

Unique ways that people with Down syndrome are impacted by Alzheimer's Disease

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A little info about me

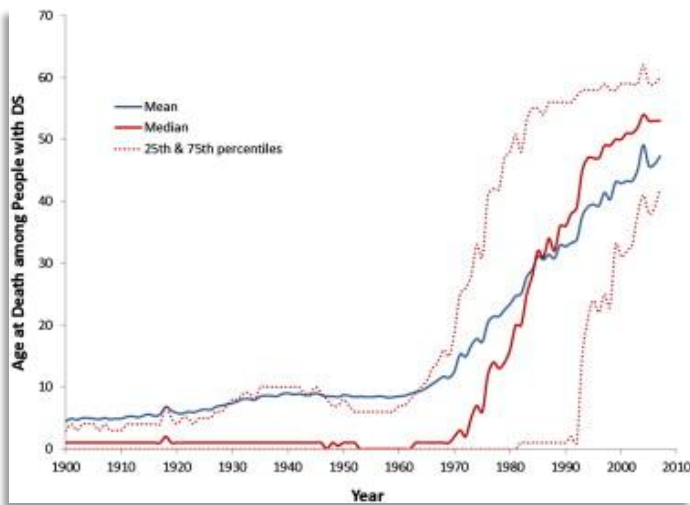
- Professor at the University of California, Irvine
- Chief Neuropsychologist in the Department of Neurology
- Co-Director of the Center for Aging Research in Down Syndrome
- PhD in Clinical Psychology at Northwestern University
- Throughout my career I have focused on key aspects of Alzheimer's disease
 - Memory loss in people with amnesia and Alzheimer's disease
 - Navigation impairments in people with Alzheimer's disease
- My work now focuses on how to prevent or treat Alzheimer's disease with lifestyle interventions
 - Exercise
 - Diet
 - Mental activity
- Also developing blood tests for detecting Alzheimer's Disease



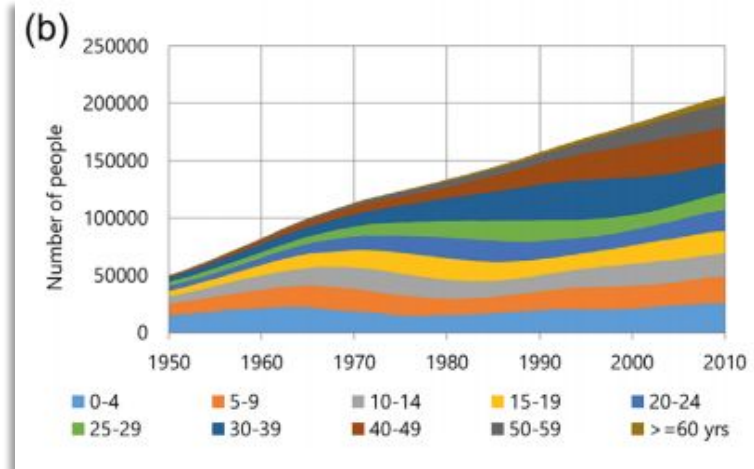
Overview

- Living longer with Down syndrome
- Links between Down syndrome and Alzheimer's Disease
- What is Alzheimer's disease
- Approved treatments – pharmacological
- Diagnosis
- Prevention
- How can we team up to find a cure?

People with Down syndrome are living longer



A 3.75-fold increase in average life expectancy since 1970 (Presson et al., J Peds., 2013).



Fastest growing segment is 40-49 years of age (Hithersay et al., 2019)

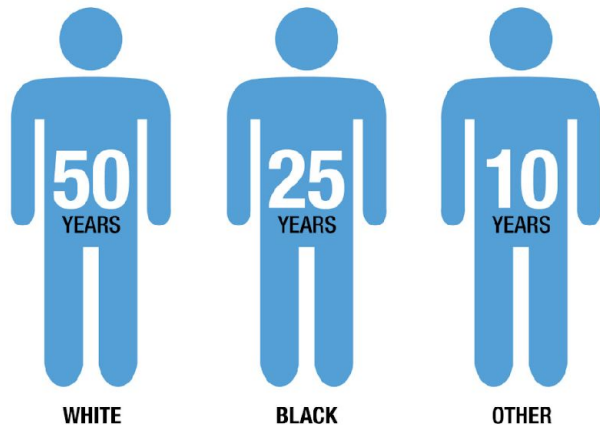
Disparities

Pediatrics
NATIONWIDE

years for other races.

About

MEDIAN AGE OF LIFE EXPECTANCY FOR PEOPLE WITH DOWN SYNDROME*



*Data from Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. *Lancet*. 2002;359:1019-25.

ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

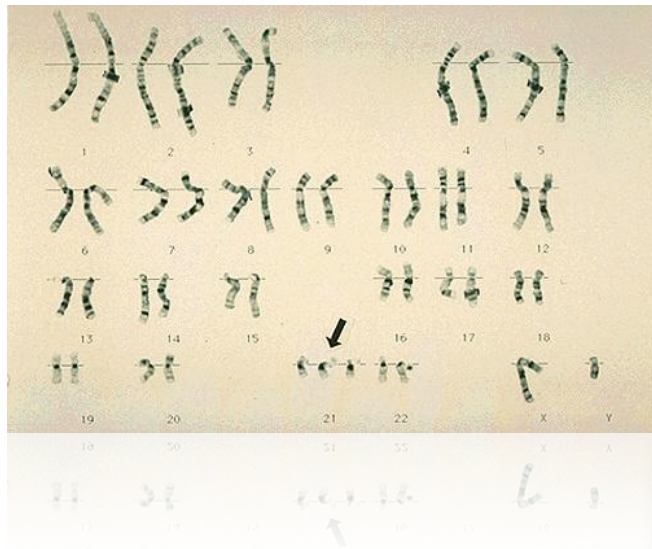


Contributions to Racial Disparity in Mortality among Children with Down Syndrome

Stephanie L. Santoro, MD¹, Anna J. Esbensen, PhD², Robert J. Hopkin, MD³, Lesly Hendershot, PsyD⁴, Francis Hickey, MD⁵, and Bonnie Patterson, MD²

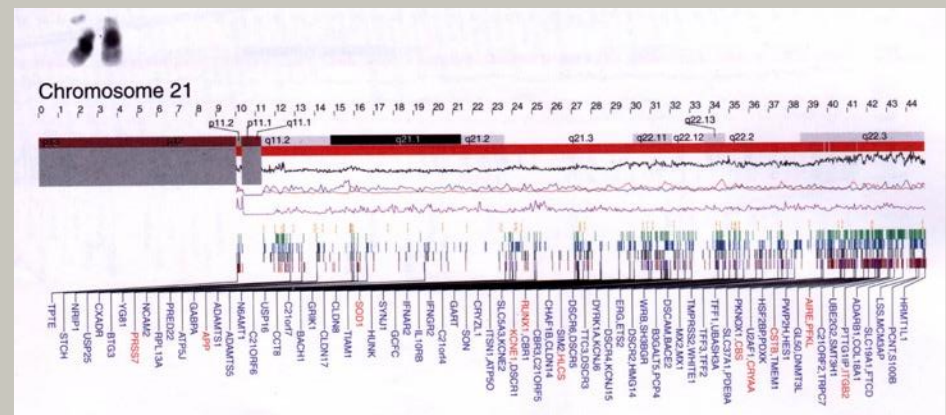


Aging people with Down syndrome are vulnerable to Alzheimer disease.

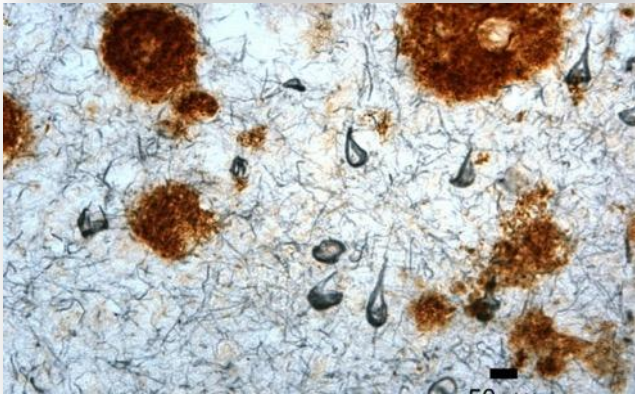


Amyloid precursor protein is present at 1.5 higher levels – overproduction of $A\beta$

People with Down syndrome are living longer and age is the biggest risk factor for Alzheimer disease

