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1 Introduction

We are increasingly becoming a 24 hour society. Many services demand a work force ready around the clock: emergency, health care, hospitality, manufacturing, telecommunications, transportation, security.

In EU-27, 17.6% of the work force has been working in shifts in 2011. In Austria, even 18.6% between 15 and 64 years were participating in shift work in this period. [EUROSTAT, 2012]

It is known for a long time that shift work involves health risks. Particularly long-term shift work is associated with a number of chronic diseases: cardiovascular disease, diabetes and certain cancers, which are part of this work. Furthermore, many shift workers report gastric problems, obesity and sleep disorders. However, exact mechanisms for the development of these diseases are still not clear. Many researchers hypothesise that disrupted circadian rhythms play a major role in the pathogenesis of these chronic diseases.

Interesting in this aspect is a study conducted in the seventies that demonstrated that the timing of food intake can significantly determine body weight: They showed that a 2 000 kcal meal within one hour after awakening can induce weight loss, while the same meal consumed after 12 hours leads to weight gain. [HOOGERWERF, 2010]

The WHO regards nutrition as a top priority in public health policies and programmes as is linked to many chronic diseases.

Shift workers are in special need for nutritional recommendations. Evidence based recommendations for this group are still missing, though. [ATKINSON et al., 2008]

Cardiovascular disease and cancer represent the majority of disease burden. Thus, the literature review concentrates on associations between these diseases and shift work. The empirical study involves 103 shift workers and 74 day workers. It compares locomotive drivers with day workers of the Austrian Federal Railway in terms of food consumption frequencies. Some research questions are: Is the BMI actually higher in shift workers, as many studies postulate? Are there significant differences in food consumption between the samples? Are some diseases more frequent among shift workers?

2 Literature Review

2.1 Definition of night shift work

The International Labour Organisation (ILO) defines night shift as work between 12 and 5 o'clock in the morning. [PESCH et al., 2010]

In comparison to day workers, night shift workers have a relative risk (RR) of 1.31 for all circulatory diseases. [TÜCHSEN et al., 2006]

2.2 Shift Work and Cardiovascular Disease

2.2.1 Incidence of Cardiovascular Disease

One third of all deaths worldwide can be attributed to cardiovascular diseases. (CVDs). [PIMENTA et al., 2011] In most industrialized countries, cardiovascular diseases (CVD) are the leading cause of death and disability.

There are multifactorial causes of CVD. The work environment can have a big impact on CVD. Substances such as carbon disulfide, nitroglycerine, lead, cobalt, arsenic, solvents, and organophosphates can cause a CVD. Besides, occupational risk factors are sedentary work, monotonous or stressful work, passive smoking and shift work. Other discussed factors are disturbed sociotemporal patterns, social support, behaviour in terms of smoking, alcohol, diet and exercise and biochemical changes. (e.g. cholesterol and triglycerides) [BOGGILD and KNUTSSON, 1999]

2.2.2 Risk factors for Cardiovascular Disease

- male gender
- age
- hypertension
- smoking
- hypercholesterolemia

- low levels of high-density cholesterol (HDL-c)
- diabetes *mellitus*
- low level of schooling
- low income
- sedentary lifestyle
- obesity
- hypertriglyceridemia
- psycho-emotional stress [PIMENTA et al., 2011]

PATHWAYS FROM SHIFT WORK TO DISEASE

Shift work can present a psychosocial stress factor due to inflexible shifts that can't be influenced by the gainfully employed people. Furthermore, shift work may imply working at unsocial hours that limit work-life balance. [PUTTONEN et al., 2010]

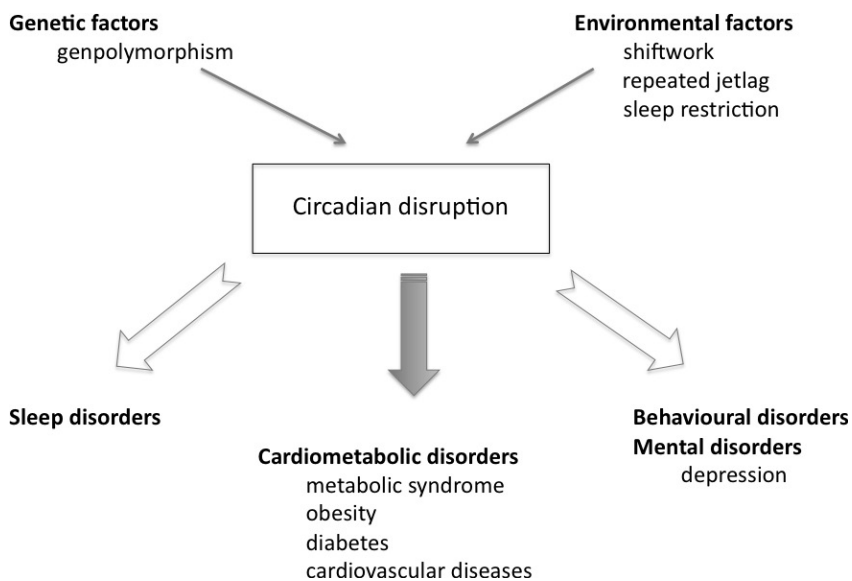


Figure 1: Causes and consequences of circadian rhythm disturbance
[JERMENDY et al., 2012]

Shift work means...

- disturbed sleep–wakefulness
- higher risk of cardiovascular disease
- people with coronary risk factors are more likely to be affected
- related to higher levels of triglyceride
- lower levels of high-density lipoprotein (HDL) cholesterol

An epidemiologic study found that mortality due to ischemic stroke was increased among shift workers. [VIITASALO et al., 2008] Recent studies even come to the conclusion that shift work is the main cause of ischaemic heart disease (IHD). Estimates speak about 10.7% of all male IHD mortality and 5.5% of female IHD mortality in working age. [TÜCHSEN et al., 2006]

The relation between shift work and cardiovascular disease has been studied for more than 50 years. Although some studies reached no definite conclusions or even found no relation, other studies have indicated an increased risk of cardiovascular disease among shift workers.

A review with 17 studies indicates that shift workers experience a 40% increase in the risk of cardiovascular disease compared with those who do not work shifts. [INOUE et al., 2003], [JERMENDY et al., 2012], [PIMENTA et al., 2011]

PIMENTA et al. (2011) even concluded that the prevalence of high cardiovascular risk was 67% higher among night shift workers. Performing over six years of shift-work is associated with higher risk of developing cardiovascular disease.(especially in women) [NABE-NIELSEN et al., 2008], [KAWACHI et al., 1995]

2.2.3. Association between shift work and cardiovascular disease

Mechanisms by which shift work causes cardiovascular disease are still not completely understood. Known contributing factors include disturbed circadian rhythms and confounding factors such as smoking, poor eating habits, and social problems causing

stress. [NABE-NIELSEN et al., 2008]. Likewise, MURATA et al. (1999) comes to the conclusion that there is some evidence that shift work contributes to higher cardiovascular morbidity and mortality, however the relation is still unclear.

A review based on 16 studies found that there is limited evidence for a causal relationship between shift work and ischemic heart disease. This indicates that a causal relationship is possible, however bias or confounding can pretend a false association. [PUTTONEN et al., 2010]

Similarly, there is still no conclusive evidence of the effect of shift rotation systems on short- or long-term health. [VIITASALO et al., 2008]

On the other hand, some scientists acknowledge the existence of a relationship between shift work and coronary artery disease, yet state that the mechanisms behind are still unknown. [INOUE et al., 2003], [KAWACHI et al., 1995], [MOSENDANE et al., 2008]

Why shift work may be associated with increased risk of CHD: They have a higher consumption of cigarettes, higher blood pressure, total cholesterol, and LDL cholesterol and lower HDL. The differences in lipids were independent of smoking, obesity, diet and physical activity.

Among day workers who had to switch to night work, increased levels of serum cholesterol, glucose, uric acid, and urinary adrenaline excretion were measured. However, as soon as those workers changed to day work, all parameters returned to normal. [KAWACHI et al., 1995]

Reasons for CVD among shift workers

A major factor by which shift work causes cardiovascular disease is disturbed circadian rhythms. [MOSENDANE et al., 2008]

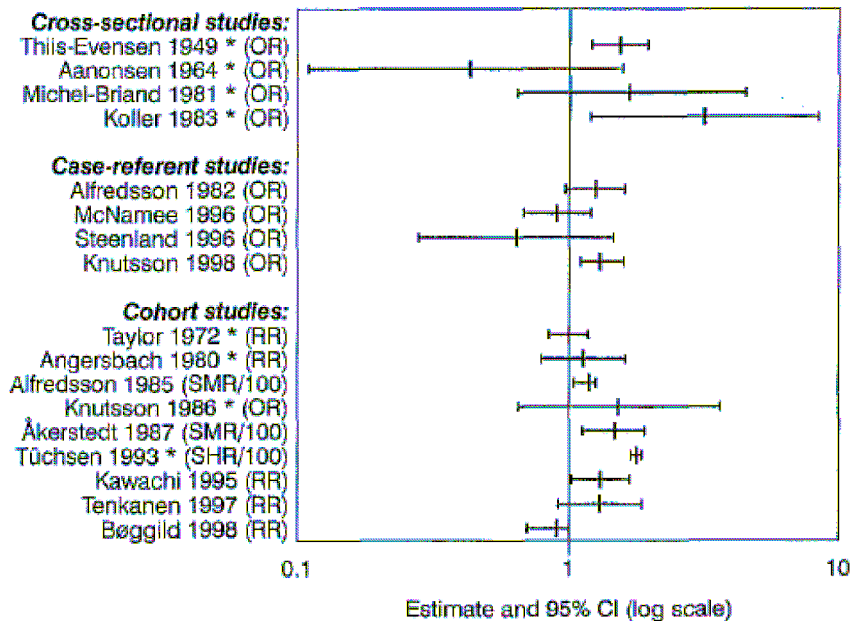


Figure 2: Epidemiologic studies on the relation between shift work and cardiovascular diseases [BOGGILD and KNUTSSON, 1999]

2.2.4 Biomarkers of CVD

Cardiovascular disease develops with atherosclerotic alteration and later thrombosis. There are markers of CVD such as cholesterol and lipids such as triglyceride and apolipoproteins, fraction A and B (Apo A, Apo B). Modifications of those biomarkers can reflect a subclinical disease or CVD.

Independent risk factors for CVD are markers of coagulation and fibrinolytic processes. (thrombocytes, fibrinogen, factor VIIc, fibrinolysis products tissue plasminogen activator (t-PA), tissue plasminogen activator inhibitor (t-PAI) and complement.

An additional risk factor is glycated haemoglobin (HbA1c), which reflects glucose metabolism, high blood pressure and electrocardiographic signs of hypertrophy. [BOGGILD and KNUTSSON, 1999]

It is assumed that CVD results from night shift work as circadian rhythms are disturbed, metabolic and hormonal functions change and smoking and inadequate diets increase. [PIMENTA et al., 2011]

In many cases, unfavourable characteristics among shift workers have been observed. In terms of systolic blood pressure, male shift workers showed higher levels than day workers. Women showed higher weight, BMI and hypertension rates. In addition, the amount of smokers was higher, HDL cholesterol was lower. Interestingly, especially (middle-aged) women working in shifts for several years have a less healthy lifestyle and are at higher cardiometabolic risk compared to daytime workers. Further, both men and women generally sleep less, do less exercise and consume more coffee. Interestingly, most workers with low and middle educational levels work in shift work, whereas higher educated people normally work during the day. [JERMENDY et al., 2012]

2.2.5 Blood pressure

As a matter of fact, night shift workers work at times opposite to the chronobiological pattern. They have to work when efficiency is at the lowest and to rest when the body is actually prepared to engage. This results in frequent fluctuations in blood pressure levels. At night, when blood pressure normally decreases, these subjects have a blood pressure that remains at the level of the day.

Permanently changing amplitudes of circadian rhythms may lead to higher mean blood pressure of night shift workers, which implies higher risk of CVD. [PIMENTA et al., 2011]

Similarly, PUTTONEN et al. (2010) found that blood pressure is higher among shift than day workers within 24 hours. Scheer et al. (2009) measured a 3mm Hg increase in mean arterial pressure during a short-term circadian disruption. Those changes are more evident in hypertensive than in normotensive patients.

However, nine of 19 studies reported no differences between shift and day workers in terms of hypertension. [BOGGILD and KNUTSSON, 1999]

→ Scientific evidence for the relationship between shift work and hypertension or elevated blood pressure is still incomplete.

A longitudinal study found that shift work is an independent risk factor for the progression of hypertension. [VIITASALO et al., 2008]

Non-dippers versus dippers

In general, blood pressure in shift workers shift from dipper to a non-dipper pattern, which indicates increased risk of hypertension.

Physiological is the fact that nocturnal blood pressure falls at least by 10% of mean arterial pressure (MAP). This effect is called dipping. On the contrary, non-dippers show very small nocturnal BP falls. It has been found that excessive morning BP surge and no nocturnal BP fall lead to worsened cardiovascular outcomes.

Several studies report that a non-dipping pattern and cardiovascular risk are associated with greater damage of heart, brain and kidney and more frequent cardiovascular events such as stroke and myocardial infarction. Cardiovascular mortality is higher in both hypertensive and normotensive individuals. Thus, non-dippers have a poorer prognosis after cardiovascular events. [MOSENDANE et al., 2008], [INOUE et al., 2003]

On the contrary, there are dippers with a normal blood pressure fall during sleep. Among them, another risk group has been identified: the extreme dippers. They have a great fall in blood pressure during sleep and elderly hypertensive patients have been found to have greater cerebrovascular damage than dippers. [INOUE et al., 2003]

2.2.6 Smoking

Smoking is a major risk factor in the development of a CVD. Interestingly, six out of 13 cross-sectional studies found that shift workers smoke significantly more than day workers. [BOGGILD and KNUTSSON, 1999]. PUTTONEN et al. (2010) confirms the fact that smoking is more prevalent among shift workers than day workers. Likewise, a Swedish prospective study found that smoking among shift workers was significantly increased. [MOSENDANE et al., 2008]. A prospective follow-up study found that the number of cigarettes smoked per day increased more among the shift workers than among the day workers. [NABE-NIELSEN et al., 2008]

Interestingly, it has been shown that night shift workers are at higher risk to start smoking. [PIMENTA et al., 2011]

Another study also concluded that shift workers had an increased risk of starting to smoke during a 2 year follow-up. [NABE-NIELSEN et al., 2008]

2.2.7 Sleep deprivation

It is generally known that shift workers sleep less than day workers. Yet there is limited evidence on a possible relationship between lack of sleep and a cardiovascular disease. [BOGGILD and KNUTSSON, 1999]

PUTTONEN et al. (2010) on the other hand, comments that reduced sleep and insomnia are associated with increased risk for CVD.

ÅKERSTEDT and KNUTSSON (1997) mentions that reduced sleep can potentially affect cardiovascular risk factors due to metabolic and immunologic changes. However, evidence is still missing.

Sleep deprivation can result in an increase in fasting blood glucose and a decrease in insulin sensitivity. Further, serum leptin levels were found to be lower, ghrelin levels higher and appetite and hunger increased, with higher consumption of carbohydrate containing foods. All these changes can lead to an increase in body weight, as leptin is normally inhibiting appetite. [JERMENDY et al., 2012],[PUTTONEN et al., 2010]

Insufficient sleep activates the sympathetic nervous system and results in increased blood pressure and heart rate.

Interestingly, only six nights in a row with four hours sleep per night already led to increased activity of sympathetic nervous system and evening cortisol, peripheral circulation of leukocytes, interleukins and C-reactive protein (CRP), with lower glucose tolerance. [PUTTONEN et al., 2010]

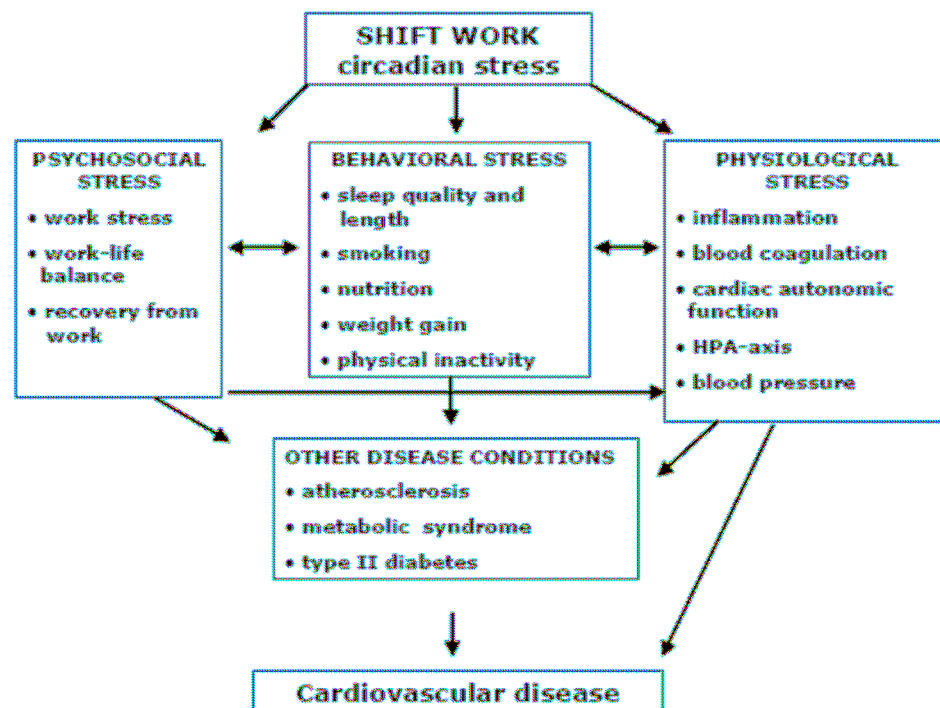


Figure 3: Model for pathways from shift work to cardiovascular disease.
[PUTTONEN et al., 2010]

2.2.8 Inflammation, homocystein and behavioural mechanisms

Numerous markers are biomarkers of the atherosclerotic process, such as inflammation, increased blood cholesterol, homocystein, and albumin levels, possible deficiencies in endothelial function and blood coagulation.

Inflammation is an essential part of atherosclerosis and CHD. It has been found that shift workers have more leucocytes and reduced T-lymphocyte and NK cell function compared to daytime workers.

Homocysteine in the plasma represents a risk factor for atherosclerosis and CVD and can influence endothelial dysfunction, oxidative stress, and atherogenic inflammation.

There is a possible association between shift work and homocysteine levels, however further evidence is needed. Studies so far have reported higher homocysteine levels among shift workers, sometimes almost double (among men) as high as among day workers.

However, shift work can also increase the risk of CVD by psychosocial, behavioural, and physiological mechanisms, yet a strong evidence for those mechanisms is still missing.

Behavioral and physiological stress reactions can be induced by low job control, work-life imbalance and insufficient recovery. Due to those factors shift workers may sleep less, start smoking and eat unhealthier. A theory is that psychosocial and behavioural stress activate the physiological stress reactions, which means that psychosocial stress is linked to the pathophysiological mechanisms of CVD.

Metabolic diseases such as the metabolic syndrome or type II diabetes increase the risk for atherosclerosis. Further, shift workers seem to have higher serum lipids and higher body weights, additional risks for the development of a CVD. [PUTTONEN et al., 2010]

2.2.9 Cardiac function

A follow-up study found that shift workers had an increased frequency of ventricular extrasystoles, which correlated with the number of night shifts.

Further, shift work leads to higher incidence of type 2 diabetes. Obesity may mediate the effect of shift work on diabetes risk. On the contrary, excess risk of incidence of diabetes in shift work has not been found [PUTTONEN et al., 2010]

Hypertension, left ventricular hypertrophy, coronary heart disease and myocardial infarction are more frequent and severe among night shift workers than in day workers. [MOSENDANE et al., 2008]

A change in, or increased arrhythmogeneity, but not in cardiac autonomic control, might explain the increased risk of cardiovascular disease in shift workers.

Coffee consumption, the body mass index, and smoking have been related with the occurrence of ventricular premature complexes. A high incidence of PVC and unfavourable heart rate variability (HRV) has been associated with increased cardiovascular morbidity and mortality. It has been observed that after one year of

working in shifts, the frequency of premature ventricular complexes (PVC) increased compared with working in daytime. The increased occurrence of PVCs is related to the number of days worked on night shift.

On the other hand, no significant one year change in heart rate variability was found in shift workers. [VAN AMELSVOORT et al., 2001]

Another possible explanation for the increased risk for cardiovascular diseases among shift workers is that there may be an association between shift work and QTc prolongation. It has been observed that the QTc of shift workers is significantly longer than that of day workers. The QTc is prognostic of sudden death in patients with myocardial infarction.

A study among nurses showed higher blood pressure and heart rate on night shifts. Additionally, adrenaline levels were elevated.

→ Shift work may influence cardiovascular functions, especially autonomic nervous functions. [MURATA et al., 1999]

2.2.10 Cholesterol and Triglycerides

In general, night shift workers have higher triglyceride levels compared with daytime workers. The reason is that the ingestion of a meal at night results in the production of higher serum triacylglycerol levels as well as lower cholesterol-rich lipoprotein levels among night shift workers. [MOSENDANE et al., 2008]

Five of 16 studies reported higher cholesterol levels for shift workers, yet the rest of the studies did not find any differences between shift and day workers.

Furthermore, four of 12 studies found higher triglyceride levels among shift workers

Interestingly, it was found that cholesterol levels correlate with the distribution of meals. Cholesterol levels were higher when a larger proportion of the diet was ingested at night.

In terms of indicators for the fibrinolytic system, plasminogen activator (t-PA) and tissue plasminogen activator inhibitor (t-PAI) were reduced in shift workers. Consequently, due to lower activity, the dissolution of thrombi may be slower.

→ Many researchers examined cholesterol and triglycerides values of both shift and day workers. Findings are still controversial. [BOGGILD and KNUTSSON, 1999], [PUTTONEN et al., 2010]

2.2.11 Doctors on- call duty

A risk factor for mortality in older adults is disturbed sleep. In addition, research has shown that individuals sleeping 6 hours a night for a period of 6 years had moderately increased death rates, compared to those sleeping 7 hours. Further, reduced sleep is associated with increased incidence of hypertension.

30 healthy physicians were observed for cardiovascular, neuroendocrine and inflammatory factors in two different 24 hour periods. One period was an 8 hour working day with a 16 hour on-call duty afterwards. The other period was work during the day.

Physicians on-call duty on average slept 70 minutes less than their counterparts who only worked during the day. Additionally, they showed increased low frequency heart rate variability during the night, increased blood pressure and noradrenaline excretion. Further, the inflammatory marker tumour necrosis factor- α (TNF- α) increased and ventricular premature beats in the early hours of the morning were also more frequent.

→ On-call duty and sleep disruption results in a shift of cardiac autonomic control towards sympathetic activation, enhanced sympathoadrenal output and increased inflammatory responses. [STEPTOE, 2009]

Middle-aged physicians who were on-call duty (OCD) for 24 hours have been the subjects. Results reflect an association of OCD with higher risk for cardiovascular disease. Frequent OCD's lead to cardiovascular alterations. Thus, physicians doing night

shifts are at higher risk for CVD. OCD is especially burdening, as it generally includes longer working hours than classical shift work and several sleep disruptions during the night.

Of negative impact on cardiovascular homeostasis may be nonphysiological timing of physical activity and nutritional intake as they influence circadian rhythms and functions of the circulatory system. (e.g. BP, heart rate, catecholamine excretion)

Further, parasympathetic activity during shift work has been found to be lower, whereas sympathetic activity during sleep was higher. This may affect cardiac autonomic activity and the risk of CVD.

Diastolic blood pressure has been observed to be higher and during sleep, systolic BP has also been higher. The study found a correlation for BP and age.

→ This study associates OCD with increased risk for CVD. Frequent OCDs may have a negative impact on cardiovascular homeostasis including over-activity of the sympathetic system, disruption of circadian BP and selective activation of inflammatory pathways. [RAUCHENZAUNER et al., 2009]

There is evidence from epidemiological studies that shift work results in increased risk for obesity, diabetes, and cardiovascular disease. This might be the outcome of physiologic maladaptation due to sleeping and eating at abnormal circadian times permanently.

2.2.12 Circadian misalignment

Chronic circadian disruption may be the cause for the adverse metabolic and cardiovascular health effects of shift work. Short-term circadian misalignment occurs acutely with jet lag and chronically with shift work. Consequences are increases in postprandial glucose, insulin, and mean arterial pressure, decreases in leptin and sleep efficiency and inversion of the cortisol profile.

High cortisol levels at the beginning of the sleep period can contribute to the development of insulin resistance and hyperglycemia. In addition, permanently

decreased leptin levels stimulate appetite and decrease energy expenditure, which may result in obesity. Decreased sleep is associated with increased risk for obesity, diabetes, and hypertension

It is suggested that internal desynchronization is caused by meals consumed at abnormal circadian times. However, evidence is still missing.

Some animal experiments have found that shift work may lead to premature death. On the other hand, mutations of circadian clock genes can result in the metabolic syndrome.

Leptin

Glucose, insulin, cortisol, vagal tone and food intake are stimulants of leptin secretion. On the other hand, epinephrine, norepinephrine and metabolic rate are inhibitants of leptin secretion.

During circadian misalignment, leptin decreases. Reduced sleep also reduces leptin. It is therefore suggested that the decrease in sleep during circadian misalignment contributes to decreases in leptin.

Furthermore, it is suggested that misalignment between meal times and central and/or peripheral (e.g., gastrointestinal) circadian rhythms might result in decreased digestion and energy uptake from meals, which may result in a negative energy balance and suppressed leptin.

→ Circadian misalignment in shift workers results in a decrease in leptin, increases of glucose, insulin and mean arterial blood pressure as well as reduced sleep efficiency. [SCHEER et al., 2009]

Besides photic information, non-photoc stimuli such as exercise, food, exogenous melatonin and serotonergic activation are also capable of shifting the endogenous circadian rhythms.

Nocturnal feeding has been shown to affect the desynchronisation of circadian rhythms. Abrupt changes in the feeding time schedule (e.g. from day to night) for several days gradually shifts the phases of the peripheral clocks, but not the central clock.

Short-term adverse effects of desynchronisation

- sleep disturbances
- shift-lag syndrome
- increased risk of errors
- workrelated accidents

Long-term effects of desynchronisation of circadian clocks

- Disturbances of the cardiovascular and gastrointestinal systems
- Impaired glucose and lipid metabolism
- reproductive difficulties
- breast cancer
- hypertension
- dyslipidemia
- insulin resistance
- obesity

2.2.13 Factors of increased risk

Factors that are associated with increased CVD risk are disturbed circadian rhythms, lifestyle changes and psychosocial stress.

Occupational health services including screening of risk factors for CVD such as history of shift work, smoking, blood pressure, obesity, alcohol use, blood lipids, physical inactivity and work stress can help to identify ill health at an early stage. [MOSENDANE et al., 2008]

The cardiovascular risk factors smoking, hypertension, diabetes, high cholesterol are more prevalent among shift workers. A possible cause may be that shift workers undergo behavioural changes as well.

On the whole, shift workers have a higher body mass index, a higher waist-to hip ratio, a higher percentage of the energy intake coming from fat and they are more often smokers. Thus, there is a difference between day and shift workers in terms of sleeping pattern, weight, diet, and smoking habits. [NABE-NIELSEN et al., 2008]

Glucose intolerance and obesity

Variable cortisol concentrations during the day result in diurnal variation of glucose tolerance.

In general, glucose tolerance decreases during the day. It is therefore suggested, that shift workers tend to have higher rates of obesity as they consume their meals during the night (when glucose tolerance is the lowest).

