May 26, 2020

The Honorable Charles E. Grassley
Chairman
Committee on Finance
United States Senate

The Honorable Richard E. Neal
Chairman
Committee on Ways and Means
U.S. House of Representatives

The Honorable Ron Wyden
Ranking Member
Committee on Finance
United States Senate

The Honorable Kevin Brady
Ranking Member
Committee on Ways and Means
U.S. House of Representatives

The Honorable Richard Blumenthal
Member
Committee on the Judiciary
United States Senate

Dear Chairman Grassley, Ranking Member Wyden, Chairman Neal, Ranking Member Brady, and Senator Blumenthal,

We, the undersigned organizations, appreciate your collective leadership on the increasingly important issue of safe, high-quality, nursing home care for older adults. We are writing today to offer comment on your April 3 inquiry to the Office of Inspector General (OIG) at the U.S. Department of Health and Human Services (HHS) to review changes in inappropriate use of psychotropic drugs, examine the adequacy of drug treatment planning/medication monitoring, and determine whether additional legislative or regulatory actions are needed to protect against the inappropriate use of these medications.

Our organizations strongly believe that a comprehensive OIG inquiry that examines nursing home practice for the diagnosis and management of neuropsychiatric symptoms (NPS) in dementia would better identify the core problems behind inappropriate use of antipsychotics. We encourage the new report to broaden its scope to include: significant provider and surveyor knowledge gaps in the diagnosis and management of NPS; under-recognition of FDA-approved uses for psychotropic and antipsychotic medications for the treatment of NPS; inadequate staffing ratios; and inherent weaknesses with the current antipsychotic 5-star quality metric. By broadening the scope of the OIG inquiry to focus on the multi-faceted structural and clinical factors behind current practices rather than just prescribing practices, we believe we can achieve our mutual goal of safer, higher-quality, nursing home care for older adults with dementia.

We would welcome the opportunity to meet with your Committee staff to discuss our comments in more detail. If your staff are available for a meeting, please have them contact Veronica Charles at vcharles@ascp.com to coordinate. Once again, thank you for your leadership on this important issue.

Background on Project PAUSE

Our organizations have joined together under Project PAUSE (Psychoactive Appropriate Use for Safety and Effectiveness), an ad hoc coalition of national patient and professional organizations collectively advocating on clinical care regulatory and legislative issues in long-term care and the community, including an improved metric on antipsychotic drug use in long-term care settings for the diagnosis and management of behavioral and neuropsychiatric symptoms (NPS) in dementia. Project PAUSE aims to educate policymakers and the public about clinical care issues in long-term care and the community, and collectively advocate for effective solutions.

Members of Project PAUSE include patient and family caregiver organizations, long-term care groups, primary care associations, geriatric and mental health specialty provider associations, Alzheimer's disease and other dementia organizations, and mental health organizations. Project PAUSE has been engaging with the Centers for Medicare & Medicaid Services (CMS) and national representatives to promote policies in LTC settings that will curb the inappropriate use of antipsychotics and ensure access and appropriate use of these medications by patients who may clinically benefit. Project PAUSE is convened by the Alliance for Aging Research and the American Society of Consultant Pharmacists.

Comments on Specific Requests to HHS

Given our collective organization's background in this critical topic, Project PAUSE is requesting that the following information be addressed when sending specific questions to the OIG.

1. *Conduct a longitudinal analysis (covering the last 10 years) examining the number and percent of nursing home residents who receive psychotropic drugs, broken down by class of drug (e.g., antipsychotic drugs, benzodiazepines, and anti-depression and anti-anxiety), and the length of time on the drug.*

a. Determine total Medicare Part A costs from hospitalizations resulting from inappropriate psychotropic use during this same period.

