Clarity in Confusion: Dementia Prevention Techniques

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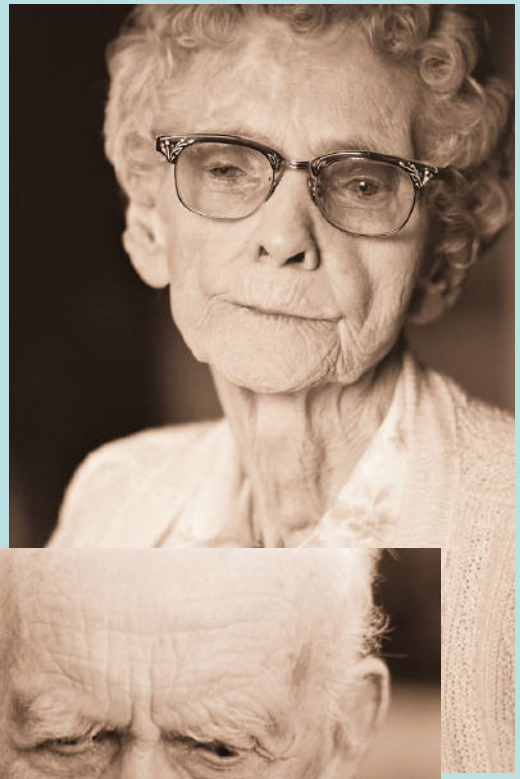
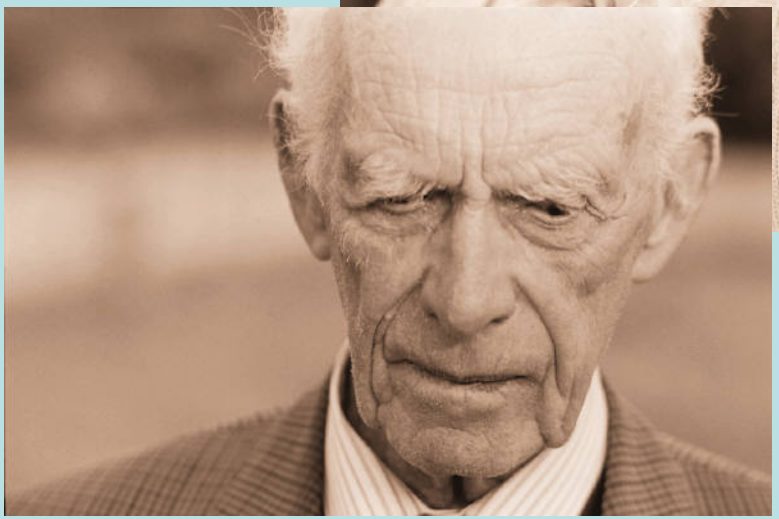
Outline

- Motivation
- Dementia
- Prevention
- Techniques
- Evidence
- Dementia and Software Engineering
- Conclusions





Motivation

- 24 million people with dementia worldwide; 81 million by 2040
- Alzheimer's Disease (AD) accounts for 64% of all dementia in Canada
- 420,000 Canadians have AD or a related dementia
- AD is the second most feared disease among Canadians (after cancer)

Cost Motivation

- $77,500 to care for one patient per year
- Cost to care for Alzheimer's patients in Canada is already $5.5 billion per year
- $100 billion per year in US, third most costly after heart disease and cancer

Government Research

- $18.7 million spent on Alzheimer's research by the Canadian government (versus $5.5 billion cost)
- Cost is 300 times research spending (0.34% = less than 1% of cost)
- $647 million (versus $100 billion cost) by the US government in 2005
- Cost is 155 times research spending (0.6% = less than 1% of cost)

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Dementia

- Dementia is mental decline beyond the normal effects of aging
- Problems with attention, language, problem solving; later disoriented and confused
- AD is 64% of all dementia in Canada
- AD first robs memory and eventually personality and independence

Alzheimer’s Disease

Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive cognitive deterioration together with declining activities of daily living and neuropsychiatric symptoms or behavioral changes. It is the most common type of dementia.

Genetic Causes

- Early AD suggests genetic mutations on 1st, 14th, and 21st chromosomes
- Late onset AD (LOAD), only one susceptibility gene has so far been identified: ApoE4 on chromosome 19
- Theory 1: AD begins as a deficiency in the production of the neurotransmitter acetylcholine. The medications that treat acetylcholine deficiency have served to only treat ***symptoms*** of the disease and have neither halted nor reversed it.

