



# Novel Approaches in the Management of AD: Considerations for Pharmacists and Pharmacy Technicians

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8-24-23

# Disclosure

Dr Lucía García , faculty for this CE activity ,  
has no relevant financial relationship(s) with  
Ineligible companies to disclose

# Objectives

► At the conclusion of the activity the pharmacist should be able to:

1. Differentiate between dementia, neurocognitive disorder and Alzheimer
2. Address the importance of vaccination as an alternative to decrease Alzheimer's risk.
3. Differentiate between current and newly approved medications for Alzheimer's disease with regards to efficacy and safety.
4. Describe the pharmacist role in the identification of drug related problems, early signs detection and referrals.
5. Discuss the role of the pharmacist in caring for the person with advancing dementia.

# Objectives

At the conclusion of the activity the pharmacy technician should be able to:

1. Describe signs and symptoms of Alzheimer.
2. Discuss the importance of vaccination as a tool to decrease Alzheimer's risk.
3. Identify current and newly approved medications for Alzheimer's disease with regards to efficacy and safety.
4. Describe how pharmacy technicians can support the patient and caregiver to prevent non-adherence, side effects, and how to support the pharmacists providing care.

# Pre and Post Test

- ▶ Pre and Post Test:
  1. Pharmacists and pharmacy technicians are likely to see persons living with dementia and care partners, on a regular basis and they can identify changes in behavior and memory and monitor for changes in persons with known pre-disposing conditions. TRUE or FALSE
  2. Pharmacists should work with prescribers to ensure medications and doses are appropriate over the course of the disease. TRUE or FALSE
  3. Influenza and other vaccines can increase the risk of Alzheimer TRUE or FALSE
  4. Aducanumab is an FDA-approved drug for AD that acts as uncompetitive antagonist of the N-methyl-D-aspartate type of glutamate receptor
  5. Pharmacists can help patients with problems with adherence by recommending the use of electronic devices, the use of medications in bubble packs , pill boxes or reminders. TRUE or FALSE

# Epidemiology

CA>Heart Disease>DM>AD

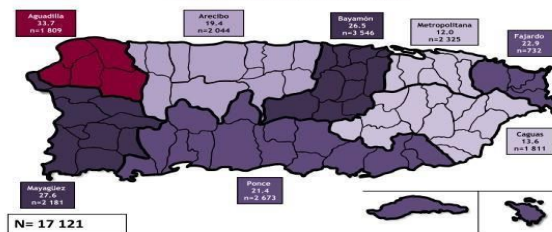


## TASAS POR REGIONES

A continuación, se presenta el mapa con las tasas de los casos de Alzheimer por región, en la población de 60 años o más. Para el cálculo de estas tasas se utilizó el estimado de la población de 60 años o más, debido a que el 98.4% de las personas en el Registro pertenecen a este grupo. La región de Aguadilla tiene la tasa más alta con 33.7 personas por cada 1,000. La región de Mayagüez se encontraba en el segundo lugar con casi 27.6 casos por cada 1,000 habitantes, seguida por la región de Bayamón con 26.5 de cada 1,000 personas.

### Tasas de Alzheimer por regiones, 2017

Por cada mil habitantes de 60 años o más



Fuente: Registro de Alzheimer, 12/31/2017  
División para la Prevención y el Control de Enfermedades Crónicas, Departamento de Salud

## CITA SUGERIDA

Santiago, M., Irizarry, J., & Adams, J. R. (2017). *Boletín trimestral del Registro de Alzheimer*. Centro y Registro de Casos de la Enfermedad de Alzheimer. División para la Prevención y el Control de Enfermedades Crónicas. Departamento de Salud.

## REFERENCIAS

Pohlador-Flow, B. and Calderón-Larrañaga, A. and Marta-Moreno, J. and Hanco-Saavedra, J. and Sicras-Mainar, A. (2014). Comorbidity of Dementia: a cross-sectional study of primary care older patients *BMC Psychiatry*, 14:84.  
Estimados anuales de la población de Puerto Rico por grupos de edad y sexo: 1 de abril de 2010 al 1 de julio de 2015. Fuente: Negociado del Censo de los Estados Unidos, División de Población, junio de 2017.

## 2023 ALZHEIMER'S DISEASE FACTS AND FIGURES



More than  
**6 million Americans**  
are living with Alzheimer's

Over 11 million  
**Americans**  
provide unpaid care for  
people with Alzheimer's  
or other dementias

These caregivers  
provided more  
than 18 billion  
hours valued  
at nearly  
**\$340  
billion**

**1 in 3**  
seniors dies with  
Alzheimer's or another  
dementia

It kills more than  
**breast cancer**  
+  
**prostate cancer**  
Combined

The  
lifetime  
risk for  
Alzheimer's  
at age  
45 is  
**1 in 5** for women  
+  
**1 in 10** for men

Between 2000 and  
2019, deaths from  
heart disease has  
decreased  
**7.3%**

In 2023, Alzheimer's  
and other dementia will  
cost the nation  
**\$345 billion**

By 2050,  
these costs  
could rise  
to nearly  
**\$1 trillion**

while deaths  
from Alzheimer's  
disease have  
increased  
**145%**

While only 4 in 10 Americans  
talk to their doctor right away  
when experiencing early  
memory or cognitive loss,

7 in 10 would want to know  
early if they have Alzheimer's  
disease if it could allow for  
earlier treatment.

ALZHEIMER'S ASSOCIATION®



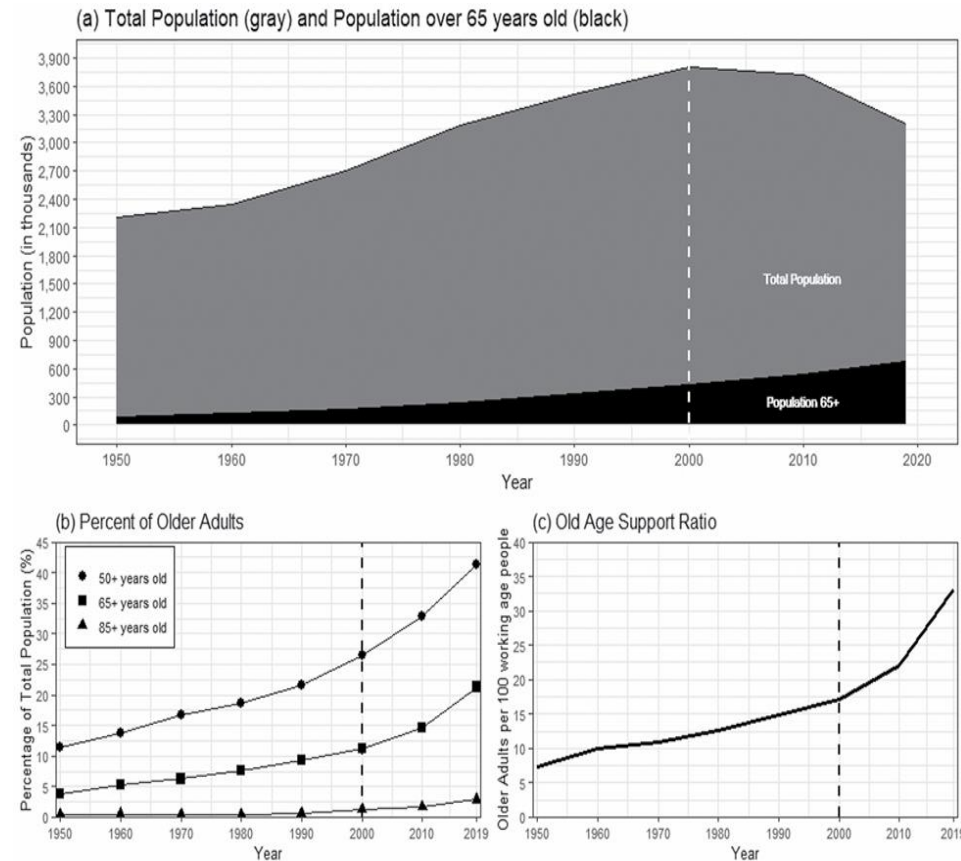
# Demography, Polypharmacy and Epidemiology

Trends in population measures in Puerto Rico from 1950 to 2019

## Alzheimers' registry

- ▶ 237 law 1999
- ▶ 20,087 cases of AD reported however there were 116,000 cases registered in Medicare by 2022
- ▶ 55.8% >85y/0
- ▶ 35.3% ♂ and 64.7% ♀

Boletín trimestral del registro de AD de PR



# Preventable risk factors- 40% risk reduction of demencia

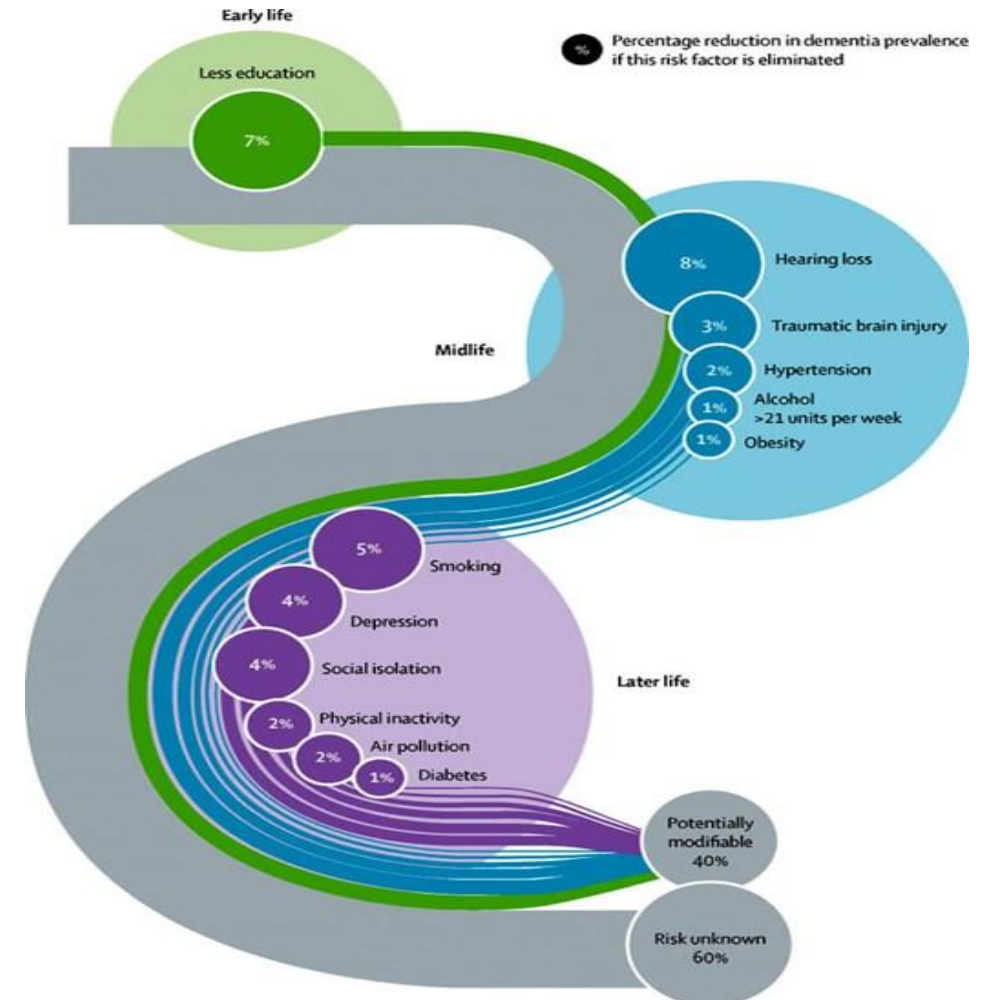
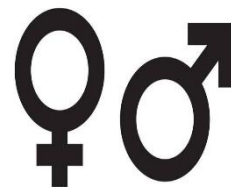
## Life course risks factors

