

Celebrating 30 years of the MIDSPAN Studies



**Lifecourse influences on
adult health: MIDSPAN
contributions**

George Davey Smith

Before Midspan



Framingham Massachusetts

Framingham Heart Disease Study

- Set up in 1949 to identify factors that contribute to cardiovascular disease
- Blood-based measures included from the start
- 5209 men and women aged 30-62 years recruited
- Subjects examined every two years to date and linked to deaths and clinical events

Framingham Study

”most significant milestones”

- 1960 Cigarette smoking increases risk of heart disease
- 1961 Cholesterol level, blood pressure, and electrocardiogram abnormalities increase risk of heart disease
- 1967 Physical activity reduces risk of heart disease and obesity to increase risk of heart disease
- 1970 High blood pressure increases risk of stroke
- 1976 Menopause increases risk of heart disease
- 1988 High levels of HDL cholesterol reduces risk of CHD
- 1994 Enlarged left ventricle (one of two lower chambers of the heart) shown to increase the risk of stroke

But interest in early life and
prenatal influences on chronic
disease in adulthood



23rd Infantry US Army Korea October 1951



Vietnam

Coronary artery disease in young US war fatalities

Korean war - early 1950s (Enos et al, JAMA 152:1090-1093, 1953)

- 200 autopsied combatants, mean age = 22 years
- 77% evidence of atherosclerosis
- 15% clinically significant narrowing of vessel(s)

Vietnam war - late 1960s (McNamara et al, JAMA 216: 1185-1187,1971)

- 105 autopsied combatants, mean age = 22 years
- 45% evidence of atherosclerosis
- 5% clinically significant narrowing of vessel(s)

Early life origins

ARTICLES

BIOLOGICAL FREUDIANISM

Lasting Effects of Early Environmental Influences

H 2585

René Dubos, Ph.D. (M.D. Hon.), Dwayne Savage, Ph.D., and Russell Schaedler, M.D.

The Rockefeller University, New York

the childhood shews the man
As morning shews the day . . .

JOHN MILTON
Paradise Regained

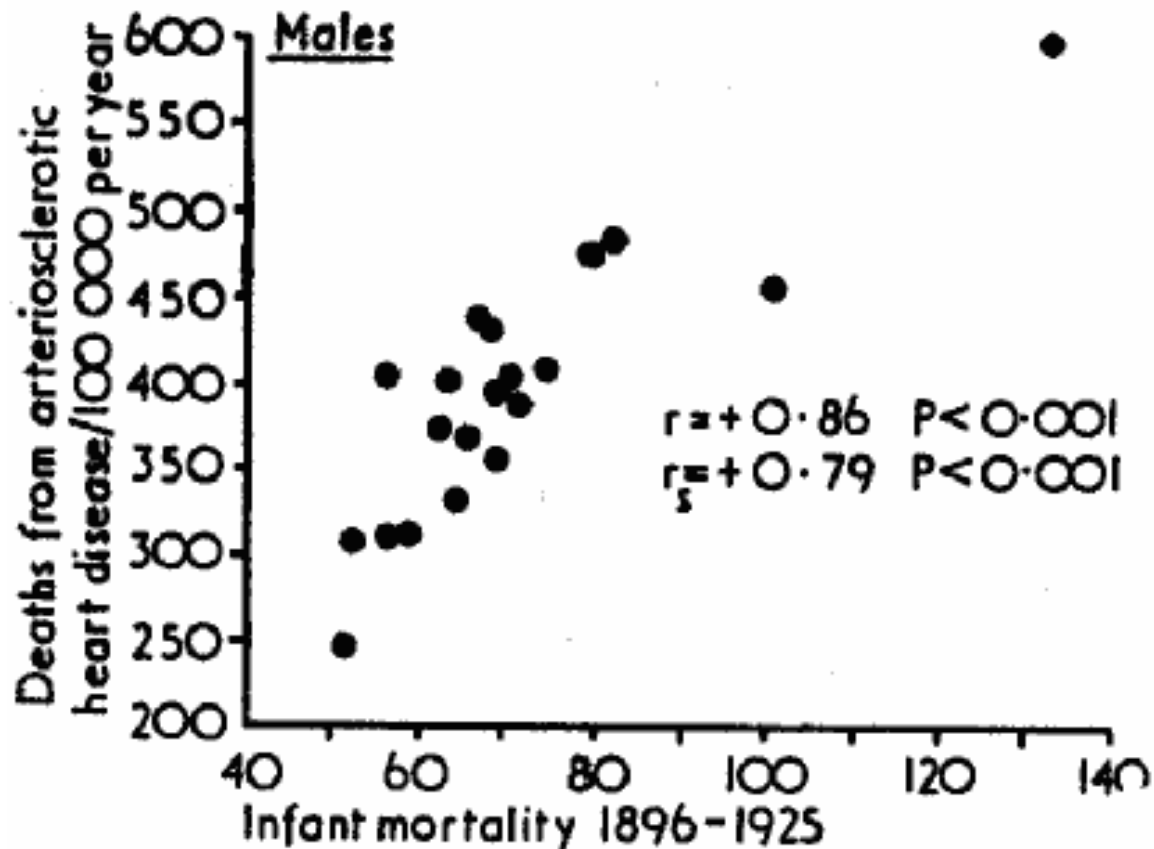
SOCIAL DETERMINANTS OF GROWTH AND HEALTH

