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Smoking and incidence and mortality of colorectal cancer

Ranjan Parajuli

A dissertation for the degree of Philosophiae Doctor-2014

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NORWEGIAN **CANCER** SOCIETY

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Summary

Smoking is one of the most important causes of cancer and premature death worldwide. Two different reports, the most recent monograph published by International Agency for Research on Cancer (IARC) in 2012 and the Unites States Surgeon General's report of 2014, concluded that smoking is risk factor for both colon and rectal cancer. In addition to being one of the most common cancers in Norway, mortality from colorectal cancer (CRC) is also high. The main aim of this thesis was to examine the association between smoking and CRC incidence and mortality overall and by gender. We examined the association between smoking and colon cancer by location and gender (Paper I), rectal cancer by gender (Paper II) and CRC mortality by subsite and gender (Paper III).

The cohort included 652,792 Norwegians (49% men) recruited from four Norwegian health screening surveys. These surveys were conducted between 1972 and 2003: the Oslo study I (1972-1973), the Norwegian counties study (1974-1988), the 40 years cohort (1985-1999) and the Cohort of Norway (CONOR, 1994-2003). The participation rate for the different surveys varied from 56-88%.

Women ever smokers had a 19% and men ever smokers had 8% increased risk of colon cancer. Furthermore, women ever smokers had an increased risk of proximal colon cancer compared to men ever smokers (Paper I). Ever smokers had an increased risk of rectal cancer at around 25% and the risk increased was similar for men and women (Paper II). Men and women ever smokers had a similar increased risk of CRC mortality of about 20%. The risk of rectal and proximal colon cancer mortality was most pronounced among men and women smokers, respectively (Paper III).

In conclusion, smoking increased the risk of colon cancer, especially proximal colon cancer among women. Furthermore, smoking increased the risk of rectal cancer, with a similar risk

being observed among women as in men ever smokers. Smoking is associated with increased CRC mortality among both men and women. The risk of rectal and proximal cancer mortality was most pronounced among men and women smokers, respectively.

List of papers

This thesis is based on the three papers listed below:

Paper I

Parajuli R, Bjerkaas E, Tverdal A, Selmer R, Le Marchand L, Weiderpass E, Gram IT. **The increased risk of colon cancer due to cigarette smoking may be greater in women than men.** *Cancer Epidemiol Biomarkers Prev.2013; 22(5), 862-71. PubMED:PMID 23632818)*

Paper II

Parajuli R, Bjerkaas E, Tverdal A, Le Marchand L, Weiderpass E, Gram IT. **Smoking increases rectal cancer risk to the same extent in women as in men: Results from a Norwegian cohort study.** *BMC Cancer (submitted)*

Paper III

Parajuli R, Bjerkaas E, Tverdal A, Le Marchand L, Weiderpass E, Gram IT. **Cigarette smoking and colorectal cancer mortality among 602,242 Norwegian males and females.** *Clinical Epidemiology, Dovepress (Online)*

List of figures and tables

Abbreviations

ASR	Age standardized rates
BMI	Body mass index
CI	Confidence interval
CONOR	Cohort of Norway
CRC	Colorectal cancer
DNA	Deoxyribonucleic acid
EPIC	European Prospective Investigation into Cancer and Nutrition
FAP	Familial adenomatous polyposis
HNPCC	Hereditary non polyposis colorectal cancer
HR	Hazard ratio
HRT	Hormonal replacement therapy
IARC	International Agency for Research on Cancer
IBD	Inflammatory bowel disease
PAH	Polycyclic Aromatic Hydrocarbons
REK	Regional komité for medisinsk og helsefaglig forskningsetikk (Regional Committee for Medical Research Ethics)
WHO	World Health Organization

1 Introduction

This thesis describes the association between cigarette smoking and colorectal cancer (CRC) incidence and mortality overall and by subsite among Norwegian men and women who participated in four different Norwegian health surveys.

1.1 Definition and epidemiology of colorectal cancer

In 2012, there were around 14 million new cancer cases (all types combined), 8 million cancer deaths and around 32 million people were living with cancer worldwide. Fifty-seven percent (8 million) of these new cancer cases and 65% (5.3 million) of cancer deaths occurred in low and medium income countries (1).

CRC is one of the major causes of morbidity and mortality around the world (2). CRC is confined to the main parts of large intestine, the colon and rectum. Adenocarcinoma is the predominant histological subtype and begins as adenomatous polyps before reaching the malignant stage. The progression from adenomatous polyps to carcinoma occurs with potential damage to DNA. Other histological subtypes of CRC include carcinoid tumors, gastrointestinal, stromal tumors, lymphomas and sarcomas. More than 95% CRC are sporadic, originating in individual without significant genetic or hereditary risk factor (3). If the diagnosis is made early, CRC is highly treatable. CRC is known as disease of western world as it is more prevalent in high-income countries.

Globally, CRC is the third most common cancer in men and the second most common cancer in women representing about 9% and 10% of all incident cancer respectively (2). CRC incidence rates worldwide have changed with time, but usually men have higher rates compared to women (2). There is a wide variation in CRC incidence across the world population but the patterns of variation in men and women are similar. The CRC incidence rates vary tenfold, with the highest estimates in Australia and New Zealand (age-standardized

incidence rate, ASR 44.8 and 32.2 per 100,000 in men and women, respectively) and the lowest in Western Africa (4.5 and 3.8 per 100,000 in men and women, respectively) (1). There is also a geographical difference in the global occurrence of CRC. High-income countries usually have higher incidence rates and accounts for almost 55% of all incident cases CRC worldwide (4).

CRC incidence rates are decreasing in the United States, whereas in Northern and Western Europe CRC incidence rates are stabilizing. However, high income countries like Japan, Singapore, and some Eastern European countries are showing a substantial increase in CRC incidence (5;6).

CRC accounts for 8% of all cancers deaths, which makes it the fourth most common cause of death from cancer worldwide (7). It has been reported that about 12% of CRC deaths are attributed to smoking (6;8). CRC mortality rates are lower in women than men except in the Caribbean region (7). Worldwide, CRC mortality rates vary less than CRC incidence rates (six fold in men, and four fold in women). The highest mortality rates are observed in Central and Eastern Europe (20.3 and 11.7 per 100.000 among men and women, respectively) and lowest in western Africa (3.5 and 3.0 per 100,000 among men and women, respectively) (1). In the United States, it is the third most common cause of cancer death although the overall mortality rates have decreased by 2.8% and 2.6% per year in men and women, respectively since 1998 (9). CRC is the second most common cause of cancer deaths in Europe (1). Latest CRC incidence and mortality rates worldwide are shown in figure 1.