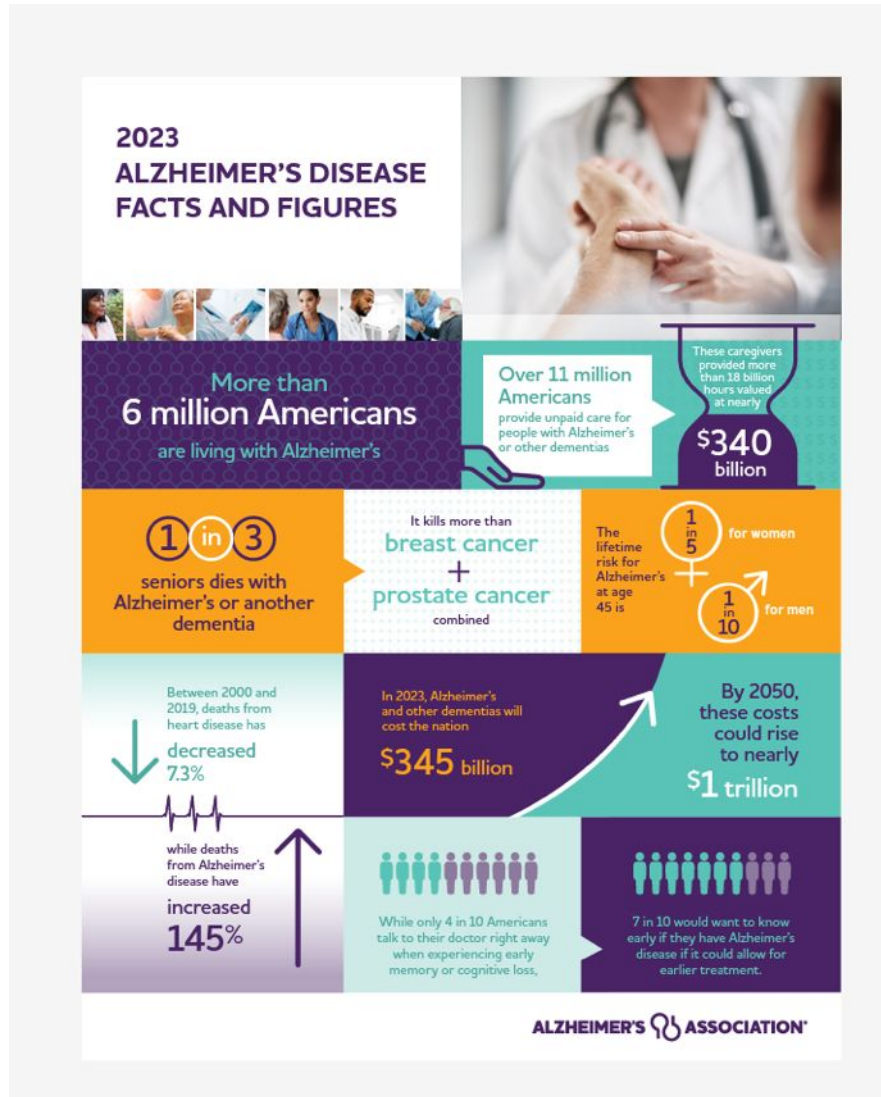


What is Alzheimer disease?

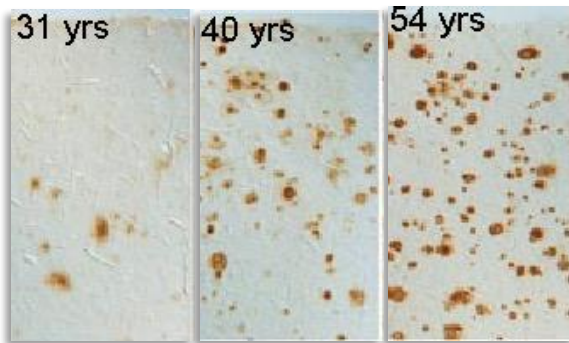


- Described by Alois Alzheimer in 1906
- The most common cause of dementia in the elderly
- Associated with a change in cognition and function that interferes with activities of daily living
- Diagnosed as possible or probable AD in the clinic
- Verified at autopsy – beta-amyloid plaques and neurofibrillary tangles

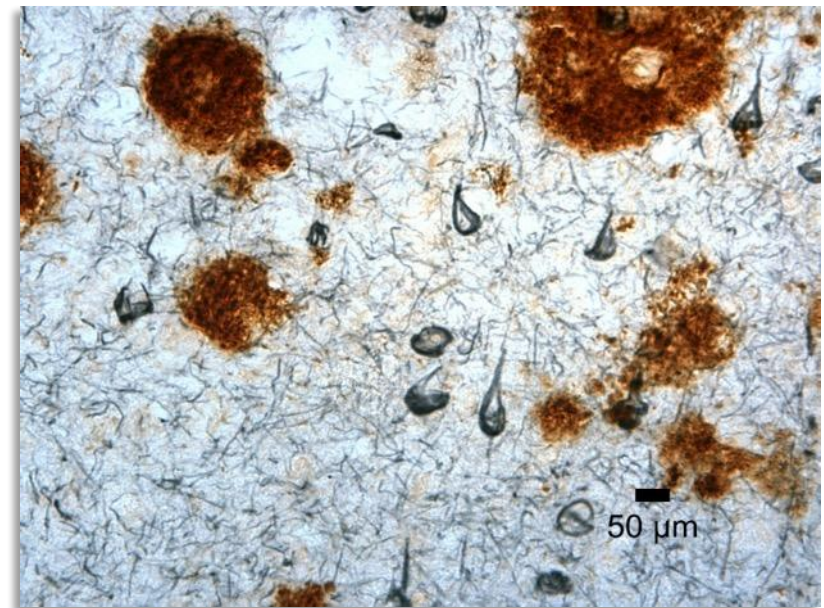
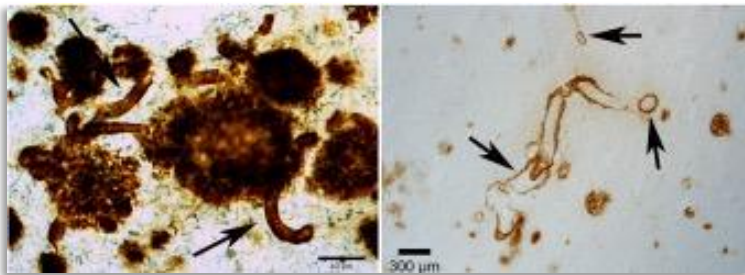
Alzheimer's Disease in USA