As commonly used, the phrase "early influences" denotes the conditioning of

girls; and by the earlier age of the first menstrual period. In England for example, the menarchal age was 15½ for the well-off townspeople in 1820, whereas it had fallen to 13 in 1960.¹

Needless to say, the trend towards earlier maturation cannot be extrapolated far back in time. In fact there is evidence that the menarchal age was 14 in Shakespeare's time,

Correlation between mortality from arteriosclerotic heart disease, 1964-67, in men aged 40 to 69 years (standardised rates/100,000 population) and infant mortality rates 1896-1925



Anders Forsdahl, Br J Prev Soc Med 1977

Age adjusted relative rates of CVD mortality by father's social class and screening social class

Screening social class

Father's social class	Non manual	Manual
Non manual	1	1.45 (1.04-2.01)
Manual	1.56 (1.29-1.88)	1.86 (1.56-2.22)

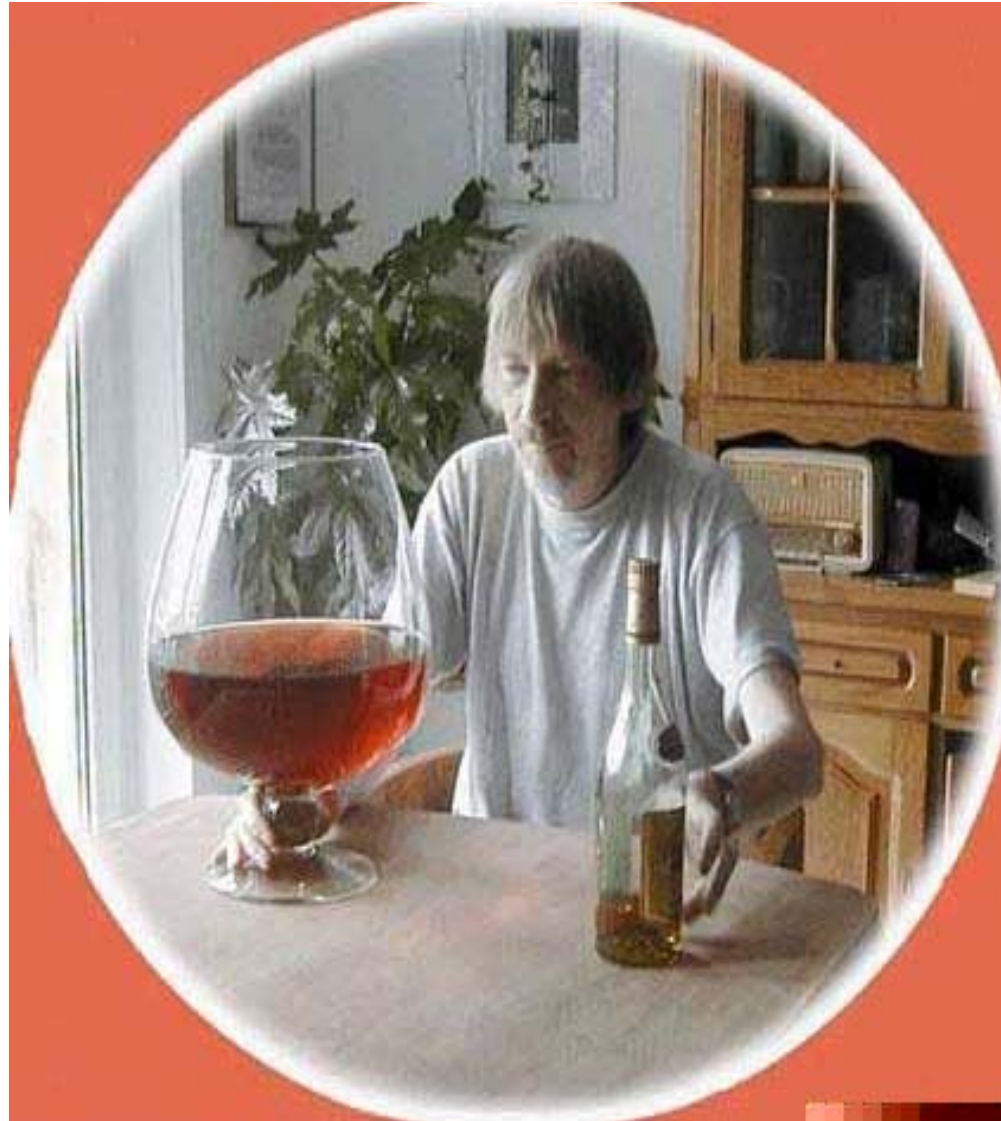
Davey Smith and Hart, AJPH 2002

Age adjusted relative rates of CVD mortality by father's social class and smoking

Father's social class	Smoking	
	Other	Current cigarette
Non Manual	1	2.20 (1.66 – 2.93)
Manual	1.80 (1.40 – 2.31)	3.11 (2.45 – 3.95)

Davey Smith and Hart, AJPH 2002

My Doctor said “Only 1 glass of alcohol a day”. I can live with that.



Age adjusted relative rates of CVD mortality by father's social class and alcohol

Alcohol

<15 units/week

≥15 units/week

Non manual

1

1.28 (0.93 - 1.76)

Manual

1.53 (1.28 - 1.82)