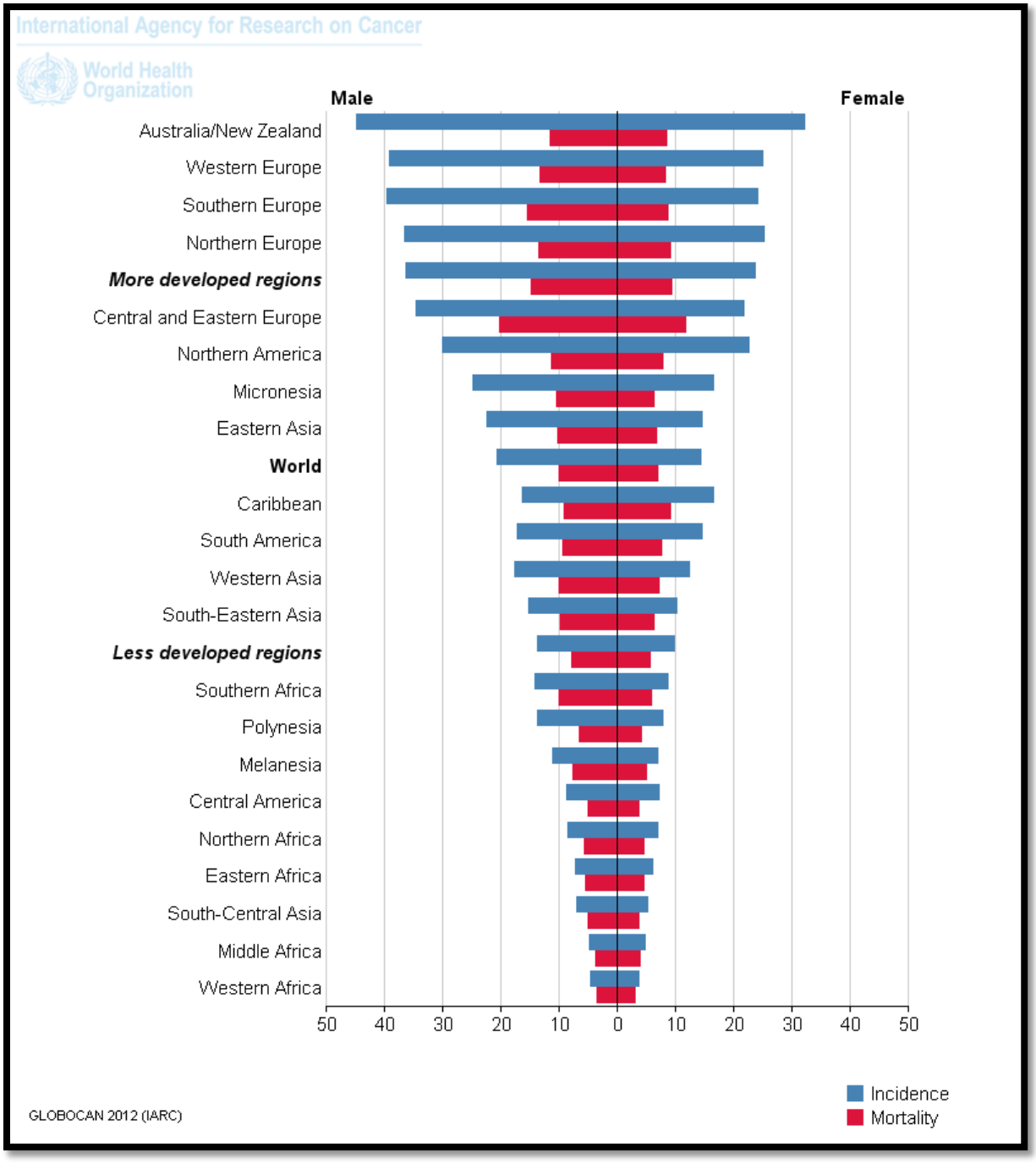

Figure 1: Worldwide estimated age standardized rates of CRC incidence and mortality rates per 100,000 by gender. (Globocan 2012, IARC)

1.2 Incidence of colorectal cancer in Nordic countries

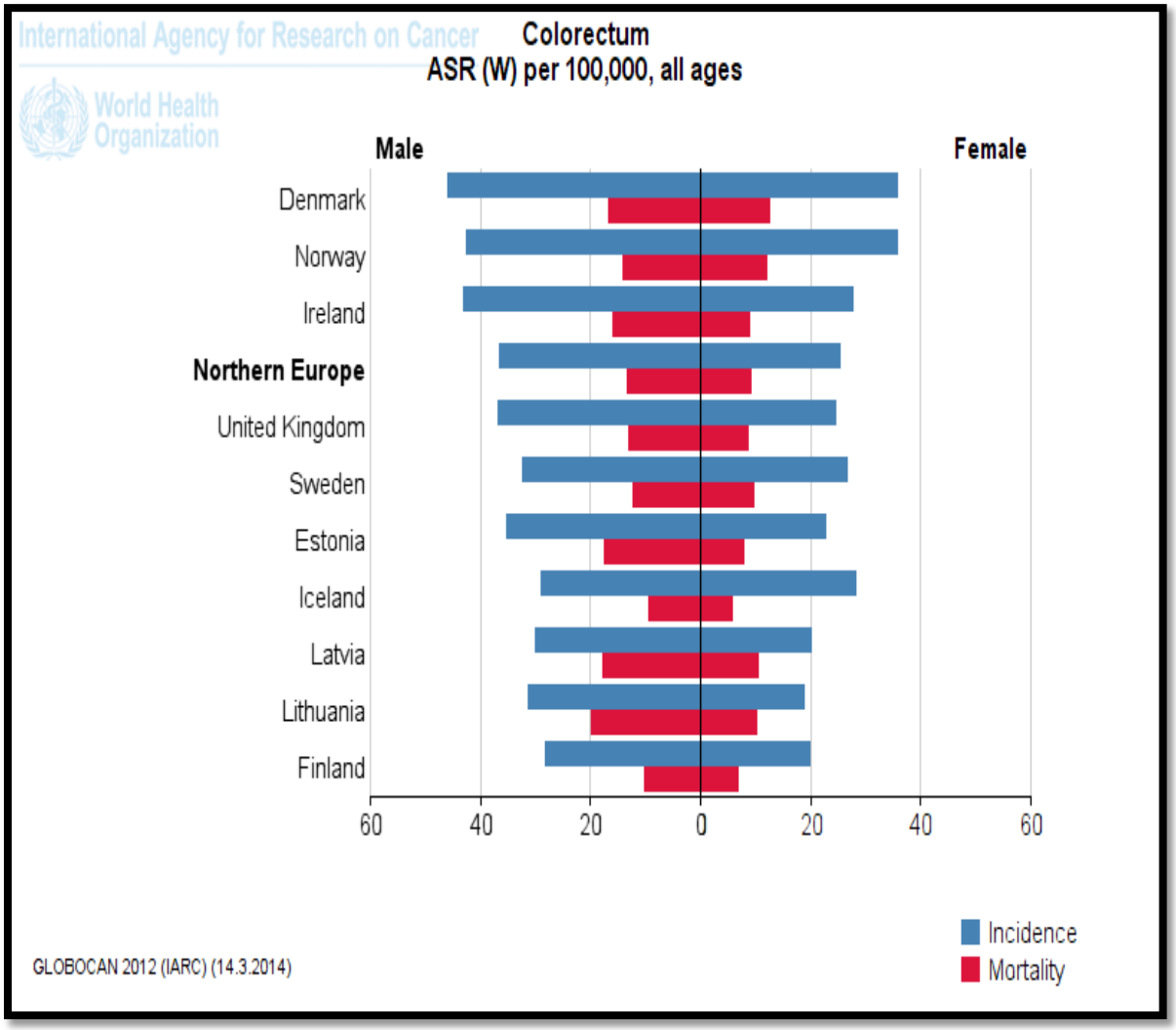

Figure 2: Estimated age standardized CRC incidence and mortality rates per 100,000 in Northern Europe by gender (Globocan 2012, IARC)

Figure 2 illustrates the present CRC incidence and mortality rates in Northern Europe among men and women.