BMI

In a Japanese study energy intake among middle-aged workers was highest during the night shift. A meta-analysis came to the conclusion that there is a relationship between reduced sleep and increased obesity rates. This indicates, that on the whole, night workers have a higher body mass index than daytime workers. [PUTTONEN et al., 2010]

Interestingly, the predictor of BMI for day workers is age, whereas for shift workers, duration of exposure to shift work was the major predictor of BMI.

Many individuals report weight gain when they start to work in shifts. This may be the result of changes in diet and exercise.

Interesting in this context is the observation, that about 15.9% of the energy content of the morning meal is used, while only 10% of the energy content in the evening meal is used. This indicates that most energy of food consumed during the night is taken up by the body and stored. [MOSENDANE et al., 2008]

Confounding factors

The association shift work and cardiovascular disease may be influenced by changes in dietary intakes, reduced physical activity, increased smoking and drinking and disrupted psychosocial factors.

In numerous cases, shift workers gain weight, which can be attributed to irregular appetites including high-fat snacking, infrequent eating during the day and over-eating at night as well as a lack of exercise. [MOSENDANE et al., 2008]

BMI (and smoking) can be related to circulatory diseases. Contrary to the studies mentioned above, some scientists state that there was no significant increase in BMI within a period of 5 years doing shift work. [TÜCHSEN et al., 2006]

Nutritional factors

Two important nutritional risk factors for cardiovascular disease are the ratio between saturated and polyunsaturated fat and the amount of energy coming from fat.

Among 13 studies, few differences between shift and day workers have been observed in terms of nutritional intake. However, changes in meal frequency and the timing of meal intake among shift workers have been reported. In some prospective studies a more frequent consummation of single carbohydrate snacks at night has been observed. [BOGGILD and KNUTSSON, 1999]

It is suggested that the metabolic response to food intake depends on the circadian phase. Yet this assumption needs further study. [ÅKERSTEDT and KNUTSSON, 1997]

Clockwise rotation

Interestingly, it has a positive effect on blood pressure to change the shift system from backward-rotating to rapidly forward-rotating.

In a short-term intervention study with clockwise shift rotation, serum levels of triglyceride and glucose decreased as well as systolic blood pressure, compared to counter clockwise shifts. A similar study found lower low-density lipoprotein (LDL) cholesterol levels, a lower total-to-HDL cholesterol ratio and higher HDL cholesterol levels after a period of 6 months.

Similarly, regular and predictable shift schedules have been found to have a positive effect on values of triglycerides and HDL cholesterol. [PUTTONEN et al., 2010], [VIITASALO et al., 2008] Furthermore, changes from slow backward-rotating shift systems (shift changes every three shifts) to very quickly forward-rotating shift schedules improved the subjective alertness of the workers, even though the working hours at night increased.

The Third EU Survey on Working Conditions reports that low individual flexibility and high variability in workhours is associated with a higher prevalence of health problems. (e.g. sleeping problems, overall fatigue, anxiety, heart disease) On the opposite, low variability in workhours combined with high autonomy has a positive association with workers' health and well-being. Thus, flexible workhours increase job satisfaction.

A fast speed of rotation and a forward direction in shift rotation reduces daytime sleepiness. [VIITASALO et al., 2008]

2.3 Shift Work and Cancer

“Cancer is the second leading cause of death worldwide after cardiovascular diseases.” [IARC, 2011]

In economically developed countries it is the leading cause of death, whereas in developing countries cancer is the second leading cause of death. [JEMAL et al. 2011]

The International Agency for Research on Cancer (IARC) is an agency that is part of the WHO. According to the IARC every year almost 7 million people die from cancer. [IARC, 2012a] Similarly, IARC (2012) states that in the year 2008, there were 7,6

million cancer deaths, accounting for 13% of all deaths worldwide. Besides, 50% of all cancer deaths can be directly attributed to cancers of lung, breast, stomach, liver and colorectum. Furthermore, as for the year 2008, about 12,7 million people were diagnosed with cancer. About 40% of all cancers were cancers of lung, breast, stomach and colorectum. [IARC, 2012]

In women, breast cancer is most frequently diagnosed, it presents 23% of cancer cases and 14% of cancer deaths. Among men, lung cancer is the most frequent cancer. 17 % of cancer cases are cancers of the lungs. Yet smoking creates 80% of the burden in males [JEMAL et al. 2011]

2.3.1 Outlook to 2030

Cancer incidence rates increase worldwide. This can be attributed to aging and a steadily growing world population. [JEMAL et al. 2011]

According to estimates, compared with 2008, there is a possible increase of 75% in the incidence of cancer in 2030. The burden of cancer can potentially rise from about 12.7 million (2008) to 22 million (2030) new cases. Especially so called “developing” countries may have the highest increase in incidence rates. [IARC, 2012]

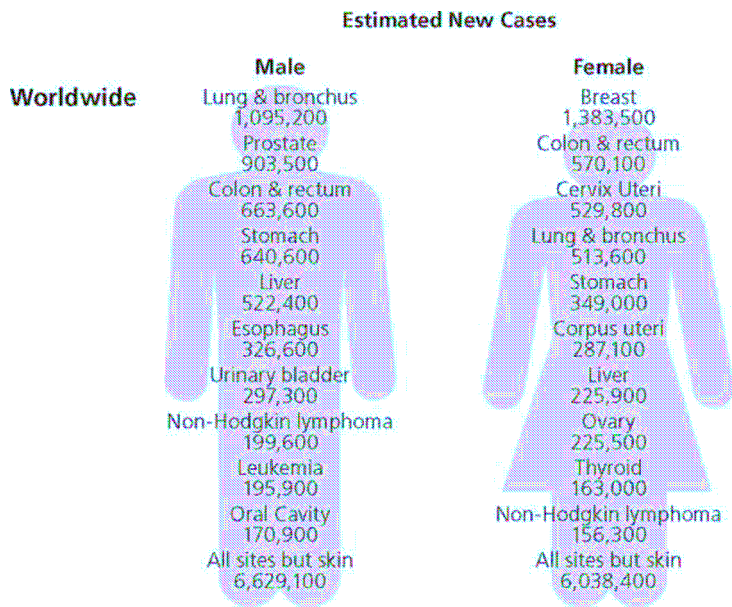


Figure 4: Estimated New Cancer Cases and Deaths Worldwide for Leading Cancer Sites by Level of Economic Development [ECO, 2008]

As figure 4 points out, the prevalence for breast, lung and prostate cancer is the highest among all cancers worldwide. In 2008 there were 1,383,500 new breast cancer cases, 1,095,200 lung and bronchus cancers and 903,500 newly diagnosed prostate cancer cases.

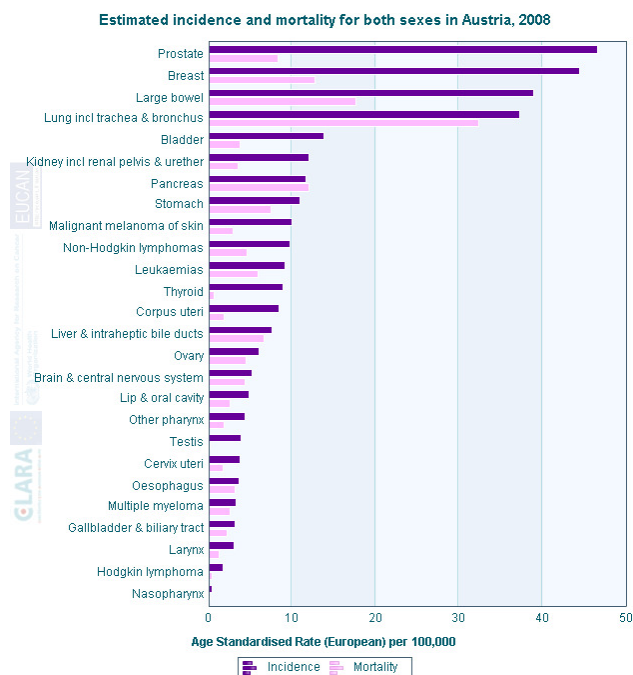


Figure 5: Incidence and Mortality of Cancers in Austria, 2008. [IARC, 2012]

2.3.2 Carcinogenesis

Certain environmental factors can trigger inappropriate activation/ inactivation of specific genes which results in neoplastic transformations. The consequence of genetic and epigenetic changes are cancers.

Diet is a potential risk factor in the development of cancer. Yet mechanisms by which single nutrients interact and how cancer is generated are not fully understood. Especially overweight and obesity, becoming more and more an epidemic, in combination with physical inactivity can lead to increased cancer risk.

The European Prospective Investigation into Cancer and Nutrition (EPIC) is a European study with about half a million subjects enrolled, from Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and the United Kingdom.

It is the largest study investigating correlations between diet, lifestyle, environmental factors and cancer/ chronic diseases incidence.

During the EPIC study, over 26,000 cases have been observed and nearly 16,000 deaths occurred.

The EPIC study has studied links between lifestyle factors and several cancers including breast, colon, gastric, prostate and lung cancers.

It confirms the results of several studies from the past years that claim the positive association between obesity and increased risk of cancers of breast, colon, oesophagus, kidney and endometrium. In addition, there is evidence of a cancer preventive effect of regular physical activity.

Cancer etiology: There is no association between fruit and vegetable consumption and breast/prostate cancer. Preliminary results indicate reduced gastric cancer risk with fruit intake. Adult weight gain indicates increased risk to develop breast cancer, whereas there is limited evidence for gastric and adenocarcinoms of the oesophagus at the moment. The intake of fibre, fish, milk, cheese, nuts and seeds (only in women) is associated with lower colon cancer incidence. On the contrary, red and processed meat show increased colon and gastric cancer risk. Besides, diet diversity can potentially decrease the development of gastric cancers.

It has been mentioned that 30% of all cancers are related to dietary intakes. In addition, some cancers are presented and how nutrition is linked to cancer development.

1) Colorectal cancer: Obesity and smoking is associated with colorectal cancer. Further modifiable variables are: nearly no physical activity, frequent consumption of red/processed meat and alcohol.

2) Lip and Oral Cavity Cancers: Smoking and alcohol consumptions, as well as HPV infections are positively related to the development of lip and oral cavity cancers.

3) Stomach cancers: Refrigeration and increased fruit and vegetable consumption, as well as smoking cessation and decreased cases of chronic H. pylori infections may decrease the incidence of stomach cancer.

4) Esophageal cancers: Factors favouring incidence of oesophageal cancers are bad nutritional status with decreased fruit and vegetable consumption, smoking, drinking of hot beverages, alcohol, obesity and chronic gastrosophageal reflux disease. [JEMAL et al. 2011]

Risk factors for cancer

- Tobacco consumption
- Chronic hepatitis B virus infection (HPV)→ liver cancer
- Human papilloma (→cervical cancer)
- Overweight and Obesity
- Dietary factors
- Alcohol
- Physical inactivity
- Occupational exposures (including several environmental chemicals)
- Radiation [IARC, 2011]

Due to the estimation that 30% of all cancers can be prevented by changing dietary intakes, there is a huge potential in terms of increasing physical activity and dietary behaviour. [IARC, 2012]

2.3.3 The role of physical activity

IARC (2011) assumes that one third of the annual 7,6 million cancer deaths can be prevented. (also through early detection) Consequently, more than 2,5 million people could avoid getting diagnosed with cancer. The World Health Organisation (WHO) has published Global Recommendations on physical activity for health advice. There are four non-communicable diseases causing more than 60% of all global deaths, namely: cardiovascular diseases, diabetes, chronic respiratory diseases and last, but not least: cancer. [IARC, 2011] Everybody, no matter what age, can actively reduce his risk for developing a NCD (non-communicable disease, including cancers). This can work through regular physical activity. Dr Ala Alwan, WHO's Assistant Director-General for Noncommunicable Diseases and Mental Health states: "Physical inactivity is the fourth leading risk factor for all global deaths. And further: "31% of the world's population is not physically active."

Recommendations for 5-17 year olds are to do at least 60 minutes of moderate to vigorous intensity physical activity per week, whereas adults over the age of 18 years should do moderate exercise at least 150 minutes a week. As everybody knows, this has a health promoting effect and can prevent the development of noncommunicable diseases. [IARC, 2011]

2.3.4 IARC

In 2007 the International Agency for Research on Cancer (IARC) came to the following conclusions:

Overall evaluation

Shiftwork that involves circadian disruption is *probably carcinogenic to humans* (Group 2A).

Cancer in humans

There is *limited evidence* in humans for the carcinogenicity of shiftwork that involves night work.

Cancer in experimental animals

There is *sufficient evidence* in experimental animals for the carcinogenicity of light

during the daily dark period (biological night).

According to the IARC, the strongest scientific support exists for shift work and increased breast cancer risk. Meta-analyses have shown that shift working women may have an increased breast cancer risk of 40 to 50% in contrast to day workers. [LANGLEY et al. 2012] Similarly, Megda et al. (2005) came to the conclusion that shift work increases breast cancer risk by 48%. Hansen (2006) confirms Megda et al. (2005) and states that there is relative consisting evidence that working during the night may increase female breast cancer risk. Likewise, Davis & Mirick (2006) reason that there is evidence for night shift work and associated increased risk of cancer. On the contrary, Anthony Swerdlow (2003) seems more critical in terms of shift work and breast cancer: He confirms the possibility that shift work increases breast cancer risk. However he doesn't exclude possible confounding that may pretend an association.

→ While there is insufficient evidence for prostate cancer, colon cancer, and overall cancer there is limited evidence for a causal association between nightshift work and breast cancer. [LANGLEY et al. 2012]

There are not yet causal links established between shift work and cancer as there are no epidemical studies. However, chronic disturbances increase cancer risk.

Empirical research has shown that disturbances of the internal clock lead to increases in breast and prostate cancer risk. However, the mechanisms are not fully understood.

Volume 98 of the IARC monograph series doesn't mention the type of shift work and type/ extent of chronodisruption that may lead to cancer development. [BONDE et al. 2012]

“Nightshift work per se is not expected to be a risk factor for cancer; but is, instead, a surrogate measure for, for example, light at night or circadian phase shift or is an influence on an intermediary risk factor (eg, sleep deprivation, diet or lifestyle that is causally related to cancer).” [KOLSTAD, 2008]

In a cohort study Schwartzbaum et al looked at Swedish inhabitants who worked 20 hours or more a week. 69 759 men (3% of men) and 3057 women (0,3% of women)

worked in shifts. The rate of incident cancers in the follow-up period was quite high: Among this shift working population, derived by the 1960 and 1970 census, 6,792 cancers occurred.

2.3.5 Shift work and breast cancer

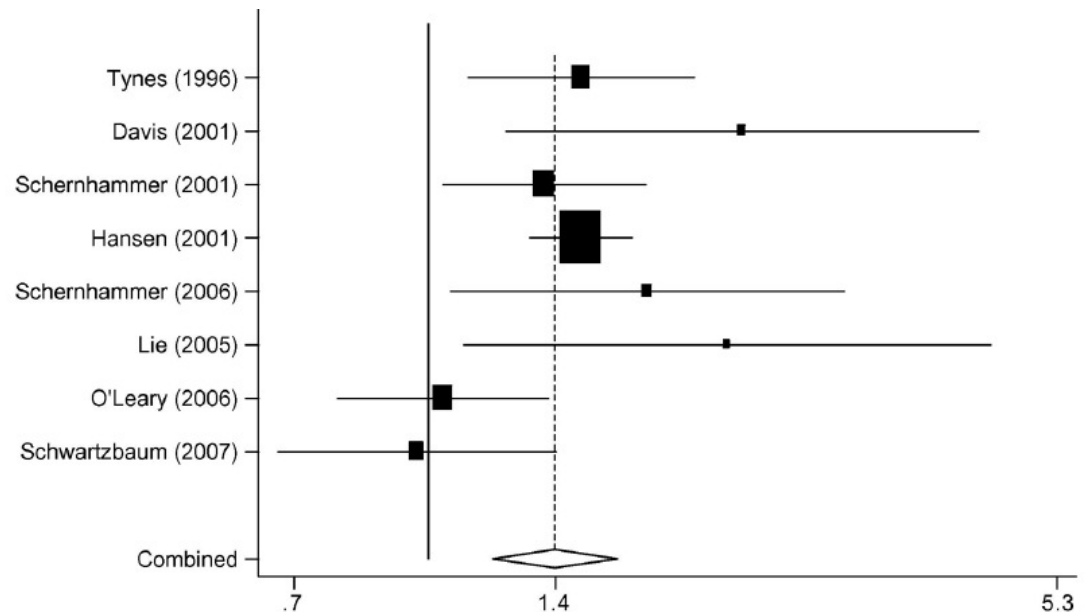


FIGURE 6: Meta-analysis of the risk of night shift work and breast cancer risk. [VISWANATHAN and SCHERNHAMMER, 2009]

“Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide, accounting for 23% (1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths in 2008.”

“Reproductive factors that increase risk include a long menstrual history, nulliparity, recent use of postmenopausal hormone therapy or oral contraceptives, and late age at first birth. Alcohol consumption also increases the risk of breast cancer.” [IARC, 2012]

Over 900 agents and exposures have been tested by the IARC in terms of their human carcinogenicity. Substances in group 1 are classified as carcinogenic to humans. In the case of breast cancer these are alcohol, diethylstilbestrol, estrogen-progestogen contraceptives, estrogen-progestogen hormone replacement therapy, exposure to X-radiation and gamma-radiation and ethylene oxide. Substances in group 2A are

“probably carcinogenic to humans”. The following factors can contribute to breast cancer: estrogen hormone replacement therapy, tobacco smoking, and shift work, especially night work involving circadian disruption.

Shift work could become the leading cause of occupational cancer in women if the association between shift work and breast cancer is confirmed. [WEIDERPASS et al., 2011]

However, several studies suggest that there is no evidence for an association between shift work and cancer incidence. (with a possible exception of thyroid cancer. Further they found no evidence for a role for melatonin in cancer development among shift workers. Eight studies have assessed the relationship between breast cancer and night work. Six of these eight studies suggest a modestly increased risk of breast cancer among long-term employees who performed night shift work.

Another occupational group of shift workers is flight cabin crew personnel, who experience circadian disruption due to the crossing of time zones. The incidence of breast cancer has been studied in eight cohorts of female flight attendants, all but one reported an increased risk for breast cancer which was greater after a longer duration of employment. A limitation is the potential detection bias among female cabin crew due to a higher prevalence of breast cancer screening among this group and potential confounding by reproductive factors and cosmic radiation.

Similarly, studies of airline pilots showed an elevated incidence of prostate cancer compared with national reference levels. However, there is a potential for detection bias due to a higher prevalence of screening for prostate cancer among airline pilots. [ERREN et al., 2009]

2.3.5.1 Possible factors rising breast cancer risk

Melatonin (or light at night) hypothesis

This hypothesis is primarily based on the idea that there is a relation between shift work and breast cancer. Light at night (LAN) suppresses melatonin release and therefore interferes with melatonin secretion. [GIRSCHIK et al., 2010]

Diet

It is suggested that fat consumption shows an association with breast cancer. However, evidence for this association is limited. Furthermore, there is evidence that obesity, especially abdominal fatness is associated with postmenopausal breast cancer risk. On the other hand, high birth weight correlates with higher premenopausal breast cancer rates. [WEIDERPASS et al. 2011]

The high intake of dietary fat at night by rotating shiftworkers (40% of total calories) causes postprandial increases in triacylglycerols and non-esterified fatty acids such as linoleic acid. Linoleic acid provides a stimulatory signal for cancer growth via its mutagenic metabolite, 13-hydroxyoctadecadienoic acid (13-HODE). Elevated melatonin levels in the blood of premenopausal women can inhibit the uptake of linoleic acid and its metabolism to 13-HODE, and tumour proliferative activity.

Exposure of these subjects to light at night suppresses melatonin production resulting in increased linoleic acid uptake, 13-HODE formation, and tumour proliferative activity in human breast cancer xenografts perfused *in situ*.

These results suggest that nocturnal circadian melatonin levels in women may protect against the breast cancer growth-promoting effects of increased dietary linoleic acid levels ingested at night. [ERREN et al., 2009]

Physical Activity

It is not yet clear how often, how long or how intense a person should be physically active, nevertheless, it probably protects against postmenopausal breast cancer. Exercising may also prevent premenopausal breast cancer. [WEIDERPASS et al. 2011]

Alcoholic beverages

The World Cancer Research Fund (WCRF) and the IARC consider alcohol “carcinogenic” to the human breast. (Group 1)

This includes all kind of alcohol beverages. There is a clear correlation between alcohol consumption and breast cancer risk. Increased alcohol consumption increases breast

cancer risk. Alcohol and occupational exposures are risk factors for breast cancer. [WEIDERPASS et al. 2011]

Duration

Risk increases statistically significant when people work night shifts for more than 20 years. However, at the moment no threshold value exists that would separate risk and no risk. [BONDE et al. 2012] Consequently, it is not clear how many night shifts may be dangerous to our health.

In 2008, 38 Danish women received monetary compensation as they had worked night shifts for several years and developed breast cancer.

It seems that people at higher age are more affected by night shifts than their younger counterparts and less able to cope with the chronic disruptions caused by overnight work. [ERREN et al., 2010] In Denmark, exposures that are considered probably carcinogenic (group 2A) are part of the occupational diseases. [BONDE et al., 2012]

The IARC calls for more epidemical evidence for the possible correlation between shift work and breast/ prostate cancer. Furthermore, preventive measures such as shorter night shifts should be taken. [ERREN et al., 2009]

Further strategies to reduce breast cancer risk:

- Maintaining a healthy body weight
- Increasing physical activity
- Minimizing alcohol intake
- Early detection through mammography

According to KOLSTAD (2008) fifty percent of all breast cancer cases can be attributed to female sex hormones, alcohol, obesity and excessive weight gain.

There is evidence indicating that nightshift workers smoke more often, have a higher body mass index, and have hormone replacement therapy less often than dayshift workers. Smoking is not an independent risk factor for breast cancer but may be a proxy

for other factors related to lifestyle and socioeconomic status that may be risk factors for breast cancer. [BONDE et al. 2012]

A great number of cancers can be prevented by implementing more tobacco and vaccination programmes (especially for liver and cervical cancers), early cancer detection systems. On the other hand, Public Health campaigns would be immensely efficient in the fight against cancer development in the long run. Reducing risk for getting cancers can often mean to reach a normal body weight (BMI between 18,5 and 25). Additionally, preventive interventions can also signify to increase physical activity, to have access to early detection programmes and to minimize alcohol consumption. [IARC, 2012]

2.3.6 The function of melatonin

- In vitro it is anti proliferative on cancer cells
- Decreases cell cycle progression through increased TP53 expression
- Inhibits DNA synthesis
- Decreases invasive/metastatic properties of cells in vitro
- Reduces induction of DNA damage by free radicals

Without the pineal gland, DNA damage would be increased when the body is exposed to the carcinogen. Similarly, there is no pineal function after pinealectomy and with constant light exposure. Consequently, melatonin exhibits a sustained decline. In contrast, the highest melatonin levels can be measured in the dark.

The rhythm of production is generated by the **suprachiasmatic nucleus (SCN)** activity in the anterior part of hypothalamus. The SCN is a region in the brain above the optic chiasm. It controls circadian rhythmicity which involves sleep, physical activity, alertness, hormone levels, body temperature, immune function and digestive activity. Many body functions are generated by neuronal and hormonal activities in a 24 hour cycle. (to be precise: the hypothalamic clock lasts a little longer than 24 hours)

The photoreceptors of circadian rhythm are retinal ganglion cells containing the pigment melanopsin. These ganglion cells send information to the pacemaker SCN via the retinohypothalamic tract. On the other hand, the SCN sends information to other hypothalamic nuclei and the pineal gland to modulate body temperature and production of hormones like cortisol and melatonin. [WIKIPEDIA, 2012]

Melatonin

- induces TP53 expression, which in turn slows down cell progression from G0 to G1 phase to S-phase
- acts antiestrogen in ER+ breast cancer cell proliferation and suppresses activity of estrogen growth response pathway
- inhibits expression and telomerase activity in breast cancer cells
- increases the number of natural killer (NK) cells and monocytes in the bone marrow
- enhances antibody-dependent cellular cytotoxicity
- has antimutagenic and oncostatic activity, and light exposure during night shift work can induce desynchrony in circadian rhythms and reduced melatonin production [SCHERNHAMMER et al. 2011]

Melatonin (N-acetyl 5 methoxytryptamine) is a hormone secreted by the pineal gland. It is synthesised from the essential amino acid tryptophan in the blood, which is converted to serotonin and finally metabolized to melatonin. It transmits information of light/darkness to the hypothalamus. [VISWANATHAN and SCHERNHAMMER, 2009]

In the 80's of the 19th century there already existed the hypothesis that the rising incidence of breast cancer is associated with increased use of lightening at night. This was justified by the suppression of melatonin secretion due to lightening at night, consequently increased estrogen levels and as a result increased risk for breast cancer. Today, melatonin is still matter of research. Of interest is melatonin and its relation to disruption of circadian rhythms or interaction with clock genes. [KOLSTAD, 2008]

Disruption of the pacemaker is primarily caused by light. When people are exposed to light at night (LAN), melatonin production decreases. Low serum melatonin levels

enhance the general tumour development. Observational studies support an association between night work and cancer risk. [SCHERNHAMMER and SCHULMEISTER, 2004]

The invention of electric light in 1879 made it possible to extend working schedules into the night. Numerous members of our society are night-active. The problem is that many of them can't adapt to changed rhythms and develop health problems. In former times people lived more according to the sun's cycle. They got up at sunrise and went to bed at sunset, which is natural and essential for various physiologic functions in humans.

Melatonin production and secretion is linked to the circadian rhythm: During the night melatonin is produced and secreted, whereas during the day it's almost zero.

Great melatonin reductions have been reported after 2 consecutive weeks of intermittent exposure to light at night. Melatonin levels recovered a little, however every disruption of a circadian rhythm reduces the ability of recovery.

2.3.6.1 Cancer protective effects of melatonin

Several experimental studies have reported a link between melatonin and tumour suppression. In vitro studies have reported a reduction in the growth of malignant cells of the breast and other tumour sites by melatonin.

In rodents, pinealectomy boosts tumour growth. On the other hand, melatonin shows anti-initiating and oncostatic activity in various chemically induced cancers. It is antimitotic and antioxidant and is able to modulate cell-cycle length through control of the p53–p21 pathway. Melatonin is believed to have antimitotic activity because it interacts with nuclear receptors and has therefore a direct effect on hormone-dependent proliferation. Further, melatonin increases the expression of the tumour-suppressor gene p53. Cells lacking p53 have been shown to be unstable and are thus more prone to tumours.

Melatonin has been shown to be oncostatic for a variety of tumour cells. Reports show that melatonin exhibits a growth-inhibitory effect on endometrial and ovarian carcinoma

cell lines, Lewis lung carcinoma, prostate tumour cells and intestinal tumors . Several clinical trials confirm the potential of melatonin, either alone or in combination with standard therapy regimens, to generate a favourable response in the treatment of human cancers.

602 women from the “Nurses Health Study Cohort” were diagnosed with colorectal cancer during follow-up. On the whole, the number of years worked in night shifts showed big differences in risk: The relative risk for colorectal cancer for 1-14 years of rotating night shifts was 1.00 (0.84–1.19), whereas women with 15 or more years in night shifts showed a much higher risk to develop colorectal cancer: 1.35 (1.03–1.77)

These observations can be explained by the oncostatic effect of melatonin. The higher the light exposure during the night, the fewer the melatonin production. Consequently, the oncostatic effect of melatonin is reduced, which results in increased risk of breast cancer and other cancers. [SCHERNHAMMER and SCHULMEISTER, 2004]

The key organ in the regulation of the circadian clock is the pineal gland. The SCN of the hypothalamus regulates melatonin secretion from the pineal gland.