Our organizations support seeking information related to utilization as we believe that additional information could provide valuable insight into practice habits and possible solutions for patients. However, it is important to note that **the current metrics in place to determine inappropriate psychotropic use would not produce real or meaningful data**. The current measure utilized to determine CMS antipsychotic quality measures uses the medication list from the MDS, discounting any residents with schizophrenia, Huntington's chorea, and/or Tourette's syndrome. Therefore this measure cannot capture the amount of hospitalizations from *inappropriate psychotropic use* during the given time period, it merely documents the number of older adults who have been hospitalized while taking a specific prescribed medication. If OIG operates under the current CMS guidelines to pursue information on Medicare Part A costs in this study, OIG will only be able to determine costs associated with hospitalizations of a large group of older adults that take psychotropic medications for a variety of different clinical conditions. Given the increasing age of nursing home and long-term care residents and therefore

the increasing complexity of their conditions, psychosis rates in this population are growing.[1] If OIG aims to find new and meaningful data on psychotropic medications in this population, looking at 10 years of medication utilization data by class will not accurately identify risk or possible benefit. **Diagnostic information, specific medication use within each class and clinical documentation supporting use would need to be included to accurately identify possible risk and benefit**. Hospitalization data could only be estimated if the definition of "inappropriate" use could be identified and studied. This would be nearly impossible short of a case by case analysis.

2. *Analyze patterns of off-label use of psychotropics in nursing homes over the last ten years, including whether there are individual nursing homes, chains of nursing homes, or homes with common ownership interests where such use is persistent.*

This question seems to assume malintent on the part of clinicians, and we ask the OIG to **consider reframing this part of the analysis to examine CMS regulatory barriers to appropriate medication prescribing by providers.** It may interest both the policymakers requesting this inquiry and the OIG that, in the Summer of 2019, the American Association for Geriatric Psychiatry—in collaboration with the American Psychiatric Association—conducted a survey of its members caring for older adults in long-term care settings.

Key results from the respondents reveal that:

- 86% reported experiencing barriers to prescribing psychotropics appropriately for their patients due to policies that penalize such prescribing;
- 73% reported patients became destabilized, requiring more acute levels of care, as a result of the failure to provide appropriate psychotropic medications due to policies limiting their use;
- 35% reported a portion of those destabilized patients treated in acute care settings were denied readmission to the long-term care facility; and
- 58% reported a facility staff member has requested that they alter their prescribing practices so the facility could achieve a higher quality rating score.

3. *Determine the extent to which Medicare drug claims for nursing home residents are erroneous or still result in inappropriate Medicare reimbursement claims (an issue identified by the OIG in its 2011 report on this subject).*

Our organizations again caution OIG against pursuing this information under the current framework as there is no clear definition of "inappropriate use" to determine whether a Medicare reimbursement claim is erroneous. **This would again need to be a case by case review in enough patients to be extrapolated to the entire population. Project PAUSE has proposed a new metric utilizing clinical rationale to help CMS determine appropriate and inappropriate use.**

[1] Folsom, David P et al. "Schizophrenia in late life: emerging issues." *Dialogues in clinical neuroscience* vol. 8,1 (2006): 45-52.

In an attempt to highlight pertinent information for the purposes of this inquiry, we encourage OIG to seek out additional qualitative research from both the patient and provider perspective.

5. *Please indicate whether there has been an increase, since CMS launched its National Partnership, in the number and percentage of nursing home residents (including non-elderly residents) diagnosed with conditions for which the use of antipsychotics is approved and use is not tracked in Medicare, specifically schizophrenia, Tourette's Syndrome, and Huntington's Disease. Please compare these data to rates of diagnosis for these conditions among the general elderly population.*

CMS currently identifies three appropriate indications for antipsychotic medication: Tourette's syndrome, schizophrenia and Huntington's chorea. However, Parkinson's disease psychosis, major depression with psychosis, and bipolar disorder have FDA-approved indications for the use of antipsychotic medications but are not currently included as appropriate by CMS. Furthermore, clinical development will soon identify additional psychoactive medications indicated to treat or manage perceptual disturbances (hallucinations, paranoia, and delusions), and behavioral disturbances (agitation and terminal restlessness), in patients who also carry a dementia diagnosis. Therefore this OIG request will continue to only produce fragmented data that do not determine inappropriate use of antipsychotic medications in nursing home residents.

