

Assessment and management of behavioral and psychological symptoms of dementia

Helen C Kales,^{1,2,3} Laura N Gitlin,^{4,5,6} Constantine G Lyketsos⁷

¹Section of Geriatric Psychiatry, Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109, USA

²Department of Veterans Affairs, Center for Clinical Management Research, Ann Arbor, MI, USA

³Geriatric Research Education and Clinical Center, VA Ann Arbor Healthcare System, Ann Arbor, MI, USA

⁴Department of Community Public Health, School of Nursing, Johns Hopkins University, Baltimore, MD, USA

⁵Division of Geriatrics and Gerontology, School of Medicine, Johns Hopkins University, Baltimore, MD, USA

⁶Center for Innovative Care in Aging, Johns Hopkins University, Baltimore, MD, USA

⁷Department of Psychiatry and Behavioral Sciences, Johns Hopkins Bayview and Johns Hopkins University, Baltimore, MD, USA
Correspondence to: H C Kales
kales@umich.edu

Cite this as: *BMJ* 2015;350:h369
doi: 10.1136/bmj.h369

This is an edited version of this paper. For full version and references see thebmj.com

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 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. This review focuses on community dwelling patients with dementia.

Sources and selection criteria

We identified articles for this review through searches of publications listed by PubMed from January 1992 to 1 June 2014. 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”.

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, increasing their impact even more.¹⁷

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 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

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} 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.

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, care giver factors, and environmental factors. Dementia may also directly cause symptoms by disrupting brain circuitry involved in behavior and emotion.

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).

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 The circuit model theorizes that three or more frontal-subcortical circuits have frontal, basal ganglia, and thalamic components that affect human behavior. Behavioral and psychological symptoms of dementia could result from synaptic or circuit disconnections in these networks.

Acute medical conditions

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} Side effects of drugs or drug-drug interactions can also 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.

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 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}

Environmental triggers

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

Non-pharmacologic treatments

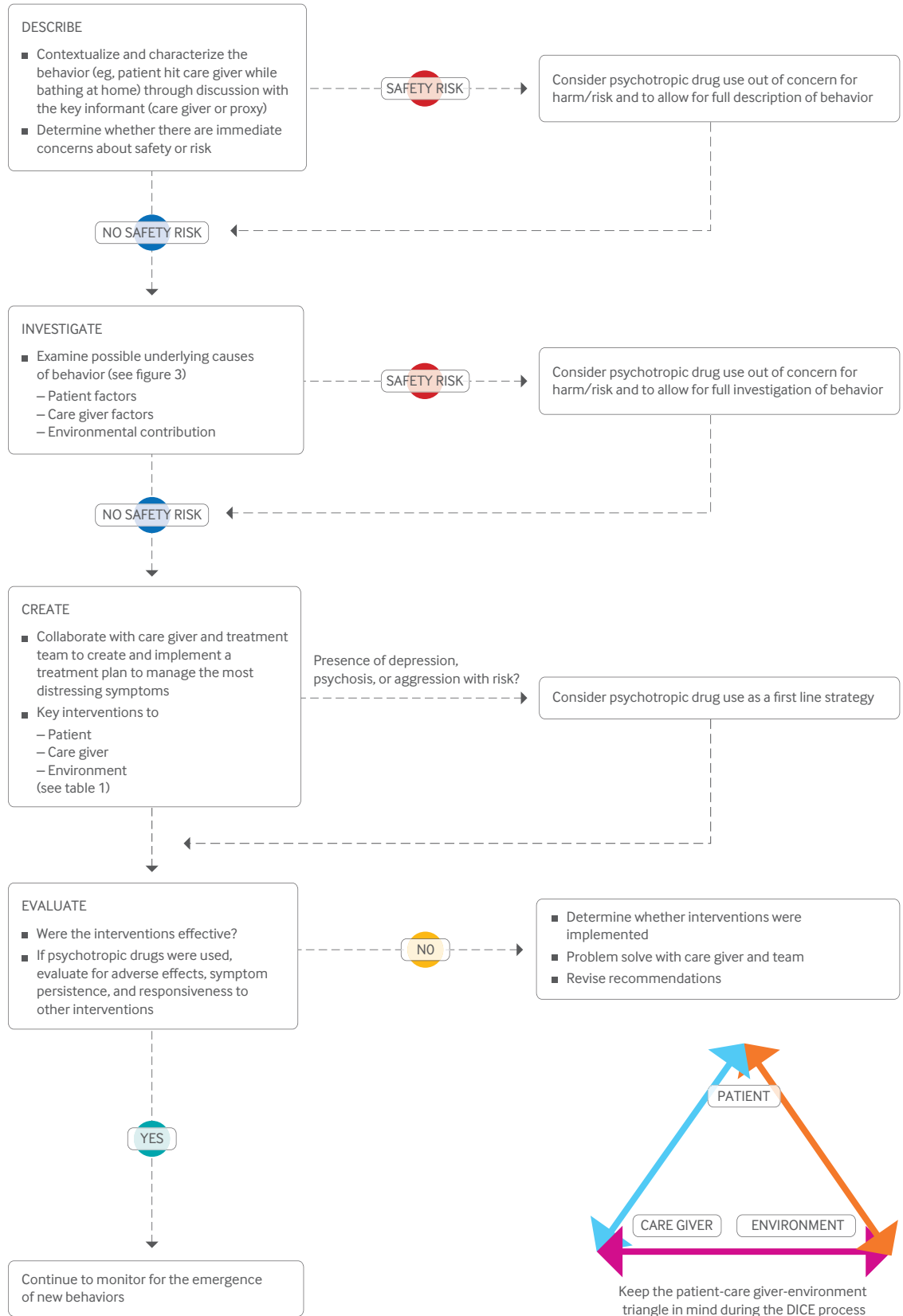
Non-pharmacologic treatments encompass a vast array of behavioral, environmental, and care giver supportive interventions. Numerous guidelines, medical organizations, and expert groups recommend non-pharmacologic strategies as the preferred first line treatment approach (except in emergency situations 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

There is a lack of clear agreement in the field about how to categorize non-pharmacologic interventions, but 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

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

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



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}

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 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.

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.

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

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. 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 syndrome¹¹⁵; 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

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.

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

Most recently, a large retrospective cohort study examined the mortality risk associated with individual antipsychotics.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

Modifiable factor	Intervention example
PATIENT	
Unmet needs	<ul style="list-style-type: none"> • 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 (eg, 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	<ul style="list-style-type: none"> • 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 choices 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 (eg, sharp objects) that could cause harm to themselves or others
Lack of activity	<ul style="list-style-type: none"> • Keep the person engaged in activities that match interests and capabilities • 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	<ul style="list-style-type: none"> • Establish daily routines • Changing the time, location, or sequence of daily activities can trigger outbursts • Allow enough time for activities • Trying to rush activities can also trigger behaviors

Fig 4 | Examples of “create” interventions

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

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.

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

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

Cholinesterase inhibitors are associated less commonly with symptomatic bradycardia and syncope.^{153 155} These drugs should therefore be used with caution in people with low resting heart rates.

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.

Tailoring assessment and management

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.

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 to bridge this gap (fig 2).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 “describe, investigate, create, and evaluate.” We have designed DICE to be used by any health professional. Fig 4 shows examples of various “create” interventions.

Discussion and challenges

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.