropic drugs, the following represents expert consensus based

Modifiable factor	Intervention example
PATIENT	
Unmet needs	• Make sure the person with dementia is getting enough sleep and rest • Deal with fear, hunger, toilet needs
Acute medical problems	Talk to the person's doctor about whether symptoms could have physical (e.g. urinary tract infection or pain) causes or be the result of a drug interaction or side effect
Sensory deficits	Encourage use of eyeglasses or hearing aids; have vision and hearing assessed
CARE GIVER	
Care giver stress, burden, depression	Care givers need to care for themselves by exercising regularly, getting help with care responsibilities, attending their own doctor's appointments, and using stress reduction techniques
Education	Understand that behaviors are not intentional or "on purpose" but are the consequence of a brain disease
Communication	• Use a calm voice • Do not use open ended questions • Keep it simple – do not over explain or discuss what events will be happening in the future • Limit the number of choice offered
ENVIRONMENT	
Overstimulating or understimulating environment	Regulate the amount of stimulation in the home by decluttering the environment, limiting the number of people in the home, and reducing noise by turning off radios and television sets
Unsafe environment	Make sure the person does not have access to anything (e.g. sharp objects) that could cause harm to themselves or others
Lack of activity	• Keep the person engaged in activities that match interests and capabilites • Relax the rules – there is no right or wrong way to perform an activity if the person is safe
Lack of structure or established routines	• Establish daily routines • Changing the time, location, or sequence of dialy activities can trigger outbursts • Allow enough time for activities • Trying to rush activities can also trigger behaviors

Fig 4| Examples of "create" interventions

on the clinical experience of the expert panel. Psychotropic drugs should be used only after serious efforts have been made to mitigate target symptoms using behavioral and environmental modifications and medical interventions if needed, with three exceptions. In each exception, the psychotropic drug suggested would be used because of concerns about serious and imminent risk:

- Major depression with or without suicidal ideation (for example, an antidepressant)
- Psychosis causing harm or with great potential for harm (for example, an antipsychotic)
- Aggression causing risk to self or others (for example, an antipsychotic or citalopram).

Given that psychosis and aggression may have underlying medical causes (for example, a urinary tract infection) and may impede the investigation of such causes, drugs may also be used as a temporizing measure for harmful symptoms during the "describe" and "investigate" steps (fig 2).

Close follow-up is needed to monitor for potential adverse effects of psychotropic drugs, and use should be time limited because behavioral and psychological symptoms of dementia may resolve over time, with or without drug treatment. If providers elect to use psychotropics, it is important to remember that their use in the treatment of these symptoms is not approved by the FDA, and that the risk:benefit ratio of the drug use must be carefully evaluated.

Psychotropic drugs are not likely to improve memory problems, not paying attention or caring about what is going on, repetitive verbalizations or questioning, rejection or refusal of care, shadowing, wandering, and behaviors that are dangerous to self (such as ingesting foreign material) or inappropriate (undressing in public).

Step 4: Evaluate

The final step is to assess whether recommended strategies were attempted and implemented effectively, whether the target symptoms improved, whether the care giver's distress was reduced, and whether there were any unintended side effects or consequences. If psychotropic drugs were judged to be needed, it is important to consider a trial of dose reduction or discontinuation to ensure that the drug is still needed. Because behaviors change and fluctuate over the course of dementia, ongoing monitoring is essential, and removal of interventions, especially drugs, should be considered at regular intervals (for example, Canadian consensus guidelines suggest every three months).[169] Such discontinuation trials are supported by a recent systematic review, which suggests that antipsychotics can be stopped in many of these patients, although caution should be exercised with those who have had severe symptoms.[170]

Once a symptom has resolved, ongoing monitoring for new behaviors, safety, care giver distress, and ongoing use of the strategies learnt during the DICE process for symptom management should continue. Previous trials have shown that care givers can learn what triggers symptoms in the person they are caring for and often become adept at spotting these triggers before the symptoms fully develop.