### Risks factors per age group

- Early life <45
  - Less education
- Midlife 45-65
  - hearing ↓ traumatic brain injury, HBP, alcohol,obesity
- Later life >65
  - Smoking,depression,social isolation air pollution,physical inactivity,diabetes



The 2020 Lancet commission on dementia prevention and intervention and care





# Shift in nomenclature as per Diagnostic and Statistical Manual of Mental Disorders DSM-V TR

- ▶ Dementia : Major neurocognitive disorder due to possible or probable [medical etiology]

And due to unknown etiology (multiple etiologies)

- ▶ MCI : Mild neurocognitive disorder

# Probable/possible AD

## (Mini-Cog)

**Step 1:** Ask the patient to repeat three unrelated words

**Step 2:** Ask the patient to draw a simple clock set to 11:10

**Step 3:** Ask the patient to recall the three words from Step 1.

Number of words recalled from Step 1	Result of clock-drawing test	Interpretation of screen for dementia
0	Normal	Positive
0	Abnormal	Positive
1	Normal	Negative
1	Abnormal	Positive
2	Normal	Negative
2	Abnormal	Positive
3	Normal	Negative
3	Abnormal	Negative

## The Mini-Mental State Exam

Patient	Examiner	Date
Maximum	Score	
5	( )	
5	( )	
3	( )	
5	( )	
3	( )	
2	( )	
1	( )	
1	( )	
1	( )	

**Orientation**  
What is the (year) (season) (date) (day) (month)?  
Where are we (state) (country) (town) (hospital) (floor)?

**Registration**  
Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record.

**Attention and Calculation**  
Serial 7's. 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.

**Recall**  
Ask for the 3 objects repeated above. Give 1 point for each correct answer.

**Language**  
Name a pencil and watch.  
Repeat the following "No ifs, ands, or buts"  
Follow a 3-stage command:  
"Take a paper in your hand, fold it in half, and put it on the floor."  
Read and obey the following: CLOSE YOUR EYES  
Write a sentence.  
Copy the design shown.



Total Score \_\_\_\_\_  
ASSESS level of consciousness along a continuum  
Alert Drowsy Stupor Coma

## Functional Assessment Scale (FAST)

1	No difficulty either subjectively or objectively.
2	Complaints of forgetting location of objects. Subjective work difficulties.
3	Decreased job functioning evident to co-workers. Difficulty in traveling to new locations. Decreased organizational capacity. *
4	Decreased ability to perform complex task, (e.g., planning dinner for guests, handling personal finances, such as forgetting to pay bills, etc.)
5	Requires assistance in choosing proper clothing to wear for the day, season or occasion, (e.g. pt may wear the same clothing repeatedly, unless supervised. *
6	Occasionally or more frequently over the past weeks. * for the following A) Improperly putting on clothes without assistance or cueing . B) Unable to bathe properly ( not able to choose proper water temp) C) Inability to handle mechanics of toileting (e.g., forget to flush the toilet, does not wipe properly or properly dispose of toilet tissue) D) Urinary incontinence E) Fecal incontinence
7	A) Ability to speak limited to approximately $\leq 6$ intelligible different words in the course of an average day or in the course of an intensive interview. B) Speech ability is limited to the use of a single intelligible word in an average day or in the course of an intensive interview C) Ambulatory ability is lost (cannot walk without personal assistance.) D) Cannot sit up without assistance (e.g., the individual will fall over if there are not lateral rests [arms] on the chair.) E) Loss of ability to smile. F) Loss of ability to hold up head independently.

\*Scored primarily on information obtained from a knowledgeable informant.

## MONTREAL COGNITIVE ASSESSMENT (MoCA)

NAME : \_\_\_\_\_  
Education : \_\_\_\_\_  
Sex : \_\_\_\_\_  
Date of birth : \_\_\_\_\_  
DATE : \_\_\_\_\_

<b>VISUOSPATIAL / EXECUTIVE</b>		Copy cube	Draw CLOCK (Ten past eleven) (3 points)	POINTS
<b>NAMING</b>				
<b>MEMORY</b>		Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.	FACE VELVET CHURCH DAISY RED	No points
<b>ATTENTION</b>		Read list of digits (1 digit/sec). Subject has to repeat them in the forward order [ ] 7 4 2 5 4. Subject has to repeat them in the backward order [ ] 4 2 5 4 7.		
<b>LANGUAGE</b>		Repeat : I only know that John is the one to help today. The cat always hid under the couch when dogs were in the room. [ ]		
<b>ABSTRACTION</b>		Similarity between e.g., banana - orange = fruit [ ] train - bicycle [ ] watch - ruler [ ]		
<b>DELAYED RECALL</b>		Has to recall words WITH NO CUE [ ] VELVET [ ] CHURCH [ ] DAISY [ ] RED [ ]		
<b>ORIENTATION</b>		[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City [ ]		

# Tests and biomarkers

- ▶ Lumipulse test :early detection beta amyloid in CSF.
- ▶ No radiation exposure ( PET Scan )
- ▶ Tau test Flortaucipir ( biomarker for PET scan)
- ▶ Finger prick test –neurofilament light,(NfL)glial fibrillary acidic protein (GFAP) , p-tau 181 and 217 AAIC 23



MMSE 18-26 M, 10-15 Mod < 9 severe

- Measures orientation
- Registration
- Attention and calculation
- Recall
- Language

# The 5 A's of AD

Anomia

Apraxia

Agnosia

Amnesia

Aphasia

DSMV : Complex attention, executive function, learning and memory, language, perceptual/motor, social cognition

# The 6 domains affected in AD

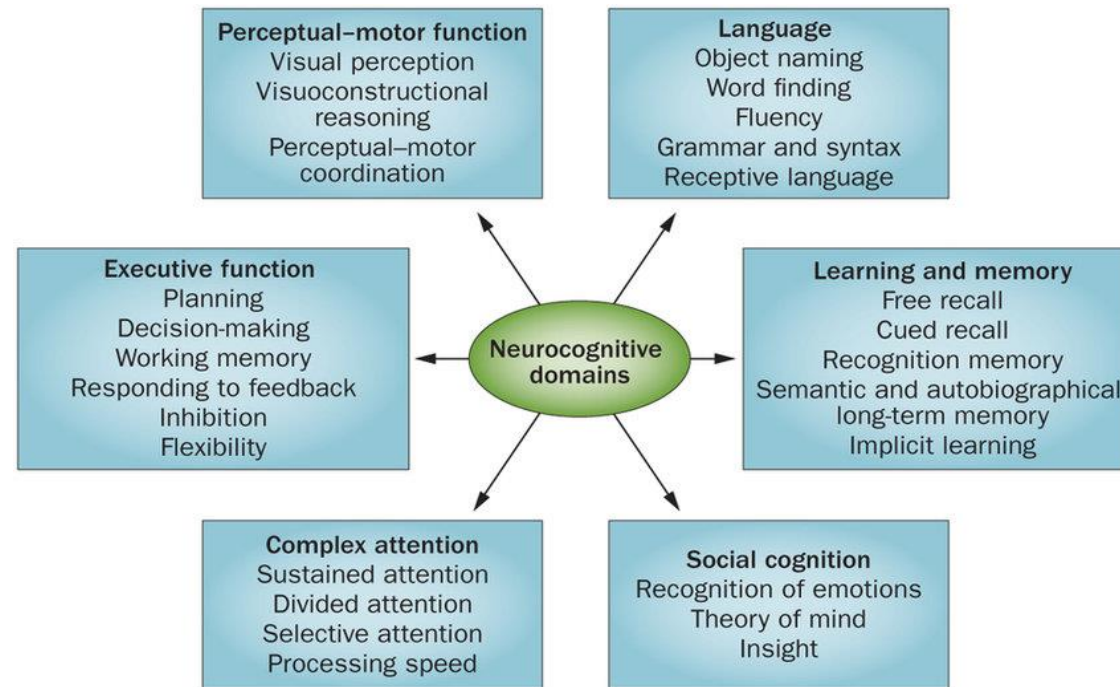
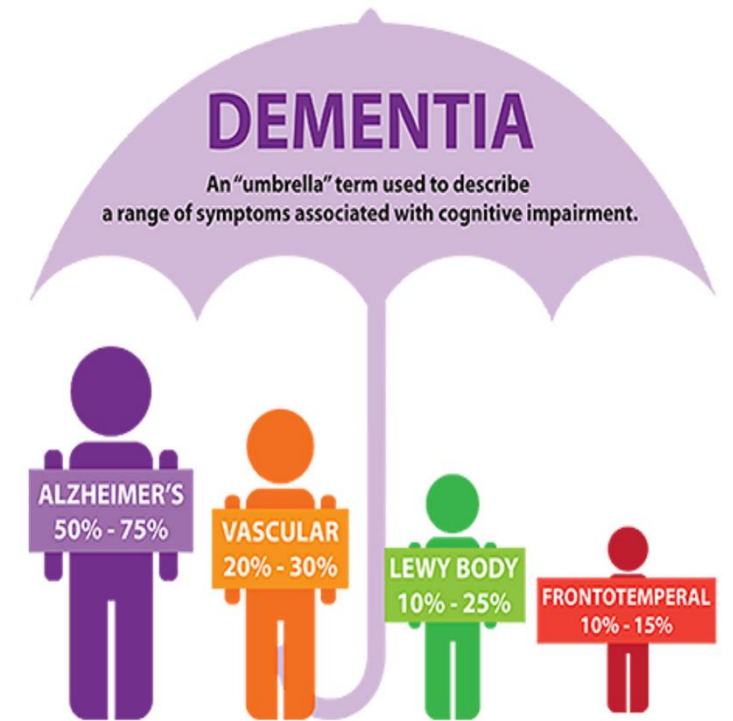


Figure 2 Sachdev et al Classifying Neurocognitive disorders the DSMV approach



# Common Types of Dementia

- ▶ Alzheimer's disease (AD >50% of cases)
- ▶ Vascular dementia
- ▶ Lewy body dementia ( Robin Williams )
- ▶ Mixed dementia ( Unknown DSM V TR)
- ▶ Other ( PD, Frontotemporal ( Bruce Willis), Huntington's disease, Creutzfeldt-Jakob Disease CJD)
- ▶ Potentially reversible causes of dementia



Dementia friendly Wyoming  
[dfwsheridan.org](http://dfwsheridan.org)

