

FACULTY GUIDE

Core Module 15:

Role of the Pharmacist in the Care of Persons Living with Dementia

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Slide 1:

- This module serves to give an overview of the ways in which pharmacists can play a role in the care of persons with Alzheimer's disease and other dementias, as well as those who participate in their care. While medication therapy management is certainly a large part of the pharmacist's duties when it comes to those living with dementia, as the most accessible health care professional, pharmacists are uniquely positioned to help persons from the time of symptom onset through the late stages of the disease by acting as an information resource, gatekeeper and advocate.

Slide 3:

- These are the topics we will address in this module. We will begin with an overview of how to identify persons who are either at risk of developing dementia, or are already exhibiting signs. Strategies and the use of tools for screening will be discussed.
- Once the diagnosis has been made by the appropriate clinician, medication therapy is typically initiated, and the pharmacist's role in choosing the correct medication at the correct dose, and in ongoing monitoring of the person will be described.
- Strategies for helping persons and care partners overcome barriers to appropriate treatment will also be discussed, as will the appropriate approach to a person with advancing disease

Slide 5:

- Pharmacists can play a unique role in the care of persons with dementia due to their accessibility, their ability to consider the impact of all medications on the person (including those not prescribed for symptoms associated with dementia), their expertise in the appropriate utilization of prescription medications and other over-the-counter (OTC) products for comorbid conditions, and their ability to direct persons and care partners to both medical and credible community resources according to individual needs.

Slide 6:

- We will begin by discussing ways to identify at-risk persons according to comorbid conditions and changes in behavior or memory. The importance of screening for medication-related reasons for cognitive decline will be addressed.

Slide 7:

- In general, short term memory loss is the first recognizable symptom of dementia. A pharmacist may notice that someone who has been diligent in getting medications refilled on time is either requesting fills late, or perhaps requesting them early. While it is known that between 25 and 50% of seniors are non-adherent with medications, a change should prompt questioning.
- Other signs may include difficulty understanding or retaining new information during the counseling process. The person may have difficulty comprehending the reasoning behind prescription or insurance changes, and may ask the same questions repeatedly.
- Additionally, display of apathy (lack of interest, enthusiasm or concern) may be an early indicator of cognitive decline.

- Individuals who are exhibiting the early symptoms of dementia may ignore them or brush them aside due to denial, or the belief that they are a normal part of aging. Social skills can often be maintained in the early stages of disease, and persons may joke about what they are characterizing as age-related memory loss.⁴
- In actuality, minor memory loss is a common complaint among seniors, and may only be a cause for concern if losses interfere with the ability of the person to function appropriately in social situations, or within their occupation if still in the work force. Mild cognitive impairment (MCI) may be present without any obvious change in the individual's ability to engage in daily activities. In such a case, it is not possible to predict if there will be progression to dementia, but referral is probably warranted as untreated Alzheimer's disease results in loss of brain function that cannot be recovered.
- Simple screening tests can be used by pharmacists to determine if referral for additional evaluation is warranted. For instance, the Mini-Cog is a widely used screening tool.⁶ However, it is not a particularly sensitive test, especially for those who have little education, or those who are highly educated.
- The Montreal Cognitive Assessment (MoCA) and the Veterans Administration/ Saint Louis University Mental Status exam (SLUMS exam) were designed to be more sensitive. Several tests are discussed in Module 2 of this curriculum. It is important for persons and families to understand that pharmacists are not diagnosing dementia through the use of these tools, but that they serve to identify those individuals who should be referred for follow-up by a diagnostician with expertise in Alzheimer's Disease and related dementias.

Slide 8:

- Several diseases have been found to be independent risk factors for the eventual development of Alzheimer's disease dementia.
- Down syndrome in particular has been definitively linked to the disease. Nearly all persons with Down syndrome who survive past the age of 40 years are likely to progress to a diagnosis of dementia due to a known link with an extra copy of chromosome #21. The disease tends to be earlier in onset in these individuals.

Slide 9:

- As previously discussed, pharmacists are often in an ideal position to identify persons who may be experiencing the early symptoms of cognitive decline associated with dementia.
- Identification of any of the signs listed on this slide should prompt additional inquiry. While many older persons may experience a decrease in memory and ability to think at their baseline level, it is not certain that these changes will result in the inability to function independently in their daily life.
- These changes can often be attributed to a diagnosis of mild cognitive impairment, or MCI. While MCI is often a precursor to the development of Alzheimer's disease, not all persons will progress to a dementia diagnosis. Estimates are that approximately 40% of persons diagnosed with MCI will progress to a diagnosis of Alzheimer's disease within 36 months.
- It is prudent to continue to routinely screen persons with MCI, two or three times per year for example, to monitor for progression so that therapeutic interventions can be initiated as soon as they are needed.

