APPENDIX A

Treatment of Cognitive Aging and Dementia

Promoting Wellness

Validation Therapy

Nursing Protocols

Other Psychosocial Initiatives

Drug Therapies for Dementia (Cholinesterase Inhibitors)

Drug Therapies for Depression, Anxiety and Psychosis Related to Dementia

Antipsychotics

Emphasize Non-drug Interventions to treat Psychosis

Comparative Effectiveness and Comparative Side Effect Prevalence Analysis Required

Anxiolytics

In a 2015 study of “Cognitive Aging,” the IOM counseled that “cognitive aging is a natural process that can have both positive and negative effects on cognitive function in older adults—effects that vary widely among individuals.” It identifies and promotes actions that individuals, organizations, communities, and society can take to help older adults maintain and improve their cognitive health. The IOM assesses the state of knowledge about cognitive aging, including definitions and terminology, epidemiology and surveillance, prevention and intervention, education of health professionals, and public awareness and education. It is a good place to start in understanding what we now know about the aging brain.¹

Similarly, researcher/clinicians like the once-controversial Peter Whitehouse have begun treating dementia and cognitive impairment on a continuum, and used a positive aging model as a way to respond.² Quality of life and the interventions to preserve and restore it differ by individual more than by diagnosis. The most demonstrated improvement is with psychosocial, rehabilitative approaches. In this view, “dysfunction and disability are more important than precise diagnosis; quality of life trumps cognitive enhancement; community engagement is key; and population health perspectives gain influence over individual health.”³

With brains, as with so much else in life, “you use it or you lose it.” Those most involved in life are the most likely to stay involved and stay well. “Neurodegenerative conditions do not ‘claim’ older people, nor do they dominate them or degrade their humanity. They simply alter how they live their lives.”⁴ Effective prevention and appropriate treatment of all kinds of dementia may be the greatest public health challenge posed by the aging of the boomers.

Promoting Wellness
As with any mental health condition, both cognitive aging and dementia are best addressed early and often. The IOM recommends that individuals should:

- Be physically active.
- Reduce and manage cardiovascular disease risk factors (including hypertension, diabetes, and smoking).
- Regularly discuss and review health conditions and medications that might influence cognitive health with a health care professional. A number of medications can have a negative effect on cognitive function when used alone or in combination with other medications. The effects can be temporary or long-term.
- Take additional actions that may promote cognitive health, including socially and intellectually engaged, and engaging in lifelong learning.
- Get adequate sleep and receive treatment for sleep disorders if needed. [and]
- Be aware of the potential for financial fraud and abuse, impaired driving skills, and poor consumer decision making, and make health, finance, and consumer decisions based on reliable evidence from trusted sources.

In 2009, MHA launched a website (no longer active) called “Live Your Life Well,” intended to promote mental wellness through ten straightforward steps:

- Connect with Others. People who feel connected are happier and healthier—and may even live longer.
- Stay Positive. People who regularly focus on the positive in their lives are less upset by painful memories.
- Get Physically Active. Exercise can help relieve insomnia and reduce depression, and reduce chronic disease.
- Help Others. People who consistently help others experience less depression, greater calm and fewer pains.
- Get Enough Sleep. Not getting enough rest increases risks of weight gain, accidents, reduced memory and heart problems.
- Create Joy and Satisfaction. Positive emotions can boost your ability to bounce back from stress.
- Eat Well. Eating healthy food and regular meals can increase your energy, lower the risk of developing certain diseases and influence your mood.
- Take Care of Your Spirit. People who have strong spiritual lives may be healthier and live longer. Spirituality seems to cut the stress that can contribute to disease. Spirituality does not necessarily involve religion. Art and music are forms of spirituality.
- Deal Better with Hard Times. People who can tackle problems or get support in a tough situation tend to feel less depressed. [and]
- Get Professional Help if You Need It. More than 80 percent of people who are treated for depression improve.

Validation Therapy
“Validation therapy” is a prototype of the psychosocial approaches now being developed for older people with cognitive impairments and dementia. Social worker Naomi Feil has written extensively and maintains a consultancy promoting validation therapy. The basic principle of the therapy is the reciprocated communication of respect, which communicates that the other's opinions and feelings are heard, understood, acknowledged, and (regardless whether or not the listener actually agrees with the content) that the person is being treated with genuine respect, rather than being marginalized or dismissed.

Validation therapy uses specific techniques, and it has attracted criticism from researchers who dispute the evidence, which is generalized rather than specific, and thus difficult to synthesize in a meta-analysis. There is not yet enough rigorous evidence proving the efficacy of validation therapy, but it is a promising practice, harmless and an important line of defense as caregivers confront the anxiety, depression and psychosis that often come with cognitive impairment.