The retina carries information on external light to the suprachiasmatic nuclei via the retinohypothalamic tract. Melatonin is a hormone which regulates circadian rhythms and is also involved in the regulating gonadal function. Decreased melatonin levels may lead to increased secretion of gonadotropins from the pituitary. This stimulates testicular testosterone and ovarian estrogen production and release.

Interestingly, visual impaired women show lower risks to develop breast cancer. A similar, but less pronounced trend has been observed for prostate cancer in visually impaired males. [PUKKALA and HÄRMÄ, 2007]

The major metabolite of melatonin, 6-sulphatoxymelatonin (aMT6s) is excreted in the urine and is highly correlated with melatonin levels in blood and saliva.

aMT6s levels measured in the first morning urine reflect plasma melatonin levels measured during the previous night. [SCHERNHAMMER and HANKINSON, 2005]

Among premenopausal women, one measurement of morning urinary melatonin is a marker for long-term melatonin levels. [SCHERNHAMMER et al., 2004]

Serum melatonin

- Rapid metabolization, mainly in the liver (short half-life)
- Metabolite of melatonin is 6-sulfatoxymelatonin (aMT6-s), an excret in the urine
- There is a strong correlation between aMT6 in urine and plasma. (morning urinary aMT6-s levels are a good indicator of nocturnal plasma melatonin. [SCHERNHAMMER et al., 2004]

2.3.6.2 Melatonin and the Circadian System

The circadian system consists of the central pacemaker in the SCN of the anterior hypothalamus and peripheral clocks which are regulated by the SCN pacemaker (nervous and neuroendocrine). Norepinephrine is the transmitter that stimulates melatonin release.

Metabolism happens mainly in the liver, where melatonin is hydroxylated and conjugated with sulphate. The excretion product is 6-sulfatoxymelatonin (aMT6s) in the urine. Melatonin is lipophil which signifies that it can act receptor dependent as well as independent. The majority of melatonin circulates in the blood, bound to albumin.

Synchronizer of melatonin secretion by the pineal gland is the light/dark cycle. Secretion of melatonin is suppressed by light. Interestingly, there is no difference between man and women in terms of concentration and suppression by light.

Light can be determined as the most powerful circadian synchronizer. There is a positive association between light and melatonin concentrations: The brighter it is the higher the reduction in circulating melatonin.

Furthermore, melatonin can be regarded as a biomarker of circadian regulation /dysregulation.

In the NHS 2 study the following inverse association was pointed out: The more night shifts the nurses worked, the lower their urinary melatonin levels.

→Disruption of the circadian rhythm correlates with increased tumor growth. Interesting in this context is the fact that blind people show lower breast cancer rate than the normal population. It is suggested that their melatonin production can't be comprised. [SCHERNHAMMER et al. 2011]

The expression "circadian" derives from the Latin phrase "circa diem," which means "about a day".

The circadian master clock provides the reference time for other peripheral clocks, similar to our Greenwich mean time. It coordinates tissue- and organ-specific 24-hour rhythms that allow proper circadian regulation, which is essential for the well-being of organisms

This circadian pacemaker was identified in the early 1970s and acts as a tumor suppressor. Failures to coordinate peripheral rhythms can lead to circadian or chronodisruption. [ERREN et al., 2009]

The Suprachiasmatic nucleus (SCN) serves as a circadian master clock, a biological oscillator, that controls biochemical, physiological and behavioral rhythms, entrained by light and other external signals. The SCN has also the unique ability to provide critical stimulus for resetting its clock phase in direct response to a light signal, which is relayed from retina via the retinohypothalamic tract

Circadian rhythms are generated by clock genes and proteins regulating many functions, including the ability to fall asleep or to snap out of sleep into wakefulness, body temperature, blood pressure, hormone biosynthesis, digestive secretion, and immune responses. Circadian rhythmicity is present in peripheral tissues too. Individual normal cells and even cancer cells keep circadian time by expressing similar clock genes. Circadian clocks in peripheral tissues regulate the expression of specific genes which control DNA synthesis, cell-division cycle and cell proliferation, coordinating physiologic processes in a circadian manner. [Savvidis and Koutsilieris, 2011]

2.3.6.3 Melatonin, a biomarker of circadian dysfunction

Melatonin is a biomarker of circadian dysregulation as it is associated with nightshift work and exposure to light at night. An advantage is that melatonin is robust in various surroundings and remains uninfluenced. In addition, urinary melatonin is stable for a long time. Furthermore it can be measured directly and indirectly in urine, blood and saliva. In contrast to melatonin, other circadian markers such as core body temperature and heart rate can be affected by excessive carbohydrate intake, cortisol and thyrotropin-releasing hormone. Additionally, core body temperature can be masked by sleep and stress. [MIRICK and SCOTT, 2008]

Melatonin synchronizes the internal hormonal environment to the light-dark cycle of the external environment. Stimulated during the dark period of the external environment, the pineal gland produces and secretes melatonin. The retina perceives light, which is a suppressor of melatonin production. Information is transmitted from the retina to the suprachiasmatic nuclei via the retinohypothalamic tract. The longer the night, the longer the duration of melatonin secretion. Among day workers, melatonin concentrations are low during the day and high at night. There is a characteristic rise in concentration after darkness and a peak near the midpoint of the dark interval. [MIRICK and SCOTT, 2008]

Melatonin acts oncostatic and growth inhibitory: A reduction in the growth of malignant cells and/or tumors of the breast, prostate and other tumor sites has been observed in several studies. Interestingly, pinealectomy enhances tumor growth in rodents.

Treatment of prostate cancer cells with melatonin significantly reduced the number of prostate cancer cells and stopped cell cycle progression in epithelial prostate cancer cells and induced cellular differentiation. Melatonin has a direct effect on hormone-dependent proliferation as it interacts with nuclear receptors and therefore exerts antimitotic activity. It is suggested that melatonin can affect cell-cycle control and increases p53 (tumor suppressor gene) expression. Furthermore, there is some evidence that melatonin is beneficial in the treatment of human cancers.

However, it is not clear if low melatonin levels during the night actually result in increased cancer risk. There are several controversial studies on this topic: Yet there is evidence that patients with breast cancer have decreased melatonin levels. It is unknown if the disease or the treatment manipulate melatonin concentrations. [MIRICK and SCOTT, 2008]

2.3.6.4 Light and Melatonin

Light is the most powerful circadian synchronizer in humans. It has a profound effect on the human circadian pacemaker.

Nocturnal illumination completely suppresses melatonin production. However, there is individual variability in LAN (light at night) sensitivity. There is a correlation between LAN and melatonin production: The brighter the light the greater the reduction in nocturnal circulating melatonin, which is a primary circadian pacemaker. [MIRICK and SCOTT, 2008]

2.3.7 Circadian rhythms

Circadian genes have clock functions. These circadian genes regulate expression of other genes with circadian rhythmicity. Disruption of clock damages organization of these gene and protein expressions. This results in deregulated cell proliferation and subsequent tumorigenesis. Circadian genes have also non-clock functions. These non-clock functions are important in regulation of cell cycle progression, DNA damage response, and genomic stability. Clock and non-clock functions build the association between disruption of circadian rhythmicity and cancer.

Circadian disruptions are induced by light at night, genetic or epigenetic variations in circadian genes and interactions between genes and environment. There is a link between disruption of circadian rhythm and cancer. A disrupted circadian peripheral clock can contribute to neoplastic transformation. [Savvidis and Koutsilieris, 2011]

All living things are influenced by circadian rhythms. Circadian rhythms include:

- Sleep/wake cycles
- Body temperature
- Blood pressure
- Hormone secretion
- Digestion
- Metabolism
- Cell turnover

All these factors are essential for survival. The central engine is the central pacemaker and biological master clock in the SCN that as well coordinates the peripheral clocks which results in time organization and function for the human body.

The light/dark cycle is the main influence of circadian rhythm (which is influenced by earth rotation in relation to the sun). Photosensitive retinal ganglion cells contain melanopsin, a photopigment with a peak absorption at 460-484 nm. (blue light). Melanopsin transmits the information to the pineal gland via SCN and sympathetic nerve system. From there, the neurohormone melatonin, a lipophilic indole is secreted and binds to melatonin receptors on organs and tissues.

2.3.7.1 Circadian disruptions

Circadian disruption is a desynchronization of circadian rhythms as a result of the dark/light cycle. This includes the desynchronization of the pacemaker SCN with peripheral clocks. It involves changed circadian rhythm like sleep disturbance and tiredness and consequent changes in physiological markers such as melatonin. (amplitudes, duration, timing of secretion) [BONDE et al., 2012]

Exposure to light at night (LAN) disturbs the circadian system. This results in alterations of sleep activity patterns, suppression of melatonin production and deregulation of circadian genes involved in cancer related pathways [ERREN et al., 2009]

Epidemiological studies correlate disruption of circadian rhythms with incidence of breast cancer. In mouse models data show that disturbed circadian clock gene expression and disruption of circadian rhythms correlate with tumor development and tumor progression [Savvidis and Koutsilieris, 2011]

2.3.8. Melatonin and Cancer

Melatonin is mainly produced during the night. On the contrary, its production during day time is almost zero. However, light exposure in the night results in immediate reductions of melatonin production. Factors influencing melatonin production reductions are: Light intensity, wavelength and duration of light exposure, all of which can cause desynchronization of the master clock from peripheral clocks.

Melatonin

- acts as a anti-cancer signal for cancer cells
- protects cells from a carcinogenic process
- **has antiproliferative effects on human cancer cells *in vitro***
- increases TP3 expression which results in the reduction of cell-cycle progression
- **reduces the invasive and metastatic properties of human cancer cells *in vitro* and increases intercellular communication between these cells.**
- inhibits or reduces the induction of DNA damage by free radicals. **Pinealectomized** rats showed a higher level of DNA damage in response to treatment with a carcinogen than did pineal-intact rats.
- **upregulates anti-oxidant enzyme systems**
- is regarded as a stable and reliable marker of circadian rhythm in humans
- The disruption of the circadian rhythm in mice is associated with the accelerated growth of malignant tumours. [COSTA et al., 2010]

Experimental studies suggest that suppression of melatonin secretion results in increases of metabolic activity of tumors due to increased intensity of light. Circadian disruption results in tumor fatty acid uptake (of linoleic acid), metabolism and accelerated tumor

growth, which is normally suppressed by the nightly secreted melatonin. (=anti-cancer signal). [BONDE et al., 2012]

2.3.8.1 Melatonin Physiology

The strongest suppression of melatonin is caused by a wavelength of 460-480 nm. Yet dim red also creates suppression. [BONDE et al., 2012],[STEVENS, 2009] Decreases in melatonin production favour an upregulation of the gonadal axis. This has been observed among female shift workers who had an increase in circulating estrogen after prolonged exposure to shift work.

An important risk factor for breast cancer is prolonged exposure and/or increased cellular response to estrogens during a woman's lifetime.

Melatonin has the ability to act as a free radical scavenger via activation of the glutathione or related antioxidative pathways and therefore protects cells from DNA damage. Further, melatonin suppresses the formation and accumulation of altered DNA and protects DNA. In addition, it helps to promote DNA repair.

Melatonin acts as a response modifier to estrogens especially estradiol. It has an anti-estrogenic effect via interaction with ER and counteracts the effects of estradiol on breast cancer cell proliferation, invasiveness, and telomerase activity.

Melatonin down-regulates both the expression of protein growth factors and proto-oncogens stimulated by estrogen and the epidermal growth factor receptor 2, the expression of which is associated with increased malignancy in some forms of human breast cancer.

Melatonin modulates local estrogen biosynthesis by reducing aromatase expression and activity. It inhibits telomerase activity and the transcription of Cyclin D1 expression. Cyclin D1 over expression is associated with tumorigenesis and metastases formation. [COSTA et al., 2010]

Why melatonin has oncostatic effects:

- Melatonin binds directly to the receptors in the tumor tissue

- Melatonin has indirect effects through entrainment of the circadian clock in the SCN, or a peripheral clock in the tumor tissue.

Large doses of melatonin have been administered in the clinical treatment of cancer. Yet this medication still needs empirical support. Further, long-term side effects, dose and circadian time point for medication are unknown.

There is a potential for more effective drugs than melatonin to restore circadian rhythms in the future. A key could be the investigation of neurotransmitters and receptors in the optic system transmitting light information to pineal gland. [BONDE et al., 2012]

Time of melatonin peak

The physiological peak of melatonin biosynthesis is between 1 and 2 o'clock in the morning.

Artificial light at night can modify the diurnal melatonin production. It has been proposed that suppressed melatonin production may lead to an increased cancer risk, but further research is needed to fully establish the mechanistic pathways leading to circadian disruption and cancer [PESCH et al., 2010]

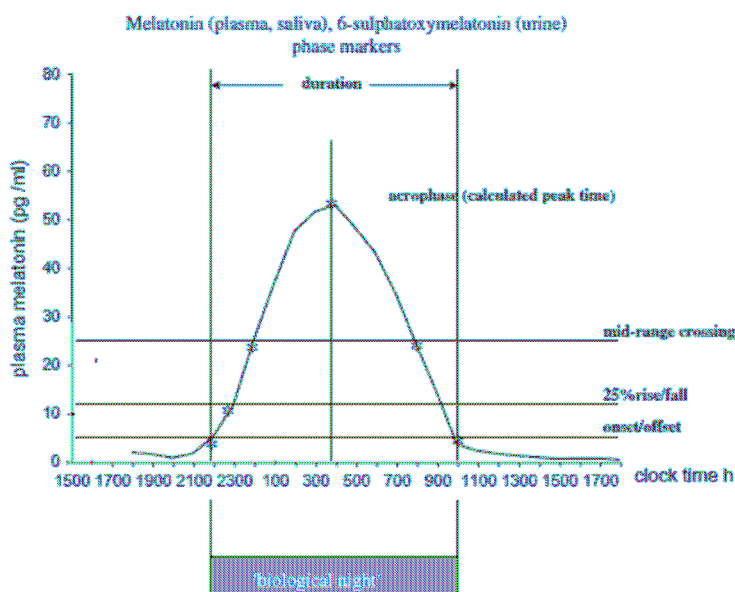


Figure 7: Melatonin rhythm [ARENDT, 2010]

2.3.9 How to minimize circadian disruption

Night and shift workers on early-morning shift sleep 2–4 hours per day less than daytime workers. This may seem irrelevant, yet sleep deprivation and accumulation of a sleep deficit may lead to increased cancer rates among shift workers.

Pinealectomy or functional depression by light at night (LAN) results in immune suppression, which favours establishment and growth of abnormal cell clones. In this case, melatonin supplementation may reverse these defects. [COSTA et al., 2010]

It won't be possible to abolish shift work with its numerous adverse effects. However, if there is ambition to change shift work schedules with better conditions for the worker, the following suggestions need to be considered:

- Shift work schedules
- Years spent in shift (night) work
- Type of shifts: rotating or fixed/permanent shifts
- Amount of night shifts (per month, per year, number of years)
- Exact times of shift periods
- Speed and direction of shift rotation: fast: 1-3 days, intermediate:4-6 days, slow >7 days; clockwise or counterclockwise
- Exposure to LAN (e.g. duration)
- Sleeping times [COSTA et al., 2010]

Number of nightshifts per month

31 showed that the higher the number of night shifts the higher the risk of breast cancer. However, other studies came up with different results.[BONDE et al., 2012]

Shift work results in reduced sleep quality and sleep duration. Reduced sleep hours may result in breast cancer.

Power naps and periods of rest during night shift may increase alertness, however there is no evidence that those measures reduce circadian disruption or prevent breast cancer in women. [BONDE et al., 2012]

Options to limit circadian disruption

- Rapidly rotating shifts (1–2 consecutive nights) result in less disruption of circadian rhythms than slowly rotating shifts (≥ 3 consecutive shifts)
- Delay of circadian phase result in less circadian disruption than advance of circadian phase. Therefore, forward- rather than backward-rotating shifts are recommended
- Modified light intensity during work at night such as working in bright white light to increase adoption or in dim red light to prevent adoption may minimize circadian disruption, yet further research on different light regimens is needed. This also includes studies addressing the optimal trade-off between effects on circadian rhythms and alertness. [BONDE et al., 2012]

Erren et al. (2009) states that establishing biomarkers would mean great progress in the research of shift work/ chronodisruption and consequent cancers, as it can a) help to study associations b) show potential success when preventing chronodisruption or keeping it at a minimum.[BONDE et al., 2012]

Adaptation

Time information is transmitted from the central oscillator to the peripheral oscillators. The central oscillator is “synchronized” by the light–dark alteration of the calendar day. The oscillators in the peripheral tissues are subject to the synchronizing effects of social routine, physical exercise and food uptake.

These secondary synchronizers which determine the phase setting of many peripheral oscillators may compete with the lighting regimen and act over the central oscillator in the SCN in a multifactorial way.

The rhythms of a person have to phase readjust, when there is a new activity–sleep schedule, as during night work or geographic displacement across several time zones.

After some time, central and peripheral oscillators follow the new schedule and adapt to the changed phase of the environmental synchronizer.

During this time of adaptation, disruption of the usual sequence and biological order of the numerous rhythmic events takes place. Some clock genes respond faster than others, which leads to a phase desynchronization within the oscillator mechanism. The circadian oscillators in the anterior region of the SCN undergo a faster time adaptation than those in the posterior part of the SCN. [ERREN et al., 2009]

2.4 Shift work and Nutrition

The World Health organisation defines 'health' as the *"state of complete physical, emotional and social wellbeing, not merely the absence of disease or infirmity."*

This definition indicates that there is a physiological, psychological and sociological aspect of health. [ATKINSON et al., 2008]

Night shift workers mostly eat more carbohydrates and cold food, as well as fast food. However, fewer meals are ingested. [MORIKAWA et al., 2008]

The human body has a circadian rhythm, which is stimulated by light and diet.

However, there is still limited scientific knowledge on how intake of food at night affects the body's metabolics.

Our metabolic system is programmed for activity during the day and rest during the night. Thus, there is a difference between meals eaten in the morning compared to the evening: from morning to midnight glucose tolerance decreases and nocturnal eating increases ratio between LDL and HDL. It is thus suggested that the endocrine system is less suitable for nightly food intake. This might be part of the explanation why there are higher rates of obesity and cardiovascular disease in shift workers.

A meal high in carbohydrates increases plasma glucose more rapidly than a high fat meal. In addition, consuming a high carbohydrate diet results in higher plasma glucose concentration. [HOLMBA et al., 2002]

To maintain circadian internal synchrony, the moment of food intake is crucial. The time of food intake influences peripheral oscillators and may be a factor promoting internal desynchrony.

Dietary intake during normal rest times may result in increased body weight and abdominal fat.

2.4.1 Obesity

The daily total food consumption is similar in both day and shift workers. Increased obesity rates in shift workers may be explained by disturbed metabolic rhythms (flattened glucose and changed TAG rhythms).

Eating during the night results in loss of blood glucose and overweight and increased abdominal fat accumulation, which is a risk factor for the metabolic syndrome, diabetes and a higher incidence of cardiovascular disease.

Thus, “out-of-phase feeding” can lead to disturbed oscillatory expression of metabolic genes and to alterations in cellular energy balance.

As already mentioned, circadian disruption and desynchrony of metabolic genes can result in metabolic disease and obesity of night shift workers.

2.4.2 Orexin

It has been observed in night workers that they ingest almost 70% of their energy intake during working hours. The orexin system in the lateral hypothalamus which has connections with monoaminergic neurons and promotes wakefulness may be responsible for the drive to eat during phases of forced wakefulness.

Orexigenic neurons have the ability to build reciprocal connections with other hypothalamic nuclei that regulate feeding behaviour. Thus, it is being argued that in times of low energy stores, orexigenic neurons may be responsible for wakefulness, which can promote food ingestion.

The hypothesis exists that disturbed feeding patterns lead to overweight and metabolic unbalance. Thus, feeding schedules and restricted food at night can prevent internal

desynchrony and obesity, and can normalize clock gene expression. [SALGADO-DELGADO et al., 2010]

The SCN interaction with the peripheral oscillators can be disturbed, which leads to internal desynchronization.

Night shift work leads to changes in feeding patterns and employees tend to increase their food intake during the night, with specially meals rich in carbohydrates. Feeding schedules have a great influence on peripheral oscillators, on behavior, visceral rhythms and on metabolic rhythms. They have the power to override rhythmic signals transmitted by the SCN and can contribute to internal desynchrony.

Obesity is promoted by disturbances in metabolic rhythmicity (flattened glucose curves and shifted TAG rhythm). Food intake at night results in loss of blood glucose rhythm and overweight. [SALGADO-DELGADO et al., 2010]

2.4.3 Physical activity and Snacking

Few studies exist that study the efficiency of exercise and diet on shift work.

However, it has been shown that fatigue at work can be minimised yet effects in terms of long term health and energy balance have not really been studied. A reason might be that recruitment of participants is very difficult.

Improved catering, recreational facilities as well as physical activity can help to alleviate the effects of shift work. The eating behaviour of shift workers is influenced by the disturbance of sleep patterns and circadian rhythms in metabolic responses to food.

Snacking

It has been reported that there is no difference in energy intakes between day and night workers. However, increased snacking of energy dense foods has been observed. This may be explained by the fact, that preferred foods are unavailable and there is a lack of time as well.

Morning shift workers ate most in the morning, while afternoon and night shift workers had a greater energy intake at noon and at dawn.

Both night and morning shift workers consumed high-energy foods and drinks during work, and most energy was derived from carbohydrates. As an example, many shift workers consume foods high in sugar to overcome tiredness.

Meal times may be influenced by working arrangements and sleeping habits.

Further, availability influences the types of foods consumed.

Inadequate canteen facilities resulted in increased usage of vending machines. The night shift workers thus consumed more energy dense food. On the contrary, shift workers who ate food brought from home consumed lower-energy dense food.

The diet of shift workers is mostly influenced by work schedules and availability of food. Social factors and the disruption of circadian rhythms play a major role.

Eating habits with the family are disrupted. Furthermore, shift work mediates sleep and circadian rhythms disruption, which change metabolic responses to food.

The human body is not designed for a nocturnal intake of energy and nutrients and glucose tolerance decreases from morning to night.

Furthermore, eating during the night increases the LDL/HDL cholesterol ratio.

Plasma triacylglycerol also has higher levels during the night, as nocturnal meals create increased triacylglycerol responses. This might be due to decreased insulin sensitivity. Insulin activates lipoprotein lipase, an enzyme for triacylglycerol clearance.

Insufficient adaptation to circadian rhythms is associated with increased insulin resistance and lipid intolerance.

There is evidence that shift work is associated with elevated lipid levels.

Insulin sensitivity

Reduced insulin sensitivity mediates a reduction in triacylglycerol clearance and is a risk factor in the development of diabetes.

At night time, there is reduced glucose utilisation because glucose metabolism in the brain is reduced. Further, insulin secretion and insulin sensitivity is decreased, which has an impact on subjects eating during the night.

In addition, sleep deprivation can cause reduced insulin sensitivity. It has been observed that glucose response was higher after restricted sleep compared to normal sleep.

Physical activity

In many cases, shift workers don't get the chance to participate in team sports or organised events. Shift workers often don't participate in leisure time exercise as they sleep during that time. Motivated shift workers might often exercise before or after sleep or late at night. The consequence of those unusual timings is unknown.

It is assumed that the majority of shift workers don't regularly exercise.

Typical excuses for not adhering to physical activity regimens are: lack of time, lack of opportunity and lack of support.

Reasons behind could be the disruptive nature of shift work, feelings that an unhealthy lifestyle is acceptable as shift work pays well or the general reluctance for a healthy lifestyle.

It is suggested that high amplitudes of circadian rhythms leads to more stable workers who can better cope with rhythm disturbances.

It has been found that physically fit subjects have higher rhythm amplitudes than inactive people. Unclear is the fact if physiological adaptation as result of improved fitness leads to higher rhythm amplitudes or if exercise is a synchroniser that mediates a stronger rhythm.

However, the suggested association between circadian rhythm amplitude and shiftwork tolerance still needs scientific confirmation.

Sleep quality

It is assumed that physical activity improves quality and duration of sleep. Furthermore, the amount of slow wave sleep (SWS) is increased. This is beneficial in terms of brain restoration and recovery during sleep.

There are several theories why physical activity improves nocturnal sleep quality.

Exercise may reduce anxiety, has a sleep-inducing thermogenic and long-term antidepressant effect and favors a circadian phase for sleep.

Exercise mediates temperature elevation which increases slow wave sleep.

On the other hand, chronic physical activity can favour the sleep-onset process by a temperature down-regulation, which promotes sleep. Attenuated temperatures at night have been detected in people with depression, sleep disruptions and insomnia.

Disrupted sleep-wake cycles and reduced sleep quality and quantity due to shift work might be alleviated by physical activity, as exercise can increase sleep quality by thermogenic effects, reductions in anxiety and depression or via circadian phase-shifting.

However, the benefits of physical activity on sleep quality and quantity of shift workers are still highly speculative.

It is advised to be physically active 4-8 hours before going to bed.

The timing of physical activity may be crucial for adjusting to night work as it can advance or delay the circadian rhythm. If exercise is correctly timed and thus circadian rhythms are adjusted to the shift, fatigue, tiredness and sleepiness may be reduced, which may increase exercise tolerance and could lead to continuing regular physical activity. It is discussed that exercise might act as a synchroniser of circadian rhythms as physical activity can alleviate some sleep disturbances.

A large epidemiologic study concluded that the number of hours of exercise per week was inversely related with the severity of sleep apnea.

To work in constantly changing schedules means that the sleep-wake cycle is constantly disturbed which may result in chronic sleep deprivation.

In general, short sleep is associated with obesity. Additionally, it is assumed that shift workers are more sedentary than day workers, which is also linked to higher prevalence of obesity.

Physical activity interventions

Unfortunately, the great advantages of exercise during shifts got only little attention so far.

There has been some success with worksite-based physical activity interventions: On average, it was demonstrated that it decreased body mass by 1–2%, 2–10 mmHg decreased blood pressure and a 15% decreased serum cholesterol. Further, small reductions in absenteeism and an average increase of 4–5% in productivity could be achieved. Additional benefits of regular physical activity are better tolerance to stress at work and better health.

A training programme for female shift workers has been developed that included between 2 and 6 training sessions per week, each time between 60–70% of maximal heart rate. After a 4-month period it was found that on the whole, sleep benefited the most: The mean sleep length increased significantly by 4.9% after the evening shift. Further, general fatigue decreased and performance rose.

Thus, it was suggested that for morning and dayshifts, exercise should be done several hours before going to bed. For night shifts, it is advisable to do physical activity before evening naps.

