Cognitive Workup in Primary Care

Challenges and Opportunities

Silvia Russo, MD

Behavioral Neurology, Providence Medical Group

Dementia Innovation Summit

Primary Care at the Forefront

Dementia Action Collaborative Washington State

Disclosures for Silvia Russo, MD

I have no relevant financial relationships to disclose

The following presentation contains my views and opinions, not the views of the Dementia Action Collaborative.

John, a 75-year-old right-handed retired teacher

Presents at the request of his family because of memory issues.

- In retrospect, symptoms started around 4 years prior with occasional forgetfulness of conversations, losing train of thought and word-finding difficulties
- In the past year he has become more forgetful and repeats questions in the span of 5-6 minutes, and he is getting lost more frequently
- History: Hypertension, Coronary Artery Disease (stent in 2021), Hyperlipidemia, Prediabetes, OSA, but he does not wear CPAP, BPH
- His MOCA score was 21/30 – showing main difficulties with memory, which did not improve with cues, and clock drawing, his fluency was low. He had trouble hearing sentences and asked to repeat. The rest of the exam is benign. Vitals: SBP 130/60, HR 72, Afebrile, SPO2 100%
- He is not quite sure why his family is concerned. He thinks he is just getting 'old'. He does not remember his full list of medications. He has always overseen finances and investments but was not sure of details when daughter asked. He reports eating "ok" but admits to skipping meals. They deny accidents while driving.
- His daughter is worried about the family history and asks what she can do to prevent dementia

<u>John's medication</u>
Benadryl
Tylenol
ASA 81
Atenolol
Metformin
Oxybutynin
Atorvastatin
MVI
Fish oil
Glucosamine

EtOH: 2 drinks per day
Former smoker
No other substances
Exercises: rarely

Pitfalls

Cognitive decline is often mistaken for “normal aging”

- About 8% of older Americans with MCI receive a diagnosis.
- About 50% of patients Alzheimer’s disease receive a diagnosis in moderate-advanced stages
- Many patients with Alzheimer’s never receive a diagnosis
- Diagnosis is more often delayed in Black and Hispanic seniors

Potential consequences of late or missed diagnosis

- Missed opportunities for prevention (brain health, substance use, mood, hearing loss)
- Delayed access to treatments and clinical trials for interested groups
- Delayed or impossible planning
- Higer cost of care, potential financial and physical harm (e.g. driving)
- Negative impact on caregivers' and patients’ mental health

Alzheimers Dement 2024;20(5).
Geront & Geriatric Med 2023; 9(1–9)

Why work up dementia in primary care

PROS

- Primary care is first point of contact
- Longitudinal trusting relationship with patients and their families
  - A person that knows the patient well is like to mention a concern
  - Annual visit questionnaire – patient answers yes to concern about memory
  - No-shows and confusion about appointments and medication
  - Worsening adherence in older patients may be a sign of cognitive difficulty
- Medicare covers separate visit to assess cognitive function/develop care plan

CONS

- Time and training needed to correctly administer/interpret cognitive assessments.
- Low confidence disclosing diagnosis and post-diagnostic care for many providers
- Lack of geriatricians, lack of specialists
- Lack of care navigators

JAMA Netw Open. 2023;6(9):e2336030.

Preventative strategies

- Sleep
- Physical exercise
- Alcohol, smoking, other substances
- Hearing and vision evaluations
- Blood pressure and other vascular risk factors
- Social isolation
- Mood