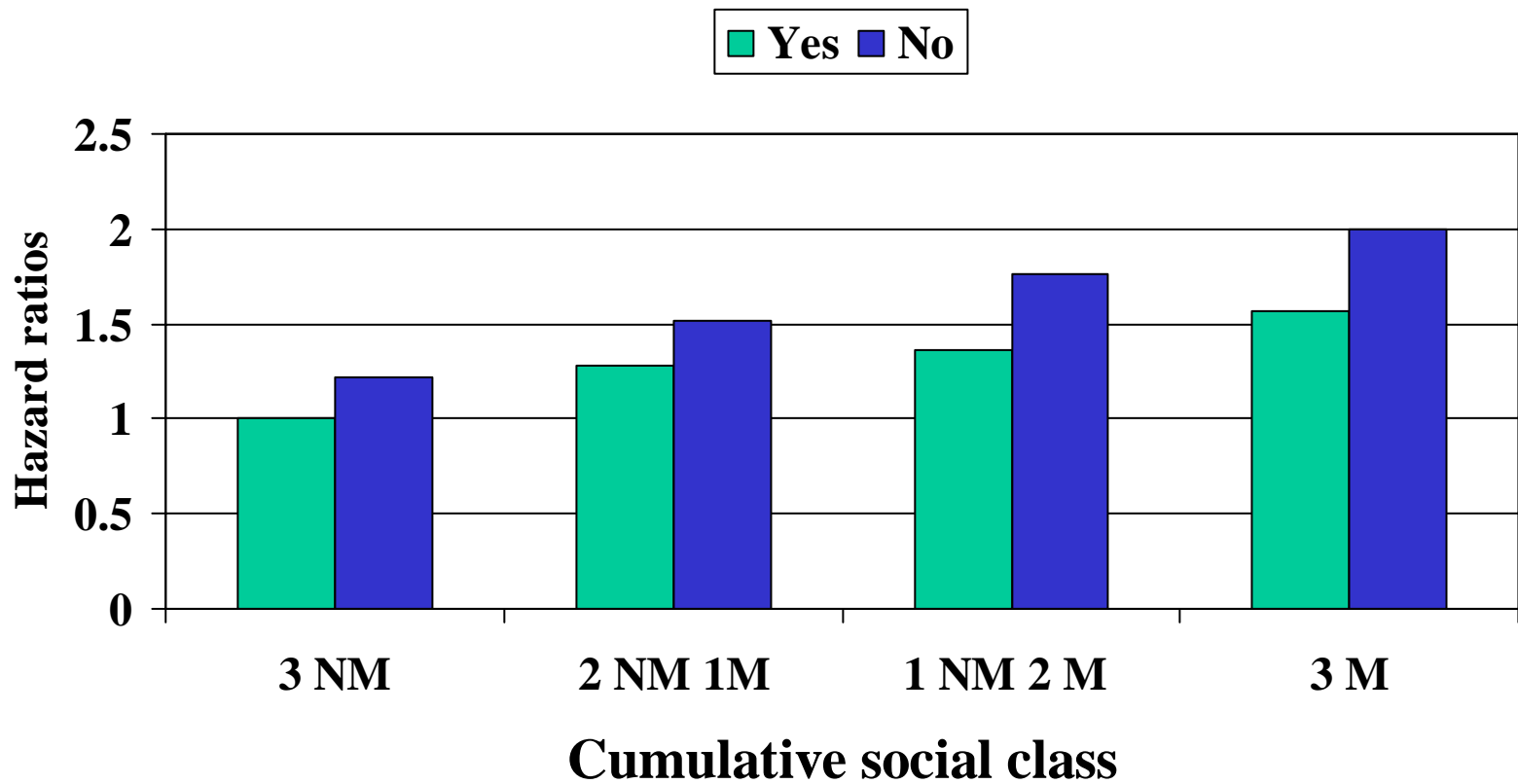
2.13 (1.77 - 2.57)

Cardiovascular mortality according to cumulative risk indicator (father's social class, screening social class, smoking, alcohol use)

	N	CVD deaths	Relative risk
4 favourable (0 unfavourable)	517	47	1
3 favourable (1 unfavourable)	1299	227	1.99 (1.45 - 2.73)
2 favourable (2 unfavourable)	1606	354	2.60 (1.92 - 3.52)
1 favourable (3 unfavourable)	1448	339	2.98 (2.20 - 4.05)
0 favourable (4 unfavourable)	758	220	4.55 (3.32 - 6.24)