**Nursing Protocols**

Nursing protocols appropriately emphasize psychosocial interventions. Thus, the AHRQ National Guideline Clearinghouse recommends:

The Progressively Lowered Stress Threshold (PLST) provides a framework for the nursing care of individuals with dementia.

- Monitor the effectiveness and potential side effects of medications given to improve cognitive function or delay cognitive decline.
- Provide appropriate cognitive-enhancement techniques and social engagement.
- Ensure adequate rest, sleep, fluid, nutrition, elimination, pain control, and comfort measures.
- Avoid the use of physical and pharmacologic restraints.
- Maximize functional capacity: maintain mobility and encourage independence as long as possible; provide graded assistance as needed with ADLs and IADLs; provide scheduled toileting and prompted voiding to reduce urinary incontinence; encourage an exercise routine that expends energy and promotes fatigue at bedtime; and establish bedtime routine and rituals.
- Address behavioral issues: identify environmental triggers, medical conditions, caregiver–patient conflict that may be causing the behavior; define the target symptom (i.e., agitation, aggression, wandering) and pharmacological (psychotropics) and nonpharmacological (manage affect, limit stimuli, respect space, distract, redirect) approaches; provide reassurance; and refer to appropriate mental health care professionals as indicated.
- Ensure a therapeutic and safe environment: provide an environment that is modestly stimulating, avoiding overstimulation that can cause agitation and increase confusion and under-stimulation that can cause sensory deprivation and withdrawal. Utilize patient identifiers (name tags), medic alert systems and bracelets, locks, and wander guard. Eliminate any environmental hazards and modify the environment to enhance safety. Provide environmental cues or sensory aids that facilitate cognition, and maintain consistency in caregivers and approaches.
Encourage and support advance-care planning: explain trajectory of progressive dementia, treatment options, and advance directives.

Provide appropriate end-of-life care in terminal phase: provide comfort measures including adequate pain management; weigh the benefits/risks of the use of aggressive treatment (e.g., tube feeding, antibiotic therapy).

Provide caregiver education and support: respect family systems/dynamics and avoid making judgments; encourage open dialogue, emphasize the patient’s residual strengths; provide access to experienced professionals; and teach caregivers the skills of caregiving.

Integrate community resources into the plan of care to meet the needs for patient and caregiver information; identify and facilitate both formal (e.g., Alzheimer’s associations, respite care, specialized long-term care) and informal (e.g., churches, neighbors, extended family/friends) support systems.

Other Psychosocial Initiatives

Many exercise, educational, hobby, craft and other initiatives have been developed to promote positive aging, and senior centers and congregate care facilities all provide some level of stimulation and wellness education. A particularly interesting model is the Intergenerational School, a three-campus charter school in Cleveland, Ohio that uses elders as an integral part of its staff and curriculum. The Intergenerational School has been nationally recognized for its innovative, intergenerational approach to learning.

Brain games are a more recent innovation, using computer software to stimulate cognition. But a 2014 Stanford consensus report largely debunked the currently-available products:

- Many claims are “exaggerated and misleading” and exploit the anxiety of healthy older adults worried about memory loss. There’s no convincing evidence that any brain training programs will improve general cognitive abilities or help prevent or treat dementia.
- The companies often boast that their programs are designed by famous scientists and supported by solid research, but most of the studies they cite are small, short, and poorly designed, and many are conducted by researchers with financial interests in the products. The findings are often only tangentially related to the advertised claims. What’s more, it’s unclear whether any improvements in skills practiced in brain games would persist until even the next day or carry over to other cognitive tasks and daily living.
- The best brain-health advice, based largely on observational findings, is to lead a physically active, intellectually challenging, and socially engaged life, the authors wisely concluded. In particular, much research shows that physical exercise is a moderately effective way to maintain and even improve brain fitness. As the report pointed out, “If an hour spent doing solo software drills is an hour not spent hiking, learning Italian, making a new recipe, or playing with your grandchildren, it may not be worth it.”

Research is desperately needed to guide essential psychosocial treatment, but more importantly, MHA calls for innovation, including increased use of peer counselling to increase stimulation and decrease anxiety, technological applications to supplement a failing memory, interactive, voice-activated programs to minimize data entry issues, sophisticated monitoring and GPS location programs to keep people oriented in space and time, and various kinds of household robots to allow people to live in their own hopes with minimal help. Over time, and with a focus on peer support, whole communities can be redesigned to promote aging well.
**Drug Therapies for Dementia (Cholinesterase Inhibitors)**

Unfortunately, current drug therapies for Alzheimer’s disease and other dementias are not very effective and, despite FDA approval, are controversial for that reason. Drug therapies to deal with the anxiety and psychosis that often accompany the cognitive symptoms of dementia are off-label, little studied, and thus even more controversial. Dementia treatment is not an issue that MHA has addressed in the past, but the serious deficiencies of existing prescribing practices demands scrutiny. The next sections of this position statement will provide guidance for the present and advocacy for the future, with the caveat that psychosocial interventions should both precede and accompany drug therapy, and that while no cure is in sight, MHA holds out hope that some of the many current research initiatives will prove fruitful.

