

ESC Congress 2005
STOCKHÖLM - SWEDEN



Interaction between APOE genotype
and cardiovascular risk factors
for Alzheimer's disease



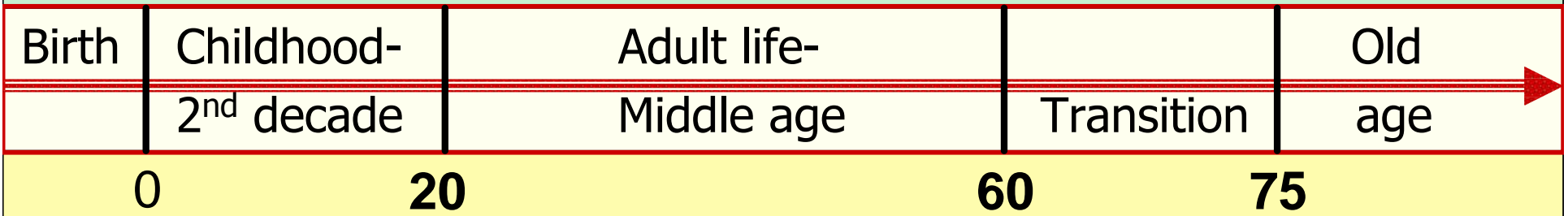
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Sweden

Risk Factors



Protective Factors

Risk Factors

Genet
Susc.

SES-
Related
factors

Life habits

Morbidity:
Vascular dis.

Environmental exp.
Solvents - EMF

Life habits

Morbidity:
Vascular dis.

Depression
Head trauma

0

20

60

75

High
education

Lyfe style:
Physical-mental act.

Drugs:
Antihypertensive

Lyfe style:
Physical-mental act.

Diet: Fish, vegetables
Mod. alcohol

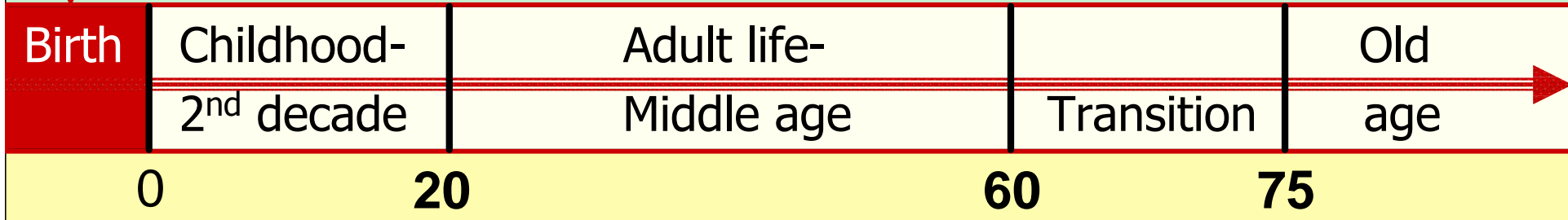
Drugs:
Antihypertensive, statin
NSAID, HRT

