

How Stress Gets Under Your Skin: psychobiological studies of social status, stress and health

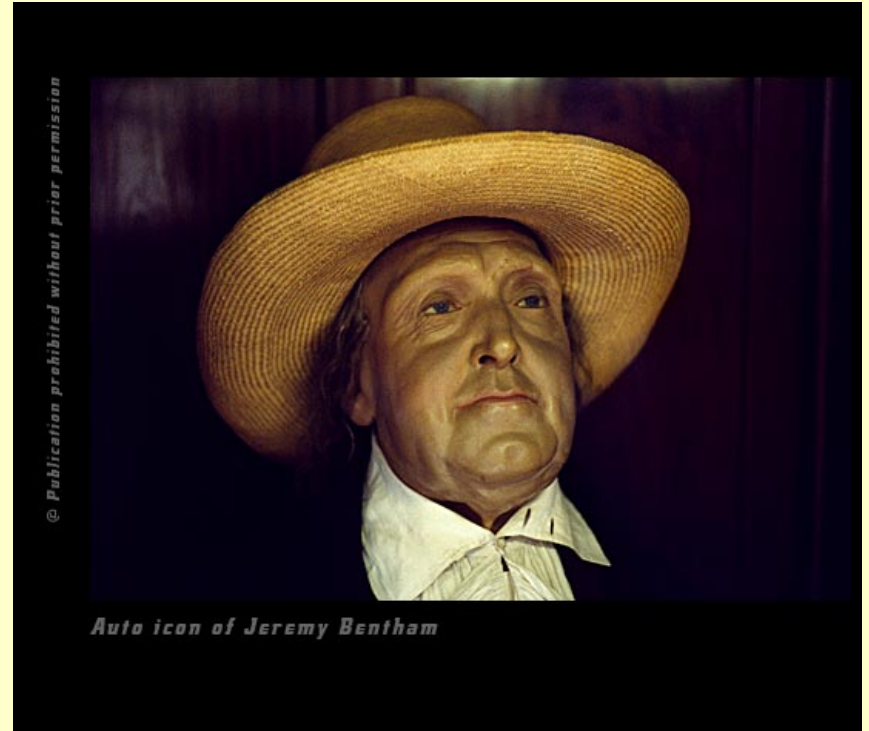
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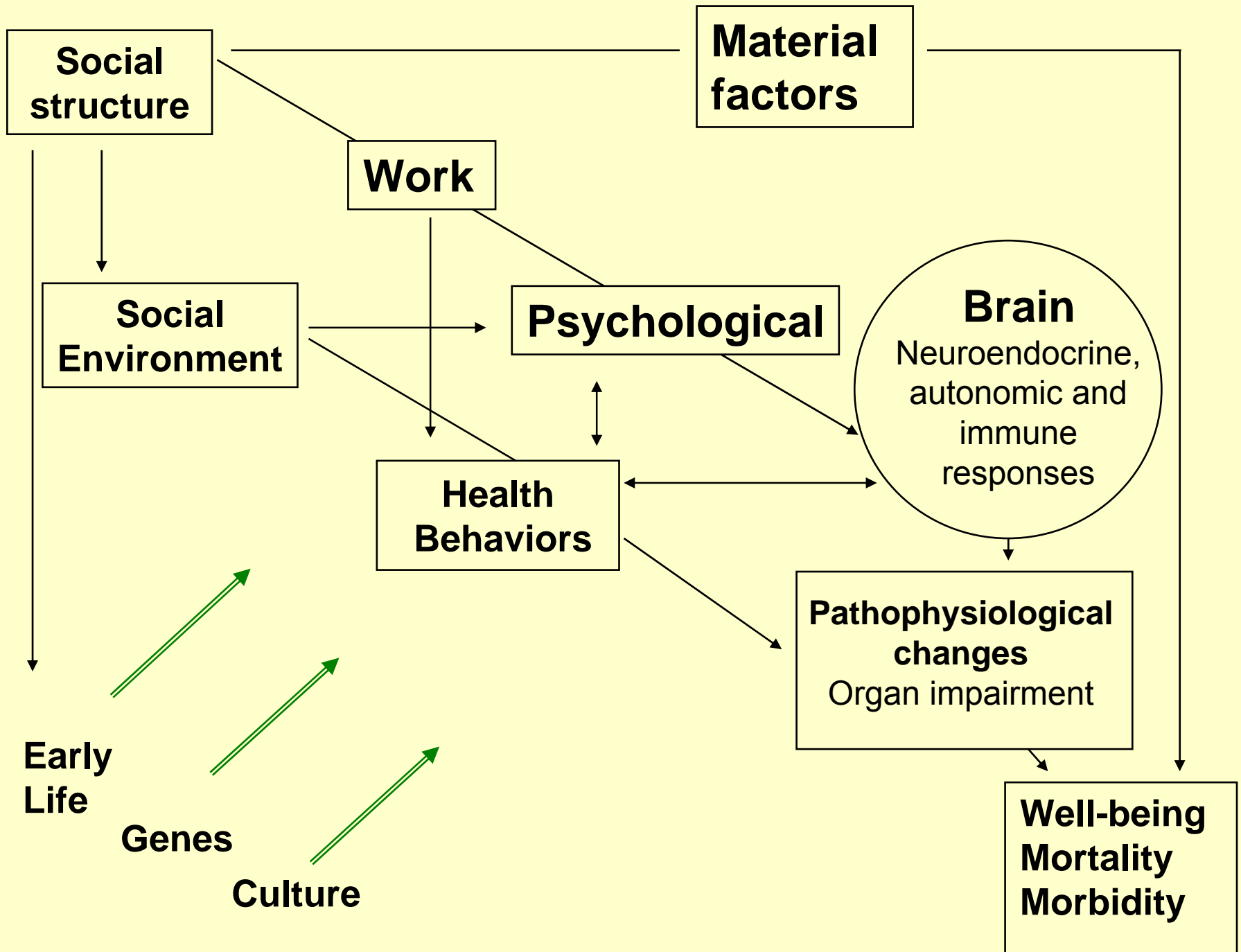
<http://www.ucl.ac.uk/psychobiology/>





Department of Epidemiology and Public Health, UCL

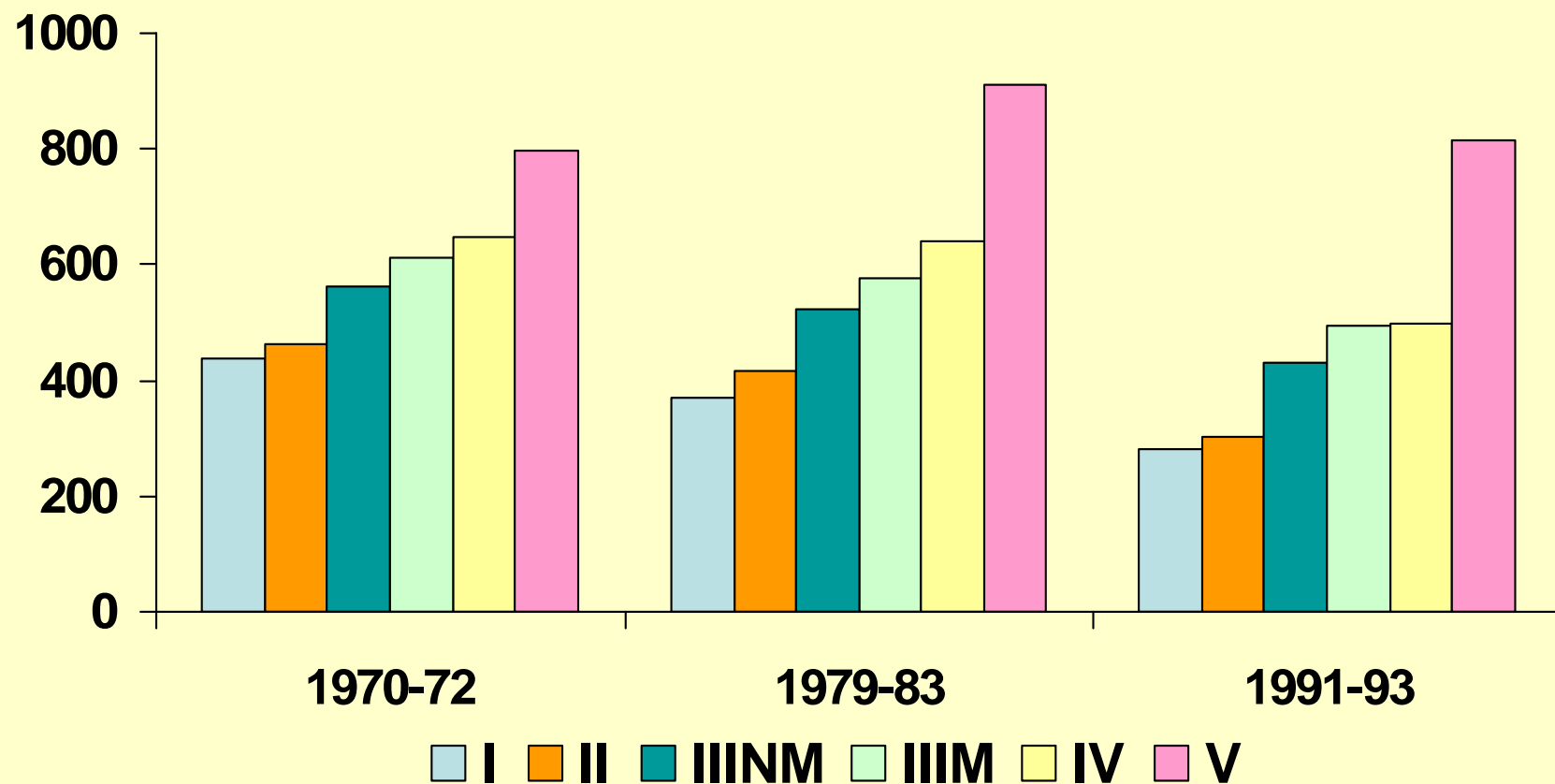
- Whitehall and Whitehall II epidemiological studies
- English Longitudinal Study of Ageing (ELSA)
- Health Survey for England
- National Child Development Study (1946)
- Psychosocial factors in Eastern Europe (HAPIEE)
- Ethnic minority psychiatric illness rates (EMPIRIC) study



How stress gets under your skin

- Psychosocial factors and physical illness
- Psychobiological processes
- Methods of investigation
- Psychobiological responses and health outcomes

Premature mortality rates (deaths per 100,000) by social class in men aged 20-64



Psychosocial factors related to the development of physical disease

- Chronic life stress

High demand/low control at work; effort-reward imbalance; financial strain; marital conflict; caregiving

- Social environment

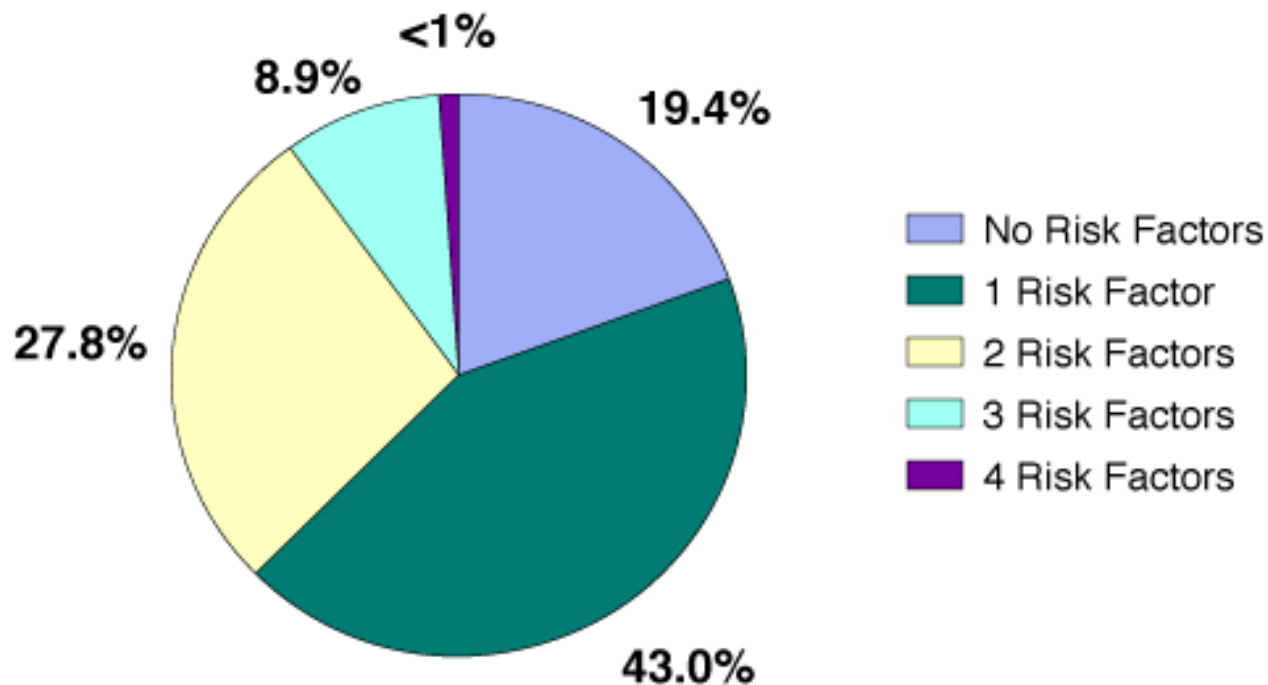
Social isolation; emotional support; social cohesion

- Psychological factors

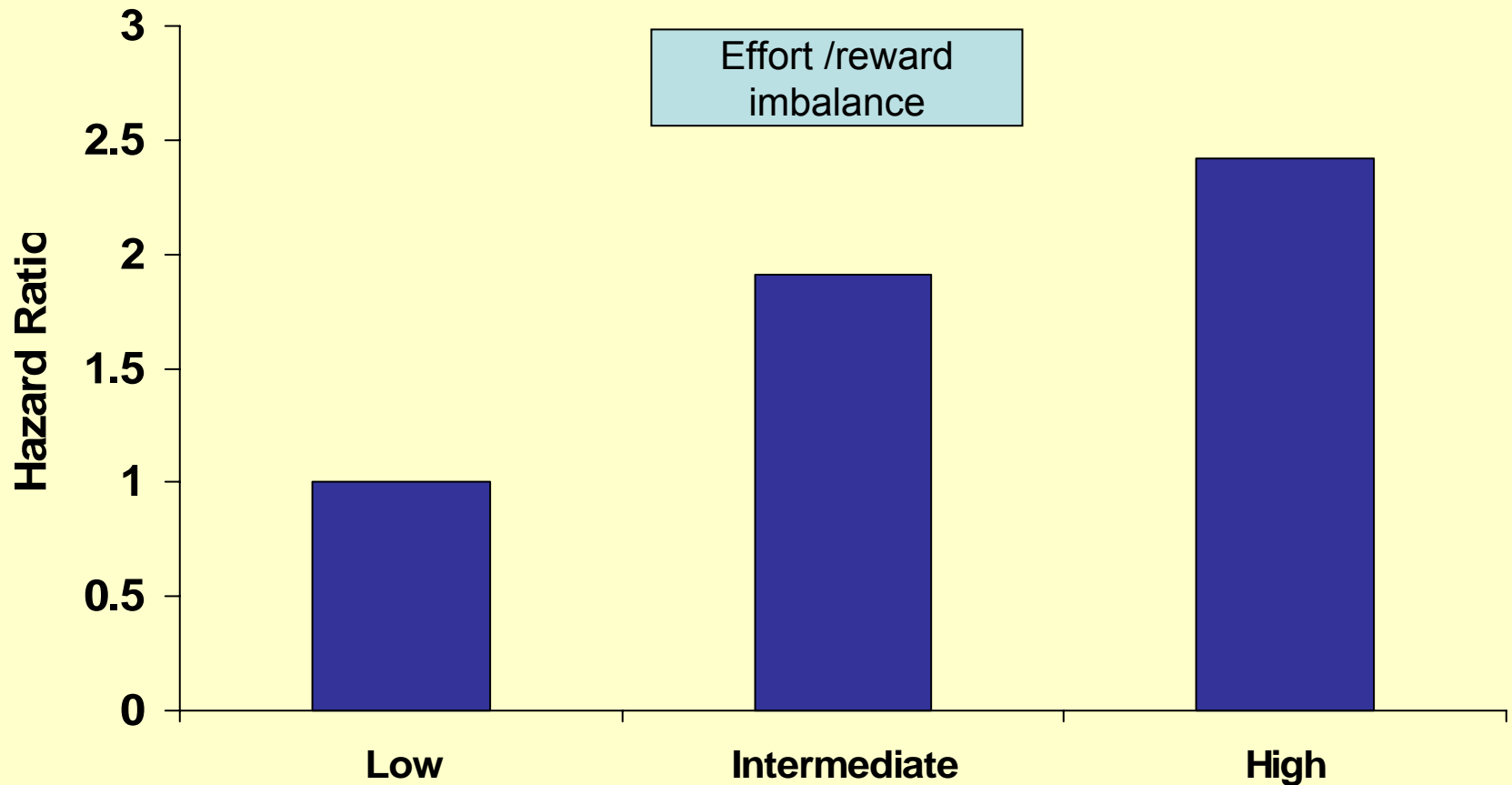
Depression, anger/hostility, anxiety/distress

