HEALTH AND QUALITY IN WORK

- Final Report -

VOLUME II

Annex I: Literature Review- Health and Quality of Working Life

Annex II: Stress and Stress Response: an Overview

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VOLUME II

ANNEX I: Literature Review – Health and Quality of Working Life

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ANNEX I: Table of Contents

1 Introduction

People spend more than a third of their working life time at the workplace. Work place characteristics, likewise material or non-material exposures (e.g. psychological distress), hence are major determinants of health. As people continuously enter and leave the labour force, the world of employment and the world of unemployment are strongly interwoven. Rates of unemployment, or economic trends like boom and recession, might have an impact on perceived as well as on de-facto job insecurity of both employed and unemployed individuals.

This literature research was performed to find out more about the relation of macro-level variables like income, income inequality, access to employment (the previously mentioned macro-level dimension 1), social dialogue, workers' rights and equality (dimension 2), education and discrimination (dimension 3) to health outcomes.

Furthermore, we would like to know how those macro-level variables are connected to, or partly can be explained through micro-level variables such as social support, work-related stress (micro-level dimension 2) and job satisfaction (dimension 3), with the latter two being not well separated in the medical literature.

Hence this overview is mainly structured by the big fields of income, education, unemployment, control, stress, and social support, and by those diseases that have the biggest influence on mortality or on the economic burden of disease, respectively.

2 Methods

A PubMed literature research was undertaken, covering publications published from 1995 onwards, or respectively, from 1985 onwards, if it was to search for reviews and theoretical papers. Selection criterion was an English abstract.

Literature was chosen on the basis of MeSH terms (Medical Subject Headings).

Input variables were employment (including unemployment), SES, income, inequality, poverty, education, social class, job satisfaction, stress (job stress, psychological stress), external/internal control, social support.

Outcome variables were: health, occupational health, occupational accidents, absenteeism, mortality, cardiovascular diseases (including ischemic heart and brain conditions), neoplasm, obstructive lung disease (including asthma), wounds or injuries, infant mortality, substance-related disorders, psychosomatic disorders, mood disorders (including depression), psychophysiology, suicide, diabetes II or HIV/AIDS.

Publications were then selected if found to be relevant on the basis of the abstracts.

If the number of publications exceeded five hundred findings, publications from the following journals were automatically included for further review: Lancet, International Journal of Epidemiology, Social Science and Medicine, British Medical Journal, Journal of Epidemiology and Community Health, European Journal of Public Health, Social Psychiatry and Psychiatric Epidemiology, Scandinavian Journal of Work and Environmental Health, International Journal of Occupational and Environmental Health, Journal of Occupational and Environmental Medicine, American Journal of Epidemiology, American Journal of Public Health, New England Journal of Medicine, JAMA, The American Journal of Psychiatry, American Psychologist, Health Psychology, Journal of Personality and Social Psychology. Furthermore, if the number of publications exceeded five hundred findings, publications from other journals were included for abstract review on the basis of their headline.

3 A Very Short History of Health in Working Life

“Industrial hygiene is one of the most important topics in preventive medicine and hygiene, as it deals with the health, the welfare and the human rights of the vast majority of the adult population. (…) [It] is a subject in which the medical, economic and sociologic aspects are closely interwoven” (Rosenau 1935, cited in Abrams 2001).

The first physicians, who describe diseases of workers, appeared in history at the verge of the middle ages. Georg Bauer, a German physician and mineralogist, better known by the Latin version of his name Agricola, wrote his “Recommendations for prevention of diseases prevalent among miners” in 1526. It took approximately 200 years more, until the fist comprehensive presentation of occupational diseases was published in 1713: “De Morbis Artificum Diatriba” (The Diseases of Workers), in which the Italian physician Bernardo Ramazzini described the various influences of the trades that were prevalent at that time on the state of health.

The first occupational cancer recorded in history was described by the British Percival Pott in 1775, resulting in the “Act for Better Regulation for Chimney sweeps and Their Apprentices” in 1788, one of the first occupational bills in Europe.

In 1790, Johann Peter Frank wrote “The peoples Misery: Mother of Diseases”, hence being regarded as a pioneer in social medicine. With the “English Factory Act” from 1819, the minimum working age was appointed 9 years – one of the first bills regarding child labour. In 1842, Edwin Chadwick reported on the “Sanitary Condition of the Labouring Population of Great Britain”. Rudolf Virchow spoke his famous words “Medicine is a social science and politics are nothing else than medicine on a large scale” in 1848. This, and particularly the German socialist workers’ movement resulted in the fist social insurance legislation in the Western world, inaugurated by the German Chancellor Bismarck in 1883. In the United States, May 1st 1886 marks the US-unions’ struggle for the 8-hour day, but it took more than fifty more years, until the 8-hour-days was regulated by law (Fair Labour Standard Act 1938).

Throughout the 20th century, more and more national and international organizations were founded; above all, the International Labour Organization in 1919, which later became part of the United Nations Organization. On a national level, US Office of Industrial Hygiene and Sanitation was founded in 1914, and federal powers of inspection and enforcement were given to the National Institute of Occupational Safety and Health (NIOSH) in 1970. In Canada, the equivalent CCOHS was created in 1978, while in Japan, JICOSH started in 1999.

For the European Union, the Safety and Health Commission for Mining and Extracting Industries (1957) can be seen as a precursor of the Community Charter of the Fundamental Rights of Workers (Social Charter) and the Framework for Health and Safety at Work (1989) and the European Agency for Security and Health at Work (1994).

According to Sigerist (1943), the history of occupational diseases reflects the history of industry and the history of labour, “in other words some of the most important chapters in the history of human civilization”.

Each individual improvement in occupational health did not come as a present, but had to be eked out by employer-employee negotiations.

Abrams HK: A short history of occupational health. *J. of Public Health Policy*. **2001**;22(1):34-80.

Sigerist HE (1943). Quoted in Rosen G: *The History of Miners' Diseases*. p. ix, Schuman, New York, **1943**

4 Income as the Driving Force of Mortality

In our models, income represented by gross domestic product (GDP) per capita – calculated at purchasing power parity (PPP) exchange rates – is the driving force behind national mortality rates and explaines the largest proportion of their variance.

The literature provides substantial and plausible evidence for that. It is well known that, but not well understood how, socioeconomic status (SES), with income being one of the three pillars of SES, is strongly and inversely related to mortality and most specific disease outcomes, including occupational health. It has been shown repeatedly, that income is equal to – if not stronger than – the other two components of SES: education and occupation status, if used as predictors of mortality (at least if based on US data: Daly et al. 2002). As for cardiovascular disease, the principal investigator of this project has already shown that CVD mortality is likely to follow economic cycles. (Brenner 1997). Additional support comes from an intervention study from San Francisco, that was designed to estimate the magnitude of health improvements resulting form a proposed living wage ordinance, and led to substantial health improvements, including increases of the other two SES indicators (Bhatia and Katz 2001).

There is also substantial evidence that income inequality at the population level effects measures of health, such as mortality, infant mortality, or life expectancy at all levels of income (US: Lynch et al. 1998, Australia: Turrel and Mathers 2001).

An ongoing dispute in the epidemiologic literature is about the question how it does. It has been suggested that this relationship might reflect an association between income and health at the individual level. This idea is known as the absolute-income hypothesis: rising income enables to buy more or better goods and services that are beneficial to health. The association is nonlinear, because the opportunity to do so diminishes as incomes increase.

The other hypotheses that have become predominant in the last ten years (which is the time span that is covered by this literature research), suggest that the population-level relationship between income inequality and health works through layers of hierarchy (see Wilkinson 1992), with health at the individual level being effected mainly by relative social status or social capital (relative-position hypothesis), or mainly by relative income (relative-income hypothesis).

In their extensive review on this subject, based on US population data and supported by the World Bank, Wagstaff and van Doorslaer concluded that “overall, the absolute-income hypothesis, although more than 20 years old, is still the most likely one to explain the

frequently observed strong association between population health and income inequality levels" (Wagstaff and van Doorslaer 2000, see also Fiscella and Franks 1997).

However, in direct comparisons between Canadian provinces or metropolitan areas, and US states or metropolitan areas, it has also be shown that Canada seems to counter the association between income inequality and mortality at the societal level, indicating different ways in which social and economic resources are distributed (Ross et al. 2000, Gorey 2000, Sanmartin et al. 2003). Kawachi and Kennedy (1997) argue, that the large gab between the rich and the poor in the US leads to higher mortality through the breakdown of social cohesion (see below). Interestingly, with data taken from the Israel Longitudinal Mortality Study, after adjustment for individual income, men living in relative disadvantage to their neighbours had lower risks of mortality than those living in concordance with their area (Jaffe et al. 2005). This would strengthen the argument that a wealthy surrounding might invest in facilities that protect the relative deprivated.

In a recent population-based cohort study during the Taiwan earthquake in September 1999, it was found that the degree of vulnerability to a natural disaster increased with decreasing monthly wage. Hence, earthquake death was strongly related to absolute individual income (Chou et al. 2004). This study illustrates remarkably the overall effect that income has on health.

A large study that compared health outcomes in a variety of wealthy countries found that income inequality and characteristics of the psychosocial environment like trust, control, and organisational membership do not seem to be key factors in understanding health differences between the 23 wealthy countries that were studied (including Russia). The authors argue that the associations that do exist are largely limited to child health outcomes and cirrhosis. (Lynch et al. 2001). John Lynch's findings largely contradict those of Wilkinson as well as those focusing largely on social capital (see last section).

In contrast, a large study from the UK found that – for British people born in the immediate post war era, socioeconomic conditions in childhood as well as early adulthood remained an independent predictor of survival, even after adjustment for income in adulthood (Kuh et al. 2002). Important differences are also shown to exist for selected specific occupations beyond those accounted for by social status, income, and education: According to a US study by Johnson et alii (1999), high risk specific occupations include taxi drivers, cooks, longshoremen, and transportation operatives; while low-risk specific occupations include lawyers, natural scientists, teachers, farmers, and "a variety of engineers".

However, other epidemiologists argue that models that focus exclusively on income as a measure of the impact of SES on mortality are not complete and that health spending and unemployment may be even more important than income growth and dispersion (Laporte and Ferguson 2003).

According to a study by Kunst et al. (1998), the European countries (EU-12) are very similar with respect to mortality by occupational class among men aged 30-64. They argue that basically data problems accounted for biasing inequality estimates.

Other very recent publications give hints that adjustments for ethnicity (USA) or education – both markers of early-life social circumstances – let the association between income inequality disappear (Pearce and Davey Smith 2003). Pearce and Davey Smith further argue across countries, the association between current income inequality and health may or may not exist “depending on the choice of countries and their historical, cultural, political, and economic context.

Bhatia R, Katz M: Estimation of health benefits from a local living wage ordinance. *American Journal of Public Health*. **2001** Sep;91(9):1398-402

Brenner MH: Heart disease mortality and economic changes; including unemployment; in Western Germany 1951-1989. *Acta Physiologica Scandinavica* Suppl. **1997**;640:149-52

Chou YJ, Huang N, Lee CH, Tsai SL, Chen LS, Chang HJ: Who is at risk of death in an earthquake? *American Journal of Epidemiogy*. **2004** Oct 1;160(7):688-95.

Daly MC, Duncan GJ, McDonough P, Williams DR: Optimal indicators of socioeconomic status for health research. *American Journal of Public Health*. **2002** Jul;92(7):1151-7. Erratum in: American Journal of Public Health2002 Aug;92(8):1212

Fiscella K, Franks P: Poverty or income inequality as predictor of mortality: longitudinal cohort study. *British Medical Journal*. **1997** Jun 14;314(7096):1724-7

Gorey KM, Holowaty EJ, Fehringer G, Laukkanen E, Richter NL, Meyer CM: An international comparison of cancer survival: metropolitan Toronto, Ontario, and Honolulu, Hawaii. *American Journal of Public Health*. **2000** Dec;90(12):1866-72

Jaffe DH, Eisenbach Z, Neumark YD, Manor O: Individual, household and neighbourhood socioeconomic status and mortality: a study of absolute and relative deprivation. *Social Science and Medicine*. **2005** Mar;60(5): 989-97

Johnson NJ, Sorlie PD, Backlund E: The impact of specific occupation on mortality in the U.S. National Longitudinal Mortality Study. *Demography*. **1999** Aug;36(3):355-67

Kawachi I, Kennedy BP: Health and social cohesion: why care about income inequality? *British Medical Journal*. **1997** Apr 5;314(7086):1037-40

Kuh D, Hardy R, Langenberg C, Richards M, Wadsworth ME: Mortality in adults aged 26-54 years related to socioeconomic conditions in childhood and adulthood: post war birth cohort study. *British Medical Journal*. *2002* Nov 9;325(7372):1076-80

Kunst AE, Groenhof F, Mackenbach JP: Mortality by occupational class among men 30-64 years in 11 European countries. EU Working Group on Socioeconomic Inequalities in Health. *Social Science and Medicine*. **1998** Jun;46(11):1459-76

Laporte A, Ferguson BS: Income inequality and mortality: time series evidence from Canada. *Health Policy*. **2003** Oct;66(1):107-17

Lynch J, Smith GD, Hillemeier M, Shaw M, Raghunathan T, Kaplan G: Income inequality, the psychosocial environment, and health: comparisons of wealthy nations. *Lancet*. **2001** Jul 21;358(9277):194-200

Lynch JW, Kaplan GA, Pamuk ER, Cohen RD, Heck KE, Balfour JL, Yen IH: Income inequality and mortality in metropolitan areas of the United States. *American Journal of Public Health*. **1998** Jul;88(7):1074-80

Pearce N, Davey Smith G: Is Social Capital the Key to Inequalities in Health? *American Journal of Public Health.* **2003**. 93(1): 122-9

Ross NA, Wolfson MC, Dunn JR, Berthelot JM, Kaplan GA, Lynch JW: Relation between income inequality and mortality in Canada and in the United States: cross sectional assessment using census data and vital statistics. *British Medical Journal*. **2000** Apr 1;320(7239):898-902

Sanmartin C, Ross NA, Tremblay S, Wolfson M, Dunn JR, Lynch J: Labour market income inequality and mortality in North American metropolitan areas. *Journal of Epidemiology and Community Health*. **2003** Oct;57(10):792-7

Turrell G, Mathers C: Socioeconomic inequalities in all-cause and specific-cause mortality in Australia: 1985-1987 and 1995-1997. *International Journal of Epidemiology*. **2001** Apr;30(2):231-9

Wagstaff A, van Doorslaer E: Income inequality and health: what does the literature tell us? *Annual Review of Public Health*. **2000**;21:543-67. Review

Wilkinson RG: Income distribution and live expectancy. *British Medical Journal.* **1992**; 304: 165-168

5 Unemployment and Health

Unemployment is consistently associated with poor health. There is no doubt that part of this association is a selection effect: people who are healthier are more likely to be employed. However, sufficient evidence exists to suggest that employment protects and fosters health. Béland et al. (2002) discuss the unemployment-health-relationship in depth. The set of modulators is very complex and includes financial strains, social support, psychosocial factors (such as stress) and contexts (e.g. business cycles).

The effects of unemployment in society on peoples' health may be mediated through pessimism about the future and financial strain. A gendered comparison of young unemployed men and women during boom and recession (survey) showed that both genders reported more somatic and psychological symptoms during recession than boom (Novo et al. 2001).

Moreover, it is not only the current economic situation, but experiences of disadvantage at any time in the life course that leads to bad health in the future. In a study by Bartley and Plewis (2002), belonging to a "semi- or unskilled social class" or being unemployed in 1971 contributed independently to an increased risk of chronic limiting illness in 1991.

In 2004, the Swedish Karolinska Institute published a huge study on unemployment and early cause-specific mortality. It is one of the most interesting studies on effects on unemployment because of its outstanding design: Voss et alii (2004) followed 20.632 females and male twins with regard to mortality from 1973 through 1996. The results from this study suggested that unemployment is associated with an increased risk of early death even after adjustment for several potential confounding factors, including socioeconomic status, lifestyle factors, and genetic and early childhood factors. In particular, unemployment was associated with increased mortality from suicide and external undetermined cause; for men, also with death from malignant neoplasms.

However, there is growing evidence, that besides experiences of disadvantage, also experiences of solidarity matter. Three studies could be identified, strengthening the public health importance of workers' organizations like unions.

A case study of the role of organized labour and smoke-free airlines illustrated the potential for successful partnerships between unions and tobacco control policy advocates when developing smoke-free worksite policies (Pan et al. 2005).

An article about the workers' health movement in the Brazilian state of Sao Paulo (Sato 2004) provides examples of some of the different actions and practices that had a key role in the battle for better working conditions. Another publication focuses on Chinese factories (Chen and Chan 2004) and finds that the input of the trade union does have a significant impact on the protection of the workers' occupational safety and health.

Workers' struggles for changes in occupation policies cannot be overrated:

"The worker played a primary role as the basis of every significant improvement in legislation, factory inspection, compensation, correction, and prevention. Labour unrest, protests, strikes, lawsuits, and catastrophes were vital catalysts in obtaining action" (Abrams 2001).

Abrams HK: A short history of occupational health. *Journal of Public Health Policy*. **2001**;22(1):34-80.

Bartley M, Plewis I: Accumulated labour market disadvantage and limiting long-term illness: data from the 1971-1991 Office for National Statistics' Longitudinal Study. *International Journal of Epidemiology*. **2002** Apr;31(2):336-41

Béland F, Birch S, Stoddart G: Unemployment and health: contextual-level influences on the production of health in populations. Social Science and Medicine. 2002; 55:2033-52

Chen MS, Chan A: Employee and union inputs into occupational health and safety measures in Chinese factories. *Social Science and Medicine*. **2004** Apr;58(7):1231-45

Gillen M, Baltz D, Gassel M, Kirsch L, Vaccaro D: Perceived safety climate, job demands, and coworker support among union and nonunion injured construction workers. *Journal of Safety Research*. **2002** Spring;33(1):33-51

Novo M, Hammarstrom A, Janlert U: Do high levels of unemployment influence the health of those who are not unemployed? A gendered comparison of young men and women during boom and recession. *Social Science and Medicine*. **2001** Aug;53(3):293-303

Pan J, Barbeau EM, Levenstein C, Balbach ED: Smoke-free airlines and the role of organized labor: a case study. *American Journal of Public Health*. **2005** Mar;95(3):398-404

Sato L, de Castro Lacaz FA, Bernardo MH: Psychology and the workers' health movement in the state of Sao Paulo (Brazil). *Journal of Health Psychology*. **2004** Jan;9(1):121-30

Voss M, Nylen L, Floderus B, Diderichsen F, Terry PD: Unemployment and early cause-specific mortality: a study based on the Swedish twin registry. *American Journal of Public Health*. **2004** Dec;94(12):2155-61

6 Education

It is well accepted that the more educated a person is, the better he or she is informed about health hazards and ways of risk management, including the use of health care facilities. The socioeconomic gradients in mortality has been described above. In most studies, income is the strongest predictor of these gradients, followed by education, especially for 'preventable' causes death – such as fatal occupational injuries (Blakely et al. 2002, Steenland et al. 2003, Sorlie et al. 1995).

Income and education are strongly linked with each other. The better a person's education, the more likely he is to get a good job; or, the less likely to get or remain unemployed. The higher the family income (or – at least in some countries – national wealth), the better the education for the children. As Davey Smith points out, "social class can change throughout adult life, while education is unlikely to alter after early adulthood" (Davey Smith et al. 1998). In that prospective study, cardiovascular disease as a cause of death was most strongly associated with education. It is concluded that "the stronger association of education with death from cardiovascular causes than with other causes of death may reflect the function of education as an index of socioeconomic circumstances in early life."

Johnson et al. (1999) analyzed data from a huge national cohort in the United States (380.000 persons, aged 25-64) and found that mortality differences obtained for social status groups of specific occupations are almost completely accounted for by adjustments for income and education. The same was true for a study from Italy: Education and income mostly explained the mortality differences by social class in men, while income showed the highest contribution in women (Mamo et al. 2005).

A broad study from the Netherlands compared differences in total and cause-specific mortality by educational level (as a proxy for SES), and explored the gender gap. Seven countries were involved and provided data from 1980 to 1990: the United States, Finland, Norway, Italy, the Czech Republic, Hungary and Estonia. Except for breast cancer, higher mortality rates among lower-educated men and women were found for most causes of death; among men, the differences were even larger (Mackenbach et al. 2003, 1999). Similar results stem from an analysis of two American Cancer Society cohorts (1959-96): "Temporal trends showed increasing mortality differences by education for coronary heart disease, diabetes, COPD and lung cancer" (Steenland et al. 2002). In contrast to Mackenbach's findings, education accounts for the frequency of cancer screening examinations, or the stage of cancer at time of diagnosis (Merkin et al. 2002).

According to Marshall et al. (1999), cancer occurrence during working life is strongly associated with SES measures, but they did not specifically control for education per se.

Regarding not mortality but disability pensions, Krokstad et al. (2002) could demonstrate that education was even a stronger predictor of disability pension than medical factors. However, it is very plausible, that a person's education accounts a lot for the kind of job he or she gets. The more formal education a person has, the more likely he or she will get a job with high decision latitude or autonomy; communication skills are also likely to be positively related to education. Thus education might be closely linked to, but much more clearly described, through variables like job strain or social support.

Blakely T, Woodward A, Pearce N, Salmond C, Kiro C, Davis P: Socio-economic factors and mortality among 25-64 year olds followed from 1991 to 1994: the New Zealand Census-Mortality Study. *The New Zealand Medical Journal*. **2002** Mar 8;115(1149):93-7

Davey Smith G, Hart C, Hole D, MacKinnon P, Gillis C, Watt G, Blane D, Hawthorne V: Education and occupational social class: which is the more important indicator of mortality risk? *Journal of Epidemiology and Community Health*. **1998** Mar;52(3):153-60

Johnson NJ, Sorlie PD, Backlund E: The impact of specific occupation on mortality in the U.S. National Longitudinal Mortality Study. *Demography*. **1999** Aug;36(3):355-67

Krokstad S, Johnsen R, Westin S: Social determinants of disability pension: a 10-year follow-up of 62 000 people in a Norwegian county population. *International Journal of Epidemiology*. **2002** Dec;31(6):1183-91

Mackenbach JP, Bos V, Andersen O, Cardano M, Costa G, Harding S, Reid A, Hemstrom O, Valkonen T, Kunst AE: Widening socioeconomic inequalities in mortality in six Western European countries. *International Journal of Epidemiology*. **2003** Oct;32(5):830-7

Mackenbach JP, Kunst AE, Groenhof F, Borgan JK, Costa G, Faggiano F, Jozan P, Leinsalu M, Martikainen P, Rychtarikova J, Valkonen T: Socioeconomic inequalities in mortality among women and among men: an international study. *American Journal of Public Health*. **1999** Dec;89(12):1800-6

Mamo C, Marinacci C, Demaria M, Mirabelli D, Costa G: Factors other than risks in the workplace as determinants of socioeconomic differences in health in Italy. *International Journal of Occupational and Environmental Health*. **2005** Jan-Mar;11(1):70-6

Marshall B, Chevalier A, Garillon C, Goldberg M, Coing F: Socioeconomic status, social mobility and cancer occurrence during working life: a case-control study among French electricity and gas workers. *Cancer causes & control*. **1999** Dec;10(6):495-502

Merkin SS, Stevenson L, Powe N: Geographic socioeconomic status, race, and advanced-stage breast cancer in New York City. *American Journal of Public Health*. **2002** Jan;92(1):64-70

Sorlie PD, Backlund E, Keller JB: US mortality by economic, demographic, and social characteristics: the National Longitudinal Mortality Study. *American Journal of Public Health*. **1995** Jul;85(7):949-56

Steenland K, Halperin W, Hu S, Walker JT: Deaths due to injuries among employed adults: the effects of socioeconomic class. *Epidemiology*. **2003** Jan;14(1):74-9

Steenland K, Henley J, Calle E, Thun M: Individual- and area-level socioeconomic status variables as predictors of mortality in a cohort of 179,383 persons. *American Journal of Epidemiology*. **2004** Jun 1;159(11):1047-56

7 Locus of Control

Although research on social and behavioural determinants of health was conducted throughout the 20th century, it has become more common since the 1980s. In those years, and specifically in the “mini-environment of the workplace” (Syme 1988), concepts of control and participation have become central (Karasek and Theorell 1990, Banduara 1995, Yen and Syme 1999). This focus is interesting as it offers more possibilities of intervention than exposure or behaviour change alone. The effect of locus of control is further reviewed in the section on stress, as it has been included into the job-strain-model.

Banduara A: *Self-efficacy: The exercise of control*. Freeman, New York, **1995**

Karasek R, Theorell T: *Healthy Work*. Basic Books, New York, **1990**

Syme SL: Social epidemiology and the work environment. *International journal of health services*. **1988**;18(4):635-45

Yen IH, Syme SL: The social environment and health: A discussion of the epidemiologic literature. *Annual Review of Public Health.* **1999**; 20: 287-308

8 Occupational Stress and Job Satisfaction: Main models and how they are linked to structural unemployment

Job satisfaction and occupational stress are often discussed as interchangeable variables. In fact, the two terms are based on two distinct concepts. The basic difference is that job satisfaction is only a measure of individual self-perception, while stress can serve both as and individual (e.g.: self-percieved stress) and as an aggregate parameter. Moreover, many aspects of stress go beyond self perception and can be measured directly.

