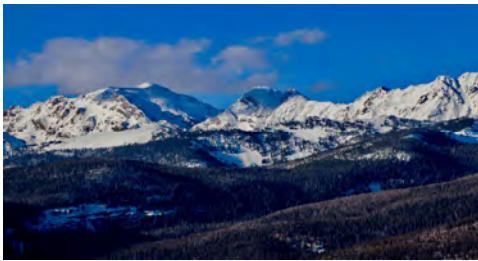
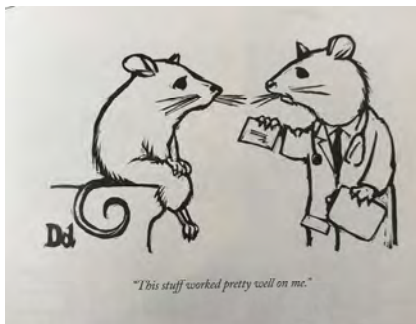


Is There a Pill that Will Help with Alzheimer's Dementia Prevention, Progression, or Behaviors Associated with Dementia?

Leslie Eber MD CMD

Medications in 2019 What do we think now?







Objectives

1. What does the current research say about prevention for Alzheimer's Dementia?
 - ▶ Are there medications that help prevent dementia?
2. Are there medications that can treat Dementia?
 - ▶ If so, how effective are they?
3. Are there medications that can help with the treatment of behaviors associated with Dementia?
 - ▶ How beneficial are these medications, and what are the risks of using them?

What does the current research say about the prevention for Alzheimer's Dementia? Are there medications that help prevent dementia?

The Scope of Alzheimer's Dementia

- ▶ Affects 5.8 million adults
- ▶ Will affect 14 million adults by 2050
- ▶ 1 in 10 adults age > 65 years old
- ▶ 1 in 3 adults age > 85 years old
- ▶ 2/3 are women
- ▶ People are living longer with fewer fatalities from other diseases → More people develop Alzheimer's Dementia

Alzheimer's Association data 2019

There are Many Types of Dementias

- ▶ Alzheimer's Dementia
- ▶ Multi-infarct Dementia
- ▶ Dementia associated with Parkinson's Disease
- ▶ Lewy Body Dementia

Most people have a combination of Dementias

Prevention is based on the cause of the dementia

- ▶ Research for the prevention of Alzheimer's disease and related dementia is prolific and ongoing
- ▶ 2 large reviews of the research for the Prevention of Alzheimer's disease and related dementias were published in the Annals of Internal Medicine and the Lancet in 2017
- ▶ There is no magic bullet, but there are things that we can do that may be beneficial by considering the cause of some dementia(s).

Livingston G, Sommerlad A, Orgetta V, et al. Dementia Prevention, Intervention and Care, Lancet, 2017
Elli B, Larson: Prevention of late-life Dementia: No Magic Bullet, Annals of Intern Med, 2017

Prevention of Alzheimer's Disease and related dementias

- ▶ There is no medication or supplement that has been proven through medical research to provide cognitive protection from developing dementia
- ▶ There are medications that can treat high blood pressure, diabetes, and heart disease. This in turn decreases the risk of diseases that can lead to some dementias (Stroke, multi-infarct Dementia)

Bulter M, Nelson VA, Davila H et. al. Over the counter supplement interventions to prevent cognitive decline, mild cognitive impairment and clinical Alzheimer type Dementia. A Systematic review. Ann Intern Med. 2018



Prevention of Alzheimer's Disease and related Dementias

Why is it so Hard to find effective interventions to prevent Alzheimer's Disease and related Dementias?

- ▶ This disease can take decades to show symptoms
- ▶ Prevention will need to be studied in people decades before symptoms appear
- ▶ Dementia has many causes and combinations in each person → prevention may need to be individualized to the specific person

Eric B. Larson. Prevention of late-life Dementia: No Magic Bullet. Annals of Intern Med. 2017

