Risk Factor Reduction and Dementia Prevalence

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San Francisco VA Medical Center
The Impending Dementia Epidemic
Global Dementia Prevalence

2010

36 million

58% low/middle income

2050

115 million

70% low/middle income

Societal Costs

- >$600 billion in 2010
  - 1% GDP
  - 70% W. Europe & N. America
- U.S. costs
  - 2010: $159-$215 billion
  - 2040: $379-$511 billion
- *Current medications do not change the disease course*

Hurd et al., NEJM 2013
Delaying Dementia Onset Could Prevent Millions of Cases

Brookmeyer et al., Alzheimer’s & Dementia, 2007
Risk Factors & Prevention Strategies
Vascular Risk Factors:
“What’s good for the heart is good for the brain.”
Vascular Disease and Dementia

- 80% Alzheimer’s or vascular
  - Most ‘mixed’ at autopsy
  - Vascular + Alzheimer’s ➔ earlier, more severe
- Risk factors for vascular disease are modifiable/treatable
  - Preventing/treating vascular risk factors may prevent/delay onset of dementia

Ligthart et al. 2010, Vascular Health and Risk Management
Diabetes and Dementia

- Diabetes → 40% higher risk
  - Esp. vascular dementia
- Impact of diabetes treatment
  - ADVANCE trial: >11,000, intensive vs. standard
  - No difference in cognitive decline
  - Slightly higher dementia risk with intensive
- Hypoglycemia → increased risk
- *Treat, but don’t overtreat*

Hypertension and Dementia

- Inconsistent association
  - Mid-life hypertension: 60% higher risk
  - Late-life hypertension: inconsistent
  - Late-life hypotension: higher risk

- Impact of hypertension treatment
  - Cochrane: 4 RCTs, ~16,000, tx vs. placebo
  - OR=0.89 (95% CI: 0.74, 1.07)

- Treatment may delay dementia onset

Power et al. 2011, Epidemiology; Ligthart et al., 2010 Vasc Health Risk Management; McGuinness et al. 2009, Cochrane Database Syst Rev
Obesity and Dementia

- Inconsistent association
  - Mid-life obesity: 60% higher risk
  - Late-life obesity: inconsistent/lower risk
  - Late-life underweight/weight loss: higher risk

- Impact of weight loss
  - Intentional weight loss in obese, mid-life → ↑ cognitive function

- Benefits of weight loss in late life unclear

Profenno et al. 2010, Biol Psychiatr; Siervo et al. 2011, Obesity Rev
Mental Health Risk Factors
Depression and Dementia

- Depression → 90% higher risk
  - True risk factor or early symptom?
- Mid-life vs. late-life depression
  - Mid-life only: 20% higher
  - Late-life only: 70% higher, esp AD
  - Mid-life + late-life: 80% higher, esp VaD
- Impact of treatment
  - Improved cognitive function, still below normal
  - Delayed dementia onset?

Byers & Yaffe, Nat Rev Neurol 2011; Ownby et al., Arch Gen Psychiatr 2006; Barnes et al., Arch Gen Psychiatr 2012; Nebes et al. J Psychiatr Res 2003; Reynolds et al., Arch Gen Psychiatr 2011
Lifestyle Risk Factors
Exercise and Dementia

- Observational studies
  - ↑ aerobic fitness → ↓ cognitive decline
  - ↑ physical activity → ↓ dementia
  - Physical inactivity → 80% higher risk

- Randomized, controlled trials
  - Aerobic/resistance → ↑ cognitive function
  - Home-based exercise → ↓ cognitive decline

Aerobic Exercise Increases Hippocampal Volume

Erickson et al., PNAS 2010
Mental Activity and Dementia

- Observational studies
  - Higher education, IQ, occupation, mental activity, brain size → ↓ dementia
  - Low education → 60% higher risk
  - **Cognitive reserve hypothesis**