Prevalence of Conventional Risk Factors in Men with Coronary Heart Disease

(n=87,869)

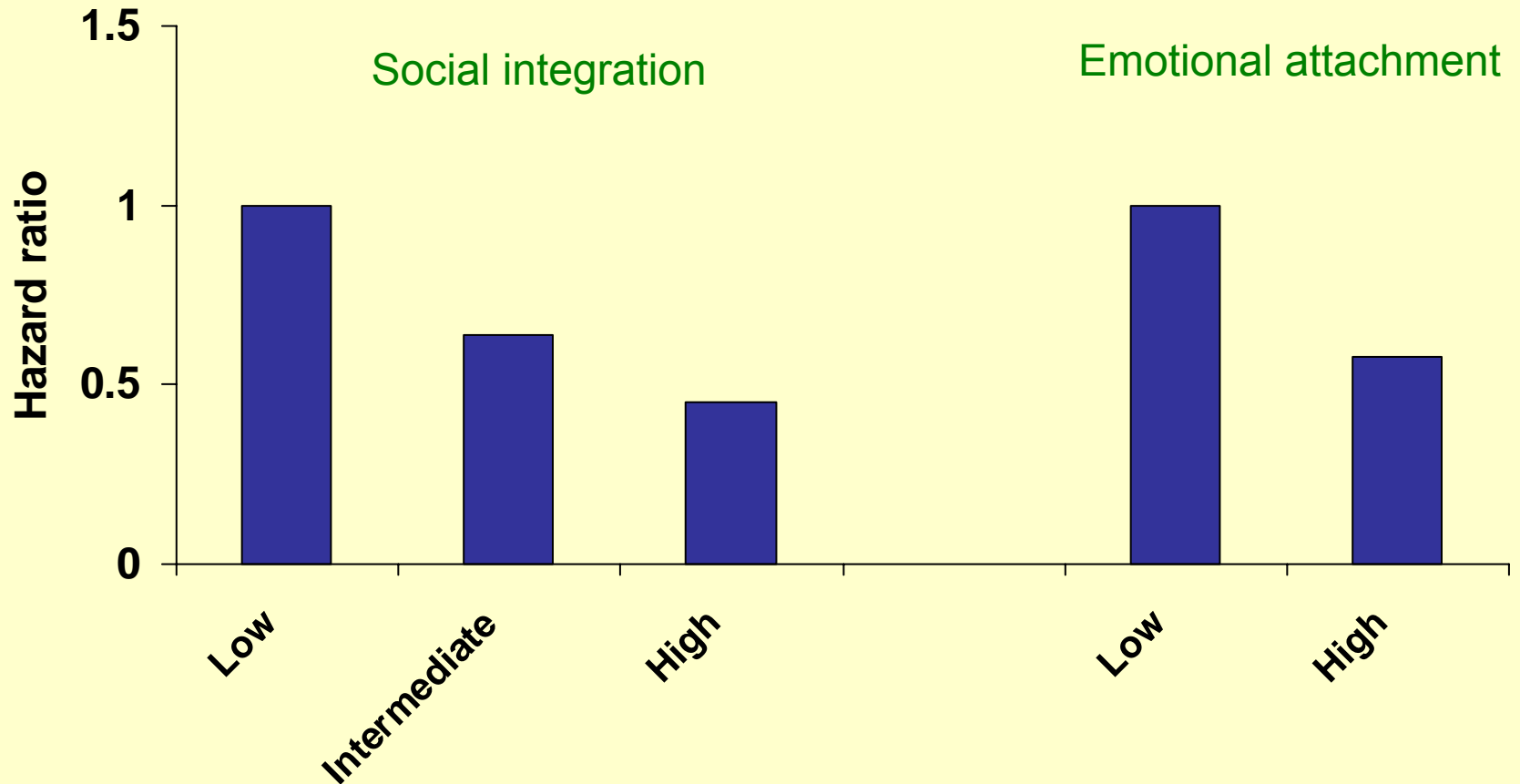


Work stress and cardiac mortality



25 year follow-up, adjusted for age, sex, smoking
Physical activity, blood pressure, cholesterol, body mass

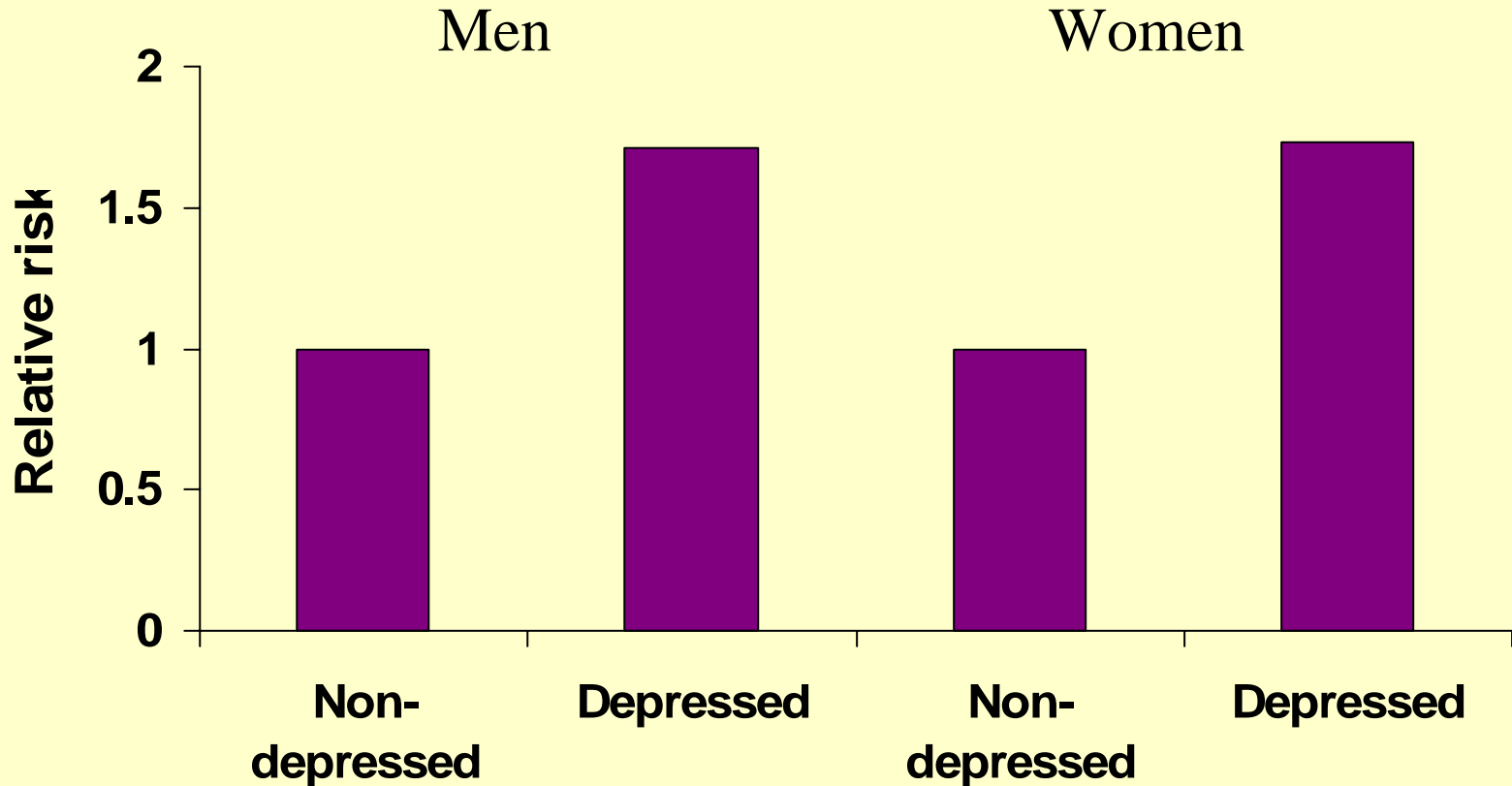
Social support and CHD



15 year follow-up, adjusted for smoking, blood pressure, cholesterol, triglycerides, BMI, waist/hip ratio, diabetes, family history, social class, stress

Rosengren, 2004

Depression and CHD incidence



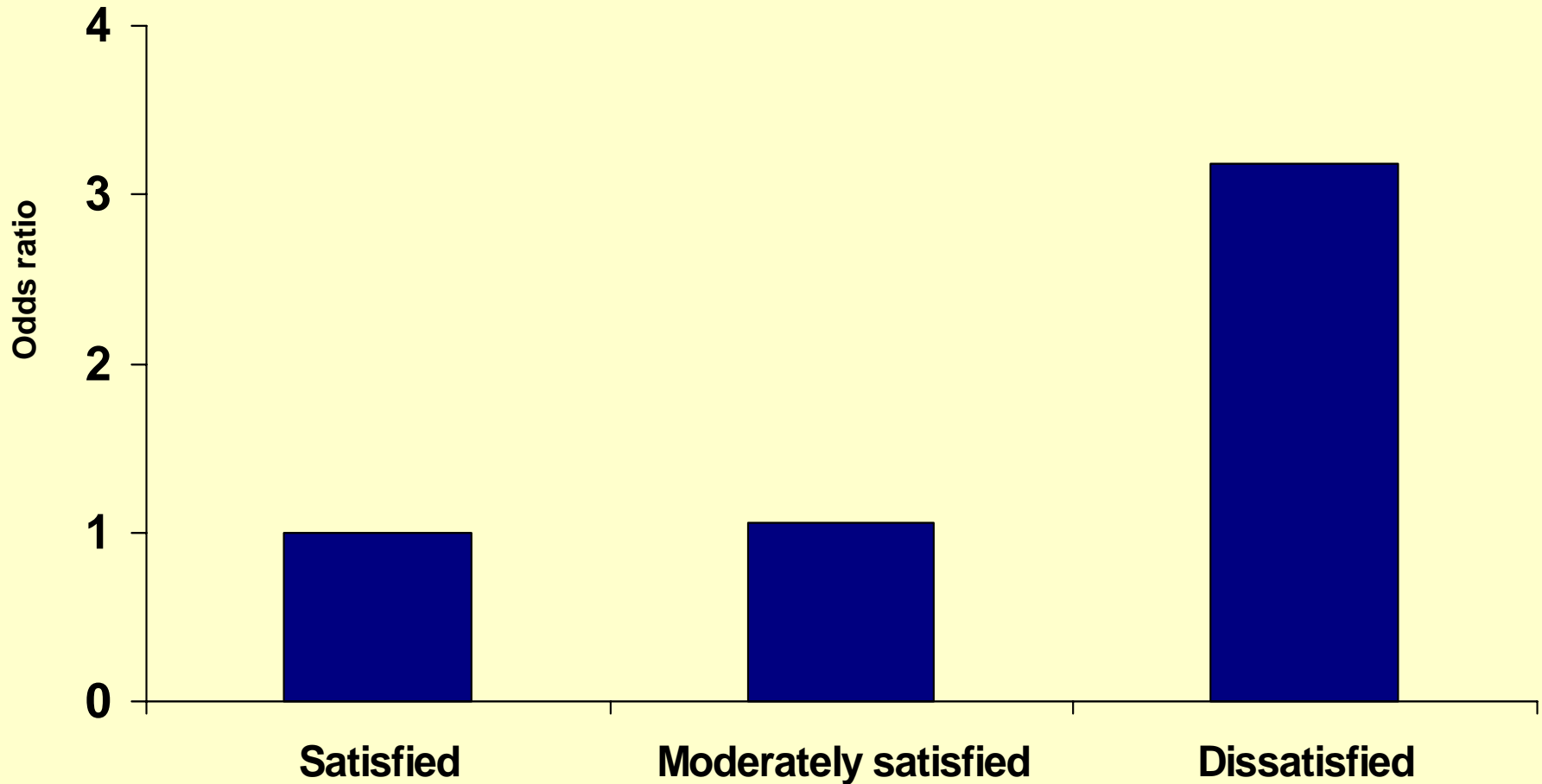
10 year follow-up. Adjusted for poverty, smoking, diabetes and body mass index (Ferketich et al, *Arch Intern Med* 2000)

Metabolic syndrome markers (ATPIII)

Three or more of:

- Waist circumference > 102 cm (men) or 88 cm (women)
- Fasting triglyceride ≥ 150 mg/dl
- Fasting HDL-cholesterol < 40 mg/dl (men), < 50 mg/dl (women)
- Blood pressure $\geq 130 / 85$ mmHg
- Fasting glucose ≥ 110 mg/dl

Marital satisfaction and the metabolic syndrome



11.5 year follow-up adjusted for baseline MS, age, race, education smoking, physical activity, alcohol, depression, anxiety

Troxel et al, 2005
Arch Intern Med

Psychosocial factors and illness

- Chronic challenges, not acute life events
- Influences on long-term development
- Not the cause, but a contribution to risk

Psychosocial factors and illness

- Mechanisms?