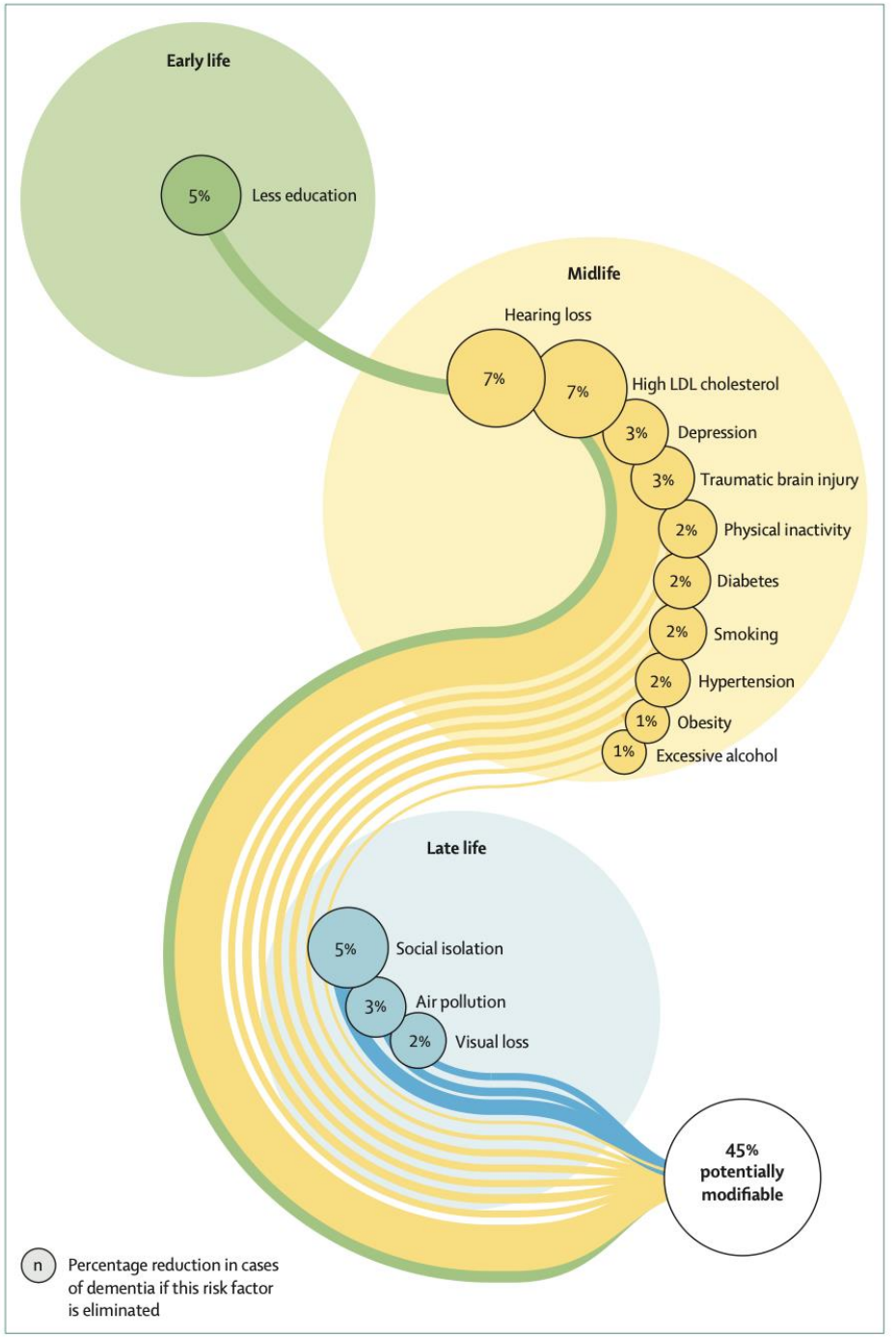
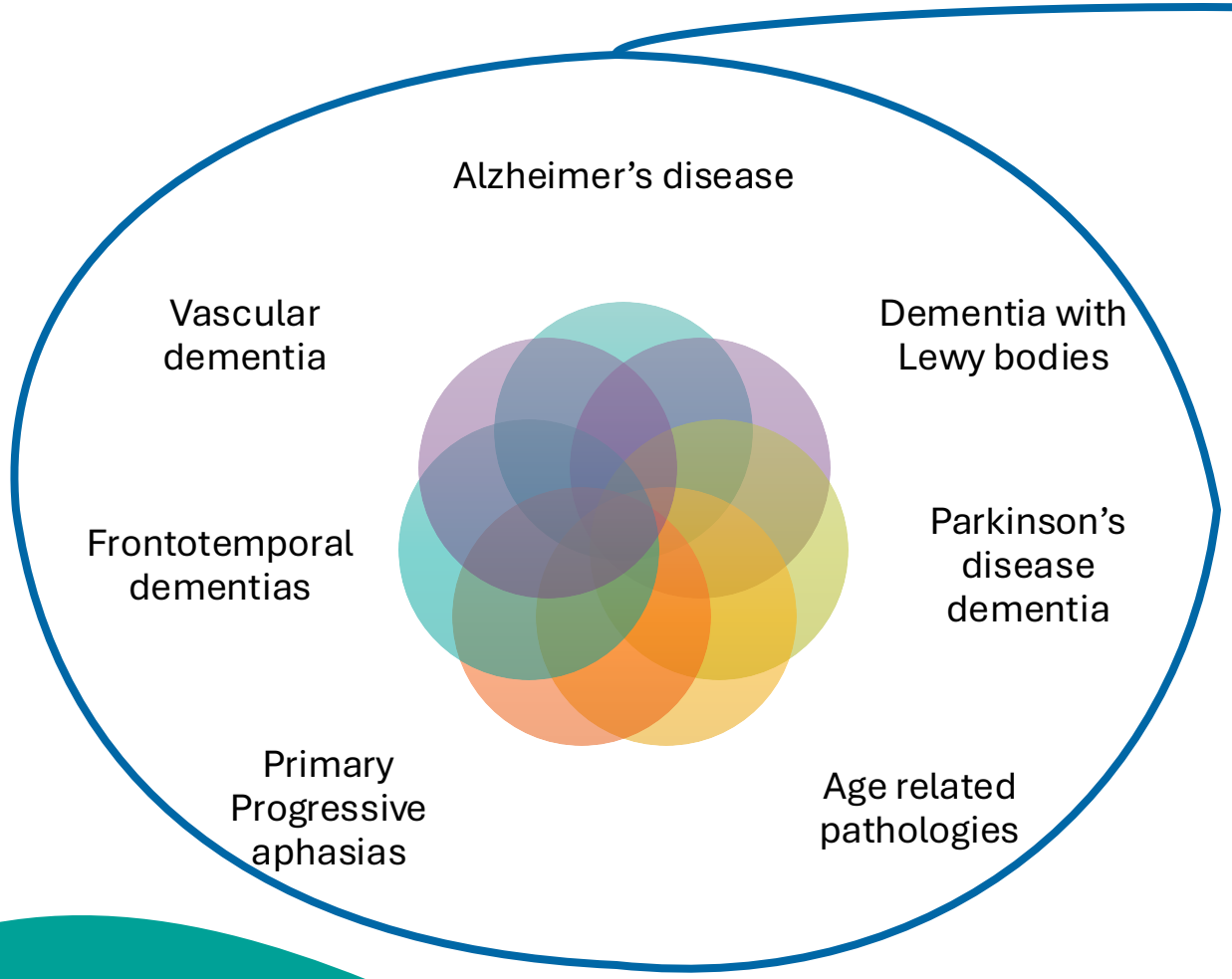