Slide 10:

- As a general rule, any cognitive symptom should be considered potentially drug-induced until another cause is determined. In one prospective study, six of 107 persons who had exhibited symptoms of global cognitive impairment suggestive of dementia for at least 3 months were found to have medication-induced symptoms.¹
- A detailed substance use history, including over the counter, nutraceutical (a food or natural supplement purported to have medical benefit) and illicit drugs is necessary to rule them out as potential culprits for cognitive decline and confusion.² In particular, it is worthwhile to look at the anticholinergic medications that the person might be using.³
- Persons living with Alzheimer's disease are known to have a decreased reserve of the neurotransmitter acetylcholine, so they become even more vulnerable to the side effects associated with these substances. Included in this group of medications are some antihistamines, including those available over the counter (diphenhydramine), muscle relaxants (cyclobenzaprine, orphenadrine), and tricyclic antidepressants (amitriptyline, nortriptyline, desipramine).
- Many antipsychotics can affect cognition, and some medications in that class also have significant anticholinergic properties (chlorpromazine, olanzapine, clozapine).
- Benzodiazepines (lorazepam, diazepam, alprazolam) are frequently associated with confusion and disinhibition.
- Systemic corticosteroids (prednisone, prednisolone, dexamethasone) have been associated with cognitive changes including decreased concentration and abnormal behavior.
- Other drugs in the antihistamine class, specifically those that work at the histamine H2 receptor for the purposes of suppression of gastric acid (ranitidine, famotidine), have been associated with mild, reversible cognitive impairment.
- Non-benzodiazepine sedative hypnotics (e.g., zolpidem) by definition and design alter the state of wakefulness of the user, and can thus cause a presentation of decreased awareness and cognitive engagement.
- Of note, the list of medications on this slide and listed in this guide is not comprehensive, but should serve to provide examples of some of the more common medications that might be encountered in practice.

Slide 11:

- The pharmacist takes HB into a counseling room, and administers one of the recommended screens, in this case the MoCA. HB scores a 21. A thorough review of HB's medication list is performed, and no highly anticholinergic medications are found, nor are other drugs that are likely to cause cognitive impairment. The pharmacist is careful to make sure that HB understands that while the test suggests that there are some memory issues that probably need to be evaluated by a specialist, the test is in no way diagnostic. She gives HB a list of practitioners that specialize in the area of Alzheimer's dementia so HB can make an appointment.
- In the case of a known pharmacy patient with a change in behaviors suggestive of memory changes, the pharmacist can administer a brief cognitive screening, review the medication list, and suggest further evaluation if indicated.

Slide 12:

- In this section, we will discuss how to choose an initial medication for the treatment of a person living with dementia according to the stage of the disease.
- An overview of individual medication properties, dosing and titration schedules will be offered.
- Person-specific considerations and important points for education will also be discussed.

Slide 13:

- Treatment for Alzheimer's disease should be initiated without delay as brain function that has been lost is irreplaceable. In the early stages, therapy is typically initiated with a cholinesterase inhibitor.
- The decrease in cortical acetylcholine activity in persons with mild-moderate disease has shown a direct correlation with an increase in cognitive symptoms. Additionally, in the hippocampus, which is associated with memory and learning, there is a deficiency of acetylcholine in the person living with Alzheimer's disease. Each of the cholinesterase inhibitors on the market has its own unique dosing and titration schedule. It has been estimated that these drugs delay cognitive decline for ~6 months.
- As the disease progresses, drug therapy will need to be re-evaluated. Only one of the cholinesterase inhibitors is approved for use in persons with moderate-severe disease. Additionally, another medication with a unique mechanism of action, memantine, is approved for the treatment of later-stage Alzheimer's disease.
- The ability of the glial cells in a person living with Alzheimer's disease to remove the excitatory neurotransmitter glutamate from the synaptic cleft is known to be impaired. Memantine blocks NMDA glutamate receptors thereby interrupting the excessive glutamatergic activity. A meta-analysis which included data from 431 persons demonstrated that memantine is not effective in earlier stages of the disease, and the combination of memantine and a cholinesterase inhibitor failed to show efficacy in mild dementia.
- In either scenario, the pharmacist should question the appropriateness of drug therapy to ensure the person is receiving the treatment most likely to allow for optimal therapeutic outcomes while not exposing the person to unnecessary drug therapy.
- In terms of specific recommendations for which cholinesterase inhibitor to choose for the initiation of therapy, from an efficacy standpoint each of the medications in the class has been shown to be equally effective. However, if it appears clear that the person is continuing to decline despite therapy, a switch to another agent is warranted, and may produce a better outcome.
- A meta-analysis of 23 clinical trials (11,024 persons) demonstrated that all of the cholinesterase inhibitors significantly stabilizes cognitive function vs. placebo in persons with mild-moderate disease. Much of the significance was due to the continued decline of persons randomized to placebo, while those on the cholinesterase inhibitors may not have improved, but were stabilized. Most of the medications also demonstrated better functional outcomes (measured on the Alzheimer's disease cooperative study--Activities of daily living inventory, or ADCS-ADL), with the exception of donepezil 5mg. This held true with all approved medications to treat Alzheimer's disease regardless of severity. Benefits seen in persons' behavior were significantly less robust, with only donepezil 10mg and galantamine 24mg demonstrating a significant