Psychosocial factors and illness

- **Behavioural processes**

Smoking, food choice, physical exercise, alcohol consumption

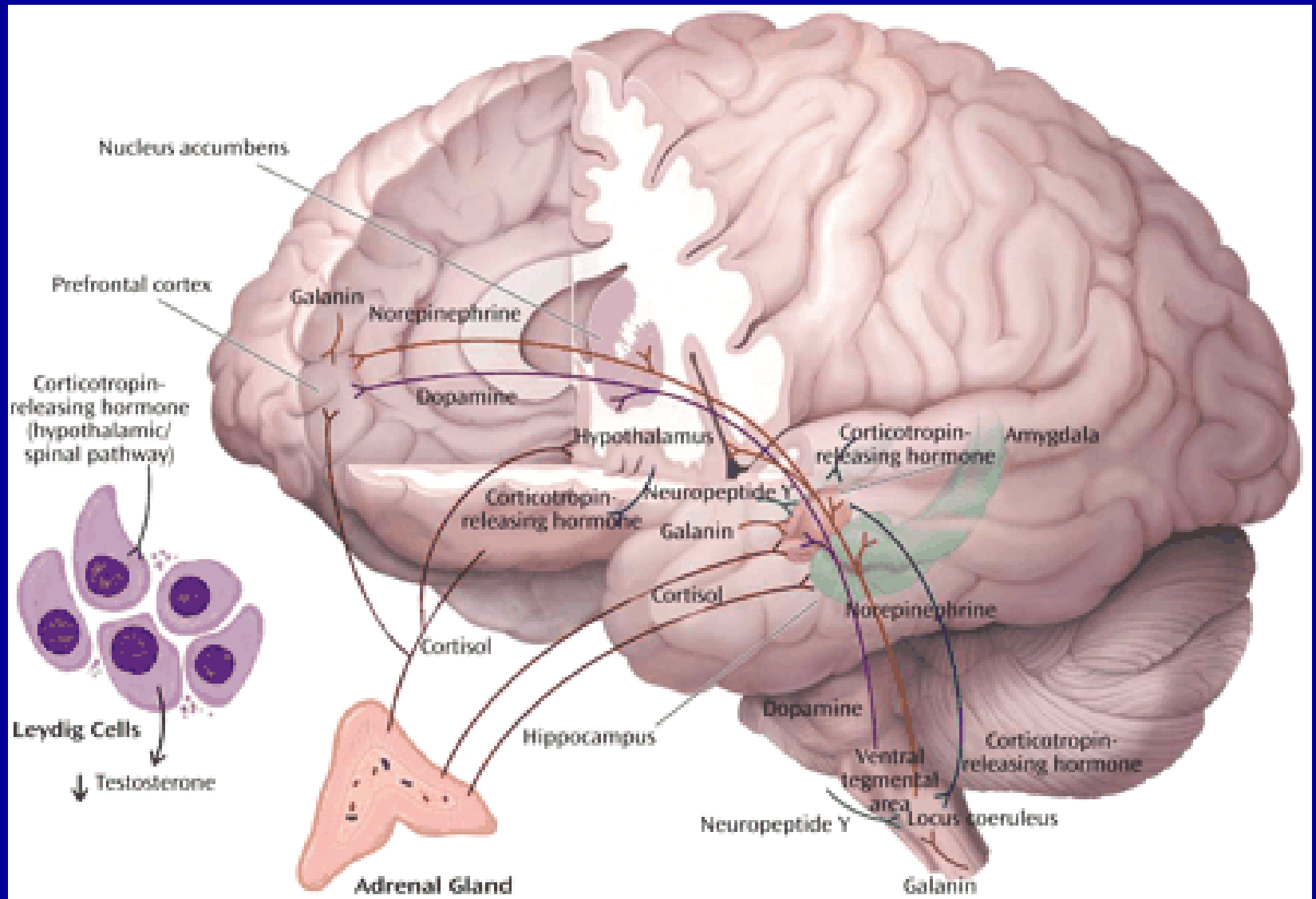
Psychosocial factors and illness

- **Behavioural processes**

Smoking, food choice, physical exercise, alcohol consumption

- **Psychobiological processes**

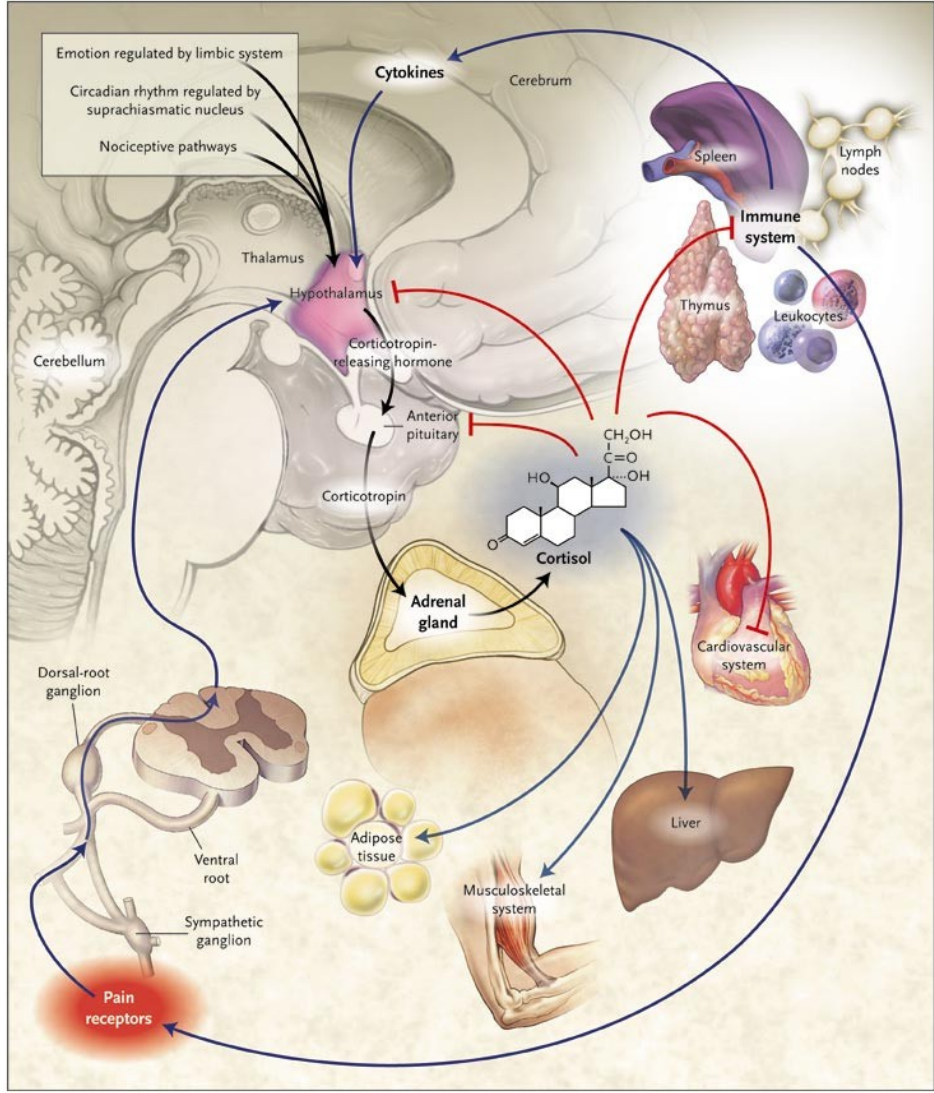
Stress-induced modifications in neuroendocrine, cardiovascular, autonomic, immunological and other physiological responses



Charney, 2004

Psychobiological responses

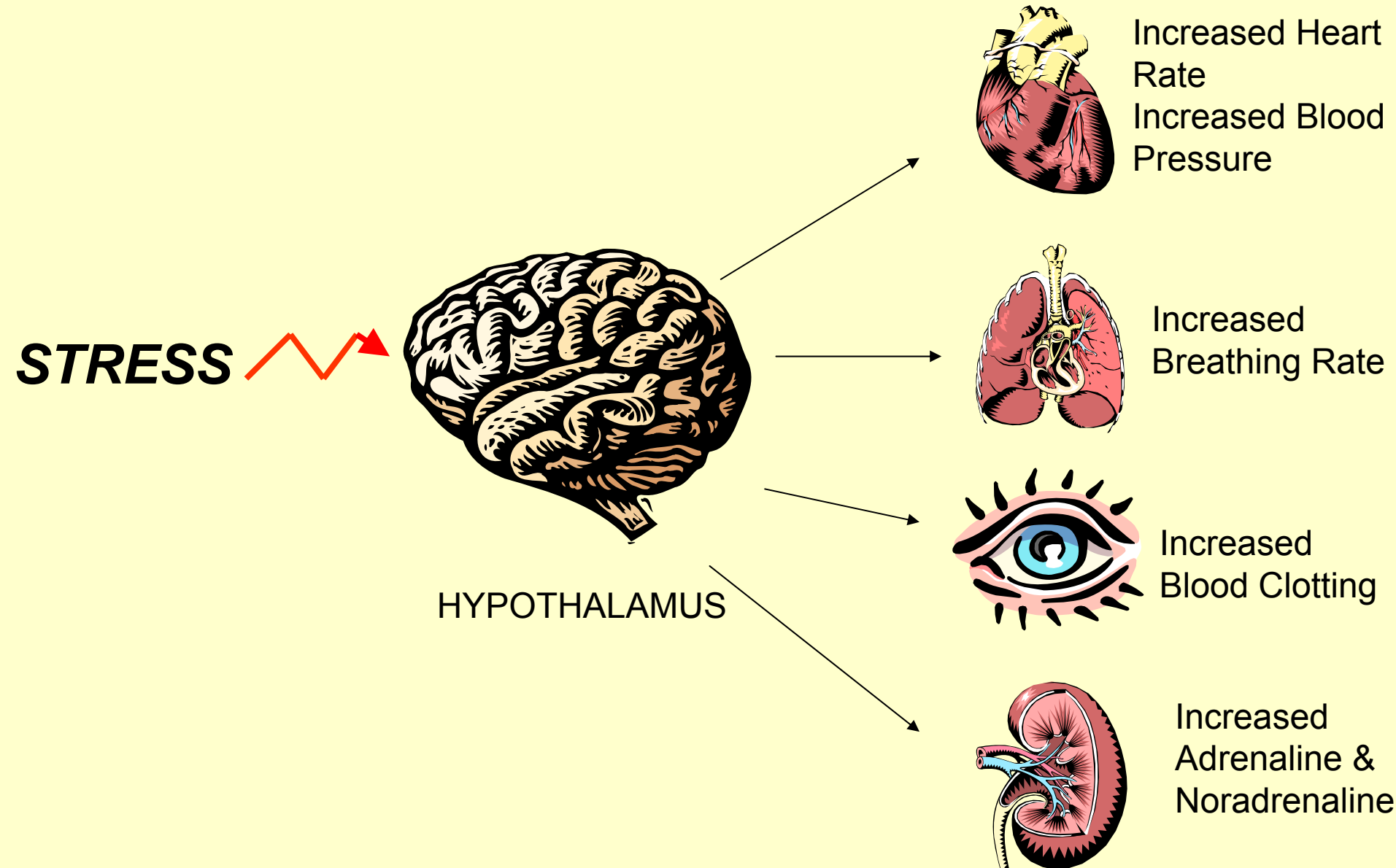
Neuroendocrine	cortisol, adrenaline, testosterone, noradrenaline
Cardiovascular	Blood pressure, heart rate
Inflammatory	C-reactive protein, interleukin (IL) 6, fibrinogen
Metabolic	Lipids, glucose, insulin
Haemostatic	Platelets, coagulation factors
Immune	Lymphocyte counts and activity, natural killer cells, immunoglobulins



Some effects of cortisol

- Stimulation of glucose production in the liver
- Release of free fatty acids from fat stores
- Regulation of water balance
- Stimulation of anti-inflammatory responses
- Immune regulation

Sympathetic Nervous System



When are psychobiological responses hazardous?

- Repeatedly elicited in conditions of everyday life
- Some people show heightened reactions or failure of post-stress adaptation

Some effects of high cortisol

Potentially damaging effects

- Increased lipid (LDL-cholesterol) in the blood
- Suppression of immune function
- Decalcification of bone
- Deposition of abdominal fat
- Damage to the hippocampus
- Muscle wasting
- Impaired reproductive function

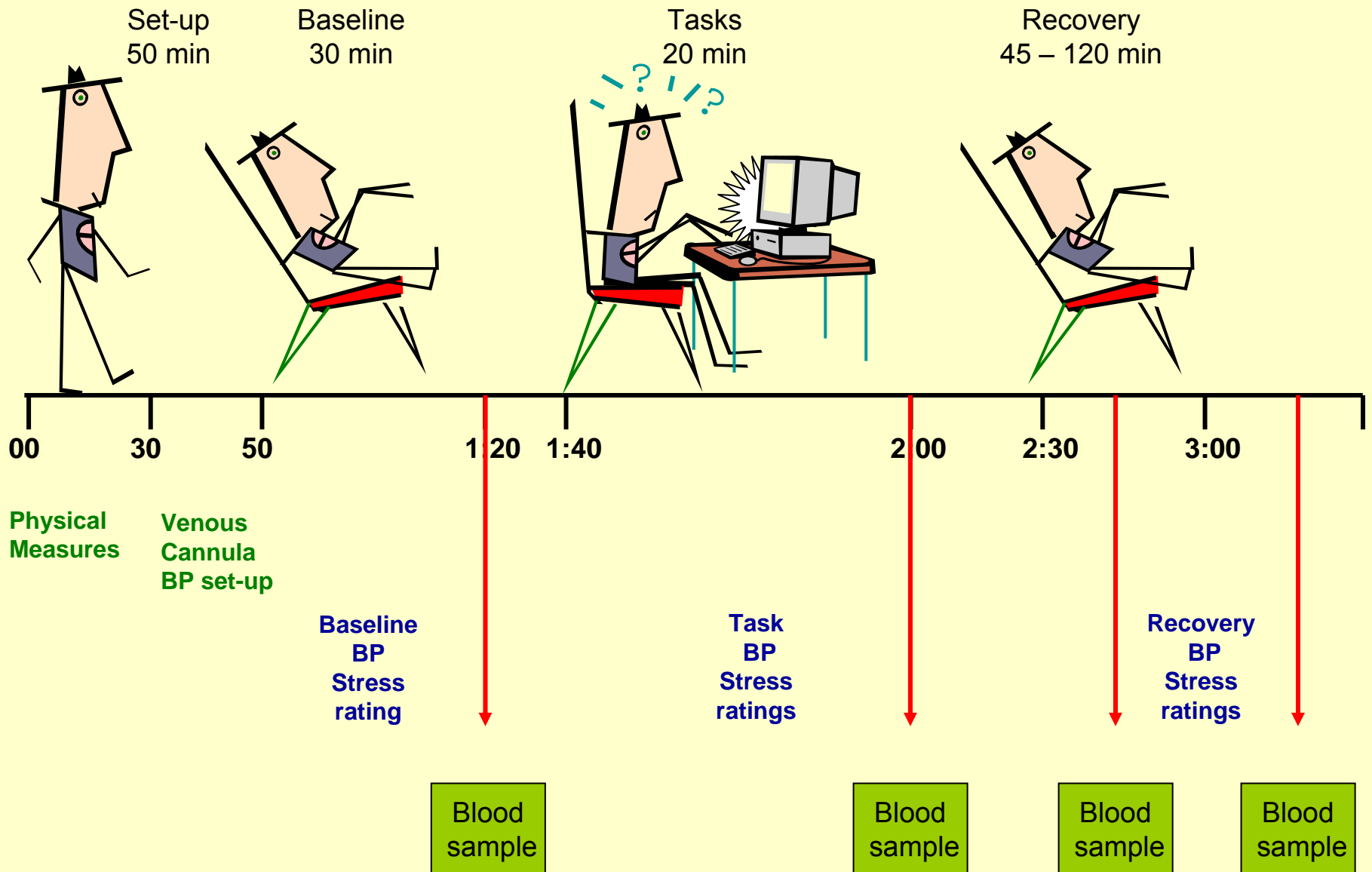
How stress gets under your skin

- Psychosocial factors and physical illness
- Psychobiological processes
- **Methods of investigation**
- Psychobiological responses and health outcomes