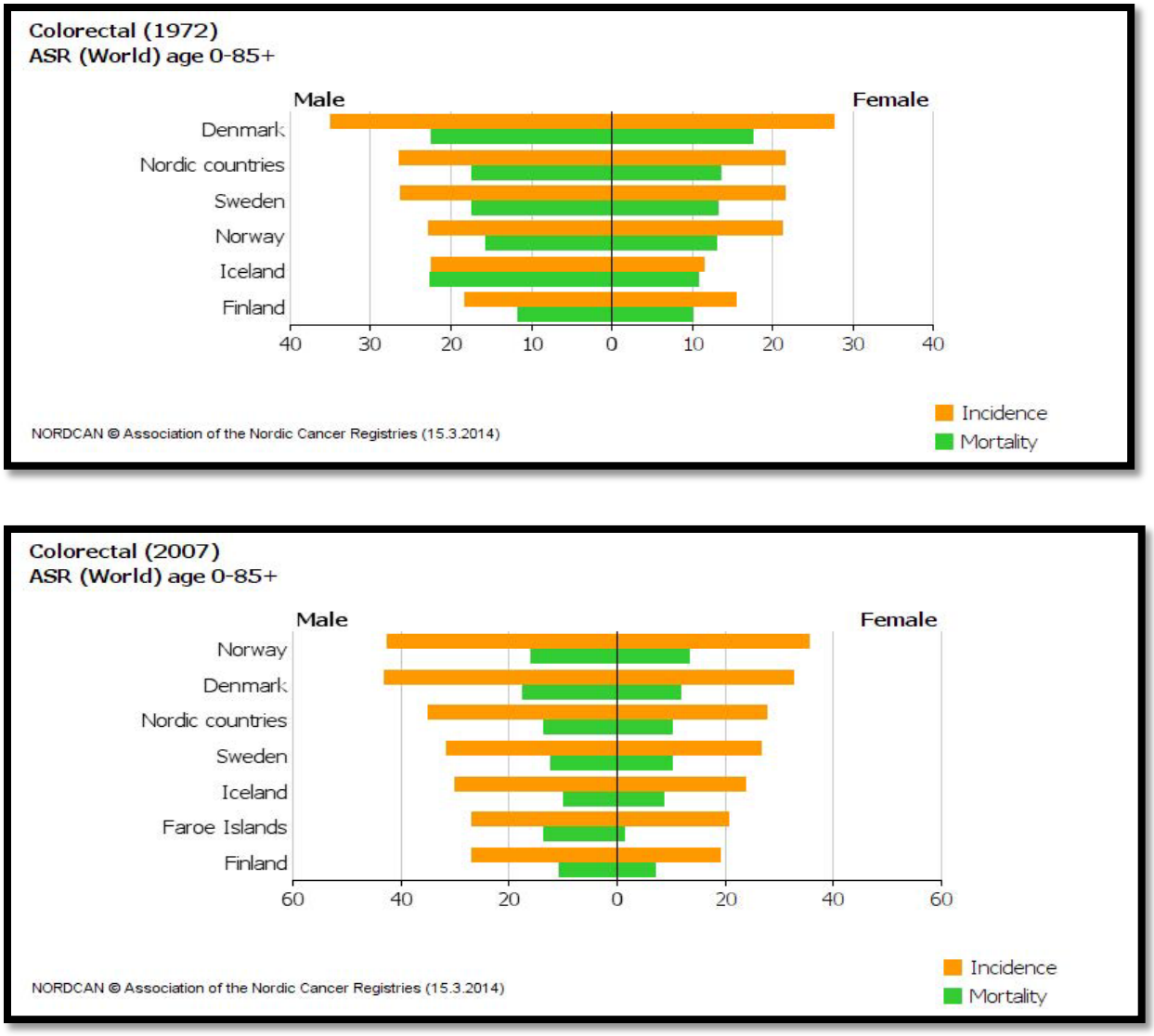

Figure 3: Age standardized rate of CRC incidence and mortality rates per 100,000 in the Nordic countries 1972 and 2007 (NORDCAN)

Figure 3 shows the incidence and mortality rates in the Nordic countries during 1972 and 2007 that is the beginning and end of our study period, respectively. Denmark had the highest incidence rate back in 1972 both among men and women. By 2007, Norway and Denmark were observing almost similar CRC incidence rates. Norwegian women had slightly higher incidence rate compared to Danish women. However, regarding mortality rates, Icelandic men had the highest rates followed by Danish men during 1972 whereas by 2007 highest rates were observed in Denmark and Norway. Danish men had highest CRC mortality rate whereas the rates were highest among Norwegian women in 2007.

1.2 Colorectal cancer in Norway

Over the last half century, Norway has experienced one of the most rapid and steady rises in CRC incidence. In the late 1950s, the age standardized incidence rate for colon cancer was 10 per 100,000 for both men and women. The incidence rate of rectal cancer in the same period was approximately around 7 and 4 for per 100,000 for men and women, respectively. By the beginning of 1970s, the incidence rate of colon cancer was around 14 for both men and women; the incidence rate of rectal cancer was 11 and 8 per 100,000 for men and women, respectively. Current incidence rates of both colon and rectal cancer are more than double what they were 50 years ago for both men and women. The present age standardized five year incidence rate of CRC for year 2007-2011 is 43 for and 35 per 100,000 for men and women respectively. Among men, the incidence rate of colon and rectal cancer is 26 and 17 per 100,000 respectively. Similarly, for women, the incidence of colon and rectal cancer is 24 and 11 per 100,000 respectively (10). The corresponding figures for CRC incidence rate and by subsite in Norway by gender from 1972-2011 are presented in the figure below (Figure 4, 5, and 6).