improvement. How long any of the benefits were likely to last remains to be seen as the majority of studies were around 6 months in duration. The authors of the analysis determined that all medications are capable of slowing the decline of Alzheimer's disease.

- Pharmacists should assure that persons are titrated to a therapeutic dose, counsel persons and care partners about common side effects and what to do if an adverse effect occurs.
- **References:** (Traynor, 2015; Bohnen et al., 2005; Allgaier & Allgaier, 2013; Wollen, 2010; Francis et al., 2012; Schneider, et al., 2001; Birks, 2006; Work Group on Alzheimer's Disease and Other Dementias, 2007; Dantoine et al., 2006; Gardette et al., 2010; Tan et al., 2014)

Slide 14:

- As with all medications, the drugs used for dementia are associated with adverse effects in susceptible persons. The nausea and vomiting that is sometimes seen with the initiation of the cholinesterase inhibitors tends to be transient, usually resolving within a matter of days.¹ In the case of rivastigmine and galantamine, concurrent administration with food should help minimize any associated gastrointestinal issues. Decreased appetite and diarrhea can be transient or chronic resulting in weight loss. Alternate dosage forms (e.g., the rivastigmine patch) may be employed so as to bypass the gut thereby minimizing nausea.¹
- Donepezil may be administered without regard to meals, so administration with food to minimize nausea is also warranted when necessary. Other adverse effects may be minimized by adhering to the titration schedule of the medications so as not to escalate too quickly. Syncope and bradycardia are associated with Alzheimer's disease treatments, and are likely underrecognized.²
- Monitoring for associated symptoms, such as dizziness and falls, is essential to avoid injury. It is important that persons understand any need for treatment interruptions should be referred to their prescriber as stopping therapy without the addition of another medication may result in a rapid cognitive decline and an increase in disability.³
- The pharmacist involved in the care of a person who starts therapy with a cholinesterase inhibitor should help to assure that the dose is being optimized. Cholinesterase inhibitors exhibit a dose-response relationship, and as such the highest approved dose should always be achieved unless the person is unable to tolerate it.⁴
- Laboratory assessment of liver function and renal function should be completed prior to the initiation of therapy so corresponding dosage adjustments can be made. No specific recommendations have been put forth with regard to the need for changes in the dose of donepezil for persons with either hepatic or renal dysfunction.⁵ Rivastigmine may require lower doses when moderate to severe renal or hepatic impairment are present due to the increased risk of side-effects. However, no specific recommendations for adjustment are available.⁶ Galantamine dosing is recommended to be limited to a maximum of 16mg daily for persons with moderate renal or hepatic dysfunction. For persons with a Child-Pugh score of 10-15 indicating severe hepatic disease, or those with a creatinine clearance less than 9ml/min, the drug is not recommended for use.⁷ Finally, memantine does not appear to require dose adjustments for hepatic disease. However, a creatinine clearance between 5-29ml/min necessitates that the daily dose be limited to 14mg/day.⁸

Slide 15:

- This slide represents the current recommended doses of the acetylcholinesterase inhibitors, along with the available dosage forms, indication and recommendations for titration. Note that each medication has a threshold for the minimum effective dose. Pharmacists should be cognizant in making sure that those doses are achieved unless there is a contraindication for doing so. In such a case, a recommendation for switching to an alternate agent should be made to the prescriber.
- **References:** (Donepezil package insert, 2015; Rivastigmine package insert, 2015; Galantamine package insert, 2015)