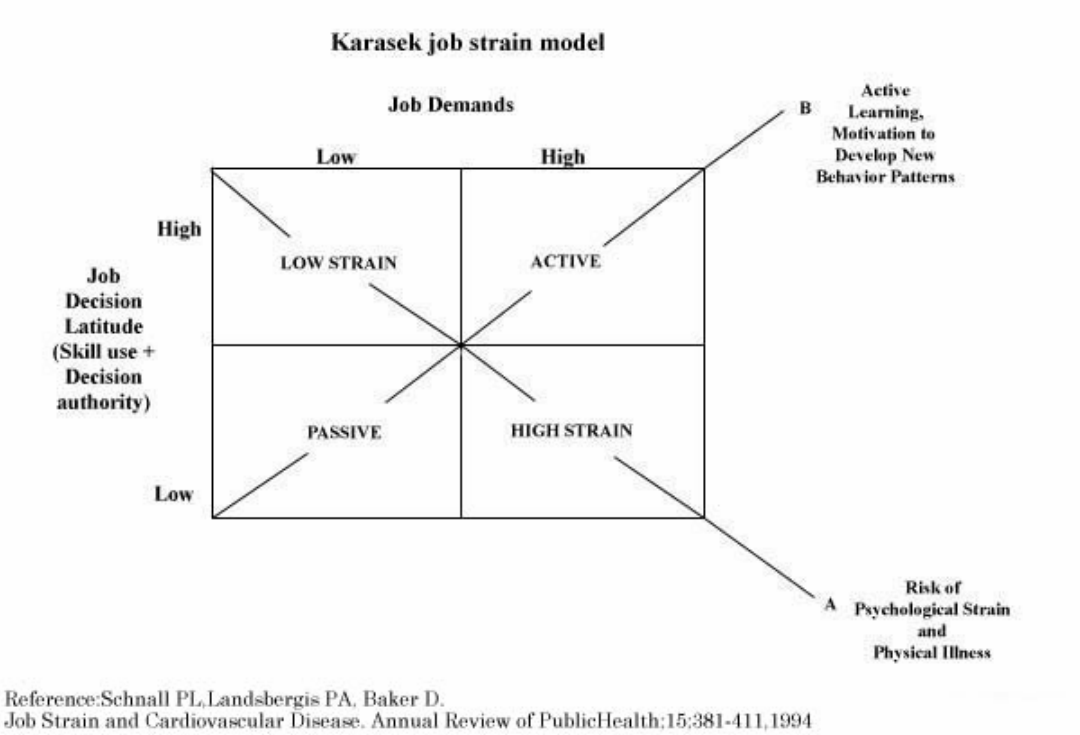
In an occupational health context, sources of stress include poor working conditions, relationships at work, an unclear role in the organisation, long hours, organisational climate, and – last but not least – lack of job security. It is plausible and has been argued repeatedly (also by the main investigator of this project), that economic recession and hence high unemployment rates create a climate of uncertainty, resulting in increases of absenteeism due to rising sickness. Interestingly, absenteeism, which is a very common measure in the epidemiologic literature, does not always reflect disease, especially not short time absenteeism (Vahtera et al. 2004, Kivimaki et al. 2003b). There is little doubt today, that ongoing recession is accompanied by decreases of short time absenteeism from work (which does not necessarily reflect decreases in illness): People are frightened to loose their jobs (Markham 1991). Already among young adults, as demonstrated by Hannan et alii (1997), unemployment is the most significant influence on the levels of psychological distress. The impact of unemployment further increases when combined with feelings of lack of control, and especially, in this context, when the responsibility of employment was attributed solely to structural or political factors.

Another argument that strengthens the role of unemployment in stress production is the fact that reemployment, especially for those moving into permanent employment, leads to a reduction of distress (Bjarnason and Sigurdardottir 2003).

Reynolds (1997) has noted that in addition to stress induced by job insecurity itself, the effect of unemployment on stress could also result from greater competition.

There have been many attempts to describe and measure key determinants of occupational stress. Unfortunately, it is difficult to establish a simple and feasible concept that can be applied for all kind of work settings.

Figure 1: Karasek's job strain model



One model of job stress developed by Robert Karasek has highlighted two key elements of work stressors. Karasek's "job strain" model (Fig. 1) states that the greatest risk to health from stress occurs to workers facing high psychological workload demands or pressures combined with low control or decision latitude in meeting those demands. Job demands means that workers feel that they are working very fast or very hard or do not have enough time to get the job done. Job decision latitude is defined as both the ability to use skills on the job and the decision-making authority available to the worker. In the Maastricht cohort study for example, decision latitude was one of the strongest predictors for sickness absence of at least one month (Andrea et al. 2003, see also Vaananen et al. 2003 and Ariens et al. 2002). Decision latitude does not only work as a “metaphor” or proxy for autonomy, but also for organizational justice (see section on social support), both at individual and work unit level (Elovainio et al. 2004).

Karasek's model emphasizes another major negative consequence of work organization; how the assembly line and the principles of Taylorism, with its focus on reducing workers' skills and influence, can produce passivity, learned helplessness, and lack of participation. Thus, this model provides a justification for efforts to achieve greater worker autonomy as well as increased workplace democracy.

The biggest cohort study to support Karasek’s model was designed to prospectively examine the relation between psychosocial work characteristics and changes in health related quality of life in a cohort of working women in the United States (Cheng et al. 2000). Low job control,

high job demands, and low work related social support were associated with poor health status at baseline as well as greater functional declines over the four year follow up period. Examined in combination, women with low job control, high job demands, and low work related social support had the greatest functional declines. These associations could not be explained by age, body mass index, co-morbid disease status, alcohol consumption, smoking status, education level, exercise level, employment status, or marital status.

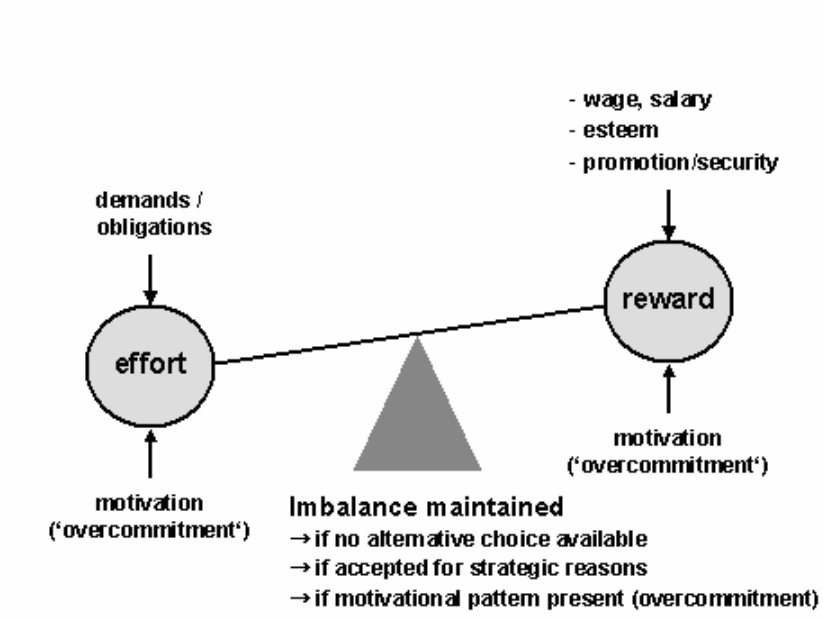
Similar results could be demonstrated by Schrijvers et al. (1998).

The issue of worktime control has to be stressed: Especially in women, worktime control is an independent predictor of health (Ala-Mursala et al. 2002). In a study of Swedish hospital employees in the 1990s, increasing work demands were accompanied by deteriorating mental health, and decreasing time to plan work showed the strongest association with increasing long-term sick leave (Petterson et al. 2005).

Another widespread model is Siegrist's effort-reward imbalance model (ERI).

This model claims that failed reciprocity in terms of high efforts spent and low rewards received is likely to provoke recurrent negative emotions and sustained stress responses in exposed workers. A major specification of this theoretical perspective concerns the work role, and in particular its contractual basis.

Figure 2: Siegrist's effort-reward-imbalance model (Source: University of Düsseldorf, Medical Sociology)



A cross sectional analysis (Niedhammer 2004) revealed that effort-reward-imbalance was significantly associated with self-reported health for both genders. It turned out that when studied as separate variables, reward remained significant for both genders, while effort was

a significant factor for men only. At this point it should be mentioned, that self-reported (poor) health is a well established predictor for mortality and disability (Mansson and Rastam 2001, Sundquist and Johansen 1997, Miilunpalo et al. 1997, Idler and Benyamini 1997).

Despite substantial evidence for the validity of both models (e.g. Baker 1996, de Jonge 2000, de Lange 2002, Kivimaki et al. 2002), difficulties arise in trying to adopt universal measures for different types of jobs. Bliese and Jex (2002) have suggested a multilevel perspective that can be incorporated into occupational stress research. This seems to be useful because there may be cases in which a group-level intervention may be far more effective than focusing on individuals.

Job satisfaction is not only a variable that influences work-related health, but also serves as an antecedent of selection from contingent to permanent employment, and thus may work as a possible confounder: The less satisfied people are with their job, the more likely it will be to remain in a fixed term job and therefore, remain at risk of unemployment. In a cohort study on hospital staff, Virtanen M et al. (2002, Finnish Institute of Occupational Health) could show that job satisfaction predicted a permanent job contract with an OR of 1.86; or, respectively, receiving a permanent job contract after fixed term employment is associated with job satisfaction (Virtanen M et al. 2003).

Interestingly, in another Finnish study (Virtanen P et al. 2002), the association of low perceived security with psychological distress was significantly stronger in permanent employees than among fixed term and subsidised employees, indicating that perceived security is more important among employees with a permanent contract.

As Leino-Arjas et alii (1999) point out, while occupational stress predicts unemployment, self-percieved stress increases further with the onset of unemployment.

Sverke et al. (2002, Stockholm University) performed a meta-analysis on job insecurity and could show a strong and significant relationship between job satisfaction and job insecurity. They also highlight the need for consensus on the measurement of job insecurity and call for a multidimensional measure reflecting both threats of imminent job loss and fear of losing important job features. Perceptions of threat to continued employment have important empirical associations with employees' job attitudes, organizational attitudes, and health.

There is also evidence from laboratory experiments (Probst 2002) and survey data (Grunberg et al. 2001), that persons faced with the threat of layoffs violated more safety rules than controls. Those threats of layoffs might work differently on people who end their job anyway after a fixed period and have already adapted to changes of work or worksite, or permanent employees who for years have not developed strategies of coping with job loss or

job change. In addition, there is also evidence that moving from temporary to permanent employment is associated with a lower risk of death than remaining continuously in permanent employment (Kivimaki et al. 2003a).

This is supported Strazdins et alii (2004). The authors introduce a new way of looking at work stress by combining job strain with job insecurity, a combination increasingly prevalent in contemporary economies. Those reporting both strain and insecurity showed markedly higher odds for mental and physical health problems (depression: odds ratio 13.88, anxiety 12.88, physical health problems 3.97, and poor self-rated health 7.12). Job strain and insecurity showed synergistic associations with health, and employees experiencing both could be at heightened health risk. Comparable results were published by D'Souza et alii (2003). In an analysis of a representative sample of the European Union total active population (aged 15 years and older), high job demands, low job control, "and high strain and passive work" were associated with higher work related sickness absence; as the authors point out, the risks were more pronounced in men compared with women, and in non-permanent compared with permanent employees (Gimeno et al. 2004).

Another Finnish study investigated the effects of workplace bullying. Of the single forms of bullying, judging a person's work unjustly or in an offending manner, restricting a person's possibilities to express his or her opinions, and assaulting one's private life were the most clearly connected with all the stress reactions measured in the study. Interestingly, not only the targets of bullying, but also bystanders, suffer when someone is bullied in the workplace (Vartia 2001).

In a large NHS study from the UK, staff who had been bullied had significantly lower levels of job satisfaction, higher levels of job-induced stress, depression and anxiety (Quine 1999). Powerlessness, or lack of control over destiny (which in our societies is closely related to having a job not) emerges as an important risk factor for disease in general, and specifically for occupational health (see also Wallerstein 1992). For example, in a recent study by Hechanova and Beehr (2001), span of control and level of empowerment predicted one third of the variance in safety measures (here: in the chemical industry, USA).

Ala-Mursula L, Vahtera J, Pentti J, Kivimaki M: Effect of employee worktime control on health: a prospective cohort study. *Occupational and Environmental Medicine*. **2004** Mar;61(3):254-61

Ala-Mursula L, Vahtera J, Kivimaki M, Kevin MV, Pentti J: Employee control over working times: associations with subjective health and sickness absences. *Journal of Epidemiology and Community Health*. **2002** Apr;56(4):272-8

Andrea H, Beurskens AJ, Metsemakers JF, van Amelsvoort LG, van den Brandt PA, van Schayck CP: Health problems and psychosocial work environment as predictors of long term sickness absence in employees who visited the occupational physician and/or general practitioner in

relation to work: a prospective study. *Occupational and Environmental Medicine*. **2003** Apr;60(4):295-300

Ariens GA, Bongers PM, Hoogendoorn WE, van der Wal G, van Mechelen W: High physical and psychosocial load at work and sickness absence due to neck pain. *Scandinavian Journal of Work, Environment & Health*. **2002** Aug;28(4):222-31

Baker E, Israel B, Schurman S: Role of control and support in occupational stress: an integrated model. *Social Science and Medicine*. **1996** Oct;43(7):1145-59

Bjarnason T, Sigurdardottir TJ: Psychological distress during unemployment and beyond: social support and material deprivation among youth in six northern European countries. *Social Science and Medicine*. **2003** Mar; 56(5):973-85

Bliese PD, Jex SM: Incorporating a multilevel perspective into occupational stress research: theoretical, methodological, and practical implications. *Journal of Occupational Health Psychology*. **2002** Jul;7(3):265-76

Cheng Y, Kawachi I, Coakley EH, Schwartz J, Colditz G: Association between psychosocial work characteristics and health functioning in American women: prospective study. *British Medical Journal*. **2000** May 27;320(7247):1432-6

Elovainio M, Kivimaki M, Steen N, Vahtera J.: Job decision latitude, organizational justice and health: multilevel covariance structure analysis. *Social Science and Medicine*. **2004** May;58(9):1659-69

Gimeno D, Benavides FG, Amick BC 3rd, Benach J, Martinez JM: Psychosocial factors and work related sickness absence among permanent and non-permanent employees. *Journal of Epidemiology and Community Health*. **2004** Oct;58(10):870-6

Grunberg L, Moore SY, Greenberg E: Differences in psychological and physical health among layoff survivors: the effect of layoff contact. *Journal of Occupational Health Psychology*. **2001** Jan;6(1):15-25

Hannan DF, ORiain S, Whelan CT: Youth unemployment and psychological distress in the Republic of Ireland. *Journal of Adolescence*. **1997** Jun;20(3):307-20

Hechanova-Alampay R, Beehr TA: Empowerment, span of control, and safety performance in work teams after workforce reduction. *Journal of Occupational Health Psychology*. **2001** Oct; 6(4): 275-82

Idler EL, Benyamini Y: Self-rated health and mortality: a review of twenty-seven community studies. *Journal of Health and Social Behavior*. **1997** Mar;38(1):21-37. Review

de Jonge J, Bosma H, Peter R, Siegrist J: Job strain, effort-reward imbalance and employee well-being: a large-cale cross-sectional study. *Social Science and Medicine*. **2000** May;50(9):1317-27

Kivimaki M, Leino-Arjas P, Luukkonen R, Riihimaki H, Vahtera J, Kirjonen J:Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *British Medical Journal*. **2002** Oct 19;325(7369):857

Kivimaki M, Vahtera J, Virtanen M, Elovainio M, Pentti J, Ferrie JE: Temporary employment and risk of overall and cause-specific mortality. *American Journal of Epidemiology*. **2003** Oct 1;158(7):663-8

Kivimaki M, Head J, Ferrie JE, Shipley MJ, Vahtera J, Marmot MG: Sickness absence as a global measure of health: evidence from mortality in the Whitehall II prospective cohort study. *British Medical Journal*. **2003** Aug 16;327(7411):364

de Lange AH, Taris TW, Kompier MA, Houtman IL, Bongers PM: Effects of stable and changing demand-control histories on worker health. *Scandinavian Journal of Work, Environment & Health*. **2002** Apr;28(2):94-108

Leino-Arjas P, Liira J, Mutanen P, Malmivaara A, Matikainen E: Predictors and consequences of unemployment among construction workers: prospective cohort study. *British Medical Journal*. **1999** Sep 4;319(7210):600-5

Mansson NO, Rastam L: Self-rated health as a predictor of disability pension and death--a prospective study of middle-aged men. *Scandinavian Journal of Public Health*. **2001** Jun;29(2):151-8

Markham SE,McKee GH: Declining organisational size and increasing unemployment rates; Predicting employee absenteeism from within and between plant perspectives. *Academy of Management Journal*. **1991**;34:952-965

Miilunpalo S, Vuori I, Oja P, Pasanen M, Urponen H: Self-rated health status as a health measure: the predictive value of self-reported health status on the use of physician services and on mortality in the working-age population. *Journal of Clinical Epidemiology*. **1997** May;50(5):517-28

Niedhammer I, Tek ML, Starke D, Siegrist J: Effort-reward imbalance model and self-reported health: cross-sectional and prospective findings from the GAZEL cohort. *Social Science and Medicine*. **2004** Apr;58(8):1531-41

Petterson IL, Hertting A, Hagberg L, Theorell T: Are trends in work and health conditions interrelated? A study of Swedish hospital employees in the 1990s. *Journal of Occupational Health Psychology*. **2005** Apr;10(2):110-20

Probst TM: Layoffs and tradeoffs: production, quality, and safety demands under the threat of job loss. *Journal of Occupational Health Psychology*. **2002** Jul;7(3):211-20

Quine L: Workplace bullying in NHS community trust: staff questionnaire survey. *British Medical Journal*. **1999** Jan 23;318(7178):228-32

Reynolds JR: The effects of industrial employment conditions on job-related distress. **Journal of Health and Social Behavior**. *1997* Jun;38(2):105-16

Schrijvers CT, van de Mheen HD, Stronks K, Mackenbach JP: Socioeconomic inequalities in health in the working population: the contribution of working conditions. *International Journal of Epidemiology*. **1998** Dec;27(6):1011-8

D'Souza RM, Strazdins L, Lim LL, Broom DH, Rodgers B: Work and health in a contemporary society: demands, control, and insecurity. *Journal of Epidemiology and Community Health*. **2003** Nov;57(11):849-54

Sverke M, Hellgren J, Naswall K: No security: a meta-analysis and review of job insecurity and its consequences. *Journal of Occupational Health Psychology*. **2002** Jul;7(3):242-64

Strazdins L, D'Souza RM, Lim LL, Broom DH, Rodgers B: Job strain, job insecurity, and health: rethinking the relationship. *Journal of Occupational Health Psychology*. **2004** Oct;9(4):296-305

Sundquist J, Johansson SE: Self reported poor health and low educational level predictors for mortality: a population based follow up study of 39,156 people in Sweden. *Journal of Epidemiology and Community Health*. **1997** Feb;51(1):35-40

Vahtera J, Pentti J, Kivimaki M: Sickness absence as a predictor of mortality among male and female employees. *Journal of Epidemiology and Community Health*. **2004** Apr;58(4):321-6

Vaananen A, Toppinen-Tanner S, Kalimo R, Mutanen P, Vahtera J, Peiro JM: Job characteristics, physical and psychological symptoms, and social support as antecedents of sickness absence among men and women in the private industrial sector. *Social Science and Medicine*. **2003** Sep;57(5):807-24

Vartia MA: Consequences of workplace bullying with respect to the well-being of its targets and the observers of bullying. *Scandinavian Journal of Work, Environment & Health*. **2001** Feb;27(1):63-9

Virtanen M, Kivimaki M, Elovainio M, Vahtera J, Ferrie JE: From insecure to secure employment: changes in work, health, health related behaviours, and sickness absence. *Occupational and Environmental Medicine*. **2003** Dec;60(12):948-53

Virtanen M, Kivimaki M, Elovainio M, Vahtera J: Selection from fixed term to permanent employment: prospective study on health, job satisfaction, and behavioural risks. *Journal of Epidemiology and Community Health*. **2002** Sep;56(9):693-9

Virtanen P, Vahtera J, Kivimaki M, Pentti J, Ferrie J: Employment security and health. *Journal of Epidemiology and Community Health*. **2002** Aug;56(8):569-74

Wallerstein N: Powerlessness, empowerment, and health: implications for health promotion programs. *American Journal of Health Promotion*. **1992** Jan-Feb;6(3):197-205. Review

9 Specific Outcomes

9.1 Neoplasm

There is clear evidence for some cancers to be related to occupational exposures, like lung-cancer in British radiologists (Doll 2005) or the adenocarcinoma of the ethmoid sinus (Bimbi G et al. 2004) in wood and leather workers, to name only two. However, despite an extensive literature, a lot of controversy remains, e.g. about the relationship between asbestos exposure and lung cancer, as the effect of mediating or confounding factors like cigarette smoking is not fully understood (see Henderson et al. 2004). Like in many rare diseases, a clear causal association for occupational exposures and neoplasm is difficult to show.

At first sight, it seems to be counterintuitive, that unemployment with its lack of industrial exposure should be a risk factor for cancer. If there is a relationship, it would have to be due to changes in risk behaviour – such as smoking, alcohol consumption, low intake of fruits and vegetables or lack of physical activity. However, Morris et al. (1994) could show in a multiple regression analysis, that mortality for cancer was still elevated, even after controlling for age, town, social class, smoking, alcohol intake, and pre-existing disease at initial screening (see also Voss et al. 2004, or Lynge 1997) . No publication could be identified that explicitly designed a study in order to address risk behaviour due to unemployment.

There are several hypotheses on the aetiopathologic association between stress and cancer. Most prominent are mechanisms of stress-induced alterations through oxidative stress and DNA damage (Cholst 1996), through corticotropin-releasing hormone (CRH) and the proopiomelanocortin (POMC) gene (Licinio 1995), or the serotonin-or-melatonin-hypothesis (Panzer 1998).

To test the hypothesis that stressful psychosocial working conditions are involved in the aetiology of cancers such as oesophageal and gastric cardia adenocarcinoma, Jansson et alii (2004) performed a nationwide population based case-control study in Sweden, but came to the conclusion that work-related stress does not seem to be of importance in the aetiology of those cancer types.

Cervical carcinoma and breast cancer are among the most prevalent malign neoplasms in women. In prospective cohort studies, no evidence of an association between self-perceived daily stress or job stress and breast cancer risk was found (Achat et al. 2000, Lillberg et al. 2001, Schernhammer et al. 2004). Besides, no support was found for an influence of negatively rated life events, social support, or distress on grade of CIN (cervical intra-

epithelial neoplasia), which is regarded as a precursor of cervical carcinoma (Tiersma et al. 2004).

A Dutch study group examined the relationship between job demands, control, support, job strain and iso-strain (defined as high job strain combined with social isolation at work) and the risk of cancer, but found not support for an association (van Loon et al. 2000). A 1999 review on major avoidable risk factors of cancer concluded that the attributable risk of occupation is negligible (Tominaga 1999).

However, despite those negative findings, it is plausible that job loss (and therefore: financial strain) could restrict access to health services and therefore to a delay in the detection of early stage cancers. Catalano and Satariano from Berkeley (2002) tested the hypothesis that unexpectedly high unemployment in a community is associated with reduced odds that registered breast tumors are local. Their findings confirmed their hypothesis. They concluded further that fear of job loss may distract women from breast self examination and the identification of suspicious breast signs.

Similar results can be demonstrated in publications that link income measures to cancer morbidity. A huge cross sectional study from New York on 37921 cases of breast cancer confirmed socioeconomic differences in the risk of advanced-stage breast cancer (Merkin et al. 2002, see also Macleod et al. 2000). The likelihood of receiving screening on breast cancer is also positively related to income (Katz et al. 2000). A population based study from Michigan among 3656 women showed that lower income was associated with advanced-stage disease, lower likelihood of receiving hysterectomy, and lower rates of survival (Madison et al. 2004). The same was true for receiving surgery on non-small cell lung cancer in Detroit, San Francisco, and Seattle (Greenwald et al. 1998).

However, there is data from Sweden, a 24-year prospective study on 1462 Swedish Women, showing a somewhat lower risk for cancer of all sites (RR=0.86, 95%CI=0.66-1.11) in women with low socioeconomic status (Cabrera et al.). The confidence interval might reflect the well known paradox for higher incidence of breast cancer in high SES women.

Achat H, Kawachi I, Byrne C, Hankinson S, Colditz G: A prospective study of job strain and risk of breast cancer. *International Journal of Epidemiology*. **2000** Aug;29(4):622-8

Bimbi G, Saraceno MS, Riccio S et al.: Adenocarcinoma of ethmoid sinus: an occupational disease. *Acta Otorhinolaryngolica Italica*. **2004** Aug;24(4):199-20

Cabrera C, Helgesson O, Wedel H, Bjorkelund C, Bengtsson C, Lissner L: Socioeconomic status and mortality in Swedish women: opposing trends for cardiovascular disease and cancer. *Epidemiology*. **2001** Sep;12(5):532-6.

Cholst S: Cancer and stress. *Medical Hypotheses*. **1996** Feb;46(2):101-6

Catalano RA, Satariano WA: Unemployment and the likelihood of etecting early-stage breast cancer. *American Journal of Public Health*. **1998** Apr;88(4):586-9

Doll R: Mortality of British radiologists: a lecture note. *Journal of Radiation Research* (Tokyo**). 2005** Mar;46(1):123-9.

