What's New in Dementia Research and Care?

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Today’s Conversation

• Who We Are
• Alzheimer’s Association International Conference 2015 Overview
• Dementia and Alzheimer’s Disease Facts
• Risk Factors
• Biomarkers
• Interventions
• Prevention Trials
• Questions

Our vision is a world without Alzheimer’s disease

Our mission:
• Advance research
• Provide care and support
• Increase Concern & Awareness
• Public Policy & Advocacy Efforts

Alzheimer’s Association International Conference (AAIC) 2015

• The world’s largest Alzheimer’s research conference
• Just took place in Washington DC
• Over 4500 researchers from 65 countries
• 489 speakers in 87 sessions
• 1225 poster presentations
• 8 corporate symposia and 106 ancillary meetings
• 135 exhibitors

AAIC 2015: Dementia Care Research and Practice Track

• Two-day track
• 2 plenary speakers
• 11 dementia care research sessions
• 4 dementia care practice session
• 132 poster presentations
**Dementia & Alzheimer’s Disease**

- Dementia is the loss of memory due to changes in the brain
- Alzheimer’s is the most common form
- Definite diagnosis used to require autopsy
- Many mixed cases
- Many memory disorders are reversible and not truly dementia

**The Alzheimer’s Epidemic Continues to Grow…**

- 5.3 million Americans of all ages will have Alzheimer’s in 2019
- 6th leading cause of death in the U.S.
- $1.1 trillion in 2019
- More than 28 million Baby Boomers will develop Alzheimer’s between 2015 and 2050
- 37% will have Alzheimer’s before they die
- In 2040, 10.3 million Boomers will have the disease — nearly twice as many as total today
- In 2050, half of Baby Boomers will have Alzheimer’s

**Baby Boom Generation = Generation Alzheimer’s**

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**Hope In Research**

- 6th leading cause of death across all ages
- 5th leading cause of death for those aged 65 and older
- Only cause of death among the top 10 in America without a way to prevent, cure or even slow its progression.

**National Plan to Address Alzheimer’s disease**

**Goals:**

- Prevent and Effectively Treat Alzheimer’s Disease by 2025
- Enhance Care Quality and Efficiency
- Expand Supports for People with Alzheimer’s Disease and Their Families
- Enhance Public Awareness and Engagement
- Improve Data to Track Progress

**Risk Factors**
Alzheimer's Disease

- Tangles and plaques

Risk Related to Cognitive Decline & Alzheimer's
- Age: The greatest known risk factor
- Heart-head connection
  - Increased risk suspected if high blood pressure, heart disease, stroke, diabetes and high cholesterol
- Head injury
- Family history
- Risk and deterministic genes

Risk Factors for Alzheimer's Disease, Dementia & Cognitive Decline
- Type 1 Diabetes (T1D) and Dementia
  - First study to report the dementia risk, including Alzheimer's, in older adults with T1D.
  - The researchers used a healthcare database of more than 490,000 people. 230 of them had T1D.
  - People in the study with T1D were 93% more likely to get dementia (73% after adjustment for heart health risk factors) compared with people without diabetes.

Early Life Risk Factors for Alzheimer's Disease, Dementia & Cognitive Decline
- School Performance and Occupation
  - 1st Study
    - Risk elevated 21% in individuals with the lowest 20% of early-life school grades.
    - Risk reduced 23% among individuals in occupations characterized by high complexity with data and numbers.
    - Lowest risk (39% reduction) found in group who had both higher childhood school performance and high occupational complexity.
  - 2nd Study
    - Risk elevated more than 50% in individuals over 75 with the lowest 20% of early-life school grades.
    - Individuals who completed secondary education had lower risk compared to individuals with only elementary education (28% lower risk).
    - Women who had an occupation with high complexity with people were at 60% lower risk of developing dementia compared to those who had an occupation with low complexity with people.

Early Life Risk Factors for Alzheimer's Disease, Dementia & Cognitive Decline
- Low Physical Activity and High TV Viewing
  - Studied the association of long-term patterns of low physical activity and high television viewing time over 25 years with cognitive function at mid-life.
  - Study participants with low levels of physical activity over 25 years had significantly worse cognition in mid-life.
  - Participants with high levels of TV watching over 25 years also had significantly worse mid-life cognitive function.
  - Study participants with both long-term low physical activity and high television viewing were almost 2x more likely to have poor cognitive function in mid-life.

Women and Risk for Cognitive Decline and Dementia
- Almost two-thirds of the 5 million Americans living with Alzheimer's are women
- 60% of Alzheimer’s & dementia caregivers are women
- Three new studies suggest there may be biological reasons women are at higher risk than men:
  1. Cognitive Decline 2X as Fast as Men
  2. General Anesthesia and Cognitive Decline
  3. APOE ε4 Alzheimer’s Risk Gene and Gender
Translating Scientific Evidence to Program Delivery

Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective

Matthew Baumgartner, Heather M. Snyder, Martha C. Carrillo, Sara Furtado, Hye-Keun Kim, Hung Jakes, Adapted from Sperling et al. 2011

What is a Biomarker?