# Common dementia types early and late symptoms

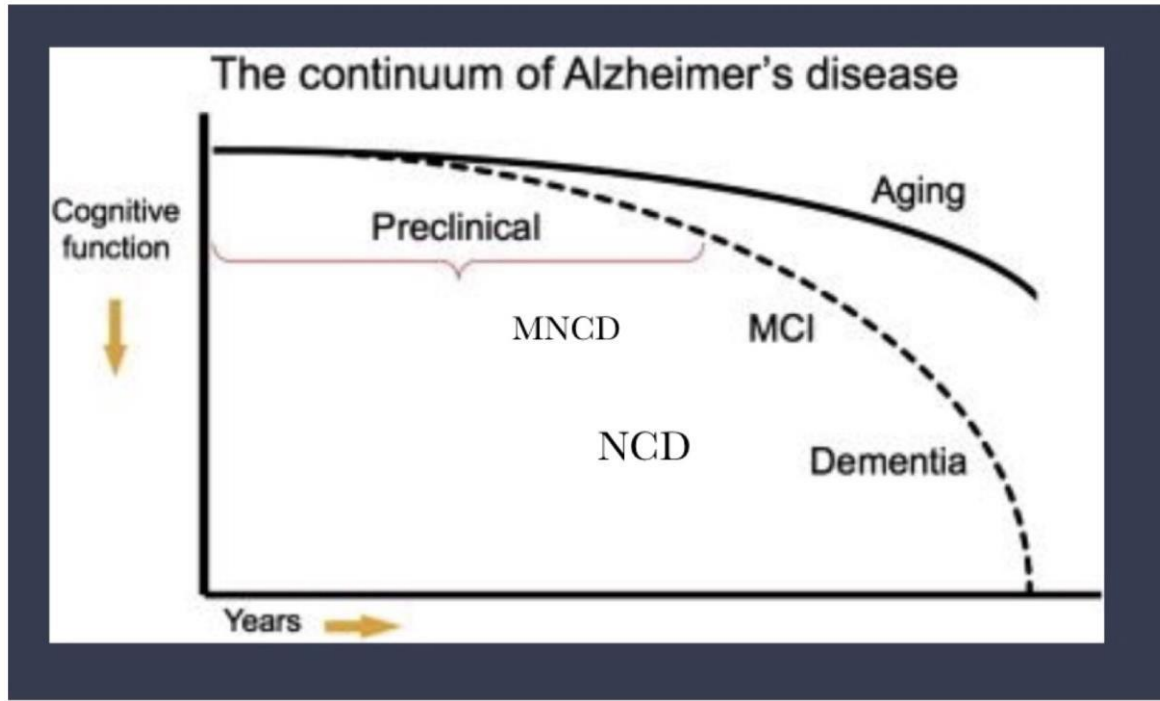
	AD	Vascular	Lewy Body	PD
Early stage	Difficulty remembering names, recent events Apathy Depression	Pre-existing CV or CVA Focal neurological signs and sxs Memory less affected than in AD	Impaired memory ~ AD but variable hallucinations, fluctuating alertness CI precedes PD sxs	PD sxs precedes CI
Late stage	Consistent rate of decline over several years	Stepwise cognitive decline Worsening vascular condition	PD symptoms progress	Dementia develops in later stages of PD

# AD screening as per ADA

- ▶ At initial visit in patients  $\geq 65$  y/o annually and as needed
- ▶ Increased in patients with DM
- ▶ Early detection and implications in DM
- ▶ Obesity (DM risk , more severe COVID 19 )
- ▶ HBP screening and monitoring

*Older Adults: Standards of Medical Care in Diabetes -2023*

# AD Stages



# Alzheimer treatment evolution



## Poll #1 ChEI

**Donepezil is the only ChEI with a therapeutic starting dose**

- ▶ **True**
- ▶ **False**



# Medicamentions to treat Sxs of AD ChE I's

Medicine	Initial Dose	Therapeutic Dose	Special Considerations	FDA Indication
Donepezil Aricept	5 mg HS	5-23mg HS	Long T1/2 (70hrs)	Mild to severe
Rivastigmine Exelon Patch	1.5mg BID 4.6mg/day	6-12mg/day 9.5- 13.3mg/day	Adm with food	Mild to moderate All
Galantamine Razadyne  Razadyne XR	4mg BID  8mg daily	8-12 BID  16-24mg/day	Adm with food  renal or hepatic dysfunction Max dose is 16mg/day . Do not use if ClCr<9ml/min	Mild to moderate

BP and pulse monitoring

Increase the dose at least q 4 weeks  
donepezil 10 mg X 3 months, then 23 mg

# ChEI Pharmacology and Pharmacokinetics

Characteristic	Donepezil	Rivastigmine	Galantamine
Chemical Class	Piperidine	Carbamate	Phenanthrene alkaloid
MOA	AChEI	AChEI BuChEI	AChEI
Binding reversibility	Noncompetitive	Noncompetitive, reversible	Competitive, reversible, allosteric modulation
Nicotinic receptor modulation	No	No	Yes
Elimination pathway	Liver	Kidney	20% Kidney (unchanged) Liver
Metabolism by CYP450 isoenzymes	Yes CYP 2D6 CYP 3A4	No	Yes CYP 2D6 CYP 3A4

## Poll # 2 Memantine

**Memantine is effective in the treatment of mild to moderate AD**

- ▶ **True**
- ▶ **False**

# NMDA Inhibitors

## Memantine ( Namenda)

- ▶ Moderate to severe AD
- ▶ Lack of evidence for the efficacy of memantine in mild Alzheimer disease. Schneider LS et al. *Arch Neurol* 2011 Apr 11
- ▶ MOA
  - ▶ Regulates glutamate activity and controls calcium amount into nerves.
  - ▶ 5-HT<sub>3</sub>, nAChRI, D2
  - ▶ Potentially ↓ Aβ toxicity, - tau, ↓inflammation, ↑neurotrophic factors
- ▶ ADR's
  - ▶ CNS, GI, fatigue

# Memantine Dosing

## ▶ Memantine Titration

- ▶ 5 mg/day x 7 days
- ▶ 5 mg twice a day x 7 days
- ▶ 5 mg in a.m. and 10 mg in p.m. x 7 days
- ▶ 10 mg twice a day
- ▶ Nemenda XR titration
  - ▶ Initial dose 7 mg ↑ 7mg a week. Max dose 28 mg daily
- ▶ CrCl 5-29 mL/minute: 5 mg twice daily, or 14 mg daily if XR capsules
- ▶ Should not be used in individuals receiving dialysis

# Donepezil + Memantine

Week 1 –  
7 mg/10 mg



Week 2 –  
14 mg/10 mg



Week 3 –  
21 mg/10 mg



Week 4 –  
28 mg/10 mg





# Alpha-tocopherol Vitamin E

- ▶ Limits free-radical formation, reduces oxidative stress and lipid peroxidation
- ▶ Promotes survival of cultured neurons exposed to beta-amyloid
- ▶ Dose 2000 IU daily
- ▶ Inconsistently associated with increased morbidity and mortality. Except for VA Cooperative study

# Comparative safety and effectiveness of Chel and Memantine for AD

Alz Res therapy 10,126(2018) 41 RCT meta-analysis

- ▶ Galantamine 32 mg daily and donepezil 10 mg daily probably the most effective on cognition for mild to moderate AD
- ▶ Memantine 20 mg combined with donepezil 10 mg recommended for moderate to severe patients
- ▶ Memantine showed the best profile of acceptability
- ▶ Rivastigmine 15-cm<sup>2</sup> patch was the best optional treatment in function and global changes None of them was likely to improve neuropsychiatric symptoms



# When to switch or D/C?

# New Era in AD treatment

# Aducanumab

## Dose

- ▶ 1m/kg q 4 weeks X2, then 3mg/kg q 4 weeks X 2 , then 6mg/kg q 4 weeks for infusions 5 &6
- ▶ Maintenance dose 10mg/kg once q 4 weeks
- ▶ Contraindications : None listed in manufacturing label
- ▶ Contains polysorbate

## Uptodate

- ▶ Controversy Engage vs Emerge

## Binding affinity

practical neurology.com

**TABLE. BINDING OF ANTIAMYLOID MONOCLONAL ANTIBODIES TO DIFFERENT SPECIES OF AMYLOID  $\beta$**

Antibody	Targets	Off-target binding
Aducanumab	Plaque	Fibrils, none to oligomer
Donanemab	Plaque	None
Gantenerumab	Plaque	Fibrils>protofibrils, monomers
Lecanemab	Protofibril	Protofibrils, oligomers>fibrils, monomers

# Lecanemab Monoclonal antibody anti-amyloid

## Who can benefit?

- ▶ MCI Y Alzheimer ( early stages)
- ▶ Amiloid +
- ▶ APOE 4
- ▶ MMSE  $\geq 26$
- ▶ How long ? 18 month data
- ▶ Dosis y administración : 10mg/kg q 2 Semanas

## Monitoring

- ▶ PET or lumbar puncture prior to initiation for A $\beta$
- ▶ MRI prior, 5<sup>th</sup>, 7<sup>th</sup> and 14<sup>th</sup> Info

## Risks or disadvantages

- ▶ Contraindications y possible interactions : lecanemab, P2Y12 inhibitors,, NSAID's, SSRI's, anticoagulants *uptodate*

Suggested precaution: pacemaker not MRI compatible

**Boxed warning** : hemosiderosis, "ARIA-H (Amyloid related imaging abnormalities-hemosiderin), ARIA-E,>ApoE4.

ADR's confusion, delirium , desorientation, microhemorrhagia, HA , diarrhea

- ▶ Route of administration IV
- ▶ SQ formulation is under development



# ARIA management recommendations

## ARIA (amyloid related imaging abnormalities)

- ▶ ARIA –E – Brain edema
- ▶ ARIA-H hemosiderin deposition – microhemorrhage and superficial siderosis
- ▶ > in APOE-4 homozygotes