Greenwald HP, Polissar NL, Borgatta EF, McCorkle R, Goodman G: Social factors, treatment, and survival in early-stage non-small cell lung cancer. *American Journal of Public Health*. **1998** Nov;88(11):1681-4

Henderson DW, Rodelsperger K, Woitowitz HJ et al.: After Helsinki: a multidisciplinary review of the relationship between asbestos exposure and lung cancer, with emphasis on studies published during 1997-2004. *Pathology*. **2004** Dec;36(6):517-50

Jansson C, Johansson AL, Jeding K et al.: Psychosocial working conditions and the risk of oesophageal and gastric cardia cancers. *European Journal of Epidemiology*. **2004**;19(7):631-41

Katz SJ, Zemencuk JK, Hofer TP: Breast cancer screening in the United States and Canada, 1994: socioeconomic gradients persist. *American Journal of Public Health*. **2000** May;90(5):799-803

Licinio J, Gold PW, Wong ML: A molecular mechanism for stress-induced alterations in susceptibility to disease. *Lancet*. **1995** Jul 8;346(8967):104-6

Lillberg K, Verkasalo PK, Kaprio J, Teppo L, Helenius H, Koskenvuo M: Stress of daily activities and risk of breast cancer: a prospective cohort study in Finland. *International Journal of Cancer*. **2001** Mar 15;91(6):888-9

van Loon AJ, Tijhuis M, Surtees PG, Ormel J: Lifestyle risk factors for cancer: the relationship with psychosocial work environment. *International Journal of Epidemiology***. 2000** Oct;29(5):785-92

Lynge E: Unemployment and cancer: a literature review. *IARC Scientific Publications*. **1997**;(138):343-51. Review

Macleod U, Ross S, Gillis C, McConnachie A, Twelves C, Watt GC: Socio-economic deprivation and stage of disease at presentation in women with breast cancer. *Annals of Oncology*. **2000** Jan;11(1):105-7

Madison T, Schottenfeld D, James SA, Schwartz AG, Gruber SB: Endometrial cancer: socioeconomic status and racial/ethnic differences in stage at diagnosis, treatment, and survival. *American Journal of Public Health*. **2004** Dec;94(12):2104-11

Merkin SS, Stevenson L, Powe N: Geographic socioeconomic status, race, and advanced-stage breast cancer in New York City. *American Journal of Public Health*. **2002** Jan;92(1):64-70

Morris JK, Cook DG, Shaper AG: Loss of employment and mortality. *British Medical Journal*. **1994** Apr 30;308(6937):1135-9

Panzer A.: Depression or cancer: the choice between serotonin or melatonin? *Medical Hypotheses*. **1998** May;50(5):385-7

Schernhammer ES, Hankinson SE, Rosner B, Kroenke CH, Willett WC, Colditz GA, Kawachi I: Job stress and breast cancer risk: the nurses' health study. American *Journal of Epidemiology*. **2004** Dec 1;160(11):1079-86

Tiersma ES, van der Lee ML, Peters AA et al.: Psychosocial factors and the grade of cervical intra-epithelial neoplasia. *Gynecologic Oncology*. **2004** Feb;92(2):603-10

Tominaga S: Major avoidable risk factors of cancer. *Cancer Letters*. **1999** Sep;143 Suppl 1:S19-23

Voss M, Nylen L, Floderus B, Diderichsen F, Terry PD: Unemployment and early cause-specific mortality: a study based on the Swedish twin registry. *American Journal of Public Health*. *2004* Dec;94(12):2155-61

9.2 Chronic Obstructive Pulmonary Disease

No publication within the time span could be identified to examine income as a risk factor or predictor for chronic obstructive pulmonary (or lung) disease (COPD) morbidity or mortality.

Instead, the selection criteria had to be broadened to include asthma as a highly prevalent disease.

There is overwhelming evidence, that income is strongly and negatively related to asthma prevalence (Chen et al. 1999, Claudio et al. 1999), especially in older people (Erzen et al. 1997) and children (Akinbami et al. 2002), or asthma mortality (Grant et al. 2000).

Income was also related to non-occupational exposures like dust mite levels or cockroach allergen levels (Kitch et al. 2000).

In one study, the relation between low income and asthma prevalence in children vanished after adjusting for passive smoking (Dales et al. 2002), but remained after adjusting for “race” (Smith et al. 2005).

One study could be found that focused on costs of occupational COPD and asthma. Relating to mortality, it was calculated from US data that the population attributable risk (PAR) for both asthma and COPD was 15%, resulting in costs of 5.0 billion US$ for COPD and 1.6 billion US$ for asthma (Leigh et al. 2002).

The biological plausibility regarding the capacity of occupational exposures to irritating dusts, gases, and fumes to cause COPD is high. Epidemiological evidence from both worker cohort and community studies supports an increased risk of COPD associated with such exposures (Balmes 2005). Like in cancer, those exposures are absent in unemployment. However, like in cancer, it is plausible to believe that loss of employment or economic recession and therefore rising rates of unemployment could lead a rise in behavioural exposures such as cigarette smoking.

Unfortunately, no publication could be identified that could strengthen or disprove that hypothesis. Two studies could be identified that support the opposite direction: people with COPD face a higher risk of job loss and work disability, or a reduced chance of being (re)employed (Eisner et al. 2002, Hnizdo et al. 2002).

However, on a molecular biological level, there is broad evidence that stress (thus including job stress) changes basic immune functions by inducing shifts in cytokine response, decreasing natural killer (NK) cell cytotoxicity, and inducing Th1/Th2 imbalance (T-helper lymphocytes type 1 and 2 resemble two pathways in the development of the immune system), or more specifically, to a selective up-regulation of Th2 cytokines during stressful exposure. Predominant Th2 profiles are associated, among others, with the worsening of asthma (Marshall 2000, Kang 2001). Both mentioned studies were not designed to test the influence of stress on chronic conditions.

Akinbami LJ, LaFleur BJ, Schoendorf KC: Racial and income disparities in childhood asthma in the United States. *Ambulatory Pediatrics*. **2002** Sep-Oct;2(5):382-7

Balmes JR: Occupational contribution to the burden of chronic obstructive pulmonary disease. *Journal of Occupational and Environmental Medicine*. **2005** Feb;47(2):154-60

Chen Y, Dales R, Krewski D, Breithaupt K: Increased effects of smoking and obesity on asthma among female Canadians: the National Population Health Survey, 1994-1995. *American Journal of Epidemiology*. **1999** Aug 1;150(3):255-62

Claudio L, Tulton L, Doucette J, Landrigan PJ: Socioeconomic factors and asthma hospitalization rates in New York City. *Journal of Asthma*. **1999** Jun;36(4):343-50

Dales RE, Choi B, Chen Y, Tang M: Influence of family income on hospital visits for asthma among Canadian school children. *Thorax*. **2002** Jun;57(6):513-7

Eisner MD, Yelin EH, Trupin L, Blanc PD: The influence of chronic respiratory conditions on health status and work disability. *American Journal of Public Health*. **2002** Sep;92(9):1506-13

Erzen D, Carriere KC, Dik N, Mustard C, Roos LL, Manfreda J, Anthonisen NR: Income level and asthma prevalence and care patterns. *American Journal of Respiratory and Critical Care Medicine*. **1997** Mar;155(3):1060-5

Grant EN, Lyttle CS, Weiss KB: The relation of socioeconomic factors and racial/ethnic differences in US asthma mortality. *American Journal of Public Health*. **2000** Dec;90(12):1923-5

Hnizdo E, Sullivan PA, Bang KM, Wagner G: Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study of data from the Third National Health and Nutrition Examination Survey. *American Journal of Epidemiology*. **2002** Oct 15;156(8):738-46

Kitch BT, Chew G, Burge HA, Muilenberg ML, Weiss ST, Platts-Mills TA, O'Connor G, Gold DR: Socioeconomic predictors of high allergen levels in homes in the greater Boston area. *Environmental Health Perspectives*. **2000** Apr;108(4):301-7

Leigh JP, Romano PS, Schenker MB, Kreiss K: Costs of occupational COPD and asthma. *Chest*. **2002** Jan;121(1):264-72

Smith LA, Hatcher-Ross JL, Wertheimer R, Kahn RS: Rethinking race/ethnicity, income, and childhood asthma: racial/ethnic disparities concentrated among the very poor. *Public Health Reports*. **2005** Mar-Apr;120(2):109-16

9.3 Wounds and Injuries

The most interesting finding stems from a study on injury and employment patterns among Hispanic construction workers (Anderson et al. 2000). According to this study, Hispanics – compared with other injured workers – had a higher proportion of serious injuries and were disadvantaged in terms of training and union status. With the exception of union status, these differences largely disappeared after controlling for trade. As argued above, union membership seems to be crucial in achieving better health.

Surprisingly, the cliché that “most injuries happen right at home” was confirmed by a Swedish study (Lindquist K et al. 2004), which – in a quasi-experimental design – investigated rates of injuries treated in health-care among members of households at different levels of labour market integration before and after implementation of a WHO Safe Community programme.

Apart from lacking effect of this programme on male members of households classified as not vocationally active, this group also displayed the highest pre-intervention injury rates. A US-American cohort study (Cinat 2004) found that the proportion of violent crime in a community is closely associated with the unemployment rate of that community.

The largest prospective study regarding the association between job satisfaction or job stress and injuries is from the Netherlands (within the Maastricht Cohort Study). While the influence of decision latitude disappeared after adjustment of confounders, several psychosocial work characteristics remained significant: High emotional demands, conflicts with the supervisor, and conflicts with colleagues showed relative risks of 2.45, 2.49, and 2.62, respectively. A weaker association (RR=1.48) could be shown for job satisfaction (Swaen 2004). These results are partly supported by previous publications on work-related upper-extremity disorders, which have a higher chance of resulting in prolonged work-disability in a climate of employer-employee conflicts (Himmelstein 1995), heightened ergonomic stress level (Melamed 1999), heightened job stress (Haufler 2000), or lower job satisfaction (Pransky 2002).

Other publications strengthen the meaning of perception of job insecurity on workplace injuries and accidents as well as the moderating effect of organizational safety climate (Probst 2004, Probst and Brubaker 2001, Probst 2000).

Anderson JT, Hunting KL, Welch LS: Injury and employment patterns among Hispanic construction workers. *Journal of Occupational and Environmental Medicine*. **2000** Feb;42(2):176-86

Cinat ME, Wilson SE, Lush S, Atkins C: Significant correlation of trauma epidemiology with the economic conditions of a community. *Archives of Surgery*. **2004** Dec;139(12):1350-5

Haufler AJ, Feuerstein M, Huang GD: Job stress, upper extremity pain and functional limitations in symptomatic computer users. *American Journal of Industrial Medicine*. **2000** Nov;38(5):507-15

Himmelstein JS, Feuerstein M, Stanek EJ 3rd, Koyamatsu K, Pransky GS, Morgan W, Anderson KO: Work-related upper-extremity disorders and work disability: clinical and psychosocial presentation. *Journal of Occupational and Environmental Medicine*. **1995** Nov;37(11):1278-86

Lindqvist K, Timpka T, Karlsson N: Impact of social standing on injury prevention in a World Health Organization Safe Community-intervention outcome by household employment contract. *International Journal of Epidemiology*. **2004** Jun;33(3):605-11

Melamed S, Yekutieli D, Froom P, Kristal-Boneh E, Ribak J: Adverse work and environmental conditions predict occupational injuries. The Israeli Cardiovascular Occupational Risk Factors Determination in Israel (CORDIS) Study. *American Journal of Epidemiology*. **1999** Jul 1;150(1):18-26

Pransky G, Benjamin K, Hill-Fotouhi C, Fletcher KE, Himmelstein J: Occupational upper extremity conditions: a detailed analysis of work-related outcomes. *Journal of Occupational Rehabilitation*. **2002** Sep;12(3):131-8

Probst TM: Wedded to the job: moderating effects of job involvement on the consequences of job insecurity. *Journal of Occupational Health Psychology*. **2000** Jan; 5(1):63-73

Probst TM, Brubaker TL: The effects of job insecurity on employee safety outcomes: cross-sectional and longitudinal explorations. *Journal of Occupational Health Psychology*. **2001** Apr;6(2):139-59

Probst TM: Safety and insecurity: exploring the moderating effect of organizational safety climate. *Journal of Occupational Health Psychology*. **2004** Jan;9(1):3-10

Swaen GM, van Amelsvoort LP, Bultmann U, Slangen JJ, Kant IJ: Psychosocial work characteristics as risk factors for being injured in an occupational accident. *Journal of Occupational and Environmental Medicine*. **2004** Jun;46(6):521-7

9.4 Diabetes (type II, or NIDDM)

The risk of type II or non-insulin dependent diabetes mellitus (NIDDM) is clearly not associated with material occupational exposures. To ascertain the effects of psychosocial job conditions on the occurrence of NIDDM in Japan, Kawamaki et al. (1999) performed an eight year prospective cohort study. Although they failed to demonstrate a statistically significant association of job strain (as defined in the job strain model) with NIDDM, diabetes was significantly higher in those who worked overtime more than 50 hours per month as well as in those who worked with new technology. A dose-response-relation was observed between overtime and the risk of NIDDM. The authors argue that long overtime causes sustained higher levels of catecholamines and therefore increased blood glucose concentrations and increased insulin resistance or, alternatively, that dietary change, such as overeating after a long interval between meals, or disturbances in glucose metabolism because of long overtime may be common underlying mechanisms of increased risk of NIDDM. These findings are supported by immunological research, showing that interleukin 6 (IL-6) and the acute phase protein “C-reactive protein” (CRP), are strongly associated with, and likely play a dominant role in, the development of an inflammatory process which leads to insulin resistance, non-insulin dependant diabetes mellitus type II, and Metabolic syndrome X (Black 2003). A review on the same subject, eight years before that, already found evidence that psychological stress produces deterioration in glycaemia in the non-symptomatic patient, which in turn makes diabetic symptoms and the diagnosis evident (Wales 1995).

However, no publication could be identified that would link unemployment or risk of unemployment to higher rates of diabetes. Yet it could be argued, as unemployment leads to higher rates of depression (Khlat et al. 2004), that through overweight there might also be an increased risk of diabetes. However, after adjustment for potential confounders, a significant association between unemployment and obesity could not be found.

Black PH: The inflammatory response is an integral part of the stress response: Implications for atherosclerosis, insulin resistance, type II diabetes and metabolic syndrome X. *Brain, Behavior, and Immunity*. **2003** Oct;17(5):350-64

Kawakami N, Araki S, Takatsuka N, Shimizu H, Ishibashi H: Overtime, psychosocial working conditions, and occurrence of non-insulin dependent diabetes mellitus in Japanese men. *Journal of Epidemiology and Community Health*. **1999** Jun;53(6):359-63

Khlat M, Sermet C, Le Pape A: Increased prevalence of depression, smoking, heavy drinking and use of psycho-active drugs among unemployed men in France. *European Journal of Epidemiology*. **2004**;19(5):445-51

Wales JK: Does psychological stress cause diabetes? *Diabetic Medicine*. **1995** Feb;12(2):109-12

9.5 Infant Mortality

Infant mortality is an established and easy-to-measure indicator of community health. In their matched case-control study, Lumey et al. (1995) could show that for an ethnically mixed population in The Netherlands, perinatal mortality was independently associated with the father's and mother's employment status, rather than with the father's or mother's country of birth.

In Poland, where the national economy undergoes a process of transformation and the unemployment rate is high, Hanke et al. (2001) observed an excess risk of preterm delivery for unemployed women. Although modestly, in a US-American case-control study, preterm delivery was also associated with high job strain (Brett et al. 1997).

The relation of work-related psychological stress to spontaneous abortion was examined in a prospective study of 3,953 pregnant, employed women in California: Results from the multivariate model indicated that, overall, stressful work was not associated with an increased risk of spontaneous abortion (Fenster 1995).

No literature could be found regarding an association between job satisfaction or job stress and infant mortality.

The main influence on infant mortality, however, is income – and only partly through more healthcare spending: Hales et al. (1999) examined the relation between infant mortality rates, gross national product, and income distribution. This re-assessment study with data from 38 countries demonstrated that infant mortality was negatively associated with GDP per capita, and positively associated with income inequality. Macinko et al. (2004) examined the relationship between wage inequality and infant mortality in 19 OECD countries with pooled data in a cross-sectional and time-series analysis. They found a significant and positive relationship, even while controlling for GDP per capita.

A recently published study that compared infant mortality rates across neighbourhoods of four world cities, concluded that in stark contrast to Tokyo, Paris, and London, the

association of average income and infant mortality rate was strongly evident in Manhattan (Rodwin et al. 2005).

A study from Spain showed that the falling rates of infant mortality (including neonatal, postneonatal, and perinatal mortality) were related to rising income on the aggregate level between 1981 and 1991, but that at any given point of time, the cluster of low income Spanish Autonomous Communities (AC) had higher infant mortality rates than the high income cluster of AC (Dominguez-Berjon et al. 1999).

US data from 1985-91 also showed that the increase in economic segregation increased infant deaths more than the increase in health care spending reduces them, so the net effect of income inequality was positively related to infant mortality, especially perinatal mortality (Mayer and Sarin 2005).

Furthermore, but for developing countries, Filmer and Pritchet (1999) have demonstrated how female education strongly and significantly contributes to explain the variance in infant mortality rates.

Brett KM, Strogatz DS, Savitz DA: Employment, job strain, and preterm delivery among women in North Carolina. *American Journal of Public Health*. **1997** Feb;87(2):199-204

Dominguez-Berjon MF, Benach J, Garcia-Arcal MD, Borrell C: Infant and perinatal mortality in Spain 1981-1991: interprovincial variations in Autonomous communities with extreme economic levels. *European Journal of Epidemiology*. **1999** Sep;15(8):723-9

Fenster L, Schaefer C, Mathur A, Hiatt RA, Pieper C, Hubbard AE, Von Behren J, Swan SH: Psychologic stress in the workplace and spontaneous abortion. *American Journal of Epidemiology*. **1995** Dec 1;142(11):1176-83

Filmer D, Pritchett L: The impact of public spending on health: does money matter? *Social Science and Medicine*. **1999** Nov;49(10):1309-23. Erratum in: *Social Science and Medicine* 2000 May;50(10):1517-8

Hales S, Howden-Chapman P, Salmond C, Woodward A, Mackenbach J: National infant mortality rates in relation to gross national product and distribution of income. *Lancet*. **1999** Dec 11;354(9195):2047

Hanke W, Saurel-Cubizolles MJ, Sobala W, Kalinka J: Employment status of pregnant women in central Poland and the risk of preterm delivery and small-for-gestational-age infants. *European Journal of Public Health*. **2001** Mar;11(1):23-8

Lumey LH, Reijneveld SA: Perinatal mortality in a first generation immigrant population and its relation to unemployment in The Netherlands. *Journal of Epidemiology and Community Health*. **1995**; 49(5): 454-459

Macinko JA, Shi L, Starfield B: Wage inequality, the health system, and infant mortality in wealthy industrialized countries, 1970-1996. *Social Science and Medicine*. **2004** Jan;58(2):279-92

Mayer SE, Sarin A: Some mechanisms linking economic inequality and infant mortality. *Social Science and Medicine*. **2005** Feb;60(3):439-55

Rodwin VG, Neuberg LG: Infant mortality and income in 4 world cities: New York, London, Paris, and Tokyo. *American Journal of Public Health*. **2005** Jan;95(1):86-90

9.6 Cardiovascular Diseases (CVD)

The main investigator of this project has already demonstrated how national economic indicators influence changes in cardiovascular disease mortality rates. More specifically, these indicators included real per capita income and social welfare expenditures, unemployment rates and business failure rates (Brenner 1997). In this study, using time-series regression and looking at Western Germany between 1951 and 1989, increased unemployment was positively, and increased income and social welfare expenditures were negatively related to heart disease mortality.

The literature offers substantial support for these findings (Ferrie et al. 2005, Alter et al. 2004, Rutledge et al. 2003, Bucher et al. 1995), but several ideas exist, how this association works: Some argue that this effect can mostly be explained through known behavioural risk factors like smoking or obesity, through known social or psychological risk factors or through a differential in healthcare access or healthcare usage. Even on a very biological level, a negative association between carotid wall thickness and income could be demonstrated (Diez-Roux et al. 1995).

However, one has to be careful when reading about “adjusted for known risk factors”, as there is no clear definition of what is included. Especially psychological and social risk factors are often not included as “known risk factors” and appear separately.

There is evidence from Finland, that all these risk factors work together and mostly depend on income (Lynch 1996), and that even the negative effects of workplace conditions like employment status and workplace social support on mortality and myocardial infarction risk depend on income levels (Lynch 1997).

Only recently, it could be demonstrated that the relation between income and CVD mortality (or more specifically: on the risk of ischemic heart disease) is the same for men and women (Andersen et al. 2003).

Apart from individual income levels, the mezzo level is also of importance: In a huge Canadian cohort study ($n \cong 50.000$), increases in neighbourhood median income were strongly associated with decreases in mortality, and increases in coronary angiography usage rates (after adjustment for individual income: Alter et al. 1999, Sundquist et al. 2004a, 2004b). However, a study from Denmark followed ~20.000 Danish men and women from 1964 through 1992, and failed to show a significant association between income inequality at the municipality level and ischemic heart disease, after controlling for individual income (Osler et al. 2003).

Regarding effects of unemployment, there are recently published findings from Whitehall II data (UK), which imply that job insecurity – not in itself, but through effects of financial insecurity – plays an important role in determining inequalities in health (Ferrie et al. 2003). Previous analysis of the data had given evidence that job insecurity (threat of unemployment) has significant effects on increases in body mass index, cholesterol concentration, blood pressure, and ischemia, even though over the same period health-related behaviours had changed only little.

Conflicting findings in the literature have made the relation between work conditions and cardiovascular diseases controversial.

An extensive review on this subject has been published by Theorell and Karasek (1996).

Many studies have suggested that occupational stress may be related to the development of CVD, independently of other known risk factors. For example, in a large case-control study from Sweden, both inferred and self-reported low decision latitude were associated with increased risk of a first myocardial infarction, although this association was weakened after adjustment for social class (Theorell et al. 1998). Another case-control study by Netterstrom et alii 1999 had a comparable result, and an extensive review by Belkic et alii 2004 largely approves this finding.

There are very few studies using longitudinal data for assessing the effect of job satisfaction on cardiovascular risk factors and events: In their cohort of Scottish workers, Heslop et al. (2002) found no evidence to suggest that persons reporting job dissatisfaction had a significant greater risk of mortality from CVD. The same was shown to be true for a pure female cohort by Lee et al. (2002). Furthermore, in a large occupational cohort from Belgium, job demands and decision latitude were not significantly related to the development of coronary heart disease after adjustment for covariates. However, coronary heart disease incidence was substantially associated with social support (see section below) independently of other risk factors, with an adjusted hazard ratio of 2.4 (de Bacquer 2005).

Using data from the Whitehall II study, it could be shown that the largest contribution to the socioeconomic gradient in coronary heart disease frequency was from low job control, a component of Karasek's job strain model (Bosma et al. 1997, Marmot et al. 1997, Bishop 2003, Malinauskiene 2004); or that low job control as well as an effort-reward-imbalance showed independent effects on coronary heart disease (Bosma et al., 1998a and 1998b); or that people with concurrent job strain (high demand, low decision latitude) were at the highest risk for coronary heart disease (Kuper et al. 2003). In a cohort study on cardiovascular mortality in general, Kivimaki et al. (2002) could demonstrate that high job

strain and effort-reward imbalance can both increase the risk of cardiovascular mortality. Comparable results were published by Hallqvist et al. (1998) and Peter et al. (2002). Data from the Czech Republic point into the same direction, looking at the association between decision latitude and nonfatal myocardial infarction (Bobak et al. 1998).

These findings are indirectly supported by a longitudinal study on women from Pennsylvania, investigating the relation between employment and cholesterol: Those who were employed had the lowest high density lipoprotein cholesterol, which serves as a protective factor for atherosclerosis, and hence, cardiovascular events (Ickovics et al. 1996). This idea is partly supported by a study from Sweden: although their findings did not support the hypothesis that job strain has an adverse impact on total cholesterol and plasma fibrinogen levels, the authors suggest that an increased risk of coronary heart disease in association with job strain, if causal, is mediated by other factors like hypertension or low levels of high-density lipoprotein cholesterol (Alfredson 2002). As for fibrinogen, a Japanese research group found that workplace characteristics are not significantly related to the plasma levels in Japanese employees (Ishizaki 2001). In contrast, an occupational French cohort resulted in significant associations between psychosocial work factors (psychological demands, decision latitude, social support) and cardiovascular risk factors such as hypertension, hyperlipidaemia, overweight and smoking (Niedhammer et al. 1998). In a cohort from Eastern Finland, men who showed stress induced blood pressure reactivity and who reported high job demands experienced the greatest atherosclerotic progression (Everson 1997). However, in another big study on Japanese rural workers, job demands had an effect on serum lipid levels, but not job strain (Tsutsumi 2003).

In a US-based cross-sectional analysis, Hellerstedt et al. (1997) found job demands to be positively associated with smoking, smoking intensity, and high fat intake in men and with body mass index and smoking intensity in women. High-strain men smokers smoked more than other male workers and high-strain women had higher body mass indices than other female workers, but not vice versa, which could be a hint for a gender specific coping strategy.

Greenlund et al. (1995), in another US-based cross-sectional analysis, found only few associations supporting the hypothesis that job strain is related to increased levels of CVD risk factors. The effect of high job strain and coronary heart disease was also examined in men and women participating in the Framingham Offspring Study (Eaker et al. 2004). The findings did not support high job strain as a significant risk factor (see also Alterman et al. 1994). Hlatky et al. (1995) analysed patients undergoing diagnostic coronary angiography but also found no significant correlation with job strain.