- Randomized, controlled trials
  - Mental activity → ↑cognitive domain trained

Cognitive Training Improves Specific Domain Trained

2,832 adults age ≥65

* * * * 

Ball et al., JAMA 2002; Willis et al., JAMA 2006
Cognitive Training Improves Specific Domain Trained

2,832 adults age ≥65

Training Group

- Memory
- Reasoning
- Speed

*p<0.05

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Tai Chi & Social Activity
Increase Brain Volume

N=120 Shanghai elders

*Mortimer et al., J Alz Dis 2012*
The Mental Activity and eXercise (MAX) Trial

Healthy, Inactive Elders with Self-Reported Cognitive Decline
N=126

Posit Science Intervention
N=63

- Aerobic Intervention
  N=32

- Stretching Control
  N=31

Educational DVD Control
N=63

- Aerobic Intervention
  N=31

- Stretching Control
  N=32
The MAX Trial

- Significant improvement in cognitive and physical function over 12 weeks
- No differences between groups
- Amount/variety of activity may be more important than type

Barnes et al., JAMA Intern Med 2013
Benefits of Physical, Mental & Social Activity in Dementia

- Physical activity $\rightarrow$ ↑ physical function, quality of life
- Cognitive stimulation $\rightarrow$ ↑ cognitive function, well-being
- Dancing $\rightarrow$ ↓ problematic behaviors, ↑ enjoyment

Potter et al., Int J Geriatr Psychiatr 2011; Aguirre et al., Ageing Res Reviews 2012; Guzman-Garcia et al., Int J Geriatric Soc 2012
Smoking and Dementia

• Early studies:
  • Smoking ➔ lower dementia
  • Many funded by tobacco industry

• Newer studies:
  • Current smoking ➔ 60% higher risk
  • Secondhand smoke + vascular dz ➔ 3X higher
  • Quitting smoking has many health benefits and may lower dementia risk

Anstey et al., 2007, Am J Epidemiol; Cataldo et al., 2010, J Alzheimer Dis; Barnes et al., 2009, Am J Epidemiol
Potential Impact of Risk Factor Reduction
What if we could change risk factor prevalence?

- Population attributable risks (PARs)
  - Tools to estimate impact of risk factor reduction
  - Used to guide public health and public policy
  - Take into account risk factor prevalence and strength of association
### PARs for AD, Worldwide

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<td>6%</td>
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<td>1.6 (1.3, 1.9)</td>
<td>3%</td>
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_Barnes & Yaffe, Lancet Neurol, 2011_
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Summary & Conclusions
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- Dementia prevalence expected to triple over next 40 years
  - High societal costs, no effective treatments
- Up to half of dementia may be attributable to modifiable/treatable risk factors
  - Physical inactivity, low education, smoking, depression, vascular risk factors
- Lifestyle interventions promising
  - Delaying onset
  - Improving function and well-being
Challenges & Next Steps

- Promote change at a societal level
  - National programs to increase educational attainment and physical activity
  - Promote smoking cessation
  - Treatment of cardiovascular risk factors and depression
- Address the needs of currently affected
  - Programs to maintain function and quality of life
  - Reduce caregiver stress
It Takes A Village...

- Kristine Yaffe, MD
- Colleagues:
  - Amy Byers, Sei Lee, Laura Middleton, Rebecca Sudore, Rachel Whitmer, Brie Williams
- Research Staff
  - Wanda Reiman, Jacy Leonardo, Ellie Dayton (Shirgul), Gina Poelke, Wendy Santos-Modesitt, Matthew Beristianos
- Volunteers
  - Yani Leyva, Serena Galloway, Gabrielle Gotta, Ann Tran, Todd Rising, Andrew Bloch
- Summer Interns
  - Sierra Ford, William Goodson, Omar Meziab
- Programming assistance
  - Katharine Kirby
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  - UCSF Department of Medicine Bridge Funds
  - VA Health Services Research
  - Community Foundation Sonoma County
  - Department of Defense
  - Bechtel Foundation
  - NARSAD

- My physical and mental activity training team