Welcome

Please stand by. We will begin shortly.

Smoking and Dementia:
Are You at Risk for Alzheimer's?

Wednesday, June 25th, 2014 · 2pm ET (90 minutes)

SMOKING CESSATION LEADERSHIP CENTER

Disclosure

Dr. Eric Larson, Dr. Steve Schroeder and Catherine Saucedo have disclosed no financial interest/arrangement or affiliation with any commercial companies who have provided products or services relating to their presentation or commercial support for this continuing medical education activity.

Moderator

Catherine Saucedo

- Deputy Director, Smoking Cessation Leadership Center, University of California, San Francisco
- **csaucedo@medicine.ucsf.edu**

Agenda

- **Welcome**
  - Catherine Saucedo
- **Presentation**
  - Eric Larson, MD, MPH, MACP
- **Q&A**
- **Closing Remarks**

Thank you to our main funders

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Housekeeping

- All participants will be in **listen only mode.**
- Please **make sure your speakers are on** and adjust the volume accordingly.
- If you do not have speakers, please request the dial-in via the chat box.
- **This webinar is being recorded** and will be available on SCLC's website, along with the slides.
- **Use the chat box to send questions** at any time for the presenter.

Poll question

- How much do you know about the prospect of preventing Alzheimer's by quitting smoking?
  - I am unfamiliar with this topic
  - I know a little about this topic
  - I know a lot about this topic

Today's Speaker

GroupHealth

Eric B. Larson, MD, MPH, MACP

- Vice President for Research, Group Health
- Executive Director, Group Health Research Institute

GroupHealth.

Smoking and Dementia: Are You at Risk for Alzheimer's?

The Evolving Story of Alzheimer's and Late Life Dementias: Prospects for Prevention

Eric B. Larson, MD, MPH
Vice President for Research, Group Health
Executive Director, Group Health Research Institute
Professor, Medicine and Health Services, University of Washington
Principal Investigator, Adult Changes in Thought Study (ACT)/ Alzheimer's Disease Patient Registry (U01-AG-06781)
June 25, 2014 Smoking Cessation Leadership Center

Disclosure

GroupHealth.

Nothing to disclose

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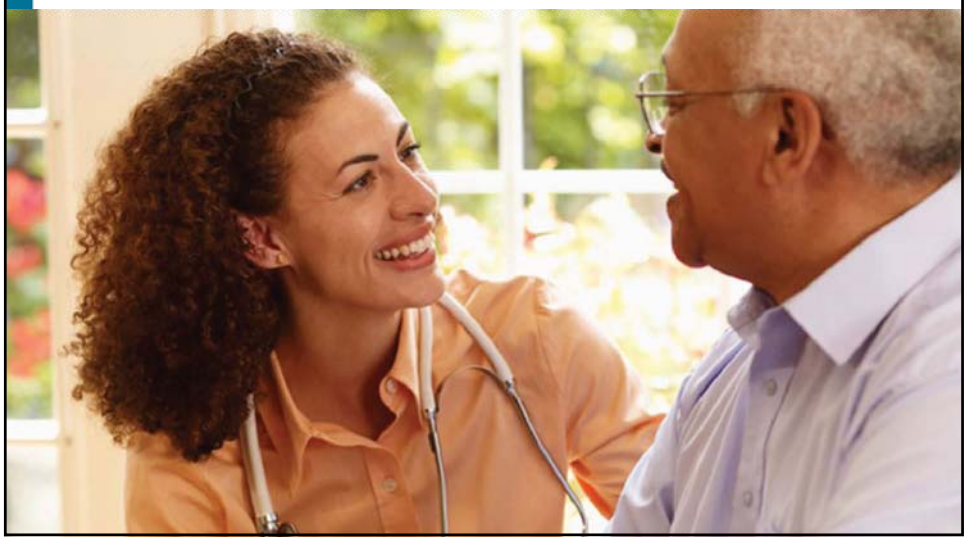
Group Health Research Institute

Practical research to help people like you and your family stay healthy

GroupHealth.



