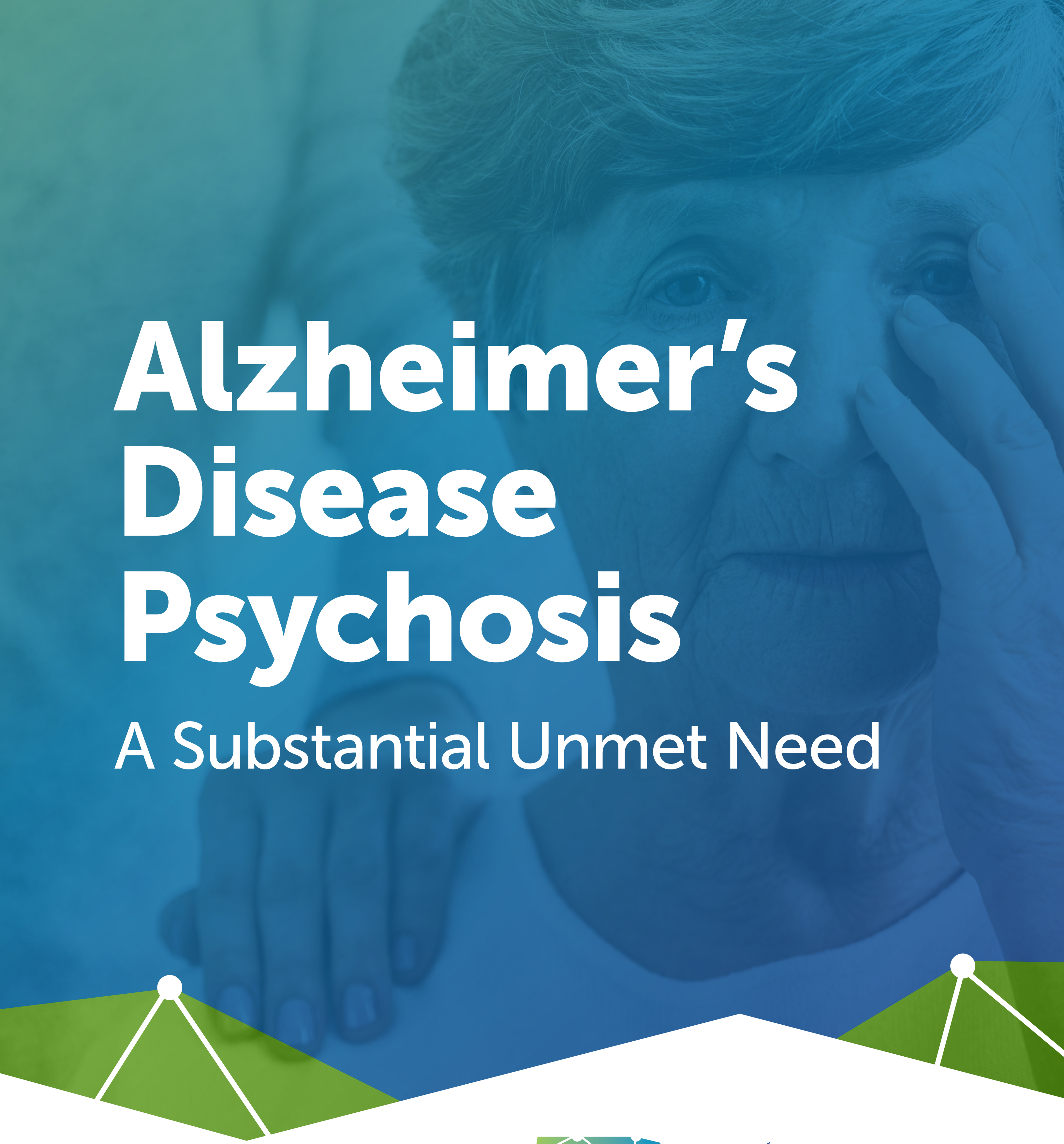

Alzheimer's Disease Psychosis

A Substantial Unmet Need

A Clinical Proceedings White Paper
August 2022

Clinical Neurological Society of America

About the Clinical Neurological Society of America

Established in 1974, the Clinical Neurological Society of America was created as an organization for neurologists practicing in clinical and academic settings. Since then, the society has grown into a nationwide organization of clinicians with a mission to improve clinical practice and patient care through education.