- Biological marker to measure change
- Reliable predictor and indicator of disease and disease progression

Example
- Glucose for Diabetes
- Cholesterol for Heart disease
Amyloid PET Imaging

RED = maximum uptake
VIOLET = minimum uptake

New Possibilities for Early Detection (Novel Biomarkers)

- Brain PET Imaging of Inflammation
  - Inflammation in the brain is clearly involved in Alzheimer’s
  - Tools to detect inflammation may be helpful in understanding what is happening in the disease and also of research studies of inflammation-targeted therapies.

New Possibilities for Early Detection (Novel Biomarkers)

- New CSF Biomarker: Neurogranin
  - Found only in the brain, involved in brain cell-to-cell communication pathways
  - Baseline levels of neurogranin were significantly higher in individuals with Alzheimer’s
  - Levels higher in MCI individuals who progressed to Alzheimer’s and were predictive of progression from MCI to Alzheimer’s
  - Neurogranin levels were strongly correlated with two other Alzheimer’s-related proteins

New Possibilities for Early Detection (Novel Biomarkers)

Saliva
- A small but intriguing study suggests it could be possible to detect Alzheimer’s-like proteins in saliva
- Researchers identified proteins in the saliva that differentiated the Alzheimer’s and MCI groups, they also predicted worse cognition

Modernizing the Diagnosis of Alzheimer’s Based on a Continuum

Normal Pre-clinical MCI Alz dementia

APOE Protein or gene “barcodes”
Family history Tau/Alzheimer (CSF, blood, eye)
MRI, CT PET, fMRI

Subjective problem in memory or another domain, informant corroborated and measurable on tests; normal overall cognition and ADLs

Clear deficits in 2 or more core cognitive domains; ADLs affected

Interventions
Pathway to Develop Interventions

Drug Discovery and Development: A LONG, RISKY ROAD

Current Alzheimer's Therapies: Symptomatic

- Cholinesterase Inhibitors
  - Tacrine (Cognex)
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Razadyne)

- Glutamate Modulators
  - Memantine (Namenda)

Combination Therapies
- Donepezil & memantine (Namzaric)

Therapeutic Agents in Phase I and II Clinical Trials for Alzheimer's Disease
- AADvac1
- ABT-957
- Alphagamma
- ANAVEX-2-73
- AZD0530
- BAN2401
- Bevacizumab
- BI 409306
- Blood plasma
- Brivatan
- CPC-201
- Crizanlumab (MABT5102A)
- DAIO-B
- DBS-f
- E2609
- Encence
- Exendin-4
- GOC21109
- IVig
- JNJ-54861911
- KH69440
- Ladinagal
- Levelacacetam
- Longitudine
- Lu AF20513
- LY3200268
- ME201814
- Membraneleak stem cells
- Methylone
- MK-762
- NCS-15
- Nicotinamide
- PO912
- PX703864
- Rassagline
- R04G0502
- RPH201
- R-Pramipexole
- Sargramostim
- S-Equol
- Simvastatin
- T-817MA
- Tetrahydrobiopterin
- TPI-287
- Transcranial magnetic stimulation (TMS)

Therapeutic Agents in Phase III Clinical Trials for Alzheimer's Disease
- AZD3293
  - Astrazeneca/ Lilly
  - BACE inhibitor
- Encence
  - Forum Pharmaceuticals
  - Nicotinic receptor agonist
- Gantenerumab
  - Hoffman-La Roche
  - Multimodal antibodies against beta amyloid Part of Data-7U
- Insulin
  - Alzheimer’s Disease Cooperative Study
- IVig and Albumin
  - Grifols
  - Intravenous immunoglobulin
- Lu AE50054
  - H. Lundbeck
  - 5HT6 receptor antagonist
- Masitinib
  - AB Science
  - Inhibitor of c-KIT cell signaling
- MK-8931
  - Merck
  - Monoclonal antibody against beta amyloid
  - Part of DIAN-TU
- Nilvadipine
  - St. James Hospital
  - Calcium Channel Blocker
- Pioglitazone
  - Takeda
  - PPAR-gamma activator
- Sodium Oligo-mannuronate
  - Shanghai Greenvalley Pharmaceutical
- Solanezumab
  - CSL Ltd
  - Humanized antibody against beta-amyloid
- Tau aggregation inhibitor
- TTP488
  - TauRx
  - Tau aggregation inhibitor
- VRT-101
  - (Axovant)
  - Results of a Phase 2a study
  - Advancing to Phase 3 trials
- TTP488 (vTv, formerly Trans Tech)
  - Oral antagonist of the Receptor for Advanced Glycation Endproducts (RAGE)
  - TTP488 has been granted Fast Track Status by FDA and is entering Phase 3
- AVP-923: Dextromethorphan/Quinidine (Avanir)
  - Investigated for Alzheimer’s-related agitation
  - Approved for pseudobulbar affect (involuntary laughing or crying) in MS and ALS
  - Provided significant improvement in agitation in patients with Alzheimer’s in 10 week trial