Types of study

- Experimental or clinical studies
- Naturalistic monitoring studies

Psychophysiological Stress Testing



BLUE

YELLOW

RED

GREEN

BLUE

GREEN

YELLOW

BLUE

RED

GREEN

YELLOW

GREEN

YELLOW

BLUE

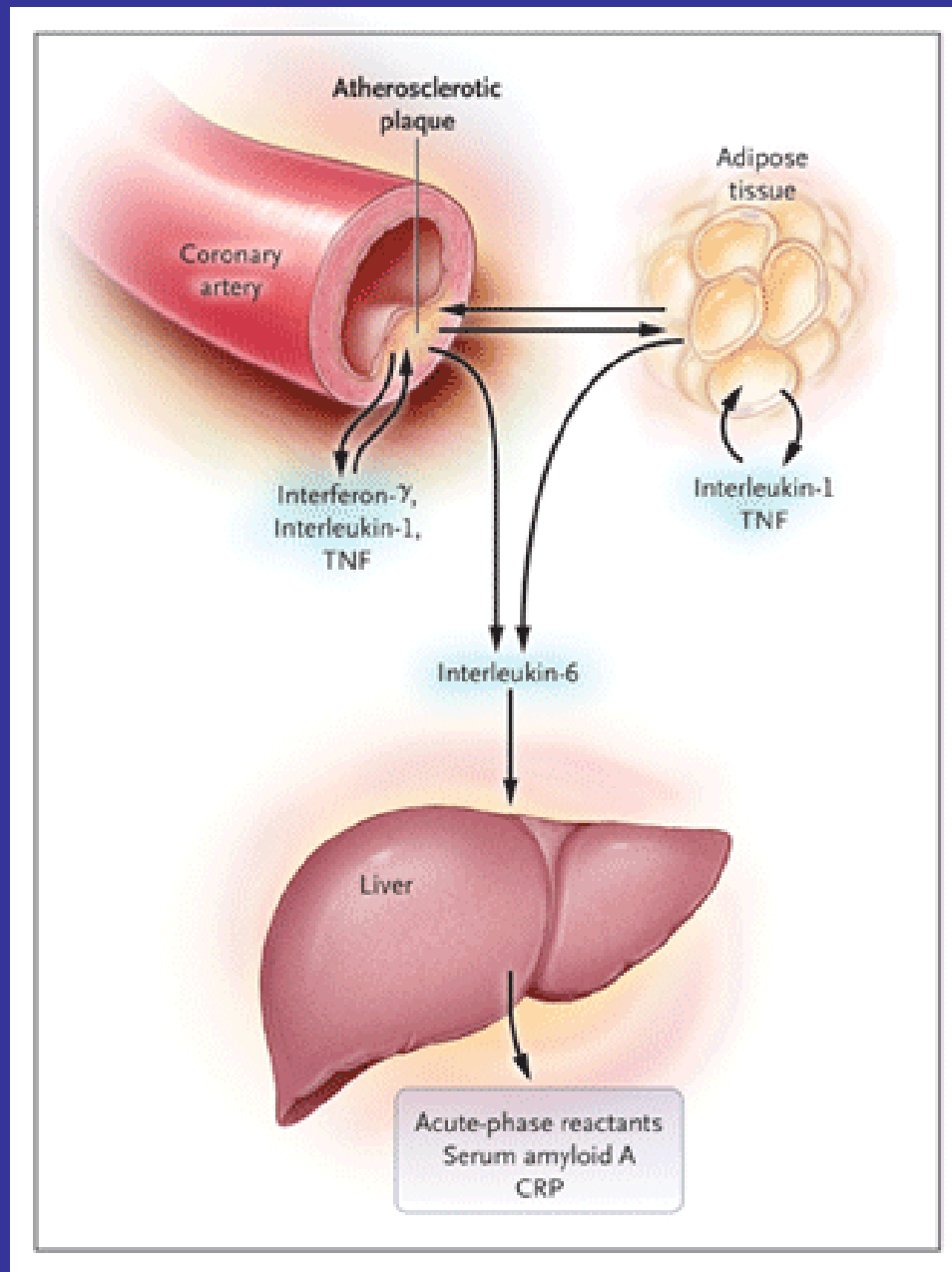
RED

Laboratory mental stress testing

- Do responses in biological measures relevant to health vary with psychosocial risk profile?

C-reactive protein

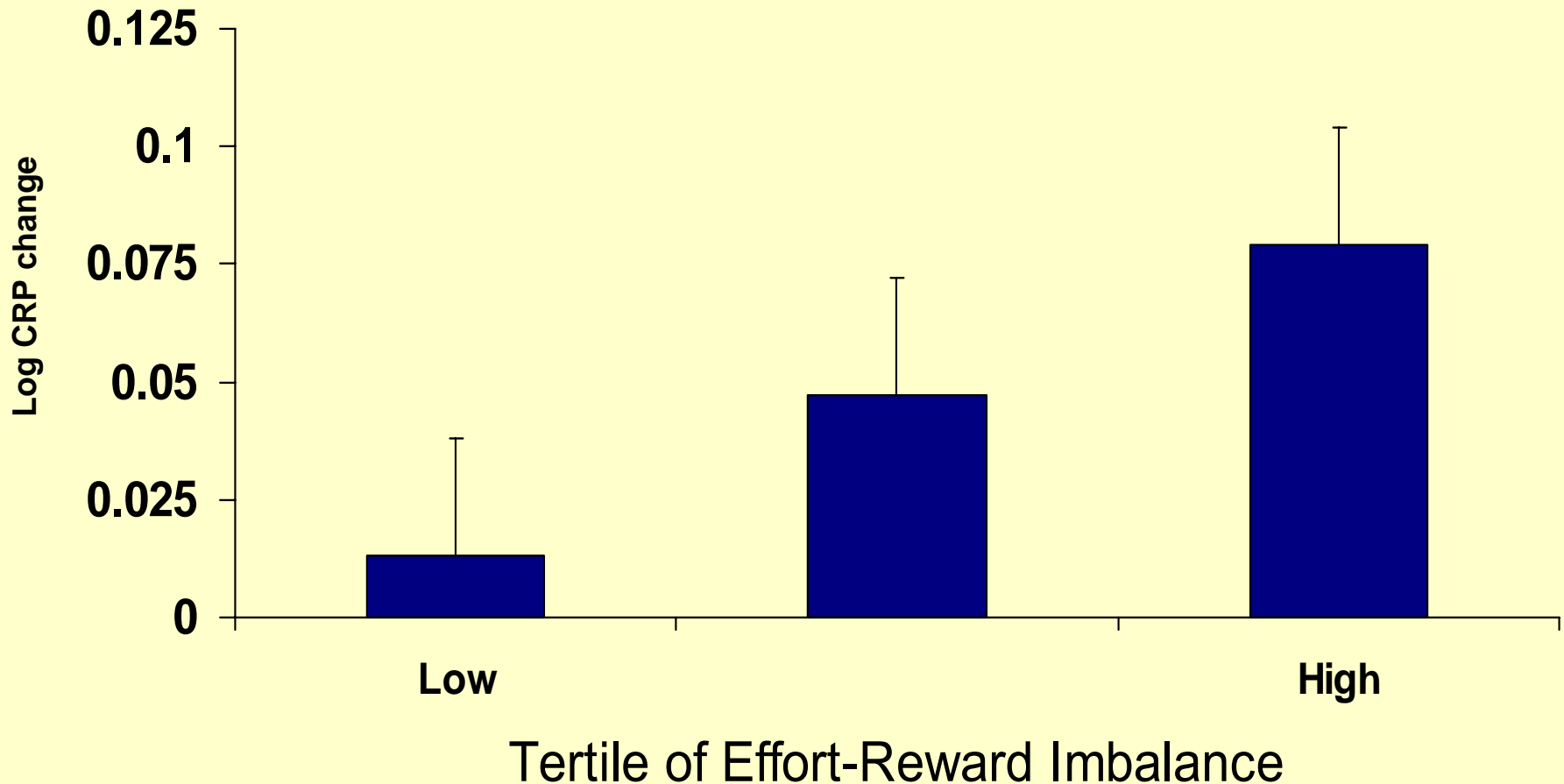
- Acute phase protein synthesized in liver
- Increases in response to inflammatory stimuli (cytokines), infection and tissue damage
- Antimicrobial, clears apoptotic cells, enhances phagocytosis
- Marker of chronic low grade inflammation
- Risk marker for CVD, functional significance debated



Work stress study

- 105 healthy nonsmoking men, mean age 32.1 years. Full-time employment
- Measures of effort-reward imbalance
- Responses to simulated public speaking and mirror tracing tasks
- Blood samples for C-reactive protein before and after tasks

Effort-reward imbalance and C-reactive protein stress responses



Adjusted for baseline C-reactive protein, age and BMI

Socioeconomic factors and illness

- Do socioeconomic inequalities stimulate biological processes relevant to cardiovascular risk?

Psychobiological responses and SEP

Participants

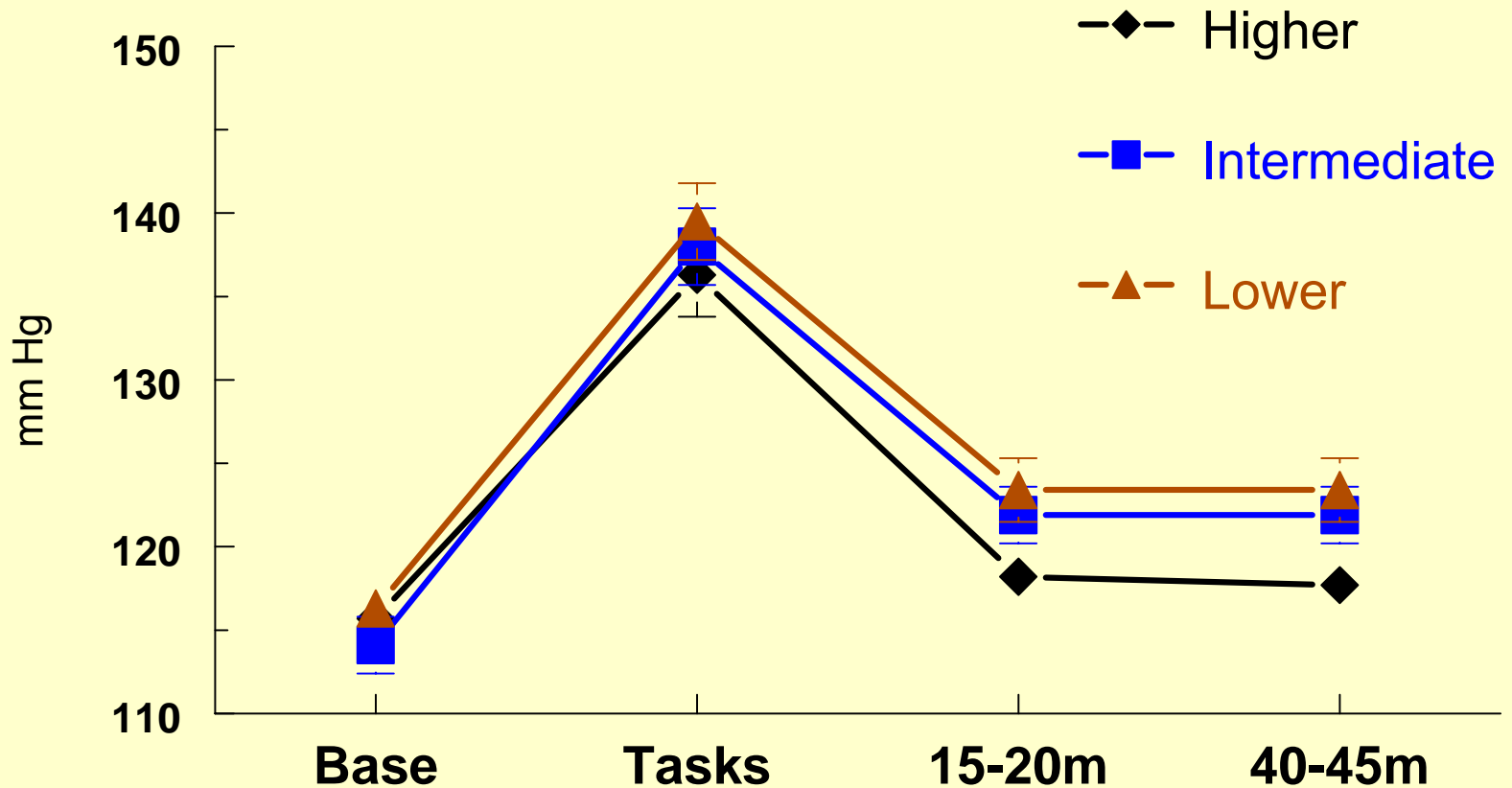
- 238 members of the Whitehall II (prospective) cohort aged 47-59 years in full-time employment.
Sampled by grade of employment:

Higher	Men	49	Women	41	Total	90
Intermediate	Men	44	Women	37	Total	81
Lower	Men	36	Women	31	Total	67

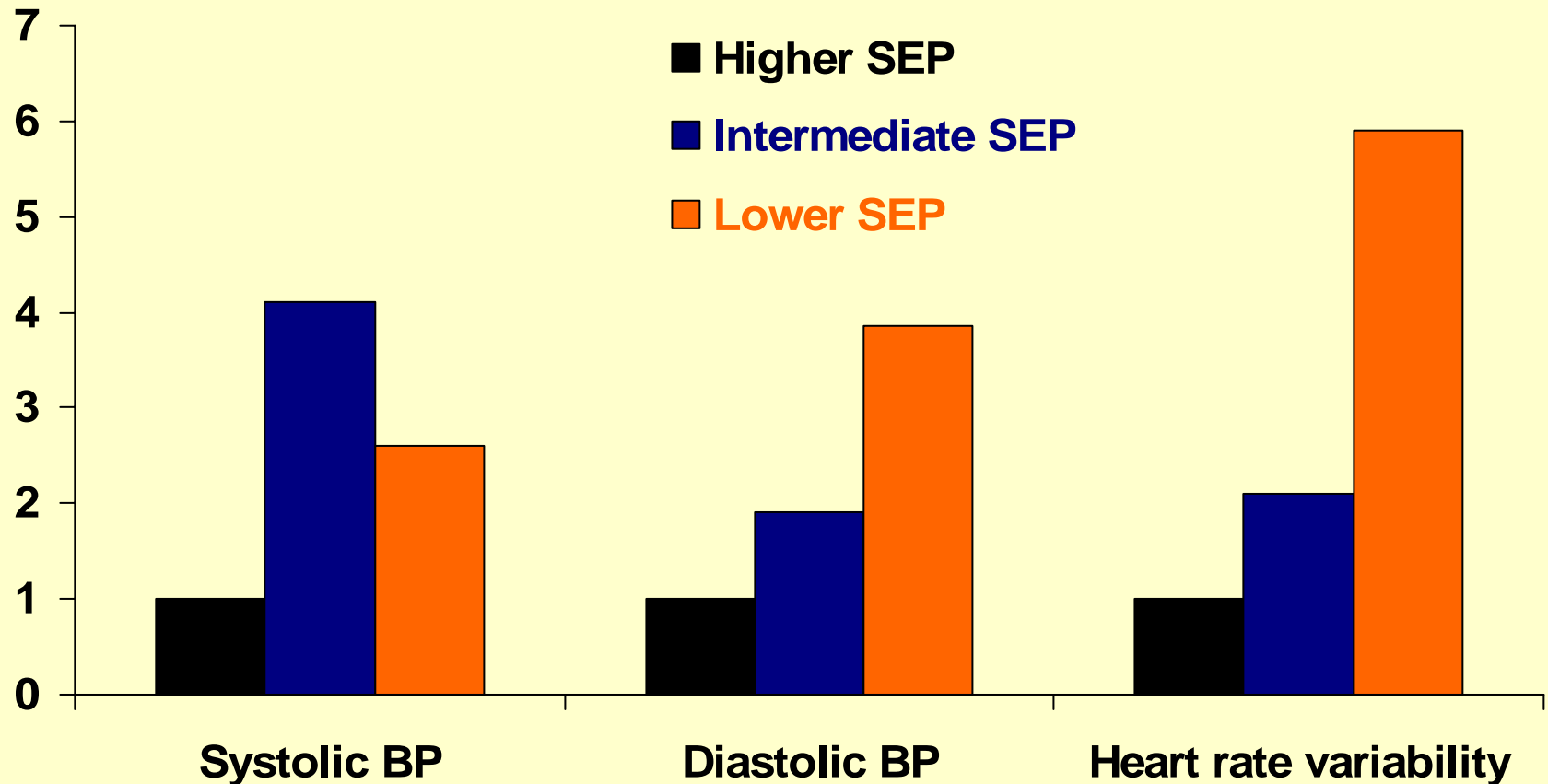
Conditions

- Cardiovascular, neuroendocrine, cytokine and hemostatic responses to colour/word and mirror tracing tasks.
Blood drawn at baseline, immediately post-task, and 45 minutes later.