Our organization's emphasize that measuring the change in the number and percentage of residents diagnosed with these conditions may not provide any statistically significant evidence of inappropriate diagnosis to avoid a poor quality rating on antipsychotic use as resident populations of patients with these conditions change over time, meaning that any small growth in number and percentage may represent organic growth. Additionally, elderly persons with these three conditions are more likely to be institutionalized in a LTCF than remain in the general population so a comparison to the rates in the general elderly population will likely not be relevant.

6. *Evaluate the effectiveness of state laws and/or regulations requiring written informed consent before administration of a psychotropic drug in changing the frequency of prescribing and appropriate use of such medications to older adults with dementia, as well as any impact of such policies on ability to hold nursing homes accountable for inappropriate prescribing and off-label use. As part of this evaluation, please include states that have monetary incentive programs and include specific target thresholds for psychotropic use among skilled nursing facility long-stay residents.*

Our organizations are concerned that this OIG evaluation will merely determine the change in the number and percentage of residents diagnosed with these conditions, which can be accounted for based on organic growth in resident population changes over the past ten years, and/or the fact that elderly persons living with conditions that require these medications are more likely to be institutionalized in a nursing facility than remain in the general population, thus making a comparison to the rates in the general elderly population not relevant.

7. *Determine the effects, if any, of regulation of psychotropic drugs on admissions to nursing homes for those struggling with mental illness.*

Project PAUSE is highly supportive of OIG's investigation of regulations of psychotropic medications hindering patient access to needed care and nursing home admission. The National Partnership's measure to determine inappropriate antipsychotic medication utilization, while not congruent with CMS' requirements for use of antipsychotics based on the State Operations Manual (SOM), deeply impact the Five-Star Quality Rating System. As mentioned previously, the rating system requires that residents on antipsychotics have a diagnosis of Schizophrenia, Huntington's disease, or Tourette's Syndrome for their use to not negatively impact a nursing home's five-star rating score. **Because the five-star system is correlated with both admissions and reimbursements, nursing homes have a large incentive to obtain the highest rating possible. This creates several disincentives to accept and retain residents who have a history of serious mental illness or who have had positive benefit from the use of antipsychotic medication in the past.**

For example, a resident with bipolar disorder could be admitted to a facility stable on an antipsychotic medication, but that facility could put pressure on the prescriber to change or discontinue the medication because of the impact on their five-star rating. It is important to note that this occurs even in cases where the medication is being used in a manner that is consistent with FDA approval and generally accepted standard of care. This resident would be at high risk for a relapse of mania and psychosis, which can result in severe adverse consequences.[2]

Residents with psychiatric illness are also more likely to have their medication discontinued in an effort to comply with the requirements of gradual dose reductions (GDRs), even if the medication is appropriate, effective, and not causing negative effects. Discontinuing antipsychotic medication upon admission to a long-term care facility can precipitate a further decline in function and behavior and set the patient on a trajectory of decline.[3] This is particularly true of recurrent, severe major depressive disorder, in whom the relapse rate of major depression is over 80%--and in whom suicide is a significant risk factor if they do relapse, especially in the geriatric population. [4]

8. *Assess the effectiveness of current quality measures for antipsychotic use under the MDS, including receipt of antipsychotics for short-stay residents and receipt of antipsychotics for long-stay residents, in reflecting the true rates of medically inappropriate prescribing.*

CMS' National Partnership effort includes only one quality measure related to dementia— the frequency of antipsychotic use, which CMS reports publicly through the Nursing Home Compare website and the Five-Star Quality Rating System for nursing homes. There exists no mechanism to adjust the quality metrics for antipsychotic use to the type of skilled nursing facility. The current narrow measure negatively impacts smaller and rural facilities. Utilizing a

[2] Connolly KR, Thase ME. The clinical management of bipolar disorder: a review of evidence-based guidelines. *Prim Care Companion CNS Disord*. 2011;13(4):PCC.10r01097. doi:10.4088/PCC.10r01097