There is no magic pill to prevent the aging of the brain or the other causes of dementia. But the U.S. Food and Drug Administration (FDA) has approved three cholinesterase inhibitors -- donepezil (Aricept), rivastigmine (Exelon) and galantamine (Razadyne) -- and one glutamate antagonist -- memantine (Namenda) — to treat the cognitive symptoms (memory loss, confusion, and problems with thinking and reasoning) of Alzheimer's disease. Doctors sometimes prescribe both types of medications together. Some doctors also prescribe high doses of vitamin E for Alzheimer's disease, although that that is becoming less common.

Although current medications cannot cure Alzheimer’s or stop it from progressing, they **may help lessen symptoms**, such as memory loss and confusion, but only **for a limited time**. As stated by *Consumer Reports*:  

“...[A]fter six months on the drugs, most of the patients show no improvement in mental functioning, based on their doctors’ assessments and tests of basic thinking skills. **Among the few who do benefit, the improvement is typically slight.** The available studies have not shown that the drugs help achieve what we would consider major goals of dementia treatment, prolonging people’s ability to live independently or improving quality of life for either patients or caregivers,” [Consumer Reports reported].

Even a small benefit or chance of improvement might be worth it if Alzheimer’s drugs were risk free. But they are not. They can cause side effects such as insomnia, nausea, muscle cramps, diarrhea, and reduced appetite, all of which can be troublesome for people with dementia. Rarely, the drugs may cause more serious side effects such as internal bleeding and a slowed heart rate that could be potentially dangerous.”

Cholinesterase inhibitors are widely endorsed and used. However, they are expensive, and the effect is modest at best. There is some evidence of permanent worsening of symptoms upon discontinuation of treatment, so once started, it may be hard to stop until late in the course of the disease. But there are inadequate data to substantiate this concern. The Cochrane Dementia and Cognitive Improvement Group’s 2006 review concluded:

“The results of ten randomized, double blind, placebo controlled trials demonstrate that treatment for six months, with donepezil, galantamine or rivastigmine at the recommended dose for people with mild, moderate or severe dementia due to Alzheimer's disease produced improvements in cognitive function, on average -2.7 points (95%CI -
3.0 to -2.3, p<0.00001), in the midrange of the 70 point ADAS-Cog Scale. Study clinicians rated global clinical state more positively in treated patients. Benefits of treatment were also seen on measures of activities of daily living and behavior. **None of these treatment effects are large.**

The effects are similar for patients with severe dementia, although there is very little evidence, from only two trials.

A 2012 Cochrane review focused on Parkinson’s disease and dementia with Lewy bodies was more positive:

The clinical features of dementia with Lewy bodies (DLB) and Parkinson's disease with dementia (PDD) have much in common. As patients with DLB and PDD have **particularly severe deficits in cortical levels of the neurotransmitter acetylcholine**, blocking its breakdown using a group of chemicals known as cholinesterase inhibitors may lead to clinical improvement. **Six trials showed a statistically significant improvement in global assessment, cognitive function, behavioral disturbance and activities of daily living rating scales in PDD and cognitive impairment in Parkinson's disease (CIND-PD) patients treated with cholinesterase inhibitors.**

However, the effect is still modest. Finally, the conclusions of a 2012 Cochrane review of studies of the use of cholinesterase for mild cognitive impairment were quite negative:

**There is very little evidence that cholinesterase inhibitors affect progression to dementia or cognitive test scores in mild cognitive impairment. This weak evidence is overwhelmed by the increased risk of adverse events, particularly gastrointestinal. Cholinesterase inhibitors should not be recommended for mild cognitive impairment.**

Until a political decision was made to make cholinesterase inhibitors generally available in the U.K., the U.K. National Health Service attempted to restrict reimbursement. And experts like Peter Whitehouse continue the dialogue in the United States. However, on balance, Whitehouse agrees that, in the current state of knowledge, he would be willing to prescribe cholinesterase inhibitors for dementia, because the effect, though small and by no means assured, could still be significant for the individual. **People in treatment need to understand this background to be able to decide whether or not to start on dementia drugs in light of the evidence, which is positive only for Parkinson’s and Lewy body dementia, demonstrates only modest relief of symptoms at best, does not demonstrate any slowing of the disease process, discourages use in mild cognitive impairment, and indicates a risk both in using and in discontinuing the medication.**