## Recommendations

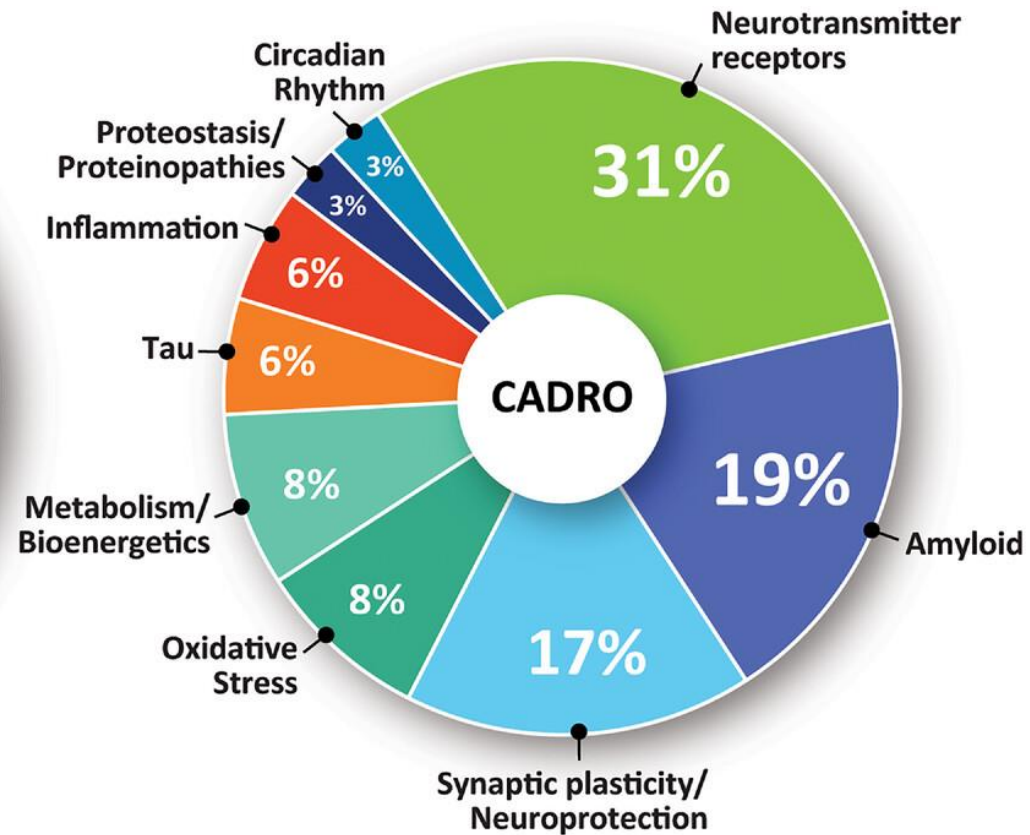
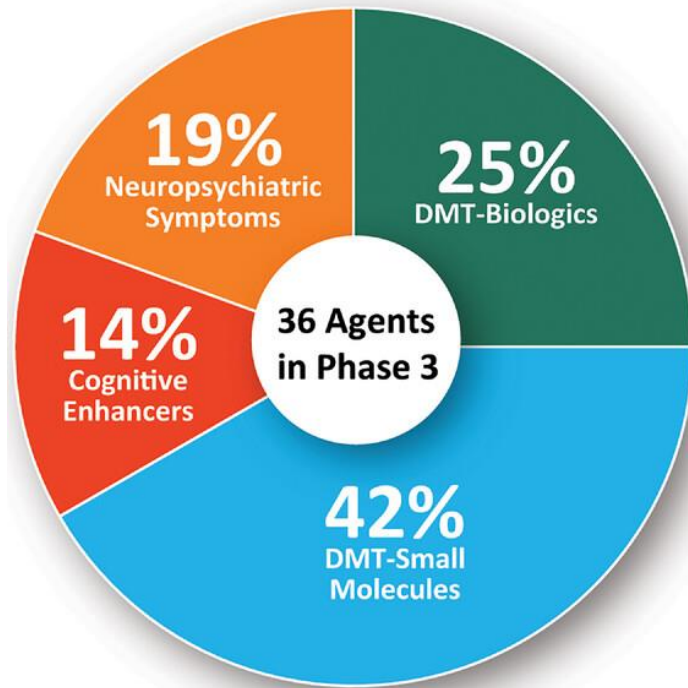
- ▶ ARIA E – if clinical symptoms or MRI is moderate to severe suspend. If symptoms are moderate to severe suspend
- ▶ ARIA-H – If the patient is symptomatic or if MRI moderate to severe suspend. Continue dosing only if asymptomatic and MRI is mild

# The TrailBlazer study

- ▶ Donanenab significantly slowed clinical progression at 76 weeks among participants with early symptomatic AD and amyloid/tau pathology

# Drug development categories

*Alzheimers Disease Drug Development Pipeline 2023 Cummings et al*



100

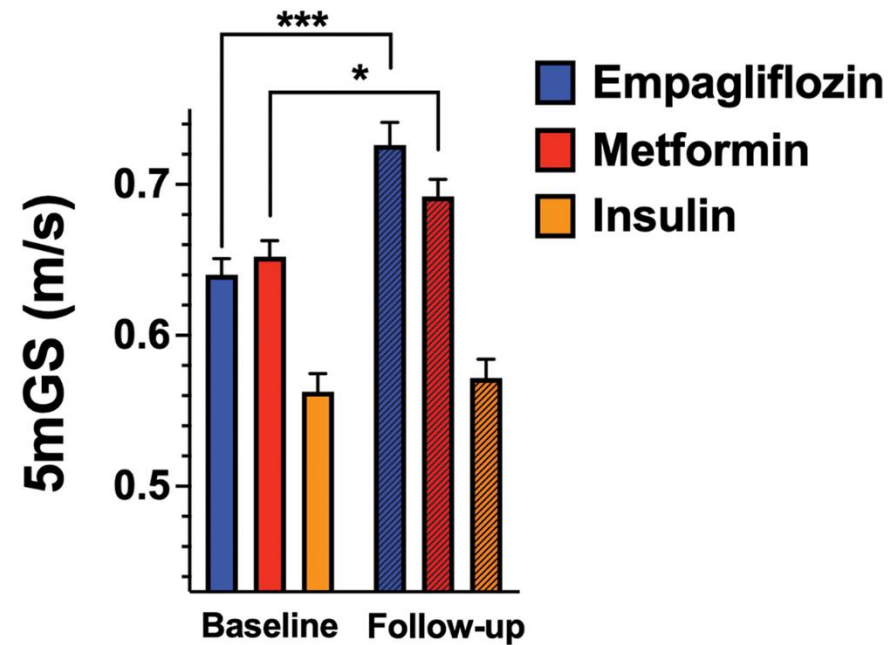


# Disease Modifying biologics

*Cummings et al*

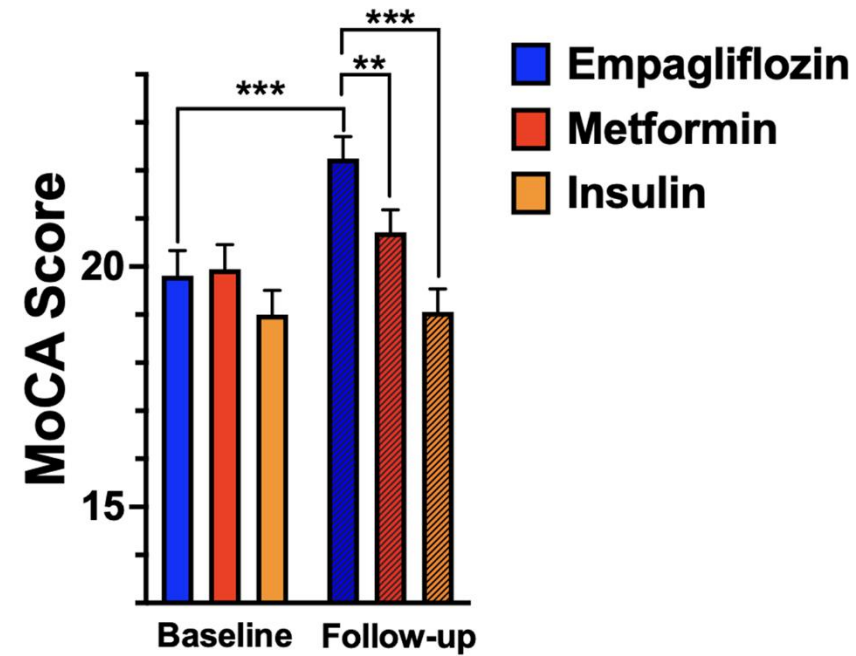
- ▶ ExPlas synaptic plasticity plasma transfusion from exercise trained donors
- ▶ Tdap Inflammation protection /immunity healthy subjects
- ▶ Insulin intranasal and intranasal insulin +empagliflozin –, pre-clinical- SGLT-2 , decrease insulin resistance and ↑ insulin signal in the brain (2026)
- ▶ GnRh-pre-clinical Growth factor hormone , antiaging
- ▶ Semaglutide- metabolism/bioenergetics, GLP-1, anti-inflammatory and insulin sensitivity
- ▶ E 2814 Anti tau MAB

Diabetes Care. 2022;45(5):1247-1251. doi:10.2337/dc21-2434

**Figure Legend:**

The 5mGS in the empagliflozin, metformin, and insulin groups measured at baseline and follow-up. Data are means  $\pm$  SD. \* $P < 0.05$ , \*\*\* $P < 0.001$ .

Diabetes Care. 2022;45(5):1247-1251. doi:10.2337/dc21-2434

**Figure Legend:**

MoCA score in the empagliflozin, metformin, and insulin groups evaluated at baseline and follow-up. Data are means  $\pm$  SD. \*\*P < 0.01, \*\*\*P < 0.001.



# Disease Modifying small molecule

*Cummings et al*

- ▶ Tricaprilin metabolism and bioenergetic caprylic tryglyceride→ketosis ↑
- ▶ Mitochondrial function Hydralazine HCl oxidative stress free radical scavenger
- ▶ Metformin metabolism/bioenergetic and insulin sensitizer
- ▶ Piromelatine circadian rhythm 9 melatonin serotonin receptor +
- ▶ Icosapent ethyl oxidative stress –purified form of omega 3 fatty acid (EPA) (VA)
- ▶ Allopregnelone neurogenesis allosteric modulator of GABA-A receptors phase 1
- ▶ Centella asiatica- synaptic plasticity/neuroprotection antioxidant and anti-inflammatory agent
- ▶ Montelukast LTRA with anti-inflammatory effects



# Cognitive enhancer *Cummings et al*

- ▶ AR1001 neurotransmitter receptors PDE-5 I  $\uparrow$  intracellular cGMP  $\rightarrow$  Synaptic plasticity
- ▶ Caffeine neurotransmitter receptor adenosine antagonist , non-specific PDE-I
- ▶ Chinese traditional medicine metabolism & bionergetic ( Rhizoma Acori tatarinowii, Paria cum Radix Pini, Radix Polygalae) mechanism unknown
- ▶ Nicotine Nicotinic acetylcholine receptor agonist
- ▶ Trazodone

# Nuropsychiatric Symptoms tx *Cummings et al*

- ▶ Dronabinol B1 and B2 endocannabinoid receptor partial agonist
- ▶ THC free cannabidiol
- ▶ IGC-AD1 THC (cannabinoid) Dr Sepúlveda
- ▶ Seltorexant circadian rhythm, dual orexin receptor antagonist
- ▶ Psilocybin neurotransmitter receptor psychedelic

# Gut microbiome/microbiota and Alzheimer's disease

- ▶ Combination of gut microbiota and plasma amyloid- $\beta$  as a potential index for identifying preclinical Alzheimer's disease : a cross sectional analysis from the SILCODE study Can Sheng et al
- ▶ Gut microbiome composition may be an indicator of preclinical Alzheimer's disease Ferreiro et al



LATINO

## Alzheimer's researchers study genes in Puerto Rican and Latino families

They have found that in Puerto Rico, people have a higher propensity for the disease, and part of the reason could be a genetic variant they have uncovered.