Systolic BP by occupational grade



Socioeconomic position and incomplete recovery 45 min post-stress



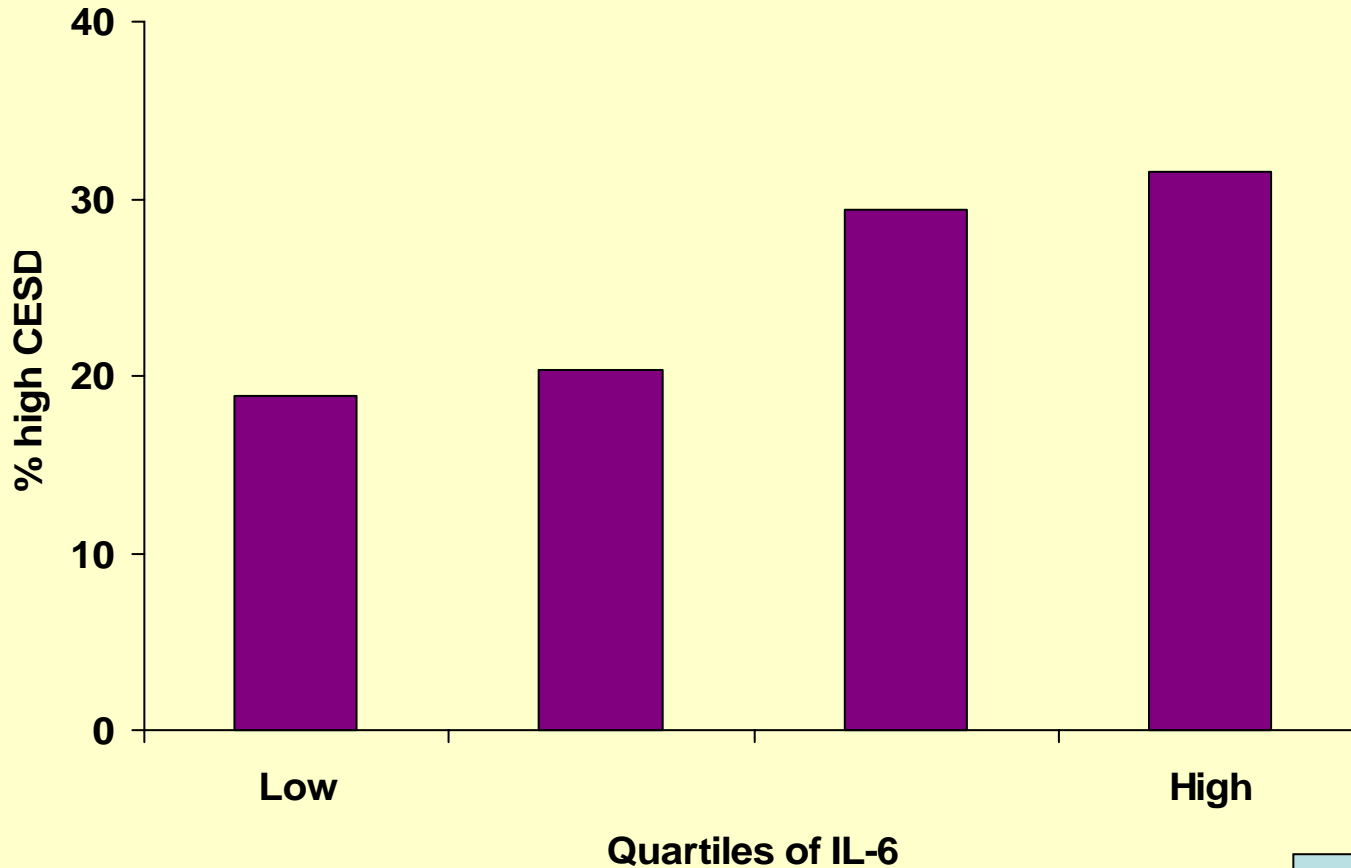
Odds of incomplete recovery adjusted for gender, age, baseline value and reaction to tasks

Interleukin 6

An 'endocrine' cytokine associated with

- Coronary heart disease
- Type 2 diabetes, insulin resistance, obesity
- Depression
- Disability
- Cognitive decline

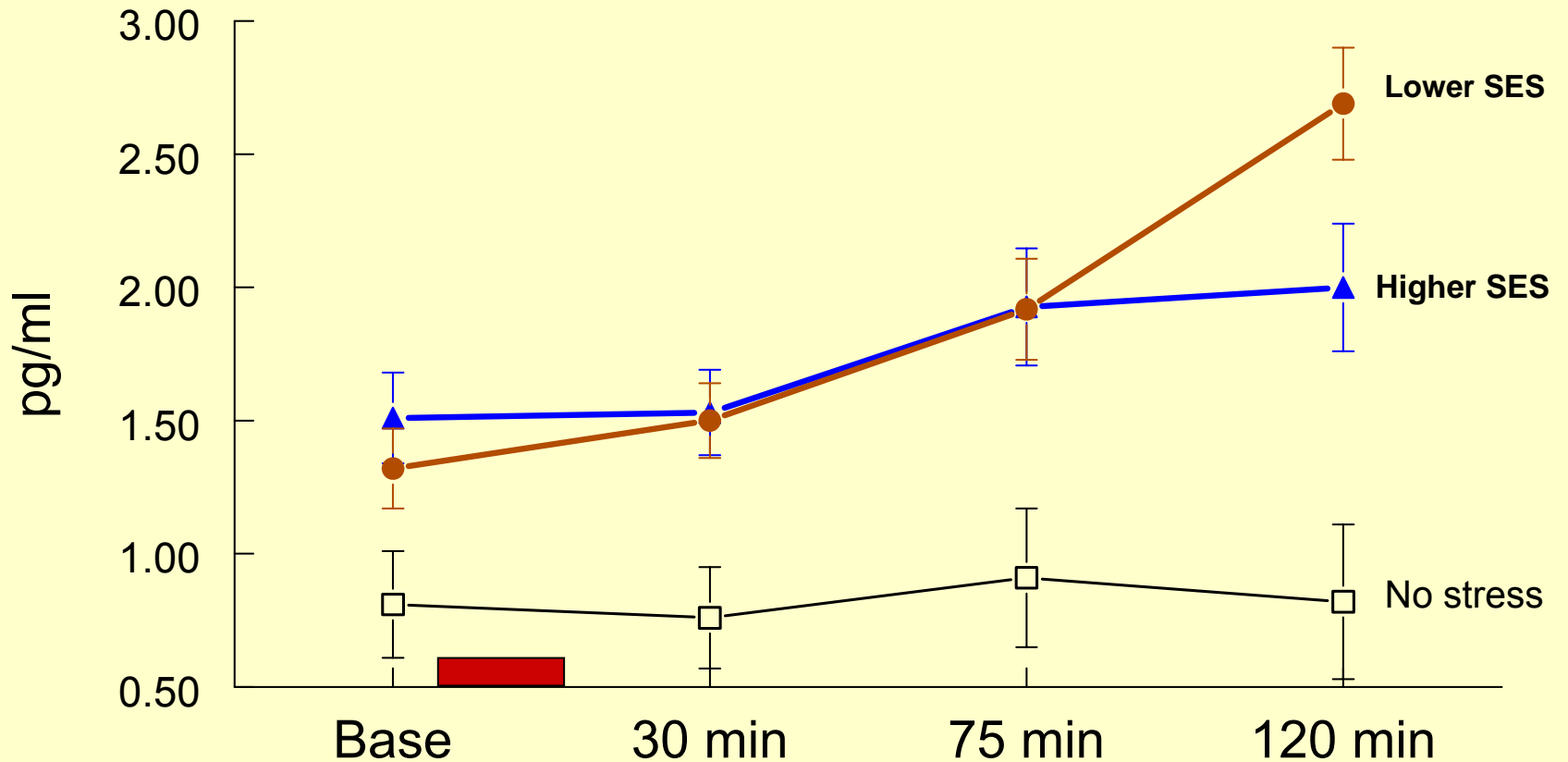
IL-6 and depressed mood



3024 men & women aged 70-79

Penninx et al,
Biol Psychiat
2005

Stress and plasma interleukin-6



Types of study

- Experimental or clinical studies
- Naturalistic monitoring studies

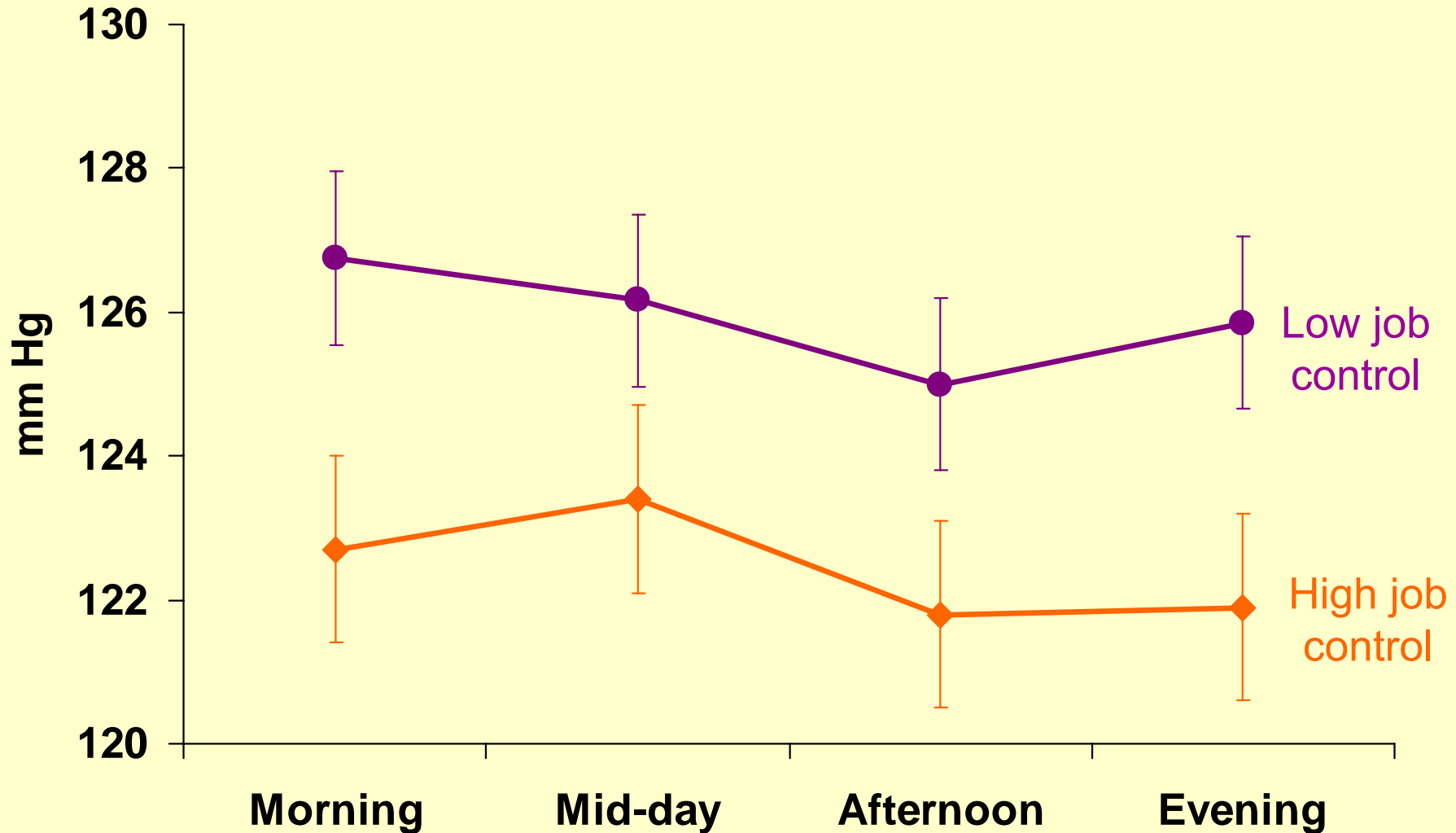
Naturalistic monitoring

- Dynamic responses in everyday life
- Covariation of biology, events and reactions

Ambulatory blood pressure

Salivary cortisol

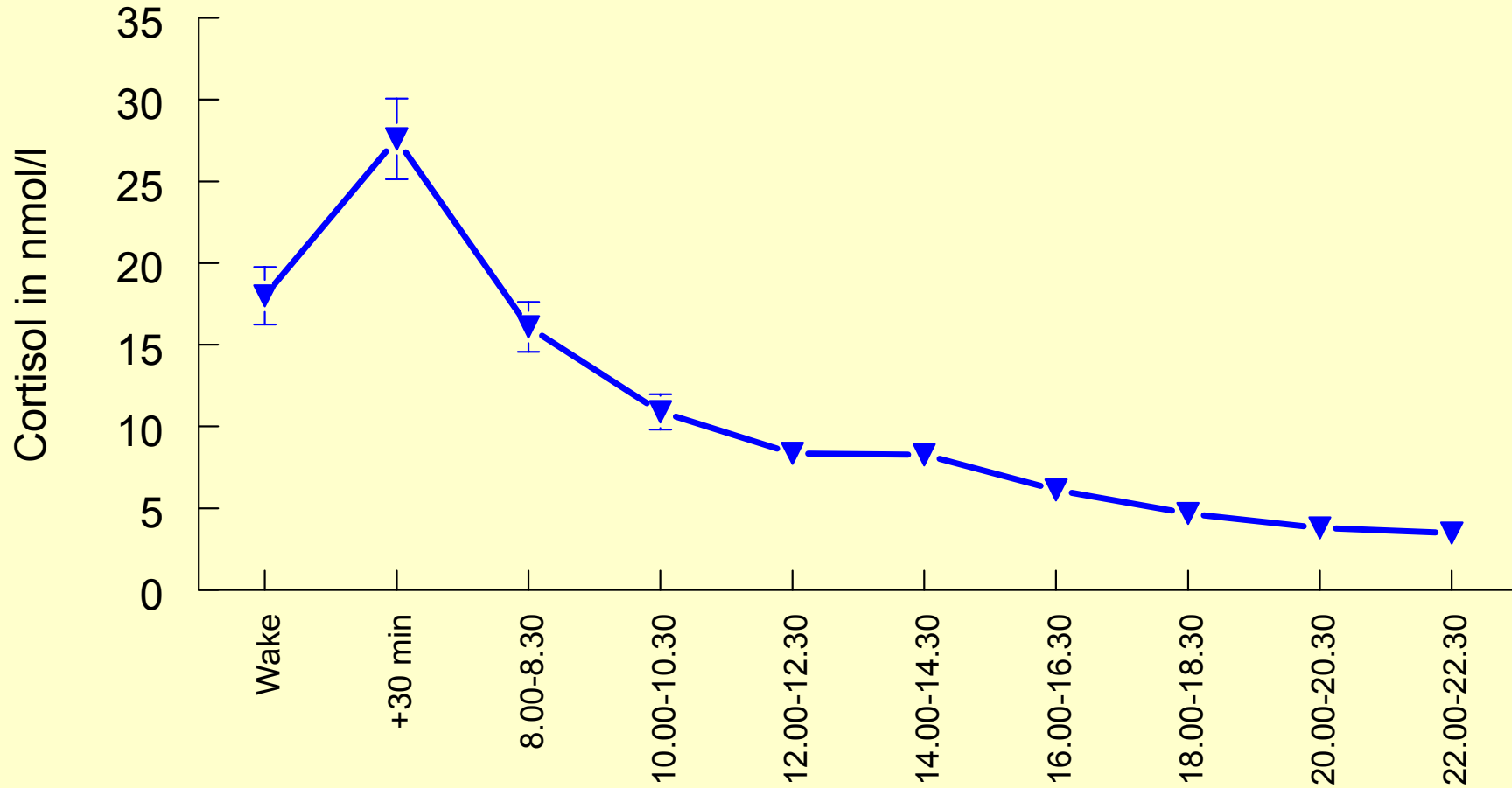
Ambulatory systolic pressure: working day