Other Possible Causes

- Environmental factors
- Toxic exposure – aluminum silicon
- Nutritional disorders
- Free radical damage
- Risk factor (not a cause): advancing age

Broad Issues, Not Included

- Head injury
- Poor cardiovascular health (smoking, diabetes)
- Exposure to metal toxins (aluminum, copper)
- Pharmaceuticals (administered after the fact)
  - antipsychotic medications

AD Risk Factors
ADEAR, NIA, USNIH

- Age
- Genetics: In 1992, researchers found that certain forms of the apolipoprotein E (APOE) gene can influence AD risk:
- APOE ε2, a rarely occurring form, may provide some protection;
- APOE ε3, the most common form, plays a neutral role; and
- APOE ε4, which is found in about 40 percent of people with AD; APOE ε4 lowers the age of onset and thus increases risk.

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Prevention

- Prevention versus delaying onset
- Average age of onset - 70 to 75 years
- Prolong by 5 years
- Prolong by 10 years – virtually eradicate it

Preventive Medicine

American Journal of Preventive Medicine is the official journal of the American College of Preventive Medicine and the Association for Prevention Teaching and Research

Alzheimer's Prevention Foundation International

- "If we can slow the progression of Alzheimer's disease by 5 years, we can cut the number of cases in half."
- "If the onset of Alzheimer's were delayed for 10 years, the disease would essentially be eradicated."
- APFI proposes an integrated complementary medical program

Alzheimer's Association

- 2nd International Conference on Prevention of Dementia, Washington, June 2007
- Current and future prevention trials
- More than 100 clinical drug trials now
- Evidence-based practices and models
- Technology-based devices and strategies

WHY NOT Prevention?

- Cognitive and blood tests are given to detect dementia. WHY NOT similar tests to prevent it?
- CT scans can show some forms of dementia. WHY NOT for prevention?
- WHY NOT treat or remove problem genes?

WHY NOT Prevention?

- WHY NOT prevent the accumulation of abnormally folded amyloid beta protein?
- WHY NOT cut out ‘the neurofibrillary tangles and amyloid plaques’ that define Alzheimer’s?
- If we can diagnose Alzheimer’s after death, WHY NOT diagnose it early in life before the symptoms present?

Hachinski Willis Lecture
October 2006

"For each person who has dementia or Alzheimer's disease, two have some cognitive impairment short of dementia... The fact that cerebrovascular and Alzheimer disease share the same risk factors provide a great opportunity for prevention, if implemented early enough (at the *"brain at risk"* stage)."

Research Questions

1. How can we prevent dementia?
2. Why do some treatments work for some subjects and not others?
3. What are the best practices in 2007?

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Sources

- US
- Canada
- Hospitals (Baycrest, Mayo Clinic)
- Universities
- Alzheimer Associations, Societies
- Government Agencies

Alzheimer Society of Canada
Alzheimer Society of BC

- Physical exercise, reasonable weight, good diet, low blood pressure, adequate sleep, minimal stress
- Social Interaction: active social life, active in retirement, positive attitudes
- Mental Agility: challenge your brain, learn new skills, varied activities

Baycrest Healthy Aging

- Nutritious diet
  - High in fruits and vegetables
  - Low in cholesterol and fatty acids
  - Vitamins B2, C, B12, Folic Acid
- Exercise your brain
- Experience new things
- Make positive friends in every generation

National Institute on Aging
U.S. National Institutes of Health

- Minimize or prevent heart disease, high blood pressure, diabetes
- Social engagement; intellectual stimulation
- Physical activity
- NSAIDs, antioxidants, estrogen, ginkgo biloba
- Immunization

Mayo Clinic: Healthy Aging

1. Maintaining a healthy weight, exercising, and controlling high blood pressure and cholesterol, may prevent Alzheimer's.
2. A low-fat diet and foods rich in omega-3s might also be helpful.
3. Life-long mental exercise and learning have been linked with delaying the onset of dementia.