Slide 16:

- This slide represents the current recommended dosing schedule of memantine in persons living with moderate to severe Alzheimer's disease, along with the available dosage forms, and recommendations for titration. Note that the dose of the extended release capsule is not a one-to-one conversion with the immediate release formulations of the drug.
- **Reference:** (Memantine package insert, 2013)

Slide 17:

- It is important to make sure that persons living with dementia, and family or care partners, understand that the presence of memory loss and other symptoms suggesting that dementia might be part of the differential do not confirm a diagnosis, nor can a diagnosis be made without ruling out other conditions that might be responsible for the symptoms that are being observed.
- It will be necessary for a diagnostician skilled in identifying dementia to see the person, conduct interviews, obtain laboratory data and perform neuroimaging tests in order to determine if treatment for dementia is warranted.¹⁻² If a diagnosis is confirmed, medication counseling should include not only information on dose and potential adverse effects, as well as how to minimize them so therapy can continue without interruption, but also the discussion about what medications can and cannot do in this setting.
- Persons respond differently to medications, and the person and care partner must be counseled that any previous experience or observations they've had with dementia persons and the use of medications may not inform their personal experience.¹ There also needs to be a clear understanding that while the currently available medications may slow the disease process, no therapy presently halts or reverses the damage.³ As such, there must be understanding that a clear improvement on drug therapy is not always seen.⁴ Additionally, if the family does not see obvious improvement, it should be emphasized that adherence to therapy is still necessary (though they can certainly discuss the issue with the prescriber), because any progression that occurs while off medications will be permanent.
- Because psychiatric symptoms and behavioral disturbances are common in advancing disease, it is prudent to counsel persons living with dementia and care partners of the limitations of the medications that are specifically approved for the treatment of Alzheimer's disease. It is very likely that at some point, additional medication therapy may need to be employed to treat these

symptoms. Other functional symptoms may also occur, and they too may require additional treatments.

- It is essential that persons and care partners are aware that over-the-counter medications may interact with the person's dementia treatment. For instance, some antihistamines used for upper respiratory conditions or to induce sleep may have anticholinergic properties and serve to counteract a prescribed medication.
- A pharmacist should always be consulted before such a medication is used. Additionally, there is a great deal of erroneous information about nutraceutical efficacy in Alzheimer's disease that might serve to prompt the use of such medications in the hope of providing additional treatment. The pharmacist has an obligation to inform the person and their care partners what the available data suggests with regard to efficacy.
- One medication frequently mentioned as a "natural" treatment for cognitive disorders is Gingko biloba.⁽¹⁰⁾ Of all nutraceutical medications, it is by far the most extensively studied with regard to Alzheimer's disease treatment. While placebo-controlled trials employing a random effect model have consistently shown that the effect of Gingko on cognition is superior to placebo, and the effect on activities of daily living is regularly reported to be favorable, the degree of heterogeneity (differences that make direct comparison difficult) across studies, and the fact that the trials are generally considered to be of low quality suggests that interpretation of study outcomes should be carefully done.⁵ Of note, no study of Gingko has ever demonstrated slowing of disease progression. Most clinicians consider the data on Gingko to be inconclusive.⁶
- Other medications often touted as having positive efficacy for persons living with dementia include vitamin E, estrogen, omega-3 fatty acids, co-enzyme Q-10 and coconut oil.⁷ Estrogen has actually been associated with an increase in Alzheimer's disease incidence in at least one study.¹⁰ There is not enough information with regard to the others to recommend their use in treating or preventing dementia. Persons and care partners who opt to use a nutraceutical medication, despite the lack of efficacy data, should be made to understand that they are not FDA regulated; the use of these agents may be a safety concern for that reason; and little information exists as to how they might interact with the prescription medications that the person is receiving.⁷
- **References:** (Traynor, 2015; DeSimone & Viereck, 2011; Ejfestad et al., 2013; Marasco et al., 2002; Yang et al, 2014; DeKosky et al.; 2008; Alternative Treatments, 2016; Miller et al., 2005; Lonn et al., 2005; Shumaker, et al., 2004)

Slide 18:

- As stated previously, pharmacists remain the most accessible health care providers for the general public. Familiarity with organizational resources is essential. While most of us take the use of the internet for granted as a common practice, it must be kept in mind that older adults may not be tech savvy, and may require the use of written materials or brochures that can be offered in the pharmacy setting. It is also prudent for the pharmacist to become familiar with local resources for persons and their care partner, whether it be support groups, or practitioners that specialize in the treatment of dementias. As an extension of that, it is helpful for pharmacists to know if any investigational studies are being conducted by local practitioners such that they might refer eligible persons.