People with DS are vulnerable to AD with an earlier age of onset



Head, Azizeh, Lott, Tenner,
Cotman & Cribbs, 2001



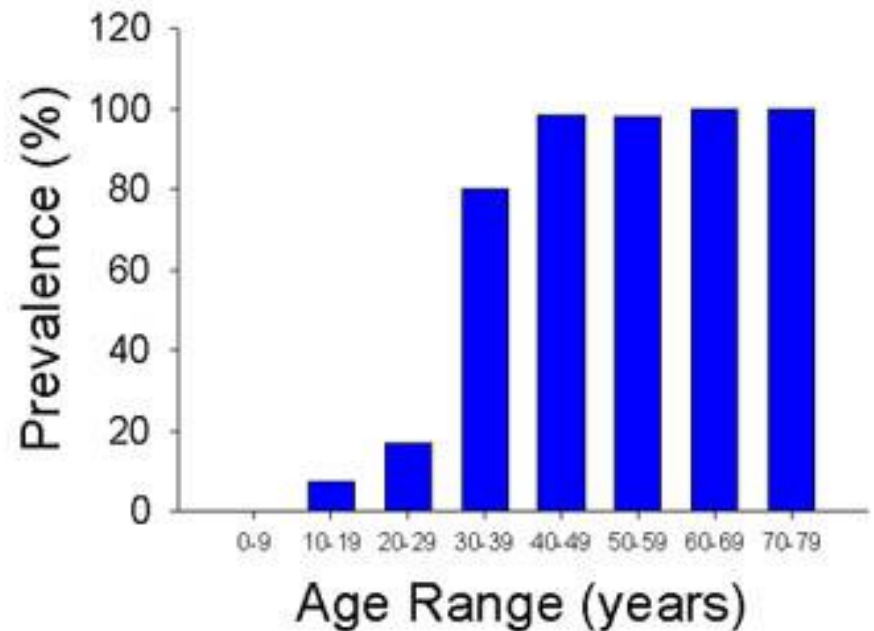
Head & Lott, 2019

Thank you to our amazing brain donors
for helping us understand how to find
ways to prevent or treat AD!

What is the age of onset of AD neuropathology in Down syndrome?

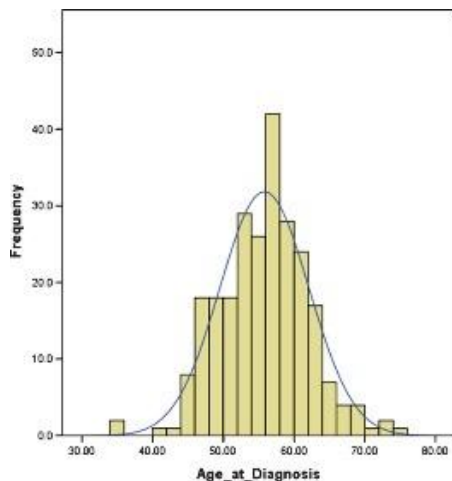
Virtually all adults with DS over the age of 40 years have sufficient neuropathology for AD (Struwe, 1929; Jarvis, 1948) – including plaques and tangles

***but wait there is more and its good news ***



Mann et al., 1993

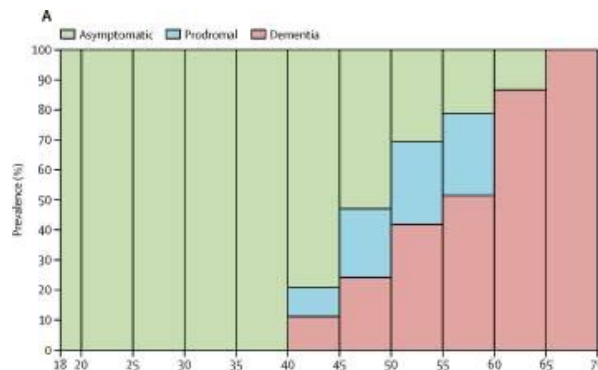
What is the typical age of onset of dementia in people with Down Syndrome (if they develop signs)?