Protective Factors

Risk Factors

Genetic Susceptibility

Dementia occurrence



Protective Factors

Risk Factors

APOE e4



**Dementia
occurrence**

Birth

Childhood-
2nd decade

Adult life-
Middle age

Transition

Old
age

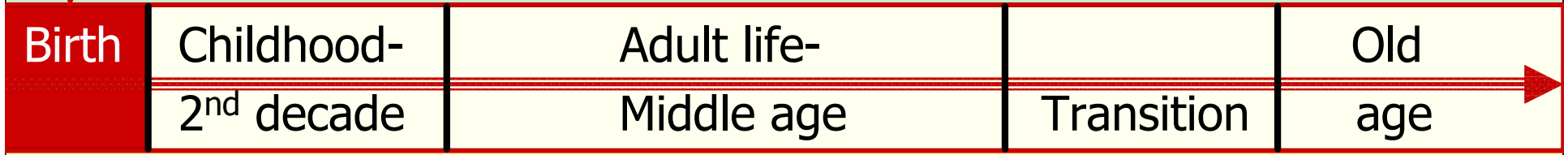
0

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60

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Protective Factors



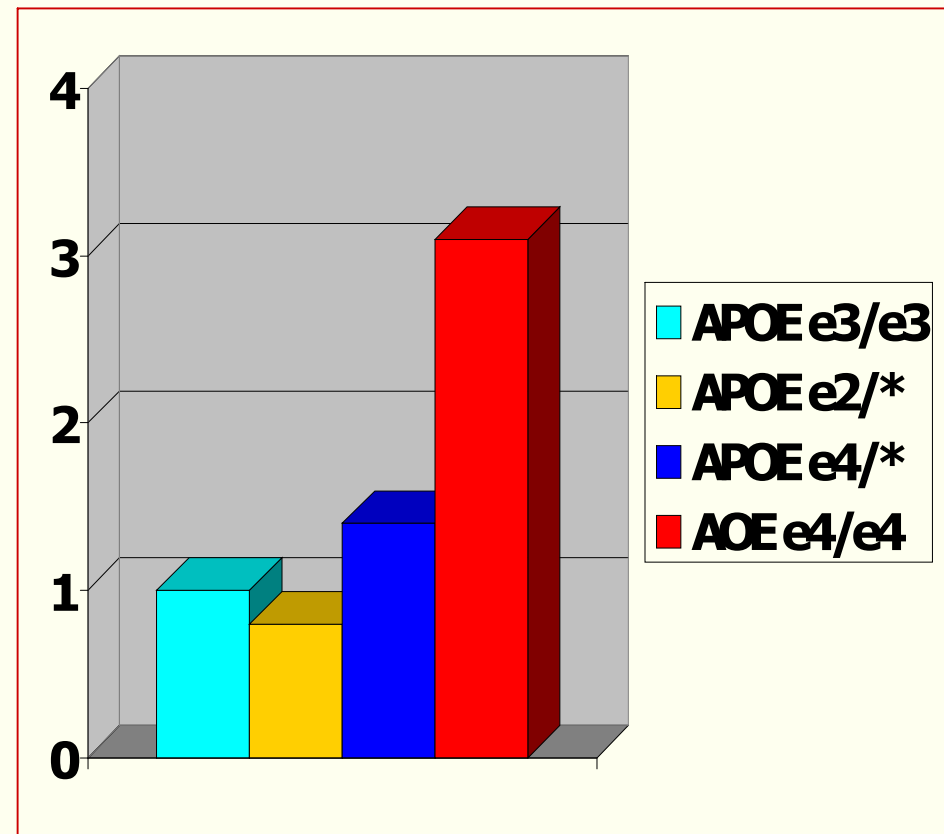
Apolipoprotein E allele $\epsilon 4$

- Consistently found associated with increased AD risk
- This association decreases with increasing age
- In 70+ subjects ApoE e4 explains 15-20% of the cases