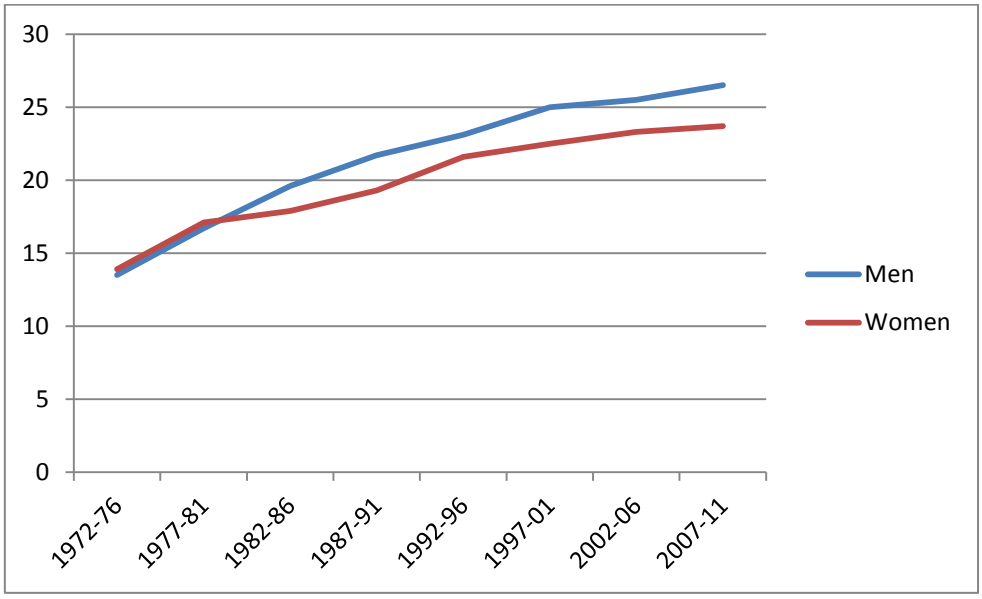

Figure 4: Age standardized incidence rate of colon cancer by gender in Norway (1972-2011) (Norwegian Cancer Registry, 2013)

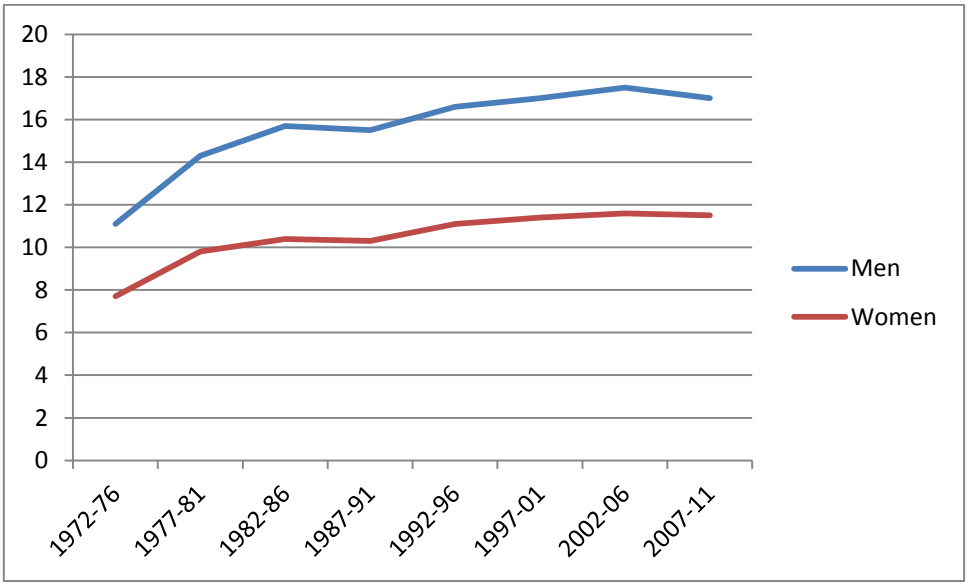

Figure 5: Age standardized incidence rate of rectal cancer by gender in Norway (1972-2011) (Norwegian Cancer Registry, 2013)

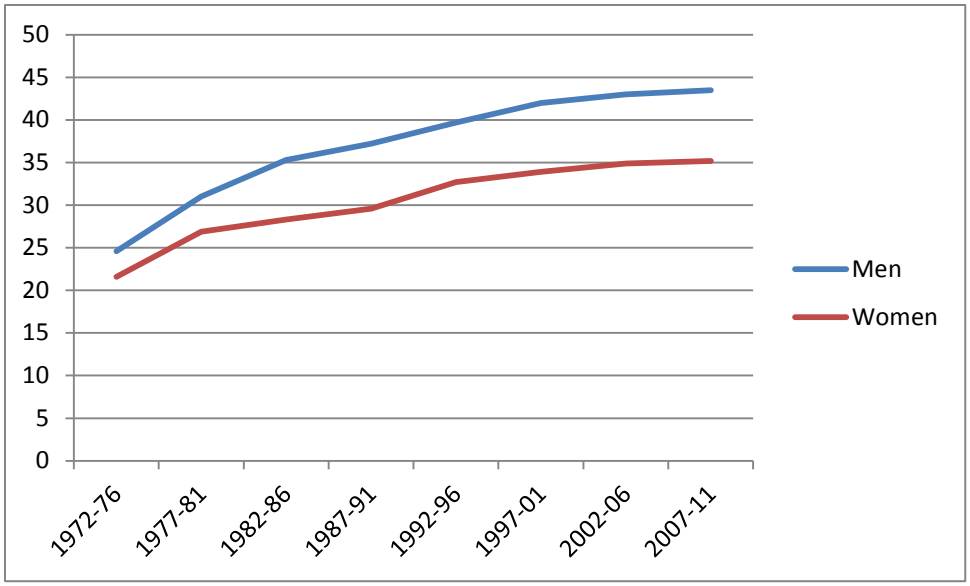

Figure 6: Age standardized incidence rate of CRC by gender in Norway (1972-2011) (Source: Norwegian Cancer Registry, 2013)

The colon cancer incidence rates among men and women are almost similar but men have higher incidence of rectal cancer than women. The gender difference in CRC incidence is due to men having more rectal but not colon cancer than women.