2023

## Landmark U.S. Pointer Study Completes Recruitment of 2,000+ Participants, Including 30% from Underrepresented Communities

### THE PUERTO RICO ALZHEIMER DISEASE INITIATIVE (PRADI): A MULTISOURCE ASCERTAINMENT APPROACH

July 2017 · *Alzheimer's & dementia: the journal of the Alzheimer's Association* 13(7):P646

DOI: [10.1016/j.jalz.2017.06.751](https://doi.org/10.1016/j.jalz.2017.06.751)

Authors:



**Briseida Feliciano**  
Central University of the Caribbean

### Trial of IGC-AD1 to Include the University of Puerto Rico

- First patient dosing commenced on May 19, 2023
- Trial enrollment completion and top line data expected in early 2024

# PR participation in Clinical Trials



# Medical Food

- ▶ “A Medical food is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles are established by medical evaluation”

As defined by Congress as part of the Orphan Drug Amendments of 1988

# Other interventions with their LOE

Non-Pharmacological Therapies in Alzheimer's Disease: A Systematic review Rayhal et al

Primary Category: Diet/Exercise	
Secondary Category: Overall Diet	
Topics	LOE SCORE
The MIND Diet	5
The MAD Diet	4
Secondary Category: Specific Foods	
Topics	LOE SCORE
Cocoa/Chocolate	4
Soy	3
Turmeric	3
Olive Oil	3
Green Tea	3
Cinnamon	2
Tomatoes	2
Saffron	2
Rosemary	2
Alcohol	2
Coffee	2
Secondary Category: Vitamins	
Topics	LOE SCORE
B Vitamins (Folic Acid, Vitamin B6, Vitamin B12)	4
Vitamin E	3
Vitamin A	3
Niacin/NAD+/Nicotinic Acid	3
Vitamin C	2
Vitamin D + Calcium	2

Secondary Category: Minerals & Other Nutrients	
Topics	LOE SCORE
Essential Fatty Acids	4
Bioactive Dietary Polyphenol Prep (BDPP)/Resveratrol	4
Magnesium Sulfate	3
Targeted Antioxidants (CO-Q-10)	3
Zinc	3
Chromium	2
Carnosine	2
Secondary Category: Prescribed Nutrition	
Topics	LOE SCORE
Souvenaid (Fortasyn Connect)	4
Axona (Ketasyn)	3
Cerefolin NAC	3
Secondary Category: Exercise	
Topics	LOE SCORE
Aerobic Exercise	5

# Non-Pharmacological interventions

## Non-Pharmacological Therapies in Alzheimer's Disease: A Systematic Review

Primary Category: Other Interventions	
Secondary Category: Modifiable Risk Factors	
Topics	LOE SCORE
Modifiable Risk Factors Body Mass Index, Type 2 Diabetes Mellitus Depression, Midlife Hypertension Smoking, Physical Inactivity Educational attainment, Sleep Disordered Breathing	5
Secondary Category: Medical Devices	
Topics	LOE SCORE
Deep Brain Stimulation (DBS)	4
Transcranial Stimulation (tCS)	4
Continuous Positive Airway Pressure (CPAP)	4
Electroconvulsive Therapy (ECT)	3
Low-Energy infrared/Laser LED Light (IRL)	2
Photobiomodulation (PBM)	2
Transcutaneous Vagal Nerve Stimulation (TVNS)	2
Hyperbaric Oxygen Chamber	2
Low Intensity Pulsed Ultrasound (LIPU)	2
Hearing Aid Placement	2

Secondary Category: Cognitive Retraining	
Topics	LOE SCORE
Cognitive Behavioral Therapy—Traditional	4
Cognitive Behavioral Therapy—Computerized	4
Tactile Tablet Stimulation	2
Serious Games	2
Auricular Point Acupressure	2
Musical-Lexical Based Therapy	2
Mindfulness Training	2
Smartphone Personal Assistant	2
Intense Piano Training Treatment	2
Secondary Category: Multimodal Interventions	
Topics	LOE SCORE
Cognitive Retraining + One Other Treatment	4
Aerobic Exercise + One Other Treatment	4
Risk Factor Modification + Cognitive Retraining + Exercise	5

APOE-4 to APOE-2  
Li et al Molecular neurodegeneration



## Poll # 3 Acetaminophen

**Acetaminophen might improve behavior, social engagement and social behavior**

- ▶ **True**
- ▶ **False**



# Non Pharmacological strategies

## First line for behavioral tx

Environmental interventions

- ▶ R/O iatrogenesis
- ▶ R/O medical illness ( pain, constipation, dehydration, or environmental triggers)
- ▶ Poor caregiving
- ▶ Physical/verbal abuse
- ▶ Unmet physical or psychological needs
- ▶ Measure risks vs benefits of pharmacotherapy

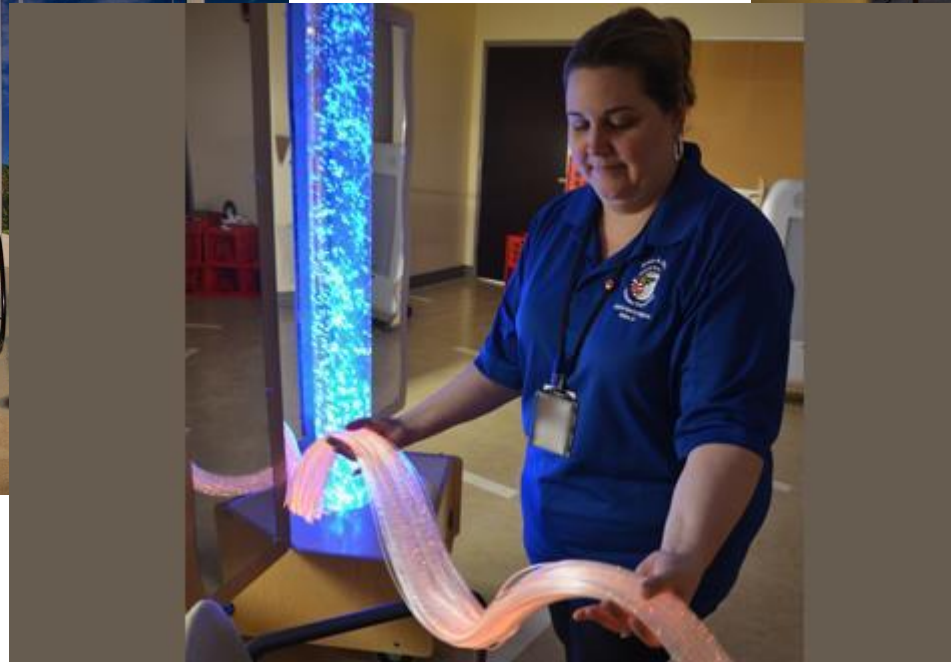
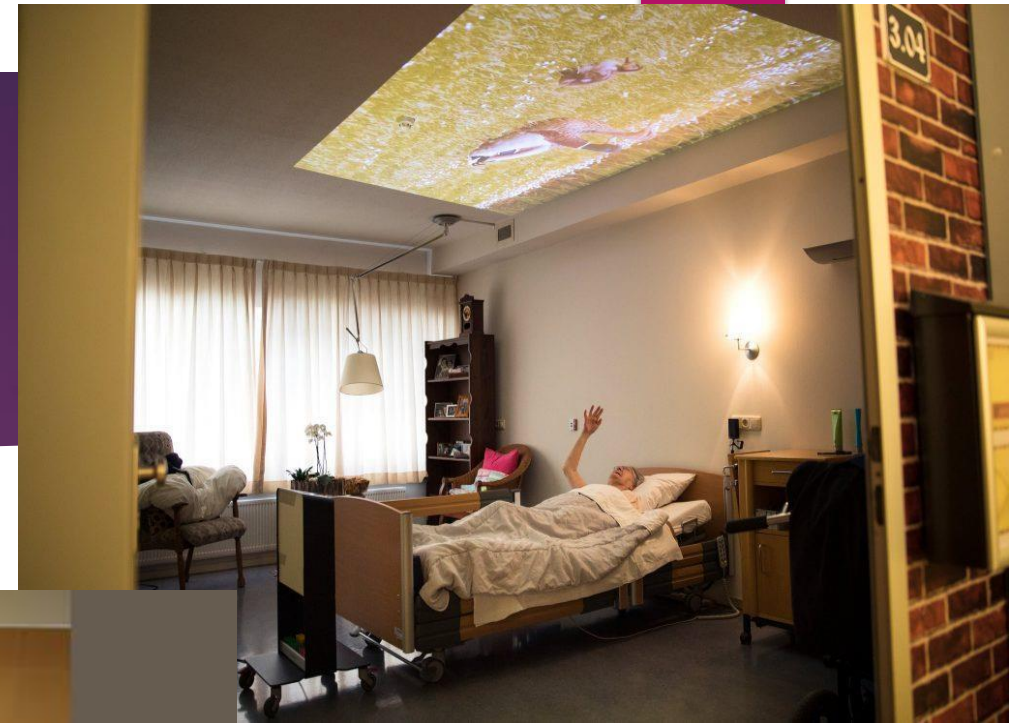
## Other strategies

- ▶ Consider impairments (visual, hearing, sensory)
- ▶ Avoid confrontation (Love , tone of voice , questions vs orders)
- ▶ Consistency and structure
- ▶ Reminders, explanation, orientation cues
- ▶ Keep it simple!
- ▶ Physical activity
- ▶ Mental activity

# Alzheimer's Disease Association position Statement on Cannabis use

- Some manufacturers of cannabis and cannabis-derived products claim their products benefit people with neurodegenerative disorders however:
- Cannabis and its components have not yet been subjected to large-scale, controlled clinical testing for these conditions.
- Research findings to date have been inconclusive and Use of cannabis or cannabis-derived products may impact participation in Alzheimer's and dementia research.
- The trials available have focused on the potential safety and effectiveness of cannabis or cannabis-derived products for the non-cognitive symptoms of dementia, such as agitation

# Other alternatives



**Snoezelen room**

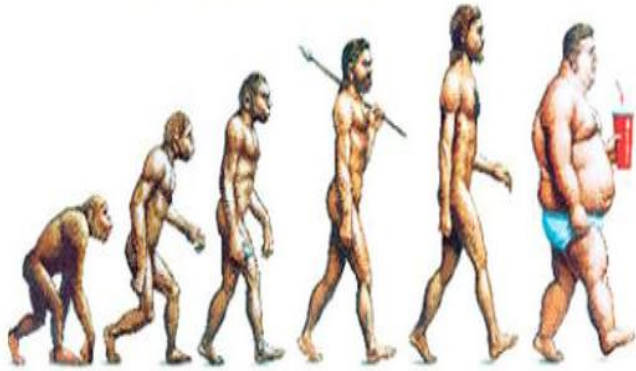


# AD Risk Reduction Strategies



# “Let food be thy medicine” Hipocrates

Pacificneuroscienceinstitute.org



## WHAT'S ON THE **MIND DIET?**

 AT LEAST **THREE SERVINGS** OF WHOLE GRAINS EACH DAY

AT LEAST ONE DARK GREEN SALAD AND ONE OTHER VEGETABLE EACH DAY



**BERRIES AT LEAST TWICE A WEEK**

 AT LEAST A ONE-OUNCE SERVING OF NUTS EACH DAY 

 **BEANS OR LEGUMES AT LEAST EVERY OTHER DAY**

**POULTRY AT LEAST TWICE A WEEK**



 **FISH AT LEAST ONCE A WEEK**

*If you don't drink alcohol, purple grape juice provides many of the same benefits.*