Alzheimer's Prevention Foundation International

The Four Pillars of Prevention

1. Diet and Vitamins
2. Stress Management
3. Exercise and Brain Aerobics
4. Pharmaceuticals and Supplements

Centre for Healthy Aging

- Eat a healthy diet
  - Low cholesterol, saturated fat, sugar, and salt
  - High dietary fibre, antioxidant fruit, vegetables
- Get a ***variety*** of regular exercise
- Stay engaged in social activities
- Exercise your mind

Summary

1. Diet
2. Nutritional Supplements
3. Physical Exercise
4. Mental Exercise
5. Social Activity
6. Stress Management

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1. Diet

1. Antioxidant fruits and vegetables ✔
2. Other antioxidants (tea, chocolate, wine)
3. Healthy weight
4. Low fat ✔
5. Omega-3 foods ✔
6. Folic acid
7. Low cholesterol, saturated fat, sugar, salt
8. High fibre

Antioxidant Fruits & Vegetables

- Blackcurrants protect neuronal cells, New Zealand researchers, *Journal of the Science of Food and Agriculture*, Jan 2006

Fruits and Vegetables

- Drinking fruit and vegetable juices frequently may significantly cut the risk of developing AD
- Almost 2,000 people for up to 10 years
- Risk was 76% lower for those who drank juice more than three times a week, compared with those who drank it less than once a week
- Dr. Harriet Millward
- ***American Journal of Medicine***, August 2006

Other Antioxidants

- Cabernet sauvignon red wine reduces the risk of AD (mouse study), 2006

Omega-3 Foods

- Docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid
- Fatty fish like mackerel, trout, herring, sardines, albacore tuna and salmon are high in DHA
- 899 people studied over 9 years
- "If you have a high level of DHA, a fatty acid found in fish, it reduced your risk of dementia by about half," said study lead researcher Dr. Ernst J. Schaefer, Human Nutrition Research Center on Aging, Tufts University, Boston
- *Archives of Neurology*, November 2006

More Diet Evidence

- Riviere S., S. Gillette-Guyonnet, T. Voisin, E. Reynish, S. Andrieu, S. Lauque, A. Salva, G. Frisoni, F. Nourhashemi, M. Micas, B. Vellas. "A nutritional education program could prevent weight loss and slow cognitive decline in Alzheimer's disease." *J Nutr Health Aging*. 2001; 5(4): 295-9.
- Emerson Lombardo, A. Martin, L. Volicer, A. Mandell, X. Wen Zhang. "Comprehensive whole foods diet to reduce risk and slow progression of Alzheimer's disease." *J Nutr Health Aging*. 2006; 10(3): 211.

2. Nutritional Supplements

1. Multi-vitamin
2. Antioxidants (Vitamins A, C, E, Zinc)
3. Vitamin B2, B12 ✔
4. NSAIDs, non-steroidal anti-inflammatory drugs, Ibuprofin (Advil, Motrin) ✔
5. Ginkgo Biloba
6. Statins ✔

Vitamin B (Folate)

- Folate is water-soluble form of vitamin B needed for formation and maintenance of new cells
- 965 dementia-free adults followed for 6 years
- 192 subjects later diagnosed with AD
- Those with the highest 25% of folate intake were 50% less likely to develop Alzheimer's disease than those with the lowest 25%.
- Archives of Neurology, 2007

Prevention through NSAIDs

- Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT) launched in 2001 to test the effectiveness of some non-steroidal anti-inflammatory drugs such as ibuprofen and aspirin in preventing AD
- Study of more than 2,500 healthy participants age 70 and over sponsored by the NIA and scheduled to run between five and seven years
- Results not yet public

NSAID Study

- November 22, 2001 New England Journal of Medicine moves the NSAID question a step forward by observing prospectively, for seven years, a population-based cohort of 6,989 initially nondemented elderly people whose NSAID prescriptions were fully documented in pharmacy records.

NSAID Study

- Erasmus Medical Center, Rotterdam, the Netherlands, those who took NSAIDs for up to two years had a 0.83 relative risk of developing AD. For those who took the drugs even longer, the relative risk dropped markedly, to 0.2.