Figure 9: **Population attributable fraction of potentially modifiable risk factors for dementia**

Lancet 2024; 404: 572–628

“Doctor, is it Alzheimer’s or Dementia?”



The short answer:

- Dementia is the umbrella term
- Alzheimer’s is a form of dementia
- There are many other causes of dementia
- These can overlap

Patient often sensitive to the word “Dementia”

- use with knowledge
- DEMENTIA IS NOT DIAGNOSED BY THE SCORE ON THE MOCA

Definitions: FUNCTION IS KEY

Subjective cognitive impairment (SCI): an at-risk state

- Patient reports cognitive changes, they are FULLY independent
- No clear deficits or declines from baseline on formal neuropsychological testing
- Relies on neuropsychological evaluation, not just MOCA/SLUMS

Mild cognitive impairment (MCI)

- Patient reports cognitive changes which are objectively demonstrated.
- **Patient is fully independent**

Dementia

- Subjective and objective cognitive decline
- Not caused by active substance abuse or other active medical conditions
- **Activities of daily living are affected**:

Mild	Only IADLS affected (Instrumental Activities of Daily Living)
Moderate	IADLS affected, starting to need reminders and prompting for ADLS (Activities of Daily Living)
Severe	Requires full assistance with IADLS and ADLS

Look for changes compared to baseline

Instrumental Activities of Daily Living
IADLs

Cooking

Housekeeping/Laundry

Shopping

Using the telephone

Managing medications

Managing finances

Driving

Using transportation

Activities of Daily Living
ADLs

Feeding

Continence

Transferring

Toileting

Dressing

Bathing/Showering

Would you feel comfortable leaving John alone for 2 weeks straight?

Definitions: FUNCTION IS KEY

Subjective cognitive impairment (SCI): an at-risk state

- Focus on prevention, research and follow up, lifestyle modification

Mild cognitive impairment (MCI)

- Focus on planning for the future, research, some medication, lifestyle modification
- **Make the bucket list happen**

Dementia

Mild	Focus on support, medication, planning, lifestyle, socialization
Moderate	More burden, most prolonged, usually institutionalization happens, be more sparing with meds
	More behavior changes. More caregiver burnout
Severe	Palliative care approaches, meds may still help but some may also need to wean off, frailty
	No established treatments.