As a non-profit 501(c)(6) professional membership organization, CNSA is led by a volunteer board of directors who, like the society's professional members, hail from across the country and treat patients with a range of neurologic conditions.

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The society's membership is known for fostering strong professional support systems and long-lasting friendships. Clinicians at any stage of practice are invited to join. Visit neuroamerica.org for more information about CNSA and to become a member.

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Introduction to Psychosis in Alzheimer's Disease

Most people know Alzheimer's disease as a condition of progressive memory loss primarily affecting older adults. However, nearly all Alzheimer's patients also experience behavioral and psychological symptoms, including psychosis, aggression, agitation and depression.[1]

Psychosis — defined as the presence of hallucinations or delusions — affects approximately 30-40% of patients with Alzheimer's disease,[2] with at least one study reporting delusions in 53% of patients.[1] Given that 5.5 million Americans currently live with Alzheimer's disease,[3] the number with psychosis is estimated to be about 2.2 million.

Delusions are persistent false beliefs that are inconsistent with external reality, as when patients erroneously believe that their husband or wife is an imposter or is having an affair. Hallucinations are sensory perceptions that seem to be real but occur in the absence of external stimulation, such as seeing or hearing someone who is not there. Fully formed silent visual hallucinations — such as seeing a person or animal — are the most common hallucinatory events in Alzheimer's disease.

Symptoms & Stigma

Psychotic symptoms in Alzheimer's disease can occur at any point during the illness, though they may be more severe later in the disease.[2] Such symptoms tend to persist over time[4] and are associated with more rapid cognitive and functional decline, as well as an increased risk of death.[5, 6] Psychotic symptoms can be particularly difficult to assess in advanced disease stages, for instance, in cases where patients are unable to speak.

Despite the prevalence of psychotic symptoms in Alzheimer's disease, families are often surprised when they occur. Such symptoms can be embarrassing to discuss, particularly if they involve sexual themes, and they can be stigmatizing — adding to the already prevalent stigma of dementia. Families may be reluctant to report that their loved one is "acting crazy," seeing or hearing things, in addition to having dementia.

It is therefore important for physicians to inquire about psychosis and, preferably, to speak with caregivers separately from patients to obtain a full report. This can be easier to do on a virtual call, where the caregiver can be in a separate room from the patient.

> "I see a lot of patients who think their husband or wife doesn't belong in their bedroom. Other patients look in the mirror and think there is a stranger in the room and start striking at the mirror or running away. One of the most common hallucinations is the presence of little people in the room talking. Many patients see relatives they believe are in the room but who are not really there."
>
> **– Howard S. Kirshner, MD**

Cultural Differences in Caregiver Patterns

Alzheimer's disease crosses cultural boundaries, affecting people of all racial, ethnic and cultural groups living in both rural and urban areas. Caregiver behaviors and patterns often differ based on cultural affiliations.

> “In our experience, white, non-Hispanic families usually rely on a single caregiver, with either the spouse or the oldest daughter being the most common. In minority families — we have many Hispanic families here in Las Vegas — it's more likely to be multiple people taking care of mom. One person comes to the house one day to be with mom and another person the next day. This is a much different pattern of caregiving than we see in the white, non-Hispanic community.”
>
> **– Jeffrey L. Cummings, MD, ScD**

> “I'm in a metro area of 250,000 people that is surrounded by rural areas. Rural families tend to keep grandma at home, with more family members involved in her care. In the more populated areas where more family members are working, they tend to leave the patient with dementia at home a lot longer, checking in with them regularly or putting cameras in the living room.”
>
> **– Christina Mayville, MD**

These scenarios illustrate the difficult problem of Alzheimer's disease and its impact on patients and caregivers. Delusions and hallucinations in Alzheimer's disease are related to aggressive behavior, increased wandering, socially inappropriate behavior, falls and worse general health.[10] All of these factors worsen care situations that are already difficult and can magnify the burden of Alzheimer's disease. Delusions and hallucinations may have different meanings and different interpretations across cultural groups.