Statins

- Statins inhibit IL-6 and TNF-α, which are proinflammatory molecules
- Since inflammation plays a role in AD, methods to suppress these molecules “may prevent dementia”
- Patients who received lovastatin or pravastatin, but not simvastatin, exhibited 70% less AD than a control group
- Statins may also promote neuron survival
- Dr. Undurti N. Das, CMAJ, October 2, 2001

Triple Supplement

- Omega-3 fatty acids, uridine and choline
- Increased the amount of membranes that form brain cell synapses
- Gerbils
- Now in clinical trials
- MIT researchers
- *Brain Research*, May 9, 2006

3. Physical Exercise

1. Minimum amount of exercise 
2. Variety of exercise 

Physical Exercise

- 1,740 seniors over 6 years
- Exercise 3 or more times a week had a 30 to 40% lower risk for developing dementia
- Even modest amounts, such as walking 15 minutes a day, appear beneficial
- The more frail the person was, the more they benefited from regular exercise
- *Annals of Internal Medicine*, January 17, 2006

More Exercise Evidence

- Crowe, M. et al. "Does participation in leisure activities lead to reduced risk of Alzheimer's disease? A prospective study of Swedish twins." *J Gerontol B Psychol Sci Soc Sci.* 58(5), (2003 Sep), P249-55.
- Briones TL. "Environment, physical activity, and neurogenesis: implications for prevention and treatment of Alzheimer's disease." *Curr Alzheimer Res.* 3(1), (2006 Feb), 49-54.

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More Exercise Evidence

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More Exercise Evidence

- Eggermont L, D. Swabb, P. Luiten, E. Scherder. "Exercise, cognition and Alzheimer's disease: more is not necessarily better." *Neurosci Biobehav Rev.* 2006;30(4):562-75.

4. Mental Exercise

1. Chess, crossword puzzles, Sudoku
2. Higher education 
3. Life-long learning 
4. Multiple languages 
5. Instrument/music

Cognitive Reserve

- Study reviewed ‘cognitive reserve’, the role of education, occupational complexity and mentally stimulating activities in preventing cognitive decline
- Never too late to build cognitive reserve
- Mental activity ***halves*** dementia risk
- 29,000 individuals across 22 studies
- *Psychological Medicine*, October 2006

Multiple Languages

- Knowledge of more than one language linked to ‘mental agility’ and significant delay in onset of dementia, Baycrest
- 184 subjects
  - Unilingual men with an average age of dementia at 70.8 and women at 71.9
  - Bilingual men at 76.1 and women at 75.1
- *Neuropsychologia*, February 2007

Mental Exercise Evidence

- Knapp M, L. Thorgrimsen, A. Patel, A. Spector, A. Hallam, B. Woods, M. Orrell. "Cognitive stimulation therapy for people with dementia: cost-effectiveness analysis." *Br J Psychiatry*. 2006 Jun;188:574-80.
- Butler, RN, F. Forette, BS Greengross. "Maintaining cognitive health in an ageing society." *J R Soc Health*. 2004 May;124(3):119-21.

5. Social Activity

- Monthly activities 
- Contact with children and relatives 
- Membership in a social club or group 
- Can be tied to other preventive aspects, such as a book club (mental exercise) or dance group (physical exercise) 

Social Networks

- Social networks offer a 'protective reserve' capacity sparing manifestation of AD
- 89 elderly people without known dementia in the Rush Memory and Aging Project, Rush University Medical Center, Chicago
- Children, relatives, monthly visits
- *The Lancet Neurology*, May 2006

6. Stress Management

1. Yoga
2. Meditation
3. Low blood pressure
4. Healthy weight

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Paul Levy, IBM

Paul Levy, one of the founders of IBM Rational, once remarked

"Ultimately, building software is the world's most important industry… Software today speeds the process of drug discovery, ***potentially curing Alzheimer's***. … And, make no mistake about it, we are just getting started."

Grady Booch, Handbook of Software Architecture

Dementia and Software Engineering

- Software Quality
- Information Quality
- Decision Support Systems
- Ontologies
- Lots of detection of symptoms, diagnosis, geriatric assessment, treatment
- Cognitive tests

Prevention Software

- Injury Prevention
- RSI Prevention (Repetitive Stress Injury)
- AIDS Prevention
- WHY NOT Dementia Prevention?

