

CAN STROKE & ALZHEIMER'S DISEASE BE PREVENTED?

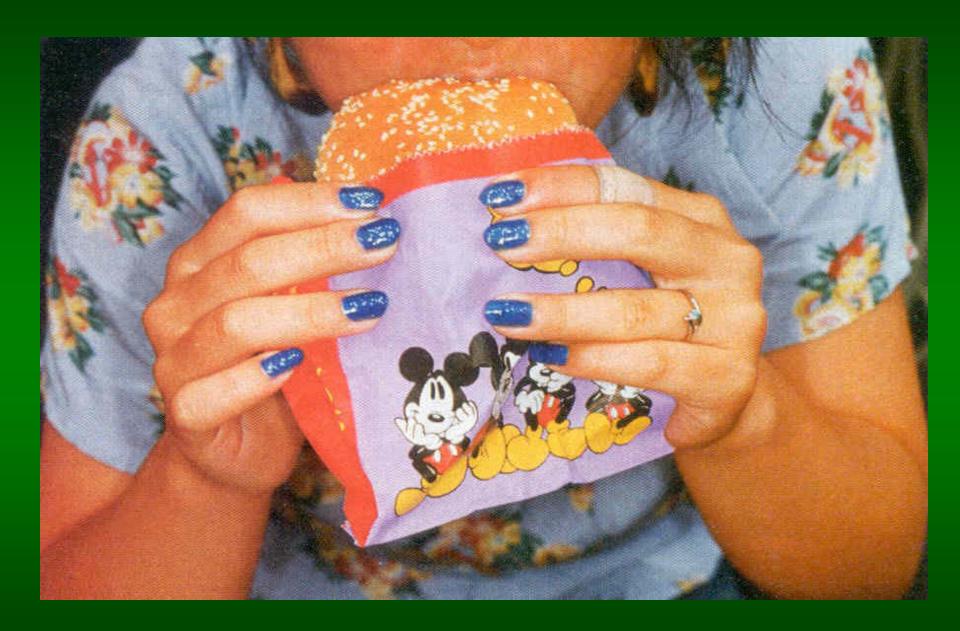
Vladimir Hachinski MD, FRCPC, DSc Department of Clinical Neurological Sciences University of Western Ontario London, Ontario

CAN STROKE & ALZHEIMER'S DISEASE BE PREVENTED?

- I THE GROWING MENACE
- II LIMITATIONS OF CURRENT APPROACHES
- III DEVELOPING A COMMON APPROACH
 - Developing a common vocabulary
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CITIES WITH MORE THAN 10 MILLION POPULATION







Tim Wong, 10, and his sister, Tiffany, 6, at a Queens KFC. Asians are especially vulnerable to diabetes

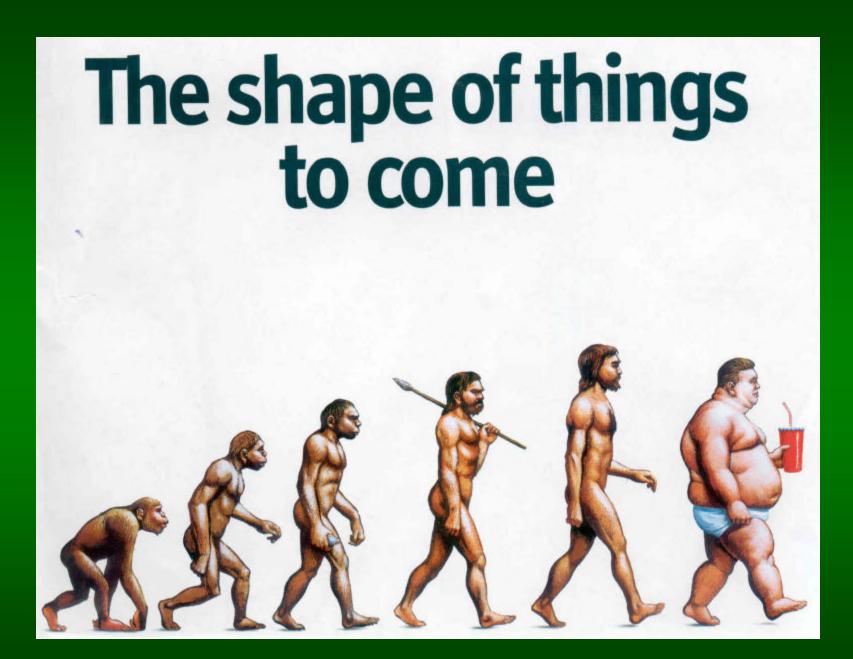
James Estrin/The New York Times, Jan 12, 2006



Librado Romero/The New York Times, Jan 12, 2006

Students at P.S. 120 have gym class just once a week, for 50 minutes.





IMPACT OF MODIFIABLE STROKE RISK FACTORS ON CANADIANS

Risk factor	Relative risk	Prevalence in Canada	Attributable risk
Physical inactivity	2.7	0.57	0.61
Hypertension	4.0	0.22	0.40
Dyslipedemia	1.5	0.43	0.18
Atrial fibrillation	11.5	0.01	0.10

LEISURE-TIME PHYSICAL ACTIVITY AT MIDLIFE AND THE RISK OF DEMENTIA AND AD

Active = physical activity \rightarrow breathlessness and sweating x 20-30 min at least twice a week

Active APO-E4

OR 95% CI OR 95% CI

Dementia 0.48 (0.25-0.91) 0.38 (0.15-0.97)

AD 0.38 (0.17-0.85) 0.18 (0.05 – 0.67)

Rovio et al, Lancet Neurology Oct 4, 2005 Online

The Queen Elizabeth sends messages for one hundredth and one hundred and fifth birthdays and then every year thereafter.