- Pharmacists must also be familiar with the limitations of their persons based not only on age but also diagnosis and level of health literacy. Accommodations should be made with regard to counseling strategies (e.g., minimize distractions, ensure good lighting, use pictograms when able, use large font with high contrast to printable medium, etc.).² The individual being counseled should always be asked to repeat the information back to the pharmacist before leaving so any misunderstandings can be caught, thus minimizing the potential for person harm.
- **References:** (Skelton, 2008; U.S. Pharmacopeial Convention. USP Pictograms, 2016)

Slide 19:

- HB, the 72-year-old customer of the pharmacy, is now diagnosed with Alzheimer's disease and is having difficulty managing side effects.
- She receives a prescription for rivastigmine, 1.5mg by mouth twice daily, and her son picks the prescription up. A week and a half later, HB arrives at the pharmacy to pick up her lisinopril prescription for her hypertension. The pharmacist asks how she is doing taking the rivastigmine. HB states that it causes such frequent nausea, that she has stopped taking it, and plans to make an appointment with her physician to discuss other options, but has not yet done so. The pharmacist reminds HB that it is important for her to be on medication to slow the progression of Alzheimer's disease since any loss of cognitive function while off medication is not recoverable.
- Upon questioning, the pharmacist finds that HB was taking her medications on an empty stomach. It is suggested that HB re-initiate therapy, and take the medication with food to reduce the nausea. It is further explained that the nausea is likely to subside within a few days. A week later, when the pharmacist checks in with HB, she is tolerating the medication well, but is almost out having received only enough for two weeks. The pharmacist contacts the prescriber to initiate the dose escalation process to make sure HB reaches the minimum maintenance dose of 6mg daily.

Slide 20:

- The approach to complications of dementia, treatment of comorbid conditions and interactions with medications used to treat such conditions will be discussed in this section.

Slide 21:

- Fortunately, on the whole there are very few drug-drug interactions that are known to occur with medications used in the treatment of Alzheimer's disease. All of the acetylcholinesterase inhibitors have been associated with bradycardia, or decreased heart rate. A population-based cohort study of 11,328 persons living with dementia revealed that individuals who had taken a drug from this class had an incidence of bradycardia of 0.82 per 1,000 person days vs. 0.47 for persons not exposed to these medications.¹ Individuals receiving beta antagonists, and those with a significant cardiac history (myocardial infarction (heart attack), congestive heart failure or hypertension) were found to be at higher risk. Additionally, the labeling contains a warning against the use of metoclopramide in persons taking rivastigmine due to the additive risk of extrapyramidal side-effects (drug-induced movement disorders). No specific recommendation

for the avoidance of any particular medication or class, other than anticholinergic medications, is found in the labeling of galantamine or donepezil. However, a general statement about the ability of medications that inhibit the enzymes cytochrome P450 3A4 (CYP3A4) (e.g., ketoconazole) and cytochrome P450 2D6 CYP2D6 (e.g., amitriptyline, fluoxetine, paroxetine) to increase the blood levels of galantamine is made.³

- A broad recommendation to use memantine with caution in the presence of other drugs that act with antagonistic properties on the NMDA receptors is found within the labeling for the drug, though the statement that these medications have not been evaluated for concomitant use is also made. Such drugs include the OTC cough suppressant dextromethorphan, as well as ketamine and amantadine.⁴
- **References:** (Hernandez, 2009; Rivastigmine package insert, 2015; Galantamine package insert, 2015; Memantine package insert, 2013)

Slide 22:

- Mechanistically, anticholinergic medications act in opposition to the acetylcholinesterase inhibitors, potentially diminishing or negating their positive therapeutic effects.
- It has been demonstrated that pharmacists can play an important role in identifying persons who have a high anticholinergic load, and act to decrease the potential for drug interactions.
- One study looked at a sample of 50 older individuals to determine what their anticholinergic burden was as measured on the Anticholinergic Drug Scale.^{1,2} A score of 2 or greater was deemed clinically significant, and worthy of an attempt at intervention with the prescriber. Fourteen persons met this criterion. At the end of the data collection period, the median score on the scale dropped from 2.5 to 1, ($p=0.009$) indicating that pharmacist monitoring of anticholinergic load can lead to a decrease in burden. Not only can this help to ensure that persons are receiving maximum benefit from acetylcholinesterase drug therapy, but intervention in non-demented persons may decrease their risk of developing the disease at a later time.³
- Several other scales for the measurement of anticholinergic load are available for use in pharmacy practice, including the Anticholinergic Cognitive Burden Scale, and the Anticholinergic Risk Scale.^{4,5}