Dementia Prevention Software

- Provide information
- Data management and ontologies
- Data visualization
- User interfaces
- Decision support systems

Repetitive Stress Prevention

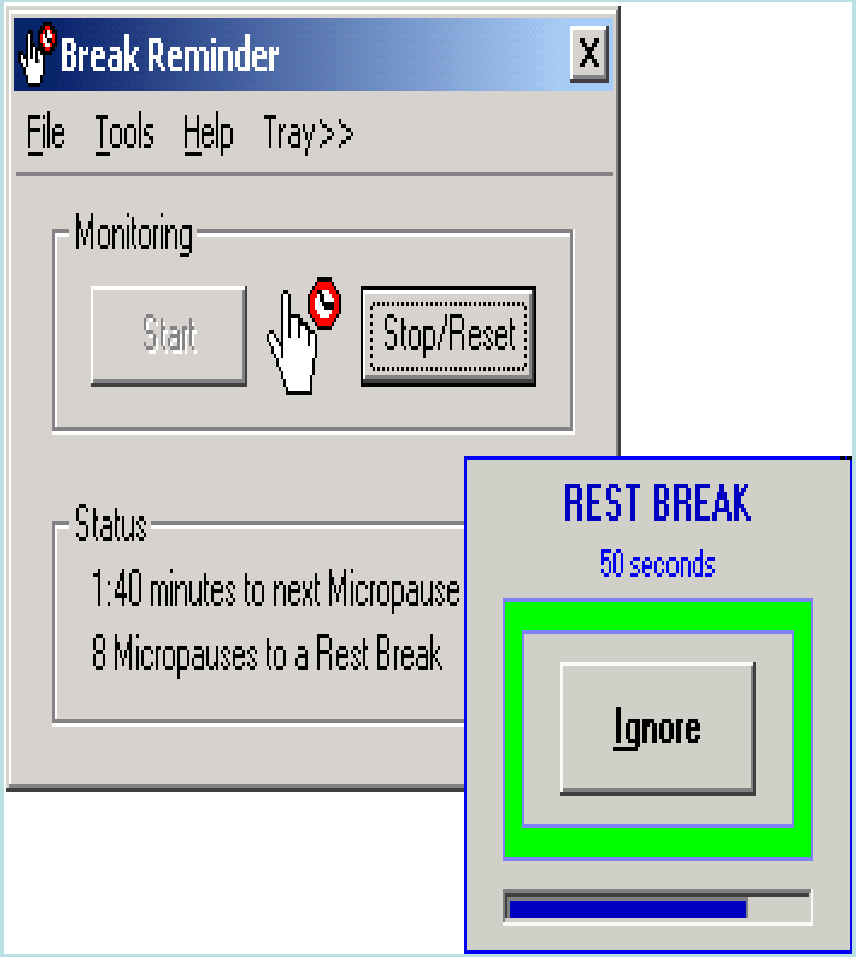
- RSI Guard
- www.rsiguard.com

WorkPace

- WorkPace helps you achieve safe and healthy work habits at your computer by:
  - **Educating** you about muscle fatigue and recovery.
  - **Alerting** you to needed micropauses and breaks.
  - **Guiding** you through regular exercises and stretches designed to reduce fatigue.
  - **Monitoring** exposure and intensity of computer use.
  - **Providing** feedback on how you are doing.
- RSI Prevention, www.workpace.com