[3] Dementia-Related Psychosis: Gaps and Opportunities for Improving Quality of Care. A report from The Gerontological Society of America. August 2019. Geron.org/dementiarelatedpsychosis

[4] Burcusa SL, Iacono WG. Risk for recurrence in depression. Clin Psychol Rev. 2007;27(8):959–985. doi: 10.1016/j.cpr.2007.02.005.

generic percentage as a quality metric does not properly capture the size and scope of the problem, which is evident in many rural facilities across the country.[5] Rural facilities are more likely to house a smaller number of residents, which means that any resident receiving antipsychotic medications, appropriate or inappropriate, has the potential to negatively impact a rural facility. This can lead to denial of care for the frailest patients living in rural communities.[6] In order to prevent undue burden on rural facilities, we encourage OIG to look into opportunities for CMS to utilize more robust, personalized patient data to properly articulate the rate of inappropriate antipsychotic utilization rates, like Project PAUSE has proposed.

It is also important to note that the current metric discriminates against facilities with high level of clinical expertise and psychotropic experience. Many nursing homes are beginning to specialize in treating residents with complex conditions[7]. A facility may choose to take in more patients with moderate dementia and psychotic symptoms due to management expertise. This facility may have a large percentage of patients appropriately treated with antipsychotics and, again, be disadvantaged by the use of the current quality measure since CMS looks at the total percentage of patients taking antipsychotic medications rather than the amount of inappropriate use. This has the unintended consequence of deemphasizing excellence in dementia and psychotic symptom care, in addition to disincentivizing truly person-centered care.

9. *Assess the potential positive and negative impacts of creating a requirement for facilities to obtain written informed consent before issuing a prescription for psychotropic drugs to nursing home residents under the Medicare and Medicaid programs.*

Project Pause appreciates this request. Informing patients and caregivers of treatment plans is important for shared understanding. Currently, when a medication is started, stopped, or changed, it is communicated to the resident, or their power of attorney, in skilled nursing facilities. In addition, some states have initiated informed consent procedures for psychotropic medications to document. Assessing the successes and failures of such programs would provide valuable information to determine value to a Federal regulation.

10. *To the extent feasible, assess the adequacy of medication monitoring, including frequency of pharmacist review and visits with the prescriber, for nursing home residents who use psychotropic drugs.*

Project PAUSE appreciates this request. Medication management is a clinical function centered around the unique pharmacologic expertise of a consultant pharmacist and a patient's primary health care provider to tailor a patient's medication usage to their individual needs.[8] Medication

[5] Assessing the Unintended Consequences of Health Policy on Rural Populations and Places; available at: http://www.rupri.org/wp-content/uploads/Evaluating-the-Impact-of-Policy-Changes-on-Rural-Populations-1.pdf

[6] Bowblis, John R et al. "The urban-rural disparity in nursing home quality indicators: the case of facility-acquired contractures." *Health services research* vol. 48,1 (2013): 47-69. doi:10.1111/j.1475-6773.2012.01431.x

[7] The Top Trends in Home Care for 2019; available at: https://homehealthcarenews.com/2019/01/the-top-trends-in-home-care-for-2019%EF%BB%BF/

[8] American Society of Consultant Pharmacists. Consultant Pharmacist Handbook: A Guide for Consulting to Nursing Facilities. Fifth Edition. 2018;4:33-57.

regimen reviews standards are published in the State Operations Manual (SOM), which provides each individual state and CMS with regulatory oversight and authority.[9] We hope that OIG will recognize and reinforce that increasing the frequency and the monitoring of medication management by pharmacists provided to nursing home residents will further alleviate concerns with inappropriate use. We encourage OIG to look into opportunities to strengthen medication management and monitoring through other CMS regulatory channels, like incorporating consultant pharmacist's review of antipsychotic medications in the documentation of antipsychotic use that is used to determine the quality measures.

Background on our organizations' rationale behind our recommendations follows.