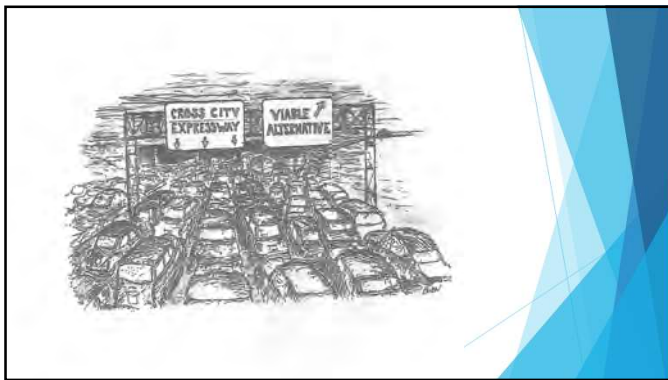
Prevention of Alzheimer's Disease and related Dementias

Why is it so hard to find effective interventions to prevent Alzheimer's Disease and related dementia?

There appears to be other factors associated with showing Symptoms of Dementia besides what is in our Brain

- ▶ Some people have the brain changes that cause Alzheimer's Dementia but show few symptoms in real life
- ▶ Some countries (USA, Sweden, Canada) have had an unexpected decline in the prevalence of Alzheimer's disease and related dementias. Other countries, like China, have not had this decline.

Sonnen JA, Larsson EB, Crane PK et. al. Pathological correlates of dementia in a longitudinal population-based sample of aging. Ann Neurol 2007



Two Schools of Thought for Dementia Prevention

- ▶ The Lancet Commission for Dementia Prevention, Intervention, and Care 2017
 - ▶ The best chance for preventing dementia is a "Life Course" approach
- ▶ The National Academy of Medicine found classes of interventions that were encouraging to help prevent dementia, though such interventions were ultimately inconclusive (2017).
 - ▶ Blood pressure management
 - ▶ Increased physical activity
 - ▶ Potentially cognitive training

Livingston G, Sommerlad A, Orgetta V, et al. Dementia Prevention, intervention and Care. Lancet. 2017
National Academy of Science, Engineering and Medicine. Preventing Cognitive Decline and Dementia: A way Forward. National Academies Press 2017

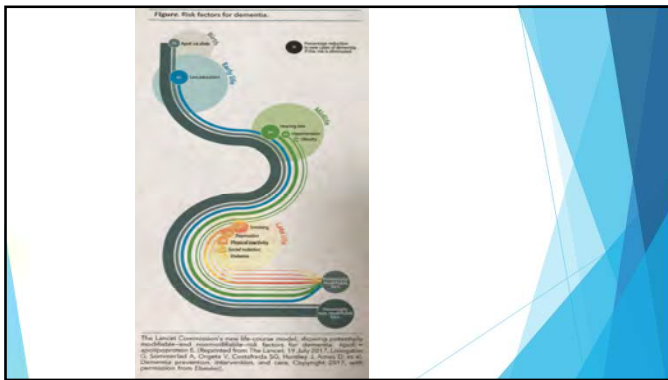
So, What does this Mean?

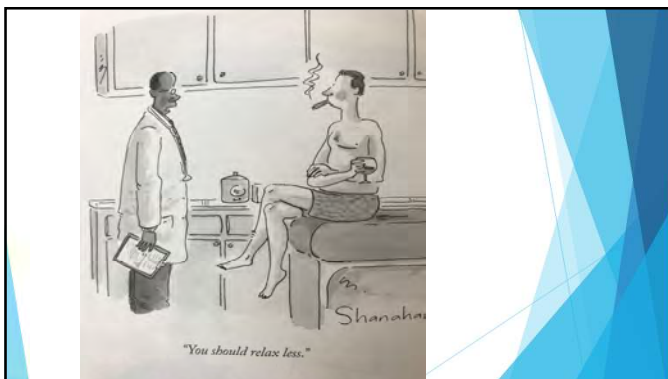
According to the Lancet Commission:

- 35% of potential risk factors for dementia are modifiable from Birth to late life :

- ▶ Hearing Loss
- ▶ HTN
- ▶ Obesity
- ▶ Smoking
- ▶ Physical Activity
- ▶ Depression
- ▶ Social Isolation

Livingston G, Sommerlad A, Orgeta V, et al. Dementia Prevention, Intervention and Care, Lancet, 2017





Research on Specific Interventions to Prevent Dementia - Hypertension Control

- ▶ **Hypertension control** decreases the risk for a stroke and resultant Dementia
- ▶ Hypertension control increases heart and cardiovascular health and decreases micro strokes in the brain
- ▶ Current research is also suggestive that hypertension that is well controlled could decrease the risk of multiple kinds of dementia

The SPRINT MIND Investigators for the SPRINT Research Group. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial (published online January 28, 2019). JAMA.