Group Health Research Institute

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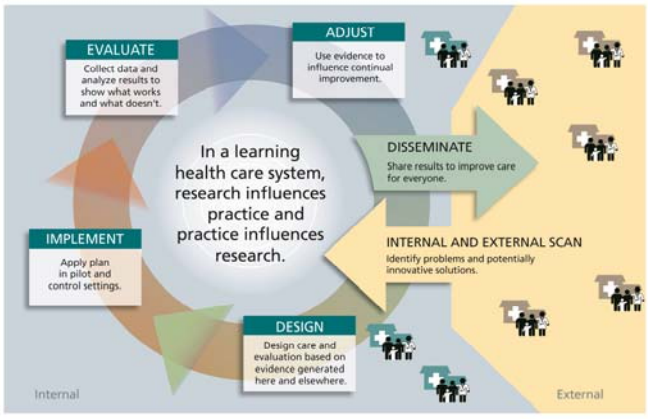
- GHRI is the independent, public-interest research arm of Group Health, a learning health care system



Greene SM, et al., Implementing the learning health system: from concept to action. Ann Intern Med 2012;157(3):207-10.

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Group Health Research Institute

- Established in 1983
- 60+ investigators (MDs, epidemiologists, biostatisticians, health services researchers, psychologists)
- Affiliations: University of Washington, Fred Hutchinson Cancer Research Center and others
- Funding: National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), PCORI, AHRQ, Robert Wood Johnson Foundation and others
- Goal: transform health care through research—including smoking quitlines for **Alere Wellbeing (a SCLC partner in evidence-based tobacco cessation)**

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GHRI and smoking cessation

- 1980s
  - Free & Clear smoking cessation programs developed at Group Health by Center for Health Promotion and Center for Health Studies
  - Best results from telephone counseling and self-help materials (23% quit)
  - Group Health one of nation's first smoke-free workplaces
- 1990s
  - Free & Clear launched in other states
  - Group Health prioritized smoking cessation services with full coverage—smoking among Group Health members is ~6% lower than the community

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GHRI and Smoking Cessation

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- 2000s
  - Washington State 6th-lowest smoking rate in nation (18.4%), in part from Free & Clear
  - Pilot study in blue collar workers (40% smokers) showed 28% quit rate and 94% participant satisfaction
  - Boeing provided Free & Clear to all employees
  - Free & Clear, Inc. spun-off as a company, **evolved into Quit for Life® and became part of Alere Wellbeing (QUIT-NOW)**

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Free & Clear-based Quitlines Today

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- Effective in 20+ clinical trials, 50 program evaluations, 80 publications in 25 years
- Telephone coaching, personalized plans, web tools, decision support for medication (nicotine replacement)
- Average quit rate (no tobacco in 30 days) = 43% (8 times better than "cold turkey")
- 500,000+ participants since 2004 with 90%+ program satisfaction
- Model for CDC and Robert Wood Johnson Foundation
- **Promoted by SCLC (QUIT-NOW cards)**

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Overview: Dementia

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- Historical overview: aging population raises dementia awareness
- The tidal wave of dementia
- Changing perspectives: mixed dementias
- Risk factors and prospects for prevention
- Exercise and smoking
- Future overview: recent trends

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Historical Overview of Alzheimer's and Dementia

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- Late 1960s, 1970s
  - Alzheimer's disease (AD) and others = "pre-senile dementias"
  - "Senile dementia" indistinguishable from classic early AD
- 1970s, 1980s
  - Focus on distinguishing AD from vascular (multi-infarct) dementia
  - Demonstrated dramatic increase in prevalence (≥50%) over age 85

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Historical Overview of Alzheimer's and Dementia

GroupHealth

- 1980s, 1990s
  - Increased awareness: disease most feared by doctors

  - Research efforts launched (from National Institute on Aging)
  - More precise definition of prevalence and causes