Cognitive Presentation Vocabulary

Not everything is "memory loss"

Amnestic

- Forgetting information repeatedly
- Forgetting names of people over and over
- Asking the same question frequently
- Forgetting appointments, bills

Executive

- Difficulty maintaining attention
- Difficulty multitasking
- Difficulty learning the rules of a new board game
- Difficulty managing finances
- Difficulty planning and making decisions
- Judgement

Visuospatial

- Spatial awareness – judging distances.
- Navigation for common and less common places
- Face recognition
- Seeing objects/obstacles

Language

- Word-finding difficulties
- Sound distortions
- Comprehending instructions
- Reading
- Writing
- Grammar

Psychiatric presentation vocabulary

Mood changes

- Late-onset depression
- Late-onset anxiety

Sleep changes

- Insomnia
- Hypersomnia
- Fragmented sleep
- Acting out of dreams

Hallucinations vs. Illusions

- Visual – get description
- Auditory – get description
- Misperceptions, Paraeidolia
- Extracampine hallucinations

Behavior changes

- Apathy
- Irritability
- Disinhibition
- Lack of empathy or sympathy
- Hyperphagia

Psychosis and delusions

- Paranoia
- Parasitosis
- Theft
- Persecution
- False memories

Motor Symptoms

- Tremors: rest, posture, action, intention
- Slow gait vs. shuffling
- Focal weakness
- Falls – How often? Caused by what?
- Diplopia
- Smaller handwriting
- Reduced Dexterity
- Parkinsonism: bradykinesia +/- rigidity
- How often do they need to do stairs?

Be ‘generous’ with PT and OT orders

Do not necessarily need to wait for a neurologist

Goal is often stability and not necessarily improvement

Clinical entities:

Alzheimer's disease: predominantly amnestic, followed by visuospatial, language, executive function in classical form. Can have atypical presentation

Dementia with Lewy bodies: two or more of parkinsonism + well formed visual hallucinations + fluctuations + acting out of dreams. Visuospatial/Executive predominant pattern

Vascular dementia: stepwise or gradual, executive predominant (from small vessel disease or cerebral amyloid angiopathy)

Behavioral variant frontotemporal dementia: early change in behavior and executive function, spared memory and visuospatial function in the first 3 years of disease.

Primary progressive aphasias: language is predominantly affected with sparing of other domains in the first 2 years.

Parkinson's disease dementia and Atypical parkinsonism

Age-related dementias in late 80s-90s-100s(!) – memory predominant, slow progressive

Rule out contributors, Get a clear picture

- Is this a sudden or gradual change, look back in time
  - Delirium
  - Medication side effects, incorrect medication administration
  - Seizures
- Collateral informant - Ask *gently* about function
- Prescription and Over-The-Counter medications:
  - Anticholinergics (bladder meds, TCAs, older SSRIs)
  - Benzodiazepines, Muscle relaxants, Z-drugs
  - Gabapentin and similar
  - First-generation antihistaminergic meds
  - Opioids
  - Certain antipsychotics
  - Certain antiseizure medications
- Active substance use, abnormal thyroid, metabolic abnormalities
- Cognitive screen in clinic is important
- What is patient/family goal?

Diazepam
Clonazepam
Alprazolam et al.
Oxybutynin
Solifenacin
Tolterodine
Trospium
Scopolamine
Baclofen
Cyclobenzaprine
Methocarbamol
Oxycodone and sim.
Naltrexone
Meclizine
Hydroxyzine
Diphenhydramine
Tylenol PM
Zzquil
Nyquil
Benadryl
Doxylamine
Unisom
SleepAid
Paroxetine
Nortriptyline
Amitriptyline
Valproic acid
Topiramate
Haloperidol
Abilify
Gabapentin
Pregabalin
Zolpidem

Diagnostics

Neuropsychological testing

- If no clear pattern on MOCA
- Normal MOCA
- Avoid in very low scoring patients

MRI Brain

- Structural evaluation of the brain: atrophy and vascular changes
- Evaluates for microhemorrhages - SWI or SWAN sequences
- Helps rule out acute or other contributing pathology (e.g. tumors, acute strokes).
- 3 Tesla ideal (better resolution), 1.5 Tesla is ok if 3T unavailable or unfeasible
- Volumetrics are NOT strictly needed – they add a cost.
- Add contrast if active or recent cancer with potential for brain metastasis, or paraneoplastic process, rapid progression, active autoimmune pathology