Future directions and research

Our approach might be used to better subtype behavioral and psychological symptoms of dementia in future trials. It could also be used to focus on particular symptoms at randomization, coupled with a systematic treatment approach—for example, a behavioral or environmental intervention using the DICE method first, followed by psychotropic testing. Future research is needed to compare the effectiveness of non-pharmacologic and pharmacologic strategies; understand the underlying biobehavioral mechanisms by which non-pharmacologic strategies work; and identify whether approaches such as the DICE method improve care and reduce costs to families and health systems, hospital admissions, and nursing home placements. A current US National Institutes of Health trial is examining the use of DICE paired with technology in an RCT of care givers.

Guidelines

Current guidelines for the management of behavioral and psychological symptoms of dementia include those from the UK National Institute for Health and Care Excellence (NICE),[68] American Psychiatric Association,[70 171] and American Geriatrics Society.[67] All recommend the use of

FUTURE RESEARCH QUESTIONS

- What specific brain areas, receptors, and neurotransmitters are involved in the neurobiology of the behavioral and psychological symptoms of dementia? Such knowledge could be used to improve pharmacologic and non-pharmacologic treatments
- What are the mechanisms by which behavioral and environmental approaches create benefits, such as stress reduction and increased tolerance of frustration? The results of such research could be used to tailor interventions more accurately
- How can behavioral and environmental approaches be better integrated into standard clinical care? What would be the cost? Is the cost offset by savings from reducing potentially preventable hospital admissions and early institutionalization?

non-pharmacologic behavioral strategies as first line, but none present the full evidence base for these approaches or give weight to the evidence for one non-pharmacologic approach over another. In terms of pharmacologic strategies, the guidelines discuss the risks of use of antipsychotic drugs but also do not detail the literature for comparative risk between individual antipsychotics and with other psychotropic drugs.[122 126] The NICE guideline offers the most comprehensive approach to assessment of underlying causes.

Discussion and challenges

The DICE approach emanates directly from successful care giver research interventions (REACH, ACT, COPE) and is compatible with the "person centered" approach commonly used in Europe. Our approach distils the content of earlier approaches as well as principles of good care (for example, assessment of underlying causes) into a streamlined, easy to use, algorithmic format.

However, tailoring treatments in this way is challenging in current care settings. Even if health professionals are adequately trained, the current US system does not allow time spent in such approaches to be reimbursed. So writing a prescription for a drug that might be modestly effective at best, and dangerous at worst, is the most common first line action.

Primary care providers also need better training in understanding the importance of assessing these symptoms, and their causes and management. They should also be reimbursed for time spent on approaches like DICE and have better access to backup specialty services (such as geropsychiatry and occupational therapy). It is our hope that healthcare systems will recognize the benefits of such approaches and compensate providers for time spent on the prevention, assessment, and management of behavioral and psychological symptoms of dementia.

In community settings, there needs to be a shift of resources from paying for psychoactive drugs and emergency room and hospital stays to adopting a more proactive approach. Although the proposed modification in healthcare organization would be a huge undertaking in most jurisdictions, without such a change policy makers may not see a meaningful reduction in the use of psychotropic drugs for these symptoms in community dwelling people with dementia. Any reductions in antipsychotics may mean just a shift to even less efficacious and similarly toxic drugs (such as anticonvulsants and benzodiazepines). Rather than using reduction in antipsychotics as the only metric of "good management," we must see the inclusion of a thorough assessment of underlying causes and greater support for the real world implementation of non-pharmacologic interventions, including the training needed to educate care givers about behavioral and environmental approaches.

Finally, more efficient and less toxic biological treatments are needed. With advances in neuroimaging and biomarkers, it is hoped that better treatment targets can be identified.

At a time when society is spending huge amounts on research into cures for Alzheimer's disease (which will take decades to find), we cannot ignore the fundamental importance of helping families and people with dementia to manage the burdensome behavioral aspects of the disease.

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