Alfredsson L, Hammar N, Fransson E, de Faire U, Hallqvist J, Knutsson A, Nilsson T, Theorell T, Westerholm P: Job strain and major risk factors for coronary heart disease among employed males and females in a Swedish study on work, lipids and fibrinogen. *Scandinavian Journal of Work, Environment & Health*. **2002** Aug;28(4):238-48

Alter DA, Iron K, Austin PC, Naylor CD; SESAMI Study Group: Influence of education and income on atherogenic risk factor profiles among patients hospitalized with acute myocardial infarction. *Canadian Journal of Cardiology*. **2004** Oct;20(12):1219-28

Alter DA, Naylor CD, Austin P, Tu JV: Effects of socioeconomic status on access to invasive cardiac procedures and on mortality after acute myocardial infarction. *New England Journal of Medicine*. **1999** Oct 28;341(18):1359-67

Alterman T, Shekelle RB, Vernon SW, Burau KD: Decision latitude, psychologic demand, job strain, and coronary heart disease in the Western Electric Study. *American Journal of Epidemiology*. **1994** Mar 15;139(6):620-7

Andersen I, Osler M, Petersen L, Gronbaek M, Prescott E: Income and risk of ischaemic heart disease in men and women in a Nordic welfare country. *International Journal of Epidemiology*. **2003** Jun;32(3):367-74

De Bacquer D, Pelfrene E, Clays E, Mak R, Moreau M, de Smet P, Kornitzer M, De Backer G: Perceived job stress and incidence of coronary events: 3-year follow-up of the Belgian Job Stress Project cohort. *American Journal of Epidemiology*. **2005** Mar 1;161(5):434-41

Belkic KL, Landsbergis PA, Schnall PL, Baker D: Is job strain a major source of cardiovascular disease risk? *Scandinavian Journal of Work, Environment & Health*. **2004** Apr;30(2):85-128. Review

Bishop GD, Enkelmann HC, Tong EM, Why YP, Diong SM, Ang J, Khader M: Job demands, decisional control, and cardiovascular responses. *Journal of Occupational Health Psychology*. **2003** Apr;8(2):146-56

Bobak M, Hertzman C, Skodova Z, Marmot M: Association between psychosocial factors at work and nonfatal myocardial infarction in a population-based case-control study in Czech men. *Epidemiology*. **1998** Jan;9(1):43-7

Bosma H, Marmot MG, Hemingway H, Nicholson AC, Brunner E, Stansfeld SA: Low job control and risk of coronary heart disease in Whitehall II (prospective cohort) study. *British Medical Journal*. **1997** Feb 22;314(7080):558-65

Bosma H, Stansfeld SA, Marmot MG: Job control, personal characteristics, and heart disease. *Journal of Occupational Health Psychology*. **1998** Oct;3(4):402-9

Bosma H, Peter R, Siegrist J, Marmot M: Two alternative job stress models and the risk of coronary heart disease. *American Journal of Public Health*. **1998** Jan;88(1):68-74

Brenner MH: Heart disease mortality and economic changes; including unemployment; in Western Germany 1951-1989. *Acta Physiologica Scandinavica* Suppl. **1997**;640:149-52

Bucher HC, Ragland DR: Socioeconomic indicators and mortality from coronary heart disease and cancer: a 22-year follow-up of middle-aged men. *American Journal of Public Health*. **1995** Sep;85(9):1231-6

Diez-Roux AV, Nieto FJ, Tyroler HA, Crum LD, Szklo M: Social inequalities and atherosclerosis. The atherosclerosis risk in communities study. *American Journal of Epidemiology*. **1995** May 15;141(10):960-72

Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB Sr, Benjamin EJ: Does job strain increase the risk for coronary heart disease or death in men and women? The Framingham Offspring Study. *American Journal of Epidemiology*. **2004** May 15;159(10):950-8

Everson SA, Lynch JW, Chesney MA, Kaplan GA, Goldberg DE, Shade SB, Cohen RD, Salonen R, Salonen JT: Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study. *British Medical Journal*. **1997** Feb 22;314(7080):553-8

Ferrie JE, Shipley MJ, Marmot MG, Stansfeld SA, Smith GD: An uncertain future: the health effects of threats to employment security in white-collar men and women. *American Journal of Public Health*. **1998** Jul;88(7):1030-6

Ferrie JE, Martikainen P, Shipley MJ, Marmot MG: Self-reported economic difficulties and coronary events in men: evidence from the Whitehall II study. *International Journal of Epidemiology.* **2005** Jun;34(3):640-8

Ferrie JE, Shipley MJ, Stansfeld SA, Smith GD, Marmot M: Future uncertainty and socioeconomic inequalities in health: the Whitehall II study. *Social Science and Medicine*. **2003** Aug;57(4):637-46

Greenlund KJ, Liu K, Knox S, McCreath H, Dyer AR, Gardin J: Psychosocial work characteristics and cardiovascular disease risk factors in young adults: the CARDIA study. Coronary Artery Risk Disease in Young Adults. *Social Science and Medicine*. **1995** Sep;41(5):717-23

Hallqvist J, Diderichsen F, Theorell T, Reuterwall C, Ahlbom A: Is the effect of job strain on myocardial infarction risk due to interaction between high psychological demands and low decision latitude? Results from Stockholm Heart Epidemiology Program (SHEEP). *Social Science and Medicine*. **1998** Jun;46(11):1405-15

Hellerstedt WL, Jeffery RW: The association of job strain and health behaviours in men and women. *International Journal of Epidemiology*. **1997** Jun;26(3): 575-83

Heslop P, Smith GD, Metcalfe C, Macleod J, Hart C: Change in job satisfaction, and its association with self-reported stress, cardiovascular risk factors and mortality. *Social Science and Medicine*. **2002** May;54(10):1589-99

Hlatky MA, Lam LC, Lee KL, Clapp-Channing NE, Williams RB, Pryor DB, Califf RM, Mark DB: Job strain and the prevalence and outcome of coronary artery disease. *Circulation*. **1995** Aug 1;92(3):327-33

Ickovics JR, Morrill AC, Meisler AW, Rodin J, Bromberger JT, Matthews KA: Employment and coronary risk in women at midlife: a longitudinal analysis. *American Journal of Epidemiology*. **1996** Jan 15;143(2):144-50

Ishizaki M, Martikainen P, Nakagawa H, Marmot M: Socioeconomic status, workplace characteristics and plasma fibrinogen level of Japanese male employees. *Scandinavian Journal of Work, Environment & Health*. 2001 Aug;27(4):287-91

Kivimaki M, Leino-Arjas P, Luukkonen R, Riihimaki H, Vahtera J, Kirjonen J: Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *British Medical Journal*. **2002** Oct 19;325(7369):857

Kuper H, Marmot M: Job strain, job demands, decision latitude, and risk of coronary heart disease within the Whitehall II study. *Journal of Epidemiology and Community Health*. **2003** Feb;57(2):147-53

Lee S, Colditz G, Berkman L, Kawachi I: A prospective study of job strain and coronary heart disease in US women. *International Journal of Epidemiology*. **2002** Dec;31(6):1147-53

Lynch J, Due P, Muntaner C, Smith GD: Social capital--is it a good investment strategy for public health? *Journal of Epidemiology and Community Health*. **2000** Jun;54(6):404-8

Lynch JW, Smith GD, Kaplan GA, House JS: Income inequality and mortality: importance to health of individual income, psychosocial environment, or material conditions. *British Medical Journal*. **2000** Apr 29;320(7243):1200-4. Review

Lynch J, Krause N, Kaplan GA, Tuomilehto J, Salonen JT: Workplace conditions, socioeconomic status, and the risk of mortality and acute myocardial infarction: the Kuopio Ischemic Heart Disease Risk Factor Study. *American Journal of Public Health*. **1997** Apr;87(4):617-22

Lynch JW, Kaplan GA, Cohen RD, Tuomilehto J, Salonen JT: Do cardiovascular risk factors explain the relation between socioeconomic status, risk of all-cause mortality, cardiovascular mortality, and acute myocardial infarction? *American Journal of Epidemiology*. **1996** Nov 15;144(10):934-42

Malinauskiene V, Theorell T, Grazuleviciene R, Malinauskas R, Azaraviciene A.: Low job control and myocardial infarction risk in the occupational categories of Kaunas men, Lithuania. *Journal of Epidemiology and Community Health*. **2004** Feb;58(2):131-5.

Marmot MG, Bosma H, Hemingway H, Brunner E, Stansfeld S: Contribution of job control and other risk factors to social variations in coronary heart disease incidence. *Lancet*. **1997** Jul 26;350(9073):235-9

Netterstrom B, Nielsen FE, Kristensen TS, Bach E, Moller L: Relation between job strain and myocardial infarction: a case-control study. *Occupational and Environmental Medicine*. **1999** May;56(5):339-42

Niedhammer I, Goldberg M, Leclerc A, David S, Bugel I, Landre MF: Psychosocial work environment and cardiovascular risk factors in an occupational cohort in France. *Journal of Epidemiology and Community Health*. **1998** Feb;52(2):93-100

Osler M, Christensen U, Due P, Lund R, Andersen I, Diderichsen F, Prescott E: Income inequality and ischaemic heart disease in Danish men and women. *International Journal of Epidemiology*. **2003** Jun;32(3):375-80

Peter R, Siegrist J, Hallqvist J, Reuterwall C, Theorell T; SHEEP Study Group: Psychosocial work environment and myocardial infarction: improving risk estimation by combining two complementary job stress models in the SHEEP Study. *Journal of Epidemiology and Community Health*. **2002** Apr;56(4):294-300

Rutledge T, Reis SE, Olson M, Owens J, Kelsey SF, Pepine CJ, Reichek N, Rogers WJ, Bairey-Merz CN, Sopko G, Cornell CE, Matthews KA: Socioeconomic status variables predict cardiovascular disease risk factors and prospective mortality risk among women with chest pain. The WISE Study. *Behavior Modification*. **2003** Jan;27(1):54-67

Sundquist K, Winkleby M, Ahlen H, Johansson SE: Neighborhood socioeconomic environment and incidence of coronary heart disease: a follow-up study of 25,319 women and men in Sweden. *American Journal of Epidemiology*. **2004** Apr 1;159(7):655-62

Sundquist K, Malmstrom M, Johansson SE: Neighbourhood deprivation and incidence of coronary heart disease: a multilevel study of 2.6 million women and men in Sweden. *Journal of Epidemiology and Community Health*. **2004** Jan;58(1):71-7. Erratum in: *Journal of Epidemiology and Community Health*. 2004 Mar;58(3):259

Theorell T, Tsutsumi A, Hallquist J, Reuterwall C, Hogstedt C, Fredlund P, Emlund N, Johnson JV: Decision latitude, job strain, and myocardial infarction: a study of working men in Stockholm. *American Journal of Public Health*. **1998** Mar;88(3):382-8

Theorell T, Karasek RA: Current issues relating to psychosocial job strain and cardiovascular disease research. *Journal of Occupational Health Psychology*. **1996** Jan;1(1):9-26. Review. Erratum in: *Journal of Occupational Health Psychology* 1998 Oct;3(4):369

Tsutsumi A, Kayaba K, Ishikawa S, Gotoh T, Nago N, Yamada S, Mizooka M, Sakai K, Hayasaka S: Job characteristics and serum lipid profile in Japanese rural workers: the Jichi Medical School Cohort Study. *Journal of Epidemiology*. **2003** Mar;13(2):63-71

9.7 Substance-related Disorders

The evidence of the association between unemployment and substance-related disorders is heterogeneous. One publication (Ettner 1997), using data from the 1988 National Health Interview Survey (USA), found that non-employment significantly reduces both alcohol consumption and dependence symptoms. Reduced income is discussed as an explanation. However, acute job loss increased the consumption of alcohol in this subpopulation. This is supported by results from a US-study by Ruhm and Black (2002), suggesting that any stress-induced increases in alcohol consumption in existing drinkers during bad economic times are more than offset by declines resulting from changes in economic factors such as lower incomes in other subgroups. This might explain the conflicting findings which derive

from comparisons of macroeconomic conditions and drinking using individual-level data. For example, with US-data from 1975-1988, the same auther (Ruhm 1995) found that alcohol consumption and traffic death vary procyclically. Analysing US-data between 1984-1995, Dee (2001) found “robust evidence” that the prevalence of binge drinking is strongly countercyclical; the fact that even among those who were employed binge drinking increased during economic downturns, suggests that not increased availability of leisure but economic stress leads to more alcohol consumption.

Conversely, data from the French National Health Survey (1991-1992) found significant relations (in men) between unemployment and addictive behaviours: heavy drinking (RR: 1.7), smoking (RR: 1.5 for “regular” and 1.7 for “heavy”), and consumption of psychoactive drugs (3.6). Overweight, as mentioned above, was not significantly related to unemployment (Khlat et al. 2004). However, from cross-sectional data, the direction of this association is unclear.

Muntaner et al. (1995) examined whether different psychosocial work environments might signal increased risk of drug dependence syndromes. After adjustment for sociodemographic risk factors and other potential confounders, they found high relative odds for drug dependence in subjects characterized by high levels of physical demands and low levels of skill discretion (OR=4.92), or respectively by high levels of physical demand and decision authority (OR=5.26), supporting the job-strain model. The same authors could show, after controlling for the other aspects of socioeconomic status, that nor income nor wealth are independent predictors of alcohol abuse or other dependence disorders (Muntaner et al. 1998).

Longitudinal data from Finland showed that temporary employment, as compared with permanent employment, was associated with increased deaths from alcohol-related causes (hazard ratio = 2.0) for both genders and from smoking-related cancer for men (HR = 2.8) (Kivimaki et al. 2003).

Longitudinal data from Sweden showed that low workplace social support, low work control, particularly in combination with low work demands, what might be called a “passive” work environment, were significantly associated with later alcoholism (Hemmingsson 1998). This is supported by other findings: Greenberg et Grunberg (1995) use the idea of work alienation, defined as low job autonomy, low use of capacities, and lack of participation in decision-making in the workplace, to show that this work setting is associated with heavy drinking and negative consequences from drinking in a sample of production workers. But also in high school students, job dissatisfaction is positively related to alcohol and cigarette use (Frone and Windle 1997).

Ettner SL: Measuring the human cost of a weak economy: does unemployment lead to alcohol abuse? *Social Science and Medicine*. **1997** Jan;44(2):251-60

Frone MR, Windle M: Job dissatisfaction and substance use among employed high school students: themoderating influence of active and avoidant coping styles. *Substance Use Misuse*. **1997** Apr;32(5):571-85

Greenberg ES, Grunberg L: Work alienation and problem alcohol behavior. *Journal of Health and Social Behavior*. **1995** Mar;36(1):83-102

Hemmingsson T, Lundberg I: Work control, work demands, and work social support in relation to alcoholism among young men. *Alcoholism, Clinical & Experimental Research*. **1998** Jun;22(4):921-7

Khlat M, Sermet C, Le Pape A: Increased prevalence of depression, smoking, heavy drinking and use of psycho-active drugs among unemployed men in France. *European Journal of Epidemiology*. **2004**;19(5):445-51

Kivimaki M, Vahtera J, Virtanen M, Elovainio M, Pentti J, Ferrie JE: Temporary employment and risk of overall and cause-specific mortality. *American Journal of Epidemiology*. **2003** Oct 1;158(7):663-8

Muntaner C, Anthony JC, Crum RM, Eaton WW: Psychococial dimensions of work and the risk of drug dependence among adults. *American Journal of Epidemiology*. **1995** Jul 15;142(2): 183-90

Muntaner C, Eaton WW, Diala C, Kessler RC, Sorlie PD: Social class, assets, organizational control and the prevalence of common groups of psychiatric disorders. *Social Science and Medicine*. **1998** Dec;47(12):2043-53

Ruhm CJ: Economic conditions and alcohol problems. *Journal of Health Economicsomics*. **1995** Dec;14(5):583-603

Ruhm CJ, Black WE: Does drinking really decrease in bad times? *Journal of Health Economicsomics*. **2002** Jul;21(4):659-78

9.8 Depression and common mental disorders

The US-American National Institute of Occupational Safety and Health (NIOSH) recognized psychological disorders as a leading occupational health risk as recent as 1988.

Over the last decade, common mental disorders, such as depression and anxiety (rather than complex psychoses), contribute most to rising sickness absence, and have replaced musculoskeletal disorders as the leading cause of incapacity benefit claims (Henderson 2005). Therefore it seems crucial to include common mental disorders, and namely depression, as a major occupational health outcome (compare Harnois 2000 (ILO)). Furthermore, mental depression is also a predictor of disability (to any cause), and non-illness based pensions. Depressed people retire younger than those without depression; in a recent Finish cohort study, the loss of working life time due to depression induced retirement was 1.5 years on average (Karpansalo et al. 2005).

“At the population level of analysis, increase in the unemployment rate indicates recession and/or structural economic decline. At the individual level, unemployment is interpreted as a stressful life event” (Brenner 1993).

Many studies have consistently found the occurrence of depression to be higher among persons with lower socio-economic status. In their study mentioned above, Khlat et al. (2004) found that unemployed men have a significantly higher prevalence of depression (RR=2.6) than the working population. This was true even if compared to low-paid employment (Theodossiou 1998). This is supported by an analysis by Muntaner et al. (1998): The relationship between income/wealth and depression/anxiety looses significance if those who are unemployed are excluded from the analysis.

Some authors point out that this relationship is age-dependent: In a Canadian study on the relationship between unemployment and mental health, becoming unemployed led to increases in distress and clinical depression only among the 31-55-year-olds, but not among younger adults 18 to 30 years of age (Breslin 2003). However, debate continues as to whether unemployment results in psychological morbidity, or whether the association is due to those who are more vulnerable to mental illness becoming unemployed. Therefore, it is useful to look at longitudinal data. The 1958 British birth cohort provides such data for men. When those who were unemployed in the year prior to onset of depressive symptoms resulting in consultation were compared to those who where not unemployed, the relative risk for symptoms of depression was 2.1. Accumulated unemployment (as compared to recent unemployment) was only significant if men with pre-existing depressive symptoms were excluded from analysis (Montgomery 1999). These findings are supported by a longitudinal study on partners, demonstrating that financial strain had not only significant effects on depressive symptoms of both partners, but also in turn led the partner to withdraw social support, leading into a vicious circle (Vinokur et al. 1996). The same author also stresses the dual role of financial strain, which on the one hand facilitates reemployment by increasing job-search motivation and job-search intensity, but on the other hand inhibits it by increasing depressive symptoms (Vinukur and Schul 2002). There is also support that changes in income and poverty status have effects on depressive symptoms in US-American women (Dearing et al. 2004).

In a study on work attributes and depression disparities among young adults, perceived job insecurity was associated with a higher depression score only for black men (Zimmerman 2004). Pikhart et alii (2004) found evidence for the validity of Siegrist’s effort-reward-imbalance model in a cross-sectional study of working men and women in Central and Eastern Europe (Russia, Poland, Czech Republic). In a cross-sectional analysis of Japanese

workers, Tsutsumi et al. (2001) found that both job stress models identify different aspects of stressful job conditions. This view is supported by Godin et Kittel (2004).

Prospective investigations on the effect of potential workplace closure, a form of job insecurity that is externally attributed by definition, could also show rises in fatigue and psychological distress (Swaen et al. 2004). Fatigue, by the way, is not only directly linked to absenteeism (Janssen et al. 2003) and decreased work productivity, but also leads to higher rates of work accidents and permanent work disability (van Amelsvoort et al. 2002). The economic impact of fatigue is severe in terms of direct and indirect costs (Chilcott et al., Metlaine et al. 2005).

In a huge cross sectional study from the United States (n=98.267) on the relationship between short- and long-term unemployment and mental distress, Brown at alii (2002) demonstrated a significant age-standardized relative odds of frequent mental distress, that was observed across race/ethnicity, education, income, and gender.

However, there are many hints for a gender difference in the effect of unemployment on mental health (Artazcoz et al. 2004). Interestingly, in a longitudinal study from France on women after childbirth – being very much involved in their maternal role – showed that those seeking a job had worse mental health than those in a stable situation, either employed or housewives (Saurel-Cubizolles et al. 2000).

The literature on the subject of interaction between job and family responsibilities for women and sources of social support is immense, but integrating the gender aspect regarding family at home would go beyond the scope of this report on occupational health.

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van Amelsvoort LG, Kant IJ, Beurskens AJ, Schroer CA, Swaen GM: Fatigue as a predictor of work disability. *Occupational and Environmental Medicine*. **2002** Oct;59(10):712-3

Artazcoz L, Benach J, Borrell C, Cortes I: Unemployment and mental health: understanding the interactions among gender, family roles, and social class. *American Journal of Public Health*. **2004** Jan;94(1):82-8

Brenner MH, Mooney A: Unempolyment and helath in the context of economic change. *Social Science and Medicine*. **1993**; 17(16): 1125-38

Breslin FC, Mustard C: Factors influencing the impact of unemployment on mental health among young and older adults in a longitudinal, population-based survey. *Scandinavian Journal of Work, Environment & Health*. **2003** Feb;29(1):5-14

Brown DW, Balluz LS, Ford ES, Giles WH, Strine TW, Moriarty DG, Croft JB, Mokdad AH: Associations between short- and long-term unemployment and frequent mental distress among a national sample of men and women. *Journal of Occupational and Environmental Medicine*. **2003** Nov;45(11):1159-66

Chilcott LA, Shapiro CM: The socioeconomic impact of insomnia. An overview. *Pharmacoeconomics*. **1996**;10 Suppl 1:1-14. Review

Dearing E, Taylor BA, McCartney K: Implications of family income dynamics for women's depressive symptoms during the first 3 years after childbirth. *American Journal of Public Health*. **2004** Aug;94(8):1372-7

Henderson M, Glozier N, Holland Elliott K: Long term sickness absence. *British Medical Journal* **2005**; 330: 802-3

Harnois G, Gabriel P (WHO/ILO): *Mental Health and Work. Impact, Issues and Good Practices*. WHO/ILO **2000**

Janssen N, Kant IJ, Swaen GM, Janssen PP, Schroer CA: Fatigue as a predictor of sickness absence: results from the Maastricht cohort study on fatigue at work. *Occupational and Environmental Medicine*. **2003** Jun;60 Suppl 1:i71-6

Karpansalo M, Kauhanen J, Lakka TA, Manninen P, Kaplan GA, Salonen JT: Depression and early retirement: prospective population based study in middle aged men. *Journal of Epidemiology and Community Health*. **2005** Jan;59(1):70-4

Khlat M, Sermet C, Le Pape A: Increased prevalence of depression, smoking, heavy drinking and use of psycho-active drugs among unemployed men in France. *European Journal of Epidemiology*. **2004**;19(5):445-51

Metlaine A, Leger D, Choudat D: Socioeconomic impact of insomnia in working populations. *Industrial Health*. **2005** Jan;43(1):11-9. Review

Montgomery SM, Cook DG, Bartley MJ, Wadsworth ME: Unemployment pre-dates symptoms of depression and anxiety resulting in medical consultation in young men. *International Journal of Epidemiology*. **1999** Feb;28(1):95-100

Muntaner C, Eaton WW, Diala C, Kessler RC, Sorlie PD: Social class, assets, organizational control and the prevalence of common groups of psychiatric disorders. *Social Science and Medicine*. **1998** Dec;47(12):2043-53

Pikhart H, Bobak M, Pajak A, Malyutina S, Kubinova R, Topor R, Sebakova H, Nikitin Y, Marmot M: Psychosocial factors at work and depression in three countries of Central and Eastern Europe. *Social Science and Medicine*. **2004** Apr;58(8): 1475-82

Saurel-Cubizolles MJ, Romito P, Ancel PY, Lelong N: Unemployment and psychological distress one year after childbirth in France. *Journal of Epidemiology and Community Health.* **2000** Mar;54(3):185-91

Swaen GM, Bultmann U, Kant I, van Amelsvoort LG: Effects of job insecurity from a workplace closure threat on fatigue and psychological distress. Journal of Occupational and Environmental Medicine. 2004 May;46(5):443-9

Theodossiou I: The effects of low-pay and unemployment on psychological well-being: a logistic regression approach. *Journal of Health Economicsomics*. **1998** Jan;17(1):85-104

Tsutsumi A, Kayaba K, Theorell T, Siegrist J: Association between job stress and depression among Japanese employees threatened by job loss in a comparison between 2 complementary job-stress models. *Scandinavian Journal of Work, Environment & Health*. **2001** Apr;27(2):146-53

Vinokur AD, Price RH, Caplan RD: Hard times and hurtful partners: how financial strain affects depression and relationship satisfaction of unemployed persons and their spouses. *Journal of Personality and Social Psychology*. **1996** Jul;71(1):166-79

Vinokur AD, Schul Y: The web of coping resources and pathways to reemployment following a job loss. *Journal of Occupational Health Psychology*. **2002** Jan;7(1):68-83

Zimmerman FJ, Christakis DA, Vander Stoep A: Tinker, tailor, soldier, patient: work attributes and depression disparities among young adults. *Social Science and Medicine*. **2004** May;58(10):1889-901

9.9 Suicide

There is overwhelming evidence that economic recession and unemployment lead to higher rates of suicide. This is true also for suicide attempts, as demonstrated by Ostamo et alii (2001). In their study, among suicide attempters, young and middle-aged men with low education had the highest risk of unemployment.

Three large longitudinal studies could be identified to support the hypothesis that unemployment or lack of job security increases the risk of suicide. In their multivariable analysis, Blakely et alii (2003) found that unemployment and marital status were the only independent determinants of suicide in New Zealand. The authors point out, that although being unemployed was associated with a twofold to threefold increased relative risk of death by suicide, about half of this association might be attributable to confounding by mental illness. For England and Wales, Lewis and Sloggett (1999) came to the same result.

Kim et al. (2004) could demonstrate with data from South Korea, that suicides increased rapidly during an economic crisis.

Gunnel et al. (1999) performed a time-series analysis using routine mortality and unemployment data over a period spanning two major economic recessions in England and Wales (1921-1995). Their findings supported the hypothesized relation for both men and women, with generally stronger associations at younger ages.