Research on Specific Interventions to Prevent Dementia - Physical Activity

- ▶ **Physical Activity**
 - ▶ Research suggests physical activity in combination with other healthy habits could be helpful to prevent cognitive decline and Dementia
 - ▶ Known to decrease heart disease and cardiovascular risk, obesity, and diabetes
 - ▶ Can lead to decreased risk of stroke and resulting dementia

M Brasure, P Desai, H Davila et. al. Physical Activity Interventions in preventing Cognitive Decline and Alzheimer-Type Dementia: A systematic Review. Ann Intern Med 2017

LE (21)

LE1

Research on Specific Interventions to Prevent Dementia - Physical Activity

- ▶ **Physical Activity**
 - ▶ May directly slow cognitive decline through increased blood flow
 - ▶ May indirectly intervene by reducing other risk factors (heart disease, diabetes, and obesity)
- ▶ **Specific Physical Activity:**
 - ▶ Aerobic training, resistance training and multicomponent physical activity are all beneficial

M Brasure, P Desai, H Davila et. al. Physical Activity Interventions in preventing Cognitive Decline and Alzheimer-Type Dementia: A systematic

Slide 20

LE1 as well as DM and Obesity decreased risk with physical activity.

Leslie Eber, 4/14/2019

LE [2]1 Leslie Eber, 4/14/2019





Research on Specific Interventions to Prevent Dementia - Cognitive Training

Cognitive Training

- ▶ In older people with normal cognition, training improves cognitive performance in that **trained domain**.
- ▶ Evidence that cognitive training prevents dementia or slows the progression of dementia is insufficient to date.
- ▶ Brain training apps or subscriptions are not harmful but are not proven to be helpful
 - ▶ **Be cautious of expensive opportunities**

Butler M, McCreedy E, Nelson VA, Desai P, Ratner E, Fink HA, et al. Does cognitive training prevent cognitive decline? A systematic review. Ann Intern Med. 2015;163(3):8. doi:10.7326/M15-1511

Research on Specific Interventions to Prevent Dementia - Medication Interventions

- ▶ Medications looked at to prevent dementia:
 - ▶ Ibuprofen, Aspirin, Estrogen, Lipid lowering Medications (statins), Evista, Aricept (Cholinesterase inhibitors)
 - ▶ NO Medications have been proven to prevent dementia
- ▶ Over the counter supplements:
 - ▶ W3 fatty acids, soy, Ginkgo Biloba, B vitamins, D vitamins + calcium, Vitamin C, B-carotene and multi-ingredient supplements
 - ▶ NO supplement was shown to prevent dementia

Butler M, Nelson W, Davila H, Ratner E, Fink HA, Hemmy LS, et al. Over-the-counter supplement interventions to prevent cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia. A systematic review. *Ann Intern Med.* 2018;168:52-62. doi:10.7326/M17-1530

Medications that can Increase the Risk of Dementia

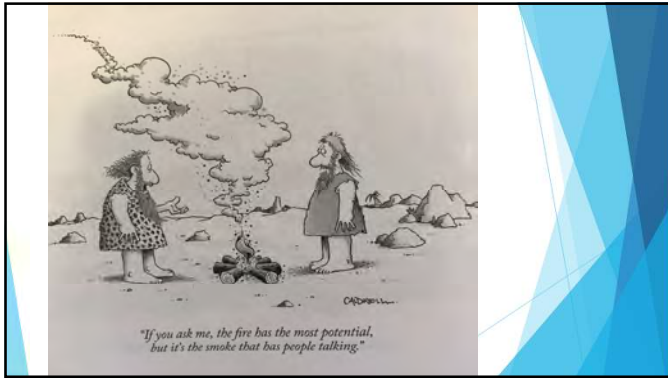
- ▶ Anti-Cholinergic Medications have now been found to increase the risk of dementia
 - ▶ Examples of medications that have high anti-cholinergic activity:
 - ▶ Benadryl, Detrol, Zanaflex and Zyprexa
 - ▶ The effect is cumulative and for long-term use