The truth is that we still know very little about the pathology of dementia, and the increasing focus on Alzheimer’s disease, while helpful in focusing attention on the riddle of dementia, obscures the individual factors that make each diagnosis unique:
Perhaps everyone’s Alzheimer’s condition or dementia is unique to them because different individual processes are involved throughout the life-course, including factors like head injuries, diet, alcohol consumption, and a panoply of social determinants of health, including air and water quality. Moreover, in the last several decades increasing overlaps between aging and dementia and among types of dementias have become more apparent. Neuronal loss, plaques, and tangles all can occur in individuals who do not have a clinically apparent dementia. Moreover, these features can occur in other conditions such as Parkinson’s and frontal lobe dementia. Our ability to differentiate these overlapping conditions from each other, much less from processes associated with aging, remain rudimentary. Even the allegedly clear-cut distinction between vascular disease and neurodegenerative disease is getting muddier the more we look at risk factors and biological markers. This aptly describes a scientific tangle every bit as complicated as the tangles associated with dementia. More research is clearly necessary and may someday help American society to cope with what is likely to become an epidemic as our population ages. The key is to pursue research into psychosocial as well as pharmacological interventions.

**Drug Therapies for Depression, Anxiety and Psychosis Related to Dementia**

**Causes of and treatments for Alzheimer’s disease and other forms of dementia are riddles that future research must address. But there are critical, practical issues that must be addressed right now in managing the psychiatric symptoms of cognitive impairment, and it is an indictment of our drug regulatory system that they are only now being addressed at all.**

People with dementia experience anguish and anxiety from life crises and loss of mental capacities and often have psychotic and depressive symptoms as well, and the agitation, depression and psychotic features impair quality of life, perhaps even more than the cognitive symptoms in many people. For example, many people with dementia do not recognize where they are, even in their own home, or who is taking care of them, and feel unsafe, anxious and depressed. In the absence of data specific to older people or people with dementia, these symptoms have been treated with medications approved for anxiety (principally benzodiazepines), depression, and psychosis. Antidepressants are effective in treating co-occurring depression and have not yet been controversial, though testing in elderly populations has lagged. The widespread off-label use of antipsychotics has raised the greatest problems. However, the use of benzodiazepines for anxiety is being called into question as well. They are effective but potentially addictive and definitely exacerbate delusions. Thus, their use should at least be minimized.

**Antipsychotics**

In the absence of U.S. Food and Drug Administration (FDA) guidance, physicians have used off-label antipsychotics to treat psychotic symptoms of dementia. As of 2010, one-quarter of nursing-home residents had used antipsychotics. The U.S. General Accounting Office (GAO)
found that by 2012, the proportion had risen to one third.\(^{20}\) MHA agrees with the GAO that these percentages are an indictment of the long-term care industry.

The available scientific evidence is weak, as pointed out in a 2005 *JAMA* review:

For typical antipsychotics,…[g]enerally, no difference among specific agents was found, efficacy was small at best, and adverse effects were common. Six RCTs [randomized controlled trials] with atypical antipsychotics were included; results showed modest, statistically significant efficacy of olanzapine and risperidone, with minimal adverse effects at lower doses. Atypical antipsychotics are associated with an increased risk of stroke. There have been no RCTs designed to directly compare the efficacy of typical and atypical antipsychotics. Five trials of antidepressants were included; results showed no efficacy for treating neuropsychiatric symptoms other than depression, with the exception of one study of citalopram. For mood stabilizers, three RCTs investigating valproate showed no efficacy. Two small RCTs of carbamazepine had conflicting results. Two meta-analyses and six RCTs of cholinesterase inhibitors generally showed small, although statistically significant, efficacy. Two RCTs of memantine also had conflicting results for treatment of neuropsychiatric symptoms.

**Pharmacological therapies are not particularly effective for management of neuropsychiatric symptoms of dementia.**\(^{21}\)

NAMI summarized the evidence on Treatment of Behavioral and Psychological Symptoms of Dementia in 2014 as follows:

- **Atypical antipsychotics (6 RCTs)** – Modest but statistically significant effects – Few adverse events at lower doses BUT: \(~1.6-1.7\) fold increase in mortality in active treatment over placebo – Rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Deaths due to heart related events (e.g., heart failure, sudden death) or infections (mostly pneumonia), cerebrovascular adverse events, hyperglycemia and diabetes mellitus.

- **Typical antipsychotics (2 RCTs)** – Minimal efficacy, frequent adverse events (may be severe) – [Associated with significantly higher adjusted risk of death relative to atypical antipsychotics -- MHA contests this assertion. Both typical and atypical antipsychotics are associated with significantly higher adjusted risk of death.\(^{22}\) ]

- **Mood stabilizers/antidepressants (5 RCTs)** – No efficacy on neuropsychiatric symptoms except depression.