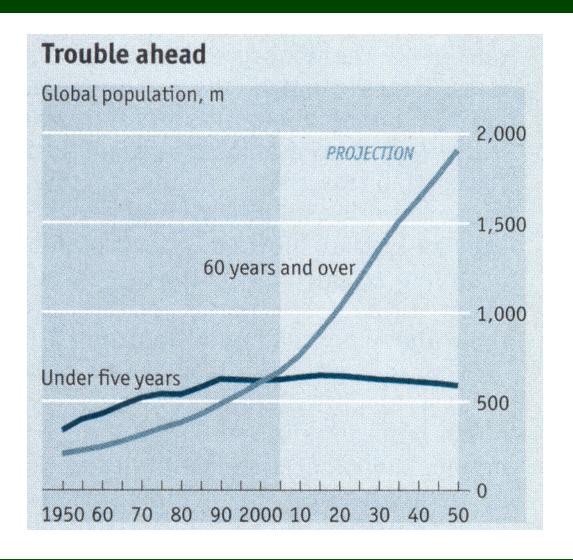
1952

255 people



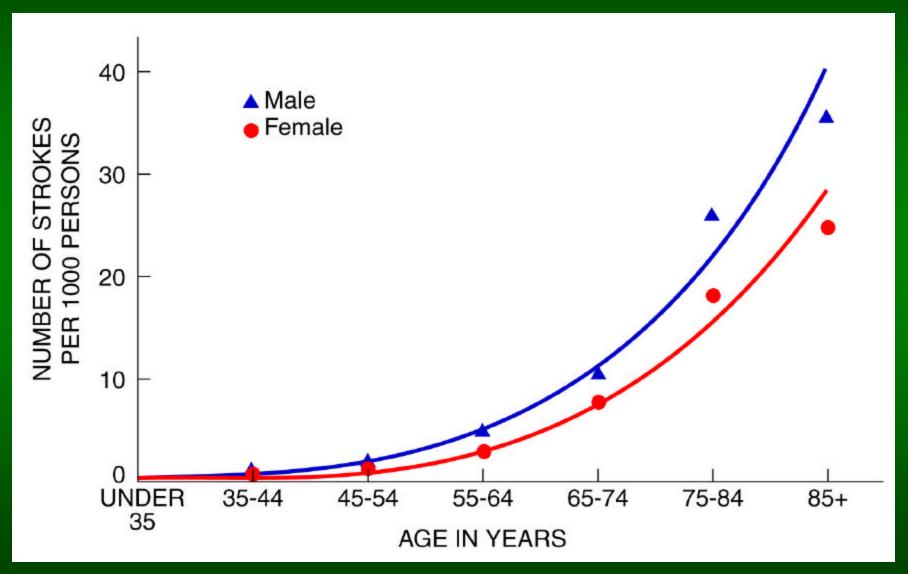
1996

5,218 people

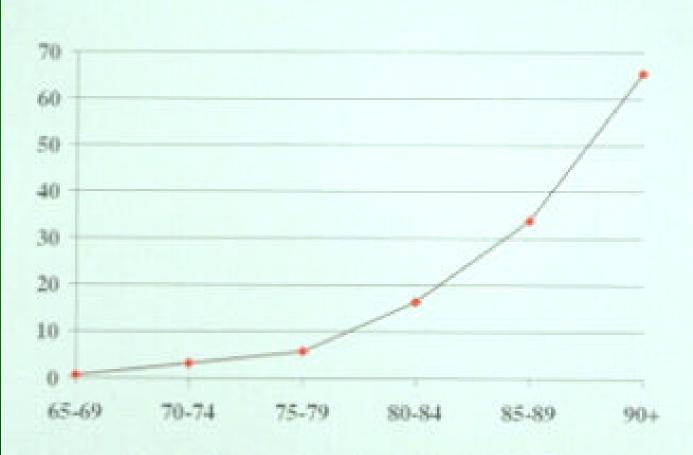


The Economist 27 March 2004

RISK OF STROKE, BY SEX



Age-Specific Incidence of Alzheimer's Disease in Canada, per thousand







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STROKE SCALES

Higher cerebral

Motor Other

Mohr et al. Cerebrovasc Dis 1998;8(suppl 1):17-22

Total

Conscious

Scale

Toronto	100	97	40	48	285
Canadian	3	2	5	0	10
NIH	3	7	21	9	40

FRAMINGHAM OFFSPRING STUDY

n = 2175

Framingham Risk Profile – 10 year risk

Age

Systolic BP

Antihypertensive medication

Diabetes

Cigarette smoking status

History of cardiovascular disease

Atrial fibrillation

Left ventricular hypertrophy (ECG)

Elias et al STROKE, 2004;35:404-409

PERFORMANCE DECREASES FOR EACH 10% INCREASE IN 10 YEAR STROKE RISK

p value

Similarities (Abstract reasonings) 0.0005

Trial-Making Test A 0.0001

Trial-Making Test B 0.0001

Paired Associates Learning (New learning and memory)

Visual Memory Composite 0.1626

Elias et al STROKE, 2004;35:404-409

0.4879

The temptation to form premature

theories on insufficient evidence is

the bane of our profession.

Sherlock Holmes, in "The Valley of Fear"

THE EFFECT OF DIFFERENT DIAGNOSTIC CRITERIA ON THE PREVALENCE OF DEMENTIA

The Canadian Study of Health and Ageing (n=1879)

DSM-III	29.1%
DSM-III-R	17.3%
DSM-IV	13.7%
ICD-9	5.0%
ICD-10	3.1%



Acknowledged ignorance is a

form of knowledge.