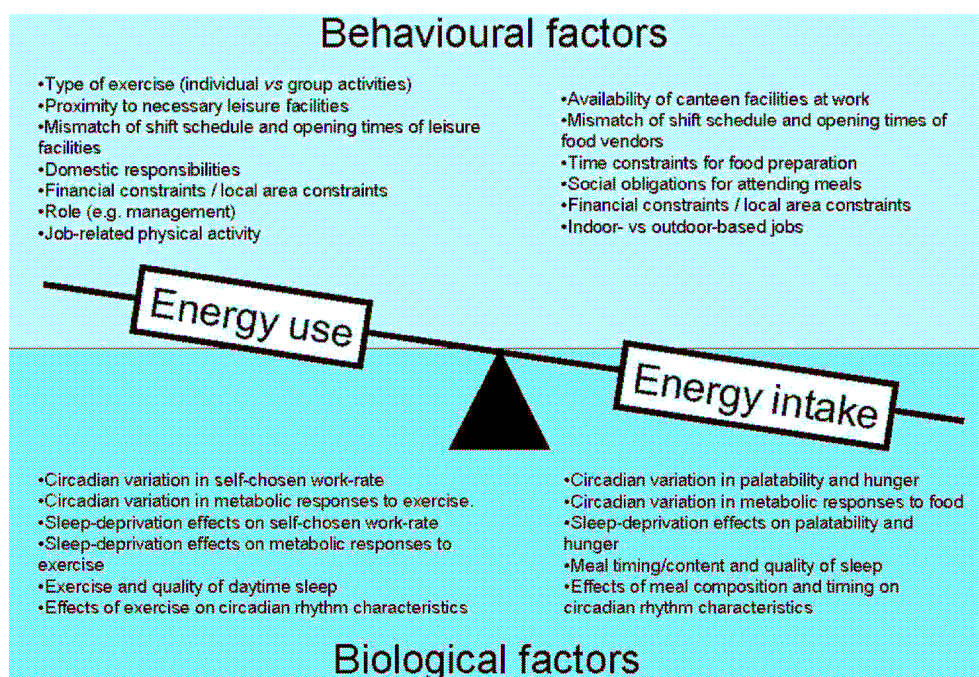


Figure 8: Behavioural and biological factors.[ATKINSON et al., 2008]

2.4.3.1. Exercise and blood pressure

As already stated, shift workers generally have higher triglyceride and lower HDL levels compared to day workers. In addition, it has been reported that obesity, diabetes and metabolic syndrome are common, resulting in increased cardiovascular risk.

Timing and type of food eaten is mostly not determined by hunger but external factors such as work schedules. As a result, night workers tend to snack a lot instead of consuming proper meals.

It has been found, that moderate exercising for one hour before an 8 hour night shift reduced the MAP in normotensive subjects.

Interestingly, a bigger decrease in diastolic BP was observed when one large meal was consumed at the start of the shift, as opposed to consuming 2 smaller meals during the shift. Yet meal frequency didn't have an impact on systolic BP and MAP.

It has been found that a meal high in fat resulted in significant increases in systolic and diastolic BP and total peripheral resistance, as opposed to a low fat meal of equal energy content.

→ Regular exercise limits increases in BP in shift workers. [FULLICK et al., 2009]

2.4.4 Hyperuricemia

Alterations in serum UA could be a consequence of stress due to night work.

Hyperuricemia is thought to be associated with metabolic syndrome and insulin-resistance syndrome. Hyperuricemia is related to higher risks for cardiovascular mortality. Among a shift working group that changed to day work, serum UA levels decreased significantly after 3 weeks. [UETANI et al., 2006]

2.4.5 Leptin and Ghrelin

Leptin is responsible for the regulation of energy balance and acts as a feedback signal from adipose tissue to the hypothalamus.

Plasma leptin levels are correlated with fat mass. Leptin is thus produced in the adipose tissues.

Short-term starvation leads to a reduction in leptin mRNA. Leptin mRNA expression has a cyclic variation: it rises after food intake and generally decreases during the day.

Increased leptin mRNA expression happens under the influence of corticosteroids and insulin. Yet, plasma leptin levels are highest during the dark and lowest during the day.

Breakfast led to a cessation of the late-night and early-morning decrease in plasma leptin levels. After breakfast, leptin levels begin to rise slowly.

This is in contrast to a report that says that the highest leptin levels are measured during the day, with a zenith in the late afternoon or early evening. This difference however, maybe due to different energy contents per each meal.

Diurnal variation in leptin levels is entrained to meal timing. Thus, insulin may change leptin production. However, this link is not strong. [SCHOELLER et al., 1997]

During circadian disruptions leptin levels decrease, which is in no association to the decrease in the leptin secretion stimulating factors glucose, insulin, cortisol, vagal tone or food intake nor in association to the increase of factors that inhibit leptin, namely epinephrine, norepinephrine, metabolic rate or a change in metabolic substrate.

In rodents it was shown that peripheral oscillators can be uncoupled from the master oscillator in the hypothalamus by restricted daytime food intake. Yet, for humans it still needs to be proven that food can be a “Zeitgeber”.

Leptin levels are mainly controlled by meals, however it needs to be found out if meals can directly have this effect or if this happens due to entrainment of central or peripheral oscillators.

→ Circadian misalignment resulted in reduced leptin and sleep efficiency, increase in glucose, insulin and mean arterial blood pressure.

Ghrelin increases food intake and alters energy metabolism by increasing respiratory quotient or carbohydrate oxidation. Ghrelin and NPY alter appetite and energy metabolism by acting on hypothalamic circuits mediating positive energy balance. [CURRIE et al., 2010]

Leptin from adipocytes inhibits food intake, ghrelin stimulates it. Both hormones are entrained to the sleep-wake cycle and thus sleep deprivation and timing of sleep has an impact on plasma concentrations. [ATKINSON et al., 2008]

Reduced sleep causes increased ghrelin and decreased leptin levels, which promotes further food intake such as snacks rich in carbohydrates. Leptin normally promotes satiety, with high concentrations in the late evening.

→ It is thus advisable to reduce food intake or not eat any food at night, especially after 3:00 hours. [LOWDEN et al., 2010]

2.4.7 Eating at night

The increased risk for ischemic heart disease associated with shift work might be related to eating habits. As a matter of fact, meal intake is mainly redistributed from day to night.

When food is frequently ingested at night, physiological functions are at the lowest point of the day, which may result in abnormal metabolic effects such as increased serum lipid levels or increased BMI.

→ Rotating shift work affects circadian distribution of energy intake, but the total amount of energy and nutrient intake remains unchanged. Yet eating at night might be associated with higher total cholesterol and LDL cholesterol levels and lower HDL cholesterol levels.

Thus, the key factor seems to be the change from diurnal to nocturnal eating.

One reason might be the changed phase relation of food intake and the circadian rhythmicity of digestive processes. There are circadian patterns for gastric emptying rate, hepatic enzyme activity, biliary excretion, anabolic and catabolic hormones (eg, insulin and cortisol).

A night meal stimulates insulin, yet the growth hormone should be released at this time. Further, the circadian rhythmicity related to sleep and wakefulness is disturbed, which may result in an imbalance in the endocrine rhythms associated with fat mobilization. This imbalance can interfere with the mobilization of free fatty acids from fat depots. (this is a hypothesis)

The best predictor of lipids is the total ingested carbohydrate, however the main cause and nutrient of increased cholesterol and LDL cholesterol is not identified. [LENNERNÄSE et al., 1994]

Contrary to the light-dark cycle, the time of food intake might be a more potent synchronizer of the phase of plasma corticosteroid levels. [KRIEGER and HAUSER, 1978]

Working in shifts alters eating behaviour. Eating at night leads to disturbances of intestinal motility, affects the digestion, absorption, and utilization of pharmacological drugs and nutrients.

The human body is diurnal, which means that, we are active during the day.

At night we are thus programmed for restitution, fasting and mobilization of blood glucose, which results in decreased appetite.

WHY DIETARY RECOMMENDATIONS FOR SHIFT WORKERS NOT YET EXIST

- It is unknown if it is advisable to eat at night or not
- It is unknown what food stuffs are recommended/less favourable
- Nutritious meals are mostly not available
- Eating at night might improve wellbeing yet can negatively impair metabolism

During sleep, anabolic processes dominate. (growth and repair) During the day, on the other hand, there are catabolic processes, the metabolic rate rises: the body ingests food and stores energy. Nevertheless, anabolic and catabolic processes occur in parallel during both day and night. During the night, growth hormone and cortisol cause internal energy mobilization of blood glucose.

The reason for impaired glucose tolerance in shift workers might be that blood glucose is reduced at night and is provided for the central nervous system, which might result in resistance to nocturnal energy in muscle tissues.

Shift workers have less regular meal patterns and eat more frequently, especially snacks instead of a full meal, which might be responsible for the higher energy intake during the night in shift workers. [LOWDEN et al., 2010]

Shift workers consume more than 50% of energy in the evening and at night, with more frequent eating but less food eaten each time. [ATKINSON et al., 2008]

Shift work seems to affect the amount eaten, the quality of the dietary intake, and energy distribution over the day.

2.4.8 The effect of shift work on metabolic disorders

Shift working is associated with metabolic disorders, especially linked to lipid and glucose intolerance. Higher rates of obesity and triglycerides, with lower concentrations of high-density lipid (HDL) cholesterol have been found in this population.

Metabolic changes in shift workers may promote the development of cardiovascular disease. Further, stress, disrupted circadian rhythms, sleep debt and health behaviour are linked to metabolic syndrome and cardiovascular disease.

Overweight

The majority of studies find an association between night work and weight gain. However, some studies can't verify this association. Still, causal factors are not established. It is assumed that weight gain can also result from changed lifestyle and health behaviours.

Obesity can lead to cardiovascular disease and sleep problems such as sleep apnea syndrome. However, obesity is a confounding factor for the shift work- CHD association. [LOWDEN et al., 2010]

Pathways from poor diet to metabolic disorders

It is not chronobiological to eat at night and sleep during the day, thus this behaviour leads to disrupted regulation and metabolism.

During the day, glucose metabolism and fat storage is induced and at night, glucose is spared and fat metabolism is active. Due to this fact, shift workers have lower glucose and lipid tolerance. Also, reduced glucose tolerance can result from small sleep disruptions.

A study of permanent night workers indicated that after two years of regular night work with 4–6 nights worked per week, adjustment of glucose and insulin secretion rhythms were still not complete.

HOMOCYSTEINE

Homocysteine shows a circadian nocturnal peak. When animal protein meals are ingested at night its level is increased.

→ Increased homocysteine, reduced glucose and lipid tolerance at night as well as sleep deprivation are risk factors for cardiovascular diseases.

In addition to light and sleep, food intake has the ability to be a “Zeitgeber” as it can influence the timing of the body clock.

Eating has an impact on peripheral clocks, yet a weak influence on the central clock SCN in the brain. Disrupted peripheral circadian oscillators could be part of the development of obesity type 2 diabetes and metabolic syndrome.

→ It is advised to adapt to the diurnal rhythm by keeping the same meal times during the shift and to restrict or avoid energy intake between midnight and 06.00 hours.

Blood glucose

After the consumption of a meal blood glucose levels increase (postprandial), insulin is secreted and consequently blood glucose decreases again.

Generally, alertness decreases after food intake and 3.5 hours after ingestion the signs of sleepiness are at the highest level. Meals rich in carbohydrate lead to more pronounced reduces in mental performance than meals rich in fat.

It was tested whether night shift workers should fast or eat during the shift. There were two groups, the fasting group got all food stuffs during the day, whereas the non-fasting group received meals regularly distributed with the 24 hour period. There was no difference in energy content.

Consequently, performance in both groups was similar, yet subjects of the fasting group felt sleepier and had lower energy levels during the night shift.

The following guidelines for dietary behaviour are directed at shift workers and the general population.

2.4.9 General guidelines

- Avoid eating, or at least restrict energy intake, between midnight and 06.00 hours, and try to eat at the beginning and end of the shift.
- Avoid “large meals” (>20% of daily energy intake) 1–2 hours prior to the main daily sleep episode.
- Provide a variety of food choices: complete or vegetarian meals and high-quality snacks are recommended.
- Avoid foods and beverages classified as low-quality snacks.
- Provide appropriate dining facilities that, for example, allow a meal to be eaten away from the workplace, with colleagues, in as pleasant a surrounding as possible.
- Maintain a healthy lifestyle with exercise, regular meal times, and good sleep hygiene when not working.

Specific guidelines for shift work

- Eat breakfast before day sleep to avoid waking due to hunger.
- Stick as closely as possible to a normal day and night pattern of food intake
- Divide the 24-hour intake into eating events with three satiating meals each contributing 20–35% of 24-hour intakes. The higher the energy needs, the more frequent the eating should be.
- Avoid over-reliance on (high-energy content) convenience foods and high-carbohydrate foods during the shift. Instead choose vegetable soups, salads, fruit salads, yoghurt, wholegrain sandwiches, cheese or cottage cheese (topped with slices of fruits), boiled egg, nuts, and green tea (promoting antioxidant activity), although this may not be palatable to some.
- Design shift schedules so as to allow adequate time between shifts for sleep, meal preparation, amongst others, avoid quick returns.

- Avoid sugar-rich products such as soft drinks, bakery items, sweets, and non-fiber carbohydrate foods (high glycemic load) like white bread. [LOWDEN et al., 2010]

2.4.10 Metabolism

Abrupt changes in the timing of sleep and work lead to significantly changed postprandial glucose and lipid tolerance and insulin secretion, which can contribute to CVD.

In general, glucose tolerance decreases throughout the day. Glucose and insulin responses are dependent on circadian rhythmicity. Additionally, glucose-dependent insulinotropic peptide (GIP), gastrin and motilin vary diurnally.

Insulin activates lipoprotein lipase, an enzyme that plays a key regulatory role in postprandial TAG clearance. Low nocturnal insulin sensitivity may be associated with lower lipoprotein lipase activity and impaired TAG clearance or higher circulating TAG levels of hepatic origin. Thus, there are higher postprandial plasma TAG levels after a meal at night compared to the day.

Non-esterified fatty acids (NEFAs) also follow a diurnal rhythm, depending on meal patterns. Insulin inhibits hormone sensitive lipase and can influence circulating NEFA levels.

Generally, insulin sensitivity is lower during the night than in the day. This results in greater amounts of insulin needed to cope with the same amount of glucose at night. [LUND et al., 2001],[RIBEIRO et al., 1998]

Plasma glucose levels are higher at night as glucose tolerance after meals or oral glucose is impaired. This is due to insulin resistance which leads to fewer glucose uptake.

Melatonin inhibits LDL receptor activity and cholesterol synthesis in mononuclear leucocytes.

Further, melatonin influences lipoprotein lipase (LPL) in adipose tissues, which is activated by insulin. Low insulin sensitivity can be linked to lower LPL activity and impaired plasma TAG clearance.

Nocturnal insulin resistance can be related to higher plasma TAG levels originating from the liver, as insulin suppresses VLDL secretion by the liver.

Insulin resistance and higher postprandial TAG levels present elevated risk factors for cardiovascular disease.

Chylomicron and VLDL remnant lipoproteins are derived from TAG-rich chylomicrons and VLDL. They have been shown to be atherogenic. In addition, when TAG levels are high, it is more likely that small dense LDL are built, which also is a risk factor for cardiovascular disease.

People working in shifts have increased plasma TAG levels independent of energy and nutrient intake. In addition, they have higher risks of developing cardiovascular diseases. [MORGAN et al., 1998]

→ Plasma glucose rhythms are not totally adapted in most night workers.

Decreased insulin sensitivity and small elevations in glucose are associated with higher cardiovascular risk. [SIMON et al., 2000]

It has been suspected that eating at unusual times of the day cause metabolic disturbances and gastrointestinal symptoms in shift workers. Circadian rhythm disturbances are related to type 2 diabetes, obesity and metabolic symptoms. [YOON et al., 2012]

IGFBP1

Disturbed sleep is a risk factor for obesity, type 2 diabetes mellitus and cardiovascular diseases. Sleep restriction and disturbances may cause glucose intolerance, insulin resistance and increased appetite. Unfortunately, the underlying mechanisms are still poorly understood. One possible mechanism may be insulin-like growth factor-binding proteins (IGFBPs). These are proteins that bind IGFs (IGF1 and IGF2), determine their bioavailability and also have direct effects.

IGFBP1 secretion is mainly regulated at transcriptional level by insulin, glucocorticoids and growth hormone (GH). Disturbed sleep may have effects on IGFBP1, which has a characteristic 24-h rhythmicity. There is an inverse association between insulin and

IGFBP1: IGFBP1 levels are high as a response to fasting. The highest IGFBP1 levels have been observed in subjects who slept during the day instead of the night.

Sleep-fasting is the main predictor of the 24-h variation of IGFBP1. A shift of sleep leads to a disturbed metabolic regulation of IGFBP1.

Disturbed sleep results in changed IGFBP1 regulation, which acts as a predictor for developing type 2 diabetes, cardiovascular and metabolic disorders.

The last part of day sleep and first hours after waking up are characterized by increased levels of IGFBP1, which is believed to be a result of impaired insulin sensitivity or sleeping at a different circadian phase or staying up longer than normal.

Insulin has the ability to suppress IGFBP1.

The first three hours of sleep are characterized by low levels of IGBP1 and high levels of insulin. After four hours of sleep, however, insulin is gradually reduced, while levels of IGFBP1 rise until one hour after breakfast. Next, IGFBP1 is cleared by insulin.

5-6 hours after a meal, IGFBP1 levels are especially high. Thus, evening and night meals may have a strong influence on morning IGFBP1.

Sleep-fasting seems to be the cause for elevated IGFBP1 and sleeping during the day results in higher levels than nocturnal sleep. [REHMAN et al., 2010]

Further, when subjects ate and slept 12 hours out of phase, their levels of leptin were decreased, as well as sleep efficiency. Increased were glucose and mean arterial pressure, which implicate cardiometabolic changes.

The SCN regulates circadian rhythms in leptin, plasma glucose, glucose tolerance, corticosteroids, and cardiovascular function. Reduced leptin stimulates appetite and reduces energy expenditure, which may lead to obesity. Additionally, decreased sleep means higher risk for obesity, diabetes and hypertension.

It is not yet confirmed that meals at abnormal times lead to internal desynchronization. Some animal models found that shift work leads to premature death. Besides, mutations of circadian clock genes can result in symptoms of the metabolic syndrome. Further, it

is suggested that vulnerable people such as hypertensive individuals are more prone to the hemodynamic effect of chronic misalignment.

2.4.11 The Metabolic Syndrome

PATHWAYS TO DISEASE

- mismatch of circadian rhythms
- social disruption
- behavioural changes
- changes in biomarkers [KARLSSON et al., 2001]

The metabolic syndrome represents several risk factors of metabolic origin and increased cardiovascular risk. [WOLK and SOMERS, 2006]

Thus it is suggested that the metabolic syndrome is a strong risk factor for CHD, which indicates the association between shift work and CHD. [KARLSSON et al., 2001]

Unclear is whether it has one or multiple causes. Predisposing risk factors are abdominal obesity, physical inactivity and insulin resistance. The latter is associated with obesity and physical inactivity.

Three of the following five criteria are decisive for the diagnosis of the metabolic syndrome:

a) abdominal obesity

(increased waist circumference: 102 cm for men and 88 cm for women)

b) elevated triglycerides (150 mg/dl)

c) decreased high-density lipoprotein (HDL) cholesterol (< 40 in men, <50 in women)

d) high blood pressure

e) increased fasting glucose (> 110 mg/dl)

The original definition of metabolic syndrome by the World Health Organization includes glucose intolerance and insulin resistance. [WOLK and SOMERS, 2006]

Insulin resistance is a major cause of the metabolic syndrome. It means lowered sensitivity in muscle, liver and fat cells to the actions of insulin. [KARLSSON et al., 2001]

There is an association between hyperinsulinaemia and glucose intolerance, elevated triglycerides, lower HDL cholesterol, elevated blood pressure, endothelial dysfunction, pro-coagulant and pro-inflammatory states. [WOLK and SOMERS, 2006]

Disruption of circadian rhythmicity may result in metabolic disturbances. Postprandial glucose concentrations have been higher after a meal when the circadian rhythm is phase shifted. In addition, quality and duration of sleep has an impact on metabolic and endocrine function. [KARLSSON et al., 2001]

Sleep disturbances may lead to weight gain and insulin resistance. [WOLK and SOMERS, 2006] Sleep deprivation may be a factor in the development of the metabolic syndrome as it affects glucose tolerance and insulin sensitivity.

[DE BACQUER et al., 2009]

The metabolic syndrome includes a disturbance in the glucose-insulin axis such as type 2 diabetes, impaired glucose tolerance or insulin resistance. This may occur combined with two of the following conditions: high triglycerides or low HDL cholesterol, increased blood pressure, central obesity or BMI>30 and microalbuminuria. [KARLSSON et al., 2001]

The relation between shift work and cardiovascular risk can be explained by disturbed metabolic regulation due to altered lifestyles, mismatch of circadian rhythms and chronic work stress.

Higher prevalence of the metabolic syndrome with all components has been observed among shift workers: increased blood pressure, raised triglycerides and glucose levels, low HDL cholesterol and abdominal overweight.

On the whole, dietary intake and general eating patterns hardly differ between day and night workers. However, it was documented that metabolic responses to meals have been impaired when there was no adaptation to night work. [DE BACQUER et al., 2009]

In an Austrian study comparing day workers and shift workers the morbidity of endocrine and metabolic diseases was increased in old shift workers.

Exposure to shift work for several years results in higher morbidity of endocrine and metabolic disease than day workers. [KARLSSON et al., 2001]

Shift workers are at greater risk of developing cardiovascular disease which may be partly due to metabolic and hormonal changes.

2.4.11.1 Sleep deprivation

Sleep deprivation is linked to obesity, hypertension and metabolic and hormonal changes associated with CVD. After partial deprivation of 5.5 hours for 14 nights or 4 hours for 6 nights significantly reduced glucose tolerance and insulin sensitivity. In addition, after 3-5 days without sleep, TAG rhythm amplitude was reduced, as well as TAG levels.

Working in shifts for a longer time could result in adaptation to sleep deprivation effects. → However, dayshift workers and long-time shift workers may show different reactions when they undergo the same sleep restrictions and dietary intake. [WEHRENS et al., 2010]

2.4.11.2 Diabetes

Rotating night shift work and diabetes (plus greater weight gain) are associated.

There may be a relation between duration of shift work and diabetes. [KARLSSON et al., 2001]

It was shown that women had higher risk for type 2 diabetes after several years in shift work, which may be mediated by body weight. The NHS I and II cohorts suggest that increased risk of type 2 diabetes is not limited to a particular age group. However, ten years of rotating shift work was associated with 64% increased diabetes type 2 risk, which disappeared after adjustment for BMI. Yet, women with 20 years in shift work had still a 44% increased risk for diabetes type 2 after adjusting for BMI.

→ This suggests that several years in night shift work may often result in type 2 diabetes development, which can't be totally explained by BMI.

Besides, a study among Japanese workers found that shift work was a risk factor for impaired glucose metabolism and diabetes.

Night shift work generally means chronic misalignment between the endogenous circadian timing system and the behaviour cycles, which often leads to metabolic and cardiovascular symptoms: decrease in leptin, increased glucose as a consequence of too strong postprandial responses, insulin and mean arterial blood pressure increase and reduced sleep efficiency.

In addition, the shift of food intake may increase BMI and influence postprandial glucose and insulin levels. However, it is still unclear what the implications of eating habits on health status of shift workers are in the long term.

Working in night shifts may influence quality and quantity of sleep.

Further, several studies suggest that sleep disorders and sleep disruptions lead to greater risk for type 2 diabetes.

Diabetes type 2 however concluded that the association shift work- diabetes can't be explained by sleep problems alone, by suggesting the additional factors disturbed socio-temporal patterns and changed biomarkers (cholesterol, lipids, plasminogen, blood pressure, cardiac activity) that can have an impact on the association. [PAN et al., 2011]

Circadian disruption may accelerate diabetes type 2 development in subjects who are prone to this disease. Insulin resistance may be the result of insufficient sleep and poor sleep quality, which also lead to increased appetite and obesity.

A meta- analysis suggests a strong association between shift work and weight gain, which is a risk factor in the development of diabetes.

Behavioural changes such as reduced physical activity may also induce processes towards diabetes type 2.

Subjects with 1-2 years of shift work have a 5% increased risk of diabetes type 2, with 3-9 years 20%, after 10-19 years 40% and for 20 years of shift work almost 60%.

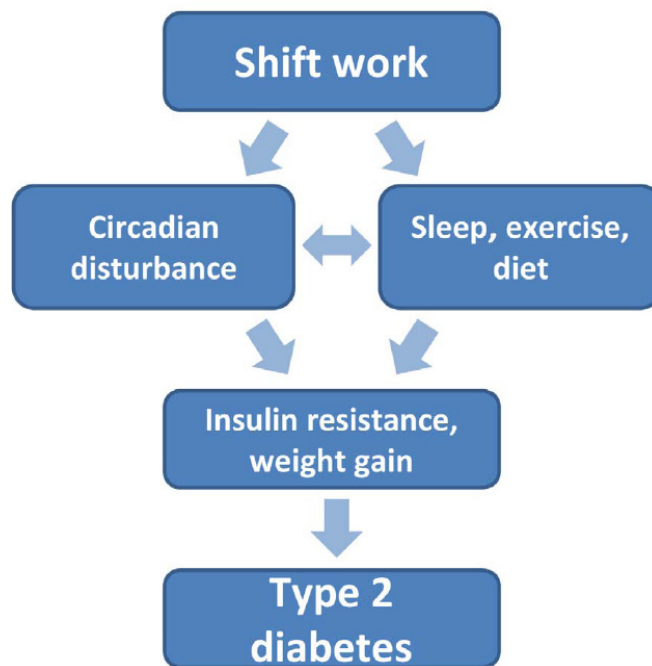


Figure 9: Links between shift work and type 2 diabetes [KIVIMÄKI et al., 2011]

Diabetes type 2 may be prevented by healthier lifestyles, weight control and early identification of prediabetic and diabetic subjects. [KIVIMÄKI et al., 2011]

The biological clock controls the sleep-wake cycle, hormones, core body temperature and heart rate.

In one study they found that 14% of night shift workers had a “shift work sleep disorder”. Almost a third of this population developed a depression.

Female shift workers were diagnosed with the following: obesity, high blood pressure, endometriosis and breast cancer. Shift workers are at higher risk to develop a metabolic syndrome over a 5 year period than dayshift workers. [GAMBLE et al., 2011]

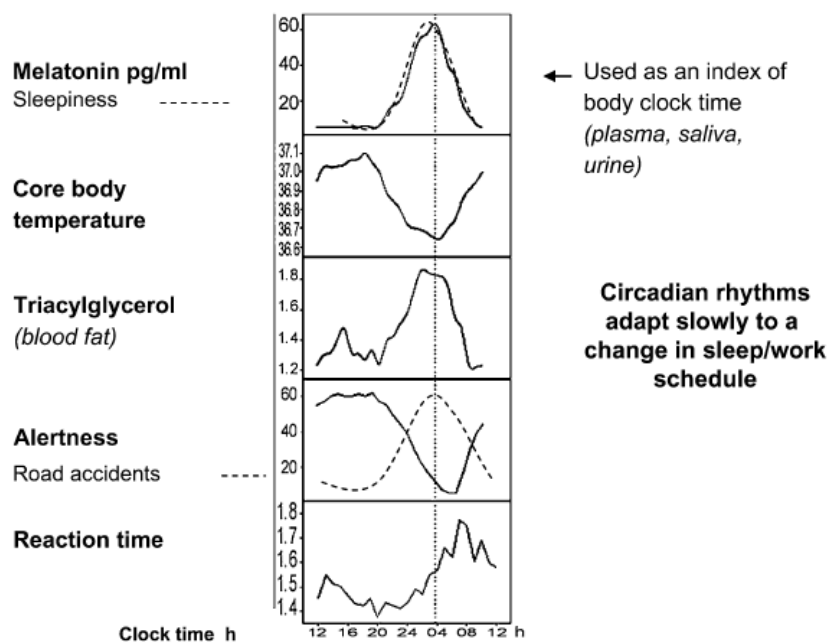


Figure 10: Examples of circadian rhythms [ARENDT, 2010]

BMI

The largest BMI increase has been observed in workers who changed from day to shift work. Weight gain is a major risk for increased blood pressure and lipids and reduced glucose tolerance. In addition, the prevalence of metabolic disturbances seems to be higher among shift workers, who tended to have higher total cholesterol.