Experimental Drug Trial Results: Potential Disease Modifying Treatments
- Solanezumab (Lilly)
  - EXP1 and EXP2 Phase 3 placebo-controlled studies did not meet endpoints
  - Delayed start analysis of solo open label
- Gantenerumab (Roche)
  - Humanized Aβ antibody in a 2-year Phase 3 trial in very mild Alzheimer’s
  - Dose-dependent reductions in brain β-amyloid and CSF Tau; Aβ42 levels unaltered
  - Trial did not meet its cognitive endpoints.
- Aducanumab (Biogen)
  - Shows solid safety and tolerability profile in Phase 1b trial
  - Dose dependent slowing of cognition loss in individuals with mild disease / confirmed β-amyloid in brain
  - Need larger, longer trial (Phase 3) – Biogen has made a $2 Billion commitment to go to Phase 3

Experimental Drug Trial Results: Potential Symptomatic Treatments
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Maximizing Independence at Home (MIND at Home)

- 18 month randomized intervention trial including 303 volunteers, 290 caregivers
- Goal: To determine if providing assistance in obtaining appropriate care for older adults with memory problems helps them remain at home longer, as well as improve life quality
- People with help at home able to stay in home 10 months longer than those without help
- Presented at AAIC in 2012

Exercise as Treatment: Living Better with Dementia

- Three new trials of aerobic exercise in Alzheimer’s, vascular cognitive impairment and mild cognitive impairment
- Exercise or regular physical activity might play a role in both protecting your brain from Alzheimer’s, and also living better with the disease
  1. Improvement on Psychiatric Symptoms with Mild Alzheimer’s
  2. Tau Levels in CSF with MCI and Diabetes
  3. Improved Memory and Attention with Mild Vascular Cognitive Impairment

AAIC Technology & Dementia Preconference

- Organized by the ISTAART Technology Professional Interest Area
- Engages ETAC awardees
- Topics include:
  - Technology integration in clinical trials to monitor intervention effectiveness
  - Global collaborative funding models
  - Technology implications for big data and dementia science
  - Emerging role of technology in dementia research – focus on mobile/ wearable technologies and use of internet

Prevention

Possible Prevention of Alzheimer’s?

- Primary prevention: Removal of amyloid plaques
- Secondary prevention: Delay and reduce cognitive impairment in individuals with evidence of pathology
- Tertiary prevention: Treatment of Alzheimer’s disease
Why is this important for this target audience? Can this group be Istaart members? Is there a recommended PIA for them?

Nancy Cullen,
Collaboration for Alzheimer’s Prevention

Alzheimer’s Prevention Initiative

ApoE Trial
- Two Copies of Risk Gene
- 1,300 adults, age 60-75
- Partnering with Novartis – two drugs:
  - CAD106: active immunotherapy
  - Beta secretase inhibitor
- Received $33.2 million from NIH

Alzheimer’s Association Leverages Support for API APOE4 Trial

- Alzheimer’s Association, GHR Foundation & FBRI $10 million to the API APOE4 Trial
- Award will enable the trial to:
  - Maximize PET imaging, including Tau, Amyloid and FDG for trial participants
  - Expand the API Registry, including APOE genotyping and online cognitive testing
  - Evaluate two remote genetic counseling approaches (telephone/ video counseling) in a sub-study population

Dominantly Inherited Alzheimer’s Network Trial (DIAN-TU)

- DIAN: Autosomal dominant Alzheimer’s disease (ADAD)
- $4.2 million award to launch
- Testing three simultaneous drugs:
  - Gantenerumab (Roche, Ab antibody)
  - Solanezumab (Lilly, Ab antibody)
- TBD
- 22 months later: Received $6 million from NIH
- A year after that: Received $23 million additional from NIH

DIAN Families Gather at AAIC15

- First ever meeting
- More than 100 participants and family members
- Joined by another 100 researchers, government officials, pharma companies, etc. in the afternoon
- Research updates, educational sessions, support groups
- Shared their unique family stories and impact with others

FINGER Study: Receipt of Lifestyle Interventions for Cognition

- Gold standard of testing any type of therapy or intervention – Randomized Control Trial (RCT)
- Large, rigorous study
- First solid evidence that receipt of lifestyle interventions reduces cognitive decline
- Needs to be replicated in more diverse populations
$300 million proposed by US House for Alzheimer's research

- US House of Representatives proposed a bill to increase funding for Alzheimer's research by $300 million
- If approved, biggest increase in Alzheimer's research funding ever
- Be informed, get involved at alz.org/advocate

What Can You Do Now?

- Learn more about AD and person-centered care
- Talk about your experience
- Participate in Longest Day or Walk to End Alzheimer's
- Talk to your legislators
- Support research
- Maintain overall health

Resources to help YOU

- Over 25,000 certified
- Have your curriculum reviewed to meet the Alzheimer's Association Dementia Care Practice Recommendations.
- www.alz.org/trainingreviews

THE END OF ALZHEIMER'S STARTS WITH YOU