**A FIVE-OUNCE GLASS OF RED WINE EACH DAY**



NO MORE THAN ONE TABLESPOON A DAY OF BUTTER OR MARGARINE; CHOOSE OLIVE OIL INSTEAD



CHEESE, FRIED FOOD AND FAST FOOD NO MORE THAN ONCE A WEEK

 **PASTRIES AND SWEETS LESS THAN FIVE TIMES A WEEK**

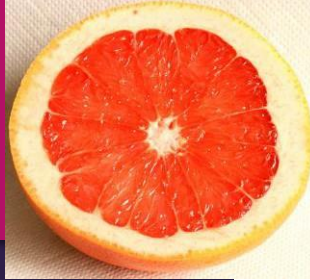


Avoid

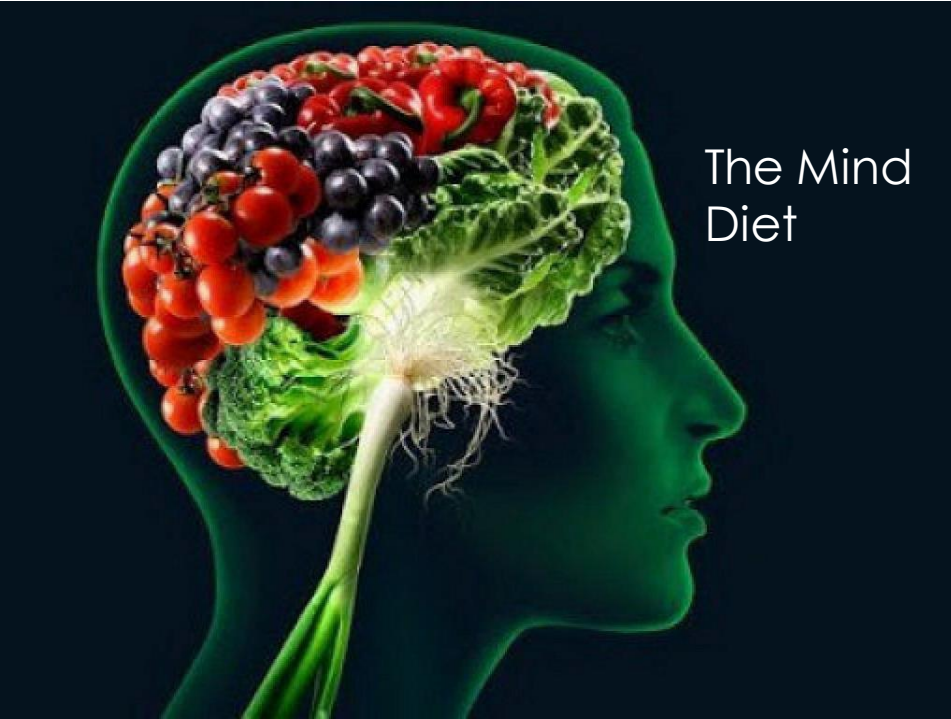
# MIND Diet associated with reduced incidence of AD

MIND diet scores (score range: 8.5 – 12.5) had a 53% (HR=0.47; 95% Confidence Interval: 0.29, 0.76) reduction in the rate of developing AD compared with participants in the lowest tertile (score range: 2.5 – 6.5). MAP participants in the middle tertile of MIND diet scores also had a statistically significant 35% reduction in AD rate compared with those in the first tertile (HR=0.65, 95% Confidence Interval: 0.44, 0.98)

US Pointer study –Lifestyle interventions that simultaneously target multiple risk factors (60-79 y/o)



# Diet :Treatment or Prevention?



The Mind Diet



Alzu.org

Weill Cornell Medicine

## DIPLOMA DIET

Dietary Intervention to Prevent Loss Of Memory due to Alzheimer's

Start Date \_\_\_\_\_



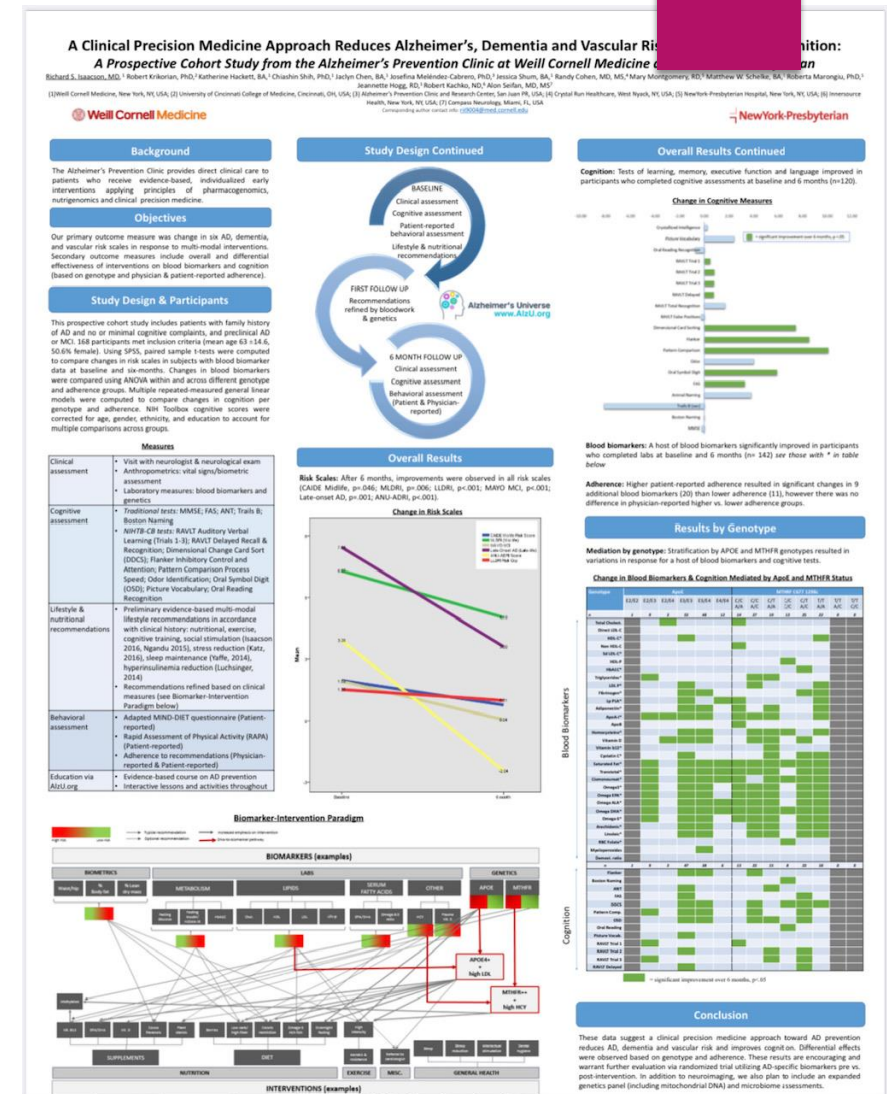
FOOD CHOICE	GOAL	SUN	MON	TUE	WED	THU	FRI	SAT	Goal Reached? 2=Yes 0=No
<b>Green Leafy Vegetables<sup>†</sup></b> <i>(ex: Kale, Dark Greens, Spinach, Romaine)</i>	6+ Servings/Wk								2
<b>Other Vegetables<sup>†</sup></b> <i>(ex: Peppers, Carrots, Broccoli)</i>	6+ Servings/Wk								
<b>Berries<sup>†</sup></b> <i>(ex: Strawberries, Blueberries)</i>	2+ Servings/Wk								
<b>Other Whole Fruits<sup>†</sup> (Low Glycemic)</b> <i>(ex: Pears, Apples, Oranges)</i>	7-14 Servings/Wk								
<b>Plant-Based Fats<sup>†</sup></b> <i>(ex: Avocado, Seeds, Hazelnuts, Almonds)</i>	5+ Servings/Wk								
<b>Legumes</b> <i>(ex: Beans, Peas)</i>	<5 Servings/Wk								
<b>Whole Grains</b> <i>(ex: Steel Cut Oats, Quinoa)</i>	1-2 Servings/Day								
<b>Fish (Not Fried/Not Shell)</b> <i>(ex: Wild Salmon, Fatty Fish, Sardines)</i>	2-4 Servings/Wk								





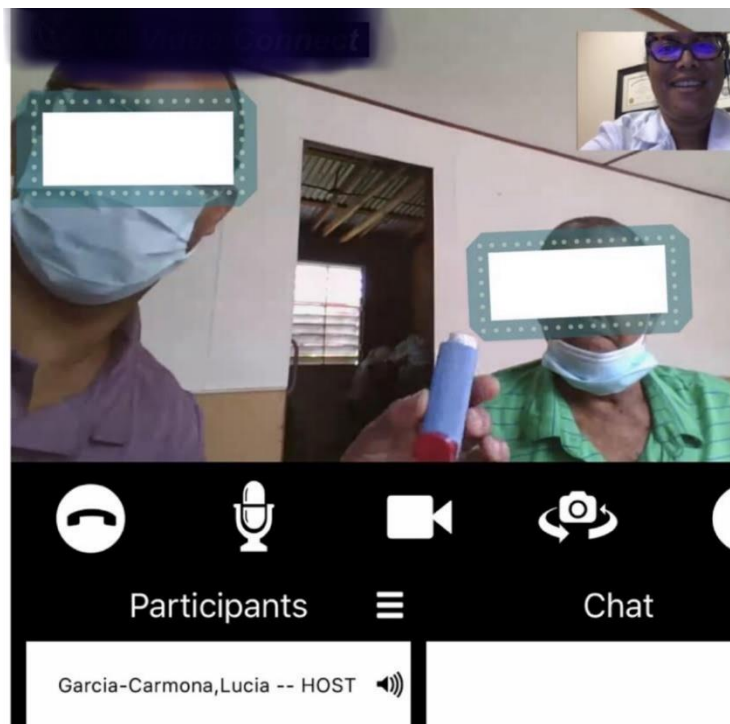
- ▶ After 6 months , Improvement was observed in all risk scales CAIDE Midlifep=0.046 , MLDR1 p=0.006, LLDR10<0.001, MAYO MCI p<0.001, Late onset AD p=0.001, ANU-ADRI p<0.001

Alzu.org





# Keeping in touch

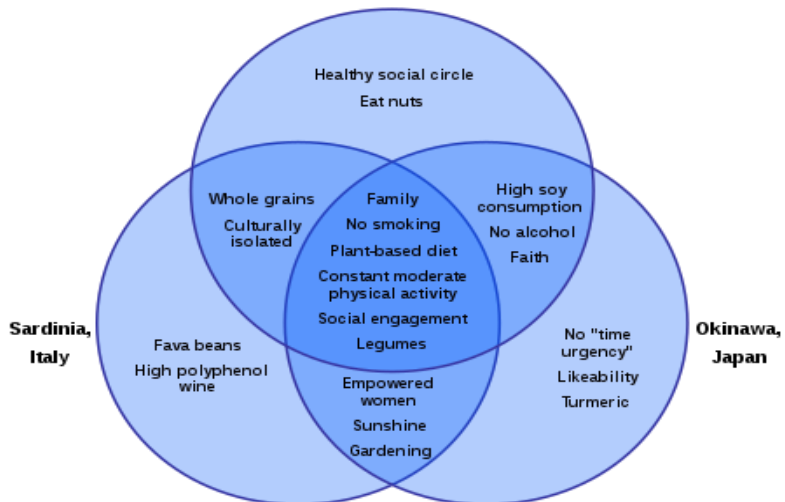


# Anecdotic data

## Blue Zones



Loma Linda, United States





# Pharmacists and Pharmacy Technicians Role

Poll





# Immunizations and AD risk

- ▶ After adjustment for age, sex and education, past exposure to vaccines against diphtheria or tetanus, poliomyelitis and influenza was associated with lower risk for Alzheimer's disease (odds ratio [OR] 0.41, 95% confidence interval [CI] 0.27–0.62; OR 0.60, 95% CI 0.37–0.99; and OR 0.75, 95% CI 0.54–1.04 respectively) than no exposure to these vaccines. Rene Verreault et al. Past exposure to vaccines and subsequent risk of Alzheimer's disease. Canadian Medical Journal
- ▶ Revaccination was associated with a reduced mortality risk of 24% (HR, 0.76; 95% CI, 0.70–0.83). Compared with a first vaccination, revaccination was associated with a reduced annual mortality risk of 15% (HR, 0.85; 95% CI, 0.75–0.96). During the epidemic periods this reduction was 28% (HR, 0.72; 95% CI, 0.53–0.96). Vordou et al. JAMA 2004. Annual Revaccination against influenza and mortality risk in elderly persons.