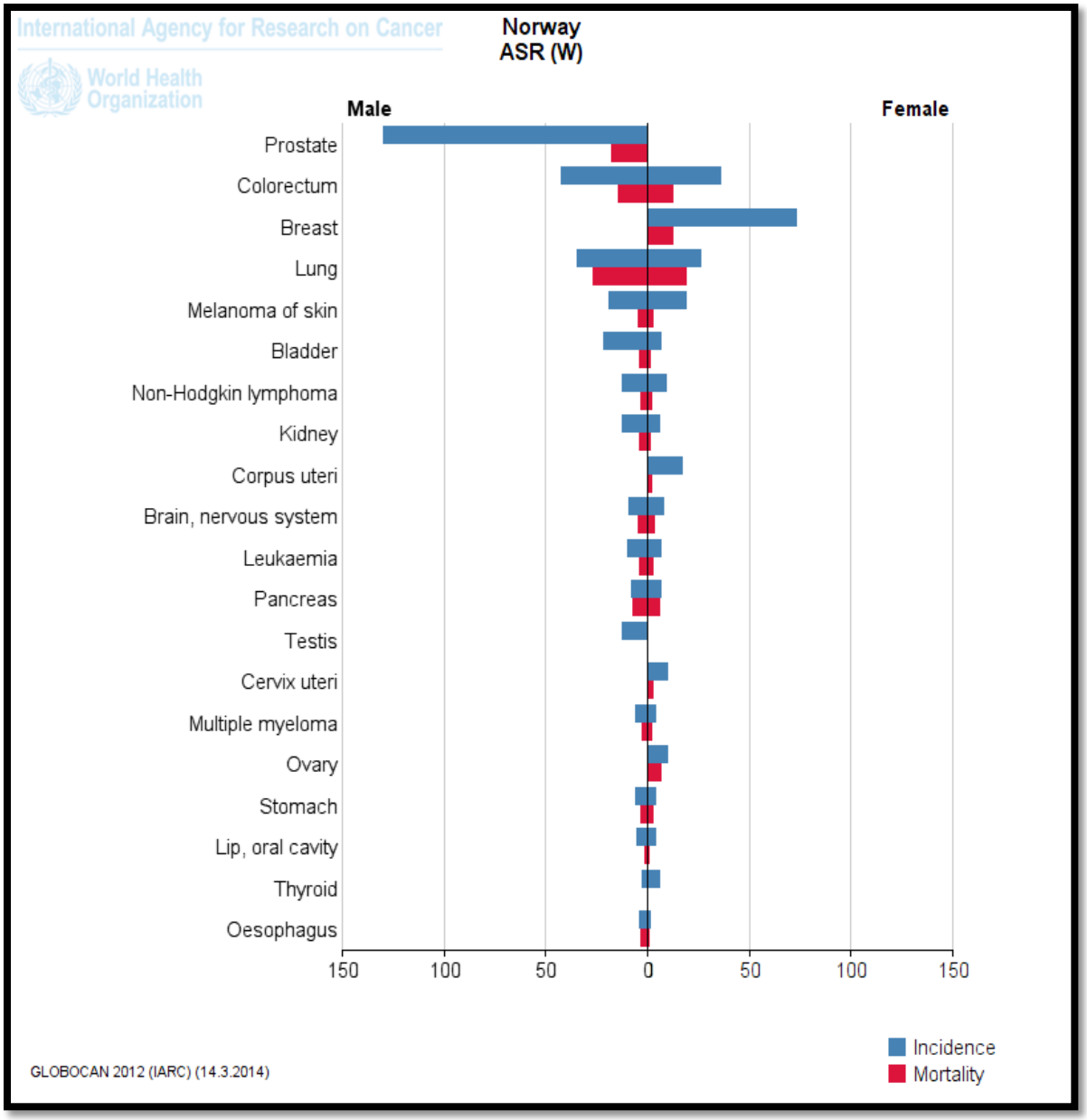

Figure 7: Estimates of age standardized incidence and mortality rate per 100,000 for different cancer sites in Norway by gender (Globocan 2012)

Figure 7 shows the ASR for different cancer in Norwegian by gender in 2012. In 2002, women in Norway had the highest CRC incidence rate in Europe and second highest incidence rate worldwide, only surpassed by women in New Zealand (11). In addition to being one of the most common cancers among Norwegian, CRC is also a cancer type with a high mortality. The latest report showed that in Norway, the CRC mortality rate is ranked

second after lung cancer among women and third after lung and prostate cancer among men (10).

1.3 Prevalence of smoking

1.3.1 Global prevalence

There are an estimated 1.3 billion smokers worldwide and that number is expected to increase to 1.6 billion by 2025 (12;13). Seventy-three percent of smokers are from low and medium income countries. Smoking is one of the major leading preventable causes of death in the world (13-15) and attributed to approximately 6 million premature deaths each year globally. If prevention measures are not implemented soon, the deaths toll could reach approximately 8 million by 2030. Recent report on tobacco from World Health Organization (WHO) reported that in the 20th century almost 100 million deaths have been caused by tobacco smoking and if this trend continues further, one billion smoking related deaths will occur in the 21st century (13).

A four stage model for describing the effects of smoking on mortality was purposed by Lopez and colleagues almost 2 decades ago (16). Women in high-income countries lagged behind men by 20-30 years in relation to smoking and its attributed mortality. This model was further reviewed in 2012 and the predictions matched recent trends in smoking and smoking related mortality (Figure 8). The authors concluded that the model reflected the situation of many high income countries reasonably well with a few exceptions in low and medium income countries (17).

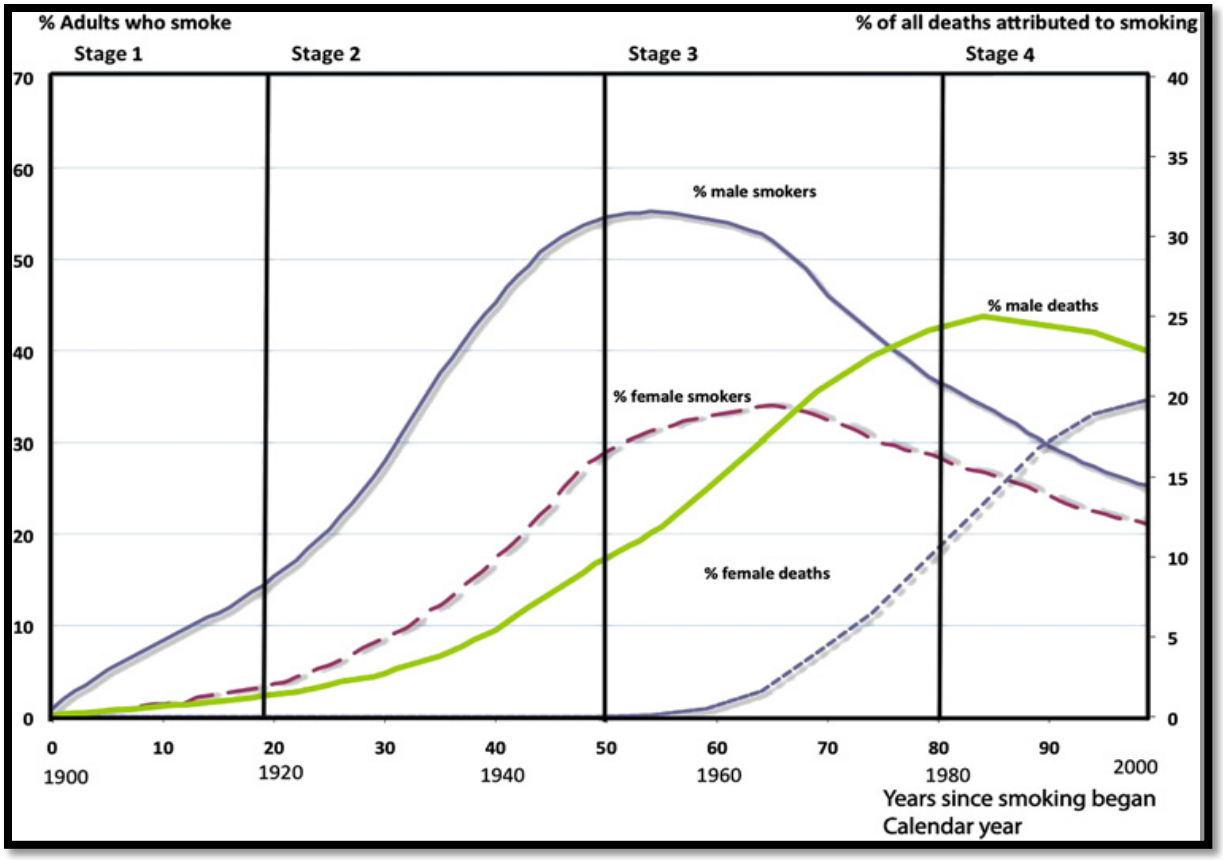

Figure 8: A descriptive model of cigarette epidemic in developed countries (Lopez et al. 1994)
Stages of the cigarette epidemic on entering its second century (Thune et al 2012):
(Reprinted with permission from BMJ publisher group)

1.3.2 Prevalence of smoking in the Nordic countries

In 1920, Denmark had the highest prevalence of smoking in the Nordic countries. A report from 2006 showed the highest prevalence in Denmark and Norway (25 and 24, respectively), and the lowest prevalence in Sweden and Iceland (18). Direct comparisons of the smoking prevalence in Nordic countries are somewhat difficult as the data on smoking habits are collected in different age groups. However, in all of the Nordic countries a decreasing trend in the prevalence of smoking was associated with an increased level of education (19).