Robert Fernquist analysed perceived income inequality and suicide rates in Central/Eastern European countries and Western countries and found that both variables were more strongly associated in men and accounted for most of the difference in the gender gap of male versus female suicide rates (Fernquist 2003). At the individual level, income does not seem to play a major role in explaining suicide rates (Blum et al. 2000, Young et al. 2005).

Surprisingly, the only study to shed light on the association between work stress or job satisfaction and suicide, was a survey data study on burnout among Finnish psychiatrists (Korkeila 2003).

Blakely TA, Collings SC, Atkinson J: Unemployment and suicide. Evidence for a causal association? *Journal of Epidemiology and Community Health*. **2003** Aug;57(8):594-600

Blum RW, Beuhring T, Shew ML, Bearinger LH, Sieving RE, Resnick MD: The effects of race/ethnicity, income, and family structure on adolescent risk behaviors. *American Journal of Public Health*. **2000** Dec;90(12):1879-84

Dee TS: Alcohol abuse and economic conditions: evidence from repeated cross-sections of individual-level data. *Health Economics*. **2001** Apr;10(3):257-70

Fernquist RM: Perceived income inequality and suicide rates in Central/Eastern European countries and Western countries, 1990-1993. *Death Studies*. **2003** Jan;27(1):63-80

Gunnell D, Lopatatzidis A, Dorling D, Wehner H, Southall H, Frankel S: Suicide and unemployment in young people. Analysis of trends in England and Wales, 1921-1995. *British Journal of Psychiatry*. **1999** Sep;175:263-70

Kim H, Song YJ, Yi JJ, Chung WJ, Nam CM: Changes in mortality after the recent economic crisis in South Korea. Ann Epidemiol. 2004 Jul;14(6):442-6

Korkeila JA, Toyry S, Kumpulainen K, Toivola JM, Rasanen K, Kalimo R: Burnout and self-perceived health among Finnish psychiatrists and child psychiatrists: a national survey. *Scandinavian Journal of Public Health*. **2003**;31(2):85-91

Lewis G, Sloggett A: Suicide, deprivation, and unemployment: record linkage study. *British Medical Journal*. **1998** Nov 7;317(7168):1283-6

Ostamo A, Lahelma E, Lonnqvist J: Transitions of employment status among suicide attempters during a severe economic recession. *Social Science and Medicine*. **2001** Jun;52(11):1741-50

Young TW, Wooden SE, Dew PC, Hoff GL, Cai J: The Richard Cory phenomenon: suicide and wealth in Kansas City, Missouri. *Journal of Forensic Sciences*. **2005** Mar;50(2):443-7

9.10 HIV/AIDS

HIV and AIDS have become one of the leading causes of death for individuals aged 15-49, not only in Sub-Saharan Africa and parts of Asia, but also in some major cities in Europe and the United States (Quinn 1996). While plausible projections exist about the impact of HIV and AIDS on the labour force in developing countries, similar projections for industrialized countries are scarce. Even the International Labour Organization (ILO) only offers data on the USA and the Russian Federation, but no data on Western or Eastern Europe. A US-American study on changes in employment, insurance, and income in relation to HIV status and disease progression, showed that persons with AIDS were 2.7 times more likely to lose full-time employment; and loss of employment was strongly associated with both loss of private health insurance and loss of income.

However, with mechanisms of the impact of HIV/AIDS on the world of labour being well understood, the opposite direction – how changes in the world of work, especially unemployment, influence HIV transmission patterns – remains an area of investigation.

The main approach to describe the connection between unemployment rates and HIV transmission runs as follows: The fall in GDP leads to increased poverty and unemployment, sometimes driving young women (and men! – see Weber et al. 2001) into prostitution, and young men (and women) into drug and alcohol abuse (Pasarín et al. 2004, Brugal et al. 2003, Rhodes et al. 1999, Kaaya et al. 1998). Globalization and – especially in the newly independent states of the former Soviet Union – the opening up of borders have contributed to cross-border sex trade. Unemployment and increased poverty have led to the expansion

of shadow economies, including those associated with crime, sex work, and “trafficking, which also form the bedrock for the spread of HIV infection” (ILO/GTZ 2004).

The involvement in sex work due to unemployment could also be shown for MSM, especially in otherwise marginalized subpopulations. In a prospective Canadian cohort study, unemployment had an adjusted Odds Ratio of 3.9 (Weber et al. 2001).

In addition, unemployment turned out to be a risk factor for inconsistent condom use – at least among US heterosexual serodiscordant couples (Buchacz et al. 2001).

Rhodes et al. describe the potential influence of the social and economic context in creating the “risk environments”, conductive to HIV and epidemic spread. This is illustrated in table 1.

Table 1: The macro risk environment influencing HIV epidemics among IDUs (Rhodes et al. 1999)

Drug injecting environment	Social and economic environment
Diffusions in drug use and size of IDU populations	Economic transition and decline
Migration, population mobility and mixing	Increased unemployment and impoverishment
Globalization in drug trade, production and transit	Growth in informal and criminal economies
Methods of drug production	Migration, population mobility and mixing
Methods of drug distribution	Trade, transport and communication links
Physical settings of drug use and injecting	Transitions in health and welfare status
Epidemics of HIV, STI and TB	Public health revenue and infrastructures
Risk behaviour norms and practices	Political, ideological and cultural shifts
Drug law enforcement and interdiction initiatives	Lack of “civil society” and community organization

“The diffusion of IDU and the emergence of HIV and STI epidemics have occurred in the context of an interplay of macro social, economic and political changes in the NIS (newly independent states) over the last decade” (Rhodes et al. 1999).

Although injecting drug use accounts for a diminishing share of newly diagnosed HIV infections in most Western European countries, it remains the most important factor in the NIS and an important factor in countries such as Italy, Spain or Portugal, and in some cities of other countries. “In most cases, this reflects declines in unsafe injecting practices probably associated with effective prevention efforts among injecting drug users in many Western European countries. Spain offers a striking example of how a comprehensive set of harm-reduction efforts (including methadone maintenance programmes and needle-exchange projects) can reverse an epidemic among injecting drug users. New HIV infections among drug injectors reached as high as 16,000 in 1985–1986, but plummeted subsequently” (WHO 2004).

In the 12 Western European countries with available data for newly diagnosed HIV infections, HIV diagnoses in people who were infected through heterosexual contact more

than doubled between 1997 and 2002. A large share of those diagnoses was in people originating from countries with serious epidemics, principally countries from sub-Saharan Africa and, for the United Kingdom, the English speaking Caribbean (see WHO 2004). Consequently, not all observed “increases” in HIV-prevalence can be connected with employment policies or the employment situation in the industrialized countries themselves.

However, it is important not to mistake data on new diagnoses as HIV incidence, since this data may reflect an increased uptake of testing services (and therefore include people who became infected several years earlier). The distinction remains a complicated task, and relevant data on test usage and test policies is not available in most European countries.

Regarding the influence of stress on the progression of HIV-infection, there is evidence that cortisol and adrenocorticotropin (ACTH) significantly inhibit the natural killer cell (NK) activity of lymphocytes (Nair 1995). Hassig et al. (1996 A, 1996 B) even postulate that continued excessive stress, “such as observed in the known risk groups” (Hassig 1996 A), is at the center of the aetiopathological process that leads to damages of T-lymphocytes, down regulation of Th1 cytokines, and therefore damage of T-cellular immunity. However, the mainstream literature in HIV research does not focus on health outcomes unrelated to HIV itself or antiretroviral therapy.

Looking at psychosocial influences not on HIV incidence, but on AIDS incidence or progression, there is growing evidence that lack of social support is a driving factor for AIDS-related mortality (Ibibarren et al. 2005), speed of disease progression (Leserman 2000 and 2002), and decline of CD4-positive T-helper cells (Persson et al. 2002).

Brugal MT, Borrell C, Díaz-Quijano E et al.: Deprivation and AIDS in a southern European city. Different patterns across transmission groups. *European Journal of Public Health* **2003;** 13: 259-261

Buchacz K, van der Straten A, Saul J et al.: Sociodemographic, Behavioral, and Clinical Correlates of Inconsistent Condom Use in HIV-Serodiscordant Heterosexual Couples. *Journal of Acquired Immune Deficiency Syndromes.* **2001**; 28(3): 289-297

Hassig A, Wen-Xi L, Stampfli K: Stress-induced suppression of the cellular immune reactions: on the neuroendocrine control of the immune system. *Medical Hypotheses.* **1996** Jun;46(6):551-5 (B)

Hassig A, Wen-Xi L, Stampfli K: Can we find a solution to the human immunodeficiency virus/acquired immune deficiency syndrome controversy? Is acquired immune deficiency syndrome the consequence of continuous excessive stressing of the body? *Medical Hypotheses*. **1996** Apr;46(4):388-92 (A)

Iribarren C, Jacobs DR, Kiefe CI, Lewis CE, Matthews KA, Roseman JM, Hulley SB: Causes and demographic, medical, lifestyle and psychosocial predictors of premature mortality: the CARDIA study. *Social Science and Medicine*. **2005** Feb;60(3):471-82

ILO/GTZ: *HIV/AIDS+ work. Country profile 1: The socio-economic impact of HIV/AIDS in Ukraine*. **2004** (http://www.ilo.org/aids)

Kaaya SF, Leshabari MT, Mbambo JK: Risk Behaviors and Vulnerability to HIV Infection among Tanzanian Youth. *Journal of Health & Population in Developing Countries* **1998**; 1(2): 51-60

Leserman J, Petitto JM, Golden RN, Gaynes BN, Gu H, Perkins DO, Silva SG, Folds JD, Evans DL: Impact of stressful life events, depression, social support, coping, and cortisol on progression to AIDS. *American Journal of Psychiatry*. **2000** Aug;157(8):1221-8

Leserman J, Petitto JM, Gu H, Gaynes BN, Barroso J, Golden RN, Perkins DO, Folds JD, Evans DL: Progression to AIDS, a clinical AIDS condition and mortality: psychosocial and physiological predictors. *Psychological Medicine*. **2002** Aug;32(6):1059-73

Nair MP, Saravolatz LD, Schwartz SA: Selective inhibitory effects of stress hormones on natural killer (NK) cell activity of lymphocytes from AIDS patients. *Immunological Investigations*. **1995** Aug;24(5):689-99

Pasarín MI, Borrell C, Brugal MT, Diaz-Quijano E: Weighing Social and Economic Determinants Related to Inequalities in Mortality. *Journal of Urban Health* **2004**; 81(3): 349-362

Quinn TC: Global burden of the HIV pandemic. *Lancet* **1996**; 348:99-106

Persson L, Ostergren PO, Hanson BS, Lindgren A, Naucler A: Social network, social support and the rate of decline of CD4 lymphocytes in asymptomatic HIV-positive homosexual men. *Scandinavian Journal of Public Health*. **2002**;30(3):184-90

Psychd ST, Troop M, Burgess AP, Button J, Goodall R, Flynn R, Gazzard BG, Catalan J, Easterbrook PJ: The relationship of psychological variables and disease progression among long-term HIV-infected men. *International Journal of STD & AIDS*. **2000** Nov;11(11):734-42.

Rhodes T, Ball A, Stimson GV et al.: HIV infection associated with drug injecting in the Newly Independent States, Eastern Europe: the social and economic context of epidemics. *Addiction* **1999**; 94(9): 1323-1336

Weber AE, Craib KJP, Chan K et al.: Sex trade involvement and rates of human immunodeficiency virus positivity among young gay and bisexual men. *International Journal of Epidemiology*. **2001**; 30: 1449-1454

WHO: Global situation of the HIV/AIDS epidemic, end 2004. *Weekly Epidemiological Record* **2004**, 50: 441-449

10 Social Capital and Social Support

The workplace has been shown repeatedly as an origin of health inequalities (Vahtera et al. 1999). In a modern occupational context, multiple exposures are involved that represent a set of conditions that people experience hour by hour, day by day over the course of their lives. This set of conditions can be called a metaexposure in the sense that the way in which work is organized produces a multiplicity of physical, chemical, psychosocial, and cultural exposures that workers encounter as a totality in actual work contexts (Gustavsen, 1991). Many models have been applied to understand this totality.

In his recently published book “The Culture of The New Capitalism” (Sennet 2006), Richard Sennet argues that the erosion of social capitalism has produced a new form of inequality (see also Lynch 2000b) linked with social isolation, in which social capital and loyalty, informal trust and accumulated knowledge decrease. For occupational safety, accumulated knowledge is a crucial value that goes hand in hand with organizational form of social networks.

Lynch (2000a) argues that not only government or legal organizations, but also business organizations play a crucial part in structuring the nature of civil society, “where informal social relations, trust and reciprocity are played out” (p. 407).

This literature review agrees with Johnson and Hall (1996), who describe the workplace as a social context that is formed by larger political, economic, and social forces. Modern industrial societies are embedded in political and economic processes that influence the character of the whole occupational field. Presently, work is undergoing a process of “permanent revolution” (Johnson and Hall 1996), in which “the intensity and rate of change itself has become one of the most significant stressors to which workers are now exposed”.

With respect to work stress, this review has already focused on the demand-control model. In many studies, control over the work process is represented by measures of autonomy, other investigators refer to the vertical structure of the work process and apply the less subjective variable of hierarchy. On the individual level, further research has expanded the demand-control model by the protective measure of social support. Social networks and social support are unexpectedly important for health, both mental and physical. In the field of social epidemiology concern about the individual-level effects has been well established under this conceptual label, long before a more recent interest in the term social capital, which is typically used to refer only to aggregate-level effects. Probably for this reason, social capital has not yet been included into the PubMed MeSH (Medical Subject Heading) terminology. Social capital has primarily been used in the fields of sociology and economics. It describes

the pattern and intensity of networks among people and the shared values and sanctions which arise from those networks. Definitions of social capital vary, but the main aspects include citizenship, neighbourhood, social networks and civic participation. There are a number of different aspects to social capital and measuring the level of social capital in communities can be complex. It is commonly focused on levels of trust, membership (in clubs, social or religious groups), networks and frequency of social contact.

According to Robert D. Putnam (2000), mortality rates are powerfully affected by social capital. Although the origins are not yet clear, Putnam brings forward the statement that the prime candidate is social isolation.

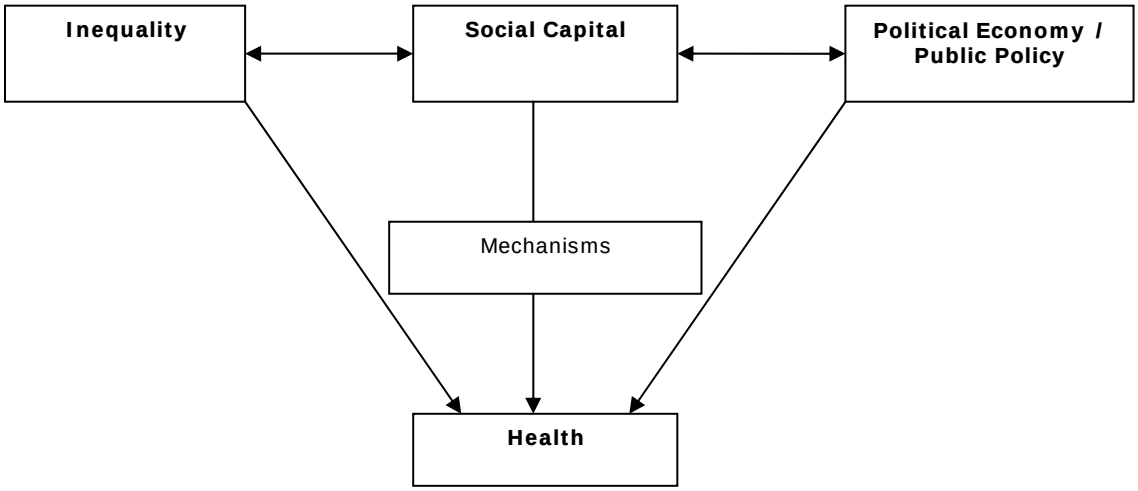
Putnam stresses that social networks can have both effects on individuals inside the social networks and aggregate effects on outsiders. Not only can social ties provide social support that enhances individual health – broader social networks of may also enhance the effectiveness of public health provision. Here, in accordance with Putnam, the term will be used in this broad sense, but it has to be stressed that most social epidemiologist use it for aggregate measures only, while social support is used for the individual level.

Figure 3 illustrates how social capital interacts with political economy and inequality. That political economy or public policy have influences on health is intuitively clear. In the sections before it has been argued, that socioeconomic inequality has influences on health as well. A positive and robust relationship also exists between measures of equality (for example: income distribution) and measures of social capital. Richard Wilkinson argues that the arrow should run from inequality to social capital, as hard reality of income distribution translates to the softer realities of social capital (Wilkinson 2002, Marmot and Wilkinson 1999). Putnam (2004) argues that both political public policy and inequality, to a certain extent, could result from social capital.

Three approaches to Social Capital Theory can roughly be described using figure 3: According to Szreter and Woolcock (2004), (1) a ‘social support’ perspective argues that informal networks are central to health (the central arrow running from Social Capital through Mechanisms to Health), (2) an ‘inequality thesis’ claiming that widening economic disparities have eroded citizens’ sense of social justice and inclusion (arrow from Inequality to Social Capital to Health), and (3) a ‘political economy’ approach meaning that the primary determinant of poor health outcomes is the exclusion from material resources, mediated socially or politically (arrow from Political Economy through Social Capital to Health). All three approaches share the final arrow running through ‘Mechanisms’, that is outlined in detail below (figure 4). Central to this understanding is the concept of perceived stress.

There is virtually no doubt that on the individual level, social support reduces perceived stress and is connected to the existence of social networks.

Figure 3: How Social Capital interacts with Political Economy and Inequality; adapted from Putnam (2004)



Debate goes on whether at the macro-level social capital is really a new and independent variable, or if it is just fogging established concepts of social class: Pearce and Davey Smith (2004) propose a 'neomaterialist' view against the 'indirect' social capital theory (hence focusing on the arrow running directly from Political Economy to Health).

However, there is a growing body of evidence today, that the broad and distinct fields of macro-sociology and micro-medicine or –biology are interlinked much more closely than it had been assumed in the more behaviour-oriented era. Differences in access to social support translate into individual physiological differences.

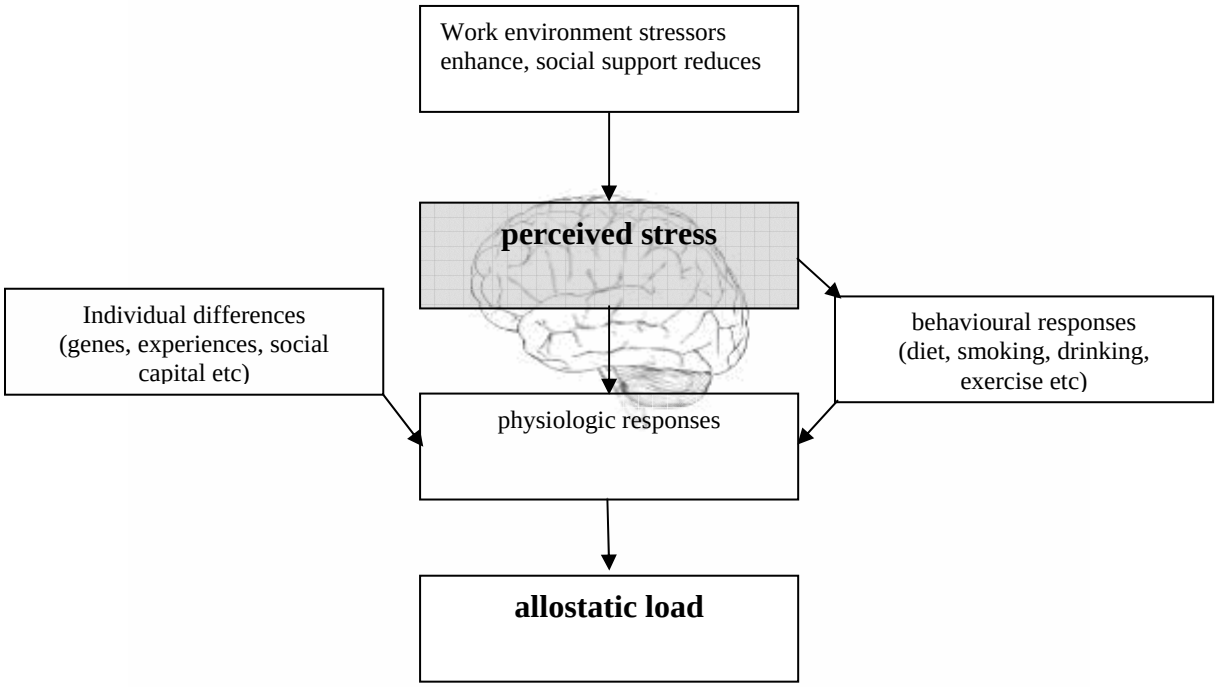
Research in the fields of psychoneuroimmunology and neuroendocrinology have begun to map out the mediators and mechanisms by which the availability of social support and other environmental conditions might influence individual health (e.g. Berkman 1995, Berkman and Kawachi 2000).

McEwen (e.g. McEwen 1998, 1999) introduced the term of allostatic load to describe that the perception of stress – being enhanced by environmental stressors, or reduced by social support (as demonstrated by Singer and Ryff 1999) – opens out into a physiologic response, that further, mediated by individual differences (as genetic predisposition, social capital, experiences) or behavioural differences (such as smoking, exercise, etc.), cumulates into an individual "storage". This "storage", the allostatic load, has major impacts on physiological

entities such as the cardiovascular, metabolic, or immune system. Outcomes like insulin resistance, abdominal obesity, atherosclerosis, hypertension, or immune suppression have been described in detail (see review by McEwen and Seeman 1999). In an experimental study by Rissen et al. (2000), perceived negative stress had influences on muscle activity, which is seen as an explanation for the high prevalence of musculoskeletal disorders associated with stressful work.

Figure 4 illustrates the concept of allostatic load.

Figure 4: Development of allostatic load, adapted from McEwen and Seeman (1999)



As mentioned, control over the working process (autonomy) and social support (low hierarchies, solidary work environment, social networks) are crucial factors underlying the health of workers and employees.

The role of social capital has been shown both on a macro and micro-level. Ichiro Kawachi is among the most prominent defender of not only social support at the individual level, but also of social capital at the aggregate level. He provided a very comprehensive list of ecological and multilevel studies, showing the different measures that are used to estimate the amount of contribution of social capital to health (Kawachi et al. 2004).

A highly significant inverse relation with age-adjusted, all-cause mortality could be demonstrated with aggregated measures of levels of interpersonal trust, norms of reciprocity, and density of associational membership across the states of the USA (Kawachi et al. 1997).

This association remained even after controlling for household poverty rates. Corresponding results could be shown by the same authors (1999a) in a multilevel study of the relationship between US-state level social capital and individual self-rated health, controlling for the most important confounders such as health insurance coverage, smoking status, overweight, as well as sociodemographic characteristics including household income level and educational attainment.

As Kawachi further points out (1999b), labour unions and comparable social institutions play a major role in stimulating citizens to participate in micro- and macro-political decision-making, in turn resulting in maintenance of social control and healthy norms. It seems plausible, that this form of participation is also true for occupational settings.

From a different angle, Wilkinson (1999) describes how different positions within a given hierarchy work on HDL/LDL ratios (high/low density lipoprotein-cholesterol), central obesity, glucose intolerance, atherosclerosis, basal cortisol levels and cortisol responses (“Social hierarchy is the human equivalent of pecking order”).

If perceived stress is responsible for the major contributions not only to mortality (above all: cardiovascular diseases), but also for long term sickness absence (the cost and importance of that have been described by Henderson et al. 2005), and if hierarchies in society and working life are a major cause of perceived stress, then more egalitarian societies and work settings must result in both decreased mortality and long term sickness absence (compare Theorell 1999). However, social capital in a given setting has been shown to be inversely related to the degree of hierarchy (reviews by Kawachi 1999 and Wilkinson 1999).

There is a growing number of studies from different OECD countries to support these ideas.

Penninx et alii (1997) studied 2928 non-institutionalized people from Amsterdam (55-85 years) in the early 1990s. After controlling for age, sex, chronic diseases, use of alcohol, smoking, and self-rated health, it turned out that fewer feelings of loneliness (social support) and greater feelings of mastery (control) were still directly linked with reduced mortality. In an additional stratified analysis, the level of perceived social support was significantly inversely associated with mortality. For men, in another study, the position in the occupational hierarchy was correlated with self-percieved health, even after adjustment for baseline health, health behaviours and psychosocial work exposures (Mustard et al. 2003).

Other authors demonstrated the role of social networks as predictors for mortality risk in middle aged men and women in Japan (Iwasaki et al. 2002) and Hungary (Skrabski et al. 2003). In the latter publication, including more than 12.000 individuals, all of the social capital variables were significantly associated with middle age mortality.

Rosengren et alii (1998) followed a random sample of a Goteburg male population (1016 men who were 50 years at baseline) for 12 years and could show that both emotional support and social activity were significantly inversely correlated with all-cause mortality. In a similar study from Norway, 1010 persons were followed for 17 year from 1976 onwards. When controlling for socio-demographic and biological factors, low social participation, and external locus of control were associated with increased mortality (Dalgard 1998).

In an ecological study from Saskatchewan (Canada), income inequality was positively, and social capital was negatively related to mortality (Veenstra 2002).

Other authors cast doubts on the importance of social capital: In an analysis with an econometric model of population health in 19 OECD countries, standard indicators of social capital (e.g. proportion of people who say that they generally trust other people, or membership in voluntary associations) was insignificant with respect to population health, while income per capita and the proportion of governmental health expenditure had a significant and positive impact (Kennelly et al. 2003). This is largely supported by the previously mentioned study by Lynch (2001), who found that on a macro-level, income inequality and characteristics of the psychosocial environment like trust, control, and organisational membership do not seem to be key factors in understanding health differences.