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The Tidal Wave of Dementia

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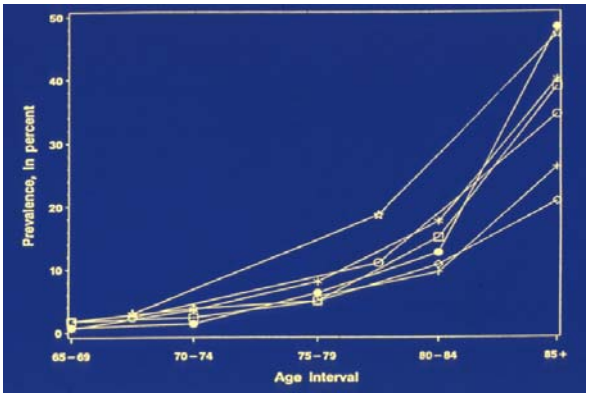
Alzheimer's Prevalence vs. Age in Seven Studies



Graves AB, et al., Prevalence of dementia and its subtypes in the Japanese American population of King County, WA: The KAME Project. Ann J Epidemiol 1996;144:760-71..

The Tidal Wave of Dementia

GroupHealth

Alzheimer's Prevalence (Kame study)

Age	Rate
65 - 69	.8 %
70 - 74	1.4 %
75 - 79	6.3 %
80 - 84	12.7 %
85 - 89	29.7 %
90 - 94	50.2 %
95+	74.3 %

Rule of thumb: Rates double every 5 years over 65 in developed countries, 7 in developing world

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The Tidal Wave of Dementia

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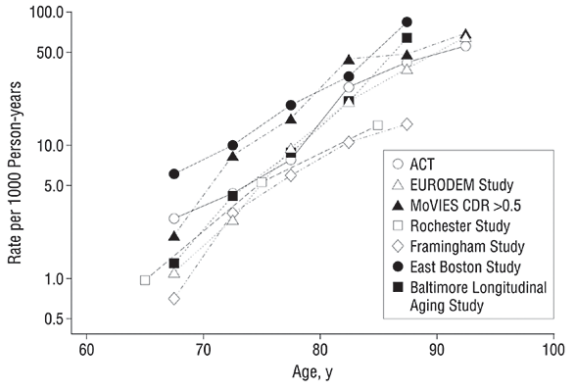
Alzheimer's Incidence vs. Age in Seven Studies



Kukull et al. Dementia and Alzheimer Disease Incidence. Arch Neurol 2002;59, 1737-46

- Currently 35 million worldwide, 5 million in the United States
- Projected 115 million worldwide in 2050

Current View of Alzheimer's and Dementias

- Currently:
  - Dementias rare before age 65
  - Incidence rises exponentially especially after 80
  - Survival differences decrease with later age of onset
  - People living to 115 years might not have neurodegenerative changes
  - Dementia rates vary in low- and middle-income countries but increasing WORLDWIDE (especially urban Latin America)

Current View of Alzheimer's and Dementias

- Aging populations worldwide = far-reaching consequences of late-life dementias
- Rising tide of late-life dementia = public health triumph and opportunity
  - Reflects life-expectancy gains with "knowledge-based" societies

The Aging Population

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- Living to 100: historical trends
  - Sweden: 3 per year in 1860s vs. 750 in 2007
- For persons born in 2007, 60,000 likely to become centenarians.
- "Two scourges of old age are cognitive impairment, often due to Alzheimer's disease, and sensory deprivations." (Vaupel, 2010)

Changing Perspectives: Mixed Dementias

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- Early efforts distinguished AD from vascular dementia
- But now we recognize mixed dementias = coexisting causes from multiple “hits” to aging brain
- Key observation 1: Vascular dementia higher than expected
  - ~50% in ≥85-year-olds with dementia in Sweden (Skoog et al. 1993, Blessed et al. 1970)
- Key observation 2: People with neuropathologically diagnosed AD also have vascular or Lewy body lesions
  - 61 of 95 with AD had other lesions on autopsy; only 34 had "pure" AD (Lim et al. 1999)

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Changing Perspectives: Mixed Dementias

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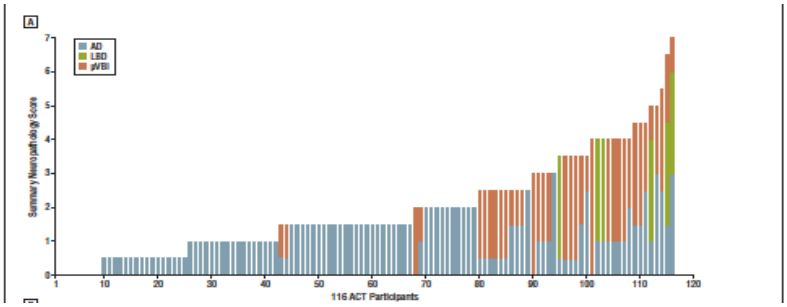
- Key observation 3: **Older adults without dementia can have brain lesions** (plaques, tangles, microinfarcts, etc.)