1.3.3 Prevalence of smoking in Norway

The trend of smoking prevalence for men current smokers has been different from that of women in Norway. The prevalence of smoking among men peaked at 65 % in the late 1950's; and then decreased to 50% in 1975 and 33% in 1999. This decrease continued through 2007, when the prevalence of smoking among men was 50% lower than that in the 1970s. This is quite different from the corresponding figures of smoking prevalence among women. In 1954, the prevalence of smoking among women which was 23% in 1954, peaked at 37% in 1970 and then stabilized to 32% for the rest of the century. After 2002, a decline in the prevalence of smoking was seen among women and by 2007 which is the end of our follow-up period; the prevalence was similar in both men and women (18;20;21). By the year 2013, 15% Norwegian men and women were current smokers (22). This smoking pattern is in accordance with the tobacco epidemic stages model suggested by Lopez et al. almost 20 years ago (16) which suggested that the smoking-attributed mortality for women, will in the same way as the smoking prevalence, lagged behind that of men and both will peak at a lower level than that of men. The difference in smoking habits is one of the main explanations for social inequalities in health in Norway. Recently, it has been reported that Norway is one of the four countries along with Canada, Iceland and Mexico that are successful in achieving reductions of smoking prevalence in both men and women by more than 50% (23). Figure 9 shows the prevalence of current smokers by gender in Norway between years 1973-2013.

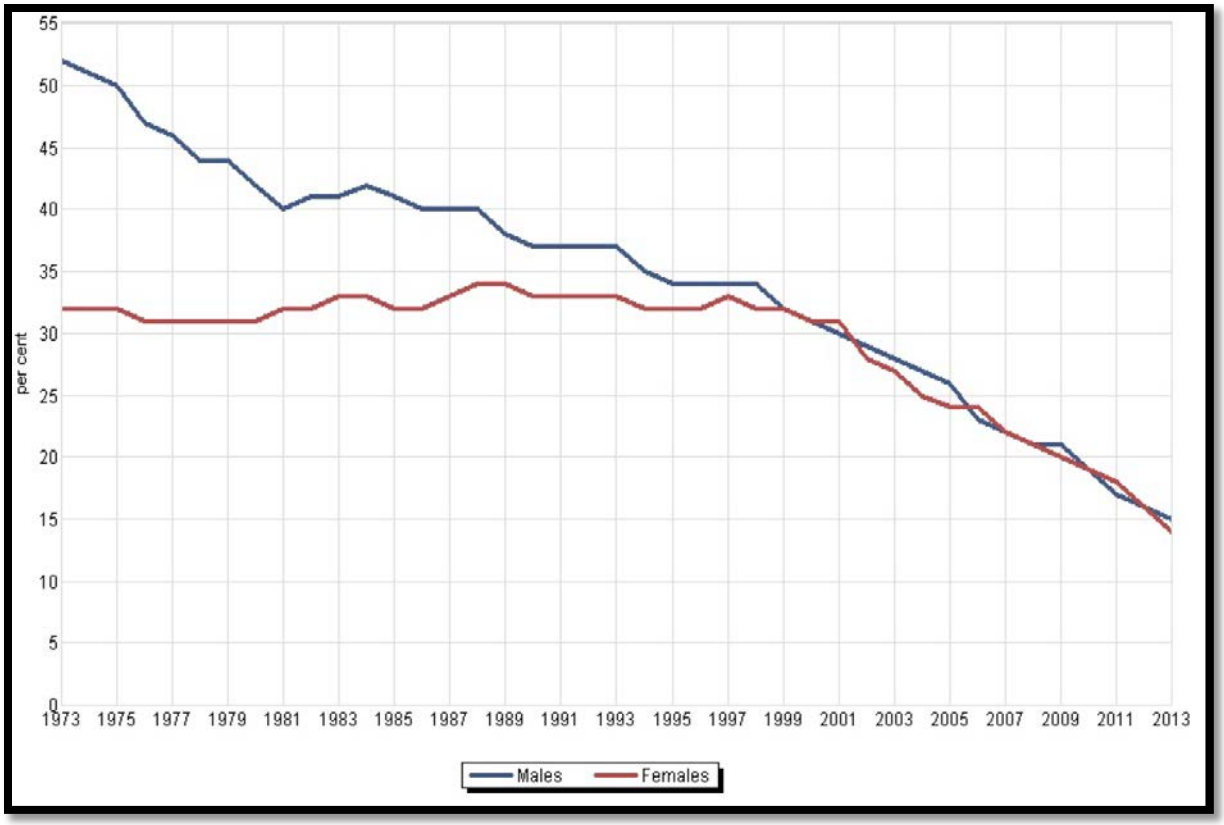

Figure 9: Men and women current smokers aged 16-74 years old since 1973-2009
Source: Statistics Norway

1.4 Assessment of risk factors for colorectal cancer

1.4.1 Non-modifiable risk factors

Age

Increased life span is one of the contributors for increasing number of cancer cases and CRC is no exception (24). CRC is common in older age groups: people aged 50 years and older accounting for more than 90% of cases and CRC incidence is low among people aged less than 50 years (25). However, recent trends show that CRC incidence is also increasing among those under 50 years of age (26;27).

Gender

As previously mentioned, CRC incidence and mortality rates are generally higher among men than women (6) and this difference may reach 35-40% higher in men compared to women(9). Differences by gender in CRC incidence are more obvious for rectal cancer which has a higher incidence among men. The reason for this difference is difficult to explain but may be partly due to exposures to different risk factors and hormones (28).

Geographical variations and race

CRC prevalence varies according to geographical locations and race. The number of CRC cases is declining in the United States, and stabilizing in most of Northern and Western Europe (25;29). Although, rates are low in Asia and Africa, CRC incidence is increasing in countries like Japan, Singapore and most Eastern European countries.

Adenomatous polyps

Adenomatous polyps are recognized precursor lesions of CRC and are common after 50 years of age. They represent almost two-thirds of colorectal adenomas and have a high potential to progress to malignancy. The majority of CRC develop from adenomatous polyps through a

series of genetic changes (30) but only around 10% of adenomatous polyps develop into cancer (31). An association between cigarette smoking and adenomatous polyps has been reported recently and it was suggested that smoking could play an important role in both the formation and aggressiveness of adenomatous polyps (32;33).