Economic Costs of Psychosis in Alzheimer's Disease

Alzheimer's disease and other dementias cost $321 billion annually — a figure that is expected to grow to just under $1 trillion by 2050.[11] Out-of-pocket costs for those with Alzheimer's disease or other dementias are $81 billion annually, with Medicare and Medicaid providing an additional $206 billion annually in total health care and long-term care costs.[11]

Psychosis in dementia increases the informal costs of care, with higher levels of psychosis requiring progressively more hours of care from unpaid caregivers.[12] The increased caregiving duties, along with the frustration and exhaustion caused by psychotic symptoms, are major factors in the decision to place a loved one in institutionalized care. Nursing home placement dramatically increases the out-of-pocket costs of Alzheimer's disease, adding an extra $47,585 per person in 2022 dollars to the lifetime costs of dementia.[13]

> “The financial consequences of psychosis are enormous. Many times, long-term care facilities will ask families of patients with aggressive or psychotic behavior to pay for another caregiver or to come there themselves because of the higher level of care needed for the patient. Some patients need a 1:1 staff-member-to-patient ratio because of aggression and psychotic symptoms.
>
> The costs are terrifying for people, and families are overwhelmed in this situation. Most don't have long-term care insurance, and many don't understand that Medicare doesn't pay for nursing home care. Psychosis makes all of this more expensive.”
>
> **– William Petrie, MD**

> “Some families may be unable to obtain optimal care for their relatives in long-term care facilities because of limited reimbursement from Medicare. I have worked with nursing home administrators who say that it is challenging to handle Medicare recipients with limited financial support for daily care for their loved ones.”
>
> **– Patrick Griffith, MD**

Lack of Approved Drugs

Despite the major impact of Alzheimer's disease psychosis on patients, caregivers and society, no drugs for this condition are currently approved in the United States. Antipsychotic drugs are often used off-label for Alzheimer's delusions and hallucinations, although they are associated with serious safety problems, including increased mortality.[14]

Efficacy and Safety of Antipsychotic Drugs for Psychotic or Behavioral and Psychological Symptoms of Dementia (BPSD)*

ANTIPSYCHOTIC DRUG	EFFICACY	RISKS	APPROVAL STATUS
Aripiprazole	↗ **Significant Improvement** in psychosis over placebo in controlled trial[15]	Death, cerebrovascular events, somnolence[15, 16, 18]	✗ **Not Approved** for Alzheimer's in the US
Olanzapine	↗ **Significant Improvement** in BPSD over placebo in controlled trial[17]	Death, cerebrovascular adverse events, somnolence, gait problems[17-19]	✗ **Not Approved** for Alzheimer's in the US
Pimavanserin	↗ **Significant Improvement** in relapse of psychosis versus placebo in controlled trial[20]	Death, QT interval prolongation, headache, constipation, urinary tract infection[20, 21]	✗ **Not Approved** for Alzheimer's in the US
Quetiapine	− **No Significant Improvement** in psychosis over placebo in controlled trial[22]	Death, somnolence[22, 23]	✗ **Not Approved** for Alzheimer's in the US
Risperidone	↗ **Significant Improvement** in BPSD (including psychosis subscale) over placebo in controlled trials[24]	Death, cerebrovascular adverse events, somnolence, extrapyramidal symptoms[24-26]	✗ **Not Approved** for Alzheimer's in the US

*Aggression, agitation, psychosis

Physicians face a difficult situation when treating psychosis in Alzheimer's disease. Although antipsychotic drugs are not approved for this use, they are often viewed as the best option despite their risks.

