KU Alzheimer’s Disease Center

Mission
To improve the lives of patients and families with Alzheimer’s disease by eliminating the disease through research into its treatment and prevention
Outline for Today

• Overview of Alzheimer’s
• Current Treatment Options
  – Current Treatments
  – Investigational Medications / Clinical Trials
  – Non-pharma Treatments
• Caregiver Support
  – Area studies and programs
• Prevention of AD / Successful Aging
  – Exercise
Alzheimer’s Facts

- 5.3 million Americans have AD in 2008
- One in ten people over 65 have AD
- Every 66 seconds someone develops AD
- $231 billion in Medicare, Medicaid, and out-of-pocket costs in 2017
- Two of every three people with AD are women
Alzheimer’s Disease is Increasing Dramatically

Projected Number of People Age 65 and Older (Total and by Age Group) in the U.S. Population with Alzheimer’s Dementia, 2010 to 2050

We are Living Longer than Ever Before

Total number of persons age 65 or older, by age group, 1900 to 2050, in millions

Note: Data for the years 2000 to 2050 are middle-series projections of the population.
Reference population: These data refer to the resident population.
Source: U.S. Census Bureau, Decennial Census Data and Population Projections.
High Prevalence of Alzheimer’s in Minority Communities

2012 AD Facts and Figures, Alzheimer’s Association
What is Alzheimer’s?
Alzheimer’s is a type of dementia
Clinical Hallmarks of Dementia

Memory and thinking problems that interfere with usual activities

- Gradual onset
- Progressive decline
- Memory loss
- Other cognitive domains impaired
- Interferes with function
Early Cognitive Changes in Alzheimer’s Disease

Memory Loss
- Forgetfulness (conversations; appointments; medicines; names)
- Repetition of questions, statements
- Misplacing items

Executive Dysfunction
- Managing household finances
- Driving
- Meal preparation
- Operating appliances
## Concerning v. Typical

<table>
<thead>
<tr>
<th>Concerning signs</th>
<th>Typical age-related changes</th>
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<tbody>
<tr>
<td>Poor judgment and decision-making</td>
<td>Making a bad decision once in a while</td>
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<tr>
<td>Inability to manage a budget</td>
<td>Missing a monthly payment</td>
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<tr>
<td>Losing track of the date or the season</td>
<td>Forgetting which day it is and remembering it later</td>
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<tr>
<td>Difficulty having a conversation</td>
<td>Sometimes forgetting which word to use</td>
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<tr>
<td>Misplacing things regularly and being unable to retrace steps</td>
<td>Losing things from time to time</td>
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Diagnosing AD

- Gold Standard: Brain autopsy
- No blood test
- PET brain scan (not covered by insurance)
- Detailed history from someone who knows the person well
- MRI or CT to r/o structural process
- Lab work (thyroid, vitamin B12)
Plaques and Tangles

- Hallmark AD changes in the brain
- Plaques are aggregations of sticky beta-amyloid protein that are toxic and interfere with cells talking to each other
- Tangles are the breakdown of the cells internal scaffolding
AD Results in Brain Atrophy
83 years old with AD
- MMSE 24/30
- May need assistance or cues with more complex tasks
85 years old
-MMSE 2/30
-Having difficulty with making a snack, choosing clothes to wear, discussing current events
Current Treatment Options
Alzheimer’s Disease Medications

- Two classes of approved medications
- Nothing new* has been approved in over 10 years!
  - **Cholinesterase inhibitors** → increase acetylcholine levels
    - Donepezil (Aricept)
    - Galantamine (Razadyne)
    - Rivastigmine (Exelon)
  - **NMDA antagonist**
    - Memantine (Namenda)
    - *Namzaric combines donepezil and memantine*
Effect of Medications on AD Course

Initiate Medications

Cholinesterase inhibitors

Donepezil
Galantamine
Rivastigmine

Namenda
Other common medications

**Antidepressants** for low mood and irritability:
- citalopram (Celexa)
- fluoxetine (Prozac)
- paroxetine (Paxil)
- sertraline (Zoloft)
- trazodone (Desyrel)

**Anxiolytics** for anxiety, restlessness, verbally disruptive behavior and resistance:
- lorazepam (Ativan)
- oxazepam (Serax)

**Antipsychotic* medications** for hallucinations, delusions, aggression, agitation, hostility and uncooperativeness:
- aripiprazole (Abilify)
- clozapine (Clozaril)
- haloperidol (Haldol)
- olanzapine (Zyprexa)
- quetiapine (Seroquel)
- risperidone (Risperdal)
- ziprasidone (Geodon)

*CMS is trying to reduce antipsychotic use in nursing homes for patients with dementia
Investigational Medicines

• Approved drugs alleviate symptoms but do not stop the underlying disease.