Slide 23:

- At some point during the disease process, nearly every person will experience some type of behavioral or psychiatric symptomatology.¹ The cumulative risk of developing a psychiatric disorder concomitantly with Alzheimer's disease is believed to be approximately 90% over the course of the disease.²
- Symptoms of depression may overlap with dementia, complicating the picture and the approach to treatment. Depression in a person living with dementia may also fluctuate symptomatically.³ Even mild depression may further impair the person's ability to function.
- Other neuropsychiatric symptoms may also worsen in the face of untreated depression.⁴ Pharmacists may identify an individual with depression through observation of behavior, and the use of simple screening tools such as the PHQ-2 or -9, or the Geriatric Depression Scale.⁵ A score of ten or more out of 30 on the latter suggests the person may be mildly depressed, and is an indicator that they should be referred to a clinician who can diagnose and treat the disorder.

- Pharmacists can continue to use the scale to monitor persons who have been started on antidepressant therapy.⁶ Of note, recurrent depression has been linked to an increased risk of developing Alzheimer's dementia.⁷⁻¹⁰ A systematic review and meta-analysis of antidepressant placebo-controlled trials in persons with depression and dementia found evidence "suggestive" of efficacy but not of sufficient strength to "confirm" efficacy. No antidepressant has been found to be superior in dementia compared to any other.⁶ However, it is prudent to avoid highly anticholinergic options such as the tricyclic antidepressants.
- Certain antidepressants are associated with side effects that can be exploited to treat other problems associated with dementia. For instance, persons living with dementia often have a decrease in food intake for a number of reasons, including inability to recognize signs of hunger, diminished sense of smell or taste, difficulty swallowing and issues related to dexterity causing difficulty in using utensils.⁴ In such a case, an appetite stimulating drug (e.g., mirtazapine) may be appropriate.⁶
- Other antidepressants may affect a person's sleep. Pharmacists can help with the timing of doses depending on whether the goal is to prevent daytime drowsiness, or to aid in inducing and maintaining sleep at night.
- Symptoms of psychosis, including aggression, can be extremely burdensome for PLWD and their care partners. This may lead to the inappropriate use of antipsychotic medications in persons living with dementia before behavioral therapy and re-direction has been employed to maximum benefit. In general, recommendations are to reserve the use of antipsychotic medications for times when these approaches have been given an adequate trial, but have failed, or for when a person is in extreme emotional distress.
- One of the reasons that the use of behavior modification prior to initiating therapy for psychotic or aggressive symptoms is recommended is that both atypical and conventional antipsychotics have been associated with an increase in mortality in elderly persons with dementia.
- Cerebrovascular events occurred at a rate of 1.9% in persons receiving atypical antipsychotic therapy compared with 0.9% of those receiving placebo in one analysis.¹³ In the same analysis, the risk of all-cause mortality was also found to be between 1.6-1.7 times greater in the population exposed to antipsychotics.
- Pharmacist-led medication reviews can help minimize antipsychotic exposure of PLWD. In general, withdrawal should be considered for those in whom the medication is not being used for acute behavioral problems.
- While benzodiazepines are often used to treat symptoms of anxiety, caution must be used in the person with dementia. Typically, these medications are not recommended due to their propensity to cause falls in older persons.⁶ They may also contribute to memory impairment, confusion and disinhibition.
- For individuals who may have marked anxiety, short term use with a carefully chosen medication from this class may be justified. The drug utilized should be short-acting, and without active metabolites (e.g., lorazepam). Longer acting medications should be avoided (e.g., diazepam, chlordiazepoxide).¹⁵
- **References:** (Savva et al., 2009; Parnetti et al., 2001; Alexopoulos, 1996; Terrie, 2015; Neugroschl, & Wang, 2011; Dotson et al., 2010; Saczynski et al., 2010; Rosenberg et al., 2011; Feinberg & Michocki, 1998; Wang et al., 2014; Schneider et al., 2006; Child et al., 2012; Rabins et al., 2007, Reus et al., 2016).