Sinai et al., 2018.
Avg age is 55.8 yrs
(n=251)



Forte et al., Lancet, 2020
Median age of diagnosis of
dementia was 50.2 years
Prevalence increases
exponentially after 40
years of age (n=388)



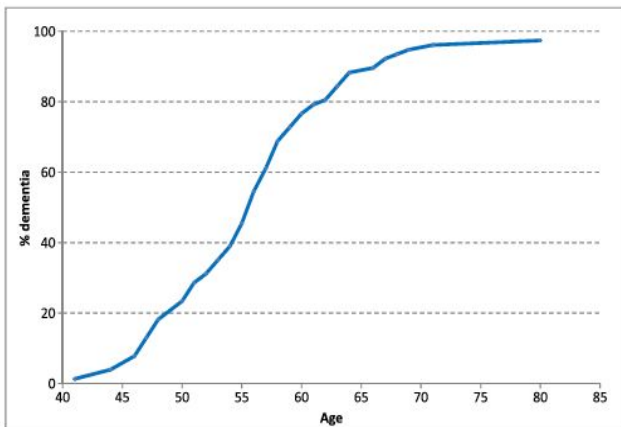
Strikingly similar age of onset across several studies of between **50 and 56 years** of age based on prevalence data

Of note, onset of dementia is over 10 years after the presence of sufficient neuropathology for a diagnosis of AD

Significant individual variability in age of onset (**up to 15% reach their 70's without signs of cognitive decline**)

Alzheimer Disease in people with Down Syndrome – some sobering facts

Near full penetrance of AD dementia



- AD limits the life expectancy for people with DS
- We need a treatment.

What are the currently approved treatments for dementia for people with Down syndrome?



From Mario D. Garrett PhD

Treatments at a glance for AD

Generic	Brand	Approved For	Side Effects
donepezil	Aricept	All stages	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
galantamine	Razadyne	Mild to moderate	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
memantine	Namenda	Moderate to severe	Headache, constipation, confusion and dizziness.
rivastigmine	Exelon	Mild to moderate	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
memantine + donepezil	Namzaric	Moderate to severe	Nausea, vomiting, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion and dizziness.

http://www.alz.org/alzheimers_disease_standard_prescriptions.asp



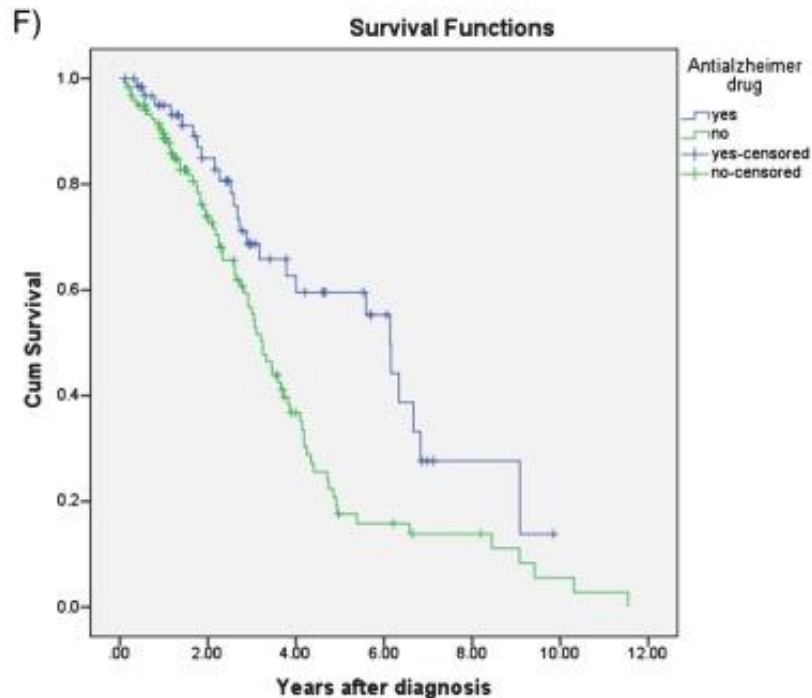
Overall

“Due to the low quality of the body of evidence in this review, it is difficult to draw conclusions about the effectiveness of any pharmacological intervention for cognitive decline in people with Down syndrome.”

Livingstone et al., 2015.

Side effects may be more frequent.