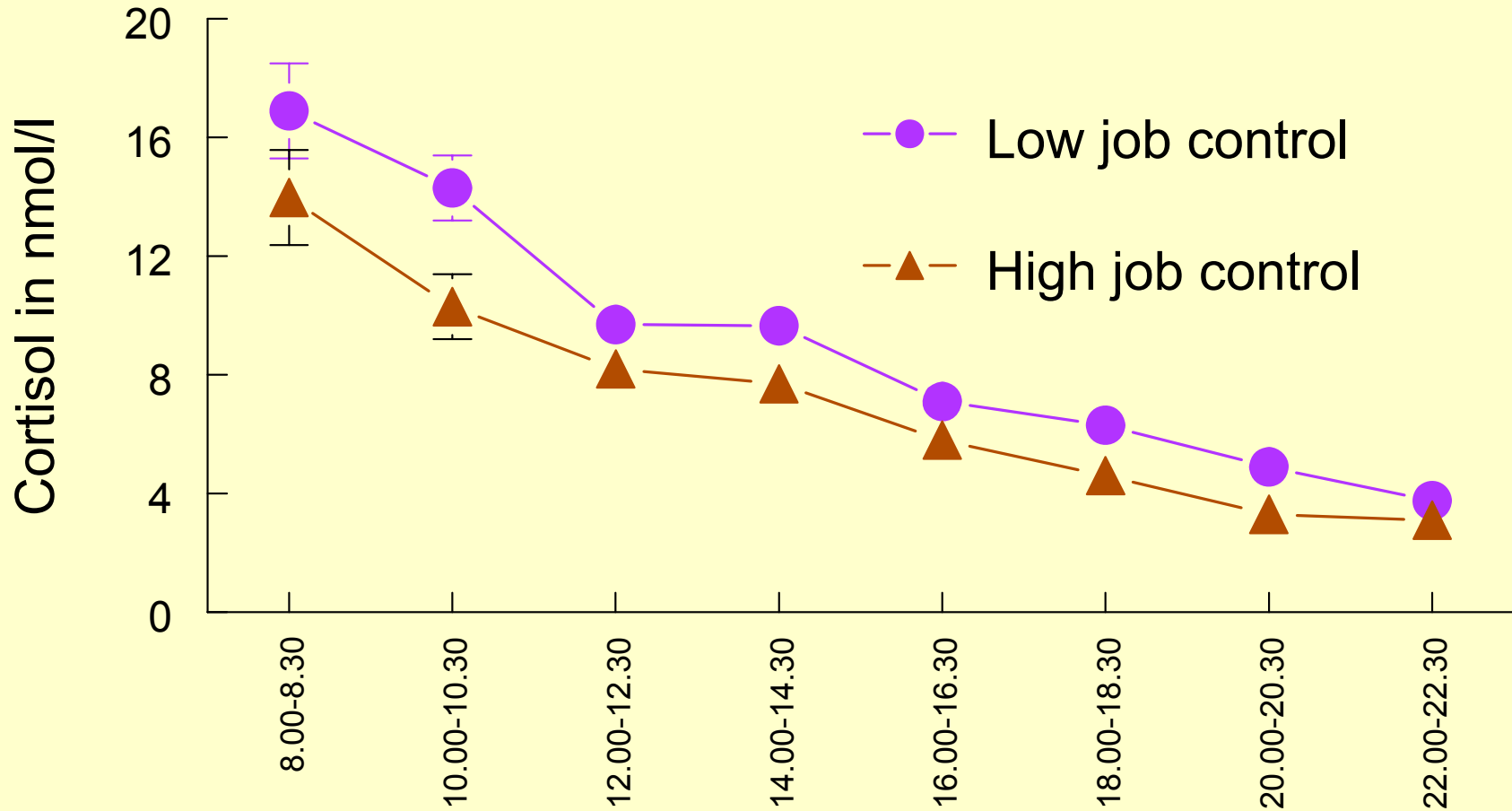
Adjusted for gender, age, occupational grade, smoking, BMI, and physical activity

Steptoe & Willemssen
J Hypertension, 2004

Cortisol profile over working day

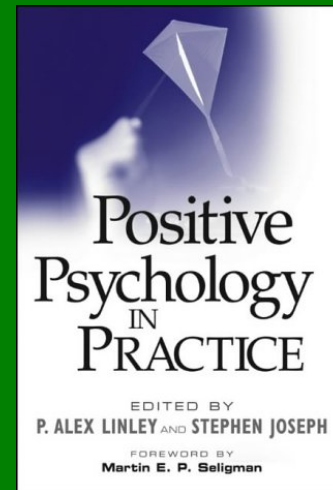
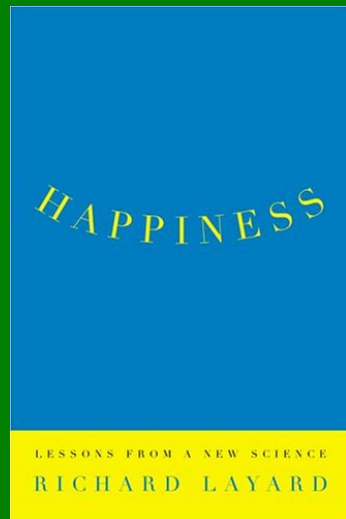
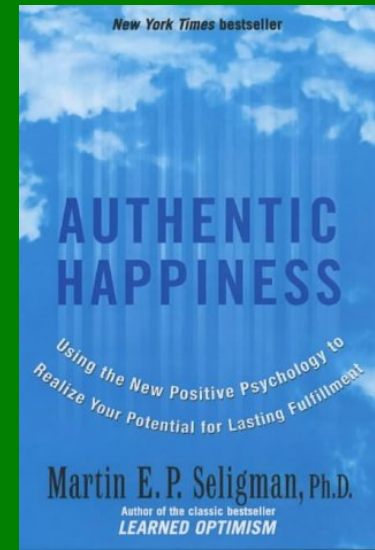
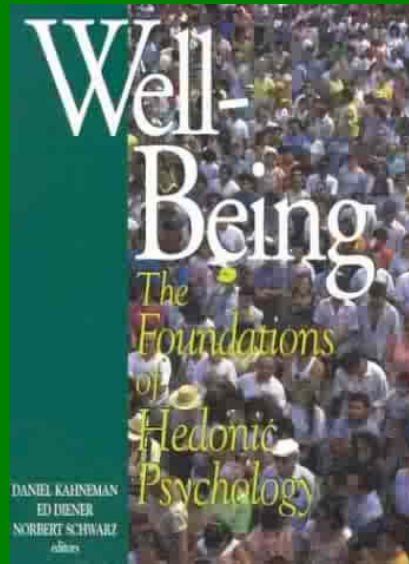
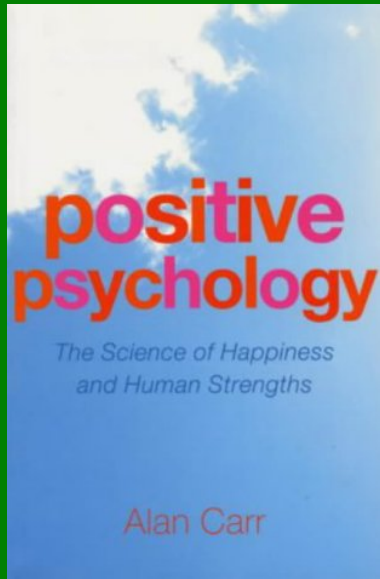


Cortisol and job control



Men, age-adjusted

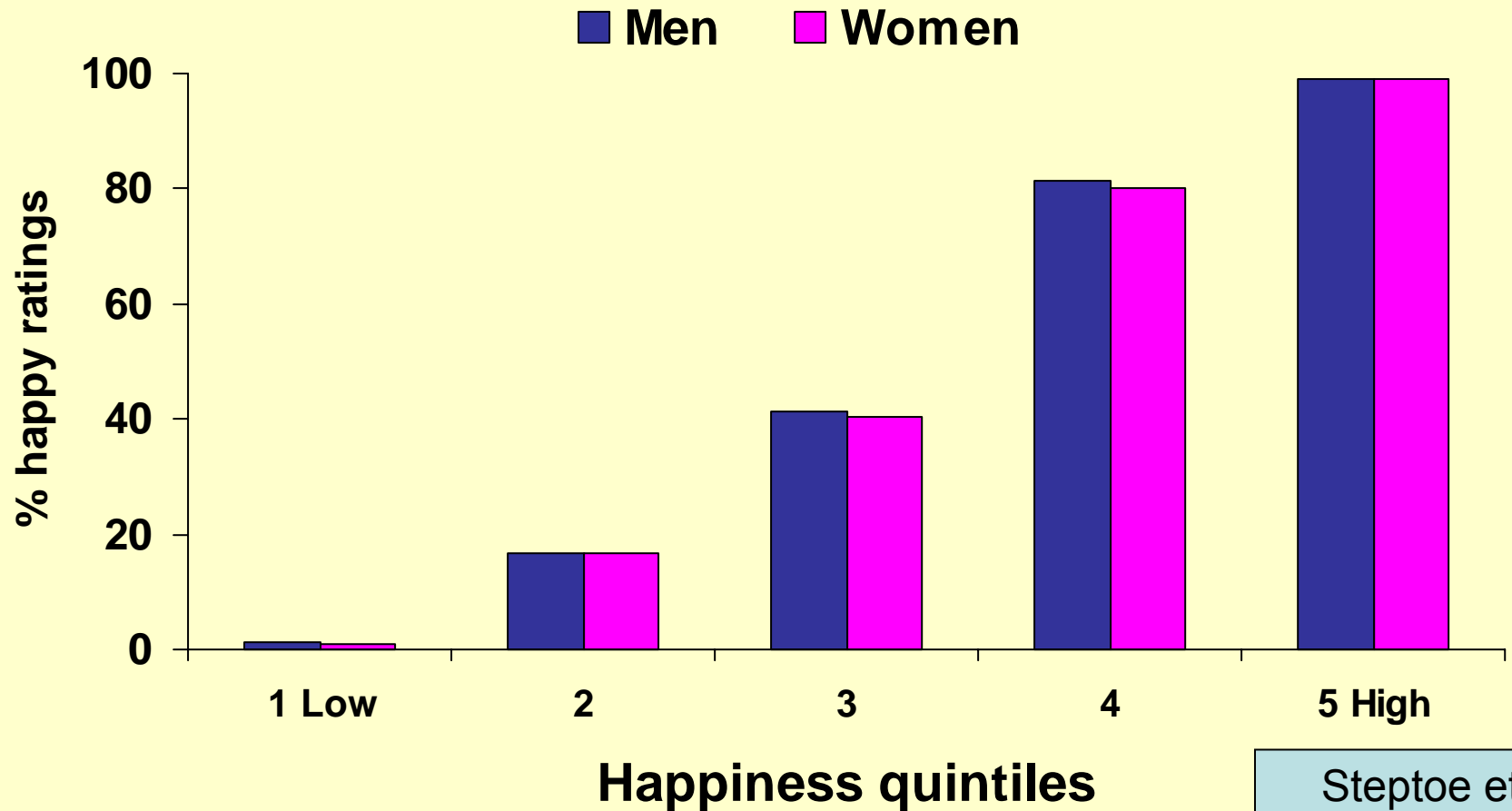
Kunz-Ebrecht et al
Soc Sci Med, 2004



Measurement of happiness

- Repeated sampling every 20 minutes from morning (07:30 – 09:30 start) until evening (22:30) on a working day
- Happiness on 5-point scale:
1 = very low to 5 = very high
- Division into 1-3 vs 4-5
- Proportion of happy ratings (4-5) over the day

Happiness in men and women



Steptoe et al
PNAS, 2005

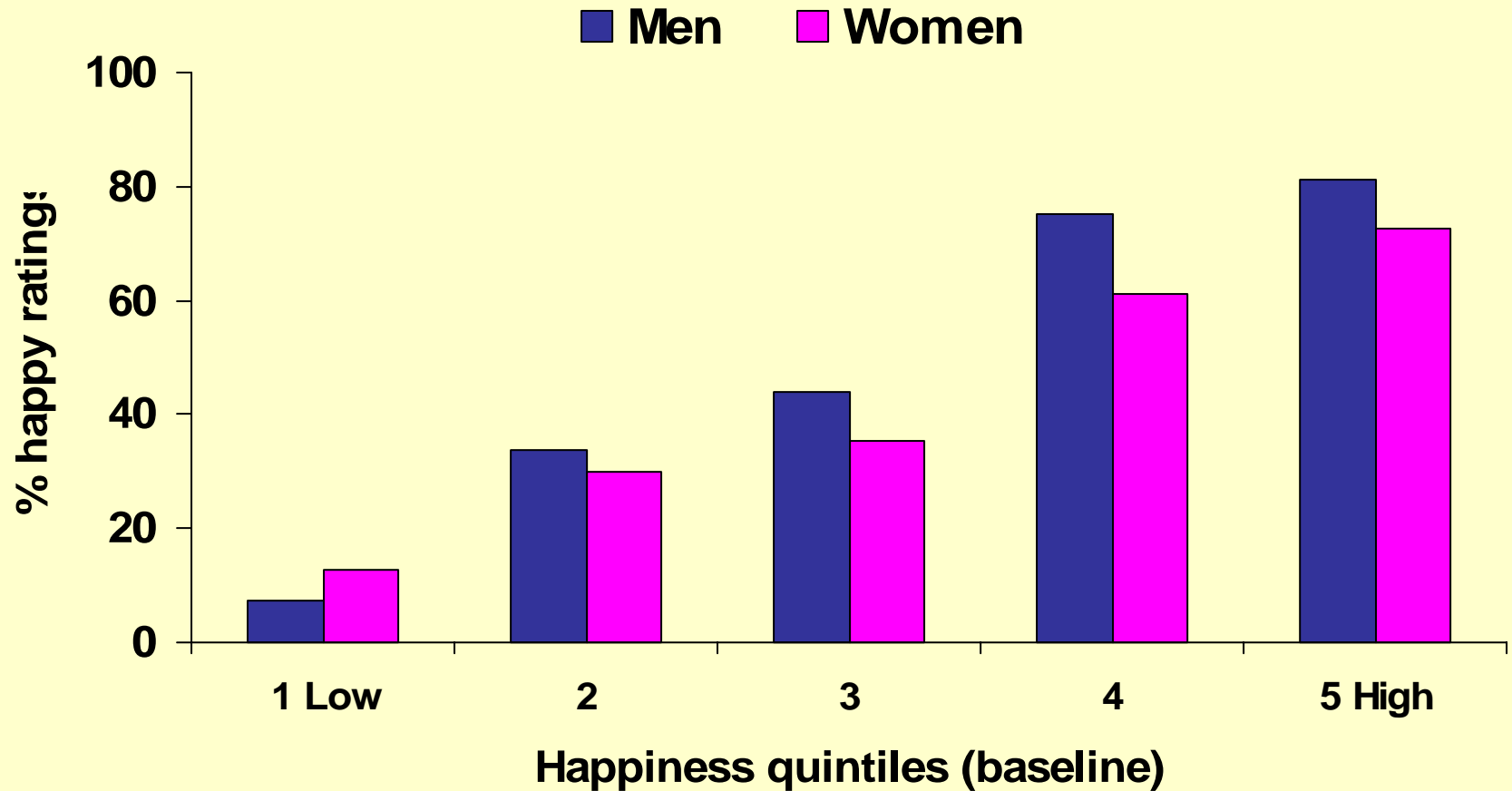
Salivary cortisol – working day



8 samples (08:00 – 22:30)