Lesion scores from autopsy of 116 cognitively normal adults
blue, signs of AD; green, Lewy bodies; red, microinfarcts



Sonnen et al. Ecology of Aging Human Brain. Arch Neurol 2011;68, 1049-1056;

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Changing Perspectives: Mixed Dementias

GroupHealth

- Recent neuropathologic studies:
  - Brain plaques and tangles AND microvascular infarcts explain dementia risk (Sonnen, et al., 2007)
  - Statin use associated with lower levels of AD pathology; likely more so for age <80 (Li et al., 2007, 2010)

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Changing Perspectives: No Magic Bullets for Dementia

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- Examples of recent failures:
  - Antioxidant vitamins (Gray et al. 2008)
  - Non-steroidal anti-inflammatory drugs (Breitner 2009)
  - Ginkgo biloba (DeKosky et al. 2008)
  - H2 Blockers (Gray et al. 2011)
- Cholinesterase inhibitors (e.g., donepezil) not likely the answer
  - Improve cognition on tests but not necessarily daily function
- To date, no trials on amyloid-targeting drugs have been successful

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Summary

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- Dementia is complex, with mixed causes
- Populations are aging as mortality is postponed
- No magic bullets for dementia
- But senescence is not inevitable: patterns of aging vary
- Neurodegenerative processes co-occur in late life—with or without dementia
- **This variation suggests an opportunity for prevention**

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Dementia Risk Factors and Prevention

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The simple message is:

Personal Health Decisions Make a Difference

Socioeconomic Factors and Policy Also Make a Difference

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Risk Factors and Prevention: Lifestyle Factors Can Be Potent

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- Four factors = 78% lower risk of chronic disease:
  - Body Mass Index <30
  - Exercise >3.5 hours/week
  - Healthy diet
  - **Never smoked**
- **What about modifiable factors and dementia?**

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Overview: Potentially Modifiable Dementia Risk Factors

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- Socioeconomic status
- Education
- Mental retirement
- Lifestyle
  - Exercise and physical activity
- Vascular
  - High blood pressure
  - Diabetes
  - Blood lipid levels
  - Atrial fibrillation
  - **Smoking**

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Dementia Risk Factors and Prevention: Early Life

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- Early life socioeconomic state (Moceri, et al., 2000)
  - Affects development: brain areas that take longest to mature (e.g. hippocampus) show earliest signs of AD
- Findings:
  - Suburbs reduce risk (odds ratio = .45)
  - Father unskilled or manual laborer increase risk (OR = 1.8)
  - Increased family size increased risk (OR = 1.08 per added sib)
  - Risk factors are multiplicative

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Dementia Risk Factors and Prevention: Early Life

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- Conclusions and other interpretations (Moceri et al. 2000)
  - Early "lifestyle" factors related to socioeconomic environment affect AD risk
  - People with higher risk based on genetics especially affected: gene-environment interaction
  - Findings support brain reserve hypothesis: ability to tolerate age- and disease-related brain changes

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Dementia Risk Factors and Prevention: Vascular Factors

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- Vascular risk factors: linked to all dementias
  - High cholesterol: likely stronger association in late midlife-early old age
  - High blood pressure: U-shaped association (disappears in old-old age)
  - Diabetes: 50-100% increased AD risk; 100-150% increased dementia mainly over age 70
  - Atrial fibrillation: increased risk for AD, all-cause dementia
  - **Smoking: increases risk by 30% for AD and 80% for all-cause dementia**

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Encouraging Prevention: Example from Physical Activity