# Potentially inappropriate medications as per Beers Criteria

- **Benzodiazepines and “Z” drugs:** Alprazolam, Diazepam, temazepam, Zolpidem. They may cause confusion, increase risk for falls and may lead to addiction
- **Anticholinergics :** Meclizine, hydroxyzine, paroxetine, cyproheptadine. May induce confusion, disorientation and constipation
- **Antipsychotics :** Quetiapine, Risperidone, haloperidol . Might increase the risk of strokes and mortality. May increase the risk of confusion and falls. They are reserved to be used, only if its benefits outweighs the risks. **Brexpiprazole** FDA approved for agitation associated with AD
- Other medications potentially inappropriate :
  - **Mineral oil** might increase the risk for aspiration pneumonia.
  - **Megestrol** commonly used to increase appetite , usually no significant improvement is observed, but might increase the risk for clots formation with chronic use.
  - **PPI’s :** Might increase risks of fractures and C.Difficile diarrhea ↓B12, ↑ AD risk

# Polypharmacy possible causes and consequences

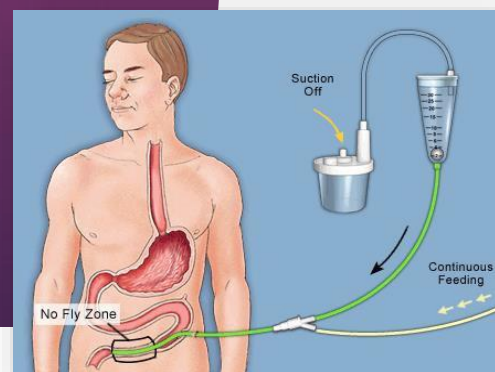
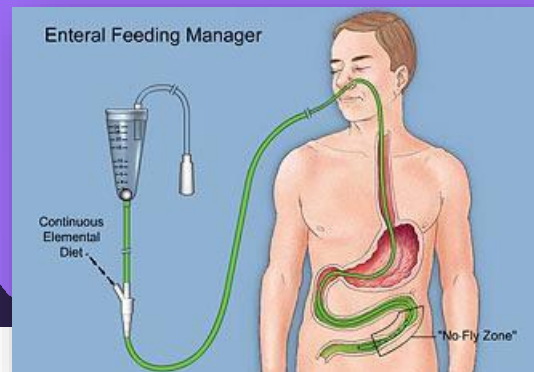


# Medication Safety

## Medicine Storage and Disposal



TAKEAWAY  
ENVIRONMENTAL



PUERTO RICO  
**POISON HELP**  
**CONTROL CENTER**  
**1-800-222-1222**



# Potential Interactions Between Herbs and Conventional Drugs.

[www.NCCAM.nih.gov](http://www.NCCAM.nih.gov)

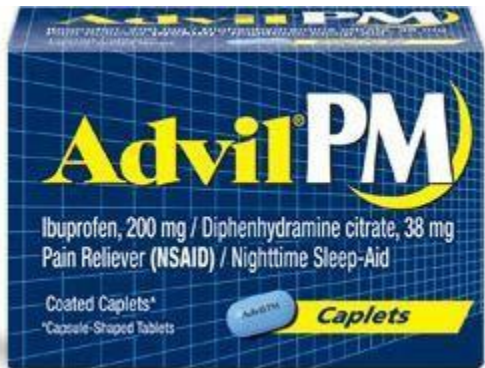
herb	Conventional drug	Comments
Ginkgo leaf	NSAID's, COOX-2, warfarin, trazodone, ChEI, SSRI's	↑ risk for bleeding ↓ seizure threshold
Huperzine A	ChEI's, negative inotropic agents	↑ side effects effects
*St. John's Wort	SSRI's, TCA's, digoxin, cyclosporin, simvastatin, warfarin, theophylline, tacrolimus	Serotonin syndrome ↓[drugs]
Asian ginseng root	warfarin	↓ INR
*Kava rhizome	Alprazolam	Lethargy and disorientation

# The prescribing cascade...

Side effects	Drug causing side effect	Side effect treatment	
Constipation	TCA's, antihistaminics, verapamil, diltiazem, opioids, calcium supplementation	psyllium, docusate/senna, lactulose	
Low levels of Vitamin B 12	Metformin, PPI's	If undetected might lead to dementia treatment	
Diarrhea	ChEI's , metformin	Loperamide	
Increased BP, D-CHF	NSAID's	Antihypertensives, diuretics	
Urinary incontinence	donepezil, rivastigmine, galantamine, memantine	Incontinence treatment ( oxybutynin)	

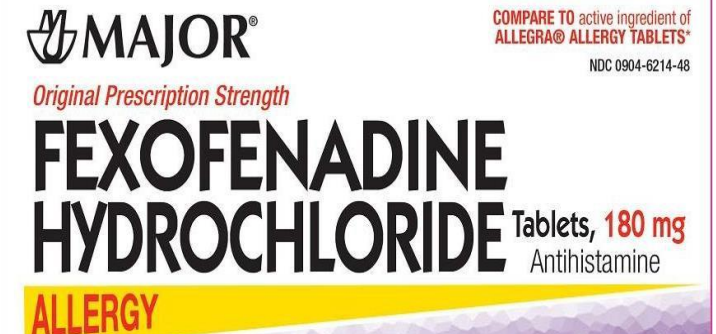
# OTC medications that might impair memory

More anticholinergic



Cyproheptadine

Less anticholinergic



“

Silver Alert

”



GOBIERNO DE PUERTO RICO  
DEPARTAMENTO DE SEGURIDAD PUBLICA  
Negociado de la Policía de Puerto Rico

PPR-614.3



## PERSONA DESAPARECIDA

1. Nombre: <b>BENJAMIN PEREZ ROSARIO</b>		2. Requisitoria Esp. Núm.: <b>2022-13</b>	
3. Dirección: <b>QUINTAS DE CANOVANAS, CALLE 4, CANOVANAS P.R.</b>			
4. Fecha de Nacimiento: <b>10/JUNIO/1944</b>	5. Lugar de Nacimiento: <b>CAROLINA</b>	6. Fecha de Radicación: <b>19/FEBRERO/2022</b>	
7. Sitio y Fecha de la Desaparición: <b>QUINTAS DE CANOVANAS (RESIDENCIA) CANOVANAS P.R. / 19 DE FEBRERO DE 2022</b>			
8. Nombre de la Persona que solicita su localización: <b>EZEQUIEL PEREZ ROSARIO</b>		9. Parentesco: <b>HERMANO</b>	

FOTOGRAFIA	DESCRIPCIÓN
	10. Edad: <b>77</b>
	11. Estatura: <b>5'-10"</b>
	12. Peso: <b>175 LBS</b>
	13. Ojos: <b>MARRON</b>
	14. Cabello: <b>CANOSO</b>
	15. Tez: <b>BLANCA</b>
16. Grupo Étnico: <b>HISPANO</b>	
17. Condición Mental: <b>ALZHEIMER</b>	
18. Señas Particulares: <b>CICATRIZ DE CIRUJIA EN EL TORAX POR CONDICION DE CORAZON.</b>	

Detalles de la Desaparición: **ADULTO MAYOR CON CONDICION DE ALZHEIMER, CAMINA LENTO Y PADECE DE CONDICION CARDIACA, SE RETIRO DE SU RESIDENCIA EN SU AUTO YARIS COLOR AZUL CON LA TABILLA: MYL-935.**

Número de Querrela: <b>2022-8-015-0693</b>	Número de Mensaje: <b>2-22-8-0228</b>	Número de NIC: <b>386663907</b>
---	--	------------------------------------

Datos de Importancia: **VESTIA POLO BLANCA, PANTALON CORTO NEGRO Y TENIS NEGRAS Y BLANCAS. DEBE ESTAR DESCOMPENSADO POR FALTA DE MEDICAMENTOS.**

De tener Información sobre el paradero de esta persona comuníquese inmediatamente con el Negociado de la Policía de Puerto Rico a cualquier de los siguientes números de teléfonos **787- 343-2020/ 787-793-1234 extensiones 2463, 2464.**