Adjusted for gender, age, occupational grade, smoking, bmi, and GHQ

Happiness ratings - 3 years



Cortisol and happiness – 3 year



N = 144

Adjusted for gender, age, occupational grade, work at follow-up, smoking, bmi, GHQ

Systolic BP and happiness – 3 year

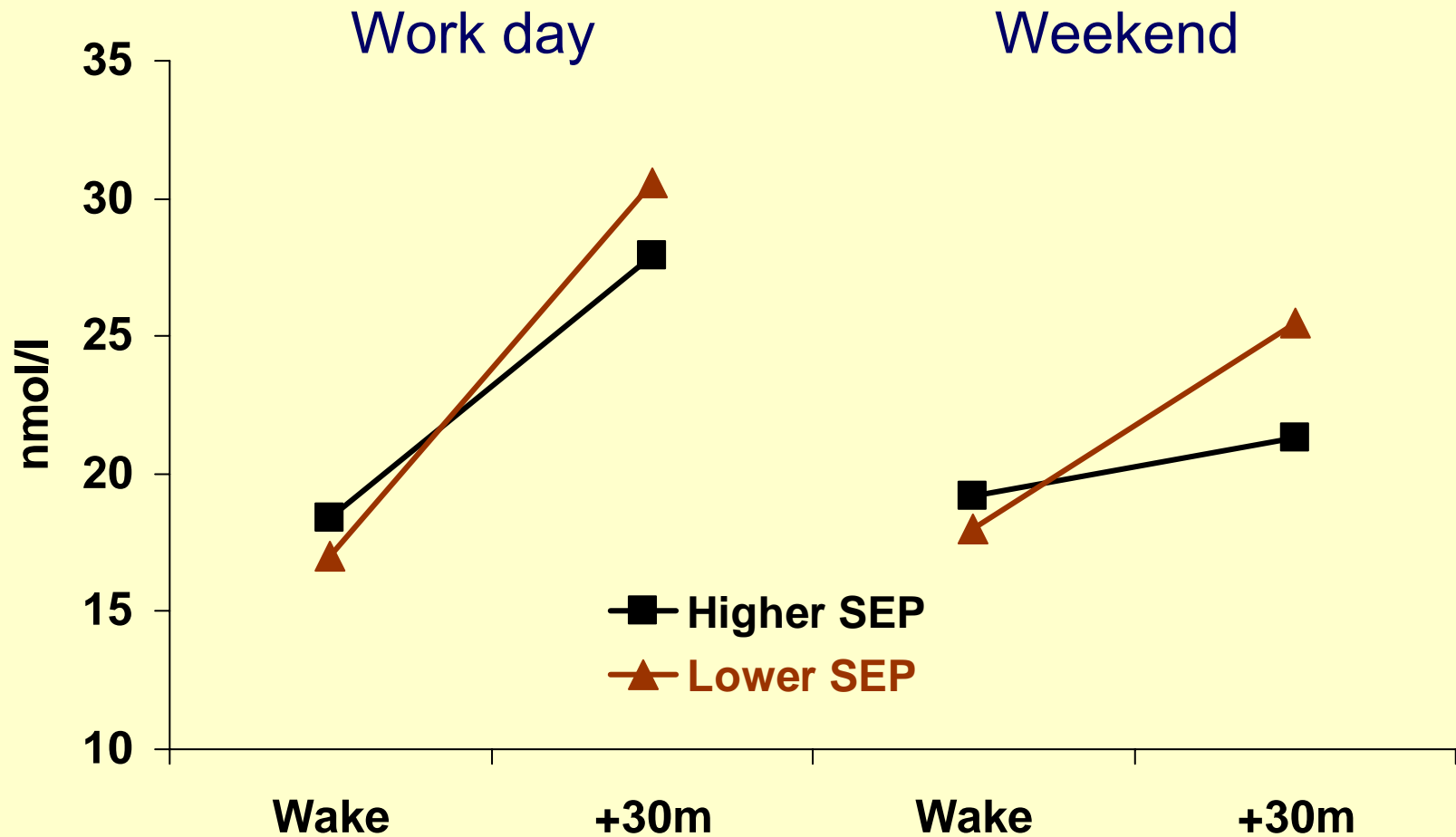


Adjusted for gender, age, occupational grade, work at follow-up, smoking, bmi, GHQ. N = 160

Problems of interpretation of cortisol data:

- Variation over the day; single readings of limited value
 - Cortisol awakening response
 - Levels over the day, slope

Cortisol waking response



How stress gets under your skin

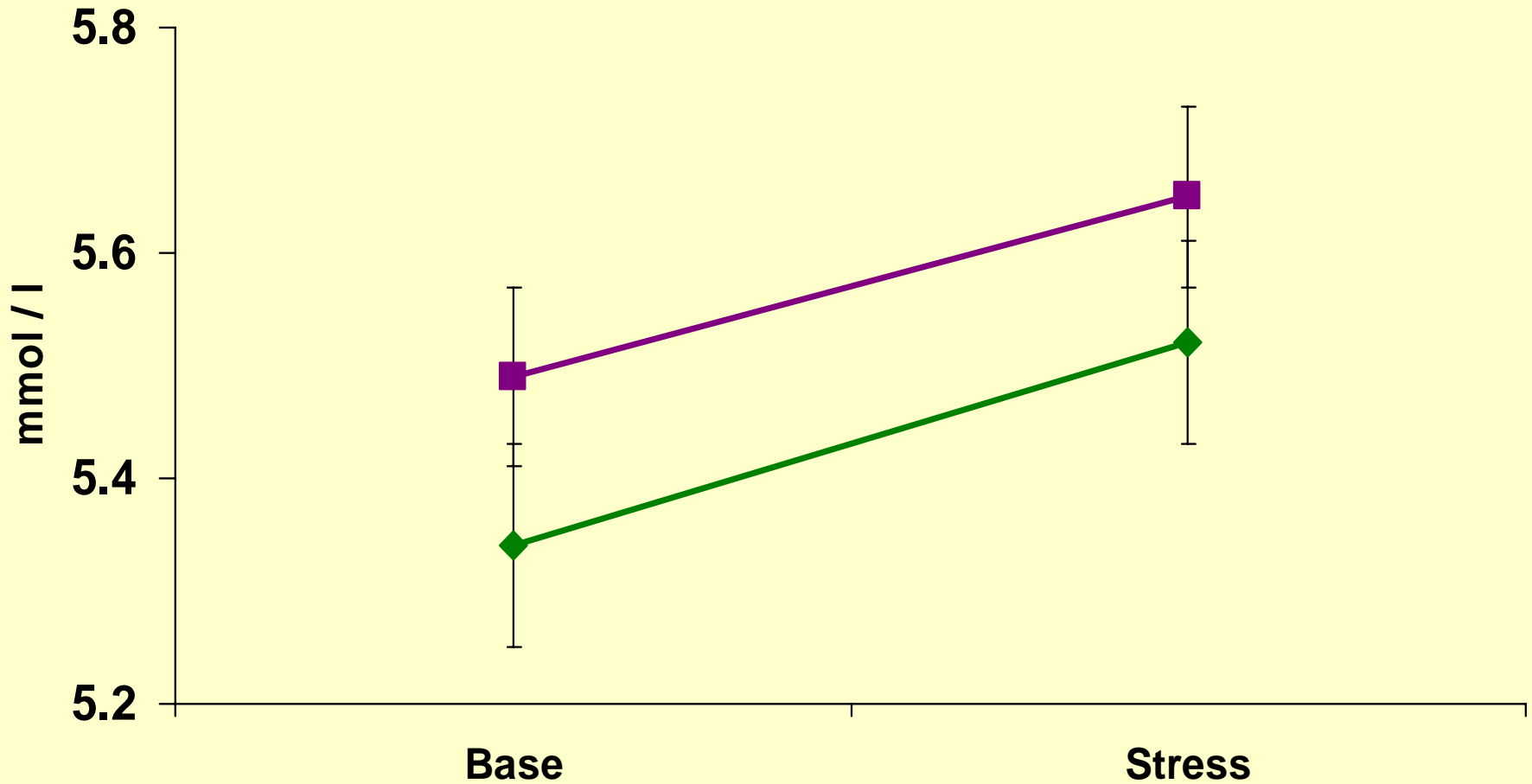
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Stress responses and the development of disease risk

Do more responsive individuals show more rapid progression of disease risk, independently of original risk profile?

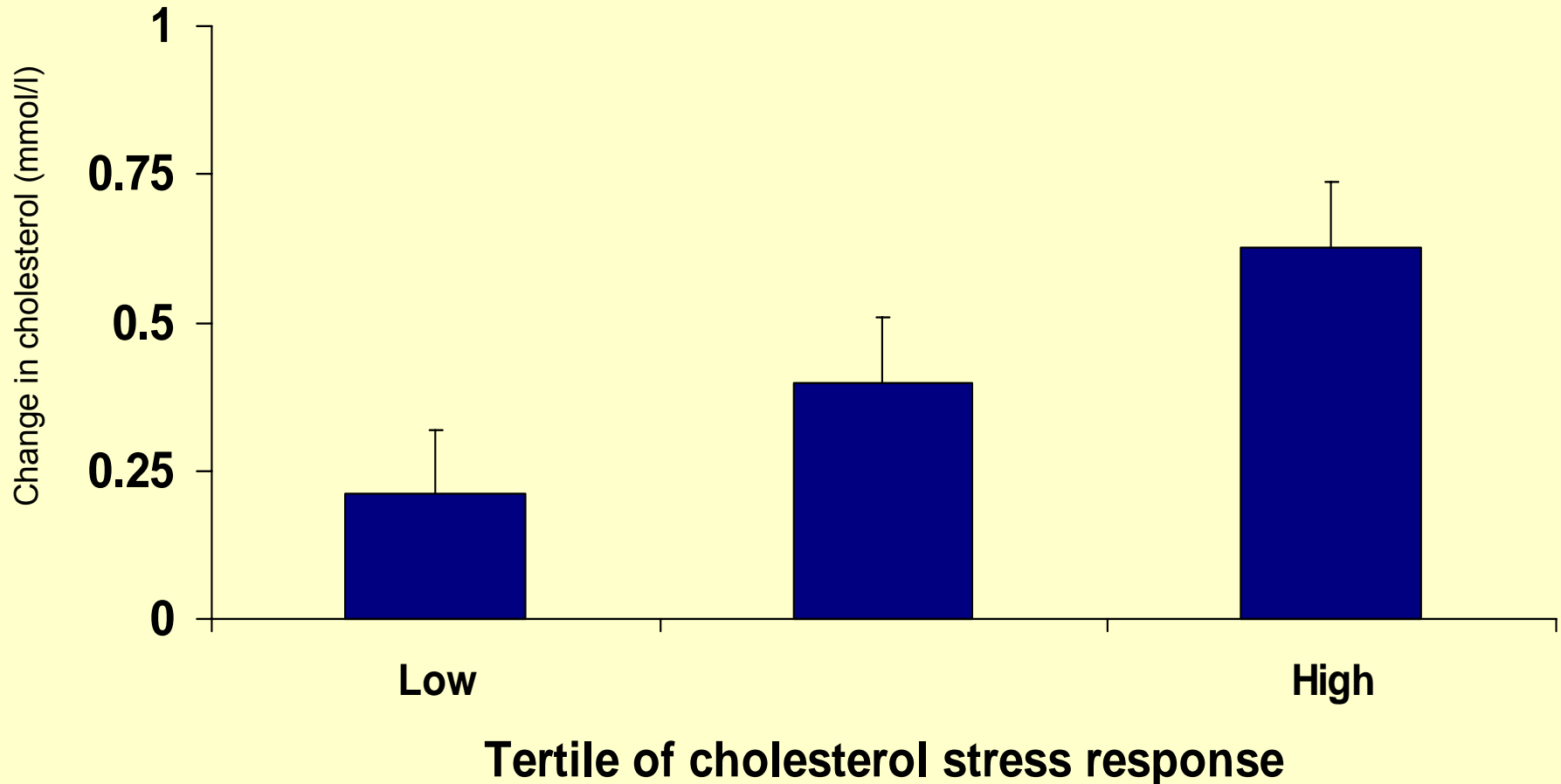
- Assessment of psychobiological responses and disease risk
- Repeat assessment of disease risk 3 years later

Cholesterol response to acute stress



Adjusted for socioeconomic status, age, body weight, smoking, and alcohol

Cholesterol stress response and cholesterol 3-years later



Adjusted for gender, socioeconomic status, age, body weight, smoking, alcohol and baseline cholesterol

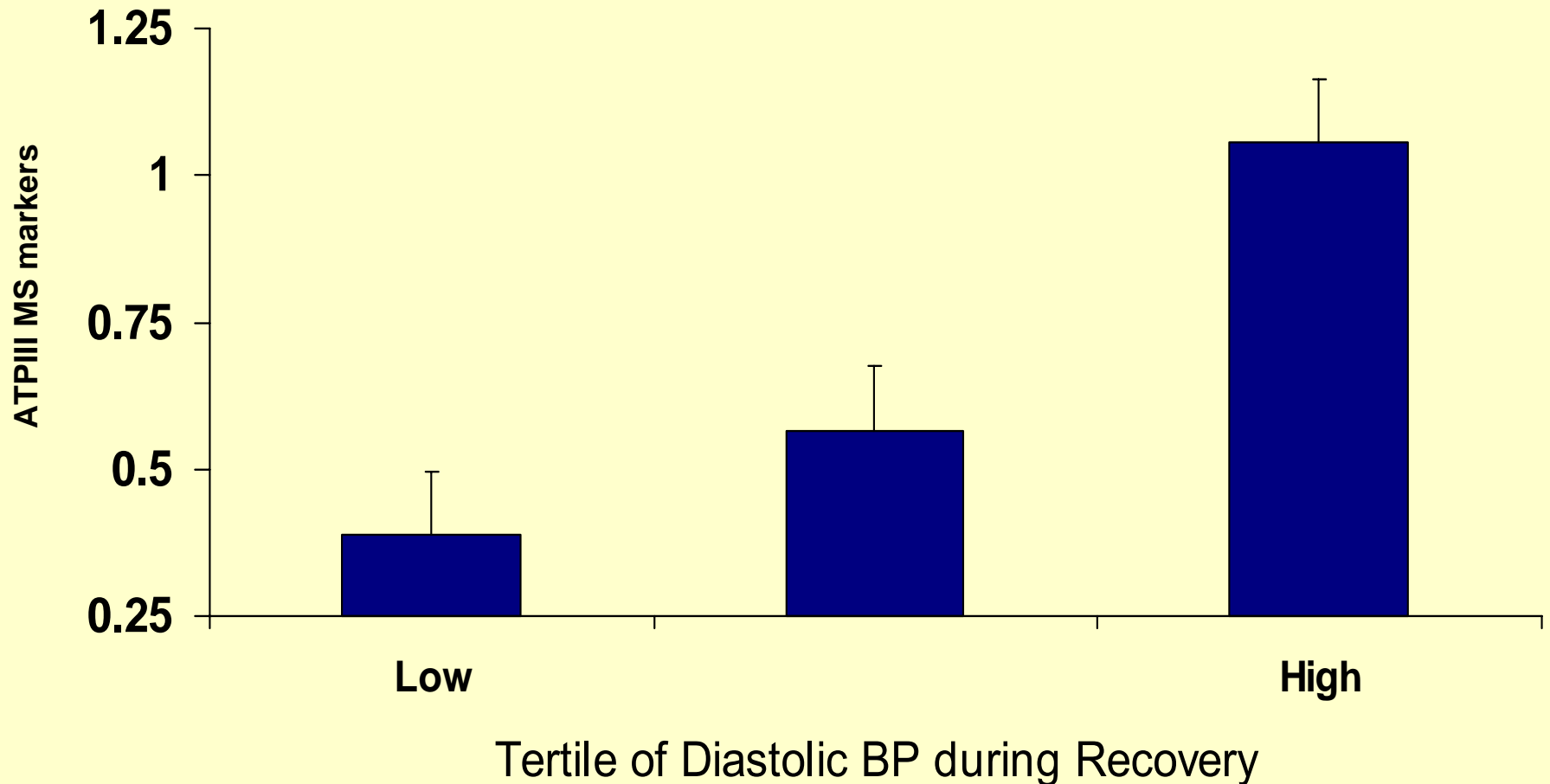
Steptoe & Brydon
Health Psychol, 2005

Metabolic syndrome markers (ATPIII)