Break Reminder

- RSI Prevention
- http://www.cheqsoft.com/break.html



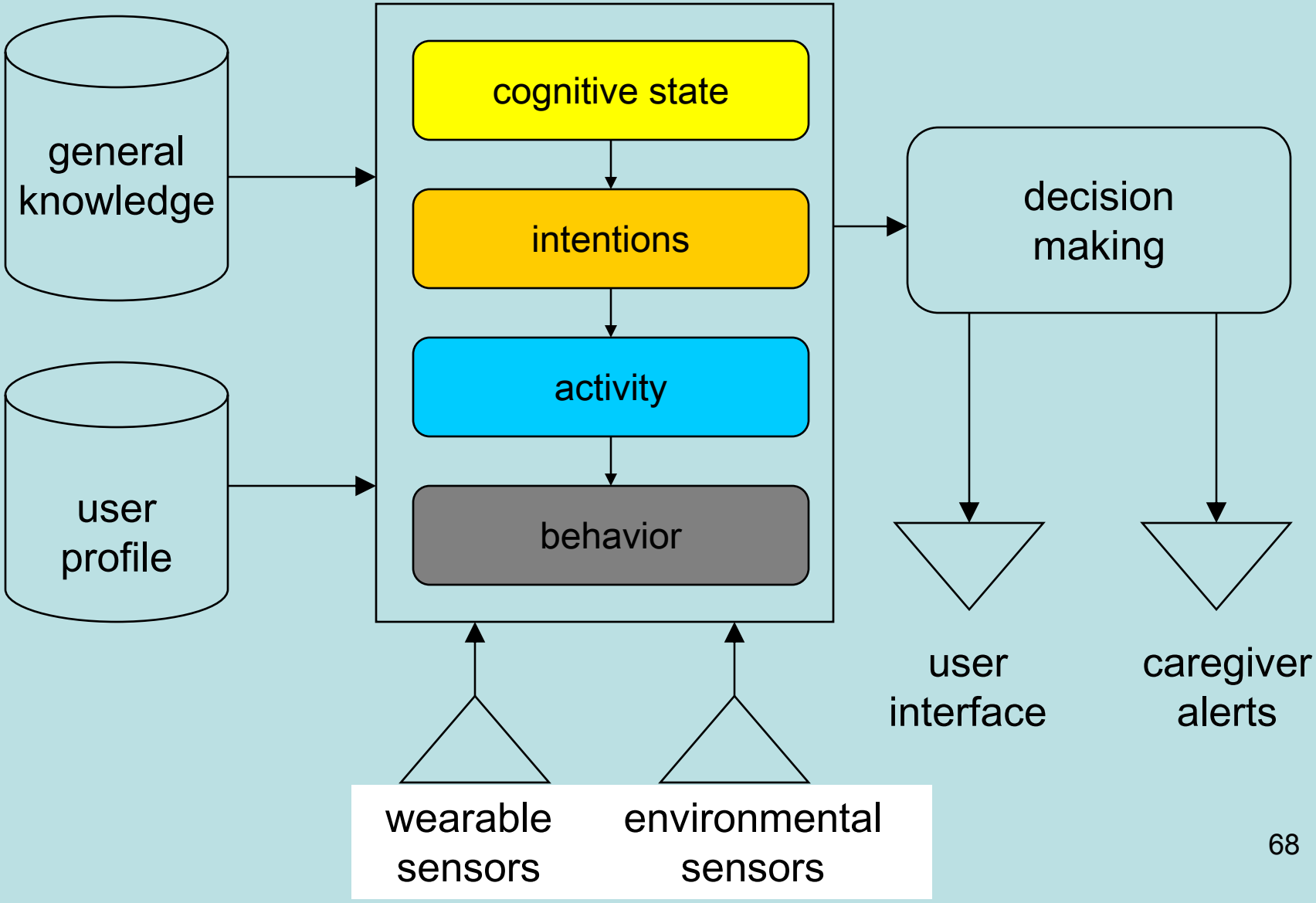
Geriatric Assessment

- Lots of software to determine cognitive awareness
- 10 point tests
- 10 minute tests
- Identify month, day, hour, address

After Dementia is Diagnosed

- Assisted Cognition Project
- Henry Kautz, University of Washington
- Artificial intelligence aids
- Helps to organize victim and to alert caregiver when a problem arises
- Use of public transport, for example – GPS cell phone to trigger correct stops
- Wearable RFID tags for ‘wanderers’