LIFETIME RISK OF STROKE AND DEMENTIA

n = 4897 stroke and dementia free at 55 years Follow up = up to 51 years

18% developed a stroke, 86% ischemic 14% developed dementia, 73% AD

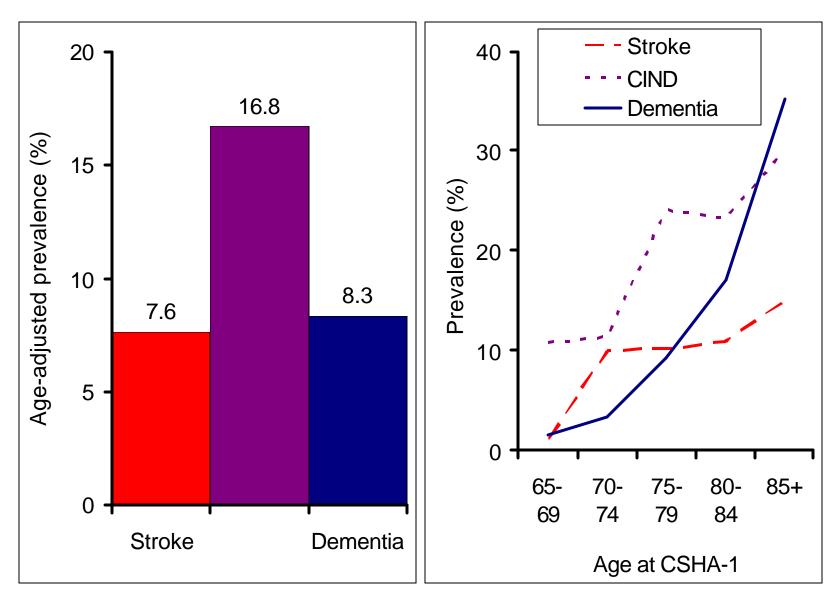
Combined lifetime risk

Male 1:4

Female 1:3

Combined lifetime risk for both sexes 1:3

Seshadri et al STROKE 2006;37:345-350

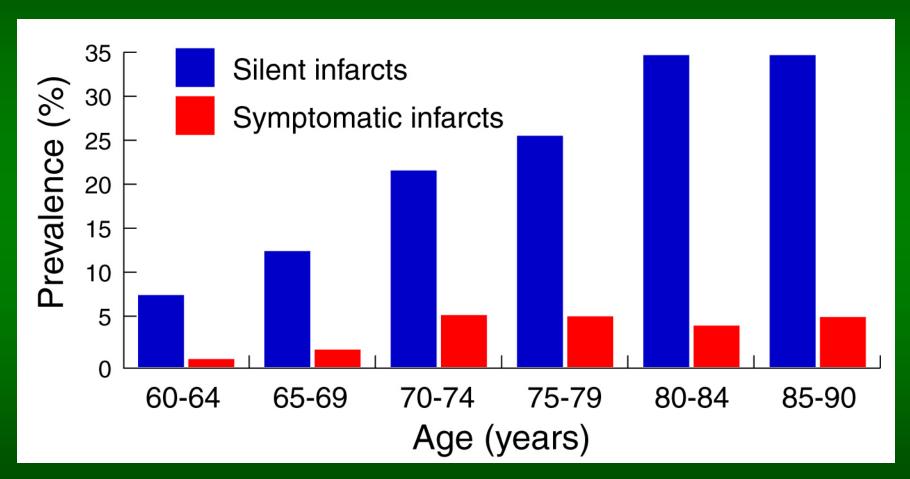


Jin et al unpublished 2005

THE THREATENED BRAIN



PREVALENCE OF INFARCTS IN THE ROTTERDAM SCAN STUDY



INCIDENCE OF FIRST SILENT STROKE

MRI population based studies:

- 1. Atherosclerosis Risk in Communities
- 2. Cardiovascular Health Study
- 3. Austrian Stroke Prevention Study

Estimates for 1998

First silent infarct	9,040,000
I hat anom marct	\mathcal{I}_{\bullet}

First silent hemorrhage 1,940,000

First symptomatic stroke 770,000

Leary and Saver. Cerebrovasc Dis. 2003;16(3):280-5

LEUKOARAIOSIS



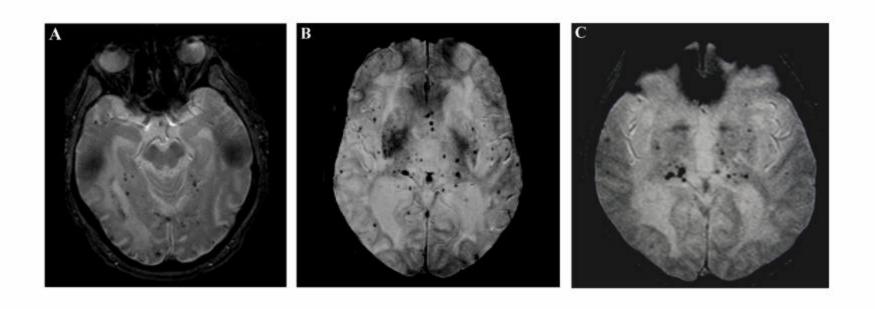
- Risk of Stroke
 - OR, 3.17-4.7

De Jong G, Stroke 2002; Vermeer SE, NEJM 2003

- Risk of intracerebral hemorrhage with anticoagulation
 - OR, 12.9

Cardiovascular Health Study; Smith EE, Neurology 2002

- Risk of Cognitive Impairment
 - OR, 1.67



Viswanathan et al. Cerebral microhemorrhage. STROKE. 2006;37:549-554

RADIOGRAPHIC PREVALENCE OF LESIONS OF PRESUMED VASCULAR ORIGIN IN 70-80 YEAR OLDS

- Lacunes: 12-15% (90% "silent")
- Intracerebral hemorrhage: 2-12% (90% "asymptomatic microbleeds")
- White matter T2 hyperintensity: 95%
- Cortical infarction: 1-2%
- Cerebral microinfarction: ?