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- Activity and dementia: initial results were confusing
- Results from 9 studies from USA, Canada, Sweden, Japan, France with different measures of activity (Fratiglioni et al. 2004)
  - 4/9 studies reported no association
  - 4/9 reported higher activity associated with lower AD risk
  - 1/9 found only DANCING was associated with lower risk

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Encouraging Prevention: Example from Physical Activity

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- ACT study: 1740 people over age without dementia, followed 6 years (Larson et al. 2006)
- **Dementia lower in people who exercised more**:
  - 13.0 per 1000 person-years for exercising 3+ times per week.
  - 19.7 per 1000 person-years for exercising less than 3 times per week (HR = 0.62 [0.44-0.86]).
  - Risk reduction greatest in those with lower performance levels.
  - Similar results for AD

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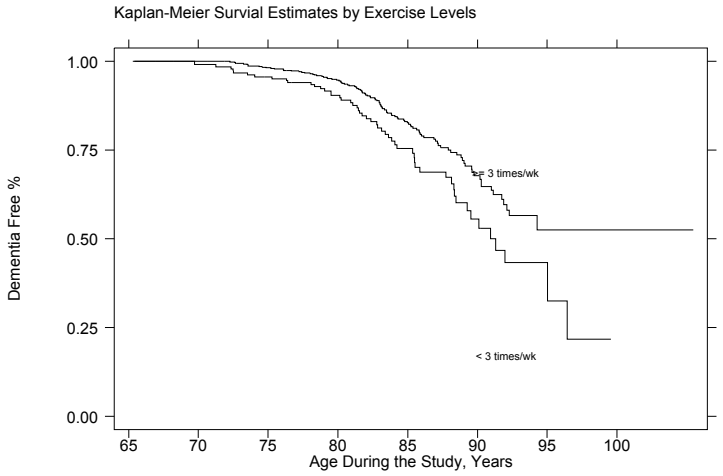
Exercise and Dementia-free Survival



Larson, et al. Exercise is associated with reduced risk for incident dementia among persons 65 years of age or older. Ann Intern Med 2006;144: 73-81

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Physical Activity and Dementia Prevention

- 2005: Seniors who exercise 3+ times per week = 30–40% lower risk for dementia than seniors with less exercise
- 2006: Good physical function linked to AD delay = re-engaging in physical activity might stop or slow decline
- 2008: Seniors in Group Health's fitness programs have lower health care costs
- Based on these findings, we advise older patients to "**use it even after you start to lose it**."

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Physical Activity and Dementia Prevention

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- Randomized trial of walking exercise (Lautenschlager et al. 2008):
  - In older persons complaining of cognitive impairment
  - **Walking improved cognitive scores** at 18-month followup
  - Greater than treatment effects of cholinesterase inhibitors (Cochrane Review)
  - No significant side effects to exercise
  - **Improving physical function might benefit cognitive function through the body-mind connection**

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Physical Function and Future Dementia

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- Measures: cognition and physical function (PPF scale for walking, grip, balance, etc.) (Wang et al. 2006)
- Outcomes: Age-specific incidence = 53.1 per 1000 person-years, PPF ≤10
- 17.4 per 1000 person-years, PPF>10
- **Physical function associated with reduced risk of dementia and AD**

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Physical Activity and Dementia Prevention

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- The hippocampus "shrinks" in late adulthood, associated with impaired memory and increased dementia risk
- Randomized controlled trial of aerobic exercise showed 2% increased anterior hippocampus and improved spatial memory (Erickson et al. 2011)
- Hippocampal volume declined in control group
- **Aerobic exercise may reverse hippocampal volume loss in late adulthood**

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Encouraging Prevention: Example from Physical Activity

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Research on activity and AD suggests **desire to prevent dementia is a powerful motivator** to exercise (Larson 2006)

Dementia prevention could also encourage smoking cessation:

"Smokers: Are you at risk for Alzheimer's?"

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New Insights into the Dementia Epidemic

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Selected Recent Studies of the Dementia Epidemic.