> “Yes, there is a mortality issue but also a major quality-of-life issue. If someone is hitting their neighbor in a long-term care facility, they are going to be treated with antipsychotics. If they are striking out at people, they will get antipsychotic drugs, or worse, benzodiazepines.”
>
> **– William Petrie, MD**

> “Current therapeutic options don't meet the need, and prescribing them feels like a liability. I tell the patient's family that these medications could be harmful but the families are desperate to try something. All my local colleagues in neurology do the same thing. We all get warning letters from insurance companies telling us that we are using a medication not indicated for this use. It feels like a terrible liability, and yet we really don't have a choice.”
>
> **– Christina Mayville, MD**

Physicians need improved treatments for Alzheimer's disease psychosis to offer patients and their families. Such treatments must be supported by robust clinical evidence and approved by the United States Food and Drug Administration so that physicians can prescribe them confidently. Additionally, insurers, including Medicare, must allow use of these medications so that patients can afford them, instead of requiring a trial on less expensive medications that have not been approved by the FDA.

The Role of a Multidisciplinary Care Team

Patients with Alzheimer's disease ideally interact with and receive care from a multidisciplinary team of health care professionals. Such professionals have different roles and can help with different patient and caregiver needs.

Medical Professionals in Alzheimer's Disease Care

Geriatricians
Physicians who specialize in the medical problems of older adults

Neurologists
Physicians who specialize in diseases of the nervous system

Nurse Practitioners
Registered nurses with advanced training in common medical conditions, including chronic illnesses

Nursing Home Directors
Registered nurses who maintain high standards of care for patients and communicate with physicians, patients, and family about patient health

Psychiatrists/ Geriatric Psychiatrists
Physicians who specialize in mental disorders

Psychologists
Professionals with advanced training in psychology

Social Workers
Professionals who help patients and families address daily needs and navigate practical resources

Skilled Nursing Home Staff
Certified nursing assistants and others trained in current clinical practice and care

> “In terms of the team approach, social workers are extremely important. They can be a bridge between physicians and patients, conducting home evaluations and helping identify support for families.”
>
> **– Patrick Griffith, MD**

> “In our Cleveland Clinic model, the physician would see the patient the first and second times to give the diagnosis. All follow-up care was assigned to a nurse practitioner. Psychosis usually evolves later in the illness, so the nurse practitioner was far more likely to be the first person to see the psychosis than the physician.”
>
> **– Jeffrey L. Cummings, MD, ScD**

Unfortunately, many Alzheimer’s patients do not have access to a multidisciplinary care team. Today, not enough health care professionals choose to enter this field, and there is a dearth of resources for Alzheimer’s care.

> “There are not enough neurologists or psychiatrists who want to work in this area. I see our residents who go into private practice, and the last thing they want is to see an Alzheimer’s patient. It typically doesn’t generate a lot of revenue, and you get a lot of phone calls after hours.”
>
> **– Howard S. Kirshner, MD**

> “We have a complete lack of medical professionals and resources for Alzheimer’s disease care in our area. We have a shortage of neurologists and just one psychiatrist who will see patients on Medicare. We have one geriatrician, and he is on the brink of retirement. We have almost no psychology support, even though psychologists may be an especially valuable resource.”
>
> **– Christina Mayville, MD**

The lack of specialists in Alzheimer’s care is alarming, particularly given that the number of people afflicted with this disease is projected to increase dramatically over the next 30 years.[11] These observations suggest that a multifactorial strategy may be needed to meet the demands. This could include increasing the incentives for professionals at all levels or issuing statements of need for professionals in the area.

Nursing home staff need training to improve their effectiveness as team members in the long-term care setting where psychosis is common. With an increased understanding of psychosis, they can report more accurately to the medical director of the facility, enabling them to make better treatment choices for patients.