Slide 24:

- Pharmacists can help PLWD and care partners manage issues with bladder and bowel dysfunction in several ways. The first is thorough education regarding the need to make sure the person makes frequent trips to the toilet, even if they are not complaining of the need to urinate or defecate. This will help to avoid incontinence from not being able to reach a toileting facility in time. Persons living with dementia may also have difficulty remembering where the toilet is located, or what it is used for. As such, leading the persons to the facility and helping them use it if necessary, including managing clothing, will be helpful.¹ For persons who continue to be incontinent, pharmacists can recommend pads or underwear that are made for this purpose. They can also discuss ways in which fiber, either through food or fiber supplements found in the pharmacy, can be used to control bowel habits. Suggesting the use of barrier creams to protect skin integrity so as to avoid ulcers and infection is prudent.
- As discussed previously, medications like benzodiazepines can contribute to falls. However, any medication that is active in the central nervous system that can cause dizziness or drowsiness may also contribute to this risk. Regular questioning of both the person living with dementia and their care partners about falls is recommended. Prescription medications may need adjustment, and pharmacists should contact prescribers to discuss options when appropriate. Additionally, OTC purchases of medications that can cause drowsiness and dizziness (e.g., antihistamines) should be monitored, and alternate suggestions should be made for persons who are at risk or who have a history of falling. Some pharmacies can supply assistive devices, such as walkers and canes. Pharmacists can facilitate obtaining prescriptions for such devices from prescribers, fit the devices, and advise on the appropriate way to use them safely.
- OTC medications for common infections and the associated symptoms are often utilized for self-treatment by persons. Immune function in the elderly is known to be compromised for a number of reasons.² Among them are naturally waning immunity, decreased nutritional status, medication-induced risk and social factors (such as isolation). Additionally, Alzheimer's disease is, in and of itself, a known risk factor. Urinary tract infections and upper respiratory infections in persons living with dementia are more likely to progress to serious conditions such as urosepsis and pneumonia that may require hospitalization and prove life-threatening. Pharmacists can monitor OTC use, and inquire of PLWD and care partners what symptoms are being treated. Education can be provided with regard to what signs to watch for that might require medical attention, or immediate referral can be made when warranted.
- Sleep disruptions occur frequently in persons living with dementia, and patterns often change depending on the stage of the disease.³ Deprivation of sleep may increase problems associated with behavior in the person living with dementia.⁴ Early in the disease process, sleep is often minimally affected, or drowsiness may actually increase, but the person may wake up confused and disoriented. As the disease progresses, sleep may become more fragmented, and daytime sleepiness may increase, while persons may have more difficulty at night going to or staying asleep. Evidence shows that normal circadian rhythms may be disrupted in the person living with dementia.³ Untreated or uncontrolled depression may contribute to sleep disturbances. Behavioral problems may increase during the nighttime hours as well due to a phenomenon known as "sundowning."⁵ Pharmacists can suggest behavioral and environmental strategies to help control sleep disturbances, including increasing the amount of light in the home at dusk, ensuring adequate physical activity and mental stimulation during the day, and maintaining a

regular sleep/wake schedule. Avoiding stimulants like caffeine may also be useful. Short-term use of prescription medications for sleep induction may be warranted if nonpharmacologic interventions are ineffective. Instructions should be offered to PLWD and care partners regarding the possibility that such agents may increase daytime drowsiness, and contribute to confusion. OTC sleep agents often contain antihistamines, which may also cause drowsiness and contribute to confusion and falls.

- **References:** (Dementia Including Alzheimer's Disease, 2016; Zagaria, 2011; Alzheimer's Disease and Sleep, 2016; Feinberg & Michocki, 1998; Alzheimer's and Dementia Caregiver Center. Sleep Issues and Sundowning; 2016)

Slide 25:

- This section will address strategies for recognizing non-adherence and steps to overcome barriers to appropriate medication use.

Slide 26:

- Lack of adherence to prescribed medication regimens is a known problem in older adults. Medication regimens may become quite complex as the number of comorbid conditions increases causing confusion about dose timing, or resulting in forgetting to take doses. Additionally, older persons in particular are often at higher risk for non-adherence due to financial reasons. Many older individuals are on a fixed income, or have minimal insurance coverage. Some skip having prescriptions filled at all due to cost. Others may stop taking medications due to side-effects that they fail to report to their health care providers. It is imperative that pharmacists ask about adherence, and do so in a non-judgmental way so as to elicit factual information. When necessary, pharmacists may contact prescribers with less expensive alternatives, or suggest discontinuing non-essential medications so that those that are necessary to slow disease progression can be obtained. Strategies for overcoming side effects can also be shared with persons, or the pharmacist may advocate for a medication change if the side effects prove to be intolerable or do not diminish with continued medication use. Additionally, pharmacists may also direct persons to programs offered by pharmaceutical companies for persons who have difficulty paying for their medications, such as Needy Meds. Manufacturers may be contacted individually as well.
- For those individuals who have difficulty organizing or remembering if they took their medications, pharmacies may offer a service to fill medication dispensers on a weekly or monthly basis. Persons living with dementia and care partners can be instructed to set reminder alarms, or place medications in conspicuous places. There are many tools on the market designed to be used for unit dose dispensing that have reminder systems. Pharmacists can help PLWD and care partners find suitable, affordable options.
- **References:** Gellad et al., 2011; Wiens, 2003; McKercher et al., 2003; Needy Meds, 2016; Caro et al., 2004; Feldman et al., 2004; Hauber et al., 2004; Migliaccio-Walle et al., 2003; Green, 2007; Pouryamout et al., 2007; Versijpt, 2014)