Data from Rotterdam study, Framingham study, Cardiovascular Health Study, Austrian Stroke Prevention Study, and American Heart Association statistics.

Eric Smith 2006

POST-STROKE COGNITIVE IMPAIRMENT

	%
France ¹	23.0
USA ²	19.3
China ³	20.0

- 1. Cordoliani-Mackowiak M. et al, Poststroke dementia. Arch Neurol. 2003;60:585-590
- 2. Ivan CS et al, Dementia after stroke. Stroke. 2004;35:1264-1269
- 3. Tang WK et al, Frequency and determinants of poststroke dementia in Chinese. Stroke. 2004;35:930-935

PATHOLOGICAL CORRELATES OF LATE ONSET DEMENTIA

n = 209

Cerebrovascular pathology 78% Alzheimer pathology 70%

Conclusion

Most patients had mixed dementia

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WORKING GROUPS

CLINICAL/EPIDEMIOLOGY
Genetics
Clinical Trials

NEUROPSYCHOLOGY
IMAGING
NEUROPATHOLOGY
EXPERIMENTAL MODELS

THE NINDS/CSN VASCULAR COGNITIVE IMPAIRMENT HARMONIZATION STANDARDS

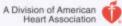
1. Alerting questions

2. Minimum data set for clinicians and nonspecialists

3. Minimum data set for researchers

Volume 33, Number 11, November 2002 ISSN 0039-2499 http://stroke.ahajournals.org

American Stroke Association



Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Cortical Topography of Stroke Lesion

■ Editorial

Stroke ASAP, Ahead of Print

■ Letters to the Editor

■ Original Contributions

Topographic and Volumetric Analysis of MCA Stroke
Local Architecture and Perfusion System of MCA Stroke
Changes of the Cerebral Arteries in CADASIL
Platelet Activation After Stroke
Bilateral Symmetry of Carotid Atherosclerosis
Infectious Burden and Progress of Atherosclerosis
Leukocyte Count and Aortic Plaque
Evaluation of Proxy Responses to Stroke Impact Scale
Frequency of Use, Benefit, and Validation of UCAs
Acupuncture for Poststroke Motor Recovery
Embolization of Ruptured Intracrunial Aneurysms in Elderly
Trunk Control as a Predictor of ADL Function
Natural History of Perihematomal Edema
Edema Volume Predicts ICH Outcome

Sensory Gating and Stroke Recovery
Hypertension Control and Stroke Recurrence
Long-Term Durability of Carotid Endarterectomy
AF Prevalence and Antithrombotic Use in the ED
Length of Stay of First-Ever Ischemic Stroke
Sildenafil and Functional Recovery After Stroke
Prevention of Vasospasm by Controlled-Release DETA/NO
NAD(P)H Oxidase and Cerebral Vasospasm
K*-Induced Conduction in Cerebral Arterioles
Tibolone Does Not Increase Carotid Atherosclerosis
eNOS Induction After Transient Focal Ischemia
Thrombolytic vs Mechanical Reperfusion in Stroke

Research Report

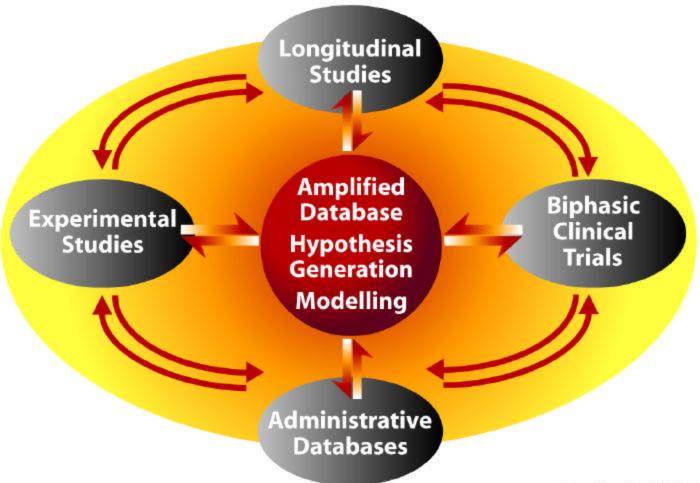
Epidemiology of Incident Stroke Signs and Symptoms

■ Comments, Opinions, and Reviews Acute Stroke With Atrial Fibrillation

■ Cochrane Corner



The Reciprocal Cycle of Discovery and Application



COMBINED EFFECT OF MIDLIFE VASCULAR RISK FACTORS

OR (95% CI)

 $BMI > 30 \text{ kg/m}^2$

2.1 (1.2 - 3.8)