The Role of Caregivers

Even in the absence of sufficient resources to manage Alzheimer's disease patients, caregivers play an important role in mitigating the effects of psychosis. Numerous options have been successfully used:[27, 28]

- Distraction
- Agreeing with the patient's perception of reality
- Explaining the situation
- Looking for an object the patient believes was stolen
- Ignoring the misperception
- Nonverbal expressions of caring, such as hugs
- Asking closed-ended questions *("Would you like a sandwich for lunch?")* instead of open-ended questions *("What would you like for lunch?")*
- Helping patients remember pleasant past events
- Responding to the emotion, not the content, of what the patient says
- Creating a safe physical environment
- Maintaining routines
- Sensory therapy, such as with music
- Symptom-specific interventions, such as an outing, pet therapy, or change of location within an institution

Some strategies that may seem logical can be ineffective. For example, attempting to reorient the person to reality can be effective early in the disease but becomes less effective as the disease progresses.

> “One of the most frequent questions I get in the clinic is, 'Do I explain to my husband or wife that this isn't true, or do I just let them go with it and try to keep them happy?' There is not just one answer to this. I think if it's the beginning of the problem and it's mild, sometimes you can reason people out of it and it's worth doing so to keep them reality based, if possible. On the other hand, when it becomes a recurring theme and it doesn't work to reorient them, then you just go with the misperception. There's an art to it.”
>
> **– Howard S. Kirshner, MD**

The Role of Long-Term Care Clinicians

There is a need for education among people who work in long-term care facilities. Caregivers need to understand how the disease operates and progresses. Increased interactions with long-term care clinicians can help with this. It may also be beneficial for Alzheimer's disease patients with psychosis. Evidence for this comes from the antipsychotic drug trials for Alzheimer's disease psychosis, many of which showed an unanticipated improvement in the placebo group.[29]

> “There is a surprisingly large placebo effect that occurs in patients who are suddenly seeing a researcher every day who wants to assess their scores and interacts more with the family to obtain informed consent. Patients are suddenly a person of interest in the nursing home due to their participation in the trial. There is a whole social structure that comes together around a trial patient, and you see the benefit in symptoms.”
>
> **– Jeffrey L. Cummings, MD, ScD**

Unfortunately, Alzheimer's disease is a relentlessly progressive condition, and most patients eventually need long-term care. Clinicians and other respected family contacts or community members can play a meaningful role in helping families navigate this move.

> “Family members feel shame and guilt for sending their loved one to a long-term care facility even though being at home may not be the best option for the patient's quality of life. Here the clinicians can play a huge role. They can say, 'I don't think you can continue to do this. The patient isn't sleeping, is psychotic, and doesn't know who you are or who they are. I think it's time to consider nursing home placement.'”
>
> **– William Petrie, MD**

> “In my experience with African American patients, there is sometimes a sort of religious guilt. Your mom or dad took care of you all of your life, so how can you say that you can't take care of them anymore? People feel extremely bad about this, like they are not good people for placing their loved ones in a nursing home. Sometimes priests or ministers within the church can help with this problem.”
>
> **– Patrick Griffith, MD**

Conclusion

Alzheimer's disease is a devastating disease that dramatically impacts patients, families and society. Psychosis — the presence of hallucinations or delusions — is a common symptom of Alzheimer's disease that complicates an already difficult experience. It is often the deciding factor in placing a loved one in a long-term care facility.

Better treatments for Alzheimer's disease psychosis are urgently needed to help reduce symptoms and permit patients to remain at home as long as possible. More professionals are also needed to specialize in this area, particularly as the Alzheimer's disease population is expected to grow considerably over the next 30 years.

CNSA's Clinical Proceedings

The Clinical Neurological Society of America has nearly 50 years of experience bringing together leading experts and clinical neurologists for educational programming. With the launch of CNSA's Clinical Proceedings — a white paper series — the organization is expanding its educational resource offerings while raising awareness about unmet needs in neurology.

CNSA recognizes the expert panel members who contributed to the development of this white paper about Alzheimer's disease psychosis.

Howard S. Kirshner, MD
Chair

Jeffrey L. Cummings, MD, ScD

Patrick Griffith, MD

Christina Mayville, MD

William Petrie, MD

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