Shift work causes food redistribution, yet calorie intake stays more or less the same. Besides, cold food and fast food is frequently consumed. [MORIKAWA et al., 2007]

The predictor of BMI for shift workers is duration of shift exposure, whereas for day workers, age predicts BMI. [KARLSSON et al., 2003]

Exposure to shift work is a predictor of increased BMI, obesity and waist-to-hip ratio. [ATKINSON et al., 2008]

Insulin Secretion

Insulin secretion has a circadian rhythm: it rises during the day and falls during the night. Correspondingly, it is assumed that the metabolic response varies according to eating. In the morning, the insulin response is at the lowest point of the day.

Generally, the lipid profile of shift workers suggests an association between shift work and the metabolic syndrome. [KARLSSON et al., 2003]

Shift work involves higher risks for the development of metabolic disorders and higher cortisol levels, which is a risk factor for type 2 diabetes, obesity and CHD. Cortisol acts as a regulator of stress and shift workers with a lot of stress and workload have increased cortisol levels. Prolonged cortisol excess may lead to insulin resistance and diabetes in the end. Cortisol predicts glycemic index as it increases hepatic glucose production and therefore rises glucose availability. However, cortisol inhibits glucose uptake and utilization by peripheral tissues

Quality and timing of food intake could play a role in metabolic response.

Food intake during the night induces an abnormal metabolic behaviour with metabolic effects such as increased serum lipids and BMI. Eating during different times may have different metabolic effects that are dependent on the circadian type of a person.

A circadian disruption of energy intakes correlates with serum lipids and the redistribution of food intake is related to serum total cholesterol, LDL, HDL, which are promoting increased CHD risk.

Insulin sensitivity has a diurnal variation, with the lowest sensitivity at night.

Insulin resistance is associated with higher CVD risk. The problem of a meal taken at night are higher glucose and TAG levels that lead to increased insulin resistance at night. In addition, TAG is a risk factor for CHD. Thus it can be concluded that meals at night contribute to increased CVD risk.

Insulin activates the lipoprotein lipase (LPL) an enzyme that is responsible for TAG uptake into cells. There is a 24h variation of LPL activity with lower activity during the night, consistent with insulin resistance at night

There is a recovery of glucose tolerance at the end of night shift by increased insulin secretion.

Raised NEFA levels are associated with increased CVD risk. NEFA also has a 24h rhythm: the highest levels can be observed in the morning, with a second increase at night. These levels are probably highly related to patterns of food intake.

There is a 24h variation in insulin sensitivity and an association of insulin resistance with increased CVD risk. Further, when shift workers eat meals at night, a circadian phase of max. insulin insensitivity causes cumulative postprandial effects.

There is a relative lipid intolerance throughout the night, yet a recovery of metabolic glucose tolerance at the end of night. This implies the suggestion to restrict fat intake throughout the night for those not adapted to night work.

Glucose tolerance has a circadian rhythmicity, similar to insulin secretion. It is lower in the evening with glucose peaks around midnight.

Sleep deprivation has effects on glucose and insulin responses. However, sleep deprivation of 10 hours or less probably has no effect on glucose tolerance.

2.4.12 Lipid metabolism

TAG and LDL cholesterol is a risk factor for coronary heart disease. LDL settle in the arterial wall, there is oxidation and further cholesterol desposition which may lead to atherosclerosis.

In addition, TAG varies diurnally. TAG levels vary much more than other lipids. Outcomes of TAG measurements vary depending on recent diet, smoking, illness, exercise, pregnancy, alcohol intake and body mass index.

Postprandial TAG responses happen after meals with even modest amount of fat. Shift workers have significantly higher fasting TAG levels than dayworkers. Eating a meal at night results in higher TAG levels compared to a meal during the day, which is an evidence for insulin resistance at night.[SOPOWSKI et al., 2001]

Men seem to be more prone to high TAG levels, which implies a higher risk for developing a heart disease. [ARENDR, 2010]

In addition, after high fat meals, huge postprandial responses were reported, with a peak 2 hours after a 04:00 meal. Generally, there is an increase in TAG levels from morning to evening. Interestingly, diets high in carbohydrates produced higher TAG concentrations than high fat diets.

It was suggested, that permanent night shift workers have adapted to night work. However, most shift workers work in two- or three-shift rotations, which means that their circadian rhythm resembles that of day workers. At this point in time, there exist no dietary recommendations specially designed for shift workers. [HOLMBA et al., 2002]

The rate of gastric emptying, intestinal triacylglycerol hydrolysis and intestinal motility contribute to the TAG entry into the circulation. Insulin and GIP influence the activity of lipoprotein lipase, an enzyme that regulates postprandial TAG clearance.

Non-esterified fatty acids (NEFAs) have a diurnal rhythm. After a meal in the morning, higher postprandial levels have been observed than in the evening. Insulin inhibits hormone sensitive lipase and therefore influences NEFA. [HAMPTON et al., 1996]

→NEFA has the highest concentrations in the morning. Throughout the day its levels decrease continuously. Overnight, there is a stepwise increase.

Insulin suppresses fat mobilization (and hormone sensitive lipase) after a meal rich in carbohydrates. Consequently, NEFA values are kept at a minimum level as the fat stores are unaffected. [HA and PARK, 2005]

After adjustment for age and lifestyle parameters, three-shift workers had higher levels of serum total cholesterol than the other workers.

Explanations are stress-induced hypercholesterolemia or dietary intake of shift workers. Redistribution of food intake to night in three-shift workers may be responsible for increased cholesterol levels or disturbance of lipid metabolism.

Cortisol and sex steroid hormones regulate the deposition of visceral fat. One reason for central obesity might be the increased activation of the hypothalamic-pituitary-adrenal

axis and insulin resistance by stress. Shift work may lead to desynchronization of hormonal circadian rhythms and imbalance of the hormonal regulation of lipids. Furthermore, abnormal food intake patterns may result in subsequent disturbance of lipid metabolism.

Shift work is associated with smoking, drinking, minor psychiatric disorders and higher levels of sleeping pill and tranquilizer use, more frequent indigestion aids and a poor social network, including disturbances of family life. [NAKAMURA et al., 1997]

Shift work influences the body by interfering with the circadian rhythm. Further, there are behavioural changes in terms of diet, smoking and exercise.

Daily energy intake is the same in all work shifts, yet the frequency of eating per day is significantly higher in night shift workers.

One mechanism is social disruption: It is more difficult for shift workers to spend time with family and friends and fulfil all the social roles. This may result in stress and one study even found higher levels of the stress hormone catecholamine among shift workers. Another study even measured increased total serum cholesterol in shift workers. [DOCHI et al., 2009], [DOCHI et al., 2008]

Lipids have a circadian rhythm. The circadian variation was 5.6% for HDL/total cholesterol ratio, 30.5% and 31.6% for HDL and total cholesterol, 33.5% for LDL and 38.5% for triglycerides.

Type of shift schedules has an influence on blood parameters: It seems that clockwise rotation of shifts is beneficial in terms of lower triglyceride levels.

GHIASVAND et al. (2006) states that even though dietary intake and quality of food is similar in both day and shift workers, there are some differences in dietary habits that may contribute to different levels in serum lipids.

There are controversial ideas considering the impact of shift work on lipid levels.

Some researchers found higher levels of triglycerides in shift workers, others described low concentrations of HDL in a shift working population.

However, another scientist found no difference between the groups in terms of cholesterol and HDL. On the other hand, one researcher concluded that high concentrations of total cholesterol and LDL cholesterol are more common among shift workers.

→In general, shift workers have higher serum total cholesterol and LDL cholesterol concentrations, with adjustment for age and food type.

On the other hand, in terms of HDL cholesterol, triglyceride, fasting blood glucose and hypertension there is no difference between the groups.

It was claimed that shift workers have increased ratios between Apolipoprotein B and Apolipoprotein A. The main protein component of HDL is Apolipoprotein A which promotes cholesterol transfer to the liver where metabolization and excretion from the body happens. [ATKINSON et al., 2008] On the other hand, Apolipoprotein B (apoB) is the protein component in LDL lipoproteins. Apolipoproteins have functions such as binding and solubilisation of lipids and removal of cholesterol from cells. The ratio between apoB and apoA is a good indicator of CHD. [KNUTSON et al., 1990]

There is a significant association between shift work and lipid disturbances (i.e. low HDL-cholesterol and high triglyceride levels). However, there is no association with hyperglycaemia.

Shift workers have higher serum levels of triglycerides and lower serum levels of HDL-cholesterol than day workers. Further, abdominal obesity is more frequent, as well as increased levels of triglycerides. [KARLSSON et al., 2003]

In Japanese non-overweight male workers, shift work was an essential factor in causing increased total cholesterol levels. In contrast, the level of cholesterol in overweight people didn't change significantly. [UETANI et al., 2011]

2.7 GASTROINTESTINAL PROBLEMS

Shift workers have a higher prevalence of gastrointestinal problems such as irritable bowel syndrome, upper gastrointestinal dyspepsia and peptic ulcer. This might be due to changes in digestion, absorption and food storage.

Shift work could potentially harm gastrointestinal movements and cause problems with digestive enzyme excretion and acid-alkaline balance. The cause may be sleep disorders.

It has been found that the incidence of peptic ulcers is generally higher in shift and night workers. A Japanese study came to a peptic ulcer prevalence of 2.38% in shift workers compared to 1.03% in day workers. Duodenal ulcer showed 1.37% in shift workers and 0.69% in day workers.

At least one GI symptom has been reported in 81.9% of shift workers and 52.2% of day shift workers. The most frequent health issue was regurgitation.(52%)

The most frequent used medication is nonsteroidal anti- inflammatory drugs (NSAIDs) and antacids. Among men, 58.8% of shift workers consume gastrointestinal medication (33.3% of dayshift workers, among women 62.6% and 27.8%, respectively) One plausible reason for greater GI problems among shift workers might be that the use of NSAIDs is quite common in this population. NSAIDs help to relieve musculoskeletal pain yet can worsen existing GI symptoms.

→ The prevalence of GI symptoms is significantly higher in shift working nurses. The reason for the symptoms is unknown.

Possible reasons for the higher incidence of GI symptoms: sleep disorders, inappropriate nutrition or irregularity in the timing of meals and mental and psychological disorders.

Defecation irregularity was more prevalent in shift-work nurses. On the other hand, the frequency for diarrhea, non-specific pains and gastric ulcers was similar among both shift and day workers.

Gastrointestinal symptoms were higher in nurses under 40 years of age. One reason might be that younger nurses are more likely to volunteer to work above average working hours or on irregular shifts. [SABERI and MORAVVEJI, 2010]

Shift nurses have a significantly higher prevalence of IBS (48% vs. 31%) and abdominal pain compared to day shift nurses, independent of sleep quality.(81% vs. 54%) In the pathogenesis of IBS and abdominal pain disruptions of circadian rhythms may be partly responsible.

Functional bowel disorders are common in the general population. Among them, the irritable bowel syndrome (IBS) is most common and includes abdominal pain or discomfort in association with altered bowel habits.

The pathogenesis of IBS involves alterations in motility, visceral sensitivity, intestinal barrier function and genetics and may also be associated with sleep disorders.

Disruption of biological rhythms due to shift work or travel across time zones has been associated with gastrointestinal symptoms such as abdominal discomfort, constipation and diarrhea. These symptoms are common in functional bowel disorders.

On the other hand, the prevalence of constipation and diarrhea, loose, mushy or watery stools, hard or lumpy stools, less than three bowel movements per week, difficulty to evacuating stools, sensation of incomplete stool emptying or feeling that the stool could not be passed was similar between all groups.

Rotating shift work is significantly associated with IBS, even after adjustment for sleep quality. Besides, poor sleep quality is also associated with IBS.

A study from Singapore came to the conclusion that the prevalence of functional bowel disorders is 38% in nurses working rotating shifts vs. 20 % in day shift nurses. One hypothesis suggests that the increased prevalence of IBS in shift workers may be due to circadian disruption rather than due to sleep disturbance.

→ The irritable bowel syndrome (IBS) is most common among functional bowel disorders. Its etiology is probably multifactorial.

- IBS has been associated with sleep disorders, however the association between IBS and night shift work is independent of sleep quality.
- Disruption of biologic rhythms has been associated with gastrointestinal symptoms.
- IBS and abdominal pain (but not functional diarrhea and functional constipation) are more frequent in nurses participating in rotating shift work. [NOJKOV et al., 2010]

2.7.1 Definition of gastrointestinal disease

Gastrointestinal diseases are diseases of the oesophagus, stomach, duodenum, jejunum, ileum, large intestine, sigmoid colon and rectum.

The most mentioned symptoms in primary healthcare are GI health issues such as peptic ulcer disease (gastric and duodenal), chronic inflammatory bowel diseases (ie, Crohn's disease and ulcerative colitis) and malignancies.

Functional disorders on the other hand, are with symptoms but without structural changes to the GI system. Non-ulcer dyspepsia manifests itself with pain and discomfort in the upper abdominal region, yet there is no structural problem like peptic ulcer.

Causes of GI disorders are:

- infections
- unhealthy diet
- stress
- travelling over time zones
- side effects of pharmaceutical agents (eg nonsteroidal anti-inflammatory drugs)

For some diseases of the GI system, socioeconomic differences have been observed: Lower socioeconomic groups have a higher risk to get a peptic ulcer, stomach or colon cancer. Smoking is also a risk factor for peptic ulcer disease.

Peptic ulcer is more prevalent among shift workers, therefore it was classified as "the occupational disease of shift workers".

Shift work may play a role in either causing gastro duodenal ulceration or in exacerbating latent or pre-existent overt disease.

Generally, the prevalence of diseases in the digestive system is more common among shift than day workers (30.1% versus 13.2%). The risk for a GI diagnosis increases three-fold in shift workers.

There is a Rome III classification system for functional GI disorders:

- (A) oesophageal
- (B) gastroduodenal
- (C) bowel
 - (C1) irritable bowel syndrome, (C2) functional bloating
 - (C3) functional constipation, (C4) functional diarrhea
- (D) functional abdominal pain syndrome
- (E) biliary
- (F) anorectal

Unfortunately, the etiology and pathogenesis of many functional GI disorders is unclear. Possible mechanisms are altered autonomic function, immune activation and altered activation of central nervous system circuits.

The rate of functional bowel disease was significantly higher among shift than day nurses in Singapore. (38% versus 20%) The prevalence of gastric ulcer was greater among Japanese shift workers than in daytime workers. (2.38% versus 1.93%) (Duodenal ulcer: 1.36% and 0.69% respectively.) Among former shift workers, the rate of gastric and duodenal ulcer was 1.52% and 0.62%, respectively. The relative risk for peptic ulcer was 2.18 for shift compared with day workers.

The large or small intestine is inflamed which results in pain and diarrhea, sometimes with bleeding, structuring, and fistulas. Most common are ulcerative colitis and Crohn's disease. The causes of these diseases are still unknown, it is however assumed, that melatonin acts as a mediator and maybe shift work plays a role.

The GI system has a circadian rhythm concerning bowel movement, secretion of gastric juices, bile acid synthesis, immune activity and appetite regulation.

Colonic motility has a circadian rhythm with increased activity during the day and a peak at midday. The activity is also increased after meals. The lowest levels can be measured late at night.

The question is, if sleep induced changes in autonomic neural input lead to sleep-related motility changes or if changes are under circadian clock control.

2.7.2 Peptic Ulcers

Gastrin stimulates the secretion of gastric acid. Besides, pepsinogen is released from cells in the stomach and transformed to pepsin, which can digest protein. It is assumed that pepsin can act as an aggressor and can cause peptic ulcers.

Shift work may cause a significant change in the gastrin/acidopepsin secretion system: They had increased levels of serum gastrin and pepsinogen.

Helicobacter pylori is a bacterium that is responsible for the development of peptic ulcer. *Helicobacter Pylori* infection was more prevalent among shift than day workers (46.1% versus 34.6%). *Helicobacter pylori*-infected shift workers had higher prevalence of peptic ulcer than infected day workers (28.7% versus 9.3%). The results may be due to deteriorated natural defense to *H. pylori* of shift workers.

Cells of the GI tract contain clock genes, which may play an important role in the coordination of rhythmic functions. The clock cells in the GI tract are entrained by the feeding time, not by the master clock in the suprachiasmatic nucleus. Varying eating times could lead to a desynchronization between circadian biological clocks. However, it still needs to be proven if this is a mechanism of GI diseases among shift workers.

→ There is an association of shift work with GI symptoms, peptic ulcer and functional GI disease. [KNUTSSON et al., 2010]

→ Shift work increases the ulcerogenic potential of H pylori infection and is a probable risk factor for duodenal ulcer in infected shift workers. Shift work and peptic ulcer disease are associated. The prevalence of peptic ulcer is higher in shift workers doing at least seven nights per month (47.6%) in comparison to other shift workers. (22.5%)

Duodenal ulcer is more frequent in shift workers than in daytime workers.

Likewise, gastric ulcer was diagnosed in 3.9% of shift workers and 1.2% of daytime workers.

Shift workers who are H.pylori positive dyspeptic are a high risk group for peptic ulcer disease. H pylori related ulcer: In the beginning, the gastric antrum is colonised, which results in the antrum predominant gastritis. Consequently, acid output is increased and gastric metaplasia in the duodenum is induced.

As a result of gastric mucosa in the duodenum, colonisation of H.pylori is possible, with a subsequent development of duodenal ulcer.

Long term stress and nocturnal sleep deprivation, often observed in shift workers, may increase gastric acid secretion and reduce mucosal defence. [PIETROIUSTI et al., 2006]

Gastrointestinal complaints are more frequent among rotating and night shift workers (20–75%) compared to day workers (10–25%)

The mentioned symptoms are:

- disturbances of appetite
- irregularity of bowel movements
- constipation
- dyspepsia
- heartburn
- abdominal pains
- grumbling and flatulence [ATKINSON et al., 2008]

Frequent snacking during the night shift may cause gastric problems. In addition, the consumption of coffee and drugs that help to stay awake may contribute to gastric complications. [LOWDEN et al., 2010]

The central clock and pacemaker is situated in the SCN and receives photic information via the retinohypothalamic tract. Besides, most of the peripheral tissues have clock genes and the SCN sends information via neuronal and humoral pathways.

However, peripheral clocks can be entrained by stimuli such as restricted or timed feeding, independent of the central clock. Lesions of the SCN can abolish behavioral, physiological, and biochemical rhythms.

A determinant of postprandial glucose tolerance is the rate of gastric emptying of a meal. [HAMPTON et al, 1996] Nocturnal eating may disturb gastrointestinal activity. The gastric emptying of meals also has a circadian variation: emptying half-times for the evening meal are significantly longer for solids (not for liquids) compared with morning emptying half-times. This indicates that the gastric emptying rate at night is reduced. [HOOGERWERF, 2010], [HAMPTON et al, 1996]

Interestingly, it was found that carbohydrates were less well absorbed when subjects were in light surroundings in the evening.

→ This suggests that shift work affects food metabolism. [ATKINSON et al., 2008]

Intestine

There is a significant variation between daytime and nocturnal propagation velocities of the migrating motor complex.

There are rhythmic changes in colonic motility. It was shown that colonic motor activity is low before meals and during sleep and increases significantly after meals and upon awakening. Similarly, a threefold increase in colonic pressure activity was observed immediately after awakening and after a meal.

Rectal motor complexes are patterns of frequent pressure fluctuations, with three or six cycles per minute. It is assumed that these complexes have a biological rhythm as the

number of rectal motor complexes is lower during sleep and duration and peak amplitudes are also decreased.

Ingestion of meals, on the other hand, increases rectal motor activity.

Colonic Clock Genes

Circadian rhythms can persist under constant conditions (eg. in the absence of light) and have the ability to be synchronized or reset by the time of feeding. This has been verified in animal experiments: mice in complete darkness with access to food and mice in complete darkness without access to food. In both groups, rhythmicity persisted and colonic clock gene expression remained rhythmic.

The colonic clock can become uncoupled and function independent of the central clock. Restricted feeding has been established as a major synchronizer of clock gene expression in tissues within and outside of the gastrointestinal tract.

2.7.3 IBS

Disruption of biological rhythms may result in gastrointestinal symptoms such as abdominal discomfort, constipation or diarrhea and altered colonic motility.

It is suggested that working rotation shifts, independent of sleep quality, is significantly associated with higher IBS rates. It was found that melatonin alleviates IBS symptoms. Interestingly, the melatonin metabolite 6-sulfatoxymelatonin differs between IBS patients and healthy subjects.

Oral melatonin for 8 weeks improved bowel symptoms in female patients with IBS by alleviating abdominal pain, abdominal distention, and abnormal sensations during defecation. Melatonin could therefore be a substance in the treatment of IBS as it may have a regulatory effect on GI motility.

Restricted feeding can uncouple peripheral clock gene expression from the central clock.
[HOOGERWERF, 2010]

All organisms have circadian and seasonal rhythms, which are responsible for daily food intake. The central pacemaker in the SCN of the hypothalamus controls the period of hunger and satiety and communicates with tissues *via* bidirectional neuronal and humoral pathways.

It has been found that clocks in the GIT are responsible for the periodic activity of its segments and transit along the GIT. In the GIT, there is a rhythm of slow waves, which is controlled by the stomach (about 3 cycles per min), the duodenum (12 cycles per min), the jejunum and ileum (from 7 to 10 cycles per min) and the colon (12 cycles per min).

The migrating motor complex (MMC) is situated in the stomach and moves along the gut causing peristaltic contractions when the electrical activity spikes are superimposed on the slow waves. The GIT hormones motilin and ghrelin are involved in the generation of MMCs. Gastrin, ghrelin, cholecystokinin, serotonin on the other hand, are involved in the generation of spikes on the slow waves, which results in peristaltic or segmental contractions in the small (duodenum, jejunum ileum) and large bowel (colon).

Melatonin is produced by neuro-endocrine cells of the GIT mucosa. It plays an important role in the internal biological clock and influences food intake (hunger and satiety) and myoelectric rhythm (which is primarily produced by the pineal gland during the dark period of the light-dark cycle).

Autonomic cells and the enterohormones gastrin, ghrelin and somatostatin arrange circadian rhythms, which influence motor and secretory activity and the rhythm of cell proliferation in the GIT and liver.

→Disrupted circadian rhythms can lead to gastrointestinal diseases like irritable bowel syndrome (IBS), gastroesophageal reflux disease (GERD) or peptic ulcer disease. In addition aging accelerates and tumorigenesis in the liver and GIT is promoted.

→Interestingly, researchers achieved improvements in patients with IBS and GERD who took melatonin. Above all, melatonin protects gastrointestinal mucosa and the liver of patients with non-alcoholic steatohepatitis (NASH).

Central and Peripheral Clock Oscillators

Mainly, the SCN coordinates daily rhythms and oscillates more than 24 hours, regulated by the light dark cycle. Several single-cell oscillators build up the SCN. When these oscillators are synchronized, they generate outputs which regulate rhythms. Peripheral oscillators in the GIT, liver, muscle and adipose tissue receive signals from the SCN. Synchronizers for central and peripheral clocks can be feeding, metabolites and light.

Chronodisruption affects the brain-gut axis and contributes to the development of several diseases of the GIT such as: gastroesophageal reflux disease (GERD), gastric dyspepsia, peptic ulcers, inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), other functional bowel disorder, non-alcoholic steatosis hepatitis (NASH) and cancer of the GIT.

Circadian oscillations affect motility, maintenance and replacement of the protective barrier, immunology and production of digestive enzymes in the GIT.

Thus, changes in circadian rhythm can lead to gastrointestinal symptoms such as abdominal pain, constipation and diarrhea.

- 1) Colonic motility is under the influence of circadian control (maximal motility during the day, minimal during the night)
- 2) Components of the molecular clock have been identified in the GIT
- 3) Neurotransmitters expressed in the myenteric plexus (*e.g.*, VIP) were identified in the neurons of SCN master clock
- 4) There is strong epidemiological evidence that alterations in colonic motility, due to the disruption of the molecular clock, have an impact on GI functions.

→The link between gut clock and colonic motility is of clinical importance as disrupted circadian rhythms increase the prevalence of functional colonic motility disorders.

A changed circadian gut clock is suggested to have effects on the integrity of the GI mucosa. The disruption of circadian oscillators could have a direct and indirect (*via* melatonin and other humoral factors) impact on protective factors of the GI mucosa and cell proliferation.

An association between shift work and development of duodenal ulcers is suggested. One reason could be the decrease of circulating melatonin during night shifts as melatonin plays a crucial role in gastric protection (*via* effects on angiogenesis, NOS system, COX-2, and gastric mucosal blood flow).

Animal studies showed the healing effect of melatonin and precursor L-tryptophan in gastric ulcerations. Further, gastric lesions by aspirin can be reduced by oral melatonin and its precursor, L-tryptophan. Besides, melatonin seemed to be efficient in combination with proton pump inhibitor (PPI) therapy as ulcer healing could be accelerated.

2.7.4 GERD, NASH, Gastric Cancer

Gastroesophageal reflux disease (GERD) is characterised by hypersecretion and frequent night reflux symptoms and can cause pain and disturbance of sleep.

It has been shown that patients with the erosive form of GERD have lower levels of melatonin than patients with non-erosive reflux form (NERD).

NASH

It is suggested that disrupted circadian rhythms have a linkage to the metabolic syndrome and non-alcoholic steatohepatitis (NASH). It is questioned if melatonin, a resynchronizing factor of central and peripheral clocks and strong anti-oxidant, has an impact on NASH. It is assumed to be beneficial in the treatment of NASH as it seems to attenuate liver enzymes levels and decreases the level of proinflammatory cytokines in NASH patients. Melatonin might act liver protective directly by an anti-oxidative effect and indirectly by a regulatory effect on the liver clock.

GASTRIC CANCER

Gastric cancer patients with total or distal gastrectomy had no marked reductions in plasma ghrelin after meals, however, high fasting and postprandial gastrin levels were measured. In animals model it was found that melatonin in the stomach can inhibit ghrelin release and gastric acid secretion.

Conclusions about the link between the gut clock and GIT carcinogenesis

- 1) A disrupted gut clock (working a rotating night shift at least 3 nights per month for 15 or more years) increases the risk of colorectal cancer
- 2) Tumor development is accelerated by down-regulated clock genes and might influence anti-cancer drug response.
- 3) Circadian disruption is associated with faster tumor growth and shorter survival
- 4) Circadian clock gene regulates tumor cell proliferation
- 5) Clock gene polymorphisms are associated with increased cancer risk
- 6) Circadian based chemotherapy may optimize therapeutic efficacy

→ Chronodisruption may result in several GIT and liver diseases such as changed colonic motility, peptic ulcer disease, NASH and obesity. [KONTUREK et al., 2011]

3 Methods

3.1 Background

This study succeeds a study that was done by “Wellcon- Gesellschaft für Prävention und Arbeitsmedizin”, a society for prevention and occupational medicine with 5 headquarters in Vienna, Graz, Linz, Innsbruck and Villach. Over 80 physicians and health experts advise companies in occupational medicine and psychology, sports and nutrition as well as health promotion, vaccinations and prophylaxis.

In 2007 the project with the title “Gesunde Ernährung im Schichtdienst” was presented by Voyta-Janda A, Schinnerer C and Gerersdorfer S. It was specially targeted at locomotive drivers representing a big group of shift workers within the ÖBB (Austrian Federal Railway). This study found, that 18% of the subjects (n=1926) had had an orthopaedic diagnosis, 14% high blood pressure and 5% suffered from gastrointestinal problems. Furthermore, it was shown that 45% of the workers were overweight and 12% were obese, with only 42% subjects with normal weight. (n=831)

They mainly concentrated on dietary habits and found that 51% of the night shift workers did not have a main meal during the shift. 30% had a meal before 22h and 6% consumed one between 22 and 24h. Working a day shift, at least 55% consumed a menu at the canteen, 30% had a cold dish from home and 3% ate fast food. On the other hand, during a night shift, 38% of all workers consumed a cold dish from home and 11% had fast food. (n=828)

The latter correlates with the study that was done at the end of 2012.