Use of anti-AD drugs and survival in people with Down Syndrome



Reduced mortality in people with Down Syndrome taking anti-Alzheimer drugs

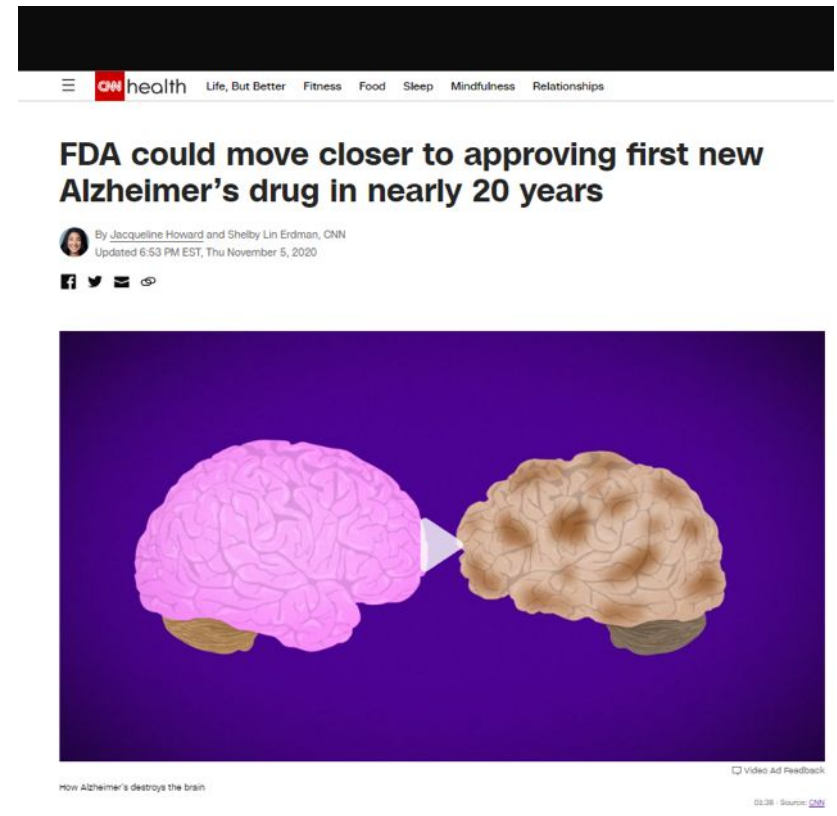
But not sure what this truly means

Sinai et al., JAD, 2018 (61): 717-728

Immunotherapies

(aducanumab, lecanumab, donanumab)

- Clinical trials have not included people with Down syndrome
- We do not know if they will help
- We do not know if there might be safety concerns
- Clinical trials dedicated to people with Down syndrome should be in 2024





Clinical Assessment of Dementia

- History of onset and progression
- Interview with patient and informant
- Compare current and previous abilities
- Identify deficits in cognitive, functional, and behavioral domains
- Directed neurologic exam
- Selected cognitive tests



Warning Signs of Dementia

- Difficulty with:
 - Learning and retaining information
 - Vocabulary
 - Daily tasks (hygiene, dressing, etc)
- Behavior changes: passive, irritable, suspicious
- Changes interfering with function
- Concerns should trigger evaluation



Mild Cognitive Impairment

- Informant reported decline in behavior or cognition
- Behavioral/cognitive decline not due to a primary medical or psychiatric condition
- Objective impairment on appropriate cognitive tests
- Functional abilities are relatively intact



Dementia

- Informant reported decline in behavior or cognition
- Behavioral/cognitive decline not due to a primary medical or psychiatric condition
- Objective impairment on appropriate cognitive tests
- Functional abilities are affected



Can We Prevent AD?

- Nothing has been proven to prevent or delay AD
- There is good reason to believe that protecting intact neurons will be more successful than repairing damaged ones
- AD is a complex disease and its likely that any reduction in risk or prevention would require multiple approaches
- Many prevention strategies will improve overall health and have minimal, if any side effects

Brain Fitness Strategies

- Manage comorbidities
- Healthy diet
- Physical activity
- Mental activity
- Social activities
- Stress reduction