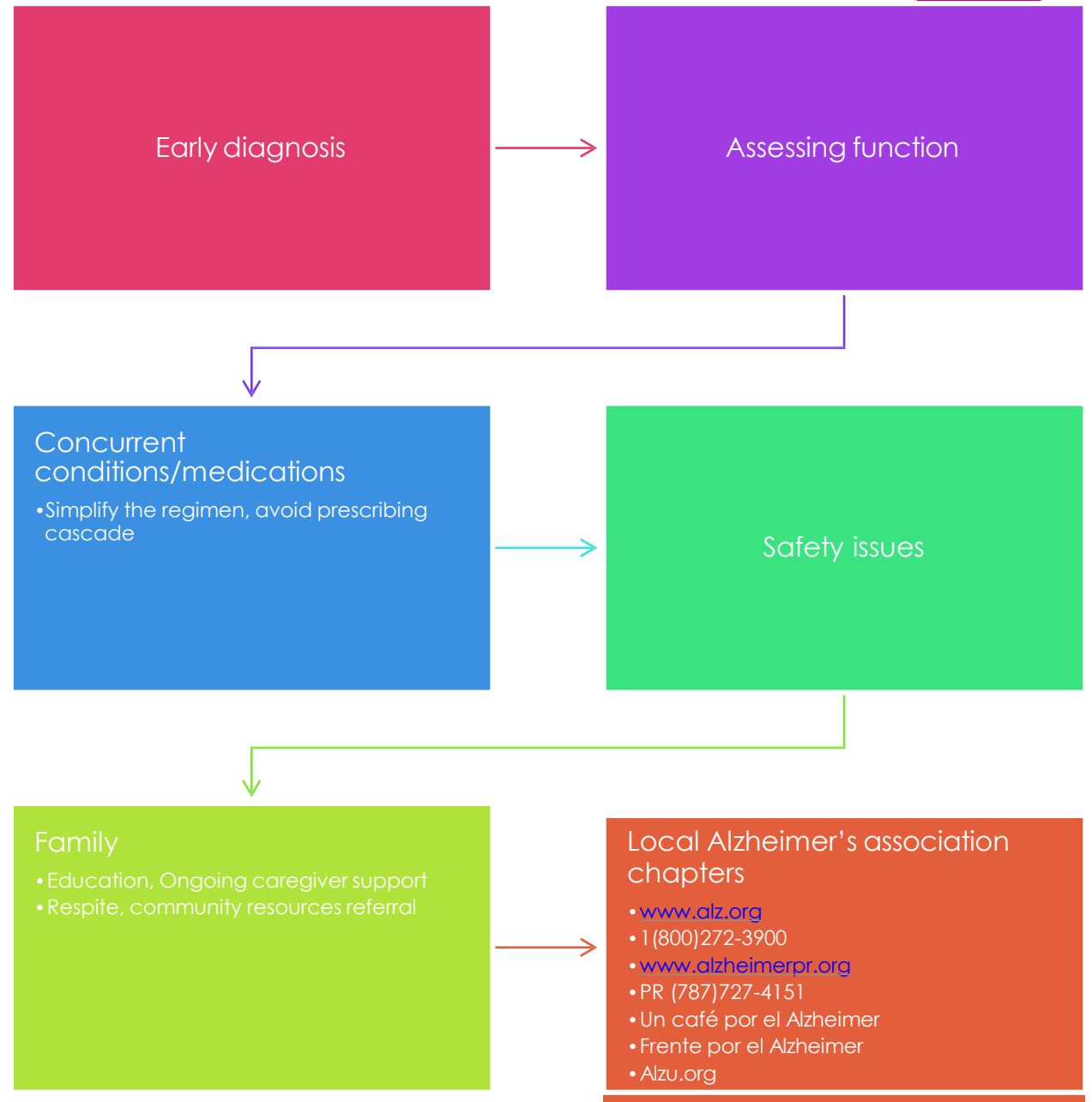
Tte. Cnel. Roberto Rivera Miranda




Comisionado Auxiliar en Investigaciones Criminales

# Silver Alert

# Summary



# Case #1

- ▶ Mr. PT is a 75 y/o male with hx of probable AD, DM, HBP, hypothyroidism.
- ▶ O: MMSE =10, FAST scale Stage 5
  - ▶ TSH=7.2 uIU/mL FBS=118mg/dL
  - ▶ BP=122/70mmHg P=70/min
- ▶ Current medications
  - ▶ Donepezil 5 mg po HS
  - ▶ Clonidine 0.1 mg po BID
  - ▶ Panadol PM 1 tab HS prn
  - ▶ Levothyroxine 0.1 mg po daily. ( The dose was increased 2 weeks ago)



## CASE #1 cont.

- A month later...
- Donepezil dose was increased to 10 mg po HS
- The caregiver called the primary care provider reporting that the patient's condition is now worse. Now she spends all day cleaning because of urinary incontinence. In the past he was able to go to the bathroom with minor assistance.
- The pt was started on oxybutynin IR 5 mg po TID



## Case #2

- ▶ Mr. MJ is a 78 y/o male patient with hx of DM type 2, ICD pacemaker MMSE 27 out of 30, CAD . The patient is independent for ADL's and IADL's
- ▶ Medications
- ▶ Glipizide 10 m daily, atorvastatin 5 mg HS, aspirin 81 m daily
- ▶ Labs HDL 37mg/dL LDL 69mg/dL, Trig 45, A1C Hgb 5.7%
- ▶ What would you recommend ?

# Case Discussion # 3

Mr. GP is a 91 y/o male patient with hx of AD, HBP, CAD, DM type 2, peripheral neuropathy, CRI, diverticulosis, CLBP, GERD, BPH, Depression, PUD, hx of fall, dementia, bradycardia AV block, S/P

Gastrostomy who is totally dependent on ADL's

## Medications

Aspirin 81 mg po daily, bisacodyl 5 mg po daily, Carbi50/Entacapone 200/ Levo 200mg po TID, clopidogrel 75 mg po daily, Ferrous sulfate 325 mg po TID, gabapentin 400 mg po daily, Glyburide 5 mg ½ tab QAM, donepezil 10 mg at bedtime, hydrochlorothiazide 25 mg ½ tab, Isosorbide dinitrate 10 mg po TID, lisinopril 40 mg ½ tab daily, loratadine 10 mg po daily, lorazepam 0.5 mg BID, omeprazole 20 mg BID, oxybutynin 5 mg BID, paroxetine 40 mg po daily, quetiapine 100mg one tab at noon and ½ tab HS, simvastatin 80 mg ½ tab QPM, valproic acid 250 mg two caps BID

# Case # 4

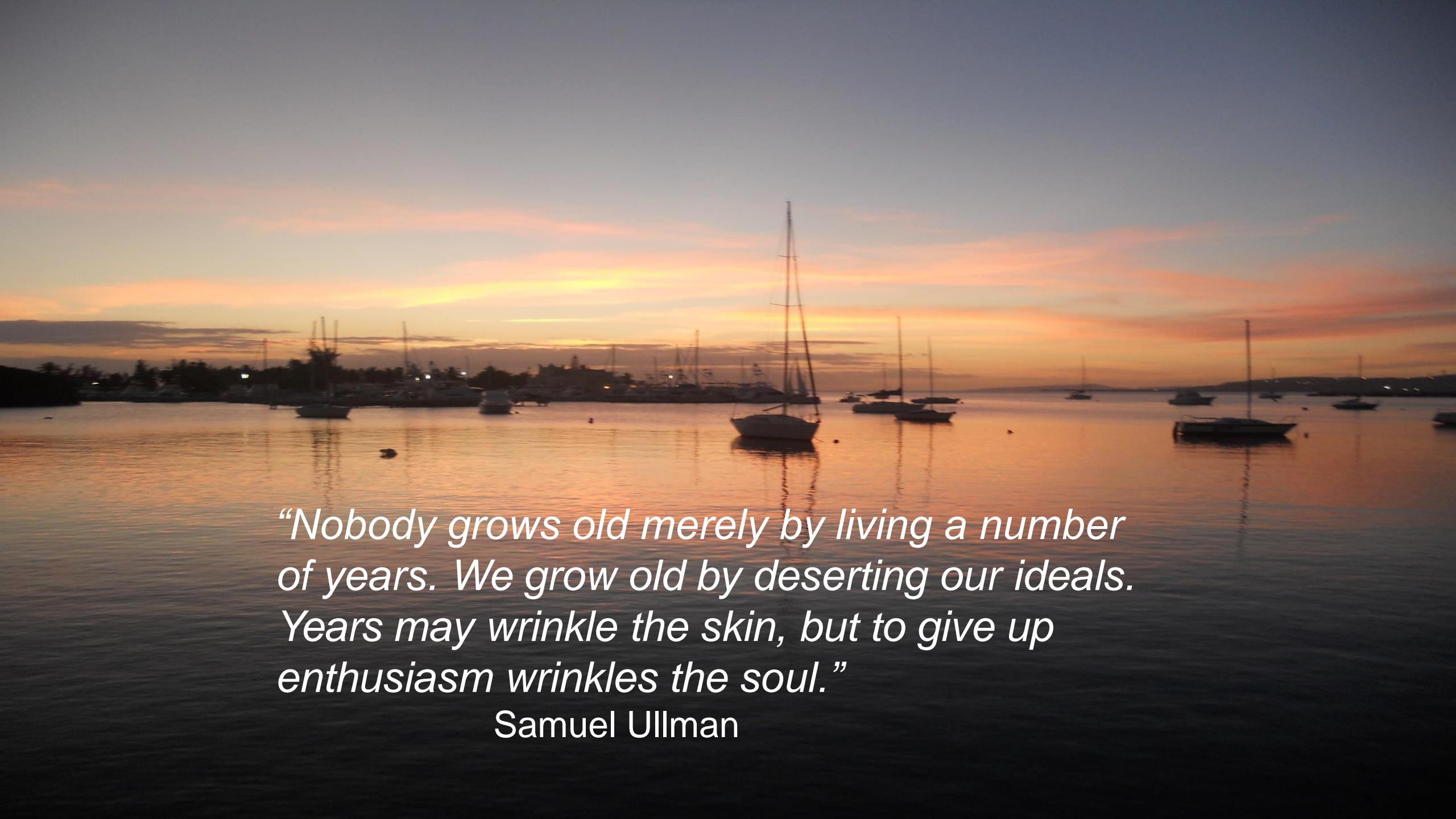
- Mr. WN is a 82 y/o male patient with hx of AD, HBP, POAG, GERD, constipation, decreased vitamin B12 levels, pre-DM, S/P PUD who went to his eye clinic appointment and C/O dry mouth.
- Labs: vitamin B12 =1,237pg/mL
- eClCr=39ml/min Hgb 12.5g/dl MCV WNL BP=131/62 P=59/min
- Medications: Clotrimazole top soln BID; docusate 240 mg po at bedtime, latanoprost 0.005% at bedtime, cyproheptadine 4 mg po BID, finasteride 5 mg po daily, ranitidine 150 mg po BID, simvastatin 20 mg ½ tab at bedtime, dorzolamide/timolol one drop both eyes BID, hydrochlorothiazide 25 mg ½ tab daily, donepezil 10 mg po at bedtime, cyanocobalamin 1000mg po daily, terazosin 2 mg po at bedtime, thiamine 100 mg po daily
- What drug related problems can you identify?

# Pre and Post Test

- ▶ Pre and Post Test:
  1. Pharmacists and pharmacy technicians are likely to see persons living with dementia and care partners, on a regular basis and they can identify changes in behavior and memory and monitor for changes in persons with known pre-disposing conditions. TRUE or FALSE
  2. Pharmacists should work with prescribers to ensure medications and doses are appropriate over the course of the disease. TRUE or FALSE
  3. Influenza and other vaccines can increase the risk of Alzheimer TRUE or FALSE
  4. Aducanumab is an FDA-approved drug for AD that acts as uncompetitive antagonist of the N-methyl-D-aspartate type of glutamate receptor
  5. Pharmacists can help patients with problems with adherence by recommending the use of electronic devices, the use of medications in bubble packs , pill boxes or reminders. TRUE or FALSE

# Pharmacist and Pharmacy Technician role in AD

- ▶ Early detection and referrals
- ▶ Education on how to decrease risk and actions to decrease risk ( smoking cessation, vaccination, etc)
- ▶ Identification of potentially inappropriate medications
- ▶ Recommendation of OTC's
- ▶ Medication reconciliation
- ▶ Monitor persons for problems such as medication failure, non-adherence and side effects, and the ways that intervention may occur. ( dosage form changes when appropriate)
- ▶ In caring for the person with advancing dementia.
- ▶ Assist individuals who are caring for persons living with dementia.



*“Nobody grows old merely by living a number of years. We grow old by deserting our ideals. Years may wrinkle the skin, but to give up enthusiasm wrinkles the soul.”*

Samuel Ullman



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