As David Halpern in his recently published work “Social Capital” – to my knowledge the most extensive work on this issue – has pointed out, it is not so much that social support stops a person getting sick, but helps him or her to recover when he or she does get sick. This notion is important not only for long term absenteeism, but also for the development of chronic diseases in general, mainly by protecting against stress (Halpern 2005).

On the individual level, there is quite some evidence that social support at work influences health outcomes:

In a cohort study from Japan, perceived job stress was “causally” related to mental health, and, in particular, the item “poor relationship with superior” showed the largest adjusted hazard ratio (Shigemi et al. 2000). Insomnia in Japanese shift workers (with a high prevalence of more than 37%), was associated independently to social support at work and job strain (Nakata et al. 2001, see also Fujita and Kanaoka 2003).

These findings are underlined by a longitudinal study from the Netherlands, where positive changes in perceived social support at work went together with decreased fatigue, decreased emotional exhaustion and decreased psychological distress (Janssen and Nijhuis 2004).

The presence of control and social support at work was also found to protect US-physicians from developing job dissatisfaction and psychiatric distress (Johnson, Hall et al. 1995). However, in a prospective cohort study on 6000 public sector employees from Finland, a similar association disappeared in logistic regression after adjustment for sociodemographic background factors, and hence only partially supported the hypothesis of work-related social capital as a health resource (Liukonen et al. 2004). Partial support also stems from a medium-sized cross-sectional study on German industrial workers, where job demands corresponded more to allostatic load than social support at work (Schnorpfeil et al. 2003).

A study on employees in Denmark showed that the influence of social support at the workplace on musculoskeletal symptoms was even higher than physical exposures (Feveile et al. 2002). Similar results stem from a prospective cohort of French workers, where biomechanical exposure worked independently from the psychosocial work environment, especially social support at work, on sick leave due to low back pain. According to a US study from 1999, back pain leading to lost work days had a prevalence of 4.6%, both in male and female industry workers (Guo et al. 1999).

In another study, high job strain and low coworker support were important factors on work injuries in Japanese female blue-collar workers (Murata et al. 2000). This harmonizes with findings from a longitudinal study from Australia, where job autonomy and communication positively predicted safe working (Parker et al. 2001).

An analysis of the Whitehall II data (UK) concluded that the extent to which people are treated with justice in workplaces seems to predict their health independently of established stressors at work (Kivimaki et al. 2004). In the literature, justice is seen as an important aspect of social support, especially in the work environment. However, analyzing the same data, Kuper and Marmot (2003) found that the effect of job strain on coronary heart disease was not modified by social support at work.

In a huge cohort of middle aged employees of France’s national gas and electricity company (GAZEL study, n=20.000), quality of the work environment, including social support at work, and social relations outside the work context, independently affected sickness absence over an extended period of time (Melchior et al. 2003). In a study from the Netherlands, high supervisor support was the most predictive variable on return to work after sickness (Janssen et al. 2003).

Hence, on the individual level, the majority of the literature suggests that social support positively influences health and negatively influences cause-specific mortality. Social support at the workplace seems to work independently from job strain variables. In addition to health

outcomes, social support also seems to influence long term absenteeism and productivity (Erikson et al. 2003, Michi and Williams 2003, Baruch-Feldman 2002, Wickstrom and Pentti 1998), both being not only of public health, but also of economical relevance.

Amick BC 3rd, McDonough P, Chang H, Rogers WH, Pieper CF, Duncan G: Relationship between all-cause mortality and cumulative working life course psychosocial and physical exposures in the United States labor market from 1968 to 1992. *Psychosomatic Medicine*. **2002** May-Jun;64(3):370-81

Baruch-Feldman C, Brondolo E, Ben-Dayan D, Schwartz J: Sources of social support and burnout, job satisfaction, and productivity. *Journal of Occupational Health Psychology*. **2002** Jan;7(1):84-93

Berkman LF: The role of social relations in health promotion. *Psychosomatic Medicine*. **1995** May-Jun;57(3):245-54. Review

Berkman L, Kawachi I (eds): *Social Epidemiology*. Oxford University Press, New York, **2000**

Bond FW, Bunce D: Job control mediates change in a work reorganization intervention for stress reduction. *Journal of Occupational Health Psychology*. **2001** Oct;6(4):290-302

Dalgard OS, Lund Haheim L: Psychosocial risk factors and mortality: a prospective study with special focus on social support, social participation, and locus of control in Norway. *Journal of Epidemiology and Community Health*. **1998** Aug;52(8):476-81

Eriksen W, Bruusgaard D, Knardahl S: Work factors as predictors of sickness absence: a three month prospective study of nurses' aides. *Occupational and Environmental Medicine*. **2003** Apr;60(4):271-8

Feveile H, Jensen C, Burr H: Risk factors for neck-shoulder and wrist-hand symptoms in a 5-year follow-up study of 3,990 employees in Denmark. *International Archives of Occupational and Environmental Health*. **2002** Apr;75(4):243-51

Fujita D, Kanaoka M: Relationship between social support, mental health and healh care consciousness in developing the industrial health education of male employees. *Journal of Occupational Health*. **2003** Nov;45(6):392-9

Gillen M, Baltz D, Gassel M, Kirsch L, Vaccaro D: Perceived safety climate, job demands, and coworker support among union and nonunion injured construction workers. *Journal of Safety Research*. **2002** Spring;33(1):33-51

Guo HR, Tanaka S, Halperin WE, Cameron LL: Back pain prevalence in US industry and estimates of lost workdays. *American Journal of Public Health*. **1999** Jul;89(7):1029-35

Gustavsen B: *Democratizing occupational health: The Scandinavian experience of work reform*. In Johnson JV & Johansson G(Eds.), *The psychosocial work environment and health: Work organization, democratization and health* (pp. 225-239). Baywood Publishing, Amityville (NY), **1991**

Halpern D: *Social Capital*. Polity Press, Cambridge, **2005**: 73-112

Hechanova-Alampay R, Beehr TA: Empowerment, span of control, and safety performance in work teams after workforce reduction. *Journal of Occupational Health Psychology*. **2001** Oct;6(4):275-82

Henderson M, Glozier N, Holland Elliott K: Long term sickness absence. *British Medical Journal* **2005**; 330: 802-3

Iwasaki M, Otani T, Sunaga R, Miyazaki H, Xiao L, Wang N, Yosiaki S, Suzuki S: Social networks and mortality based on the Komo-Ise cohort study in Japan. *International Journal of Epidemiology*. **2002** Dec;31(6):1208-18

Janssen N, Nijhuis FJ: Associations between positive changes in perceived work characteristics and changes in fatigue. *Journal of Occupational and Environmental Medicine*. **2004** Aug;46(8):866-75

Janssen N, van den Heuvel WP, Beurskens AJ, Nijhuis FJ, Schroer CA, van Eijk JT: The Demand-Control-Support model as a predictor of return to work. *International journal of rehabilitation research*. **2003** Mar;26(1):1-9

Johnson JV, Hall EM, Ford DE, Mead LA, Levine DM, Wang NY, Klag MJ: The psychosocial work environment of physicians. The impact of demands and resources on job dissatisfaction and psychiatric distress in a longitudinal study of Johns Hopkins Medical School graduates. *Journal of Occupational and Environmental Medicine*. **1995** Sep;37(9):1151-9

Johnson JV, Hall EM: Dialectic between conceptual and causal inquiry in psychosocial work-environment research. *Journal of Occupational Health Psychology*. **1996** Oct;1(4):362-74. Review

Kawachi I, Kennedy BP, Lochner K, Prothrow-Stith D: Social capital, income inequality, and mortality. *American Journal of Public Health*. **1997**; 87: 1491-98

Kawachi I, Kennedy BP, Glass R: Social capital and self-rated health: a contextual analysis. *American Journal of Public Health*. **1999**; 89: 1187-1193

Kawachi I, Kim D, Coutts A, Subramanian SV: Reconciling ther three accounts of social capital. *International Journal of Epidemiology*. **2004;**33(4):682-690

Kawachi I: Social capital and community effects on population and individual health. *Annals of the New York Academy of Science*. **1999**;896:120-30. Review

Kennelly B, O'Shea E, Garvey E: Social capital, life expectancy and mortality: a cross-national examination. *Social Science and Medicine*. **2003** Jun;56(12):2367-77

Kivimaki M, Ferrie JE, Head J, Shipley MJ, Vahtera J, Marmot MG: Organisational justice and change in justice as predictors of employee health: the Whitehall II study. *Journal of Epidemiology and Community Health*. **2004** Nov;58(11):931-7

Kuper H, Marmot M: Job strain, job demands, decision latitude, and risk of coronary heart disease within the Whitehall II study. *Journal of Epidemiology and Community Health.* **2003** Feb;57(2):147-53

Liukkonen V, Virtanen P, Kivimaki M, Pentti J, Vahtera J: Social capital in working life and the health of employees. *Social Science and Medicine*. **2004** Dec;59(12):2447-58

Lynch J, Smith GD, Hillemeier M, Shaw M, Raghunathan T, Kaplan G: Income inequality, the psychosocial environment, and health: comparisons of wealthy nations. *Lancet*. **2001** Jul 21;358(9277):194-200

Marmot M, Wilkinson R (eds): *Social Determinants of Health*. Oxford University Press, Oxford, **1999**

McEwen BS: Protective and damaging effects of stress mediators. *New England Journal of Medicine* **1999**; 338: 171-79

McEwen BS, Seeman T: Protective and damaging effects of mediators of stress. Elaborating and testing the concepts of allostasis and allostatic load. *Annals of the New York Academy of Science*. **1999**;896:30-47. Review

Melchior M, Niedhammer I, Berkman LF, Goldberg M: Do psychosocial work factors and social relations exert independent effects on sickness absence? A six year prospective study of the GAZEL cohort. *Journal of Epidemiology and Community Health*. **2003** Apr;57(4):285-93

Michie S, Williams S: Reducing work related psychological ill health and sickness absence: a systematic literature review. *Occupational and Environmental Medicine*. **2003** Jan;60(1):3-9

Murata K, Kawakami N, Amari N: Does job stress affect injury due to labor accident in Japanese male and female blue-collar workers? *Industrial Health*. **2000** Apr;38(2):246-51

Mustard CA, Vermeulen M, Lavis JN: Is position in the occupational hierarchy a determinant of decline in perceived health status? *Social Science and Medicine*. **2003** Dec;57(12):2291-303

Nakata A, Haratani T, Takahashi M, Kawakami N, Arito H, Fujioka Y, Shimizu H, Kobayashi F, Araki S: Job stress, social support at work, and insomnia in Japanese shift workers. *Journal of Human Ergology* (Tokyo). **2001** Dec;30(1-2):203-9

Ostry AS, Kelly S, Demers PA, Mustard C, Hertzman C: A comparison between the effort-reward imbalance and demand control models. *BMC Public Health*. **2003** Feb 27;3(1):10

Parker SK, Axtell CM, Turner N: Designing a safer workplace: importance of job autonomy, communication quality, and supportive supervisors. *Journal of Occupational Health Psychology*. **2001** Jul;6(3):211-28

Pearce N, Davey Smith G: Is Social Capital the Key to Inequalities in Health? *American Journal of Public Health.* **2003**. 93(1): 122-9

Penninx BW, van Tilburg T, Kriegsman DM, Deeg DJ, Boeke AJ, van Eijk JT: Effects of social support and personal coping resources on mortality in older age: the Longitudinal Aging Study Amsterdam. *American Journal of Epidemiology*. **1997** Sep 15;146(6):510-9

Putnam RD: *Bowling Alone: The Collapse and Revival of American Community*. Simon & Schuster, New York, **2000**

Putnam RD: Commentary: 'Health by association': some comments. *International Journal of Epidemiology*. **2004;**33(4):667–671

Rissen D, Melin B, Sandsjo L, Dohns I, Lundberg U: Surface EMG and psychophysiological stress reactions in women during repetitive work. *European Journal of Applied Physiology*. **2000** Oct;83(2-3):215-22

Rosengren A, Orth-Gomer K, Wilhelmsen L: Socioeconomic differences in health indices, social networks and mortality among Swedish men. A study of men born in 1933. *Scandinavian Journal of Social Medicine*. **1998** Dec;26(4):272-80

Schnorpfeil P, Noll A, Schulze R, Ehlert U, Frey K, Fischer JE: Allostatic load and work conditions. **Social Science and Medicine**. **2003** Aug;57(4):647-56

Sennet, R: *The Culture of The New Capitalism*. Yale University Press, New Haven and London **2006**. (Sennet, R: *Die Kultur des Neuen Kapitalismus*. Berlin Verlag, Berlin **2005**

Shigemi J, Mino Y, Ohtsu T, Tsuda T: Effects of perceived job stress on mental health. A longitudinal survey in a Japanese electronics company. *European Journal of Epidemiology.* **2000** Apr;16(4):371-6

Singer B, Ryff CD: Hierarchies of life histories and associated health risks. *Annals of the New York Academy of Science*. **1999**;896:96-115

Skrabski A, Kopp M, Kawachi I: Social capital in a changing society: cross sectional associations with middle aged female and male mortality rates. *Journal of Epidemiology and Community Health*. **2003** Feb;57(2):114-9

Soderfeldt B, Soderfeldt M, Jones K, O'Campo P, Muntaner C, Ohlson CG, Warg LE: Does organization matter? A multilevel analysis of the demand-control model applied to human services. *Social Science and Medicine*. **1997** Feb;44(4):527-34

Szreter S, Woolcock M: Health by association? Social capital, social theory, and the political economy of public health. *International Journal of Epidemiology.* **2004**; 33(4): 650-67

Theorell T: How to deal with stress in organizations?--a health perspective on theory and practice. *Scandinavian Journal of Work, Environment & Health*. **1999** Dec;25(6):616-24. Review

Tubach F, Leclerc A, Landre MF, Pietri-Taleb F: Risk factors for sick leave due to low back pain: a prospective study. *Journal of Occupational and Environmental Medicine*. **2002** May;44(5):451-8

Vahtera J, Virtanen P, Kivimaki M, Pentti J: Workplace as an origin of health inequalities. *Journal of Epidemiology and Community Health*. **1999** Jul;53(7):399-407

Veenstra G: Social capital and health (plus wealth, income inequality and regional health governance). *Social Science and Medicine*. **2002** Mar;54(6):849-68

Wickstrom GJ, Pentti J: Occupational factors affecting sick leave attributed to low-back pain. *Scandinavian Journal of Work, Environment & Health*. **1998** Apr;24(2):145-52

Wilkinson RG: Liberty, fraternity, equality. *International Journal of Epidemiology*. **2003**; 31: 538-543

Wilkinson RG: Health, Hierarchy, and Social Anxiety. *Annals of the New York Academy of Science*. **1999**; 896: 46-63

11 Conclusions from the Literature

The evidence from the literature suggests that high national wealth, low income inequality, hight percentage of secundary education, low unemployment rates, low inequality, low hierarchy, low (work) stress, high internal control, high social support are crucial factors that are responsible not only for good general health, but also for good occupational health.

Table 2 roughly summarizes the main influences and outcomes.

While individual level indicators are well established, efforts should be made to introduce and harmonize national (macro-level) and institutional (company-, mezzo-level) indicators especially for aspects of hierarchy, equality, autonomy (control) and social support, as these are the main factors associated with perceived stress.

Policy efforts should be directed to strengthening sources of social capital and reducing occupational hierarchies, external control, long work hours, inadequate workspeed, anonymity, fixed-term contracts, and focus on high job security, good working climate and consequently job satisfaction, while maintaining a low percentage of unemployment and low income inequality. However, one has to be careful with respect to bureaucracy, as big institutions are associated with strong hierarchies, and therefore with negative impacts on autonomy and internal control, but also provide resources for social contacts, social networks and hence can be regarded as sources of social capital. Policy makers might consider strengthening work forms that combine high autonomy with high participation.

Table 2: Summary of main findings, effects of variables, independently explaining SES differences with respect to occupational health

outcomes\due to influence	income (inequality)*	education	unemployment	stress	control	social support
mortality	++	- -	++	++	- -	- -
neoplasm	++	-	(+)	(+)		
chronic obstructive pulmonary diseases (COPD)	+	-	(+)	(+)		
wounds & injuries		- -	+	++		- -
diabetes II		-		(+)		
infant mortality	++	- -	+			
cardiovascular diseases (CVD)	++	-	++	++	- -	- -
substance related disorders	+		++	++	- -	- -
depression &mental disorders	(+)		++	++	-	- -
suicide	(+)		++	(+)		- -
HIV/AIDS	++	- -	++	(+)		- -

Legend:

++	strong evidence from the literature for a positive association
+	clear support for a positive association, but few publications
(+)	some support for a positive association, but few publications
- -	strong evidence from the literature for a negative association
-	clear support for a negative association, but few publications
(-)	some support for a negative association, but few publications
no entry	no support for an independent association, or no relevant literature found

*most of the associations reported from the literature within the time span used (1995-2005) are with respect to income inequality rather than absolute income (especially on aggregate levels), so the association, if published, will be positive.

ANNEX II: Stress and Stress Response – an Overview

ANNEX I: Table of Contents

1 General Issues

1.1 Stress hormones and proteins

The stress response can be described as an unspecific defence mechanism to support physical action – i.e. combat or escape. Hans Selye (1985) defined stress response as a set of phase-wise neuro-endocrine reactions, in which the sympathetic nervous system and the limbic-hypothalamic-pituitary-adrenal axis (HPA) are co-activated.

The primary stress response is initiated in the hypothalamus. Immediately after the hypothalamus receives an input from sensory nerves and chemical mediators reporting the presence of stressors, it starts to secrete corticotrophin-releasing factor (CRF). The CRF stimulates the pituitary gland to release a number of stress hormones, most notably adrenocorticotropic hormone (ACTG), enkephalins and endorphins.

In the stress-response continuum, adrenocorticotropic hormone induces downstream release of cortisol from the adrenal cortex and aldosterone from the adrenal medulla. Aldosterone is a mineralocorticoid that acts to retain sodium and water. This provides increased blood pressure, in unison with the renin-angiotensin system during the stressful experience.

Cortisol – a glucocorticoid – stimulates glucose release into the serum from the stored glycogen in the liver and from the conversion of amino acids and fats. In skeletal muscle, cortisol facilitates the breakdown of proteins to amino acids, which are then carried to the liver. Therefore, plasma osmolarity is increased. Thus, in turn, pulls intracellular fluid into the circulating plasma, increasing blood pressure and cardiac output (Stanford 1994). Cortisol – together with aldosterone – enhances fluid retention, further increasing blood pressure.

On the other hand, cortisol has a major role in suppressing the inflammatory and immune responses. It acts to decrease the number of circulating white blood cells (leucocytes) and inhibits migration of leucocytes to the site of infection by decreasing capillary permeability and inhibition chemotaxis (Guyton & Hall 1996 p957-970; Lusk & Lash 2005). Cortisol also stabilises lysosomal membranes, thus preventing release of their infection-fighting proteolytic enzymes. Furthermore, cortisol inhibits the release of inflammatory substrates – such as histamine and prostaglandins – decreases fibroblast proliferation and function at the site of injury, and depresses phagocytosis (Guyton & Hall 1996 p957-970; Shelby & McCanse 2002 p272-289). Finally, increased cortisol levels also inhibit production of some cytokines – interleukins – which are essential for inflammatory and immune response (Stanford 1994).

Cytokines are soluble mediators released by various cells both at the periphery by macrophages and lymphocytes and in the brain by astrocytes and microglia.

At the same time, the so-called acute phase reactants are produced in liver in the early phase of stress. They include α_1-antitrypsin and α_2-antitrypsin, which protect normal tissues from inflammatory mediators, α_1-acid glycoprotein, C-reactive protein, haptoglobin, fibrinogen, fibrinogen-stabilising factor, and cold-insoluble globulins (Stanford 1994).

On another front, the sympathetic division of the autonomous nervous system stimulates the release of epinephrine from the adrenal medulla. Essentially, this is an extension of the sympathetic nervous system. Norepinephrine is released by the peripheral nerve endings. Both of these chemicals increase myocardial contractility, heart rate and venous return through peripheral vasoconstriction of arteriole smooth muscle, leading to an enlarged cardiac output. Epinephrine also stimulates the pancreas to produce increased glucagon and decreased insulin, to further raise blood glucose (Shelby & McCanse 2002 p272-289).

Catecholamines, cortisol, glucagon, and some cytokines collectively promote hyperglycemia through insulin resistance.

In sum, the acute stress response increases blood flow to the brain and other vital organs, whereas blood flow to the periphery is decreased. Therefore, there is a hypermetabolic state with lipolysis, protein degradation and gluconeogenesis.

Table 1 presents the list of major stress-related hormones and their effects.

Selye (1985) has identified three stages of stress reactions:

(1) The Alarm Reaction is equivalent to fight-or-flight response. It is an immediate reaction to acute stress. Alarm mobilises bodily energetic resources and maximises the expenditure of energy (“attack mode”).

(2) The Stage of Resistance is a continued state of arousal. If the stressful situation is prolonged, the high level of hormones during the resistance phase may upset homeostasis and harm internal organs leaving the organism vulnerable to disease. There is evidence from animal research that the adrenal glands actually increase in size during the resistance stage, which may reflect the prolonged activity.

(3) The Exhaustion Stage occurs after prolonged resistance. During this stage, the body's energy reserves are finally exhausted and breakdown occurs.

Table 1: Major stress-related hormones and their effects

Stress hormones	Source	Major effects
Adrenocorticotropic hormone (ACTG)	Anterior pituitary	Stimulates adrenal cortex to release cortisol
Catecholamines (epinephrine, norepinephrine, adrenaline)	Adrenal medulla and the sympathetic nervous system	Increases overall strength, blood flow to vital organs, gluconeogenesis. Increases myocardial contractility (inotropic effect), heart rate (chronotropic effect), venous return to the heart and cardiac output. Constricts smooth muscle in all blood vessels, increases blood pressure, dilates pupils, inhibits gastrointestinal activity
Cortisol	Adrenal cortex (following stimulation by ACTG from the anterior pituitary)	Gluconeogenesis; hyperglycemia; decreases protein synthesis, number of lymphocytes and leukocytes (at inflammatory site); promotes muscle and lymphoid tissue catabolism; delays healing; suppresses cell-mediated immune response
Antidiuretic hormone	Posterior pituitary	Increases water retention
Aldosterone	Adrenal cortex	Increases sodium and water retention
Growth hormone (somatotropin)	Anterior pituitary	Increases immune function; levels are increased during acute stress; chronic stress is associated with inhibition of growth hormone secretion
Prolactin	Anterior pituitary	β -cell activation and differentiation, levels can be increased during acute stress but decreased during the chronic stress
Testosterone	Testis	Regulates male secondary characteristics, levels are reduced during chronic stress
Endorphins	Anterior pituitary	Endogenous opiate; elevated during stress, downregulate pathways to the stress response
Enkephalins	Adrenal medulla	Endogenous opiate; elevated during stress, downregulate pathways to the stress response

Source: adapted from Lusk & Lash (2005)

In accordance with Selye's ideas, there is evidence of decreased levels of some major stress hormones under chronic stress. For instance, a glucocorticoid corticosterone – which structure and effects are similar to cortisol – appeared to have significantly lower basal concentrations and reduced responses to acute stress, when animals were chronically stressed (Rich & Romero 2005).

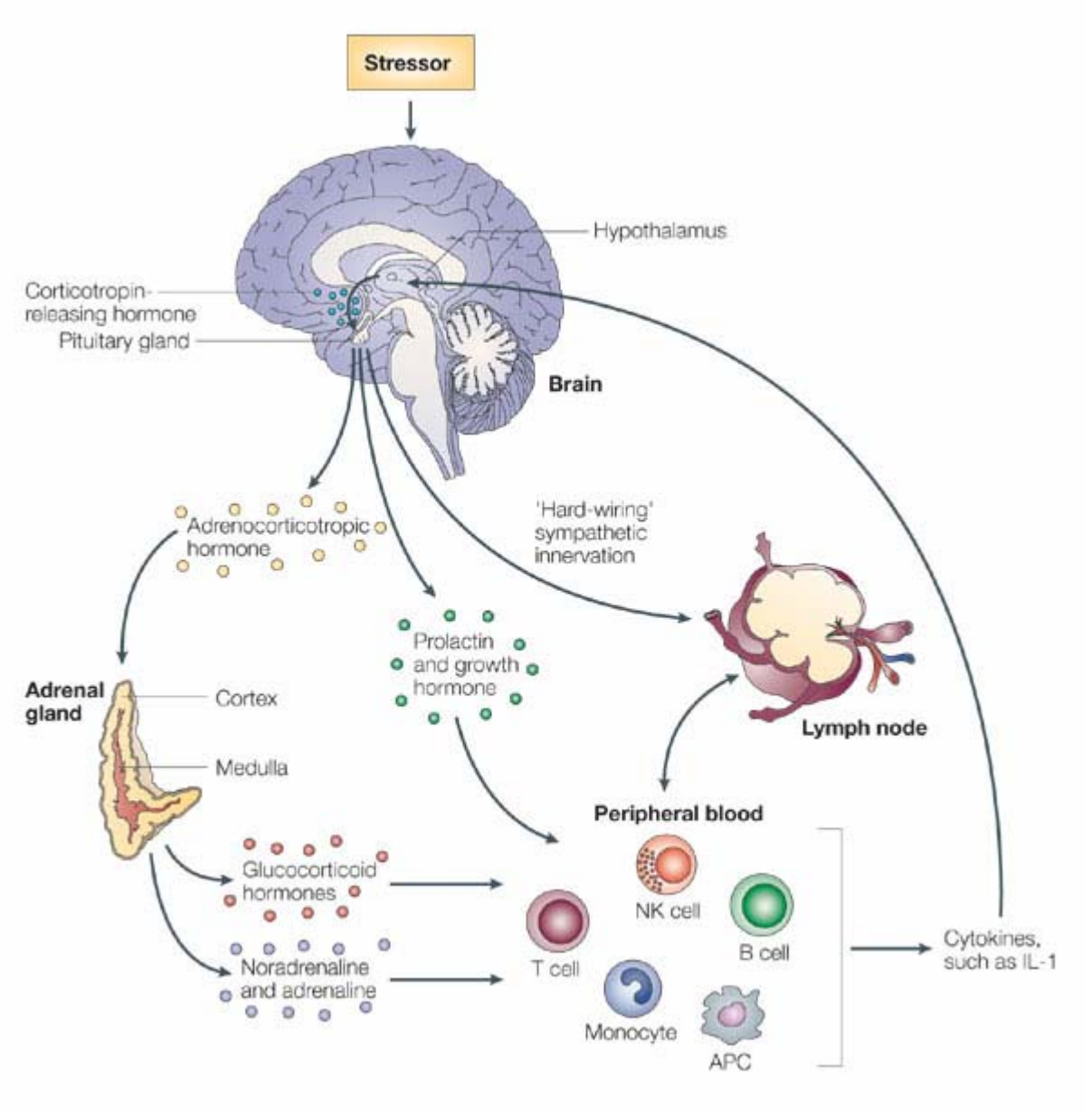
In recent properly controlled human study designs – which took into account the circadian fluctuations in cortisol secretion, age, sex, medication, smoking habits and wake-up times – there was a blunted cortisol awakening response in patients with posttraumatic stress disorders (PTSD) (Wessa et al 2006). In addition, this has also been reported for patients with chronic fatigue syndrome (Roberts et al 2004) and with uni- or bilateral lesions of the hippocampus (Buchanan et al 2004; Wolf 2005).