SBP > 140 mmHg

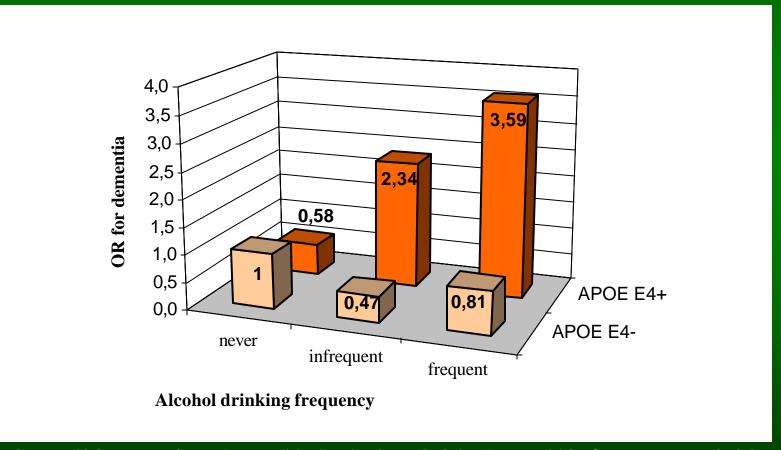
2.0 (1.0 - 3.9)

Cholesterol > 6.5 mmol/l 1.9 (1.94-3.5)

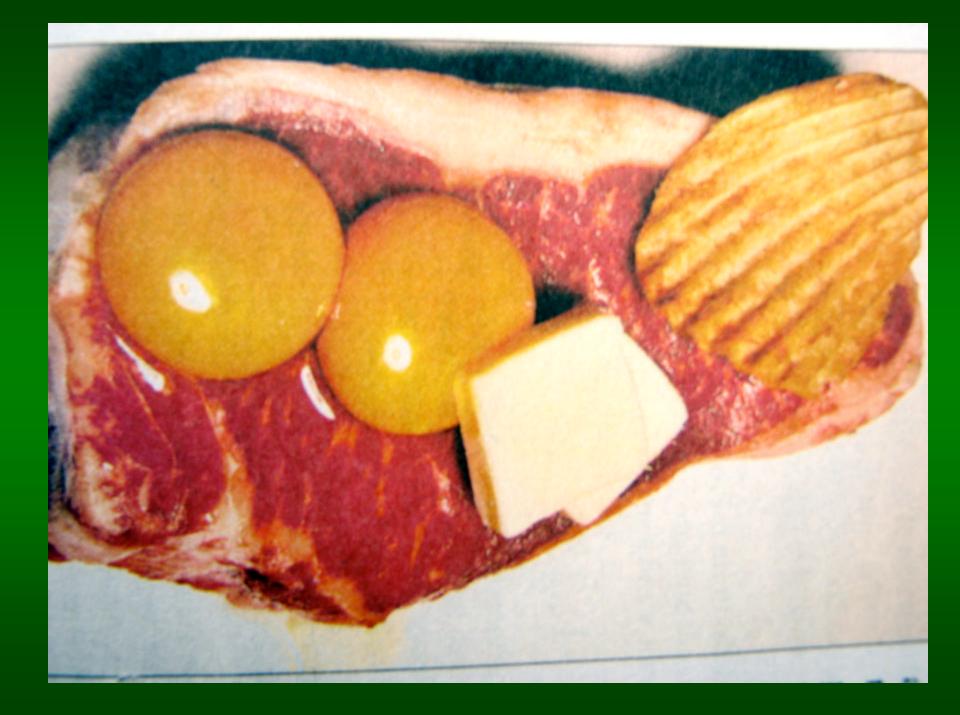
Combined

6.21(1.94 - 19.92)

INTERACTION BETWEEN ApoE4 AND ALCOHOL DRINKING – THE RISK OF DEMENTIA



Overall interaction ApoE4*alcohol p=0.04; ApoE4*infrequent p=0.02, and ApoE*frequent drinking p=0.03



FEBS 30116 FEBS Letters xxx (2005) xxx-xxx

High cholesterol diet induces tau hyperphosphorylation in apolipoprotein E deficient mice

3

5

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^c Karolinska Institutet, Neurotec Department, Division of Geriatric Epidemiology, ARC, Stockholm, Sweden

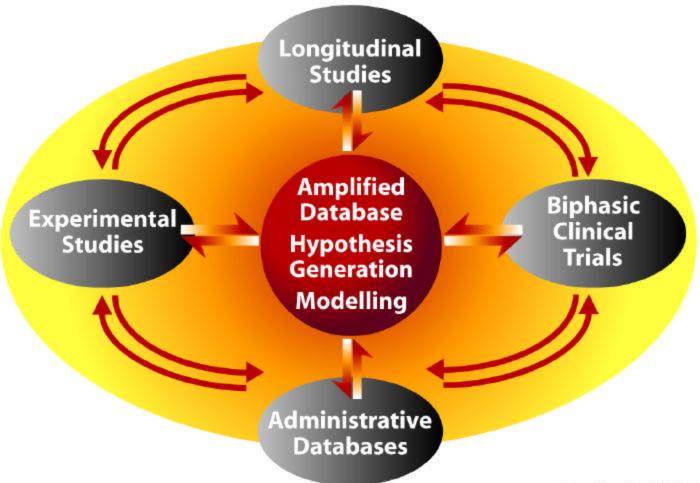
Received 15 August 2005; revised 14 October 2005; accepted 14 October 2005