General Approach



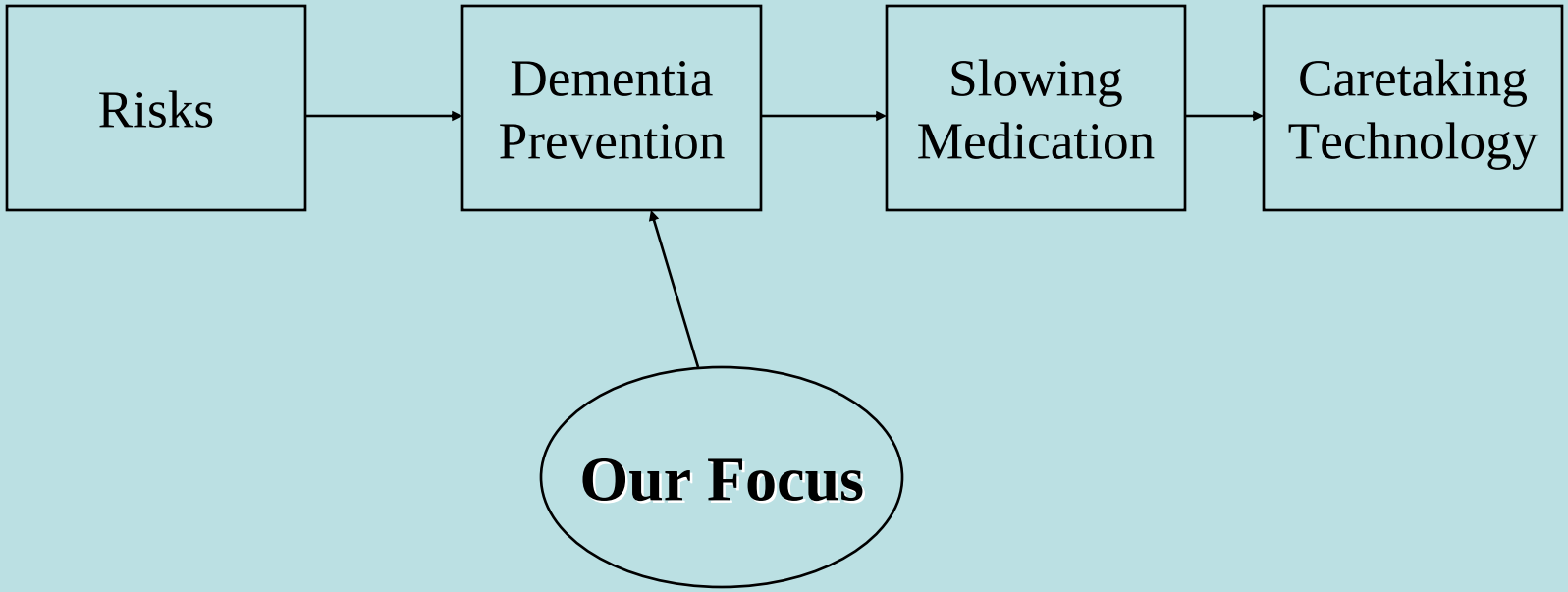
AD Dementia Challenges

- Large volumes of information
- Large numbers and variety of sources
- Before diagnosis
  - Risk factors
- After diagnosis
  - Medications to slow dementia progress
  - Support services and technologies