Inflammatory bowel diseases

Inflammatory bowel diseases (IBD) such as ulcerating colitis and Crohn's disease might predispose to CRC development though these diseases account for very few cases of CRC in the general population and only around 15% of all CRC deaths occur among individuals with IBD (34;35). Factors such as early age at IBD diagnosis, longer duration of symptoms and severity of dysplasia and inflammation increase the risk of CRC.

Family and personal history of colorectal cancer or adenomatous polyps

A family history of CRC is a well-established risk factor (28) and is associated with an increased risk of the CRC (36). Individuals with a family history of CRC and colorectal adenomas mainly adenomatous polyps have higher risk of CRC (37). The risk of CRC is increases when a first degree relative has one or more colorectal adenomas mainly adenomatous polyps (38) and the risk is doubled when a first degree relative is affected with CRC. Similarly, individuals with multiple relatives affected with CRC who were diagnosed at a young age have a risk of CRC that is three to six times than that of general population (39). Almost 20% of all CRC cases have a close relative who have been diagnosed with the same cancer (40). Person who had CRC are more likely to develop it again in other areas of colon and rectum. This can occur even when the first cancer is removed completely. The risk further increases if the first cancer is diagnosed at 60 years of age or younger (9). Furthermore, person with previous adenomatous polyps are in increased risk of CRC and this is more probable if the polyps were multiple and were of large sizes (41).

Genetic risk factor

The risk of CRC associated with hereditary conditions is about 5 to 10% (42). The two types of hereditary conditions are familial adenomatous polyps (FAP) and lynch syndrome, which is also known as hereditary non-polyposis colorectal cancer (HNPCC). The genes that mutate and lead to carcinogenesis have been identified in both of these conditions. MLH1 and MLH2 are responsible for mutations in individuals with HNPCC (43) whereas APC genes are responsible for mutation in FAP (44). HNPCC is the most common of these genetic syndromes and accounts almost 2- 4% of CRC (45), whereas AFP accounts for less than 1% (46).

1.4.2 Modifiable risk factors

Physical activity and obesity

The association between a high level of physical activity and decrease colon and rectal risk of cancer has been reported previously in a recent meta-analysis which included 52 cohort and case control studies (47). The study reported around a 20-30% decreased risk of colon cancer among physically active individuals compared with less active ones. Similarly, another meta-analysis concluded that physical activity is associated with reduced risk of both proximal and colon cancer which did not differ by location (48). Lack of physical activity can also lead to obesity, another major risk factor for CRC (49), but a high level of physical activity can lower the risk of CRC even without the significant weight loss (50). Nevertheless, many studies have supported the notion that obesity leads to the development of CRC, and have reported that obesity as an independent risk factor (51-56).

Diet

Diet is a major modifiable risk factor for CRC. It has been reported that changes in dietary patterns can reduce the CRC burden by 70% (49;57). Diets that are high in fat and high meat consumption have been implicated in the development of CRC (49;58;59). Diets consisting of large amounts of red meat and highly refined carbohydrates increase the risk of CRC as do diets low in vegetables and fruits (50;60-62).

Alcohol consumption

The IARC has concluded that alcohol consumption is a potential risk factor for CRC (33). Indeed, alcohol consumption is one of the most important modifiable risk factors for all human cancers (63). Heavy alcohol consumption is linked to an increased CRC and could even give rise to CRC at younger age (8;64). Metabolic product of alcohol such as acetaldehyde is considered to be carcinogenic (65). Alcohol can also work as a solvent which could allow other carcinogenic molecules into the colon and rectum mucosa (66). Similarly, an individual with high alcohol consumption and a diet low in essential nutrients is more vulnerable to the carcinogenic effects of alcohol. Several meta-analysis and pooled studies carried out in different parts of the world reported an increased risk of CRC with high regular alcohol consumption (67-75).

Medications, supplements and hormonal replacement therapy

There is growing evidence that COX inhibitors such as aspirin, calcium supplements and hormonal replacement therapy (HRT) may have preventive effects towards the CRC (9;76;77) Calcium supplements have been shown to reduce the risk of recurrent polyps (78). The long-term use of aspirin has been shown to have preventive effects on CRC (77;79) but it is not prescribed routinely for this purpose because of its side effects which includes gastrointestinal bleeding (9). Although, HRT has shown protective effects against CRC, it can increase the

risk for breast and other cancers, and therefore is not presently used for CRC prevention (76;77;79;80).

1.5 Smoking and colorectal cancer

Smoking is a major contributing factor to human carcinogenesis and is one of the most important modifiable risk factors for cancer and premature death worldwide (24). The main hazards of smoking are related to exposures such as age at smoking initiation, numbers of cigarettes smoked per day, smoking inhalation or type of cigarettes such as either tar and nicotine, or content or filter type (81). Cigarette smoke contains more than 7000 chemical compounds majority of which are carcinogens such as polycyclic aromatic hydrocarbons (PAH) and nitrosamines in addition to other promoters. These mixtures contribute to complete carcinogenesis in the mucosa of the colon and rectum (82). The carcinogenic effects of smoking could be initiated through multiple pathways such as DNA binding and mutations, oxidative stress, epigenetic changes, or inflammation (14). Figure 10 shows the pathway for causation of cancer via the carcinogenic effects of smoking. In the most recent monograph published in 2012 (33), and the report from the Unites States Surgeon General (15), the conclusion was that there is a casual association between smoking and CRC. The association between smoking and CRC risk has been shown to be dose-related (83-85). A longer exposure to or duration of smoking (35-40 years) has been shown to be associated with increased risk of CRC (86;87). The association between smoking and colorectal adenomas which are precursor lesions for most CRC was confirmed in a recent meta-analysis (32).