CT head wo contrast is better than no image at all

- Very frail or advanced patient
- Metal contraindicating MRI

Labs

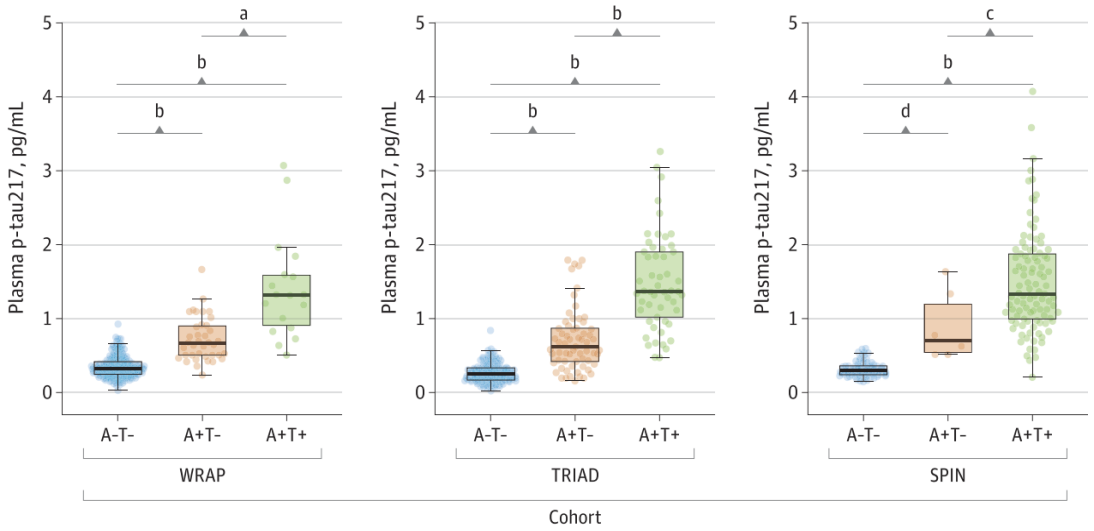
- General labs, B12, TSH in everyone.
- Add RPR, HIV in high-risk or rapidly progressive cases
- Add whole blood B1 if significant weight loss, alcohol use disorder, risk of malnutrition
- pTAU217 is a new blood biomarker for AD

Sleep test if suggestive history

JAMA Neurol. 2024;81(3):255-263
JAMA Neurol. 2024;81(2):197-200

pTAU217

Figure 1. Plasma Phosphorylated Tau 217 (p-Tau217) Levels According to Amyloid β (A) and Tau (T) Profiles



Blood biomarkers: ptau 217 has the most promise.

- Still out of pocket – ~$400-500
- 89% accurate in ***symptomatic*** individuals in predicting amyloid presence. Some studies indicate it can predict tau presence.
- Careful selection of patients.
- Only for patients above 50 years old.
- NOT for use in asymptomatic individuals!!!
- **AVOID in patients with EGFR < 60** – higher risk of false positives

FDG PET scan- helps determine pattern of hypometabolism.

Can have prognostic + diagnostic impact.

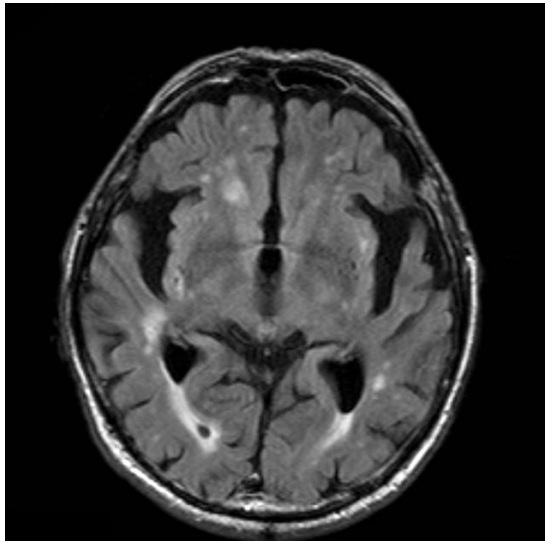
CSF biomarkers: special kits, neurology mostly still