• Current investigational disease-modifying medications are primarily focused on amyloid:
  – Tricking the body into digesting amyloid by tagging it with an antibody (like when you have an infection)
  – Blocking the formation of amyloid
The Amyloid Hypothesis

Amyloid plaques trigger the AD pathophysiological cascade

Production

Enhance Clearance

Downstream effects

Cell Death

KU Alzheimer’s Disease Center
The University of Kansas Medical Center
Thinking Beyond Amyloid

• Tau (tangles)
  – Antibody trials underway

• Vascular (blood flow)
  – Controlling BP, lowering cholesterol

• Metabolism
  – Insulin resistance, controlling diabetes
  – Compounds that improve energy use in the brain

• Genetics
  – Targeting in those at higher risk
Drugs in Phase 3

UsAgainstAlzheimer’s, 2016
Treatment Trials: KU ADC Clinical Trial Unit

• **Anti-Amyloid**
  – Aducanumab/ENGAGE (Biogen)
  – Azeliragon/STEADFAST (vTv)

• **Neuroprotection**
  – NOBLE/TCAD study (Toyama)
  – Bryostatin (Neurotrope)
  – Asprin/ASPREE (NIH)

• **Metabolic Studies (KU led)**
  – Metabolic approaches (Diet, Exercise, OAA, S-equol)
Non-pharmaceutical Treatment Options
Supplements have not shown benefit

- **Ginko biloba**
  - 2008 study, not effective in reducing conversion to AD

- **Huperzin**
  - 2011 study showed no benefit

- **Omega-3/DHA**
  - Trials of fatty acids have not demonstrated consistent benefit

- **Axona / Coconut oil**
  - Possible benefit but maker chose not to do a large study
Exercise has shown modest benefit

- Aerobic exercise has shown modest benefit for people in early stages of AD. (Baker, 2010; Vidoni, 2012; Burns, 2008)
  - Even with AD, fitness is associated with healthier brains and slower progression.

- Resistance training has also shown some benefit. (Fiatarone-Singh, 2014; ten Brinke, 2015; Nagamatsu, 2012)
  - Evidence for brain and thinking benefit.
Alzheimer’s Disease Exercise Program Trial (ADEPT)

- Randomized trial of 26-weeks of aerobic exercise vs. stretching in early AD

80 individuals with Early AD

26 weeks of Intervention

Aerobic Exercise
N=40

Control/Stretching
N=40

Assessments
Cognitive
Functional
Fitness
Brain Imaging
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0170547
Caregiver Support
Caregiver Support

• Respite - hours to days
• Support groups and finding community
• Transportation
• Day programs
• Education on disease
• Management strategies for challenging situations
A program to help caregivers and maintain function

Reducing Disability in Alzheimer’s Disease (RDAD)

• Teri et al. (2003) demonstrated that a 12-week program could reduce disability and increase active days.
  – Coaching caregiver on behavior management
  – Exercise with caregiver and PWD

• Menne et al. (2010) replicated across Ohio using the Alzheimer’s Associations
  – Reduced caregiver unmet needs
New Program to Teach Caregivers Ways to Manage Challenging Behaviors

mobile Reducing Disability in Alzheimer’s Disease (mRDAD)

- Coaching caregiver on behavior management
- Exercise with caregiver and PWD delivered via phone and iPad

- Alzheimer’s Association, Heart of America Chapter
- Jewish Family Services of Greater KC
- Shepherd’s Center Kansas City Central
- Developmental Disability Services of Jackson Co.
- KUMC and UMKC
Using Technology to Support Caregivers

• FamTechCare
  – Caregiver gets an iPad to can record challenging situations
  – Expert panel provides feedback on the recordings
AD Prevention and Successful Aging: What we know
Two simple tenets

• Heart Health = Brain Health
  – Exercise
  – Eat a heart-healthy diet (Mediterranean diet) [Scarmeas, 2009; Morris, 2015]
  – Sleep well

• Stay Engaged
  – Socially (faith groups, clubs) [Bassuk, 1999; Saczynski, 2006]
  – Mentally (book clubs, classes) [Gatz, 2006]
Exercise is Related to Reduced Risk of Cognitive Decline in Older Women

• Long term, regular physical activity associated with less cognitive decline in 18K. (Weuve, 2004, JAMA)

• Greater baseline physical activity associated with less cognitive decline at 6 years later, even after adjusting for education and comorbidities (Yaffe, 2001, Arch Neurol)
Trial of Exercise on Aging and Memory (TEAM)

- “Dose Response” Study
  - Is there a minimum dose?
  - Is more better?