Background on Neuropsychiatric Symptoms (NPS) of Dementia

While cognitive impairment is regarded as the hallmark indicator of dementia, neuropsychiatric symptoms (NPS) are nearly as universal, with one or more symptoms affecting nearly all people with dementia over the illness course. NPS may include wandering, sleep issues, agitation, depression, apathy, aggression, and psychosis, and evidence finds such symptoms often result in greater impairment in activities of daily living, poorer quality of life, more rapid disease progression, greater morbidity, an increase in direct cost of care, and earlier institutionalization.[10,11,12,13,14,15] These symptoms also result in increased caregiver burden due to the emotional, financial, and physical difficulties associated with caring for the persons exhibiting them.[16] NPS can also pose a risk to other residents and staff members in LTC settings, when residents exhibit violent or physically aggressive behavior.

Among people with Alzheimer's disease (AD), depression is the earliest observable symptom in at least one-third of cases.[17] Milder agitation may manifest early and increase in prevalence and severity with worsening of dementia, often leading to an increase in caregiver burden, greater morbidity, poorer quality of life, increased cost of care, early institutionalization, and rapid disease progression.[18] Long-term care staff caring for residents with depression, agitation, and other NPS, also experience decreased quality of life, increased risk of injury, increased workload, lost days of work, burnout, and staff turnover.[19] [20]

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[9] CMS State Operations Manual; available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/som107ap_pp_guidelines_ltcf.pdf

[10] Karttunen K, Karppi P, Hiltunen A, et al. Neuropsychiatric symptoms and quality of life in patients with very mild and mild Alzheimer's disease. Int J Geriatr Psychiatry. 2011;26(5):473–482.
[11] Lyketsos C, Carrillo M, Ryan J, et al. Neuropsychiatric symptoms in Alzheimer's disease. Alzheimer's Dement. 2011;7(5):532–539.
[12] Banerjee S, Smith SC, Lamping DL, et al. Quality of life in dementia: more than just cognition. An analysis of associations with quality of life in dementia. J Neurol Neurosurg Psychiatry. 2006;77(2):146–148.
[13] Steele C, Rovner B, Chase GA, et al. Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. Am J Psychiatry. 1990;147(8):1049–1051.
[14] Brodaty H, Donkin M. Family caregivers of people with dementia. Dialogues Clin Neurosci. 2009;11(2):217–228
[15] Murman D, Chen Q, Powell M, et al. The incremental direct costs associated with behavioral symptoms in AD. Neurology. 2002;59(11):1721–1729.
[16] Kales H, Gitlin L, Lyketsos C. Assessment and management of behavioral and psychological symptoms of dementia. BMJ. 2015;350:h369.
[17] Masters MC, Morris JC, Roe CM. Noncognitive Symptoms of Early Alzheimer disease: A longitudinal analysis. Neurology 2015;84:617–622.
[18] Smith Z, Smith EE, Geda Y, et al. Neuropsychiatric Symptoms as Early Manifestations of Emergent Dementia: Provisional diagnostic criteria for mild behavioral impairment. Alzheimer's Dement 2016; 12:195–202.
[19] Lachs MS, Rosen T, Teresi JA, et al. Verbal and Physical Aggression Directed at Nursing Home Staff by Residents. J Gen Intern Med 2013;28:660-667.
[20] Zeller A, Hahn S, Needham I, et al. Aggressive Behavior of Nursing Home Residents Toward Caregivers: A systematic literature review. Geriatr Nurs 2009;30:174-187.

Background on Clinical Care for NPS

While antipsychotics have been used to treat NPS since the 1950s, people with neurodegenerative disorders were previously excluded from trials of psychotropic medications in general, and antipsychotics specifically, despite the fact that both brain changes and biological aging may impact psychotropic dosage needs and response, carrying significant risks.