Three or more of:

- Waist circumference > 102 cm (men) or 88 cm (women)
- Fasting triglyceride ≥ 150 mg/dl
- Fasting HDL-cholesterol < 40 mg/dl (men), < 50 mg/dl (women)
- Blood pressure $\geq 130 / 85$ mmHg
- Fasting glucose ≥ 110 mg/dl

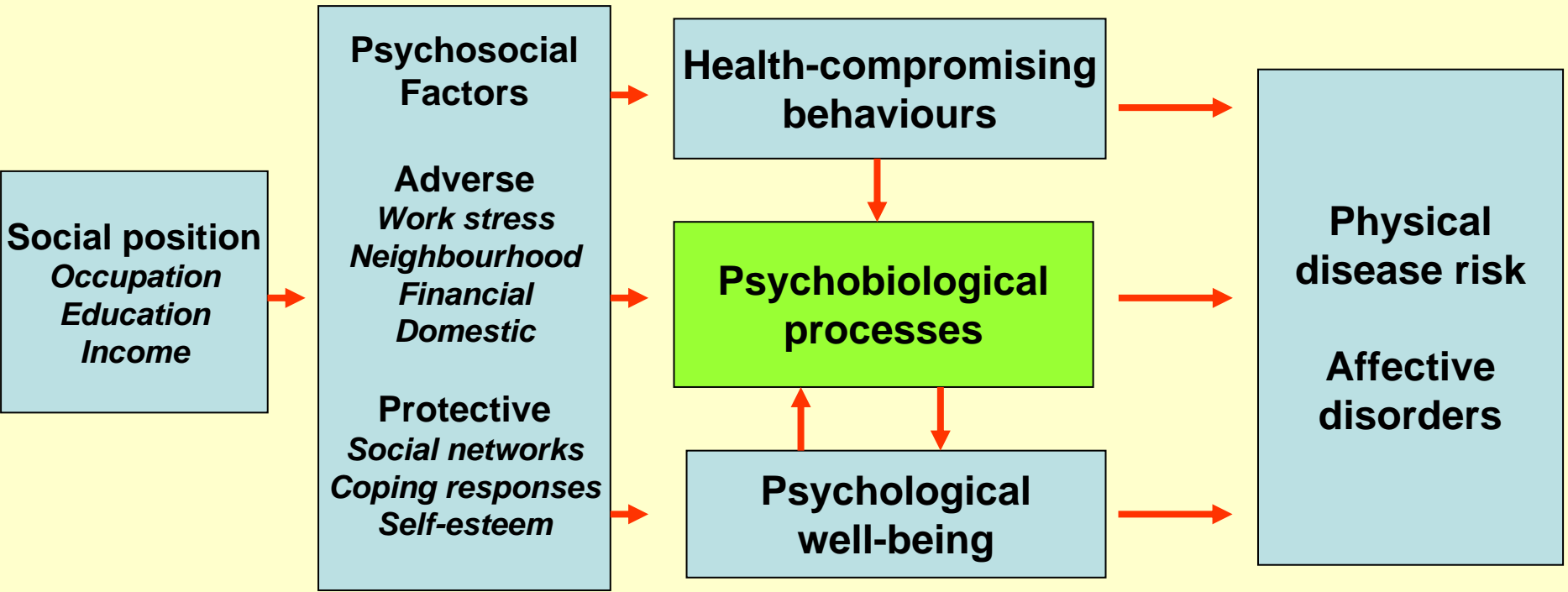
BP Stress Recovery and Metabolic Syndrome 3-years later



Adjusted for baseline ATP III metabolic syndrome markers, gender, BMI, physical activity
SES, age, smoking, alcohol consumption, medication, and baseline diastolic BP

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Acknowledgements

- University College London:
Sir Michael Marmot, Professor Jane Wardle, Dr Sabine Kunz-Ebrecht, Dr Pamela J Feldman, Dr Natalie Owen, Dr Lena Brydon, Dr Mark Hamer, Bev Murray, Dr Caroline Wright
- University of Dresden
Professor Clemens Kirschbaum
- University of Glasgow
Professor Gordon Lowe, Dr Ann Rumley

Medical Research Council

British Heart Foundation

Cortisol waking response

Heightened response

- Depressive symptoms (Pruessner 2003)
- Patients with clinical depression (Bhagwagar 2003)
- Chronic work stress (Steptoe 2000)
- Working vs weekend days (Schlotz 2004)
- Loneliness (Steptoe 2004, PNEC)
- Abdominal adiposity (Steptoe, 2004, IJO)

Reduced response

- Chronic fatigue (Roberts 2004)
- Some physical illness groups (Kudielka 2003)

IL-6 and cognitive impairment

4 year follow-up of 2632 men and women aged 70-79 years

Cognitive impairment, adjusting for baseline cognitive score, age, education, race, depression, alcohol, stroke and statins

- High inflammation RR: 1.66 (1.19 – 2.18)
- Low inflammation RR: 1.08 (0.89 – 1.30)

Heart rate variability

- Beat-to beat variation in heart rate
- Interplay between sympathetic and parasympathetic (vagal) branches of autonomic nervous system

Assessed in the

- Time domain (R-R variability)
- Frequency domain (spectral analysis)
 - High frequency (parasympathetic)
 - Low frequency (sympathovagal balance)
 - Low/High (sympathovagal balance)

Low heart rate variability

- Higher risk of death or recurrent events in patients with CHD (Atrami study, 1998)
- Incident CHD in apparently healthy cohorts (Liao, 1997)
- Future hypertension (Schroeder, 2003)
- Post-stroke mortality (Makikillio, 2004)
- Depressive symptoms (Lim, 2005)

Low heart rate variability

- Poorer cognitive executive function (Hansen et al, 2003)
- Less effective impulse control in children (Allen et al, 2000)
- More negative moods in alcohol abuse (Ingjaldsson et al, 2003)
- Reduced sleep efficiency (Hall et al, 2004)

Whitehall autonomic function study

Low heart rate variability related to:

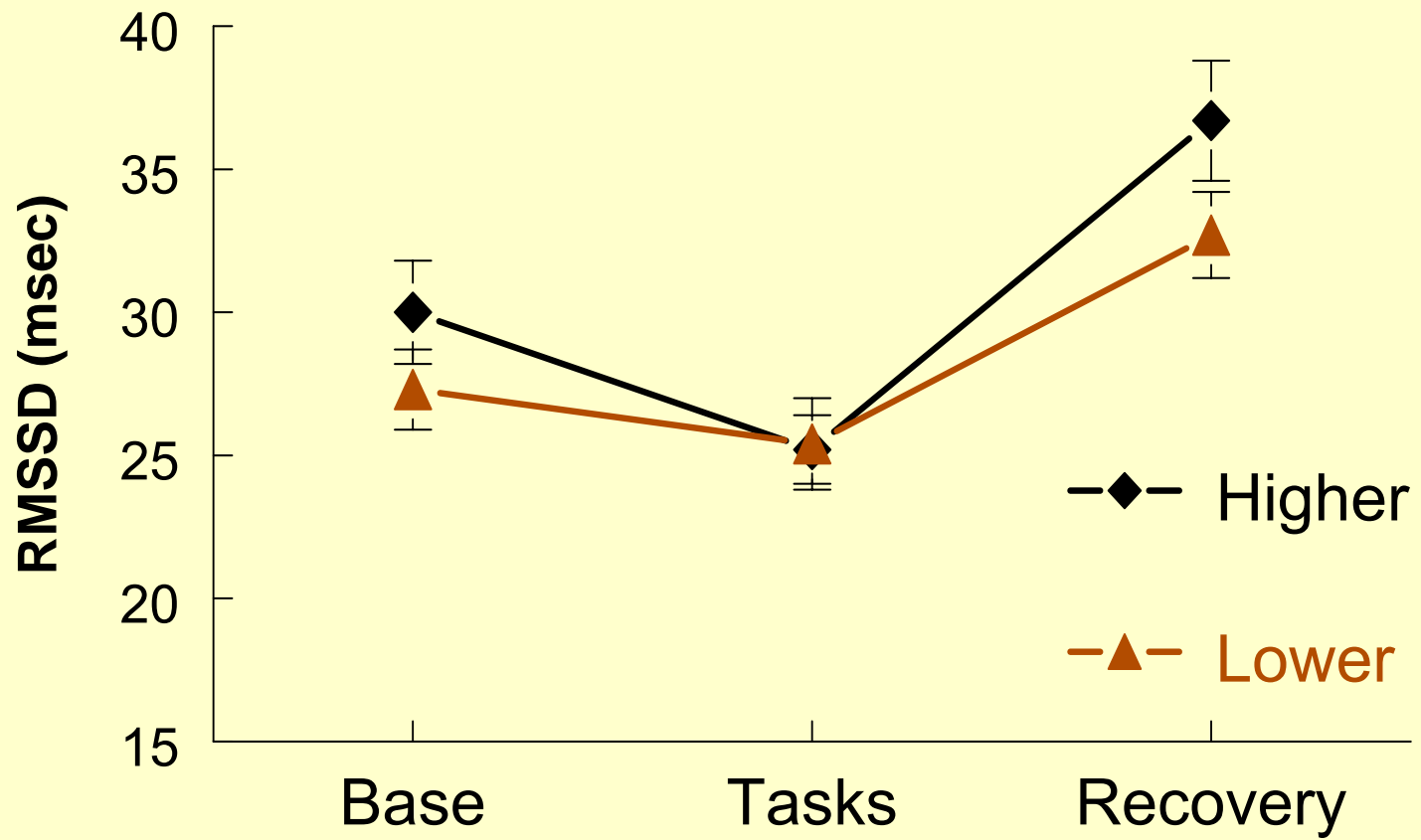
- Low employment grade
- Lower job control
- Smoking, inactivity, high alcohol intake
- Metabolic syndrome

Hemingway et al
Circulation, 2005

Low heart rate variability

- Social isolation (Horsten, 1999)
- High effort/reward imbalance (Vrijkotte, 2000)
- Depressive symptoms (Lim, 2005)
- Depression in post-MI patients (Carney, 2001)

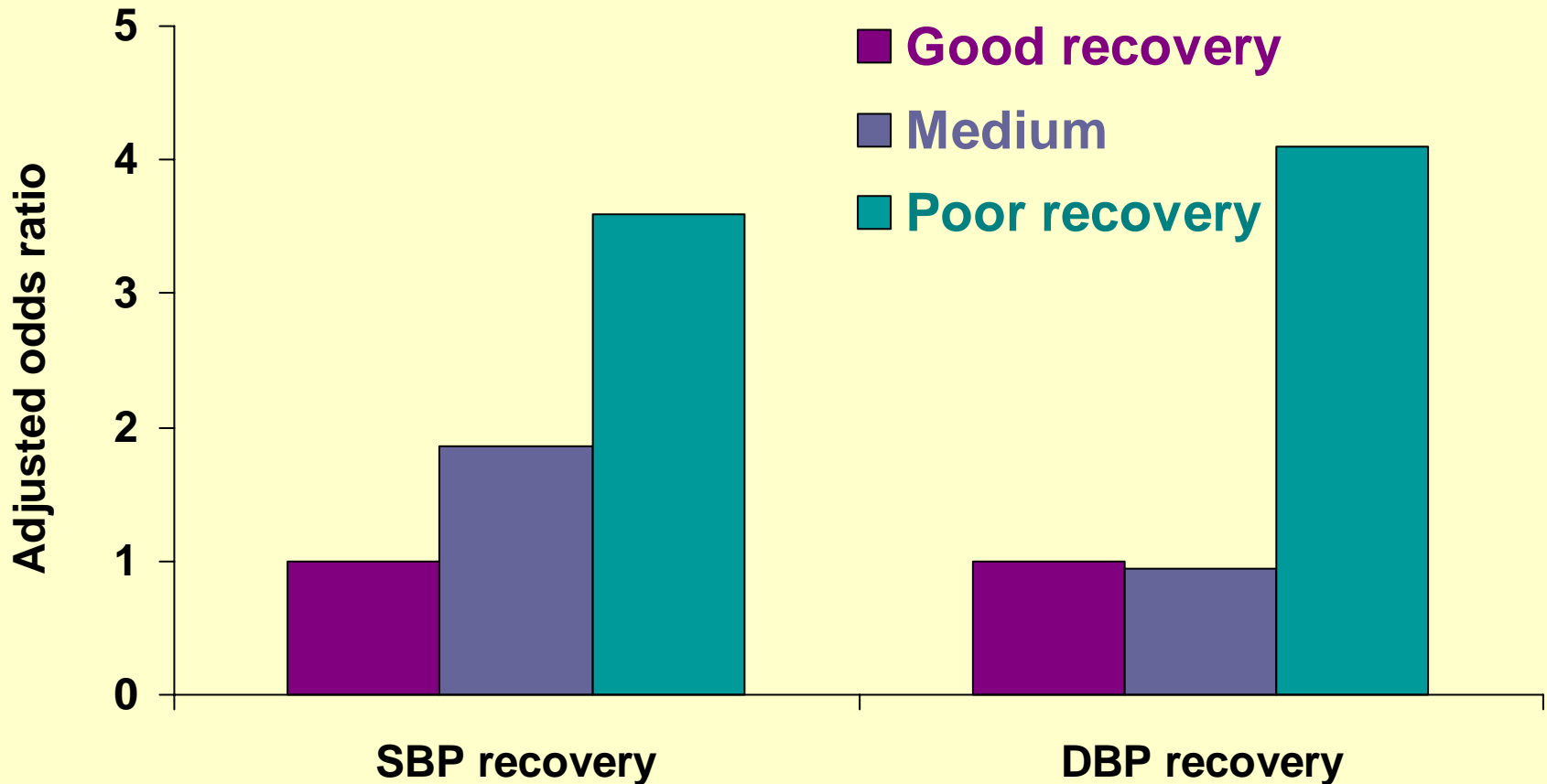
Heart rate variability by grade



Whitehall Psychobiology Follow-up

- Assessment of 209 participants 3 years after mental stress testing (92% response rate)
- Measurement of
 - resting blood pressure
 - fasting lipid profiles
 - BMI, waist and hip circumference
 - Ambulatory BP in a subset (153)

3 year systolic BP increase ≥ 5 mmHg



Adjusted for baseline BP, age, gender, grade of employment, hypertensive medication, BMI, and smoking

Steptoe & Marmot
J Hypertension, 2005

Some effects of sympathetic activation

- Increased blood pressure and heart rate
- Reduced gut motility and salivation
- Stimulation of clotting processes
- Acute immune activation
- Release of free fatty acids from fat stores