In addition, a food stuff that is mostly consumed as a snack is meat and sausages. (56%) However, 52% of the subjects also name fruits and vegetables as part of their regular snacks. Similar to the study that was recently done, a small food frequency questionnaire was also part of the survey.

Most interesting outcomes:

67% of the subjects consume bread every day.

These food stuffs are consumed almost every day:

- meat and sausages (63%)
- cheese (by 62%)
- rice and noodles (60%)
- fruits (57%) and vegetables (44%)
- sweets (41%)
- whole meal products (54%)

These foods are consumed once a week:

- Joghurt and milk (46%)
- Eggs (36%)

37% consume poultry once a fortnight and 41% consume fish only once a month.

96% of the subjects prefer water and mineral water when it comes to drinks. Tea and fruit juice is also often named. (43% and 36%)

On the whole perceived problems are:

- Night shift workers mostly consume fatty and indigestive meals which induce fatigue.
- Nutrition composition is not adequate.
- Both shifts and breaks are irregular.
- Shift workers are generally sedentary, 46% have increased cholesterol levels and the consumption of warm dishes among night shift workers is practically zero.

3.2 Data collection

The study was built upon the project of 2007 by Wellcon. It was done in collaboration with the university of Vienna, ÖBB and Wellcon and is an empiric study.

The survey is based on a food frequency questionnaire, which is kept very short (2,5 pages) to keep compliance high. A food frequency questionnaire asks how often a food is consumed and eaten. Furthermore, questions about country of origin, place of living, family status, household size and education were included. In addition, it was asked whether there are diseases and what the shift times are.

The main collection phase was from October 15th to December 20th 2012.

The original sole headquarter of collection was Wellcon Innsbruck, a society where ÖBB workers from the west part of Austria regularly have to undergo physical examinations. However, after several weeks, it was found that two to three shift workers a week is not enough to get sufficient subjects. As a result, contact was established with Pletzer Caroline, responsible for the locomotive drivers in Innsbruck and Hechenberger Wilfried from Bludenz. In addition, Wiesner Leopold from Linz collected most questionnaires from day shift workers, serving as the control group. More than 70 locomotive drivers came from Hörzenberger Manfred, Linz.

Fortunately, the obligatory number of at least 80 subjects of shift workers could therefore be achieved shortly before Christmas. As a result, 103 shift workers (locomotive drivers) and 74 dayshift workers took part in the survey, aged 20 to 56 years.

The food frequency part of the survey included 33 key food stuffs for energy intake in the Austrian population: 22 questions about food items and 11 questions about drink consumption.

The following items were included:

Rice and noodles, Bread, White bread, Wholemeal bread, potatoes, vegetables, fruits, compote, milk, beef and pork, poultry, sausages, fish, eggs, pulse, nuts, butter and oil, cakes, chocolates and sweets, fruit and vegetable drinks, lemonades, drinks with gas, tea, coffee, (mineral) water, alcoholic drinks, tinned food, fast food, French fries, popcorn, drinks in tetrapak, drinks in PET bottles, drinks in plastic cups.

3.3 Data evaluation

The survey was based on a food frequency questionnaire and some basic questions about educational level and living circumstances, including personal health data. In total, the questionnaire is 2,5 pages long. Evaluation was done with Excel.

To be able to compare the two samples shift workers (locomotive drivers) and day shift workers and search for significant consumption differences between the groups, the t-test is the method of choice.

3.3.1 t-test for independent samples

The t-test for independent samples is used for comparing two means. The hypothesis is tested that the means of the sample characteristics x_1 and x_2 in two populations are different. Preconditions are that the two samples are independent of each other. In addition, the normal distribution of the random variables x_1 and x_2 and the homogeneity of variance of x_1 and x_2 are requirements.

The random variable is t-distributed with n_1+n_2-2 degrees of freedom, when

$T = (x_1 - x_2) / S * \sqrt{((n_1 * n_2) / (n_1 + n_2))}$ and the validity of the null hypothesis $H_0 : \mu_1 = \mu_2$
 μ_1 and μ_2 are the unknown population means, n_1 and n_2 are the range of the partial samples. S is the standard deviation of x_1 and x_2 .

x_1 and x_2 are the means of the random variables x_1 and x_2 in the two samples.

Statistical hypotheses:

$$H_1 : \mu_1 \neq \mu_2 \quad H_0 : \mu_1 = \mu_2$$

$$H_1: \mu_1 > \mu_2 \quad H_0: \mu_1 \leq \mu_2$$

$$H_1: \mu_1 < \mu_2 \quad H_0: \mu_1 \geq \mu_2$$

Election of the level of significance

For example $\alpha = 0,05$

Calculation of arithmetic means and standard deviation of both samples.

Calculation of the standard deviation of the pooled samples:

$$s_p = \sqrt{(((n_1-1)*s_1^2 + (n_2-1)*s_2^2) / (n_1-1)+(n_2-1))}$$

Calculation of the value of the test statistic:

$$t = (x_1 - x_2) / s_p * \sqrt{((n_1 * n_2) / (n_1 + n_2))}$$

Test decision with the use of the quantile of the t-distribution (with n_1+n_2-2 degrees of freedom)

$|t| > t_{n_1+n_2-2, \alpha} \rightarrow$ Refusal of H_0

H_0 : there is no difference between the means of the two populations

H_1 : there is a difference between the means of the two populations [RUDOLF and KUHLSCH, 2008]

With a mistake of 0,1 or 10% ($\alpha=0,1$), there are significant differences between the two samples locomotive drivers and dayshift workers in the categories sausages, chocolates and sweets, (mineral) water, alcohol and fish.

p-value < 1%: fast food, French fries and plastic cup drinks $\rightarrow$ the difference is very sure

1% < p-value < 5%: alcohol $\rightarrow$ the difference is sure

5% < p-value < 10%: sausages, chocolates and sweets, (mineral) water and fish $\rightarrow$ there is a tendency

Example of fast food: 5,119780111 > 1,653919942 $\rightarrow$ refusal of H_0 :

There is a significant difference between locomotive drivers and dayshift workers in terms of the consumption of fast food. Locomotive drivers eat significantly more fast food than day workers.

Furthermore, there is a significant difference in terms of French fries and plastic cup drinks.

$\rightarrow$ with $\alpha=0,05$ locomotive drivers consume significantly more fast food, French fries and plastic cup drinks than day workers.

$\rightarrow$ with $\alpha=0,10$ day workers consume more fish, (mineral)water, chocolates and sweets than shift workers. However, locomotive drivers seem to eat more sausages than day workers.

sp	9	13,7	0,07	3,2	0,2
t	-1,8	0,05	1,3	-0,8	-0,7
Proband	Alter	Körpergewicht	Körpergröße	BMI	Geburtsland
alpha:	0,1	0,1	0,1	0,1	0,1
Freiheitsgrad	175	175	174	174	174
t_krit	1,7	1,7	1,7	1,7	1,7
	WAHR	FALSCH	FALSCH	FALSCH	FALSCH
	0,07	1	0,2	0,4	0,5
	*				

0,6	0,2	1,3	0,8	0,8
-0,5	0,2	-2,0	-0,1	0,7
Geburtsland				
Eltern	Nationalität	Bundesland	Wohngebiet	Familienstand
0,1	0,1	0,1	0,1	0,1
174	174	174	175	174
1,7	1,7	1,7	1,7	1,7
FALSCH	FALSCH	WAHR	FALSCH	FALSCH
0,6	0,8	0,0	0,9	0,5

1,3	0,5	0,5
-0,3	-2,4	-2,1
		Dauer
Haushaltsgröße	Ausbildung	Ausbildung
0,1	0,1	0,1
174	174	175
1,7	1,7	1,7
FALSCH	WAHR	WAHR
0,8	0,02	0,03
	**	**

1,3	1,1	1,5	1,5	1,9	1,1
1,3	0,1	-1,2	1,5	-0,2	-0,9
Krankheiten	Reis/Nudeln	Misch/Hausbrot	Weißbrot	Vollkornbrot	Kartoffeln
0,1	0,1	0,1	0,1	0,1	0,1
167	173	169	168	168	170
1,7	1,7	1,7	1,7	1,7	1,7
FALSCH	FALSCH	FALSCH	FALSCH	FALSCH	FALSCH
0,2	0,9	0,2	0,1	0,8	0,4

1,4	1,6	1	1,9	1,2	1,0
-0,8	-1,5	-0,6	-0,6	-0,4	0,5
Gemüse	Obst	Kompott/Fruchtmus	Milch(getränke)	Rind/Schweinefleisch	Geflügel
0,1	0,1	0,1	0,1	0,1	0,1
174	173	170	173	174	172
1,7	1,7	1,7	1,7	1,7	1,7
FALSCH	FALSCH	FALSCH	FALSCH	FALSCH	FALSCH
0,5	0,1	0,6	0,6	0,7	0,6
			*	*	

1,3	1,0	1,1	1,0	1,2	1,6
1,8	-1,8	-1,5	0,3	-1,0	-1,2
Wurst(waren)	Fisch	Eier	Hülsenfrüchte	Nüsse	Butter/Öle
0,1	0,1	0,1	0,1	0,1	0,1
172	171	173	171	169	173
1,7	1,7	1,7	1,7	1,7	1,7
WAHR	WAHR	FALSCH	FALSCH	FALSCH	FALSCH
0,1	0,1	0,1	0,8	0,3	0,2
				*	

1,5	1,6	1,8	1,9	2,1	
-0,5	-1,8	-0,8	-0,1	-0,4	
				KH-	
Mehlspeisen/Kuchen	Schokolade/Süßigkeiten	Obst/Gemüsesäfte	Limonaden	Getränke	
0,1	0,1	0,1	0,1	0,1	
173	172	168	168	170	
1,7	1,7	1,7	1,7	1,7	
FALSCH	WAHR	FALSCH	FALSCH	FALSCH	
0,6	0,1	0,4	0,9	0,7	
1,9	2,0	1,4	1,4	1,1	1,1
0,2	-0,4	-1,9	-2,4	-0,3	5,1
Tee	Kaffee	Leitungs/Mineralwasser	Alkohol	Konserven	Fast Food
0,1	0,1	0,1	0,1	0,1	0,1
171	171	173	171	169	169
1,7	1,7	1,7	1,7	1,7	1,7
FALSCH	FALSCH	WAHR	WAHR	FALSCH	WAHR
0,8	0,7	0,1	0,02	0,8	8,3E-07
		*	**		***
0,8	0,5	1,6	2,1	1,6	
3,3	0,2	-0,7	0,1	4,4	
		Tetrapak-		Plastikbecher-	
Pommes	Popcorn	Säfte	PET-Getränke	Getränke	
0,1	0,1	0,1	0,1	0,1	
170	168	170	170	169	
1,7	1,7	1,7	1,7	1,7	
WAHR	FALSCH	FALSCH	FALSCH	WAHR	
0,001	0,8	0,5	0,9	1,6E-05	
***				***	

Table 1: Values of t-test

4 Results and Discussion

4.1 General description of the study population

4.1.1 Sample size

There are 103 locomotive drivers and 74 day workers who filled the FFQ. Whenever the left questions blank, the cell was filled with NaN (not a number).

4.1.2 Age

The average age among day workers was $42,2162 \pm 8,48087$ and $39,7087 \pm 9,28274$ for locomotive drivers. The age ranged from 20 to 54 years among day workers and from 23 to 56 years among shift workers.

→ There is a tendency towards younger workers in shift work, as confirmed by other studies. In the age group 20-40 years, there are more subjects working in shift work than in day work. On the other hand, observing the age group 41-60 years, there are more people in day work than in shift work.

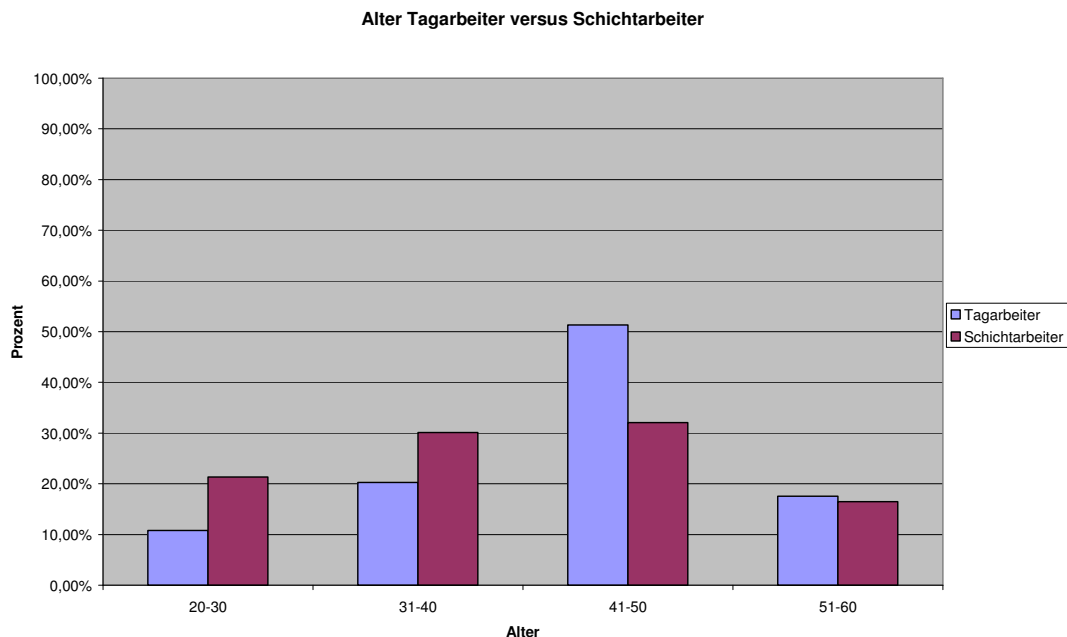


Figure 11: Age of day and shift workers

4.1.3 BMI

Mean BMI values for day workers are $26,23129519 \pm 3,483977789$ and $25,82617377 \pm 2,945660334$ for shift workers (locomotive drivers). Overweight (Übergewicht) was

classified as having a BMI between 25 and 29,9. Obesity (Adipös) was grouped as having a BMI over 30.

The figure shows a tendency of the shift workers to have a smaller group of normal weight and obesity compared to day workers. Nevertheless, they have a higher percentage of overweight. (BMI between 25 and 29,9)

Day workers:

- 39,73% have normal weight
- 46,58% are overweight
- 13,70% are obese

Shift workers:

- 36,89% have normal weight
- 53,40% are overweight
- 9,71% are obese

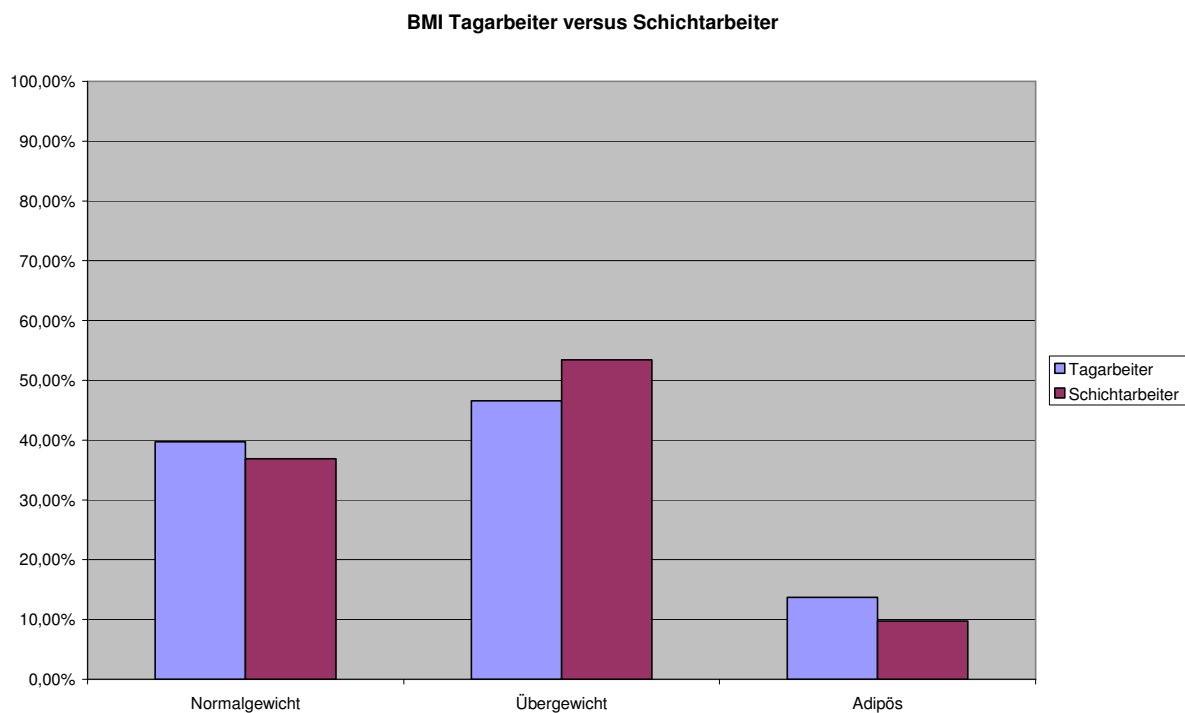


Figure 12: BMI of day and shift workers

4.1.4 Habituation

With only minimal exceptions, participants are mainly born and raised in Austria. Parents of this minority came from Croatia, Paraguay, Bosnia, Rumania, Germany and Serbia. Other mentioned nationalities are Bosnian and German, in which subjects were also born. However, these numbers are very small and are not worth looking at.

4.1.5 Household size

Among day workers the household size is $3,123287671 \pm 1,257700784$ and $3,067961165 \pm 1,315534156$ among locomotive drivers.

→ In terms of household size there is no real difference between the samples.

4.1.6 Education

The highest achieved level of education among day workers is $3,202702703 \pm 0,596329635$ and $3,029411765 \pm 0,357546157$ among shift workers. This is according to a scale ranging from 1 to 5, with 5 as the highest level of education (university).

→ Most workers of both samples have completed at least an apprenticeship or vocational school.

4.1.7 Jobs and work shifts

Day workers who took part in the survey work in a range of different jobs: technical worker, planning, administration, wagon master, debtor, engineer, garage service, logistician, engine fitter, plumber, communications, electronics engineer, production manager, design draftsman, electrician, purchasing, team leader, marketing staff, locomotive instructor, headman, team leader workshop, skilled worker, order processing and movements inspector.

Work shifts among day workers are very diverse, ranging from 06:00 to 21:45 hours.

Likewise, shifts for the locomotive drivers are widely distributed, practically around the clock.

4.1.8 Diseases

Day workers:

- 21,62% have high blood pressure
- 4,05% have high cholesterol levels

- 2,70% have or had cancer (one case of testicle tumor and thyroid gland cancer)
- 1,35% have Morbus Crohn
- 1,35% have diabetes type 2
- There are no cases of stroke and myocardial infarction

Locomotive drivers (Shift workers):

- 13,59% have high cholesterol levels
- 11,65% have high blood pressure
- 4,85% have or had cancer (testicle tumor, intestine cancer, thyroid gland cancer, osteosarcoma)
- 1,94% have sleep disorders
- 0,97% had a stroke or myocardial infarction
- 0,97% have diabetes type 2
- 0,97% have Morbus Crohn
- 0,97% suffer from nervous affection

sp	0,4	0,1	0,3	0,1
t	-1,8	0,8	2,1	-0,2
	Bluthochdruck	Schlaganfall/Herzinfarkt	Hoher Cholesterinspiegel	Diabetes Typ 2
alpha	0,1	0,1	0,1	0,1
Freiheitsgrade	175	175	175	175
	1,7	1,7	1,7	1,7
	WAHR	FALSCH	WAHR	FALSCH
p-Wert	0,1	0,4	0,03	0,8
	*		**	

sp	0,1	0,1	0,1	0,1	1,3
t	-0,2	0,8	1,2	0,8	1,3
	Mb. Crohn	Arthritis	Schlafstörungen	Nervenleiden	Krankheiten
alpha	0,1	0,1	0,1	0,1	0,1
Freiheitsgrade	175	175	175	175	167
	1,7	1,7	1,7	1,7	1,7
	FALSCH	FALSCH	FALSCH	FALSCH	FALSCH
p-Wert	0,8	0,4	0,2	0,4	0,2

Table 2: t-test of diseases (shift and dayworkers)

Means and standard deviation values are shown in the following compilation in both day and shift workers (locomotive drivers):

DAY WORKERS

	Alter	Körpergewicht	Körpergröße	BMI	Geburtsland	Geburtsland Eltern	Nationalität
	1	2	3	23	4	5	6
x	42,2	84,4	1,8	26,2	1,0	1,1	1,00
Sd	8,5	15,2	0,1	3,5	0,2	0,6	0,1
n	74	74	73	73	74	74	74

	Bundesland	Wohngebiet	Familienstand	Haushaltsgröße	Ausbildung	Dauer Ausbildung
	7	8	9	10	11	12
	2,6	2,3	1,4	3,1	3,2	2,8
	1,1	0,9	0,8	1,3	0,6	0,5
	74	74	74	73	74	74

	Reis/Nudeln	Misch/Hausbrot	Weißbrot	Vollkornbrot	Kartoffeln	Gemüse
	3,5	5,3	3,8	3,3	3,7	4,2
	1,1	1,4	1,5	1,9	1,1	1,4
	73	71	71	71	72	73

Obst	Kompott/Fruchtmus	Milch(getränke)	Rind/Schweinefleisch	Geflügel	Wurst(waren)
4,9	1,9	3,9	3,8	3,0	4,3
1,6	1,0	1,9	1,3	1,1	1,4
72	72	73	73	72	72

Table 3: Means and standard deviations of day workers

SHIFT WORKERS (LOCOMOTIVE DRIVERS)

	Alter	Körpergewicht	Körpergröße	BMI	Geburtsland	Geburtsland Eltern	Nationalität
	1	2	3	23	4	5	6
x Sd n	39,7	84,5	1,8	25,8	1,0	1,1	1,0
	9,3	12,5	0,1	2,9	0,2	0,6	0,2
	103	103	103	103	102	102	102

Bundesland	Wohngebiet	Familienstand	Haushaltsgröße	Ausbildung	Dauer Ausbildung
7	8	9	10	11	12
2,2	2,3	1,5	3,1	3,0	2,6
1,4	0,8	0,8	1,3	0,4	0,5
102	103	102	103	102	103

Krankheiten	Reis/Nudeln	Misch/Hausbrot	Weißbrot	Vollkornbrot	Kartoffeln
15	1601	1602	1603	1604	1605
0,7	3,5	5,0	4,2	3,3	3,5
1,5	1,1	1,5	1,6	1,9	1,1
97	102	100	99	99	100

Gemüse	Obst	Kompott/Fruchtmus	Milch(getränke)	Rind/Schweinefleisch	Geflügel
1606	1607	1608	1609	1610	1611
4,0	4,5	1,8	3,8	3,7	3,0
1,4	1,6	1,0	1,8	1,1	1,0
103	103	100	102	103	102

Wurst(waren)	Fisch	Eier	Hülsenfrüchte	Nüsse	Butter/Öle
4,7	2,5	2,7	2,1	2,2	4,2
1,2	1,0	1,0	0,9	1,2	1,7
102	101	102	100	100	102

				KH-
Mehlspeisen/Kuchen	Schokolade/Süßigkeiten	Obst/Gemüsesäfte	Limonaden	Getränke
3,4	3,7	3,1	2,9	3,6
1,4	1,5	1,9	1,8	2,1
102	101	99	98	99

Tee	Kaffee	Leitungs/Mineralwasser	Alkohol	Konserven	Fast Food
3,1	6	6,7	2,6	2,1	2,4
1,8	1,9	1,6	1,3	1,0	1,3
100	101	103	101	99	99

Pommes	Popcorn	Tetrapak-Säfte	PET-Getränke	Plastikbecher-Getränke
2,1	1,2	2,2	3,4	2,4
0,9	0,5	1,6	2,0	1,9
99	97	100	99	99

Table 4: Means and standard deviations of shift workers

The four most significant items are shown in a figure (fast food, French fries, plastic cup drinks and alcohol): there is a comparison between shift workers (Schichtarbeiter, locomotive drivers, blue) and day workers (purple).