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RR for AD in the KP



Qiu et al, J Neurol Neurosurg Psych 2004

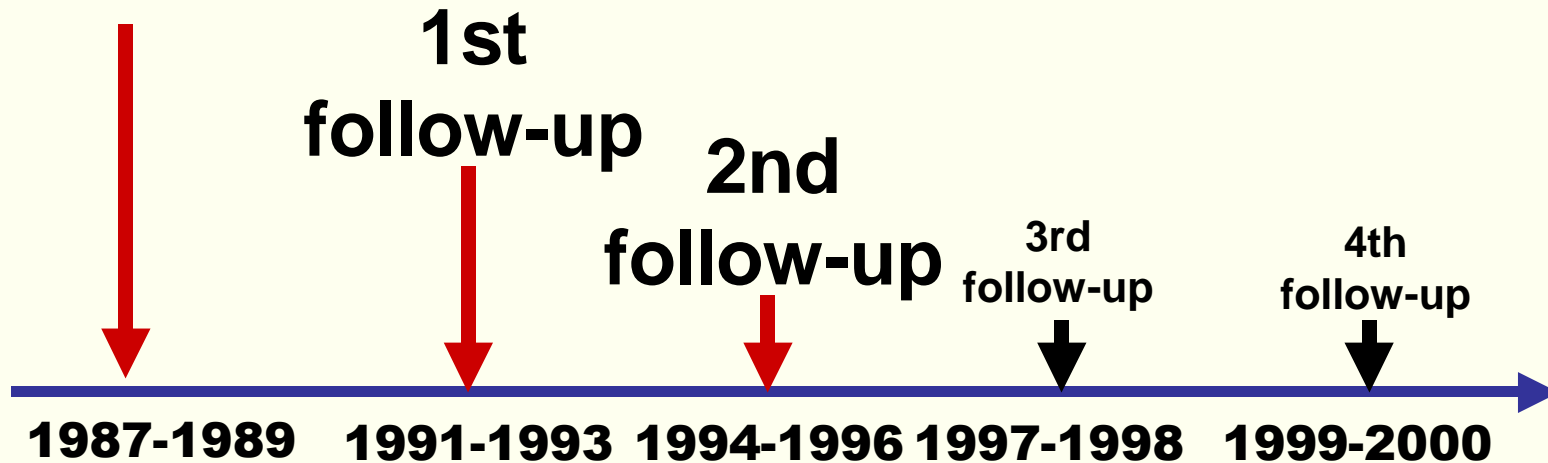


The Kungsholmen Project

Stockholm, Sweden

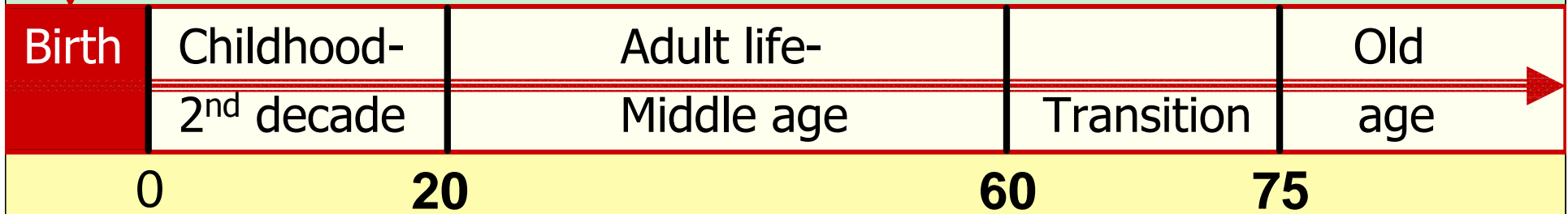
1810 participants at baseline
75+ old
Living in a central area of Stockholm

Baseline



Risk Factors

Is it possible to modify the genetic susceptibility of Alzheimers 's disease?



Protective Factors



Kungsholmen Project

1. Hypertension

National Public Health Institute



**CAIDE –
Cardiovascular risk factors,
Ageing and Dementia**

**2. Alcohol
3. Physical
activities**



The Kungsholmen Project

Stockholm, Sweden

STUDY 1

Guo et al, Arch Neurol 1999; 56: 991-996

Subjects with antihypertensive treatment had 40% reduced risk of dementia

STUDY 2

*Guo et al,
Am J Epidemiol
2001; 153:225*

Adjusted RR	Antihypertensive therapy	
	Yes	No
$\epsilon 4-$	0.9 (0.6-1.3)	1
$\epsilon 4+$	0.8 (0.4-1.5)	2.3 (1.5-3.5)



STUDY 3 *Qiu et al, Neurology 2003; 61:655*

APOE ϵ 4, BP & incident dementia

		No. of AD	Adj. RR	95% CI
ϵ 4 carrier	SBP, mmHg			
No	<140	20	1.0	Ref.
No	\geq 140	112	1.8	1.0–3.3
Yes	<140	15	2.3	1.1–4.7
Yes	\geq 140	57	3.0	1.6–5.5



STUDY 3

Qiu et al, Neurology 2003

Adjusted RR

Antihypertensive therapy
Yes No

High SBP/ ϵ 4+

1.5
(0.7-3.2)

3.2
(1.6-6.4)

Subjects with normal BP, ϵ 4-, and no drugs
as reference

The Honolulu Aging Study

APOE e4, midlife BP and antihypertensives

Peila et al, *Stroke* 2001

Adjusted RR

Subjects with
normal BP and
e4- as reference

Antihypertensive therapy

Yes

No

Midlife high BP/ ϵ 4-

1.5
(0.8-2.4)

2.4
(0.6-10.4)

Midlife high BP/ ϵ 4+

1.9
(0.7-4.5)

10.8
(1.4-83.5)