C. Fox, K. Richardson, I. Maidment et. al. Anticholinergic Medication Use and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study. *J Am Geriatr Soc* 59:1477-1483, 2011.
Shelly L. Gray, PharmD, MS, Melissa L. Anderson, MS, Sascha Dublin, MD, PhD, et al. Cumulative Use of Strong Anticholinergics and Incident Dementia: Prospective Cohort Study. *JAMA Intern Med.* 2015;175(13):401-407. doi:10.1001/jamainternmed.2014.7869. Published online January 26, 2015.

Pseudo Medicine: What is it and Why do We Need to Know about It?

- ▶ Pseudo Medicine:
 - ▶ Supplements and medical interventions that exist within the law and are often promoted as scientifically supported treatments but lack credible efficacy data

Joanna Hellmuth, MD, MHS: The Rise of Pseudomedicine for Dementia and Brain Health, January 25, 2019. doi:10.1001/jama.2018.21560



PseudoMedicine: What Do We Need to Know?

- ▶ \$2-3 billion industry
- ▶ Uses individual testimonials as established fact
- ▶ The supplement is often widely available and appears to gain legitimacy when sold by a major U.S. retailer
- ▶ Supplements are **not** regulated by the FDA
- ▶ Some supplements can be harmful and even cause a stroke, lead to dementia, or result in death (Vitamin E)

Joanna Hellmuth, MD, MHS: The Rise of Pseudomedicine for Dementia and Brain Health, January 25, 2019. doi:10.1001/jama.2018.21560

PseudoMedicine: What Do We Need to Know?

The Alzheimer's Association has taken the initiative to highlight these concerns

- ▶ Notes these supplements are promoted by testimonies, not science

Joanna Hellmuth, MD, MHS: The Rise of Pseudomedicine for Dementia and Brain Health, January 25, 2019. doi:10.1001/jama.2018.21560

PseudoMedicine: What Do We Need to Know?

- ▶ Pseudo medical interventions are not ethically, medically, or financially benign
- ▶ Effective interventions for common diseases would already be widely used and be the standard of care.

Joanna Hellmuth, MD, MHS: The Rise of Pseudomedicine for Dementia and Brain Health, January 25, 2019. doi:10.1001/jama.2018.21560

Treatment of Dementia

- ▶ There is no current treatment that has been proven to stop the progression of dementia

LE B11

Medications to Treat Dementia

Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors)

- ▶ Symptomatic therapy
- ▶ No neuro-protection
- ▶ Does not alter the underlying disease trajectory
- ▶ Patients with mild to moderate dementia are more likely to respond, but the effect is modest.
 - ▶ Dementia continues to progress
- ▶ Most often, benefits are short-lived (3-6 months)

Side Effects: Gastro-intestinal and Cardiac

Langa KM, Foster NL et al. Mixed dementia: emerging concepts and therapeutic implications. JAMA 2004;292:2901

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LE [3]1 target the acetylcholine deficit arising from loss of neurons

Leslie Eber, 4/14/2019

Medications to Treat Dementia

Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors)
Continued:

- ▶ Effectiveness varies person-to-person
- ▶ Aricept is also approved for use in severe Alzheimer's dementia in combination with Memantine
 - ▶ Effect is variable, short lived and there are many side effects

Reeve E, Farrell B, et al. EvidenceBased Clinical practice guideline for deprescribing cholinesterase inhibitors and memantine. Sydney, Australia: University of Sydney;2018

Medications to Treat Dementia

Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors)
Continued:

- ▶ 2018 guidelines -30% of prescriptions for these medications are inappropriate
- ▶ Up to 80% of patients have adverse drug reactions

Reeve E, Farrell B, et al. EvidenceBased Clinical practice guideline for deprescribing cholinesterase inhibitors and memantine. Sydney, Australia: University of Sydney;2018

LE2

Medications to Treat Dementia

Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors)
Continued:

- ▶ **Particular concern:** if a patient take these medications in combination with a class of medications called Anticholinergics (used for urinary leakage), muscular spasms or seasonal allergies could result
- ▶ These 2 types of medications work directly opposite one another and can both negatively affect Dementia medication and cause harm

Reeve E, Farrell B, et al. EvidenceBased Clinical practice guideline for deprescribing cholinesterase

LE2 Adverse Drug Reactions: slow heart rate, drug to drug interactions,
like anticholinergics , diarrhea

Leslie Eber, 4/20/2019

Medications to Treat Dementia

Since these medications only help for a while, what is the RIGHT way to stop them after starting?