Therefore, cortisol – together with other hormones of the hypothalamic-pituitary-adrenal axis – has been widely investigated in both animal and human studies as an important stress-related biological marker (Hasson et al 2005; Glaser & Kiecolt-Glaser 2005)

1.2 Stress-induced immune changes

Stress hormones can induce quantitative and qualitative changes in immune function. Almost all immune cells have receptors for one or more hormones associated with the hypothalamic-pituitary-adrenal (HPA) or sympathetic-adrenal-medullary (SAM) axis.

Figure 1: Stress-associated modulation of the hormone and immune response by the central nervous system



APC – antigen-presenting cell
IL-1 – interleukin-1
NK – natural killer

Source: Glaser & Kiecolt-Glaser (2005)

The neuro-endocrine and immune systems share, therefore, common signal mediators and receptors, suggesting that the brain has an immunoregulatory role and the immune system – a sensory function. In mice, the interaction with the immune system involves most of the brain, where high to moderate densities of receptors for cytokines (interleukin 1) have been detected (Reiche 2004).

Experiencing a stressful situation, as perceived by the brain, results in the stimulation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medullary (SAM) axis. The production of adrenocorticotropic hormone by the pituitary gland results in the production of glucocorticoid hormones. The SAM axis can be activated by stimulation of the adrenal medulla to produce the catecholamines adrenaline and noradrenaline, as well as by "hard-wiring", through sympathetic-nervous-system innervation of lymphoid organs.

Leukocytes have receptors for stress hormones that are produced by the pituitary and adrenal glands and can be modulated by the binding of these hormones to their respective receptors. In addition, noradrenaline produced at nerve endings can also modulate immune-cell function by binding its receptor at the surface of cells within lymphoid organs.

In general, immune modulation by stress hormones might act through two pathways: directly, through binding of the hormone to its cognate receptor at the surface of a cell; or indirectly – for instance, by inducing dysregulation of the production of cytokines, such as interferon-γ (IFN-γ), interleukin-1 (IL-1), IL-2, IL-6 and tumour-necrosis factor (TNF).

These interactions are bidirectional in that cytokines produced by immune cells can modulate the activity of the hypothalamus. For example, IL-1 influences the production of corticotropin-releasing hormone (CRH). In turn, CRH can affect the HPA axis and thereby trigger increases in stress hormone levels, which result in dysregulation of immune function. In addition, lymphocytes can synthesise hormones such as ACTH, prolactin and growth hormone (Glaser & Kiecolt-Glaser 2005).

Therefore, there are different pathways through which stressors might affect immune function. Many researchers are now focussing their efforts on immune-system-to-brain communication and how the activation of inflammatory-cytokine networks might shape mood, cognition and behaviour (Capuron et al 2004; Maier 2003). Table 2 summarises the effects of hormones and immune cells interactions.

Table 2 Interactions of hormones and immune cells

Hormone	Expression of receptors by immune cells	Examples of effects on cell function
Glucocorticoids	T and B cells, neutrophils, monocytes and macrophages	Inhibit inflammation; inhibit the production of IL-12 by antigen-presenting cells; induce a shift from production of $T_H 1$ to $T_H 2$ cytokines
Substance P	T and B cells, eosinophils, mast cells, monocytes and macrophages	Stimulates mitogen-induced blastogenesis; increases trafficking of cells from lymph nodes to peripheral blood; stimulates monocytes to produce several cytokines, such as IL-1, IL-6 and TNF
Neuropeptide Y	T and B cells, dendritic cells, monocytes and macrophages	Can downregulate antibody production to T-cell-dependent antigens by its effect on dendritic cells, and T and B cells
Corticotropin-releasing hormone	T-cells, monocytes and macrophages	Increases production of IL-1 by monocytes; evidence for autocrine and/or paracrine modulation of inflammation
Prolactin	T and B cells, granulocytes, NK cells, monocytes and macrophages	Can stimulate lymphoid-cell clonal expansion; might function as an in vitro co-mitogen for NK cellsand macrophages
Growth hormone	T and B cells, monocytes and macrophages	Helps to maintain competence of T and B cells and macrophages; stimulates antibody production and NK-cell activity
Catecholamines (adrenaline and noradrenaline)	T and B cells, NK cells, monocytes and macrophages	Induce a shift to a $T_H 2$ response, involving antigen-presenting cells and $T_H 1$ cells
Serotonin	T and B cells, NK cells, monocytes and macrophages	Modulates the synthesis of IFN-γ by NK cells; stimulates the production of IL-16 (a chemotactic factor) by T cells

Source: Glaser & Kiecolt-Glaser (2005)

1.3 Stress and genetic changes

Poor immune function might have consequences at the molecular level in terms of the speed and quality of deoxyribonucleic acid (DNA) repair. These mechanisms are assumed to mediate an increased cancer risk (Kiecolt-Glaser et al 1985; Cohen et al 2000; Reiche et al 2004). If DNA damage goes unrepaired, the damaged cells may proliferate, leading to carcinogenesis. Therefore, DNA repair is crucial to maintaining a normal cell cycle. Several research groups have tried to examine the effects of stress on DNA damage or DNA repair capacity.

Thus, Kiecolt-Glaser and co-authors (1985) compared 28 non-psychotic, non-medicated new psychiatric patients with 28 blood-bank controls matched by age and gender. After exposure to x-radiation, peripheral blood leucocytes of psychiatric patients showed greater impairment of DNA repair. The high-distress subgroup of patients demonstrated a significantly worse repair of damaged DNA than low-distress subjects.

By contrast, DNA repair capacity was positively associated with levels of perceived stress in sixteen healthy medical students (Cohen et al 2000). The psychological and physiological

responses measured during the exam block were compared to a time of low stress after a vacation. The authors used a host-cell reaction assay to assess the DNA repair capacity.

How can we explain these contradictory findings? There are some important methodological differences between these studies – such as, characteristics of the populations, assays used to measure DNA repair, and the effects of acute versus chronic stress. Irrespective of the interpretation of these results, both studies suggest that psychological factors have an effect on DNA repair.

Other biological processes may also be relevant to explain the variations in outcomes of some types of cancer – for instance, increases in DNA damage and inhibition of apoptosis. Apoptosis is an important defence mechanism against the development of malignant cells. It acts via genetically programmed alterations in cell structures which lead to failure in proliferation and differentiation. Eventually, it may result in cell death. Apoptosis is induced by a variety of toxic insults including growth factor deprivation and ionizing radiation. This process may protect against the appearance of heritable phenotypic changes in cells; it might be a critical factor in normal cellular immune function.

Tomei and colleagues (1990) demonstrated that an acute psychological stress – i.e. taking examinations – may induce physiological changes regulating the ability of immune cells to initiate apoptosis. In this study, peripheral blood leukocytes were treated with phorbol ester to inhibit gamma-radiation-induced apoptosis. Lymphocyte death was decreased during examination compared with a lower stress baseline.

1.4 Stress, neuro-anatomic changes and aging

For decades, it was assumed that the adult brain did not produce new neurons, at least to any great extent (Altman & Das 1965; Rakic 2002). However, numerous studies now succeeded to reveal that adult brain – including the human – continues to produce new neurons throughout life (Cameron et al 1993; Eriksson et al. 1998; Gould et al 1999; Shors 2005). Most of these cells seem to be generated in the hippocampal formation, a brain structure intimately involved in some aspects of learning, notably those related to formation of declarative or episodic memory (Fortin et al 2002; Squire & Zola 1996).

Evidence from human neuroimaging studies has suggested areas of the brain that may be damaged by an intensive distress and posttraumatic stress disorders (PTSD). The most replicated findings include hippocampal volume reduction, as well as decreased functions of amygdala and some portions of the frontal lobe (Hull 2002; Bremner 2002). These findings

may have important implications for cognitive functioning of people affected by the traumatic experiences (Horner & Hamner 2002; Bremner 2003).

Different types of stressful experiences decrease cell proliferation (Cameron & Gould 1994) as does normal aging (Cameron & McKay 1999). In a recent study, Epel and colleagues (2004) provided evidence that psychological stress is significantly associated with accelerated aging. In particular, the authors investigated the determinants of cell senescence and longevity in peripheral blood mononuclear cells from healthy premenopausal women. Women with the highest levels of perceived stress had telomeres shorter on average by the equivalent of at least one decade of additional aging compared to low stress women. It remains to be discovered whether these cellular markers of aging affected by stress are restricted to blood cells.

Therefore, distress may promote earlier onset of age-related diseases and memory deficits.

1.5 How is stress assessed?

When events or environmental demands exceed an individual's ability to cope, the ensuing psychological stress response typically includes negative thoughts and emotions (Cohen et al 1991; Glaser & Kiecolt-Glaser 2005). Various studies of stress and its health consequences often use measures of negative mood that assess symptoms of general distress, anxiety or depression.

Researchers might also assess the number and type of recent significant stressful life changes, or they might ask participants to rate their perceptions of stress on a scale by answering certain questions. Here are some examples of such questions:

- How frequently in the past week did you feel you could not control important things in your life?
- How often did you feel that things were piling up so high that you could not overcome them (Cohen et al 1991)?

In addition, researchers often examine the psychological and immunological responses of individuals who are experiencing an acute distress-generating event, like examination or divorce, or a more chronic stressor – such as, caring for a spouse with Alzheimer's disease (Segerstrom & Miller 2004). Other commonly studied long-term stressors include "burnout" at work, job strain, unemployment, isolation, exposure to a hostile climate (Mehta et al 2000), and pressures as home – e.g., conflicts, arguments, responsibilities and finances.

Traumatic events of an exceptionally threatening or catastrophic nature have been extensively studied in relation to various mental health and immunological responses. In the past, stress following trauma was associated mainly with combat-related events and was called: “shell shock”, “combat neurosis”, “soldier’s heart” or “operational fatigue” (Zohar et al 1998). Later it become evident: even non-combative events can cause similar responses, termed as “traumatic neurosis” or “post-traumatic stress disorders” (PTSD). Such events may include a severe automobile accident, violent personal assault – e.g., rape, physical attack, robbery – terrorist attack, natural or man-made disaster, witnessing serious injury or death due to any of the above, as well as other situations, such as being kidnapped or being held hostage.

Adverse immunological changes have been documented for weeks and months following natural disasters – e.g., earthquakes and hurricanes, with more persistent immune dys-regulation among those who suffered greater personal losses (Ironson et al 1997).

Stressors that are perceived as unpredictable and/or uncontrollable might continue to be associated with increased levels of stress hormones, even after repeated exposures (Delahanty et al 2001 p335-348). The ability to “unwind” after stressful events – i.e. to return to one’s neuro-endocrine baseline in a relatively short time – is thought to influence the total burden that stressors place on an individual (Lundberg & Frankenhaeuser 1999).

There has been relatively little research that directly examined a “cross-over” of different stressors – for instance, home/work stresses (Kalia 2002). Recent theory suggests that an individual’s situation at home can influence performance at work.

The definition of stressors should include careful, behaviourally anchored terminology. When measuring the stressor, the exposure should be measured independently of the symptoms exhibited in reaction to the exposure. In addition, the timing and intensity of the exposure should be determined since the reaction might occur long after the initial exposure.

Although work stress is one of the most commonly examined form of stress, other types of stressors – such as home stress, trauma leading to PTSD and adjustment disorders – need to be included in any comprehensive analysis of stress-related outcomes (Kalia 2002).

2 Health Consequences

2.1 Burden of psychological distress

Stress is often considered as a modern day hidden epidemic. Its outcomes and related comorbide conditions are responsible for a large proportion of disability worldwide. The World Health Organisation (WHO) Global Burden of Disease Survey estimated that mental diseases, including stress-related disorders, will be highly prevalent and will become the second leading cause of disabilities by the year 2020 (WHO 1996).

It has been consistently demonstrated that individuals with stress and related disorders experience impaired physical and mental functioning, more work days lost, increased impairment at work and a high use of health care services. The disability caused by stress is just as great as the disability caused by workplace accidents or other common medical conditions – such as hypertension, diabetes and arthritis (Kalia 2002). Therefore, the problem of early recognition and management of stress is extremely relevant.

Stress-related disorders have a considerable negative economic impact. In the United Kingdom, the Mental Health Foundation reports that stress costs British industry 3 billion British pounds annually (The Mental Health Foundation 2001).

In France, 1.3-1.7 percent of the working population was affected by illnesses attributable to work-related stress in 2000. These illnesses included cardiovascular diseases, depression, musculoskeletal diseases and back pain. Work-related stress cost the French society between Euro 1 167 million and Euro 1 975 million – or 14.4-24.2% of the total spending of social security occupational illnesses and work injuries branch (Bejean & Sultan-Taieb 2005).

In the United States, stress-related disorders cost the nation more than 42 billion dollars each year. More than half of that is due to the repeated use of health care services. People suffering from stress-related illnesses are 3 to 5 times more likely to visit the doctor and 6 times more likely to be hospitalised than non-sufferers. Approximately 43% of these people are depressed or have alcohol or substance abuse problem (Kalia 2002).

In addition, there are sunk costs of stress-related disorders, which include substantial losses of human lives. In 2000, more than 2 300 deaths cases in the French working age population have been attributed to occupational stress (Bejean & Sultan-Taieb 2005).

Psychosocial stress is regarded in the epidemiologic literature as a key factor in the transition mortality crisis. This epidemic upsurge in mortality occurred recently in the former socialist

countries of Central and Eastern Europe, including the new Member States of the European Union – e.g., Estonia, Latvia and Lithuania. The estimates of excess deaths oscillate around 3 million people during the period 1989-1996 (Cornia 2000 p63).

In all transitional countries, mortality fluctuations are largely attributed to changes in cardiovascular and violent death levels – i.e. stress-related conditions. The major mortality fluctuations were concentrated around the most difficult years of important socio-economic changes. First of all, the mortality crisis affected working age population – particularly men. The underlying causes of stress are related to large unanticipated changes – like unemployment and reallocation of labour under difficult circumstances, migration and shifts in social hierarchies (Cornia 2000 p77-80).

2.2 Stress and cardiovascular diseases

Cardiovascular mortality has been often used as the index rapidly reacting to socio-economic changes and related psychological stress (Denisova et al 2005; Kalediene & Petrauskiene 2004). This cause-of-death category represents “Killer No. 1” both in the industrialised countries with developed market economies and in transitional countries. At present, there is sufficient evidence to accept that psychological stress is associated with cardiovascular diseases.

Acute stress of high intensity may trigger transient myocardial ischemia or infarction, ventricular arrhythmia and sudden cardiac death. After an earthquake, the number of hospital admissions for acute myocardial infarction increases by about 35% (Lampert et al 2000). In young men (before 55 years), high level of anger in response to stress is associated with an increased risk of subsequent premature cardiovascular diseases – particularly, myocardial infarction. These results were obtained in a prospective study with a median follow-up period of 36 years (Chang et al 2002).

Reacting with anger can also detonate stoke. In a longitudinal study, anger was significantly associated with an increased risk of incident stroke among younger participants and those with higher cholesterol levels. This relationship persisted after a multivariate adjustment for the established biological and socio-demographic stroke risk factors (Williams et al 2002).

Psychosocial stress has been intensively examined as a known risk factor for myocardial infarction. In a large case-control multicenter INTERHEART study involving 24 767 people from 52 countries, presence of psychosocial stressors was significantly associated with

increased risk of acute myocardial infarction. These relationships were consistent across regions, in different ethnic groups, and in men and women (Rosengren et al 2004).

In the famous prospective Framingham study, a significant relation between psychosocial stress factors and the 20-year incidence of myocardial infarction or coronary death has been found for women (Eaker et al 1992).

A well-known association between educational attainment and coronary heart disease has been consistently reported. However, much of the increased risk of coronary heart disease in people with low education appears to be linked to psychosocial stress and lifestyle factors (Wamala et al 1999).

Vale (2005) reviewed reports on chronic psychosocial stress associated with cardiovascular diseases (Table 3).

Table 3 Chronic psychosocial stress (PSS) associated with cardiovascular diseases (CVD)

PSS associated to CVD	Mediator mechanisms proposed	References
Work stress: – High effort and few reward – Exhaustive coping style (competitive)	 – Increased body mass index and cholesterol concentration – Impaired fibrinolitic capacity	 – Kuper et al (2002); Kivimäki et al (2002) – Vrijkotte et al (1999)
Home stress: – Marital dissolution in women – Care-giving for a spouse with dementia	 – Mental stress no otherwise specified – Mental stress no otherwise specified	 – Orth-Gomer et al (2000) – Lee et al (2003)
Social isolation (and self-neglect)	Hyperfibrinogenaemia and hypercortisolism	Brummett et al (2001); Steptoe et al (2004);House (2001)
Low income (poverty)	Blunted serotonergic responsivity	Matthews et al (2000); Woodward et al (2003)
Chronic emotional disorders: – Anxiety – Hopelessness* – Hopelessness plus depression – Depression	 – Low grade inflammation and atherosclerosis – Autonomic dysfunction (vagal withdrawal) – Low grade inflammation and atherosclerosis – Low grade inflammation and atherosclerosis	 – Strike & Steptoe (2004) – Schwarz et al (2003) – Stern et al (2001) – Strike & Steptoe (2004)

* Hopelessness may reflect a current or past “life situation” or can be a symptom of depression
Source: Vale (2005)

The main pathophysiological mechanisms linking mental stress to cardiovascular diseases differ for acute and chronic stress.

In the case of an intense acute stress, a rapid increase of arterial pressure and heart rate occurs – by means of augmented sympathetic activity and vagal withdrawal. Higher blood

pressure and heart rate cause a higher demand for oxygen in the myocardium. In people affected by atherosclerosis, there is an impaired vascular endothelium response, which may predispose blood vessels to spasm and favour the development of acute ischemia.

In addition, acute stress induces activity of blood clotting factors and platelets. There is a clustering of thrombotic risk factors, which might result in circulatory occlusive effects.

Further, these effects may be coupled with transitory endothelial dysfunction inducing prothrombotic changes in the disrupted atherosclerotic plaques. Finally, acute stress causes modifications in the immune status (Vale 2005). However, the cardiovascular consequences of these changes become more obvious if the psychological stress persists. In sum, acute stress might favour the development of an acute vascular damage. These outcomes take place mostly in people already suffering from atherosclerosis.

During a chronic stress, the onset and course of cardiovascular diseases appear as a result of the psychosocial insult, sometimes concurring with other risk factors – for instance, those lifestyle-related. Nevertheless, cardiovascular outcomes develop not in all stressed people. There is an important biological reason behind the differential responses to chronic stress. Namely, stress-induced alterations in the endocrine and immune system can be skewed towards immunosuppression or towards the inflammatory side. Some individuals are prone to immune hyper-reactivity, a low grade chronic inflammation and atherosclerotic complications.

Since there are differences in chronic stress response, not all prospective studies have reported a significant relation between psychological stress and ischemic heart disease (Vale 2005). Researchers are looking for specific biological markers to stratify adequately individuals with a chronic stress who are susceptible to suffering a low grade chronic inflammation and a severe cardiovascular disease. However, a definite systematic approach has not been yet elaborated.

To make the story about chronic stress even more complicated, it should be mentioned that chronic stress presents itself in clusters. Poverty, a known risk factor for stress, is an example of the cumulative burden that may overcome the human capacity of tolerance. It may exert its effects by creating non-satisfactory conditions for living, family disruption, unemployment and hostile neighbourhoods. At the same time, poverty might promote unhealthy activities like misuse of alcohol or drug abuse, criminal behaviours and other risks. On the biological side, malnutrition during poverty can produce depression (Bottiglieri et al 2000; Corwin 2003) with a synergistic effect for stress responses.

The impact of chronic stress on cardiovascular outcomes may be substantially mediated by other comorbide conditions. Chronic cortisolaemia in the stress range redistributes stored fat toward an intra-abdominal reserve, resulting thereby in abdominal obesity. On one hand, this happens due to bulimia caused by glucocorticoids. On the other hand, visceral fat tissue has more cells per mass units, higher blood flow and more glucocorticoid receptors than subcutaneous fat. Abdominal obesity represents an important risk factor associated with atherosclerosis, as the intra-abdominal adipose tissue is an essential source of the pro-inflammatory cytokine interleukin 6 (Fried et al 1998). Additionally, stress hormones cause salt retention, insulin resistance, and higher concentrations of low-density lipoprotein (LDL) cholesterol. Most of these effects are also atherogenic (Chrousos & Gold 1998).

Deregulated responses to a chronic stress may also include other specific and non-specific conditions, which are known to be risk factors for cardiovascular diseases. For instance, some of the circulating pro-inflammatory cytokines cause a systemic syndrome – anorexia, fatigue, asthenia, somnolence and fever – collectively identified as sickness syndrome (Vale 2005). Another glaring example is depression – a possible consequence and source of chronic stress, increasing mortality due to cardiovascular diseases (Lesperance et al 2004).

In conclusion, stress is probably a mediator or moderator risk factor in the chain of causal factors for cardiovascular diseases.

2.3 Stress, immune dysfunction and cancer

At present, the complex associations between physical health and stress are still poorly understood. Although studies have shown that stress alters the way the immune system functions[1], they have not provided sufficient evidence of a direct causal relationship between these immune system changes and cancer onset.

On the basis of speculation that chronic inflammation might be a contributing factor in up to 15% of all cancer cases (Marx 2004), stress-induced increases in the inflammatory response could be a broader pathway that links stress with cancer. Other possible pathways linking stress and cancer include genetic alterations - e.g., increases in DNA damage, poor DNA repair and inhibition of apoptosis[2].

Reiche and colleagues (2004) reviewed the possibility that stress-related physiological changes could be the key factors in cancer risk and progression. The authors referred to the

[1] see Section 1.2 – stress-induced immune changes
[2] see Section 1.3 – stress and genetic changes

studies, in which innate lymphocytes of stress-exposed animals had a reduced ability to kill foreign target cells. Decreased activity of natural-killer (NK) cells is discussed as one of the primary mediators of the tumour-enhancing effects of stress. Rats unable to escape from electric shock had earlier tumour appearance, enlarged tumours, and decreased survival time compared with those which could escape.

Suppressed immunity has also been reported in humans after severe psychological stress – for instance, depressed lymphocyte function, their suppressed stimulation and reduced NK activity after conjugal bereavement (Bartrop et al 1977; Schleifer et al 1983; Irwin et al 1988). Women who were separated from their husbands had significantly poorer immune function than did socio-demographically matched married women, with impaired proliferation in response to mitogens, lower proportion of NK cells and helper T-cells, and higher antibody titres to Epstein-Barr virus capsid antigen (Kiecolt-Glaser et al 1987).

Lower NK-cell activity is one of the most consistent observations reported in studies of depression and immunity in adults and children (Schleifer et al 1996).

Despite the numerous reports documenting alterations of immune and genetic parameters after a severe stress, there are only few notions about an increased occurrence of incident malignant diseases in prospective human studies. One of these notions concerns a cohort of 6284 Jewish Israelis who lost an adult son. In this cohort, there was an increased incidence of lymphatic and haematological malignancies and melanomas after 20 years of follow-up – compared to non-bereaved members of the population. Accident-bereaved parents also had an increased risk of respiratory cancer. The survival study showed that the risk of death was increased by bereavement if the cancer had been diagnosed before the loss, but not after (Levav et al 2000).

The relation between stressful life experiences and breast cancer has been frequently examined. However, these research efforts did not result in a certainty about the role of any specific factor. A retrospective study of Roberts and co-authors (1996) did not confirm any important association between self-reported stress factors and breast cancer. A meta-analysis concluded that the few well-designed studies that have been done failed to find evidence of a link (Petticrew et al 1999). The results of a more recent meta-analysis including studies carried out between 1966 and December 2002 (Duijts et al 2003) also did not support an overall association between stressful life events and breast cancer risk. Only a modest association between death of spouse and breast cancer risk has been identified. A prospective study of Graham and colleagues (2002) failed to confirm that severely stressful life events increase the risk of breast cancer relapse.