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- Another way in which pharmacists can help ensure adherence is to make sure that the dosage form that is being received by the PLWD is convenient and safe to take. For instance, in the case of a person who has dysphagia, the risk of coughing or choking on certain dosage forms exists.
- Pharmacists can suggest that persons be referred to speech therapists who can offer techniques for minimizing risk as the person is likely also having difficulty swallowing food or liquids that are not medication related.
- Exploring the alteration of dosage forms is another option. It is important, even if the person is currently not experiencing difficulty taking the medication, that counseling include information about which dosage forms may be crushed or cut lest the person or family do so potentially causing a safety issue (such as a bolus of medication from a dosage form that is intended to be extended release). Some medications are available as liquids, and might be better options for persons who have difficulty with the solid dosage forms. Thickeners may be utilized for liquid medications in some cases, to minimize the risk of choking. Rivastigmine is available in patch form, which bypasses the need to swallow entirely.
- Side effects may require that a drug switch be made, or the pharmacist may be able to provide strategies to overcome side effects as described previously.

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- As persons living with dementia advance in their disease, the approach to their care changes. While there is no clear answer on when medication therapy should be discontinued, thought should be given to whether or not the benefits of ongoing therapy outweigh the risks.

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- Cholinesterase inhibitor therapy for Alzheimer's disease is dependent on the person having a high enough number of intact, functional cholinergic neurons for the drug to act upon.¹ In the later stages of the disease, cholinergic neurons have been shown to be particularly at risk from the neurotoxicity associated with the disease.
- The average life span of a person with Alzheimer's disease after diagnosis is approximately 7 years. Each time the pharmacist sees the care partner, an inquiry should be made about progression of symptoms, as this may begin to occur rapidly in between visits with the prescriber. There is no clear guideline on when it is appropriate to consider discontinuation of treatment for dementia. However, in general, if the person is non-adherent and strategies for increasing adherence have proven unsuccessful, or if the efficacy has clearly waned as evidenced by advancing symptoms, the pharmacist should contact the prescriber, or suggest that the person be seen to discuss the pros and cons of continuing treatment.³
- It is widely assumed that the clinical benefits of medications for Alzheimer's disease have a finite duration of significant activity, and for some persons that might be no longer than 12 months.⁴ If discontinuation is being considered, it is also prudent to look at the person's other maintenance medications to see if they too might be stopped (e.g., cholesterol lowering medication, medications for osteoporosis prevention), so as to decrease the pill burden and cost to the person and family.

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- Individuals involved in the care of persons living with dementia face their own challenges and are at risk for declining health. Pharmacists also have a place in the care of these individuals.

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- Responsibility for the care of someone with dementia frequently falls to a family member. As dementia progresses, care partner burden will naturally increase as long as the person living with dementia remains at home. Both the PLWD and the care partner may experience physical and mental deterioration.² Factors associated with higher care partner burden include neuropsychiatric symptoms and the need for help with activities of daily living.³ Care partners should be screened for symptoms of depression, and pharmacists may consider utilizing the tools previously discussed to do that, and to refer persons when it seems prudent. In addition, pharmacists should be on the lookout for signs that the person is not being adequately taken care of, or may even be experiencing neglect or abuse at the hands of the care partner. Alerting the prescriber, or a local agency to advocate for the person may be necessary. In some jurisdictions, such reporting is mandatory.

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Answers:

1. b. Diagnose the person and refer to a prescriber.
2. d. Consider rivastigmine for persons who have difficulty swallowing.

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Answers:

3. b. Medications for the treatment of Alzheimer's disease should be titrated to the maximum tolerated approved dose.
4. d. Should be screened for unnecessary maintenance medications unrelated to the diagnosis of dementia.