- **Antiepilepsy drugs (5 RCTs)** – No efficacy with valproate; conflicting results with carbamazepine.

- **Cholinesterase Inhibitors (6 RCTs)** – Minimal effect/conflicting results; statistically significant in 2 RCTs.
• Memantine (2 RCTs) – Conflicting results.\textsuperscript{23}

Few studies of these drugs have been done in older people and in dementia of various types. Antipsychotics are widely used even though they increase the risk of death in elders. As has been documented in a recent (2015) serialized book by Steven Brill, published by the Huffington Post,\textsuperscript{24} drug companies have promoted off-label use of antipsychotics without seeking FDA approval for their claims.

This situation requires a little explanation. The FDA reviews drugs for efficacy and safety and approves drugs for specific conditions. These are the labeled indications. The FDA does not regulate or monitor physicians, who are governed only by state licensure and civil malpractice. Clinicians with appropriate state licensure may prescribe any drug approved by the FDA for any purpose for any other condition that they believe warrants using the drug, without regard to the FDA label. This is called “off-label use.” In recent years, drug companies have been more assertive in marketing drugs. They have sometimes promoted off-label use, as illustrated by the following cautionary tale:

Despite the lack of FDA approval of its “second generation” “atypical” antipsychotic Risperdal (risperidone) for use in older people or in people with dementia, and a 2005 express FDA “black box” WARNING -- \textit{Warning: Increased mortality in elderly patients with dementia-related psychosis} – the manufacturer thereafter aggressively marketed risperidone “for simple symptoms of dementia or restlessness.”\textsuperscript{25} In a plea agreement resolving these charges, it conceded that it illegally promoted Risperdal to health care providers “for treatment of psychotic symptoms and associated behavioral disturbances exhibited by elderly, non-schizophrenic dementia patients.”\textsuperscript{26}

The dilemma for a family or a person in treatment is that there is no pharmaceutical treatment approved by the FDA for treatment of psychotic symptoms and associated behavioral disturbances exhibited by elderly people with dementia who do not have schizophrenia, even though the DSM 5 expressly states that antipsychotics are used for that purpose. Thus, if available psychosocial care is inadequate to deal with the symptoms, when the family or the care facility has run out of options, a typical or atypical antipsychotic will be prescribed off-label. Based on an unscientific sample collected by MHA, hospice programs often prescribe haloperidol (Haldol), an older and cheaper typical antipsychotic, while psychiatrists generally use atypical antipsychotics. But all use extremely low doses, and clinicians and care workers alike claim that the drugs are effective in a significant number of patients, based on their experience.

Yes, the evidence is weak, and there is a significant risk of stroke and other side effects, but if available psychosocial approaches fail, antipsychotic drugs will be used to deal with psychotic symptoms, especially when needed to preserve the safety of the staff and other people in treatment, and to avoid the use of seclusion and restraints. Why then is someone not busy studying risperidone and other anti-psychotics and working on comparisons and improvements right now?
The general answer is that private funding now dictates the direction of most research. “When looking at the numbers, I see an imbalance,” said Stephan Ehrhardt, an associate professor in the Johns Hopkins Bloomberg School of Public Health’s Department of Epidemiology, in a 2015 study. “Industry doesn’t fund trials most important for public health because they have no incentive to do that.”

This trend has emerged as the budget for the National Institutes of Health—the primary source of government funding for clinical trials—has been slashed 24 percent since 2006 amid belt-tightening in Washington. The drug and medical device industry now funds six times more clinical trials than the federal government, according to the Johns Hopkins University researchers. That means companies with financial interests in the studies now have more control over what doctors and patients learn about new treatments. And pharmaceutical companies are unlikely to address the use of antipsychotics in dementia care:

First, because most antipsychotics are now out-of-patent, and there is little profit to be made.

Second, because there are significant ethical issues whenever people have complicated medical conditions, as the elderly always do, and whenever competency is in question, as it is in anyone with dementia.

And third, because the risk/benefit equation is skewed, and the public policy that favors finding a reliable drug and demonstrating its reliability to treat the psychiatric symptoms of dementia has been ignored in prioritizing punishing manufacturers for promoting off-label uses.

MHA believes that a more significant additional sanction would be to require the manufacturer to conduct and disclose studies to back up its claim. If additional authority is needed for the FDA to insist on full disclosure and additional studies of drugs being marketed and used off-label as frequently as are antipsychotics, MHA strongly supports congressional action to grant such authority. In addition, the FDA should use the full range of enforcement incentives and “nudges” that it can devise to get these drugs properly evaluated and controlled. Academic researchers and public interest organizations like the Cochrane Collaboration should be recruited to help. And NIH funding should be increased to focus more research on these drugs and others with major public health implications.