In general, the effects of psychological stress factors have been more convincingly shown for cancer progression than for cancer initiation. Thus, stress reduction through social support, presence of social network or psychological intervention has been found to increase survival time and decrease the rate of metastases (Spiegel et al 1989; Garssen & Goodkin 1999; Reiche et al 2004).

Conflicting results on the association between tumour development and psychological stress might be explained by the variations in stress chronicity, timing of stress and types of tumours. Cancers induced by chemical carcinogens might be less responsive to psychological factors than those associated with a DNA tumour virus, retrovirus insertion near a cellular oncogene or other viruses, such as Epstein Barr virus (Reiche et al 2004).

2.4 Stress, mental health and behavioural problems

The group of mental stress-related disorders is very large and heterogeneous. They are frequent in general populations and associated with a wide range of disabilities and functional impairment. Depending on case definition and instruments used, one in four or one in ten meets the criteria for any mood or anxiety disorder throughout life (Alonso et al 2004).

Mental and behavioural disorders result in increased suicide risk. Approximately 60% of suicides are related to depressions (Bejean & Sultan-Taieb 2005). This figure testifies that depressive disorders are poorly diagnosed and insufficiently treated in general populations, despite the availability of successful therapeutic regimens – psychotherapy, drugs or both.

In the research literature, depression is commonly regarded as a deregulated response to a chronic distress. Psychosocial stressors are associated with the onset, symptom severity and course of major depressive disorders (Burke et al 2005). The abnormal functioning of hypothalamic-pituitary-adrenal axis (HPA) – assessed through the levels of stress hormones3 – is a very common finding in depressed patients, along with serotonergic abnormalities (Sher & Mann 2003 p300-315).

Few human diseases are as painful as depression – due to its inherent subjective burden of suffering, possible chronicity and a frequent occurrence of comorbide conditions – e.g., cardiovascular diseases. Many depressed patients continue aging with cognitive problems or cerebral vascular damage related to their unrelieved depressive states (Vale 2005).

[3] see Section 1.1 – stress hormones and proteins

Quite often, depressions precede the onset of post-traumatic stress disorders (PTSD). They might also coexist with PTSD or develop subsequently. PTSD is a pathological protracted response to a severely traumatic event. Most people experience at least one significant traumatic event over the course of their lives, but only a few succumb to PTSD (Breslau 2002).

Women are at a higher risk for PTSD than are men, following exposure to traumatic events. Approximately 5% of men and 10-12% of women suffer from PTSD sometime in their lives; for victims of traumas such as rape, the rate may be as high as 60% to 80%. For at least a third of sufferers, PTSD is a persistent condition lasting many years. Yet, most patients are not being diagnosed and, consequently, not being treated. Many trauma victims also experience marital, occupational, financial and health problems. They are disproportionate users of the health care system. This results in a considerable economic burden for the affected individuals, for the health care system and society as a whole (Solomon & Davidson 1997).

Recent findings of biological alterations in PTSD delineate that this condition is associated with distinct, often circumscribed alterations in the same hormonal, immune, neurochemical, and physiological systems involved in other stress-related somatic and psychiatric illnesses (Yehuda 2002).

Severely stressful life events have been shown to predispose individuals to both psychoses and substance abuse. The latter is more prevalent among people who report histories of physical and sexual abuse as well as other early adverse events during childhood (Scheller-Gilkey et al 2004).

However, current physical, social and emotional stress might also facilitate initiation and maintenance of alcohol and drug abuse, as well as a precipitation of relapse. These effects have been repeatedly confirmed in both animal and human research (Suwaki et al 2001; Stewart 2003; Walter et al 2005). They seem to be related to the same brain systems which are involved in other stress-related conditions – the corticotrophin-releasing factor (CRF) and noradrenergic (NA) systems. In general, drug or ethanol use can be regarded as a form of self-medication for stress-related emotional and physical discomfort.

Repeated exposure to a psychoactive substance can cause the development of dependence syndrome, which is characterised by behavioural, cognitive, and physiological phenomena, including a strong desire to take the substance, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to substance use than to other activities and obligations, increased tolerance, and a physical withdrawal state.

Similarly to stress, the withdrawal from alcohol, cannabioids and cocaine is accompanied by the increased CRF-release (Suwaki et al 2001). Alcohol withdrawal is associated with painful symptoms – such as, anxiety and negative depression-like affect. Since stress might induce these symptoms in abstinence, it can be perceived by abstinent alcoholics as a withdrawal. Therefore, stress enhances the likelihood of relapse – and with relapse an inability to limit an abusive pattern of alcohol intake (Breese et al 2005). A vicious circle begins, perpetuating distress and reinforcing the anxious or depressive symptoms related to emerging distress syndromes. The progression of alcoholism is frequently associated with comorbide conditions – e.g., other substance-related disorders, anxiety and affective disorders. Following alcohol dependence, severe somatic and psychosocial consequences have to be anticipated.

Prospective epidemiological studies revealed the close links between stress and heavy drinking. Thus, stressful environment in “disadvantaged neighbourhoods” has been found to promote alcohol abuse behaviour in women (Hill & Angel 2005). Women who live in neighbourhoods they characterize as having a lot of problems with drugs, crime, teen pregnancy, unemployment, idle youth, abandoned houses, and unresponsive police drink more heavily or get drunk more often than those who report more order in their neighbourhoods. In dynamics, increasing perceived levels of “neighbourhood disorder” resulted in increased levels of drinking at the end of the two years follow-up period, even with an adjustment for heavy drinking at baseline.

The results of a longitudinal study performed by Russel et al (1999) with representative samples of the black and non-black adult household populations in Erie County, New York also support a causal relationship between stress and alcohol use.

The relationship between stress and tobacco smoking has been debated for some time. Virtually all adult smokers attribute their smoking – at least in part – to its anxiolytic and sedative properties. Therefore, there is a good reason to believe that nicotine, smoking in general – as well as other psychoactive substances – is used as a mean of mood regulation and coping with stress (Kassel et al 2003).

This positive connection between smoking tobacco and relieving stress leads to a regular pattern of smoking. Once dependence is established, evidence suggests that tobacco motivation is strongly influenced by a reduction in withdrawal symptoms, an expectation of stress reduction and conditioned reinforcement (Baker et al 2004).

On the other hand, tobacco dependency is known to be associated with heightened stress. When smokers stop, they gradually become less stressed over time (Long 2003).

Many people use both alcohol and nicotine (i.e., cigarettes and other tobacco products). The behavioural effects of these two drugs differ, and they do not act on the same target sites in the brain, although they may share – or partly share – certain properties. The initiation of alcohol or nicotine use may be precipitated by similar personality characteristics in the user, such as impulsivity and sensation seeking. The mechanisms underlying the development of dependence may be similar for alcohol and nicotine. Stress is widely discussed as one of them (Little 2000).

Summarising this chapter, it is possible to conclude that population-based and workplace-related programs of stress management could probably be very useful in reduction of stress-induced morbidity and mortality. Perhaps, the best preventive effect of such programs is to be expected for highly prevalent conditions, in which stress is convincingly found to increase morbidity and mortality risks – e.g., cardiovascular diseases. The costs of such programs could be much lower than national health insurance expenditures for treatment of these conditions and their complications.

3 References

Alonso J, Angermeyer MC, Bernert S et al (2004) Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta psychiatrica Scandinavica. Supplementum* (420): 21-27

Altman J & Das GD (1965) Autoradiographic and histological evidence of postnatal hippocampal neurogenesis in rats. *The Journal of comparative neurology* 124(3): 319-335

Baker TB, Brandon TH & Chassin L (2004) Motivational influences on cigarette smoking. *Annual review of psychology* 55: 463-491

Bartrop RW, Luckhurst E, Lazarus L, Kiloh LG & Penny R (1977) Depressed lymphocyte function after bereavement. *Lancet* 1(8016): 834-836

Bejean S & Sultan-Taieb H (2005) Modeling the economic burden of diseases imputable to stress at work. *The European journal of health economics* 6(1): 16-23

Bottiglieri T, Laundy M, Crellin R, Toone BK, Carney MW & Reynolds EH (2000) Homocysteine, folate, methylation, and monoamine metabolism in depression. *Journal of neurology, neurosurgery, and psychiatry* 69(2): 228-232

Breese GR, Overstreet DH & Knapp DJ (2005) Conceptual framework for the etiology of alcoholism: a "kindling"/stress hypothesis. *Psychopharmacology* 178(4): 367-380

Bremner JD (2002) Neuroimaging studies in post-traumatic stress disorder. *Current psychiatry reports* 4(4): 254-263

Bremner JD (2003) Functional neuroanatomical correlates of traumatic stress revisited 7 years later, this time with data. *Psychopharmacology bulletin* 37(2): 6-25

Breslau N (2002) Epidemiologic studies of trauma, posttraumatic stress disorder, and other psychiatric disorders. *Canadian journal of psychiatry. Revue canadienne de psychiatrie* 47(10): 923-929

Brummett BH, Barefoot JC, Siegler IC, Clapp-Channing NE, Lytle BL, Bosworth HB, Williams RB Jr & Mark DB (2001) Characteristics of socially isolated patients with coronary artery disease who are at elevated risk for mortality. *Psychosomatic medicine* 63(2): 267-272

Buchanan TW, Kern S, Allen JS, Tranel D & Kirschbaum C (2004) Circadian regulation of cortisol after hippocampal damage in humans. *Biological psychiatry* 56(9): 651-656

Burke HM, Davis MC, Otte C & Mohr DC (2005) Depression and cortisol responses to psychological stress: a meta-analysis. *Psychoneuroendocrinology* 30(9): 846-856

Cameron HA & Gould E (1994) Adult neurogenesis is regulated by adrenal steroids in the dentate gyrus. *Neuroscience* 61(2): 203–209

Cameron HA & McKay RD (1999) Restoring production of hippocampal neurons in old age. *Nature neuroscience* 2(10) 894–897

Cameron HA, Woolley CS, McEwen BS & Gould E (1993) Differentiation of newly born neurons and glia in the dentate gyrus of the adult rat. *Neuroscience* 56(2):337-344

Capuron L, Ravaud A, Miller AH & Dantzer R (2004) Baseline mood and psychosocial characteristics of patients developing depressive symptoms during interleukin-2 and/or interferon-alpha cancer therapy. *Brain, behavior, and immunity* 18(3): 205-213

Chang PP, Ford DE, Meoni LA, Wang NY & Klag MJ (2002) Anger in young men and subsequent premature cardiovascular disease: the precursors study. *Archives of internal medicine* 162(8): 901-906

Chrousos GP & Gold PW (1998) A healthy body in a healthy mind--and vice versa--the damaging power of "uncontrollable" stress. *The Journal of clinical endocrinology and metabolism* 83(6): 1842-1845

Cohen L, Marshall GD Jr, Cheng L, Agarwal SK & Wei Q (2000) DNA repair capacity in healthy medical students during and after exam stress. *Journal of behavioral medicine* 23(6):531-544

Cohen S, Tyrrell DA & Smith AP (1991) Psychological stress and susceptibility to the common cold. *The New England journal of medicine* 325(9): 606-612

Cornia GA (2000) Short-term, long-term, and hysteresis mortality models: a review. In: Cornia GA & Paniccià R (eds.) *The mortality crisis in transitional economies*. New York: Oxford University Press

Corwin EJ, Murray-Kolb LE & Beard JL (2003) Low hemoglobin level is a risk factor for postpartum depression. *The Journal of nutrition* 133(12): 4139-4142

Delahanty DL, Dougall AL & Baum A (2001) Neuroendocrine and immune alterations following natural disasters and traumatic stress. In: Ader R, Felten DL & Cohen N (eds.) *Psychoneuroimmunology 3rd ed.* San Diego, CA: Academic Press

Denisova TP, Shkoda AS, Malinova LI & Astaf'eva NG (2005) Social stress as a risk factor for ischemic heart disease. *Terapevticheskii arkhiv* 77(3): 52-55

Duijts SF, Zeegers MP & Borne BV (2003) The association between stressful life events and breast cancer risk: a meta-analysis. *International journal of cancer* 107(6): 1023-1029

Eaker ED, Pinsky J & Castelli WP (1992) Myocardial infarction and coronary death among women: psychosocial predictors from a 20-year follow-up of women in the Framingham Study. *American journal of epidemiology* 135(8): 854-864

Epel ES, Blackburn EH, Lin J, Dhabhar FS, Adler NE, Morrow JD & Cawthon RM (2004) Accelerated telomere shortening in response to life stress. *Proceedings of the National Academy of Sciences of the United States of America* 101(49): 17312-17315

Eriksson PS, Perfilieva E, Bjork-Eriksson T, Alborn AM, Nordborg C, Peterson DA & Gage FH (1998) Neurogenesis in the adult human hippocampus. *Nature medicine* 4(11): 1313-1317

Fortin NJ, Agster KL & Eichenbaum HB (2002) Critical role of the hippocampus in memory for sequences of events. *Nature neuroscience* 5(5): 458-462

Fried SK, Bunkin DA & Greenberg AS (1998) Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid. *The Journal of clinical endocrinology and metabolism* 83(3): 847-850

Garssen B & Goodkin K (1999) On the role of immunological factors as mediators between psychosocial factors and cancer progression. *Psychiatry research* 85(1): 51-61

Glaser R & Kiecolt-Glaser JK (2005) Stress-induced immune dysfunction: implications for health. *Nature reviews. Immunology* 5(3): 243-251

Gould E, Tanapat P, Hastings NB & Shors TJ (1999) Neurogenesis in adulthood: a possible role in learning. *Trends in cognitive sciences* 3(5):186-192

Graham J, Ramirez A, Love S, Richards M & Burgess C (2002) Stressful life experiences and risk of relapse of breast cancer: observational cohort study. *BMJ (British Medical Journal* 324(7351): 1420

Guyton AC & Hall JE (1996) *Textbook of medical physiology. 9th ed.* Philadelphia: Saunders

Hasson D, Anderberg UM, Theorell T & Arnetz BB (2005) Psychophysiological effects of a web-based stress management system: a prospective, randomized controlled intervention study of IT and media workers [ISRCTN54254861]. *BMC Public Health* Jul 25; 5:78

Hill TD & Angel RJ (2005) Neighborhood disorder, psychological distress, and heavy drinking. *Social science & medicine* 61(5): 965-975

Horner MD & Hamner MB (2002) Neurocognitive functioning in posttraumatic stress disorder. *Neuropsychology review* 12(1): 15-30

House JS (2001) Social isolation kills, but how and why? *Psychosomatic medicine* 63(2):273-274

Hull AM (2002) Neuroimaging findings in post-traumatic stress disorder. Systematic review. *The British journal of psychiatry* 181: 102-110

Ironson G, Wynings C, Schneiderman N, Baum A, Rodriguez M, Greenwood D, Benight C, Antoni M, LaPerriere A, Huang HS, Klimas N & Fletcher MA (1997) Posttraumatic stress symptoms,

intrusive thoughts, loss, and immune function after Hurricane Andrew. *Psychosomatic medicine* 59(2): 128-141

Irwin M, Daniels M, Risch SC, Bloom E & Weiner H (1988) Plasma cortisol and natural killer cell activity during bereavement. *Biological psychiatry* 24(2): 173-178

Kalediene R & Petrauskiene J (2004) Socio-economic transition, inequality, and mortality in Lithuania. *Economics and human biology* 2(1): 87-95

Kalia M (2002) Assessing the economic impact of stress--the modern day hidden epidemic. *Metabolism: clinical and experimental* 51(6 Suppl 1): 49-53

Kassel JD, Stroud LR & Paronis CA (2003) Smoking, stress, and negative affect: correlation, causation, and context across stages of smoking. *Psychological bulletin* 129(2): 270-304

Kiecolt-Glaser JK, Fisher LD, Ogrocki P, Stout JC, Speicher CE & Glaser R (1987) Marital quality, marital disruption, and immune function. *Psychosomatic medicine* 49(1): 13-34

Kiecolt-Glaser JK, Stephens RE, Lipetz PD, Speicher CE & Glaser R (1985) Distress and DNA repair in human lymphocytes. *Journal of behavioral medicine* 8(4): 311-320

Kivimäki M, Leino-Arjas P, Luukkonen R, Riihimaki H, Vahtera J & Kirjonen J (2002) Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. *BMJ (British Medical Journal* 325(7369): 857

Kuper H, Singh-Manoux A, Siegrist J & Marmot M (2002) When reciprocity fails: effort-reward imbalance in relation to coronary heart disease and health functioning within the Whitehall II study. *Occupational and environmental medicine* 59(11): 777-784

Lampert R, Jain D, Burg MM, Batsford WP & McPherson CA (2000) Destabilizing effects of mental stress on ventricular arrhythmias in patients with implantable cardioverter-defibrillators. *Circulation* 101(2): 158-164

Lee S, Colditz GA, Berkman LF & Kawachi I (2003) Caregiving and risk of coronary heart disease in U.S. women: a prospective study. *American journal of preventive medicine* 24(2): 113-119

Lesperance F, Frasure-Smith N, Theroux P & Irwin M (2004) The association between major depression and levels of soluble intercellular adhesion molecule 1, interleukin-6, and C-reactive protein in patients with recent acute coronary syndromes. *The American journal of psychiatry* 161(2): 271-277

Levav I, Kohn R, Iscovich J, Abramson JH, Tsai WY & Vigdorovich D (2000) Cancer incidence and survival following bereavement. *American journal of public health* 90(10): 1601-1607

Little HJ (2000) Behavioral mechanisms underlying the link between smoking and drinking. *Alcohol research & health: the journal of the National Institute on Alcohol Abuse and Alcoholism* 24(4): 215-224

Long D (2003) Smoking as a coping strategy. *Nursing times* 99(33):50, 53

Lundberg U & Frankenhaeuser M (1999) Stress and workload of men and women in high-ranking positions. *Journal of occupational health psychology* 4(2):142-151

Lusk B & Lash AA (2005) The stress response, psychoneuroimmunology, and stress among ICU patients. *Dimensions of critical care nursing* 24(1): 25-31

Maier SF (2003) Bi-directional immune-brain communication: Implications for understanding stress, pain, and cognition. *Brain, behavior, and immunity* 17(2): 69-85

Marx J (2004) Cancer research. Inflammation and cancer: the link grows stronger. *Science* 306(5698): 966-968

Matthews KA, Flory JD, Muldoon MF & Manuck SB (2000) Does socioeconomic status relate to central serotonergic responsivity in healthy adults? *Psychosomatic medicine* 62(2): 231-237

Mehta SK, Pierson DL, Cooley H, Dubow R & Lugg D (2000) Epstein-Barr virus reactivation associated with diminished cell-mediated immunity in antarctic expeditioners. *Journal of medical virology* 61(2): 235-240

Petticrew M, Fraser JM & Regan MF (1999) Adverse life events and risk of breast cancer: a meta-analysis. *British journal of health psychology* 4(1): 1-17

Rakic P (2002) Neurogenesis in adult primates. *Progress in brain research* 138:3-14

Reiche EM, Nunes SO & Morimoto HK (2004) Stress, depression, the immune system, and cancer. *The lancet oncology* 5(10): 617-625

Rich EL & Romero LM (2005) Exposure to chronic stress downregulates corticosterone responses to acute stressors. *American journal of physiology. Regulatory, integrative and comparative physiology* 288(6): R1628-R1636

Roberts AD, Wessely S, Chalder T, Papadopoulos A & Cleare AJ (2004) Salivary cortisol response to awakening in chronic fatigue syndrome. *The British journal of psychiatry: the journal of mental science* 184: 136-141

Roberts FD, Newcomb PA, Trentham-Dietz A & Storer BE (1996) Self-reported stress and risk of breast cancer. *Cancer* 77(6): 1089-1093

Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA, Blackett KN, Sitthi-amorn C, Sato H, Yusuf S & INTERHEART investigators (2004) Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 364(9438): 953-962

Russell M, Cooper ML, Frone MR & Peirce RS (1999) A longitudinal study of stress, alcohol, and blood pressure in community-based samples of blacks and non-blacks. *Alcohol research & health: the journal of the National Institute on Alcohol Abuse and Alcoholism* 23(4): 299-306

Scheller-Gilkey G, Moynes K, Cooper I, Kant C & Miller AH (2004) Early life stress and PTSD symptoms in patients with comorbid schizophrenia and substance abuse. *Schizophrenia research* 69(2-3): 167-174

Schleifer SJ, Keller SE, Bartlett JA, Eckholdt HM & Delaney BR (1996) Immunity in young adults with major depressive disorder. *The American journal of psychiatry* 153(4): 477-482

Schleifer SJ, Keller SE, Camerino M, Thornton JC & Stein M (1983) Suppression of lymphocyte stimulation following bereavement. *JAMA: the journal of the American Medical Association* 250(3): 374-377

Schwarz AM, Schachinger H, Adler RH & Goetz SM (2003) Hopelessness is associated with decreased heart rate variability during championship chess games. *Psychosomatic medicine* 65(4): 658-661

Segerstrom SC & Miller GE (2004) Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychological bulletin* 130(4): 601-630

Selye H (1985) History and present status of the stress concept. In: Monat A & Lazarus RS (eds.) *Stress and coping. 2nd ed.* New York: Columbia University

Shelby J & McCance KL (2002) Stress and disease. In: McCance KL & Huether (eds.) *Pathophysiology. 4th ed.* St. Louis: Mosby

Sher L & Mann JJ (2003) Psychiatric pathophysiology: mood disorders. In: Tasman A, Kay J & Lieberman JA (eds.) *Psychiatry*. Chichester, UK: John Wiley & Sons

Shors TJ (2005) Significant life events and the shape of memories to come: A hypothesis. *Neurobiology of learning and memory* Nov 9; [Epub ahead of print]

Solomon SD & Davidson JR (1997) Trauma: prevalence, impairment, service use, and cost. *The Journal of clinical psychiatry* 58 Suppl 9:5-11

Spiegel D, Bloom JR, Kraemer HC & Gottheil E (1989) Effect of psychosocial treatment on survival of patients with metastatic breast cancer. *Lancet* 2(8668): 888-891

Squire LR & Zola SM (1996) Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences of the United States of America* 93(24): 13515-13522

Stanford GG (1994) The stress response to trauma and critical illness. *Critical care nursing clinics of North America* 6(4): 693-702

Steptoe A, Owen N, Kunz-Ebrecht SR & Brydon L (2004) Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women. *Psychoneuroendocrinology* 29(5): 593-611

Stern SL, Dhanda R & Hazuda HP (2001) Hopelessness predicts mortality in older Mexican and European Americans. *Psychosomatic medicine* 63(3): 344-351

Stewart J (2003) Stress and relapse to drug seeking: studies in laboratory animals shed light on mechanisms and sources of long-term vulnerability. *The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions* 12(1): 1-17

Strike PC & Steptoe A (2004) Psychosocial factors in the development of coronary artery disease. *Progress in cardiovascular diseases* 46(4): 337-347

Suwaki H, Kalant H, Higuchi S, Crabbe JC, Ohkuma S, Katsura M, Yoshimura M, Stewart RC, Li TK & Weiss F (2001) Recent research on alcohol tolerance and dependence. *Alcoholism, clinical and experimental research* 25(5 Suppl ISBRA): 189S-196S

The Mental Health Foundation (2001) *Burnt out or burning bright? The effects of stress in the workplace*. London: The Mental Health Foundation

Tomei LD, Kiecolt-Glaser JK, Kennedy S & Glaser R (1990) Psychological stress and phorbol ester inhibition of radiation-induced apoptosis in human peripheral blood leukocytes. *Psychiatry research* 33(1): 59-71

Vale S (2005) Psychosocial stress and cardiovascular diseases. *Postgraduate medical journal* 81(957): 429-435

Vrijkotte TG, van Doornen LJ & de Geus EJ (1999) Work stress and metabolic and hemostatic risk factors. *Psychosomatic medicine* 61(6): 796-805

Walter M, Dammann G, Wiesbeck GA & Klapp BF (2005) Psychosocial stress and alcohol consumption: interrelations, consequences and interventions. *Fortschritte der Neurologie-Psychiatrie* 73(9): 517-525

Wamala SP, Mittleman MA, Schenck-Gustafsson K & Orth-Gomer K (1999) Potential explanations for the educational gradient in coronary heart disease: a population-based case-control study of Swedish women. *American journal of public health* 89(3): 315-321

Wessa M, Rohleder N, Kirschbaum C & Flor H (2006) Altered cortisol awakening response in posttraumatic stress disorder. *Psychoneuroendocrinology* 31(2): 209-215. [Epub 2005 Sep 9]

WHO (1996) The global burden of disease. In: Murray CJL & Lopez AD (eds.) *The global burden of disease. A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected.* Cambridge, MA: Harvard School of Public Health

Williams JE, Nieto FJ, Sanford CP, Couper DJ & Tyroler HA (2002) The association between trait anger and incident stroke risk: the Atherosclerosis Risk in Communities (ARIC) Study. *Stroke* 33(1): 13-19

Wolf OT, Fujiwara E, Luwinski G, Kirschbaum C & Markowitsch HJ (2005) No morning cortisol response in patients with severe global amnesia. *Psychoneuroendocrinology* 30(1): 101-105

Woodward M, Oliphant J, Lowe G & Tunstall-Pedoe H (2003) Contribution of contemporaneous risk factors to social inequality in coronary heart disease and all causes mortality. *Preventive medicine* 36(5): 561-568

Yehuda R (2002) Preface. Recent advances in the study of biological alterations in post-traumatic stress disorder (PTSD). *The Psychiatric clinics of North America* 25(2): xi-xv

Zohar J, Sasson Y, Amital D, Iancu I & Zinger Y (1998) Current diagnostic issues and epidemiological insights in PTSD. *CNS Spectrums. The international journal of neuropsychiatric medicine* 3(7): 12-14