In April 2005, the FDA issued a boxed warning for atypical antipsychotics in the treatment of NPS in older patients with dementia because of a 1.6- to 1.7-fold higher death rate in those taking such drugs, compared with those taking a placebo. In a pivotal randomized control trial (RCT) of demented patients already on conventional or atypical antipsychotics, 3-year survival doubled in those randomized to cease treatment.[21] However, a large longitudinal observational study published in the September 2013 issue of the *American Journal of Psychiatry* challenged these findings by showing that **the primary correlate of adverse outcomes was the psychiatric symptomatology and not the drugs used to treat these symptoms**.[22]Additionally, a 2015 study in the same journal analyzed data from the Cache County Dementia Progression Study to examine the link between clinically significant neuropsychiatric symptoms in mild Alzheimer's dementia and progression to severe dementia and death, found that psychosis, affective symptoms, agitation/aggression, mildly symptomatic neuropsychiatric symptoms, and clinically significant neuropsychiatric symptoms, were all associated with earlier death.[23] It is important to note that neurodegenerative disorders are progressive and fatal. The treatments for such diseases, whether pharmacologic or non-pharmacologic, are primarily symptomatic.

While no medication has been specifically approved at this time for the treatment of agitation or other NPS in Alzheimer's disease, a number of studies have been published with information strong enough to provide guidance to clinicians. For example, two studies with almost identical design have shown efficacy of methylphenidate in the treatment of apathy in Alzheimer's disease.[24] [25] With regards to the treatment of agitation in Alzheimer's disease and other dementias, there is a large amount of literature clearly showing a small but consistent effect of atypical antipsychotics, although those benefits were generally outweighed by risk of intolerability. Nonetheless, with careful monitoring some clinicians have used these short of any alternatives;[26] and studies have shown that carefully dosed citalopram (<30mg/day) and the combination of dextromethorphan and quinidine can be safe and effective for agitation.[27] [28]

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[21] Maust DT, Kim H, Seyfried LS, et al. Antipsychotics, Other Psychotropics, and the Risk of Death in Patients with Dementia:Number needed to harm JAMA Psychiatry 2015;72:438-445.

[22] Lopez OL, Becker JT, Chang YF, et al. The Long-Term Effects of Conventional and Atypical Antipsychotics in Patients with Probable Alzheimer's disease. Am J Psychiatry 2013;170:1051-8.

[23] Peters ME, Schwartz S, Han D, et al., Neuropsychiatric symptoms as predictors of progression to severe Alzheimer's dementia and death: The Cache County Dementia Progression Study, Am J Psychiatry. 2015 May 1; 172(5):460–465.

[24] Padala, Prasad & Padala, Kalpana & Lensing, et al. Methylphenidate for Apathy in Community-Dwelling Older Veterans With Mild Alzheimer's Disease: A Double-Blind, Randomized, Placebo-Controlled Trial. The American journal of psychiatry. 2017:175. https://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2017.17030316

[25] Rosenberg PB, Lanctôt KL, Drye LT, et al. Safety and efficacy of methylphenidate for apathy in Alzheimer's disease: a randomized, placebo-controlled trial. J Clin Psychiatry. 2013;74(8):810–816. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902018/

[26] Schneider LS, et al. "Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer's Disease". The New England Journal of Medicine. 2006. 355(15):1525-38.

[27] Porsteinsson AP, Drye LT, Pollock BG, et al. Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial. JAMA. 2014;311(7):682–691. https://www.ncbi.nlm.nih.gov/pubmed/24549548/

[28] Jeffrey L. Cummings, MD, ScD; Constantine G. Lyketsos, MD, MHS; Elaine R. Peskind, MD; et al. Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial, JAMA. 2015;314(12):1242-1254. https://jamanetwork.com/journals/jama/fullarticle/2442936

When the appropriate population is targeted, the size of the effect is magnified, and the safety profile improved. A study by Devanand, Mintzer, and colleagues showed significant improvement in relapse rates of agitation in patients that responded to treatment with an atypical antipsychotic (risperidone).[29] These results underscore that in certain situations, it may be inappropriate to discontinue these medications if a patient has shown a clear symptomatic improvement and is monitored for signs of risk.