Study	Outcome	Data Source	Key Findings	Factors
Manton et al. (United States)[1]	Prevalence of severe cognitive impairment	National long-term care survey interviews, 1982–1999	Decline in dementia prevalence among people ≥65 yr of age (5.7% to 2.9%)	Higher educational level, decline in stroke incidence
Langa et al. (United States)[2]	Prevalence of cognitive impairment	Ongoing population-based survey of people ≥51 yr of age	Prevalence of cognitive impairment among people ≥70 yr of age (12.2% in 1993 vs. 8.7% in 2002)	Higher educational level; combination of medical, lifestyle, demographic, and social factors
Schrijvers et al. (Rotterdam)[3]	Incidence of dementia	Population-based cohort ≥55 yr of age in 1990, extended in 2000	Incidence rate ratios (6.56 per 1000 person-yr in 1990 vs. 4.92 per 1000 person-yr in 2000)	Higher educational level, reduction in vascular risk, decline in stroke incidence
Qiu et al. (Stockholm)[4]	Prevalence of DSM-III-R dementia*	Cross-sectional survey of people ≥75 yr of age, 1987–1989 and 2001–2004	Age- and sex-standardized dementia prevalence (17.5% in 1987–1989 vs. 17.9% in 2001–2004); lower hazard ratio for death in later cohort suggests decreased dementia incidence	Favorable changes in risk factors, especially vascular risk; healthier lifestyles
Matthews et al. (England)[5]†	Prevalence of dementia in 3 regions	Survey interviews of people ≥65 yr of age, 1989–1994 (in CFAS I) and 2008–2011 (in CFAS II)	Dementia prevalence (8.3% in CFAS I vs. 6.5% in CFAS II)	Higher educational level, better prevention of vascular disease

* In the study by Qiu et al., dementia was diagnosed according to the criteria provided in the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (DSM-III-R).
† CFAS denotes Cognitive Function and Ageing Study.

Larson, et al. New insights into the dementia epidemic. New Engl J Med 2013;369(24):2275-77

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Future Overview: Positive Signs for the Dementia Tidal Wave

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- Decline in chronic disability prevalence 1982-1999 (Manton et al. 2005)
- Possibly from **overall decline in severe cognitive impairment** (prevalence down from 5.7–2.9%)
- Decline is in mixed dementia
- Suggested reasons: increased education in the oldest old, decrease in strokes from hypertension treatment, and "neuroprotective meds"

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Future Overview: Positive Signs

- **Lower dementia rates** in persons born in the later 20th century in four studies (US, Rotterdam, Stockholm, England)
- Factors: education, decreased vascular risk, healthier lifestyles, better living conditions

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Future Overview: Opportunities for Prevention

- Address mental retirement (Rohwedder and Willis 2010)
  - Retirement policies are associated with cognitive performance
  - Suggest: "Estimated effect of retirement on cognition…is very large indeed"
  - Today's rapid information environment might profoundly affect brain development—**building our brains might reduce neurodegeneration**
- Address the worldwide obesity epidemic
  - **Higher blood sugar levels = increased dementia risk**—even in people without diabetes (Crane et al. 2013)

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Future Overview: Trends

- Large population of very old people at high risk of late-life dementia is predicted (Brayne 2006)
- Baby boomers entering retirement age fear burdens of long life
- We can't absolutely prevent late-life dementias
- **However**, biodemographic trends predict senescence is already postponed 10 years (and continuing)
- Delay of dementia onset is possible and increased longevity does not result in excessive disability in the very old (Christensen 2008)

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Future Overview: Opportunities for Prevention

- Reducing the burden of late-life dementias requires major global **changes in behavior**, health care priorities, and social policy:
  - Promote education, strong communities, social and economic wellbeing
  - Reduce disparities and extreme poverty
  - Encourage work in later life
  - Continued progress in reducing vascular risk is currently best option.

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Future Overview: Opportunities for Prevention

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- General midlife health improvement + activity + healthy diet + vascular risk factor and disease control **(including smoking) =**

Potential for More Advances in Cognitive Health

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Questions and Answers

- Submit questions via the **chat box**

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Call us toll-free

- 1-877-509-3786

Closing remarks

- Please help us by completing the post-webinar survey.
- Thank you for your continued efforts to combat tobacco.

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