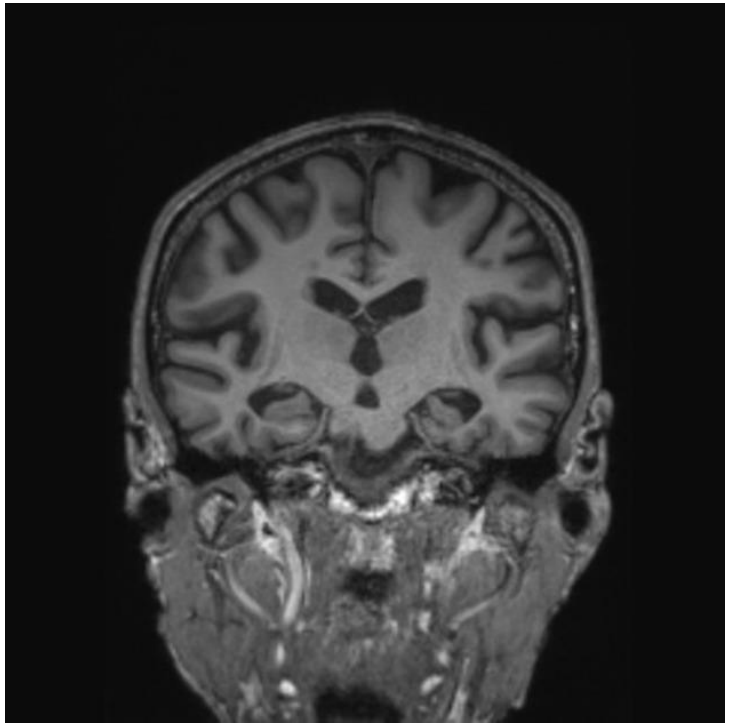
Amyloid PET and (in future) Tau PET: newer technologies, less available to primary care still especially in suburban and rural areas.

Recommendations for John

- Would recommend starting to work on reversible factors:
  - Oxybutynin is an anticholinergic.
  - Benadryl is an antihistaminergic
  - Should try to wear CPAP – you discover his machine was recalled and he did not get replacement
  - Hearing evaluation
  - Try to reduce alcohol
  - Counsel on lifestyle
- Counsel on potential safety issues
  - Ask family to help monitor meds, driving, finances. Involve patient.
  - Use pill box or automated reminder
  - Check BP at home.
- Orders
  - Labs: CBC, CMP, B12, TSH with reflex
  - MRI brain wo contrast

3 months later:





- Off Oxybutynin and Benadryl
- Better use of CPAP and sleep schedule
- Exercises and meets up with friends
- Ongoing forgetfulness
- His wife is making more soups, adds spinach to many meals. They cut out the fast food to about 1-2 times a month.
- Family noticed some financial mistakes; he needs some reminders for medications. He is doing better driving locally
- MRI with hippocampal atrophy and vascular disease
- Labs and home BP ok

"Doctor, does he have Alzheimer's or dementia?"

"Can we do something about it?"

"I don't want to be a burden!"

Diagnosis:

- Memory predominant progressive cognitive decline.
- Despite correcting reversible factors, he is still having difficulties
- MRI without other pathology, but suggestive for pattern of atrophy
- Patient is needing some assistance in iADLS (finances)

MILD DEMENTIA

Likely due to Alzheimer's disease, with vascular contributions

Interventions for John

- Brain health promoting interventions are the cornerstone
- The new anti-amyloid agents are a very limited new option
- We have other, older medication that can help delay
  - Counsel that they may not see a clear benefit
  - Know what alternatives you have if side effects
  - Medication does not “prolong” the misery
- Planning: local and national support resources.
- Longitudinal follow up: “I’m going to see this through with you"

Who should see the neurologist?

- Complex presentation, unclear diagnosis, second opinion
- Severe multiple symptoms at onset
  - Caveat is advanced cases
- Visual hallucinations or significant psychiatric presentation
  - Psychiatry may also be needed
- Significant Motor component: resting tremor, dystonia, parkinsonism
- Predominant speech component
- Predominant visual presentation or other atypical presentation
- Age < 65 (after ruling out contributors or if no contributors)
- Rapid progression: from first symptom to dementia *truly* in < 6 months
- Predominantly behavioral changes
- If more management needed after you have done first steps.
- High stakes occupations

Memory medications

Cholinesterase inhibitors > Extend the half-life of Acetylcholine.