Finally, MHA urges the pharmaceutical industry, in the public interest, to help build an evidence base of published and unpublished studies that it has conducted of the use of anti-psychotics to treat psychiatric conditions associated with dementia. Whenever possible, the federal government should insist, in the interest of science, that ALL such studies be made available to the public.

Psychotic symptoms of dementia are difficult for patients, clinicians, families and caregivers to deal with. Medication needs more study, but it must be stressed: It is not the only answer. We need good research on psychosocial treatments as well.
Comparative Effectiveness and Comparative Side Effect Prevalence Analysis Required

Haloperidol (Haldol) is an older antipsychotic used frequently to treat the psychotic features of dementia, especially as part of a program of palliative care, but there are no studies validating its use for that off-label purpose. It went out of patent in 1986. Risperidone (Risperdal and generics), Seroquel (quetiapine) and Zyprexa (olanzapine) are the “atypical” antipsychotics currently being used off-label for psychotic symptoms of dementia, which are thought by psychiatrists to be preferable because the side effects (especially tardive dyskinesia) are less frequent than with haloperidol. However, the listed side effects are substantial in the more recent drugs as well, and there are no data on the relative prevalence of side-effects. The FDA refused to allow any comparative effectiveness or comparative side effect language on the risperidone label. Risperidone is now out-of-patent as well. All antipsychotics have serious side effects.

Major government and professional society efforts have emerged to try to decrease the use of antipsychotic drugs, particularly in long-term care. For all antipsychotics, the FDA requires a warning that the drug is not approved for treatment of dementia-related psychosis and may increase the risk of death. Quetiapine has the anti-depressant black box warning concerning the increased risk of suicide as well. Obviously, these warnings have had little if any effect in discouraging off-label use.

Other antipsychotics that may be used to treat psychotic features of dementia include asenapine (Saphris), iloperidone (Fanapt), paliperidone (Invega or Sustenna), and ziprasidone (Geodon). These have side effects and warnings similar to those of the three drugs discussed above. MHA advocates that all of these drugs be carefully tested through a comparative effectiveness and safety analysis for use to alleviate psychotic features of dementia and that the labels be amended to give more guidance as soon as possible.

Emphasize Non-drug Interventions to treat Psychosis

Although there are times when drug treatment is the only alternative, psychosocial techniques should be tried first, and may be more effective, according to 2015 British Medical Journal study. Dr. Helen Kales, a psychiatrist who directs the University of Michigan's Program for Positive Aging, examined more than two decades of scientific studies, along with her coauthors, Laura N. Gitlin and Dr. Constantine Lyketsos, both of Johns Hopkins University. They say the treatments that showed the best results were the ones that trained caregivers how to communicate calmly and clearly, and to introduce hobbies or other activities for the person in treatment. The treatments also followed up with caregivers.

"I think the caregiver interventions work… because they train caregivers to look for the triggers of the symptoms," says Kales. "And when [caregivers] see the triggers of the symptoms, they train them to manage them...It's inherently patient- and caregiver-centered." The study showed that antipsychotic drugs were only about half as effective as the caregiver interventions. Health care providers use antipsychotics, says Kales, partly because they haven't been trained to use non-drug approaches. And even if they did know how to use them, they're rarely reimbursed for doing so by Medicare or private insurance.
Thus, caregivers need to refocus on interventions that respond to the idiosyncratic needs of the individual. This is sometimes very difficult when the person in treatment is at home, but it is essential to train and support caregivers as well as nursing home staff in psychosocial options that reduce the risks of using antipsychotic medications whenever possible.

As previously stated, a 2015 GAO Report recommended an expansion of U.S. Department of Health and Human Services (HHS) efforts to decrease antipsychotic use, which were initiated in 2012 in nursing homes under the National Alzheimer’s Plan. GAO recommended that HHS expand its outreach and educational efforts aimed at reducing antipsychotic drug use among older adults with dementia to include those residing outside of nursing homes by updating the Plan.

Alternatives exist. The GAO recommended emotional therapies and sensory stimulation:

An example of an emotion-oriented approach is Reminiscence Therapy, which involves the recollection of past experiences through old materials with the intention of enhancing group interaction and reducing depression. An example of a sensory stimulation approach is Snoezelen Therapy, which typically involves introducing the individual to a room full of objects designed to stimulate multiple senses, including sight, hearing, touch, taste, and smell. This intervention is based on the theory that behavioral symptoms may stem from sensory deprivation. A 2012 white paper published by the Alliance for Aging Research and the Administration on Aging, a part of the ACL, noted that advancements have been made with regards to the evidence base supporting some nonpharmacological interventions, but that evidence-based interventions are not widely implemented. Experts referenced in the white paper identified the need for clearer information about the interventions, such as a system to classify what interventions exist and who might benefit from those interventions. Experts also noted that additional research is needed to develop effective interventions.