Available online

Edited by Laszlo Nagy



The Reciprocal Cycle of Discovery and Application



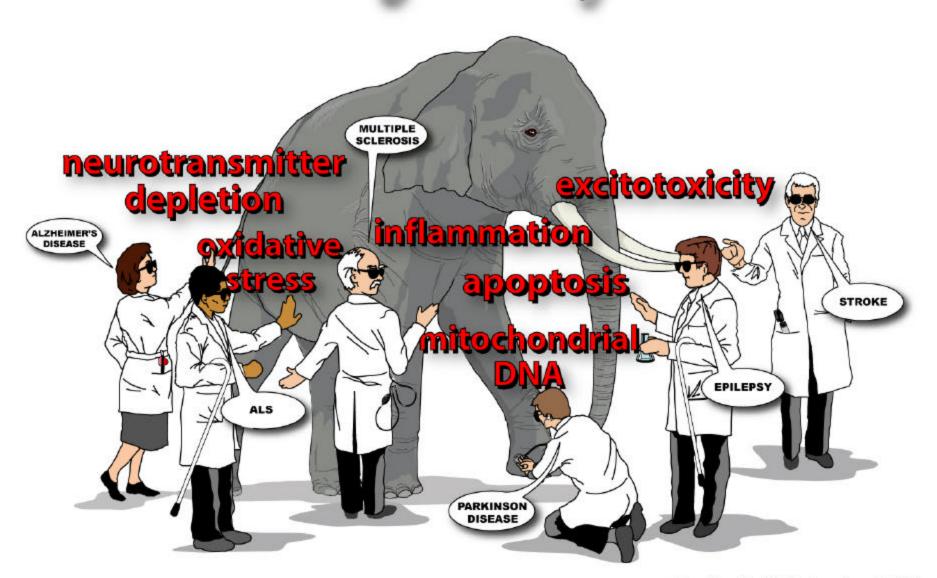
Knowledge is acquired in pieces,

but understood in patterns.

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The Pathogenesis Pachyderiii



A lot, it turns out. This a make is that folio acid may stave off a scentia.

By Didne Decembership

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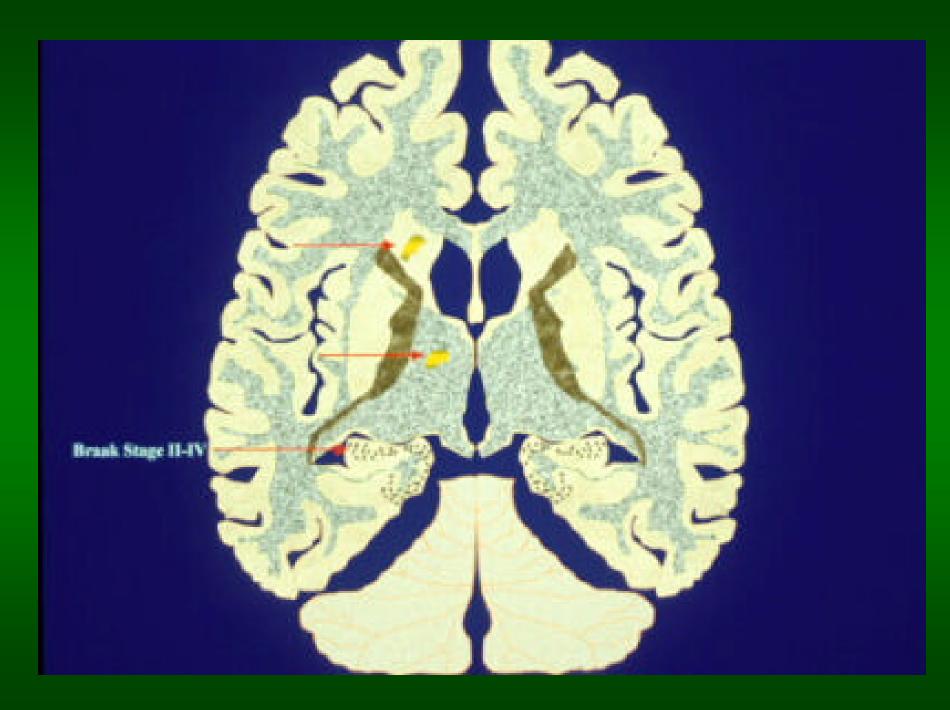
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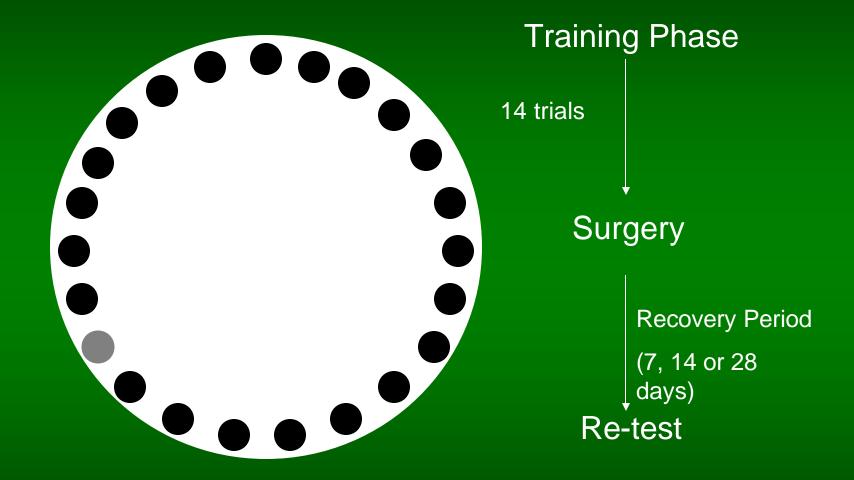
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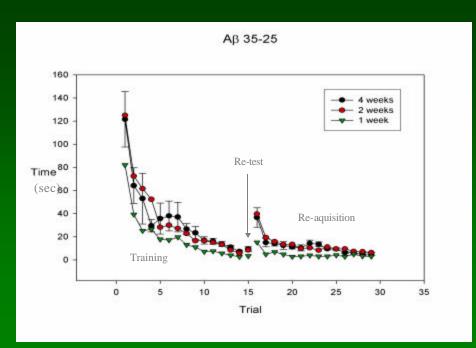
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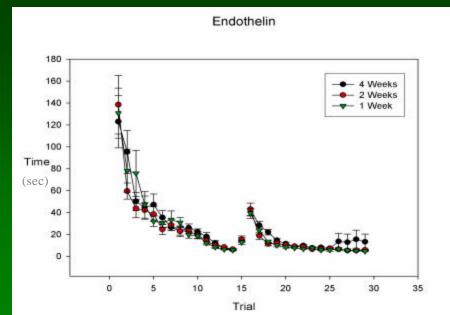
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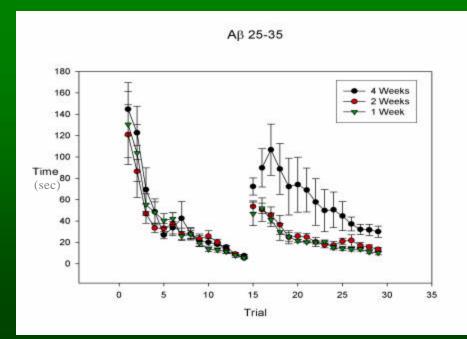