Approved for Mild-moderate dementia due to AD, can be started in MCI stages of AD

Very helpful in DLB for hallucinations, anxiety and fluctuations

Avoid in frontal/behavioral syndromes (e.g. FTD) – can make them worse

GI side effects, muscle cramps, urinary frequency, mostly with PO donepezil and galantamine.

Bradycardia is a class effect – caution with beta-blockers and heart problems.

Would keep long-term even if no effect noted esp. in AD – stopping may mean faster progression

Donepezil 5-10 mg daily in the morning
Galantamine (more side effects) 8-32 mg
Rivastigmine capsules 1.5- 3 mg BID
Rivastigmine patch – pre-auth needed 4.6-9.5 mg/24h
Donepezil patch once a week – not covered yet, coupons

Higher doses used in DLB for hallucinations and fluctuations

NMDA Receptor Antagonist - Memantine (gradual up-titration to 10 mg bid)

FDA Approved for moderate-severe Alzheimer's disease (when ADLS are impacted)

- Halve dose if EGFR < 30 (i.e. max dose 5 mg BID)
- Dizziness, confusion, constipation, sleepiness
- Sometimes used in vascular disease – results are usually mixed
- Can have calming effect
- Only keep if it helps

Week 1: memantine 5 mg daily
Week 2: memantine 5 mg BID
Week 3: memantine 10 mg QAM 5 mg QPM
Week 4: memantine 10 mg twice daily

Behavioral and sleep problems

Mood, anxiety and behavioral changes:

- SSRIs are a good second step in addition to nonpharmacologic steps
- Avoid tricyclics, avoid paroxetine.
- Brexpiprazole (Rexulti*) for agitation due to Alzheimer's disease ($$$)
- Off label quetiapine can help some *
- FDA black box warning for antipsychotics
- Avoid strong anti-D2 antipsychotics in dementia with Lewy bodies

Sleep:

- Low threshold for OSA screening in *early* stages
- Avoid Z-drugs (e.g. NO zolpidem), avoid benzodiazepines
- Melatonin a couple hours before bed (sundowning, dream enactment)
- Low dose mirtazapine (7.5 mg-15 mg), Trazodone, Suvorexant

First step is nonpharmacological:

- Behavioral techniques
- Caregiver learning curves
- Sleep hygiene and sleep therapy early on

If medication needed:

- Monitor EKG for QTc prolonging drugs (marked*)
- Slow changes, allow time for steady state
- Use lower doses than younger adults

Sertraline 25 -200 mg

- Choice in Aggression/Agitation
- Choice in Frontotemporal dementia
- Imbalance at high doses
- Some urinary frequency

Lexapro* 5-10 mg (max 10 in age > 60)

- Can help with anxiety in Alzheimer's disease
- Paradoxical initial anxiety.

Citalopram* 10-20 mg

- Can help with anxiety in Alzheimer's disease

Mirtazapine 7.5 mg-30 mg

- Low doses (7.5 mg esp.) most help with sleep
- High doses most help with anxiety

Vortioxetine (with psych help, $$$):

- Very selective SSRI – may need psych to Rx

Advocate for use of resources

Hope for the best, prepare for the worst, so you have a choice in this

Powerful tools for caregivers https://www.powerfultoolsforcaregivers.org/

Caregivers who take these free classes demonstrate:

Increased self-care behaviors.

Reduced guilt, anger and depression.

Increased confidence and coping skills.

Increased use of community resources

Alzheimer's association: https://www.alz.org/help-support

24/7 National Helpline 800.272.3900.

Staffed by social workers.

Provides urgent advice.

Makes referrals to local chapters and programs.

Free service available to all.

(Available even if main diagnosis is not Alzheimer's)

Area agency on Aging (AAA): https://eldercare.acl.gov/

1-800-677-1116

Every county in the United States has an AAA. Name may vary.

AAAs help adults, families, and professionals facing aging and disability issues get the information and support they need to make informed decisions.