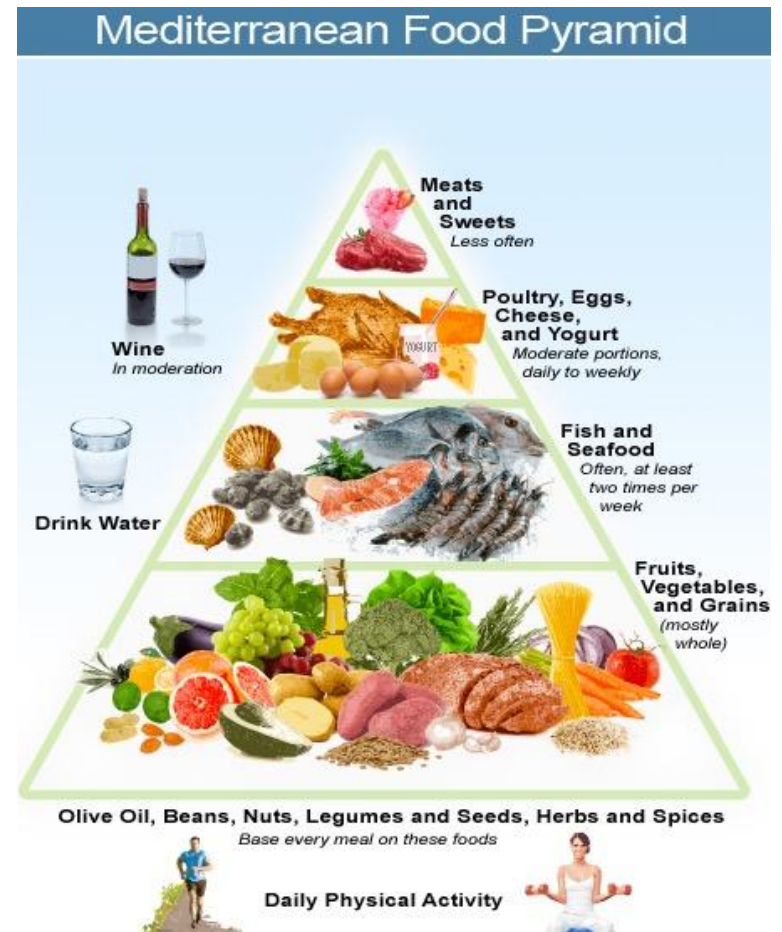


Manage Comorbidities

- Obesity, type II diabetes – raises risk for AD
- Poor cardiovascular function – can lead to blood vessels in the brain not working well
- Sleep apnea can lead to losses in brain volume in regions important for memory
- Stay on top of hypothyroidism treatment
- Vitamin deficiencies (e.g. vitamin D, B)
- Epilepsy
- Psychiatric conditions (e.g. Depression)

Healthy Diet

- Fruits and vegetables are high in antioxidants – better than supplements
- Mediterranean diet – lots of fish, nuts and healthy oils, fruits and vegetables
- A healthy diet can reduce obesity and associated risk factors



Physical Activity

- Reduces risks associated with obesity and cardiovascular function
- Can help the brain grow new neurons!
- Stimulates the brain to make growth factors to support healthy cells
- How much? What kinds?



Mental Activity

- Accelerates the rate new brain cells are created
- Enhances the chances of new neurons' survival
- Strengthens the synapses (connections) among neurons
- Chemicals released in the brain make existing neurons happier and healthier



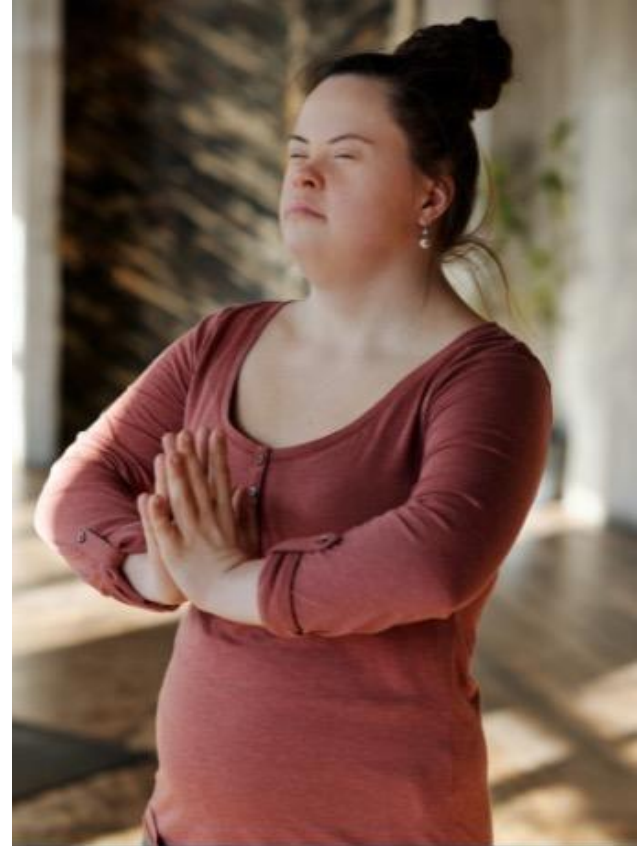
Social Activities

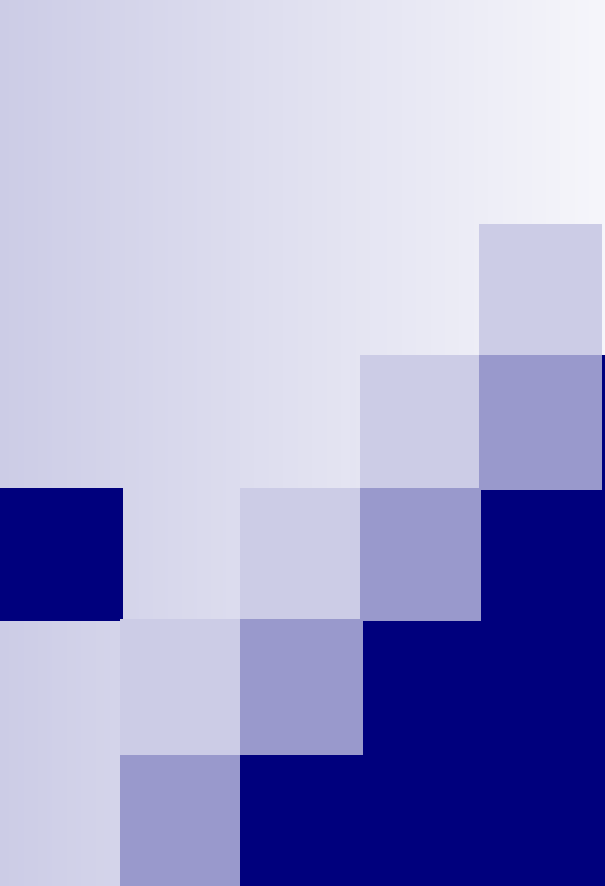
- Social activity engages the brain and the more active your brain, the more neurons are stimulated to make connections and stay healthy
- People with very active social lives, lots of friends tend to be more protected against AD