Pimavanserin is currently the only approved medication by the U.S. FDA for the treatment of NPS in neurodegenerative disorders. This agent is approved for the treatment of hallucinations and delusions occurring in Parkinson's Disease (PD) psychosis.[30] Other uses of psychotropics for NPS would be considered "off-label," although they may be considered medically reasonable and necessary when practicing evidence-based patient-centered care. There are multiple FDA-approved indications for first-and-second-generation antipsychotics that include bipolar disorder, major depression, and nausea and vomiting. Off-label usage for any psychotropic medications tends to be based on extensive experience and evidence, and some are endorsed by treatment guidelines.[31] [32]

All treatment decisions should be patient-centric and although the current choices are not ideal, a recent *Current Psychiatry Reports* paper provides a summary of potential pharmacologic treatments for NPS for situations where there is no other option:[33]

[29] Devanand, et al. (2012). Relapse risk after discontinuation of risperidone in Alzheimer's disease. The New England Journal of Medicine, 367 16, 1497-507 .
[30] Cummings J, Isaacson S, Mills R, Williams H, Chi-Burris K, CorbettA, et al. Pimavanserin for Patients with Parkinson's Disease Psychosis: A randomised, placebo-controlled phase 3 trial. Lancet 2014;383(9916):533–40. https://doi.org/10.1016/S0140- 6736(13)62106-6.
[31] Alexopoulos GS, Jeste DV, Chung H, Carpenter D, Ross R, Docherty JP. The EConsensus Guideline Series:Treatment of dementia and its behavioral disturbances. Introduction: methods, commentary, and summary. Postgrad Med 2005;Spec No:6–22.
[32] Kales HC, Gitlin LN, Lyketsos CG; Detroit Expert Panel on Management of Neuropsychiatric Symptoms of Dementia in Clinical Settings: Recommendations from a Multidisciplinary Expert Panel. J Am Geriatr Soc2014;62(4):762–9. https://doi.org/10.1111/jgs.12730.
[33] Cummings J, Ritter A, Rothenburg K. Advances in Management of Neuropsychiatric Syndromes in Neurodegenerative Diseases. Curr Psychiatry Rep 2019; 21:79, published online August 8, 2019. https://link.springer.com/article/10.1007/s11920-019-1058-4.

Since there are no highly effective disease-modifying treatments for dementia; clinicians focus on symptoms and decreasing patients' suffering and improving their quality of life.
The underlying cause of these behaviors may be neurobiological, an acute medical condition,

Table 1 Recommended treatments for neuropsychiatric syndromes

Neuropsychiatric syndrome	1st-line therapies*	2nd-line therapies	3rd-line therapies
Agitation in AD	Citalopram (10–30 mg/day)** Risperidone (0.5–1 mg/day)	Aripiprazole (10 mg/day) Carbamazepine (300 mg/day) Dextromethorphan/quinidine (20/10 mg BID) Olanzapine (5–10 mg/day) Quetiapine (200 mg/day) Trazodone (50–100 mg/day)	Lamotrigine (25–100 mg/day) THC (2.5–7 mg/day)
Apathy in AD	Methylphenidate (20 mg/day)	Modafinil (200 mg/day)	
Depression in AD	Citalopram (10–40 mg/day)** Escitalopram (5–20 mg) Sertraline (50–150 mg)	Aripiprazole as augmentation (2 mg–15 mg/day) Bupropion (100 mg–300 mg/day) Carbamazepine (augmentation) (300 mg/day) Duloxetine (20–60 mg/day) Fluoxetine (20–40 mg/day) Mirtazapine (7.5–30 mg/day) Paroxetine (10–40 mg/day) Quetiapine as augmentation (25–200 mg/day) Venlafaxine (37.5–225 mg/day)	Electroconvulsive therapy Tricyclic antidepressants
Depression in PD	Pramipexole (0.3–4.2 mg/day) Ropinirole (10 mg/day)	Citalopram (10–20 mg/day) Desipramine (25–75 mg/day)*** Nortriptyline (25–75 mg/day)*** Sertraline(25–50 mg/day)	Electroconvulsive therapy Buproprion (100–300 mg/day) Duloxetine (30–60 mg/day) Mirtazapine(30 mg/day) Paroxetine (10–40 mg/day) Venlafaxine (37.5–225 mg/day)
Psychosis in PD	Pimavanserin (40 mg/day)	Clozapine (6.25–50 mg/day) Quetiapine (25–100 mg/day)	Risperidone (0.5–2 mg/day) Olanzapine (5–7.5 mg/day)