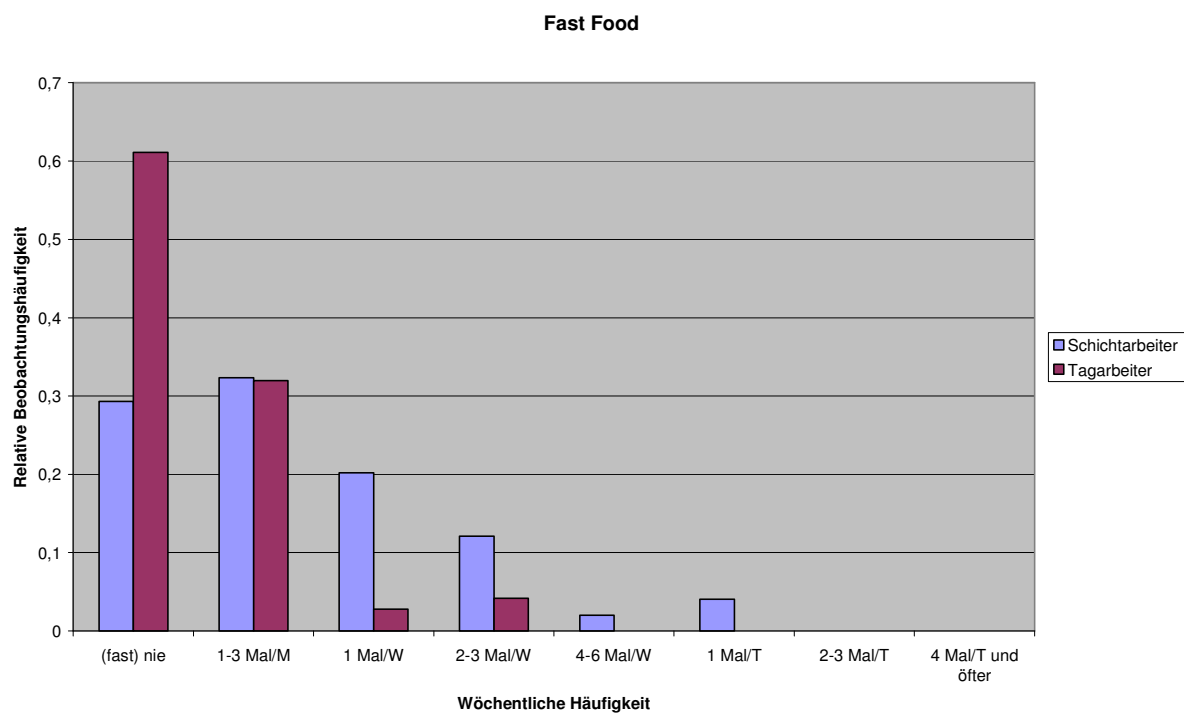


Figure 13: Fast Food consumption of day and shift workers of ÖBB

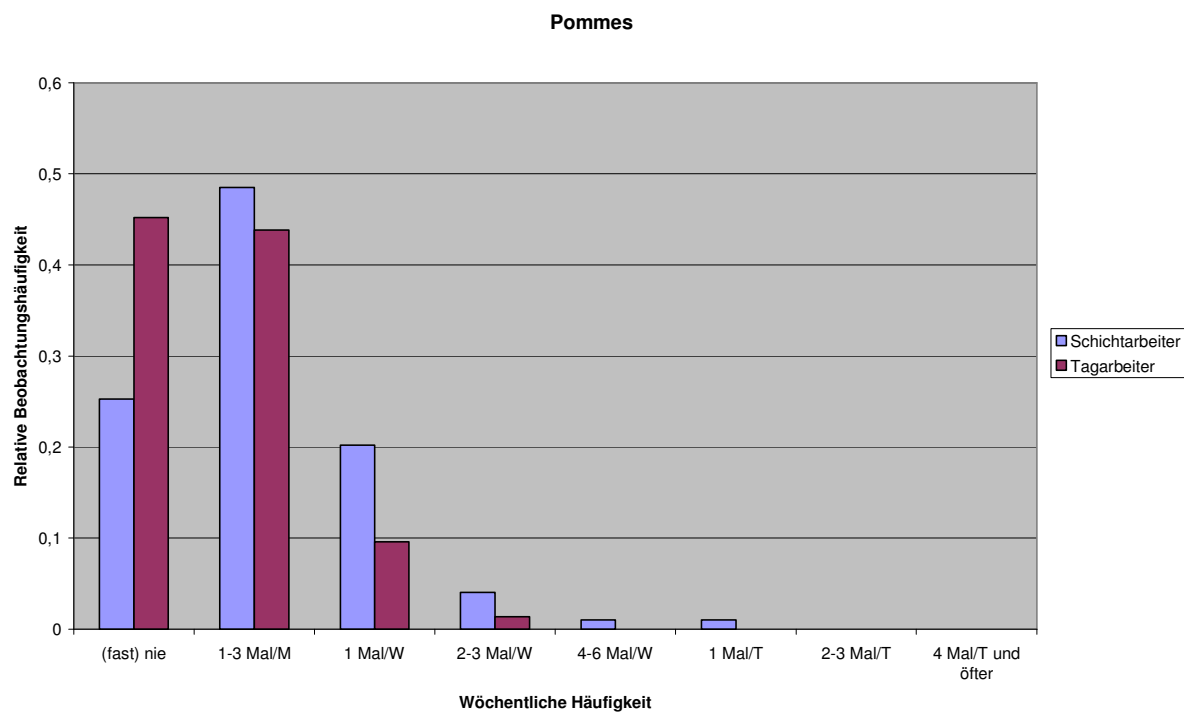


Figure 14: French Fries consumption of day and shift workers of ÖBB

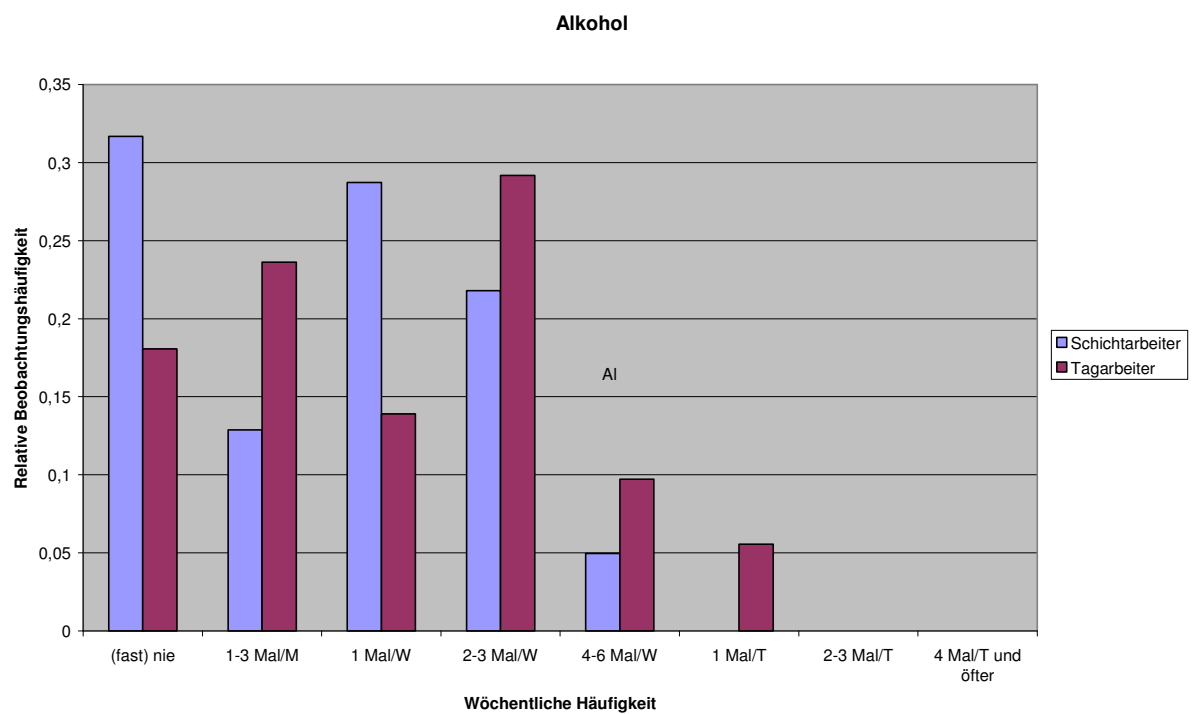


Figure 15: Alcohol consumption of day and shift workers of ÖBB

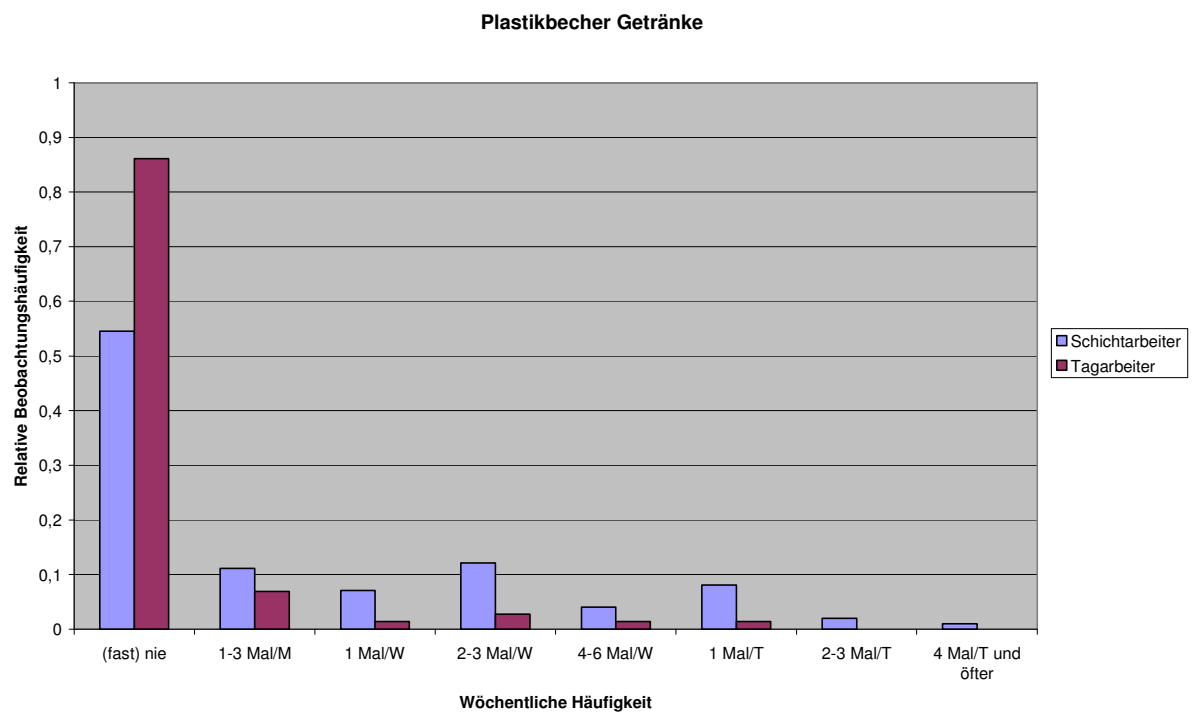


Figure 16: Plastic cup drinks consumption of day and shift workers of ÖBB

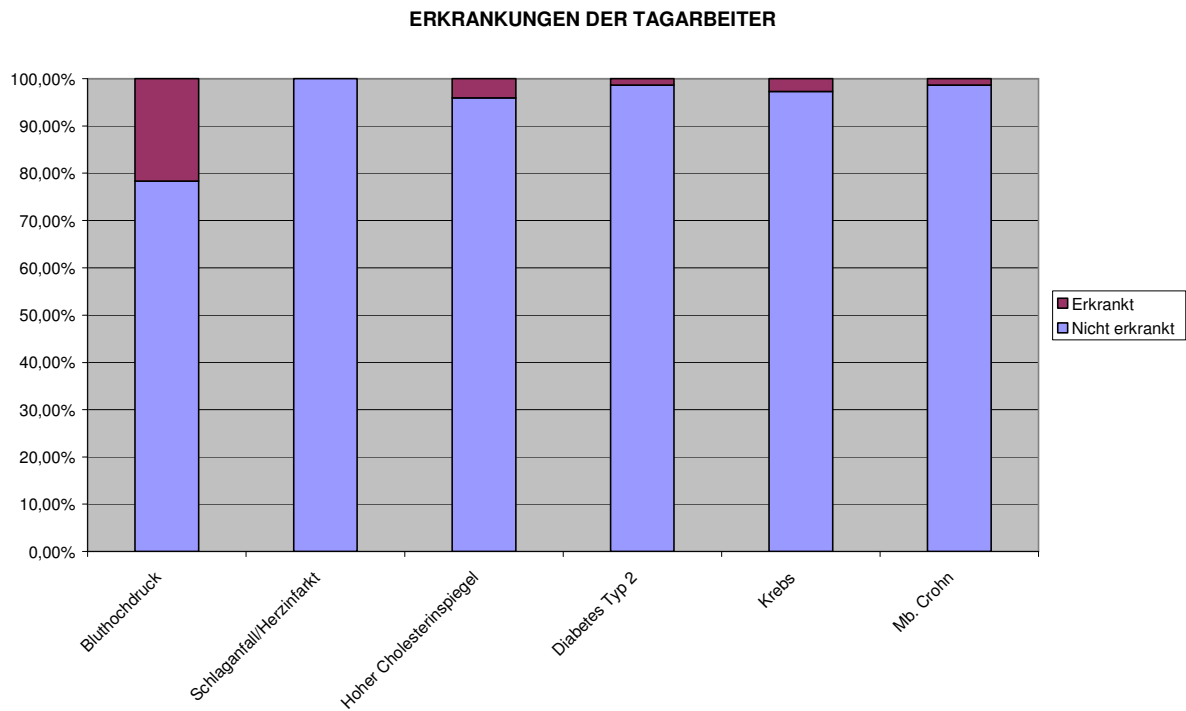


Figure 17: Diseases of day workers

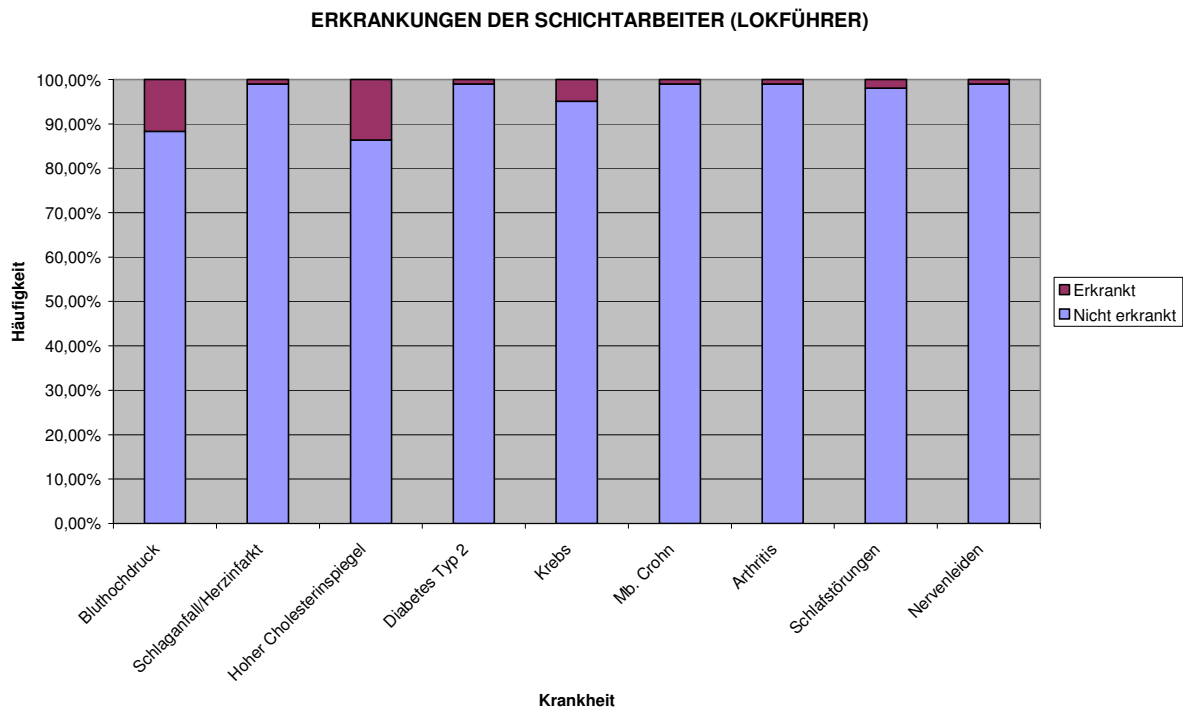


Figure 18: Diseases of shift workers

Frequency of Consumption during work hours : Day versus Shift Workers

Vegetables: 3 portions a day are recommended. 41% of dayworkers eat vegetables once a week during the shift, whereas 40% of shift workers consume vegetables 2-3 times a week.

Fruits: 25% of Day workers and 28% of shift workers eat fruits once a day. 2 portions a day are recommended

Potatoes and Grains: 50% of day workers eat potatoes once a week and 45% eat rice once a week. Of shift workers, 60% eat potatoes and 46% eat rice 2-3 times a week. 4 portions a day are recommended.

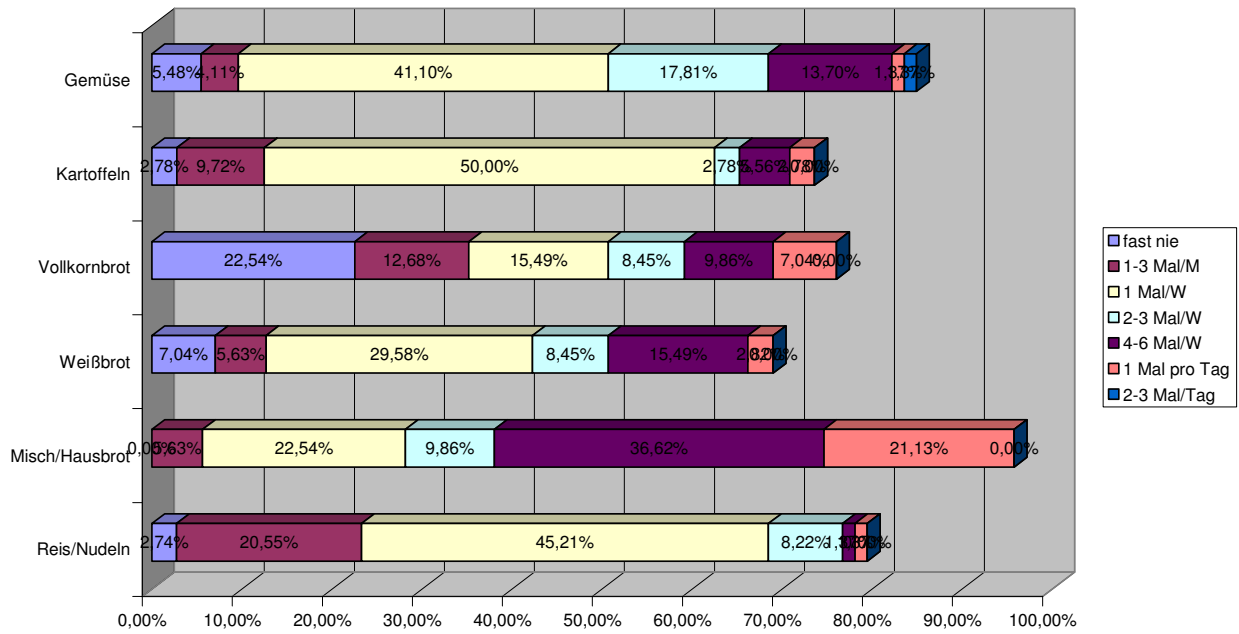
Milk: 29% of day workers have milk and milk products 2-3 times a week, whereas 24% of shift workers consume it once a day. 3 portions a day are recommended.

Meat and Sausages: There is no big difference between the samples: 44% day workers and 45% shift workers eat pork and beef 2-3 times a week and 25% day workers and 33% shift workers eat sausages 4-6 times a week. 3 portions a week are recommended.

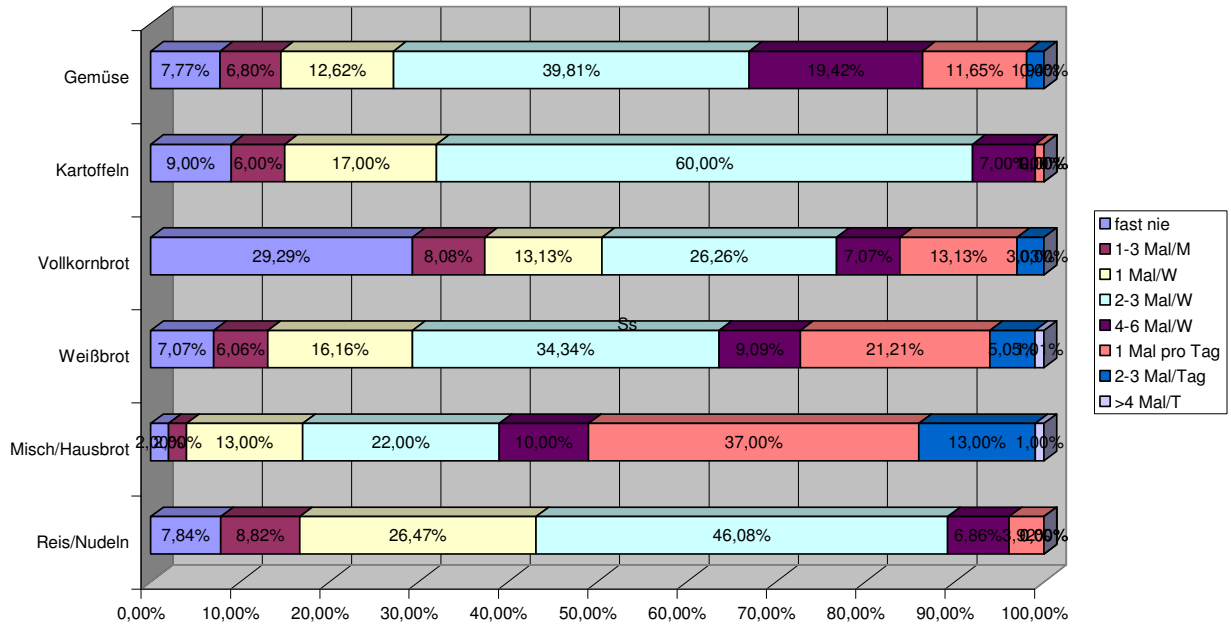
Eggs: 37% of day workers and 46% of shift workers eat eggs once a week. It is recommended to consume a maximum of 3 eggs a week.

Fish: 37% of day and 41% of shift workers consume fish once a week, which is in accordance with the guidelines. [ELMADFA et al., 2012]