Kungsholmen Project

1. Hypertension

National Public Health Institute

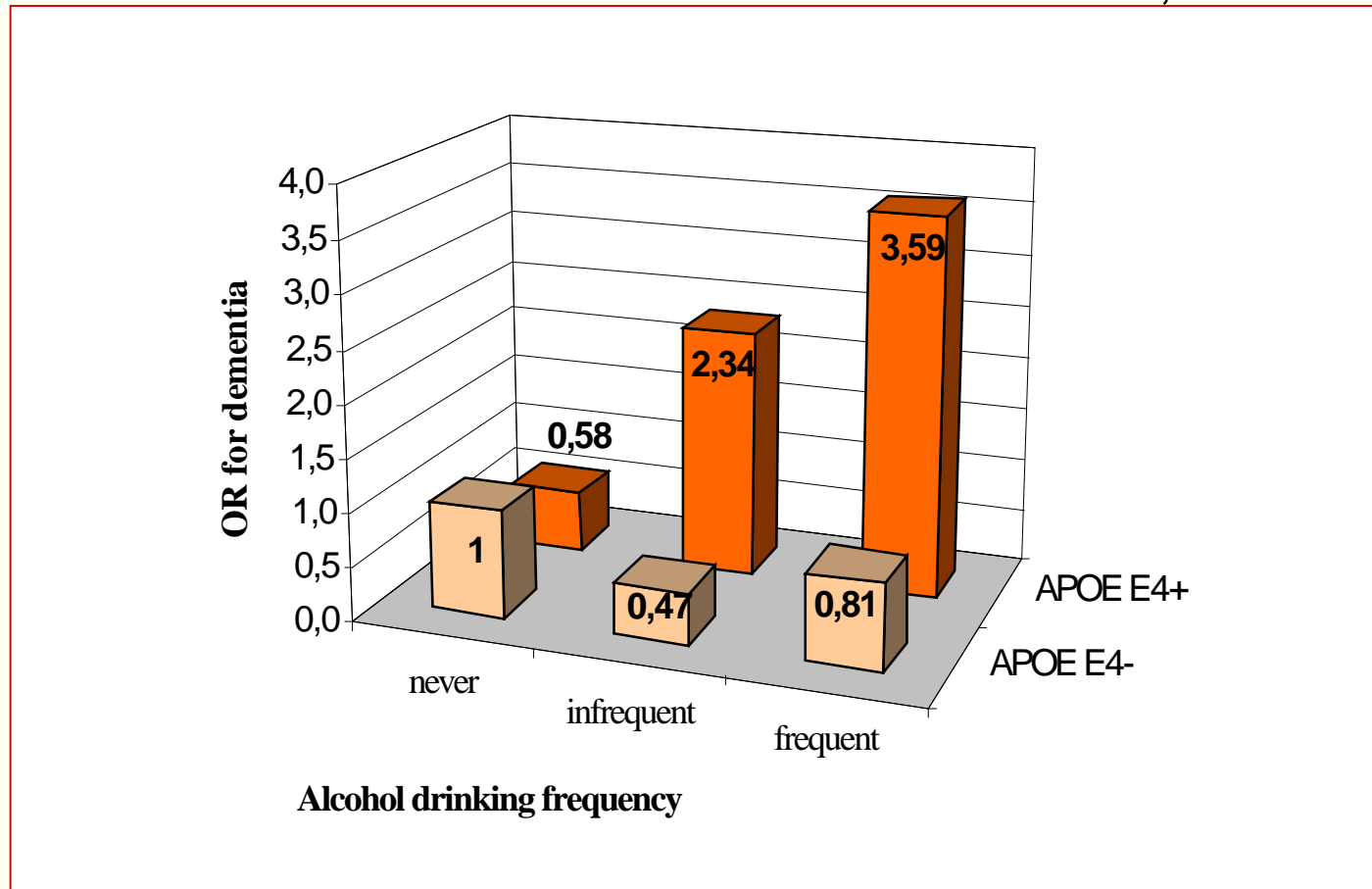


**CAIDE –
Cardiovascular risk factors,
Ageing and Dementia**

**2. Alcohol
3. Physical
activities**

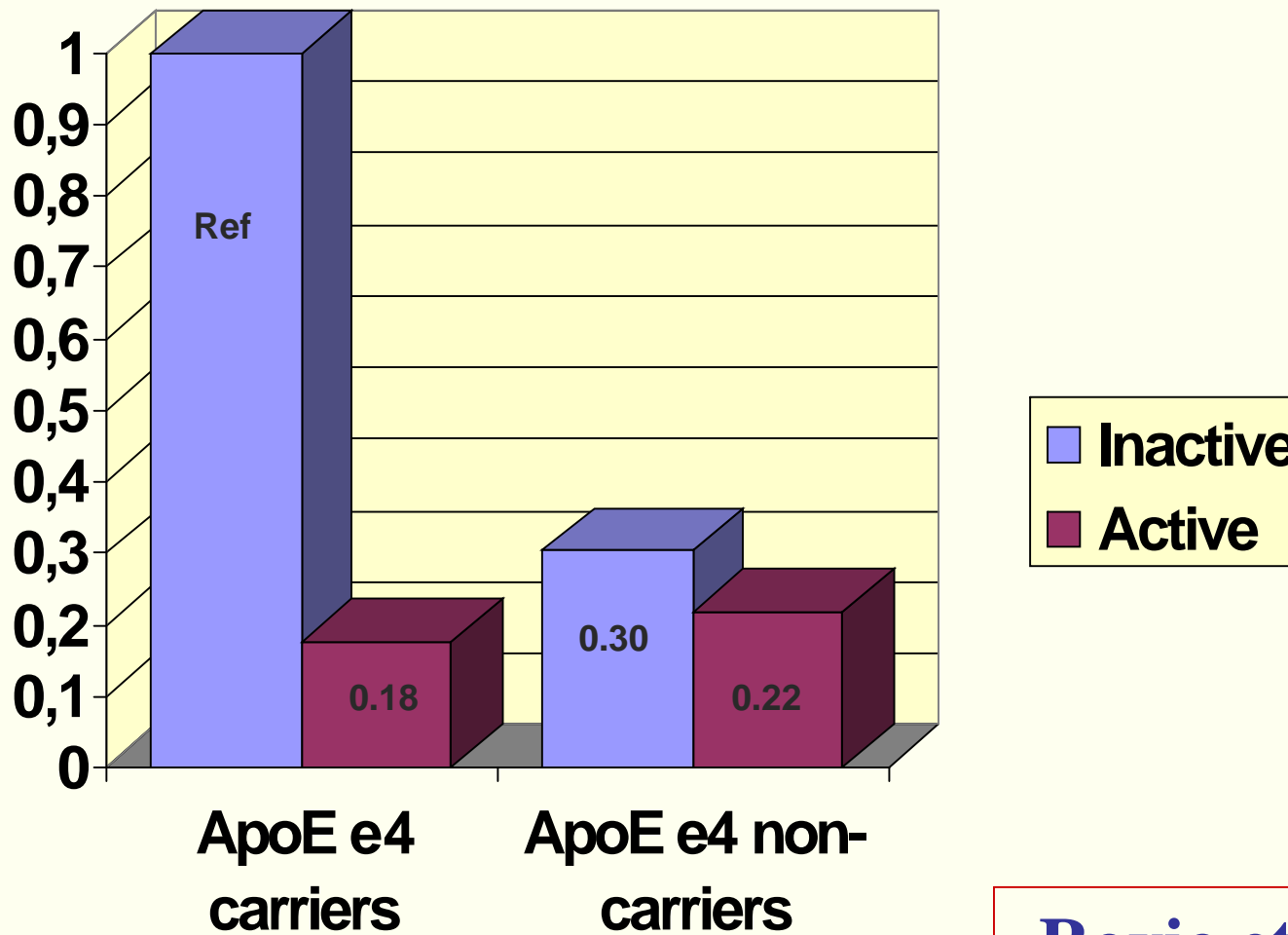
Interaction between ApoE4 and alcohol drinking - the risk of dementia

Anttila et al., BMJ 2004



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

ApoE ϵ 4 allele, physical activity at midlife and AD risk



Rovio et al, 2005

Is it possible to prevent dementia?

Control the BP

- **Even during middle age**
- **Not too low**
- **Special focus on ApoE e4 carriers**

Be and maintain an active life

- **Social integration**
- **Physical activities**
- **Mental activities**