Educating health care workers reduces the inappropriate use of antipsychotics. A two-day education program in Norwegian nursing homes, followed by a six-month period of monthly group guidance, reduced both the use of restraints and patient agitation. The study included four Norwegian nursing homes housing 145 total residents with dementia, with each home randomly assigned to receive either treatment as usual or an intervention consisting of the two-day educational seminar and monthly group guidance for six months. The co–primary outcome measures were the proportion of residents subject to interactional restraint and the severity of agitation using the Cohen-Mansfield Agitation Inventory (CMAI). The CMAI score declined from baseline to 6 and 12 months’ follow-up in the experimental groups compared to a small increase in the control groups.

A study in Northern Ireland utilized specially trained pharmacists, who visited one group of nursing homes regularly over a year and used an algorithm to assess the appropriateness of using psychotropic drugs on residents. By the end of the study, the proportion of residents taking inappropriate psychotropic medications in the experimental group of homes was 19.5 percent, compared to 50.0 percent in the control group.
In another Norwegian study, lowering the dose of antipsychotic medication proved effective in lowering Neuropsychiatric Inventory scores, which measure agitation, apathy, psychosis, and restlessness. And in the same study that utilized the memory test, the residents taken off antibiotics and receiving benzodiazepines or antihistamine hypnotic agents reported more stable or improved anxiety levels over the residents in the control group. At the very least, health care providers, especially those in nursing homes, should regularly monitor and reevaluate elderly patients on antipsychotic medication, and make efforts to stop use or wean off use of them over time.

**Anxiolytics**

Benzodiazepines are the most common psychotropic drugs taken for anxiety in the United States:

- alprazolam (Xanax)
- chlordiazepoxide (Librium)
- clonazepam (Klonopin)
- clorazepate (Tranxene)
- diazepam (Valium)
- estazolam (Prosom)
- flurazepam (Dalmane)
- lorazepam (Ativan)
- oxazepam (Serax)
- temazepam (Restoril)
- triazolam (Halcion)
- quazepam (Doral)

Although causation has not been established, in 2014, a team of researchers from France and Canada established a convincing link between use of benzodiazepines and the development of dementia. People who had taken a benzodiazepine for three months or less had about the same dementia risk as those who had never taken one. Taking the drug for three to six months raised the risk of developing Alzheimer’s disease by 32%, and taking it for more than six months boosted the risk by 84%. Psychiatrists consulted for this position statement all warn that benzodiazepines can exacerbate delusions in anyone with dementia. An FDA WARNING counsels that benzodiazepines are: “not recommended in the treatment of psychotic patients.” Benzodiazepines are definitely contraindicated in dementia with Lewy bodies, and thus in Parkinson’s disease, though the Parkinson’s Association only recommends “caution” in Parkinson’s dementia.

MHA urges that elders consider use of alternative treatments for anxiety that do not have such cognitive associations. For anyone with dementia, benzodiazepines should be used sparingly, and some psychiatrists avoid using them altogether. Pharmaceutical manufacturers should respond to the challenge of creating a new generation of anxiolytic drugs. Integrative/complementary (“CAM”) treatments for anxiety with varying assessments of efficacy include cranial electrical stimulation, rhodiola *rosea*, valerian, kava (in small amounts to avoid liver toxicity), relaxation techniques and meditation. Cranial electrical stimulation has recently been found in a pilot study to have positive effects on cognition, virtually ruling out that concern. And psychosocial
techniques should always be used before trying drug interventions. Validation therapy has an important role in coping with anxiety, as do techniques to refocus the person’s attention like hobbies and exercise.

Common drugs like antihistamines and benzodiazepines may exacerbate dementia symptoms in some people under some circumstances and should be used with caution by people with any kind of dementia or mild cognitive impairment. Overall, there is an inadequate evidence base for use of these drugs in older people.

**MHA urges much more research and public education concerning the dangers of using anxiolytics and antihistamines in people with dementia. CAM treatments are often a better alternative, with fewer side effects. And again, psychosocial techniques should be emphasized before considering drug therapy and as an essential adjunct if anxiolytics are used.**

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4. *Id.*, introduction, at xi.