Dementia Roadmap* https://www.dshs.wa.gov/altsa/dementia-action-collaborative

A 28-page guide available in English or Spanish for families and caregivers that explains:

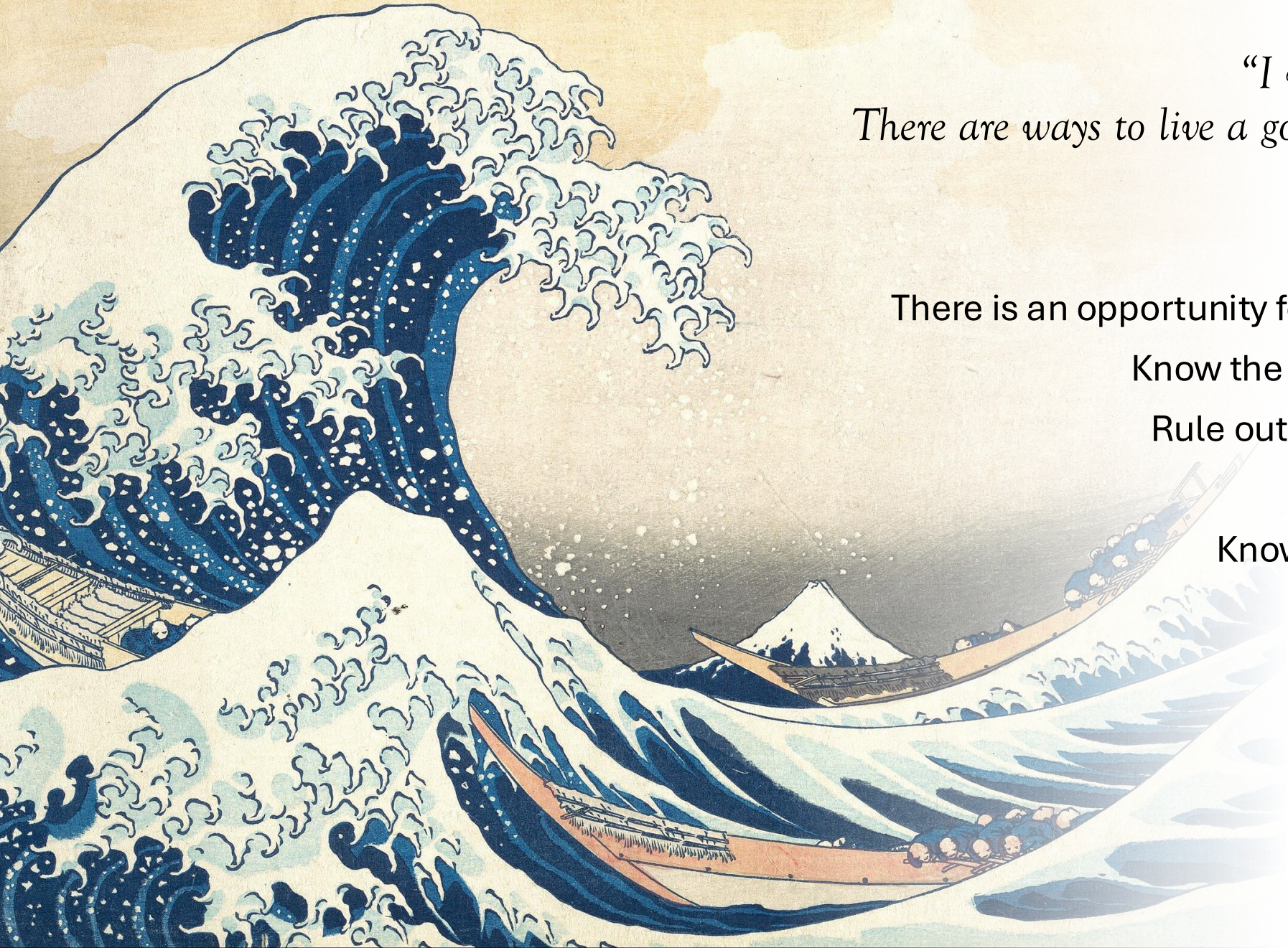
What to do when a person experiences changes in memory and thinking.

What to expect and steps to take if someone in your family has been diagnosed with Alzheimer's or other dementia.

This guide is specific to Washington State; similar guides for a national audience are in development.

A knowledgeable social worker in the clinic for select cases:

- caregiver burnout
- unsafe situation
- needing institutionalization quickly to avoid ER admission



"I will see this through with you,
There are ways to live a good life in spite of the disease"

There is an opportunity for a safe haven in primary care

Know the definitions and the vocabulary

Rule out contributors and confounders

Prevention and lifestyle matter

Know diagnostic/therapeutic tools

Know what to avoid

Know when to ask for help

Be "Cockroaches" of Hope