- Primary Study Goal:
  - What is the optimal exercise dose for cognition and physical function?

Four Exercise “Doses”

- Control
- 50%
- 100%
- 150%

Cognitive & Physical Testing

26 week intervention

Cognitive & Physical Testing

26 weeks unstructured

Cognitive Testing
Any is good, more is better...
Exercise is Related to Reduced Risk of Developing Dementia

• Moderate exercise in mid- and later life associated with lower risk for MCI in 1200 older adults. (Geda, 2010)

• Compared with no exercise, physical activity associated with lower risk of cognitive impairment, Alzheimer disease, and dementia of any type in 4600 older adults. (Laurin, 2001)
Good evidence that fitness can help delay or prevent AD. This gap represents a delay in AD onset just by regularly exercising.
Endurance

• Endurance is the ability of your heart, lungs and muscles to meet the requirements of your daily activity.

• Find time for 30 minutes. It doesn‘t have to be all at once (but at least 10 minute bouts)
  – Walking/jogging * (Kramer, 1999)
  – Dancing * (Coubard, 2011)
  – Bicycling
  – Swimming
Endurance

• Alternatively, some advocate aiming for 10000 steps* a day (15000 if you are already active)

• Simple pedometers make it difficult to monitor intensity.

• Accelerometers (Fitbit, Jawbone, etc…) can provide some information on intensity.
Strength

• Strength is the ability of your muscles to generate enough power to overcome gravity or objects you encounter throughout the day

• 2-3 days a week
  – Lifting weights * (Liu-Ambrose, 2011; Nagamatsu, 2012 in MCI)
  – Using resistance bands
  – Gardening
  – Home and car repair
Balance

• Balance is your ability to keep your nose over your toes and requires good sensation, coordination, quick reflexes and strength

• Brief and daily
  – Standing on one foot or heel-toe walking
  – Dancing
  – Gardening
  – Tai Chi * (Man, 2010 cross-sectional evidence only)
  – Hiking uneven ground
Flexibility

- Flexibility is the ability to move your joints through an extended and useful range of motion
- Brief and daily
  - Yoga * (Oken, 2006 no effect on cognition seen)
  - Stretching
  - Cleaning
Current AD Prevention Trials

• Alzheimer’s Prevention thru Exercise (APEX)
• Reducing Risk in Alzheimer’s Disease (rrAD)
• Anti-amyloid Treatment in Asymptomatic Amyloidosis (A4)
• GeneMatch Screening
Sit Less, Move More!

• Sitting is the new smoking!
  – Increased mortality with > 7 hrs a day

• Move More: Take a Day-Long Approach
  – Reduce prolonged sitting
    • Gentle walks during the day, commercials, on phone
  – Benefits even at the lowest doses
    • Not necessary to achieve the “threshold” of 150 minutes a week or 10,000 steps
Exercise your brain!

- Mentally stimulating activities
  - Give your neurons a workout!
    - Lectures, social activities, reading, puzzles
    - There is nothing special about crosswords!
- Scientific data is limited
  - Improvement at what you practice… but
  - Not yet clear that your daily activities improve
  - But it can’t hurt!
Why we need you!

In next 3 years we need to have over 750 volunteers participate in our studies and trials.
– 650 need to have normal memory
– 100 need to have memory problems

– To get that number, we will need to consider over 14,000 people!
What Can You Do?

1. Join us in a study
2. Spread the word. Be an advocate!
3. Support research financially
4. Be proactive!

www.KUAlzheimer.org  (913) 588-0555
Resources

• Alzheimer’s Association
  – www.alz.org
  – 24-hour hotline: 1-800-272-3900

• Alzheimer’s Disease Education and Referral (ADEAR)
  – www.nia.nih.gov/Alzheimers
  – 1-800-438-4380

• Alzheimer’s Research Forum
  – www.alzforum.org