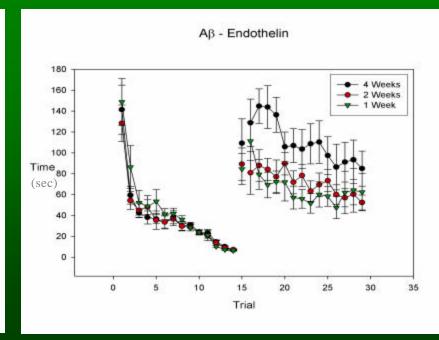
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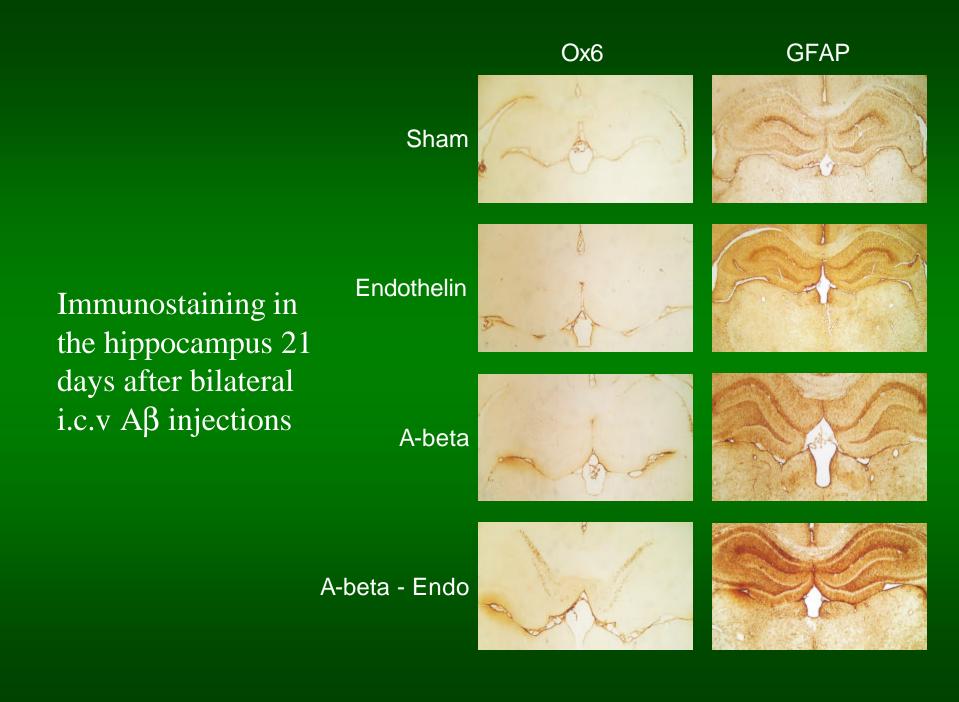












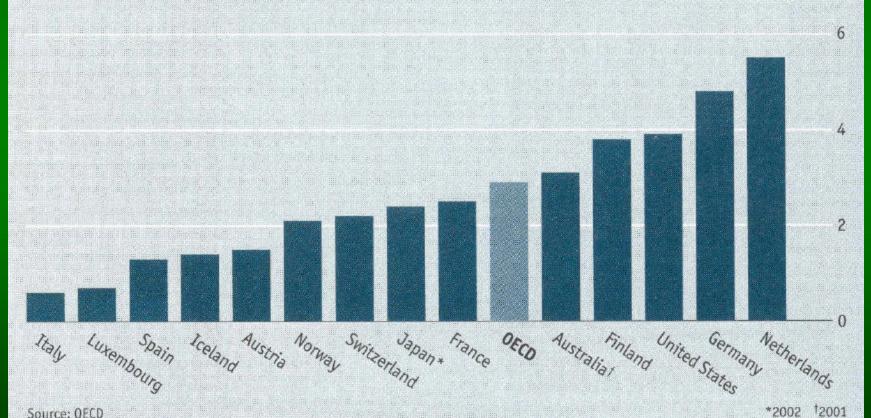
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Public-health programmes

Since the late 1990s, average health spending in rich countries has risen in real terms at double the rate of economic growth. Since public money generally predominates in the financing of health care, this is straining government budgets. Yet public-health and prevention programmes, which are especially cost-effective, account on average for only 3% of current health-care spending.

Public health and prevention as % of current health expenditure, 2003



In the Treatment of Diabetes, Success Often Does Not Pay

By IAN URBINA

Published: January 11, 2006

With much optimism, Beth Israel Medical Center in Manhattan opened its new <u>diabetes</u> center in March 1999. Miss America, Nicole Johnson Baker, herself a diabetic, showed up for promotional pictures, wearing her insulin pump.