Davey Smith and Hart, AJPH 2002

All cause mortality by cumulative social class and car driving



Davey Smith et al, BMJ 1997

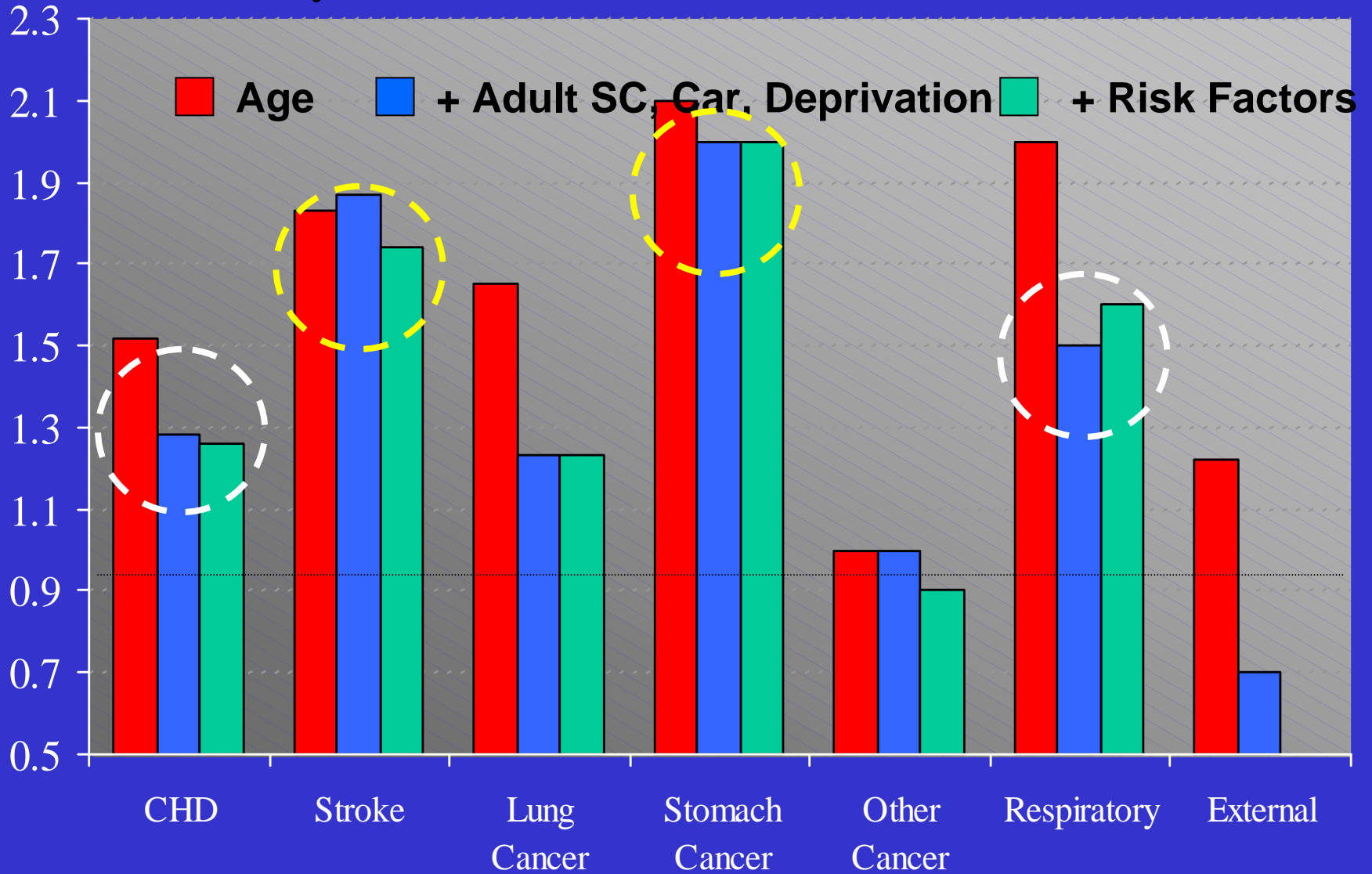
The Prince's sorrows
accumulating day by day would
in the end be the real cause of his
death

Giuseppe Tomasi di Lampedusa
“The Leopard”, 1958

Relative rates for all-cause mortality for men with manual social class fathers in the Collaborative study.