*Initiation of pharmacological interventions should occur after non-pharmacological approaches, cognitive enhancers, and comprehensive assessment of medical and environmental factors has been completed

**Maximum recommended dose for citalopram in patients over the age of 60 is 20 mg/day

***TCA should not be used in patients with cognitive impairment

unmet needs, or a preexisting psychiatric illness. Because of this complexity, treatment should begin with an assessment to rule out potentially reversible causes of NPS. These causes can range from environmental to pharmacologic. For mild to moderate NPS, short-term behavioral interventions, followed by pharmacologic interventions, are commonly used. For moderate to severe NPS, pharmacologic interventions and behavioral interventions are often used simultaneously. This stepped approach to prescribing is possible to implement, and necessary to develop clear guardrails for appropriate use of antipsychotics.

Nonpharmacologic Approaches to NPS

After environmental and other medications are ruled out as a potential cause, turning to nonpharmacologic interventions, alone, is not standard practice. It is important to recognize that neuropsychiatric symptoms of dementia are clinically characterized as progressing in severity over time. On the one hand, neither healthcare workers nor family members want to see people with dementia oversedated and with a poor quality of life. Conversely, the reality of needing to protect family members staff and other residents from potentially dangerous symptoms should be recognized. Effectively diagnosing, managing or preventing behaviors that disturb and can cause harm to self and others is valuable to residents, LTC staff, family caregivers, and payers.

Specific diagnostic criteria have been developed for psychosis in AD[34][7], depression in AD[35], apathy in AD and other neurodegenerative disorders[36], and agitation in cognitive disorders including AD.[37] In Parkinson's Disease (PD), criteria have been developed to include psychosis in PD[38]and depression in PD[39]. Diagnostic criteria, combined with clinical guidelines, are essential to inform prescribers and to explain the use of the medication to patients, as well as professional and family caregivers. ***Currently, CMS does not integrate diagnostic criteria and clinical guidelines into nursing home operator, prescriber, medical director, nursing, and surveyor trainings, or in standardized patient assessment elements (SPADEs) for the Minimum Data Set (MDS), Outcome and Assessment Information Set (OASIS), Inpatient Rehabilitation Facility–Patient Assessment Instrument (IRF-PAI), or LTCH Continuity Assessment Record and Evaluation (CARE) Data Set (LCDS).***

We greatly appreciate your attention to these concerns and look forward to meeting with your office to discuss our aforementioned recommendations.

Sincerely,

Project PAUSE

[34] Jeste DV, Finkel SI. Psychosis of Alzheimer's Disease and Related Dementias: Diagnostic criteria for a distinct syndrome. Am J Geriatr Psychiatry 2000;8(1):29–34. https://doi.org/10.1097/00019442-200002000-00004.
[35] Olin JT, Schneider LS, Katz IR, Meyers BS, Alexopoulos GS, Breitner JC, et al. Provisional Diagnostic Criteria for Depression of Alzheimer's Disease: Description and review. Expert Rev Neurother 2003;3(1):99–106. https://doi.org/10.1586/14737175.
[36] Robert P, Onyike CU, Leentjens AF, Dujardin K, Aalten P, Starkstein S, et al. Proposed Diagnostic Criteria for Apathy in Alzheimer's disease and Other Neuropsychiatric Disorders. Eur Psychiatry 2009;24(2):98–104. https://doi.org/10.1016/j.eurpsy.2008.09.001.
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