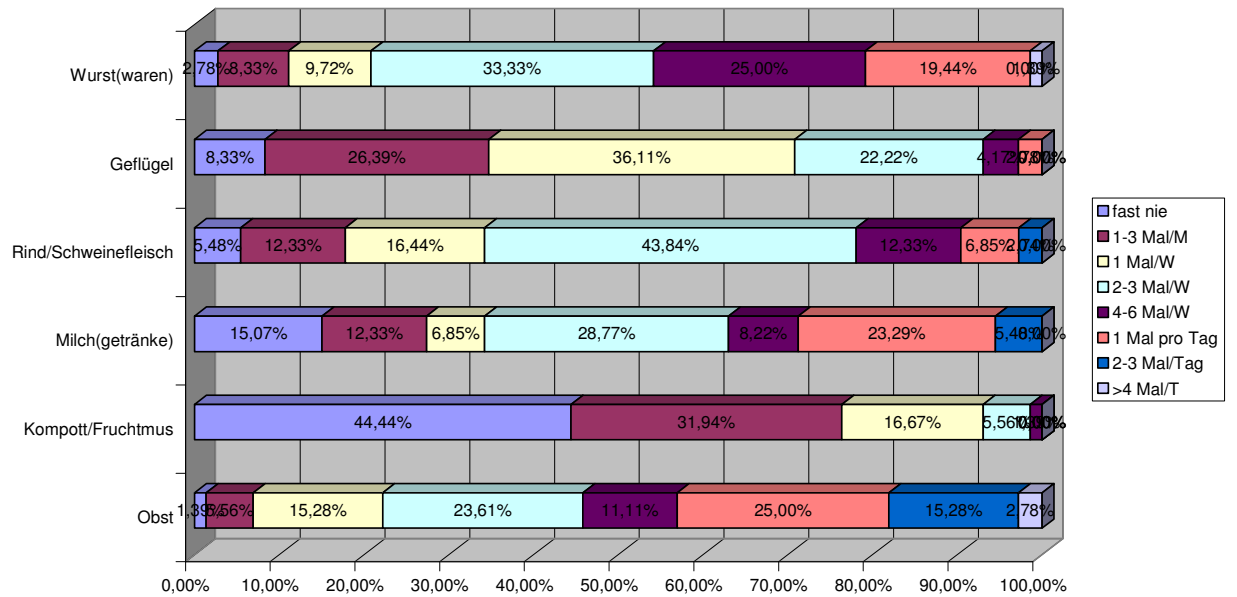
Tagarbeiter



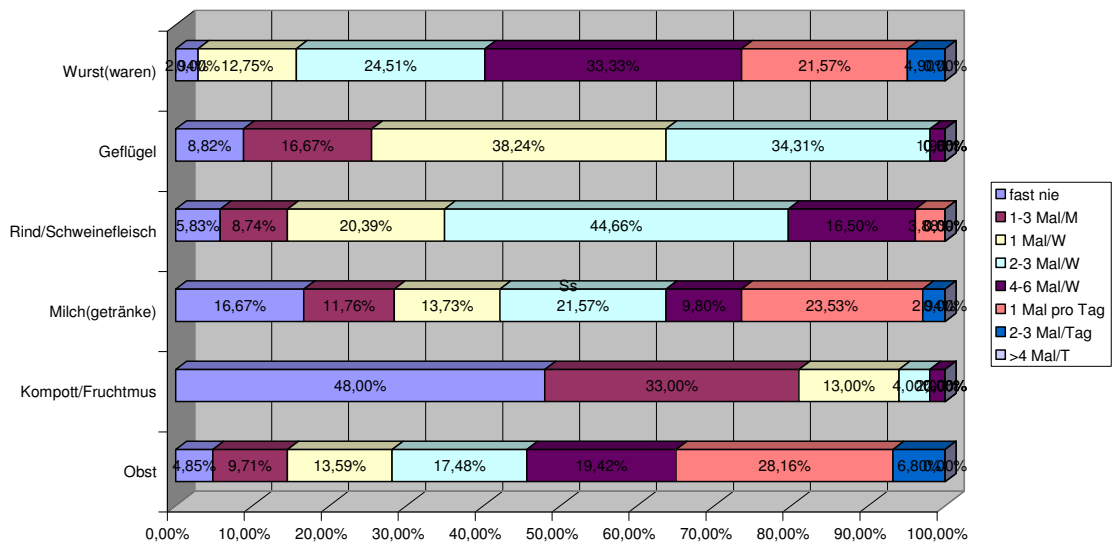
Schichtarbeiter



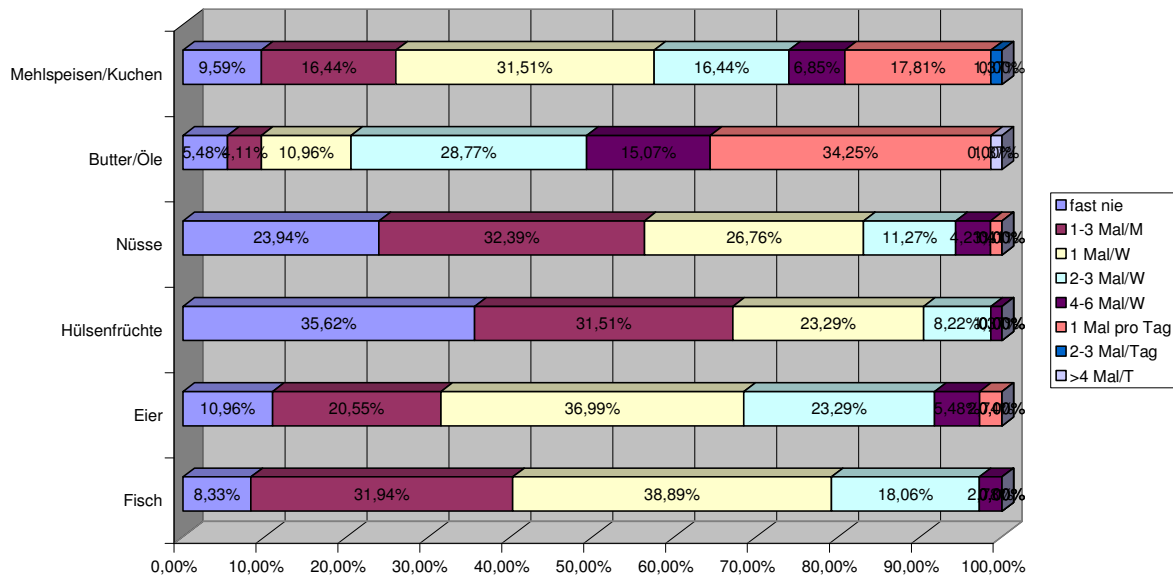
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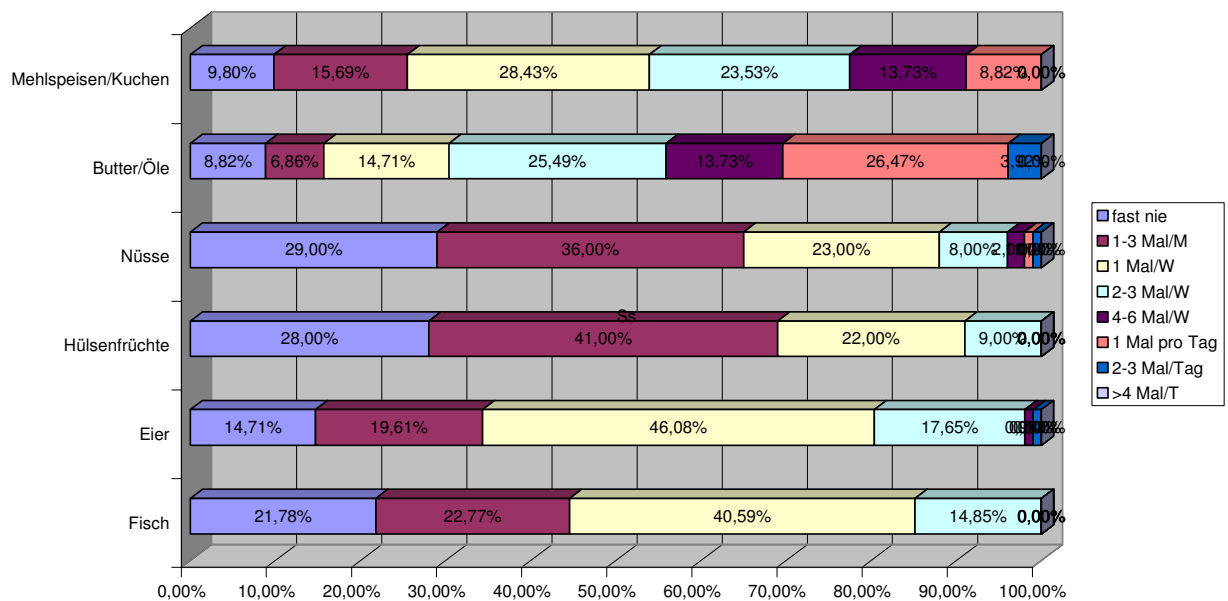
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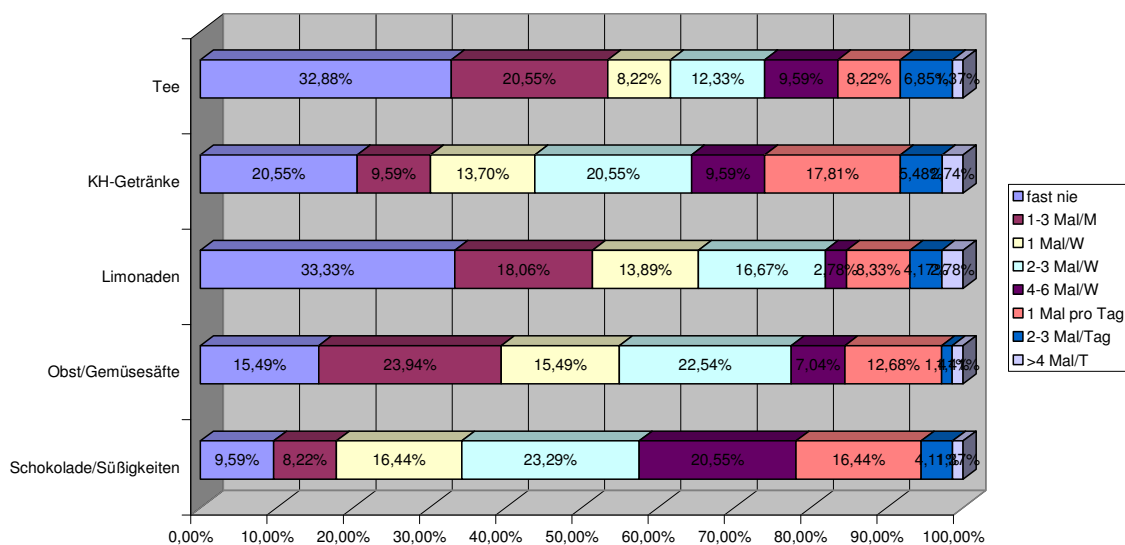
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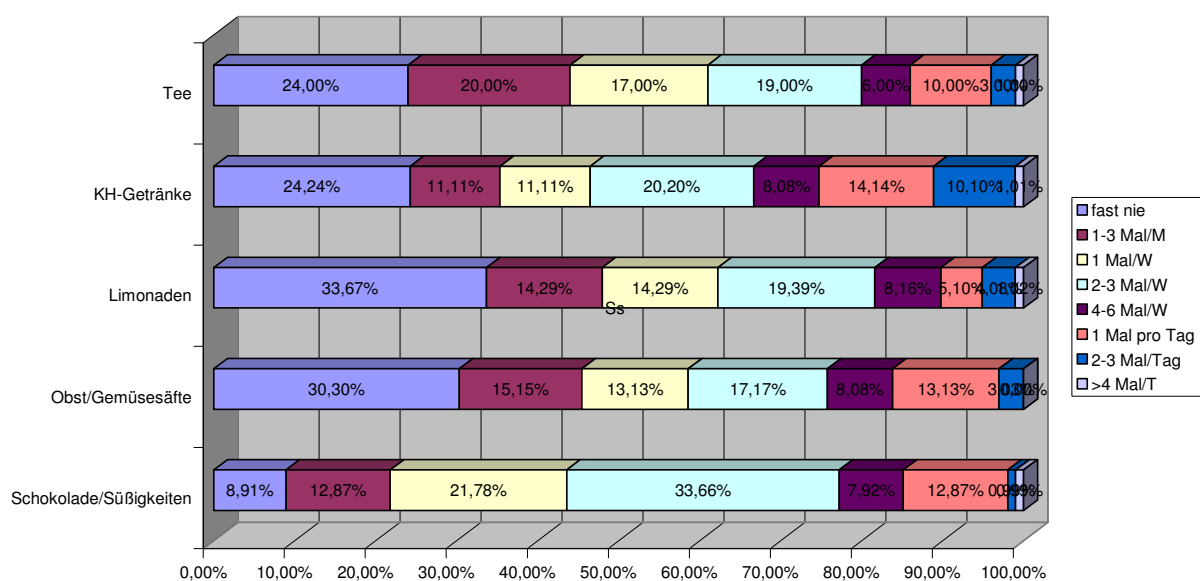
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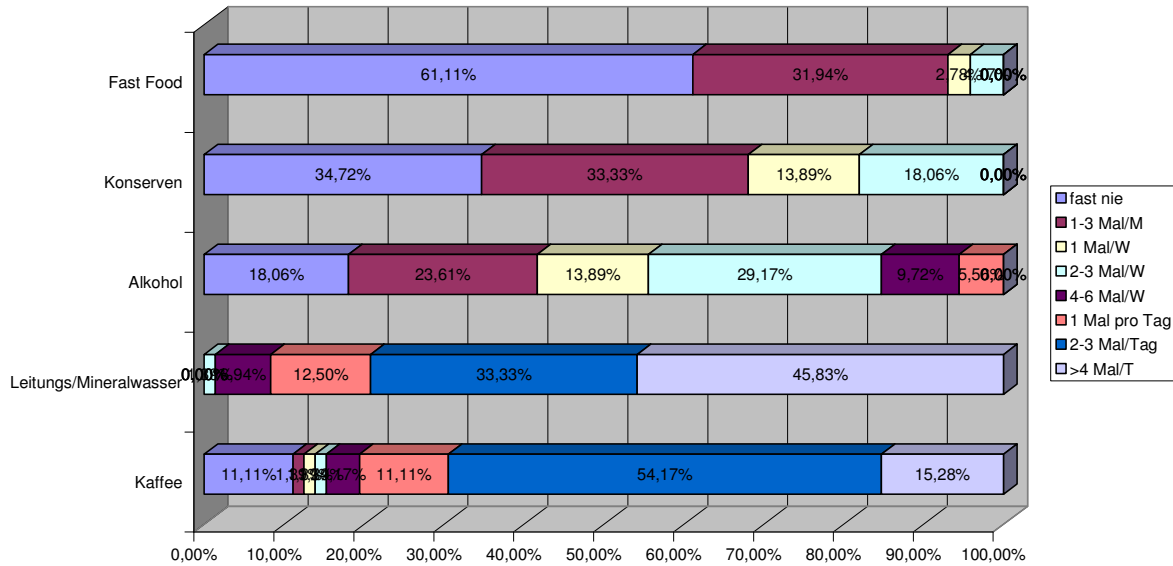
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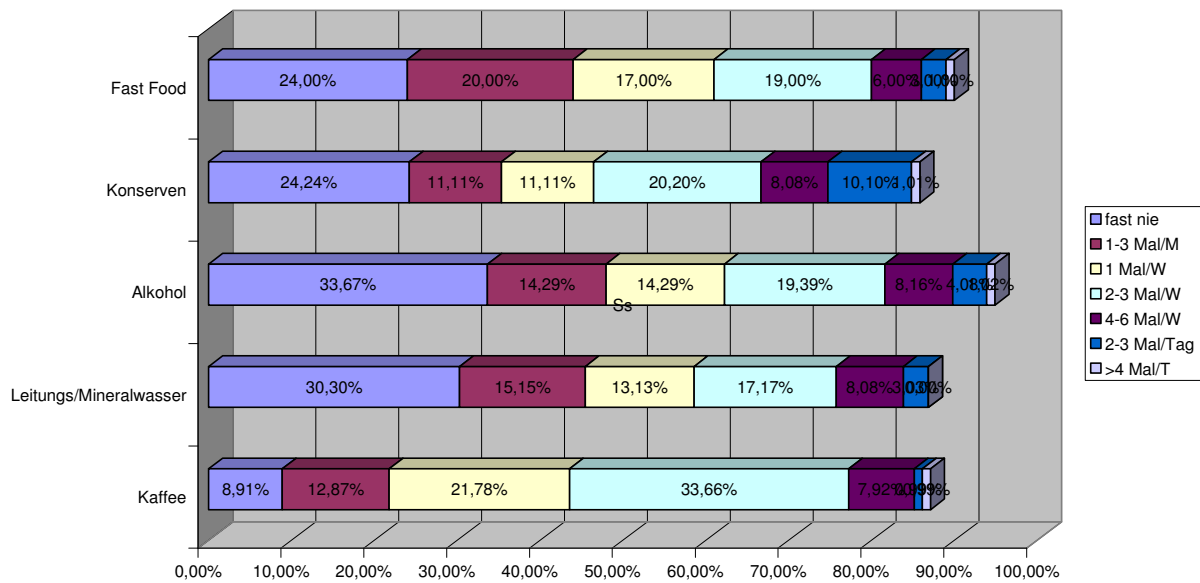
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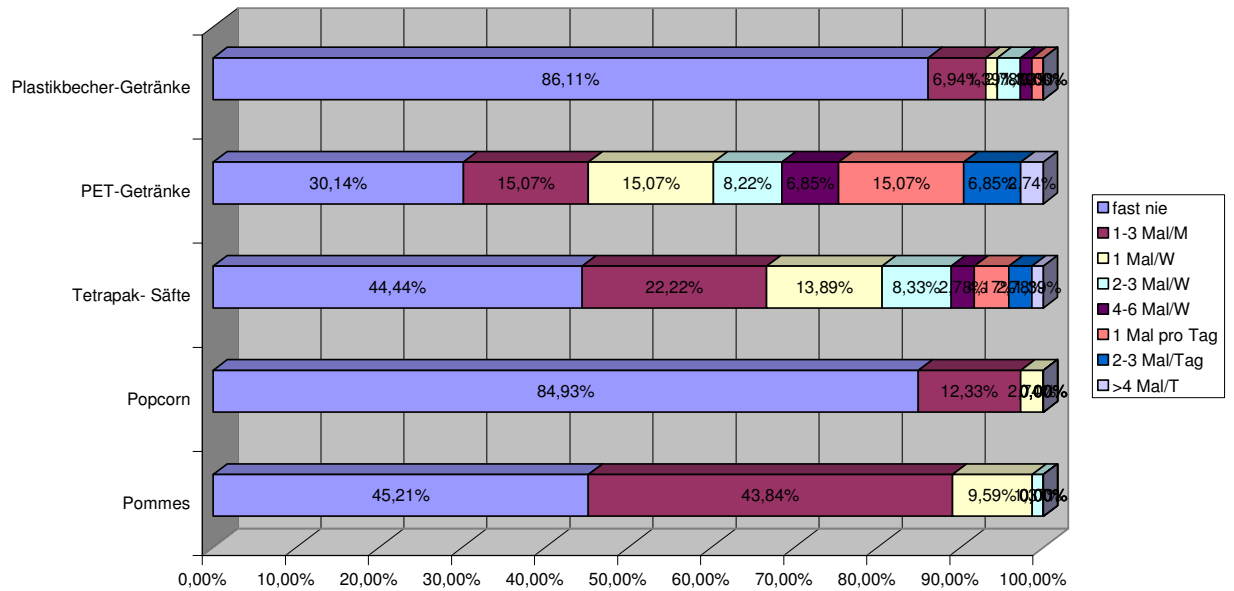
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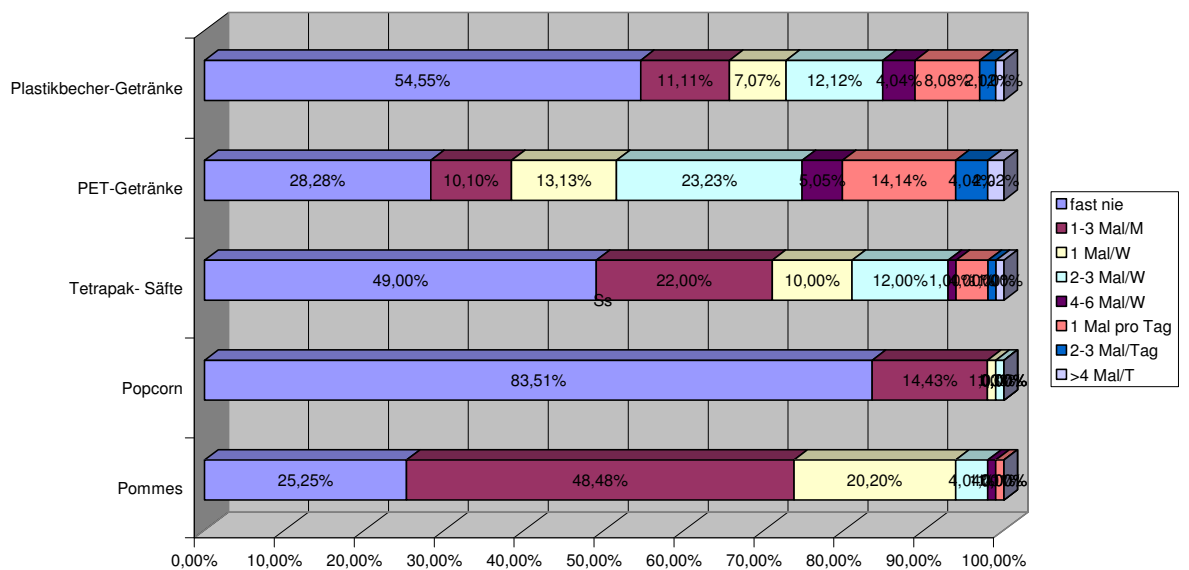
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Schichtarbeiter



Figures 19-30: Frequency of food consumption of day and shift workers of ÖBB

5 Conclusion

The aim of this study was to show how shift work can influence dietary habits. (Night) shift work with resulting changed dietary behaviour has a major role in the development of chronic diseases such as cardiovascular disease, cancer and gastrointestinal diseases. This paper highlighted a few studies which concluded that nutrition and exercise can improve adaptation to changing circadian rhythms.

At the moment, to our knowledge, no evidenced based nutrition recommendations especially for shift workers exist. For example, the DGE (Germany Society for Nutrition) has developed a folder for shift workers. However, these recommendations hardly differ from general guidelines for the population.

This study found that there is a tendency towards younger workers in shift work: in the age group 20-40 years, there are more subjects working in shift work than in day work. On the other hand, observing the age group 41-60 years, there are more people in day work than in shift work.

In addition, 63% of shift workers in this survey have overweight or are obese, compared to 60% of day workers. Yet, this difference is not significant.

Finally, locomotive drivers eat significantly more fast food and French fries than day workers and drink more plastic cup drinks. ($\alpha=0.05$)

As a matter of fact, 14 % of the locomotive drivers have significantly increased levels of cholesterol ($1\% < p\text{-value} < 5\%$) and 12% have significantly increased blood pressure. ($5\% < p\text{-value} < 10\%$)

Interestingly, 5% of locomotive drivers have or had cancer (3% in day workers) and 2% noted to suffer from sleep disorders, even though this disease was not a category.

Limitations of this survey are that the assessment of nutritional status is very limited with this short food frequency questionnaire. Exact analysis of both macro and micronutrients is missing. Withdrawal of blood and urine samples, as in the Nutrition Report of Austria 2012 would have provided much exacter data. Also, more study subjects would have given a higher explanatory power. Last but not least, questions

about lifestyle and exercise habits as well as risk factors would probably have delivered interesting findings.

Further research on the mechanisms of shift work-changed exercise and dietary behaviour-chronic disease is needed in order to prevent diseases in shift workers and to be able to improve their health status. Public Health Nutrition and Prevention of Disease should be of huge importance among shift workers, who constantly have to adapt to changed circadian rhythms and should draw their attention towards healthier dietary and exercise behaviour.

6 Summary

Objective: To assess food consumption frequencies in shift work compared to day work.

Design: The survey included 103 locomotive drivers and 74 day workers from ÖBB (Austrian Federal Railway) who filled a food frequency questionnaire. On the whole, the questionnaire comprised 2.5 pages. The study period lasted about two months, from October 15th to December 20th of 2012.

Subjects: 103 locomotive drivers (shift workers) and 74 day workers from ÖBB, with an age ranging from 20 to 56 years.

Setting: ÖBB Bludenz (Vorarlberg), Innsbruck (Tyrol) and Linz (Upper Austria).

Methods: The two samples locomotive drivers and day workers filled the same questionnaire. It included questions about body weight and height, country of birth, place of living, household size, education and diseases. Nutritional questions included 33 basic food and drink items such as fish and nuts. (22 questions about food items and 11 questions about drink consumption.)

Frequency of consumption during working hours had to be marked in the following eight categories: (almost) never, 1-3 times a month, once a week, 2-3 times a week, 4-6 times a week, once a day, 2-3 times a day and 4 and more a day.

Results: The t-test for independent samples was used to compare the two samples. There is a significant difference between locomotive drivers and dayshift workers in terms of the consumption of fast food, French fries and plastic cup drinks. Locomotive drivers eat significantly more fast food and French fries than day workers and drink more plastic cup drinks. ($\alpha=0.05$)

Conclusion: The assumption that the diet of shift workers includes significantly higher intake of fatty meals can be confirmed by this study. Noticeable in this respect is the fact that 14 % of the locomotive drivers have increased levels of cholesterol and 12% have increased blood pressure. Interestingly, 5% of locomotive drivers have or had cancer (3% in day workers) and 2% noted to suffer from sleep disorders, even though this disease was not a category.

7 Zusammenfassung

Zielsetzung: Vergleich der Häufigkeit des Nahrungsmittelverzehr zwischen Schicht- und Tagarbeit.

Design: Diese Studie umfasste 103 Lokführer und 74 Tagarbeiter der ÖBB, die einen „Food Frequency Questionnaire“ ausfüllten. Insgesamt beinhaltete dieser 2.5 Seiten. Die Studiendauer betrug etwa 2 Monate, vom 15.Oktober bis 20.Dezember 2012.

Studienteilnehmer/Innen: 103 Lokführer (Schichtarbeiter) und 74 Tagarbeiter der ÖBB, zwischen 20 und 56 Jahre alt.

Studienort: ÖBB Bludenz (Vorarlberg), Innsbruck (Tirol) und Linz (Oberösterreich).

Methoden: The beiden Gruppen Lokführer und Tagarbeiter füllten den selben Fragebogen aus. Dieser beinhaltete Fragen zum Gewicht und Körpergröße, Geburtsland, Wohnort, Haushaltsgröße, Ausbildung und Krankheiten. Es gab 33 Fragen zu Grundnahrungsmitteln und Getränken wie etwa Fisch und Nüsse. (22 Fragen über Grundnahrungsmitteln und 11 Fragen über Getränke). Die Häufigkeit des Verzehr während der Arbeitszeit musste aus den acht folgenden Kategorien angekreuzt werden: (fast) nie, 1-3 Mal pro Monat, 1 Mal pro Woche, 2-3 Mal pro Woche, 4-6 Mal pro Woche, 1 Mal täglich, 2-3 Mal täglich und 4 Mal und öfter täglich.

Ergebnisse: Der t-Test für unabhängige Stichproben wurde zum Vergleich der beiden Gruppen herangezogen. Es gibt einen signifikanten Unterschied zwischen Lokführern und Tagarbeitern in Bezug auf Fast Food, Pommes und Getränken im Plastikbecher: Lokführer essen signifikant mehr Fast Food, Pommes und trinken mehr Getränke aus Plastikbechern. ($\alpha=0.05$)

Schlussbetrachtung: Die Vermutung, dass Schichtarbeiter signifikant fettreicher essen, wird durch diese Studie bestätigt. Bemerkenswert in dieser Hinsicht ist die Tatsache, dass 14% der Lokführer erhöhte Cholesterinwerte angaben und 12% erhöhten Blutdruck. Weiters gaben 5% der Lokführer an, an Krebs zu leiden oder gelitten zu haben. (3% der Tagarbeiter).

2% der Schichtarbeiter gab an, an Schlafstörungen zu leiden, obwohl dies keine Kategorie in der Frage war.

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Studie zur Ernährung im Schichtdienst



Informationen zum Fragebogen

Bitte nehmen Sie sich für den Fragebogen ausreichend Zeit und lesen ihn aufmerksam durch. Sehen Sie sich die Fragen und die möglichen Antworten genau an. Die meisten Fragen können Sie beantworten, indem Sie ein einziges Kästchen ankreuzen ☒.

In wenigen Fällen werden Sie gebeten die Fragen frei zu beantworten, wofür Sie eine Linie zum Ausfüllen vorfinden: _____

Manche Fragen werden Sie leichter beantworten können und manche werden eine längere Nachdenkphase erfordern.

Bitte füllen Sie den Fragebogen dennoch gewissenhaft und wahrheitsgemäß aus.

Vergewissern Sie sich, dass Sie keine Frage vergessen haben auszufüllen und blättern Sie den Fragebogen am Ende noch einmal durch.

Wir möchten uns schon jetzt für Ihre Mithilfe bedanken!

Mit freundlichen Grüßen

Univ.-Prof. Dr. Jürgen König

Vorstand des Instituts für
Ernährungswissenschaften
Universität Wien



Ihre persönlichen Daten und Befunde unterliegen der ärztlichen Schweigepflicht sowie dem Datenschutzgesetz und werden daher streng vertraulich behandelt und nicht an Dritte weitergegeben!

Fragen zu ihrer Person

1. Alter: _____ Jahre

2. Körpergewicht: _____
kg

3. Körpergröße: _____ cm

4. In welchem Land wurden Sie geboren? _____

5. In welchem Land wurden Ihre Eltern geboren? _____

6. Welcher Nationalität gehören Sie an? _____

7. In welchem Bundesland leben Sie? _____

8. Wohngebiet (derzeit): ☐ städtisch

☐ in Stadtumgebung

☐ ländlich

9. Familienstand: ☐ verheiratet/Lebensgemeinschaft ☐ ledig

☐ getrennt lebend/geschieden ☐ verwitwet

10. Wie viele Personen leben insgesamt in Ihrem Haushalt?
_____ Personen

11. Was ist Ihre höchste abgeschlossene Ausbildung?

☐ Volksschule

☐ Hauptschule/AHS-Unterstufe

☐ Berufsschule (Lehre)/Berufsbildende mittlere Schule (**ohne Matura**)

☐ Berufsbildende höhere Schule/AHS-Oberstufe (**mit Matura**)

☐ Universität/Fachhochschule

☐ andere (bitte angeben): _____

12. Wie lang hat Ihre Ausbildung (einschließlich Schulausbildung) gedauert?

☐ 0 – 8 Jahre

☐ 9 – 11 Jahre

☐ 12 Jahre oder mehr

13. Welchen Beruf üben Sie derzeit aus?

- ☐ Lokführer
- ☐ Zugbegleiter
- ☐ anderer Beruf (bitte angeben) _____

14. Welche Schichtarbeitszeiten haben Sie normalerweise?

- ☐ Beginn: Uhr.....Ende: Uhr
- ☐ Beginn: Uhr.....Ende: Uhr
- ☐ Beginn: Uhr.....Ende: Uhr

15. An welchen Krankheiten (Krankheitsbildern) leiden Sie/ haben Sie gelitten?

- ☐ Bluthochdruck
- ☐ Schlaganfall/Herzinfarkt
- ☐ Hoher Cholesterinspiegel
- ☐ Diabetes Typ 2
- ☐ Krebs Welcher?.....

16. Wie oft essen oder trinken Sie normalerweise die folgenden Dinge IM SCHICHTDIENST?

Lebensmittel		pro Monat	pro Woche			täglich		
	(fast) nie	1-3 mal	1 mal	2-3 mal	4-6 mal	1 mal	2-3 mal	4 mal und öfter
Reis, Nudeln (Spaghetti, Hörnchen,...)	☐	☐	☐	☐	☐	☐	☐	☐
Mischbrot, Hausbrot	☐	☐	☐	☐	☐	☐	☐	☐
Weißbrot (Semmeln, Toastbrot,...)	☐	☐	☐	☐	☐	☐	☐	☐
Vollkornbrot	☐	☐	☐	☐	☐	☐	☐	☐
Kartoffeln	☐	☐	☐	☐	☐	☐	☐	☐
Gemüse (frisch oder gekocht)	☐	☐	☐	☐	☐	☐	☐	☐
Obst (frisch)	☐	☐	☐	☐	☐	☐	☐	☐
Kompott, Fruchtmus	☐	☐	☐	☐	☐	☐	☐	☐
Milch und andere Milchgetränke	☐	☐	☐	☐	☐	☐	☐	☐
Rind- oder Schweinefleisch	☐	☐	☐	☐	☐	☐	☐	☐
Geflügel	☐	☐	☐	☐	☐	☐	☐	☐
Wurst und Wurstwaren	☐	☐	☐	☐	☐	☐	☐	☐
Fisch	☐	☐	☐	☐	☐	☐	☐	☐
Eier	☐	☐	☐	☐	☐	☐	☐	☐
Hülsenfrüchte (Bohnen, Linsen,...)	☐	☐	☐	☐	☐	☐	☐	☐
Mandeln, Erdnüsse oder Nüsse	☐	☐	☐	☐	☐	☐	☐	☐
Butter, Öle	☐	☐	☐	☐	☐	☐	☐	☐
Mehlspeisen, Kuchen	☐	☐	☐	☐	☐	☐	☐	☐
Schokolade oder Süßigkeiten	☐	☐	☐	☐	☐	☐	☐	☐
Obst- oder Gemüsesäfte	☐	☐	☐	☐	☐	☐	☐	☐
Limonaden	☐	☐	☐	☐	☐	☐	☐	☐
Kohlensäurehaltige Getränke	☐	☐	☐	☐	☐	☐	☐	☐
Tee (Früchtetee oder Grüner Tee)	☐	☐	☐	☐	☐	☐	☐	☐
Kaffee	☐	☐	☐	☐	☐	☐	☐	☐
Leitungswasser, Mineralwasser	☐	☐	☐	☐	☐	☐	☐	☐
Alkoholische Getränke	☐	☐	☐	☐	☐	☐	☐	☐
Lebensmittel in Konserven	☐	☐	☐	☐	☐	☐	☐	☐
Fast Food, Take away	☐	☐	☐	☐	☐	☐	☐	☐
Pommes Frites	☐	☐	☐	☐	☐	☐	☐	☐
Mikrowellen Popcorn	☐	☐	☐	☐	☐	☐	☐	☐
Säfte in Tetrapak	☐	☐	☐	☐	☐	☐	☐	☐
Getränke in PET Flaschen	☐	☐	☐	☐	☐	☐	☐	☐
Getränke im Plastikbecher zum mitnehmen	☐	☐	☐	☐	☐	☐	☐	☐

Curriculum vitae

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Education:

10/2010: Medical Student at the Medical University of Innsbruck
07/2008-11/2008: Exchange semester in Australia, Brisbane at the University of Queensland
10/2005: Student of Nutritional Science at the University of Vienna
09/2004-06/2005 Year of Service at Maxwell International School, Canada and India
09/2000-06/2004: Student at Bundesoberstufenrealgymnasium Perg

Professional Experience:

07/2010 – 08/2010: Intern at FAO, Rom
08/2009 -09/2009: Intern at SIPCAN („Special Institute for Preventive Cardiology and Nutrition”)
02/2009-07/2009: Intern at Danone (Communication)
06/2009: Summer course „EU Basics in Public Health Nutrition in Stockholm, Sweden
02/2008- 03/2008: Intern at „forum.ernährung heute“
2003: Peereducation seminar: a project for prevention of addiction in schools