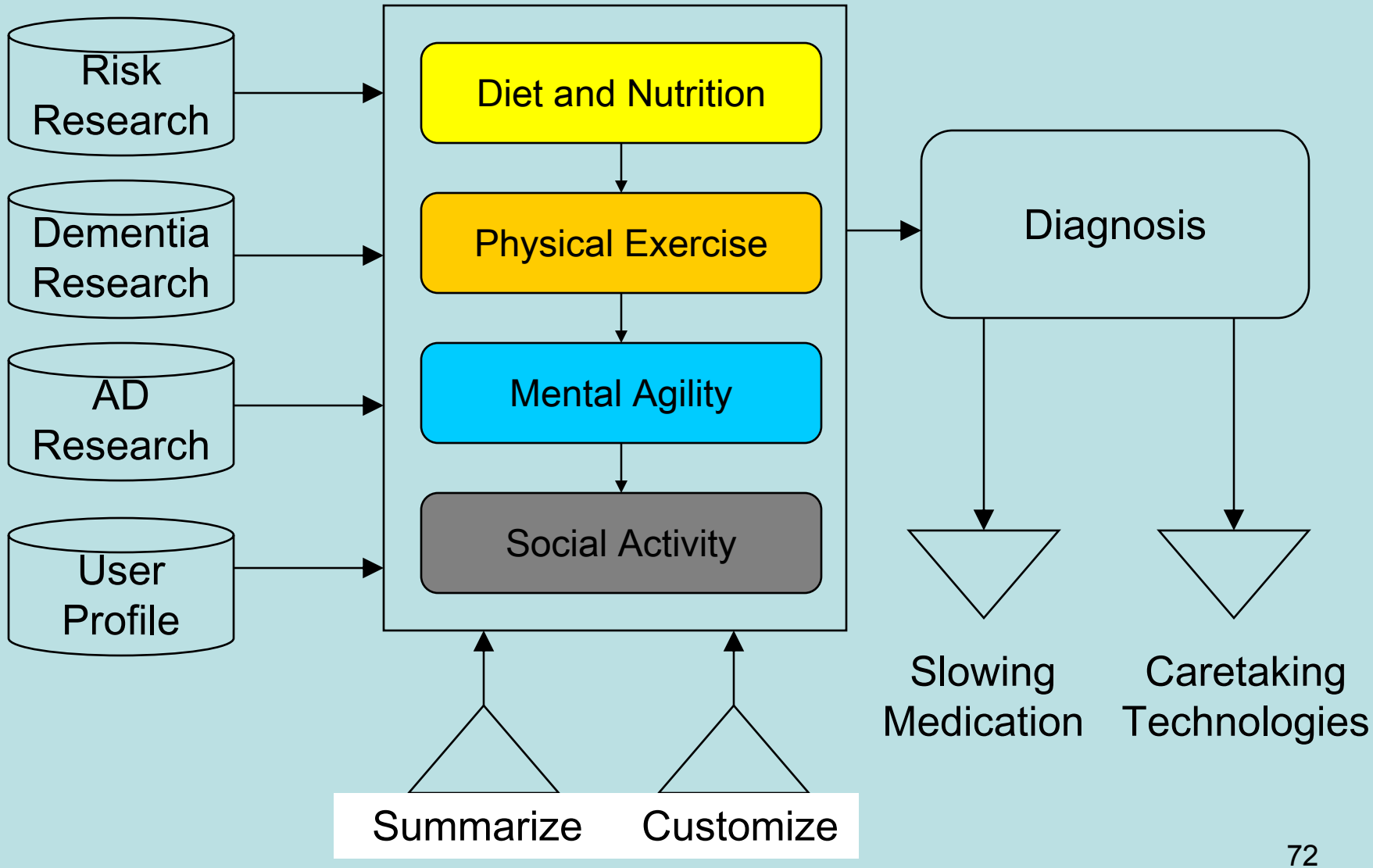
Our Framework

- Focus on prevention
- Focus on current research (2006+)
- Best practices, summaries, graphics
- Customization to particular circumstances
  – genetic or environmental factors
- Links to current
  – Risks before diagnosis
  – Treatments and technologies after diagnosis

Current Dementia Theory



Dementia Prevention Model



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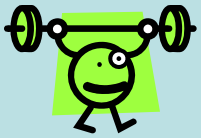
3. Physical Exercise 
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Major Findings

1. Dementia Prevention Evidence
2. Healthy Brain
3. Effect of Age
4. Risks before diagnosis
5. Treatment and technology after

Contributions

- Documented current dementia research
- Increased understanding of dementia and AD complexities
- Provided new insight linking dementia and many diseases
- Developed a Dementia Prevention Model

Future Prevention Research

- Vaccines
- Brain imaging (to identify risk)
- Drugs
- Blood test
- Spinal tap
- Surgery (to remove tangles)

Vaccine 2001, 2002

- The vaccine worked by stopping deposits of beta-amyloid in the brain.
- Animal studies were so encouraging that human trials began in 2001.
- Positive results for 20% of subjects.
- Unfortunately, 6% experienced serious inflammation of the brain (encephalitis).
- Work is continuing for less-toxic vaccine.

Brain Imaging

"Today, an estimated 4.5 million Americans have Alzheimer's disease, and that number could triple by 2050 as the population ages. We urgently need techniques to see brain changes in the earliest stages of cognitive decline so that we can identify people at risk and test drugs to stop or slow the progression of Alzheimer's," says NIA Director Richard J. Hodes, M.D.

FDDNP Imaging

- A new imaging molecule that can detect and map plaques and tangles in the brains of people with Alzheimer's disease could eventually lead to earlier diagnosis.
- The compound, FDDNP, was developed at UCLA.
- *New England Journal of Medicine, December 21, 2006*

Current Work

- ADEAR is ***recruiting*** for 36 clinical trials related to AD as of February 2007
- Drugs being tested ***after symptoms appear*** to slow progression of AD

Drugs – Future Prevention?

- Drug AF267B tested on mice
- Reversed memory loss, learning problems
- Reduced levels of protein clumps, tangles
- After 3 days, plaques were reduced
- After 5 days, so were tangles
- Maybe tangles are induced by plaque?
- Dr. Frank LaFerla, U California, Irvine
- *Neuron*, March 2006

References

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- Alzheimer Society of British Columbia
- Alzheimer's Prevention Foundation International
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- Baycrest
- Canadian Medical Association Journal (CMAJ)
- Journal of Alzheimer's Disease
- Mayo Clinic
- U.S. National Institutes of Health
  - National Institute of Mental Health (NIMH)
  - National Institute on Aging (NIA)