- ▶ Tapering these medications to off is not “giving up”
 - ▶ It is assessing if this medication is helping and weighing the risk/benefit of the medication
- ▶ **Do Not Stop Abruptly** - This can lead to worsening cognition, behaviors, and withdrawal symptoms

Rieve E, Farrell B, et al. EvidenceBased Clinical practice guideline for deprescribing cholinesterase inhibitors and memantine. Sydney, Australia: University of Sydney;2018





Medications to Treat Dementia

- ▶ Namenda (NMDA Receptor Antagonist)
 - ▶ For moderate Alzheimer's Dementia patients
 - ▶ Again, modest effect for 3-6 months
 - ▶ Question of benefit when combined with Cholinesterase Inhibitors
 - ▶ Studies find this medication to be less effective than Cholinesterase Inhibitors
 - ▶ there was no statistical signs of effectiveness at 12 months

R Knigh, M Khondoker et al. A systematic Review and Meta-Analysis of the Effectiveness of Acetylcholinesterase inhibitors and memantine in treating the cognitive symptoms of Dementia. Dement Geriatr Cogn Disord 2018;45:131-151

Slide 37

LE3 1/2 the medication every 4 weeks with close monitoring, Trial discontinuation

Leslie Eber, 4/20/2019

LE4 Note: discontinuation deterioration may also be due to the progression of the disease it's self

Leslie Eber, 4/20/2019

EBE1 what kind of behaviors???

Eber, Benjamin E., 4/21/2019

Behaviors Associated with Dementia

What are some of the behaviors associated with dementia?

- ▶ Agitation, anxiety, irritability, depression, apathy, disinhibition, delusions, hallucinations, and sleep or appetite changes, refusal of care
- ▶ These behaviors are also called behavioral and psychological symptoms of dementia

Kersta Scales, PhD Sheryl Zimmerman, PhD et al. Evidence-Based Nonpharmacological Practices to Address Behavioral and Psychological Symptoms of Dementia. *The Gerontologist*, Volume 58, Issue suppl_1, February 2018, Pages S88-S102

Are There Medications that Can Help with These Behaviors?

Medications that have been tried:

- ▶ Benzodiazapines (Ativan, Klonopin, Valium)
- ▶ Atypical antipsychotics (Seroquel, Zyprexa, Respidal)
- ▶ Antipsychotics (Haldol)

- ▶ None of these medications have been showed to be helpful to decrease behaviors
- ▶ They can ALL be harmful

Are there Medications that can Help with these Behaviors?

There have been many studies on medications to see if they can help with the behaviors associated with dementia

None have been successful

A Maher, MD, G Theodore, PhD. Summary of the Comparative Effectiveness Review on Off-Label Use of Atypical Antipsychotics. *Journal of Managed Care Pharm.* June, 2012, Vol 18
Dorovan T. Maust, MD, MS; Hyunjin Myra Kim. Antipsychotics, Other Psychotropics, and the Risk of Death in Patients With Dementia Number Needed to Harm. *JAMA Psychiatry*. 2015;72(5):438-445. doi:10.1001/jamapsychiatry.2014.3018

Are there Medications that can Help with these Behaviors?

- ▶ There are now national, federal, and international initiatives to discourage the use of these medications for dementia behaviors
 - ▶ Because of their harm and lack of effectiveness
- ▶ There is now a **BLACK BOX** warning on the use of some medications like Seroquel, Risperdal and Zyprexa
 - ▶ Increased risk of diabetes and mortality.

A Maher, MD, G Theodore, PhD. Summary of the Comparative Effectiveness Review on Off-Label Use of Atypical Antipsychotics. Journal of Managed Care pharm. June, 2012, Vol 18
 Donovan T. Maust, MD, MS; Hyungjin Myra Kim, Antipsychotics, Other Psychotropics, and the Risk of Death in Patients With Dementia Number Needed to Harm. JAMA Psychiatry. 2015;72(5):438-445.
 doi:10.1001/jamapsychiatry.2014.3018

Behaviors with Dementia: What can we do?