Adjustments	Manual social class	P value for trend
Age	1.44 (1.27-1.63)	0.0001
Age, adult social class, deprivation category, car	1.22 (1.06-1.39)	0.024
Age, adult social class, deprivation category, car, risk factors	1.19(1.04-1.37)	0.042

Mortality of Men with Father's of Manual Social Class



Risk factors for cardiovascular disease in relation to father's social class and own social class included simultaneously

	<u>Father's social class</u>		<u>Own social class</u>	
Risk factor				
✓ Diastolic blood pressure (mm Hg)	0.37	0.018	0.50	0.0002
✓ Serum cholesterol (mmol/l)	-0.05	0.001	-0.19	<0.0001
? Recreational exercise (hours/week)	-0.16	0.06	-0.23	0.002
Current smokers (%)†	1.01	0.68	1.36	<0.0001
✓ Body mass index (kg/m ²)	0.20	<0.0001	-0.05	0.23
✓ FEV ₁ score (%)	-1.06	0.0003	-2.29	<0.0001

†Logistic regression for smoking: odds ratio reported

Childhood social class and stroke subtype

	Manual vs non-manual	Manual vs ⁺ non-manual
Haemorrhagic	2.84 (1.12-7.20)	3.22 (1.15-9.03)
Ischaemic	1.25 (0.77-2.03)	0.92 (0.53-1.61)

⁺risk factor adjusted

Hart&Davey Smith, J Epidemiol Community Health 2003

Relative risk of death in relation to 10cm lower height

	Male	Female
All cause	1.13 (1.07-1.19)	1.19 (1.11-1.26)
CHD	1.14 (1.05-1.24)	1.29 (1.15-1.45)
Stroke	1.32 (1.11-1.57)	1.23 (1.04-1.45)
Respiratory	1.45 (1.21-1.72)	1.75 (1.40-2.18)
Stomach cancer	1.43 (0.95-2.14)	1.54 (0.98-2.41)
Colorectal cancer	0.71 (0.53-0.96)	0.80 (0.58-1.10)
Haematopoietic cancer	0.63 (0.39-1.03)	0.45 (0.28-0.73)

Davey Smith et al. J Epidemiol Community Health 2000;54:97-103

Stroke by height: Paisley and Renfrew study

	<i>Height quintile</i>					<i>RR associated with 10 cm increase in height</i>
	1	2	3	4	5	
<i>All stroke</i>						
Relative rate	1	0.96	0.82	0.77	0.70	0.80 (0.73 to 0.88)
<i>Haemorrhagic</i>						
Relative rate	1	1.16	0.93	0.66	0.54	0.70 (0.51 to 0.97)
<i>Ischaemic</i>						
Relative rate	1	1.16	1.17	1.02	0.91	0.87 (0.71 to 1.06)

McCarron et al. J Epidemiol Community Health 2001;55:404-405

Sir or Madam

I am an O.A.P
& I've just read the headlines
regards your 'Richer the taller'
investigations & I have this to
say.

We were six children and
one parent (mother) & once we
had but one egg between us all,
& eating apple cores found in the
gutter was common. Our groceries
were bought on Saturday & gone
by Tuesday. I cannot believe
you didn't see the connection
between 'height & money' in the
first place and you got paid for
this? Unbelievable.

yours.

Jane Lutzey

P.S I'm 5' 2", & weigh 8½ stone & all
of my family tend to be small.

Family size and mortality

Per sibling relative risk of mortality

	Adjustments			
	Age	Age, smoking	Age, SEP	Age, SEP, risk factors
All-cause	1.04*	1.04*	1.01	1.01
CHD	1.04*	1.03*	1.01	1.01
Stroke	1.03	1.03	1.01	1.01
Lung cancer	1.08*	1.07*	1.03	1.03
Stomach cancer	1.16*	1.13*	1.14*	1.14*

*p<0.05

Hart, J Epidemiol Community Health 2003

Stroke subtype by number of siblings

	0-2	3-4	5-6	7+	per sib	per sib ⁺
Haemorrhagic	1	1.63	1.79	2.33	1.11	1.11
Ischaemic	1	0.86	1.00	1.36	1.03	1.01

⁺adjusted SEP and risk factors

Other relevant Midspan findings

Education

Birthweight

Offspring birthweight

Leg Length

IQ