Stress Reduction

- Stress is bad for the brain and is related to AD risk
- Stress affects memory and promotes anxiety
- Stress leads to inflammation and chronic stress leads to chronic inflammation





Working to understand Alzheimer's
Disease risk in people with Down
Syndrome

COMMUNITY
PARTNERSHIP!

How do we become good partners?

- Ensure that community members with DS have a seat at the table
 - Seek feedback at every stage of research
 - Advertising
 - Informed consent
 - Procedures
 - Setting/ Location
- Acknowledge that traditional sources of DS recruitment have failed to engage diverse community members.
 - Care providers
 - Support Groups
 - Conferences
- Meet the community where they are
 - Identify how research can be of service to the community
 - Community is acutely aware of "hit and run" approach
- Identify challenges and barriers to participation
 - Costs both monetary and time
 - Acknowledge that these factors may differ in diverse communities and attempt to design research studies that can be as inclusive as possible.

Community Resources

HHH ABC-DS

Home

About Us

For Participants & Caregivers

For Researchers

News & Publications



Join more than 200 people like you driving breakthroughs

By partnering with us, you're joining the fight against Alzheimer's disease in the Down syndrome community.

 **The KNOWLEDGE FORUM**
Presents...an Evening Workshop

A Look at the Connection Between Down Syndrome and Alzheimer's Disease: A Research Study

When: Tuesday, May 30, 2023

Where: Online via Zoom

Time: 6:30 - 8:00pm

Admission: Free

Register: Sign Up Here (or scan the code) to register and receive further instruction to attend.

Note: The Forum is being recorded and will be posted online for future viewing.



The Alzheimer Biomarkers Consortium-Down Syndrome (ABC-DS) is a longitudinal study to follow a cohort of adults with Down syndrome over time to identify early biomarkers that may herald the onset of Alzheimer's disease. The investigators hope that these biomarkers can be used to inform clinical trials and improve the quality of life in people with Down syndrome and for the general population.



Presenters



JOIN US as Dr. Anne Cohen introduces the study being conducted on Alzheimer's Disease and Down Syndrome. Dr. Handen, one of the principal investigators of ABC-DS, will discuss recent findings from this large study of the aging brain in Down Syndrome. Dr. Kati, Principal Investigator of the Alzheimer's Clinic Trial Consortium Down Syndrome will discuss findings from the Trial Ready Cohort-Down Syndrome study and the potential for future clinical trials for Alzheimer's disease therapies in adults with Down Syndrome.

Center Region Down Syndrome Society (CRRSS) | 221 W. Hamilton Avenue # 215, State College, PA 16801 | centerregiondownsyndrome.org



Aging and Down Syndrome

On Saturday, April 1, 2023, please join the Albert Pajula Wellness Center for Adults with Down Syndrome and Dr. Beau Asmus from Washington University for a discussion on Aging and Down syndrome.

In 1983, the life expectancy for individuals with Down syndrome was 25 years. With advances in medicine and education individuals with Down syndrome are now living into their 60s and beyond. Adults with Down syndrome will show physical, medical, and cognitive signs of aging much earlier than what is expected for their age.

Topics to be discussed include:

- Potential health concerns associated with aging
- Behavioral and mental health concerns associated with aging
- Recognizing and dealing with an Alzheimer's disease diagnosis



Understanding Alzheimer's and Dementia: A Focus on People Living with Down Syndrome





Summary

- People with DS are at a higher risk for AD with an earlier age of onset but NOT EVERYONE DEVELOPS DEMENTIA
- Current treatments for Alzheimer's disease include both pharmacological and nonpharmacological interventions
- Prevention approaches are very promising and include modifying lifestyle risk factors
- New treatments are in the pipeline



Take home messages

- A healthy diet – lots of fruits and vegetables
- Exercise – make it fun! Dancing counts 😊
- Make friends – and then make more friends and keep visiting with friends
- Play (board games, computer games), learn new things (music, drawing, cooking), take classes
- Make sure you are getting lots of good sleep
- All of these reduce your risk factors
- Prevention is more powerful than treating a disease

Be active and proactive!

Advocate and self-advocate for more research to help us find ways to improve health in aging people with Down syndrome

Volunteer 😊





Thank you!