Alzheimer's Association Tools

- ▶ **Person-centered Care**
- ▶ **Sensory practices:** aromatherapy, massage, multi-sensory stimulation, bright light therapy
- ▶ **Psychosocial practices:** validation therapy, reminiscence therapy, music therapy, pet therapy, meaningful activities
- ▶ **Structured care protocols:** bathing, mouth care

Kezia Scales, PhD Sheryl Zimmerman, PhD et al. Evidence-Based Nonpharmacological Practices to Address Behavioral and Psychological Symptoms of Dementia. The Gerontologist, Volume 58, Issue suppl_1, February 2018, Pages S58-S102

Behaviors with Dementia: What can we do?

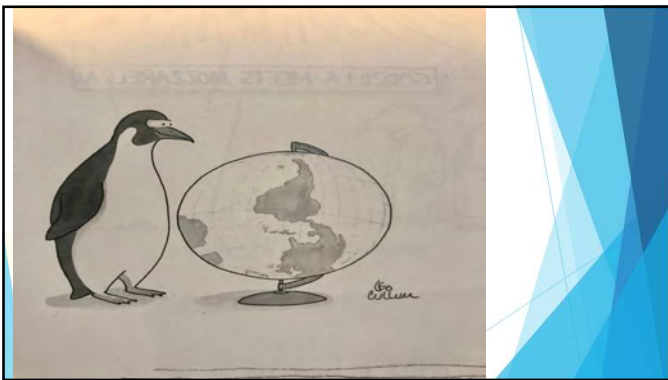
Alzheimer's Association Tools: undesirable behavior observed

- Detect:** Who is involved?
 What is happening?
 Where is this happening?
 When is it happening? What time?
 Why do you think it is happening?

Behaviors with Dementia: What can we do?

Alzheimer's Association Tools: Undesirable behavior observed

- Connect:**
- Approach calmly and respectfully
 - Be friendly first
 - Use your knowledge of the person
 - Join their reality
 - Focus on feelings and emotions
 - Validate their concerns
 - Reassure and redirect



Behaviors with Dementia: What can we do?

Alzheimer's Association Tools: Undesirable behavior observed

- Check for Physical Needs:**
- Pain
 - Hunger
 - Thirst
 - Bathroom
 - Cold/Hot

Behaviors with Dementia: What can we do?

Alzheimer's Association Tools: Undesirable behavior observed

Check for Emotional Needs: Fear

- Anxiety
- Frustration
- Boredom
- Overstimulation
- Loneliness

Reassess and plan for next time: What worked?
What didn't?

Behaviors with Dementia: What can we do?

Alzheimer's Association Tools: Other helpful recommendations

- ▶ Respond without taking offense or arguing
- ▶ Logic and reasoning are not helpful
- ▶ Allow the person to make simple choices
- ▶ Consider doing the task at a different time/in a different way

Behaviors with Dementia: What can we do?

The Colorado Dementia Partnership

A Collaboration with:

Geriatric Doctors, The Colorado Society for Post-Acute and Long-Term Care Medicine, Geriatric Psychiatrist, Alzheimer's Association, Colorado Health Care Association, and the Colorado Department of Health

Mission: To Enhance the Care of people with Dementia

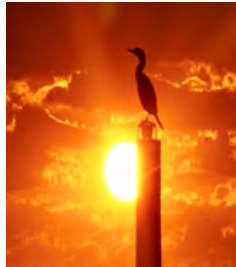
Behaviors with Dementia: What can we do?

The Colorado Dementia Partnership

- R Rule out acute illness, pain, or discomfort
- E Engage the senses: sight, touch, smell, taste, and sound
- S Soothe: Evaluate the environment of noise, climate and other stimulators
- P Practice calm, adjust your body to be at their eye level
- O Offer meaningful choices and things to do
- N Never argue, confront, or tell the resident they are wrong
- D Develop a plan for physical movement, exercise, and fresh air

Behaviors with Dementia: What can we do?

Caring for the
Care Giver!



Thank you!
Questions?