- B Printer-Friendly
- Single-Page
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- Save Article



Vincent Laforet for The New York Times

Dr. Gerald Bernstein directed Beth Israel's diabetes center, with its focus on education. In one photo, she posed with a man dressed as a giant foot - a comical if dark reminder of the roughly 2,000 largely avoidable diabetes-related amputations in New York City each year. Doctors, alarmed by the cost and rapid growth of the disease, were getting serious.

At four hospitals across the city, they set up centers that featured a new model of treatment. They would be boot camps for diabetics, who struggle daily to reduce the sugar levels in their blood. The centers would teach them to check those levels, count calories and exercise with discipline, while undergoing prolonged monitoring by teams of specialists.

But seven years later, even as the number of New Yorkers with Type 2 diabetes has nearly doubled, three of the four centers, including Beth Israel's, have closed.

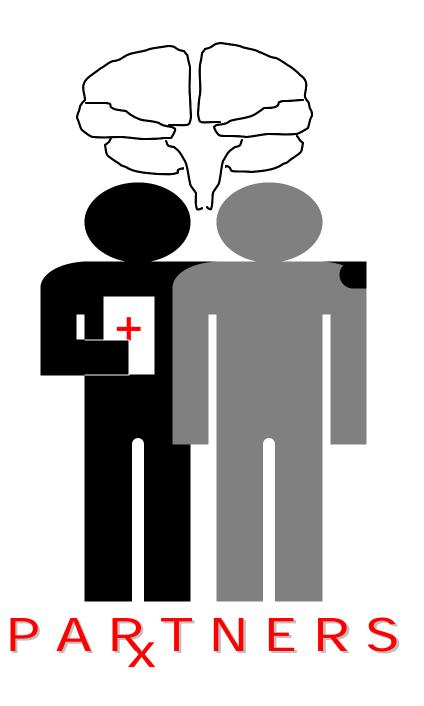
GOOD CARE, BAD BUSINESS BAD HEALTH, GOOD BUSINESS

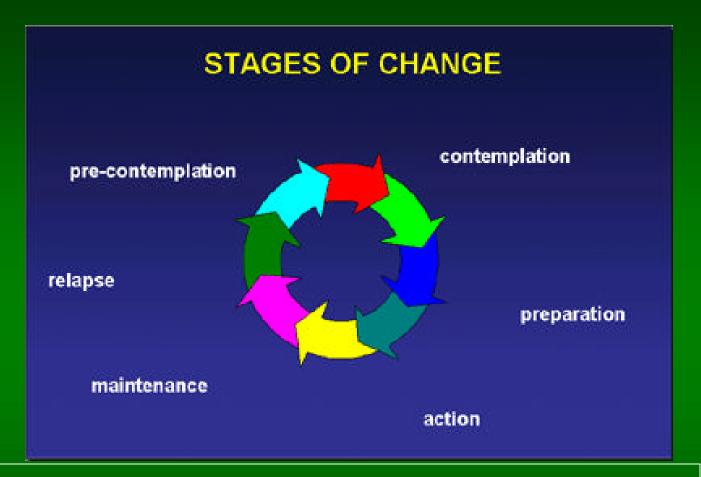
	Time	Cost	Reimbursement	Balance
Nuritionist	60 min	\$70	\$15-20	Loss
Bariatric surgery	40 min	\$50,000		Profit
Podiatrist	35 min	\$150-20	00 \$30-90	Loss
Foot amputation			\$30,000 NY Times 12 Jar	Profit n 2006

THE FUTURE OF STROKE AND ALZHEIMER'S DISEASE PREVENTION

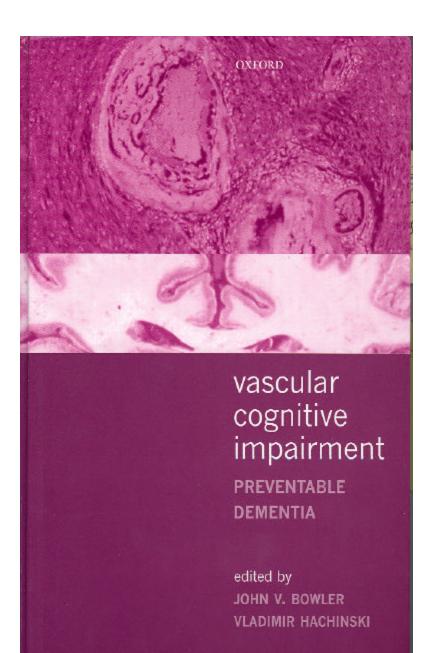
1. More

- a) Population health and social and norms policies
- b) Responsibility of individual
- c) Involvement of non-medical health professional and non-experts
- 2. More coordinated approach to preventing chronic disease
- 3. Genetic individualization





Stages of change indicate the patient's 'readiness' to change



CRITERIA FOR VASCULAR DEMENTIA

The California Criteria	Sensitivity 50%	Specificity 87%
NINDS-AIREN Criteria	50%	87%
DSM – IV Criteria	50%	87%
Ischemic score	89%	89%

Knopman et al Neurology, 2001;56:1143-53

HOW CAN YOU HELP?

- 1. Join a working group at vas-cog.org and help develop standardized and priortized clinical, imaging, biological and pathological descriptors
- 2. Survey the prevalence of vascular cognitive impairment in populations at risk e.g. hypertension, diabetes, lipid, peripheral vascular disease and cardiology clinics
- 3. Write critical reviews integrating current knowledge and suggesting new analyses and directions



VAS-COG 2007

San Antonio, Texas, USA • 11-15 July

Lifetime Risk of Dementia: Women - 65 yrs