9. Rather surprisingly, because their scientific foundation was weaker than for cholinesterase inhibitors, a glutamate antagonist, Namenda (memantine), was approved in 2003, but in general its effects are less consistent than those of the cholinesterase inhibitors. Frequently, cholinesterase inhibitors and glutamate antagonists are prescribed together, although the Cochrane Dementia and Cognitive Improvement Group’s last review (in 2006) concluded that:

   Memantine has a small beneficial, clinically detectable effect on cognitive function and functional decline measured at 6 months in patients with moderate to severe Alzheimer’s Disease (AD). In patients with mild to moderate dementia, the small beneficial effect on cognition was not clinically detectable in those with vascular dementia and barely detectable in those with AD.


13 All Cochrane reviews can be accessed at http://onlinelibrary.wiley.com/cochranelibrary/search


15 M.D., Ph.D., Professor of Neurology and current or former Professor of Psychiatry, Neuroscience, Psychology, Cognitive Science, Bioethics, Nursing, History, and Organizational Behavior, Case Western Reserve University.


17 In 2015, Mental Health America began collecting data related to the mental health conditions of people with dementia through its online screening program at www.mhascreening.org.

18 One review links SSRIs with dementia, and speculates: “Contrary to a widely held belief in psychiatry, studies that purport to show that antidepressants promote neurogenesis are flawed because they all use a method that cannot, by itself, distinguish between neurogenesis and neuronal death. In fact, antidepressants cause neuronal damage and mature neurons to revert to an immature state, both of which may explain why antidepressants also cause neurons to undergo apoptosis (programmed death).” The FDA has not required a warning or restricted the label, and antidepressants are used to treat depression in the elderly. See Andrews et al., “Primum Non Nocere: An Evolutionary Analysis of Whether Antidepressants Do More Harm Than Good,” Frontiers in Psychology 3:117 (2012).

19 http://www.nytimes.com/2010/10/03/business/03psych.html?pagewanted=all&_r=0

20 “Antipsychotic drugs are frequently prescribed to older adults with dementia. GAO’s analysis found that about one-third of older adults with dementia who spent more than 100 days in a nursing home in 2012 were prescribed an antipsychotic, according to data from Medicare’s prescription drug program, also known as Medicare Part D. Among Medicare Part D enrollees with dementia living outside of a nursing home that same year, about 14 percent were prescribed an antipsychotic.” U. S. Government Accounting Office, Antipsychotic Drug Use, GAO 15-211 (January, 2015), http://www.gao.gov/assets/670/668221.pdf, available online at http://www.gao.gov/products/GAO-15-211


22 http://doh.dc.gov/service/prescription-drug-marketing-costs-access-rx


24 http://highline.huffingtonpost.com/miracleindustry/americas-most-admired-lawbreaker/chapter-1.html

25 Id.


See American Psychiatric Association, *Practice Guideline for the Treatment of Patients With Alzheimer’s Disease and Other Dementias* (October 2007); American Geriatrics Society, “Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults,” *Journal of the American Geriatrics Society* 60:4 (2012); and American Medical Directors Association, Excerpts from the *Dementia in the Long Term Care Setting Clinical Practice Guideline: American Medical Directors Association* (Columbia, MD 2012).


http://www.npr.org/sections/health-shots/2015/03/05/390903112/for-dementia-patients-behavioral-therapy-helps-more-than-drugs


GAO 15-211 at 9


Billioti de Gage, S., Moride, Y., Ducruet, T., Kurth, T., Verdoux, H., Tournier, M., Pariente, A & Bégaud, B., “Benzodiazepine use and risk of Alzheimer’s disease: case-control study,” *BMJ* 9:349:g5205 doi: 10.1136/bmj.g5205 (2014): “Benzodiazepine ever use was associated with an increased risk of Alzheimer’s disease (adjusted odds ratio 1.51, 95% confidence interval 1.36 to 1.69; further adjustment on anxiety, depression, and insomnia did not markedly alter this result: 1.43, 1.28 to 1.60). No association was found for a cumulative dose <91 prescribed daily doses. The strength of association increased with exposure density (1.32 (1.01 to 1.74) for 91-180 prescribed daily doses and 1.84 (1.62 to 2.08) for >180 prescribed daily doses) and with the drug half life (1.43 (1.27 to 1.61) for short acting drugs and 1.70 (1.46 to 1.98) for long acting ones).”

**CONCLUSION:**
“Benzodiazepine use is associated with an increased risk of Alzheimer’s disease. The stronger association observed for long term exposures reinforces the suspicion of a possible direct association, even if benzodiazepine use might also be an early marker of a condition associated with an increased risk of dementia. Unwarranted long term use of these drugs should be considered as a public health concern.”
37 http://www.parkinson.org/understanding-parkinsons/non-motor-symptoms/anxiety/What-are-the-Treatment-Options-for-Anxiety

38 MHA maintains a website giving the evidence for these complementary treatments, at http://www.mentalhealthamerica.net/sites/default/files/MHA_CAM.pdf