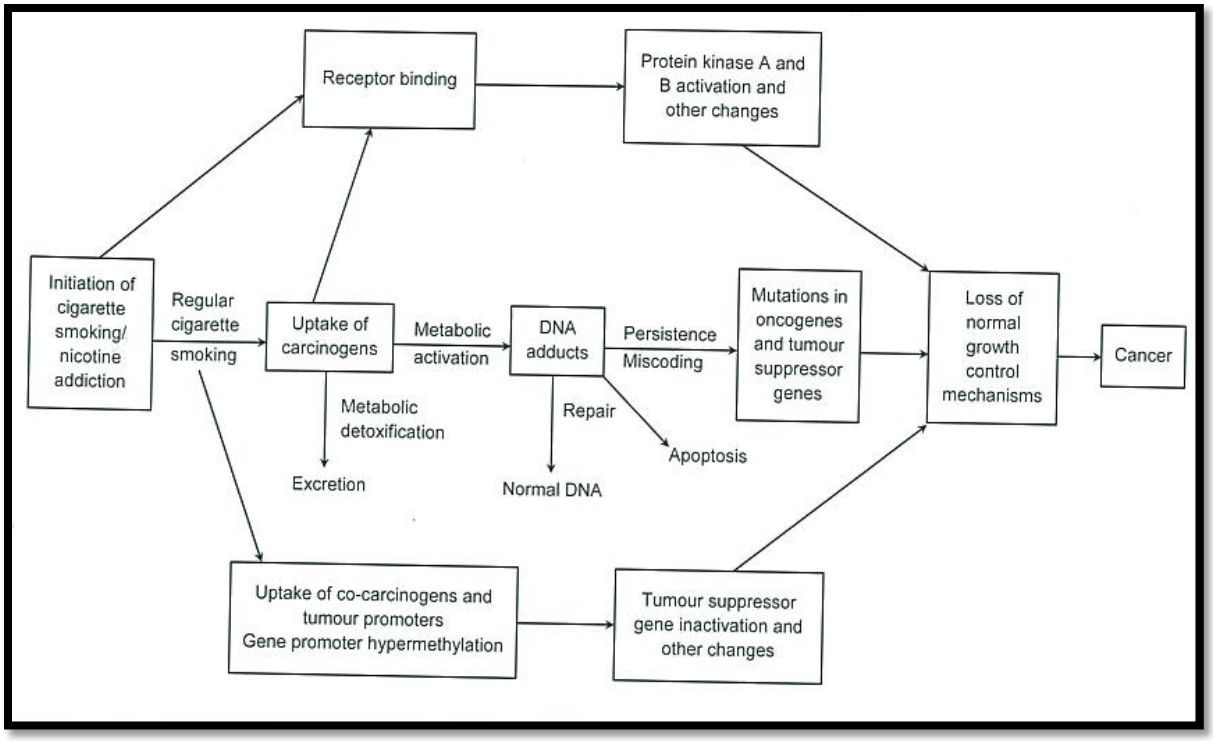

Figure 10: Pathway for causation of cancer by carcinogens in tobacco smoke
(Reprinted from the United States Department of Health and Human Services (2004). *The Health consequences of Smoking: A Report of the Surgeon General*. Atlanta, GA: The United States Department of Health and Human Services, Center for Disease Control and Prevention, National Center for Chronic Disease)

2 Aims of the thesis

The main aim of this thesis was to examine the association between smoking and CRC incidence and mortality overall and by subsites and gender.

The specific objectives were:

1. To investigate the association between smoking and the risk of colon cancer overall, and by localization and gender.

2. To investigate the association between smoking and the risk of rectal cancer by gender.

3. To examine the association between smoking and CRC mortality overall, by subsites and gender.

4. To examine the association between different smoking exposures i.e., age at smoking initiation, numbers of cigarettes smoked per day, smoking duration and number of pack-years smoked and colon and rectal cancer by gender.

5. To examine the association between different smoking exposures i.e., age at smoking initiation, numbers of cigarettes smoked per day, smoking duration and number of pack-years smoked CRC mortality by gender.

3 Materials and Methods

3.1 Study population

The cohort included 652,792 Norwegians (49% men) born between 1897 and 1975, recruited from several Norwegian health screening surveys initiated by the National Health Screening Service (now included in the Norwegian Institute of Public Health). These surveys were conducted between 1972 and 2003 and are as follows: the Oslo study I (1972-1973), the Norwegian counties study (1974-1988), the 40 years cohort (1985-1999) and the Cohort of Norway (CONOR, 1994-2003).

In all surveys included, information was gathered through questionnaires and a short health examination. The design and protocol of these surveys were very similar, but there were some modifications during different time periods, mainly in the questionnaires regarding questions on smoking, alcohol consumption, physical activity and other lifestyle factors. In most surveys, the attendees were given another supplementary questionnaire which they completed at home and mailed back in a pre-addressed stamped envelope. The participation rates for the different surveys varied from 56-88%. A flow chart with a detailed description of study participants has been provided below (Figure 11).

The Oslo study I

This survey was conducted in 1972-1973 among men living in the municipality of Oslo. Men aged 40-49 years in Oslo and a random sample of 7% of the general male population aged 20-39 years were invited to participate in screening for tuberculosis and cardiovascular disease. About 30,000 men were invited and almost 18,000 attended the screening (i.e., a participation rate of approximately 60%). The participants answered one-page questionnaire which focused on symptoms of cardiovascular disease and diabetes, smoking habits and physical activity. This was one of the first large epidemiological studies of that period and became a model for

establishing other population based health studies in Norway later on. Height, weight and blood pressure were measured during screening using a standard procedure (88-91).

The Norwegian counties study

These surveys included participants of cardiovascular disease screening in three Norwegian counties (Finnmark, Sogn og Fjordane and Oppland) during three different time periods: 1974-1978, 1977-1983 and 1985-1988. All residents aged 35-49 years as well as random sample of 10% of the general population aged 20-34 years were invited to a first screening. A second and third screening was carried out, and included a combination of previous cohort as well as new ones. Similar protocols and questionnaires were applied for these surveys. The attendance rates were 88%, 88% and 84% at the three screening rounds, respectively (91-93).

The 40 years cohort

These surveys included about 420,000 Norwegian men and women, and were carried out in all of the 19 counties of Norway in 1985-1999 for cardiovascular disease screening. Men and women aged 40-42 years were the largest invited population. Individuals aged 65-67 years were also invited to the first round of surveys in some of the counties (Nord-Trøndelag, Møre and Romsdal and Hordaland). The participation rate was 69% (94;95). Of all the surveys included in this thesis, the 40 years cohort had the largest number of participants.

The Cohort of Norway

CONOR is a very large collaborative project including regional data from 10 epidemiological studies conducted in 1994-2003 which have been merged into a national database (please refer to Table 1 for details of surveys included in CONOR). Standardized protocols, procedures and questionnaires were used together with a short health examination. The questions used in CONOR have been validated previously. The response rate varies across the surveys. The average response rate for the 10 different surveys in the CONOR study was

56%. Altogether, around 309,000 individuals were invited of which about 181,000 accepted to participate and provided consent (91;96;97).

Table 1: List of different surveys included in the study

Name of Survey	**Year Conducted**	**Populations from**	**Surveys**
The Oslo study I	1972	Oslo (only men)	1
The Norwegian counties study	1974-88	Oppland, Sogn og Fjordane, Finnmark	9
40 years cohort	1985-99	All Norwegian counties included	19
CONOR			
Tromsø Health Study IV	1994-95	Tromsø	1
The second Nord-Trøndelag Health study (HUNT 2)	1995-1997	Nord-Trøndelag	1
Hordaland Health Study(HUSK)	1997-99	Hordaland	1
Oslo study II	2000	Oslo	1
HUBRO(The Oslo Health Study)	2000-2001	Oslo	1
Oppland and Hedmark Health Study (OPPHED)	2000-1	Oppland and Hedmark	1
Tromsø Health Study V	2001	Tromsø	1
I-HUBRO(The Oslo Immigrant Health Study)	2002	Oslo	1
Troms and Finnmark Health Study (TROFINN)	2002	Troms and Finnmark	1
MoRo II(The second part of the Romsås in Motion Study	2003	Romsås	1
Total			**39**

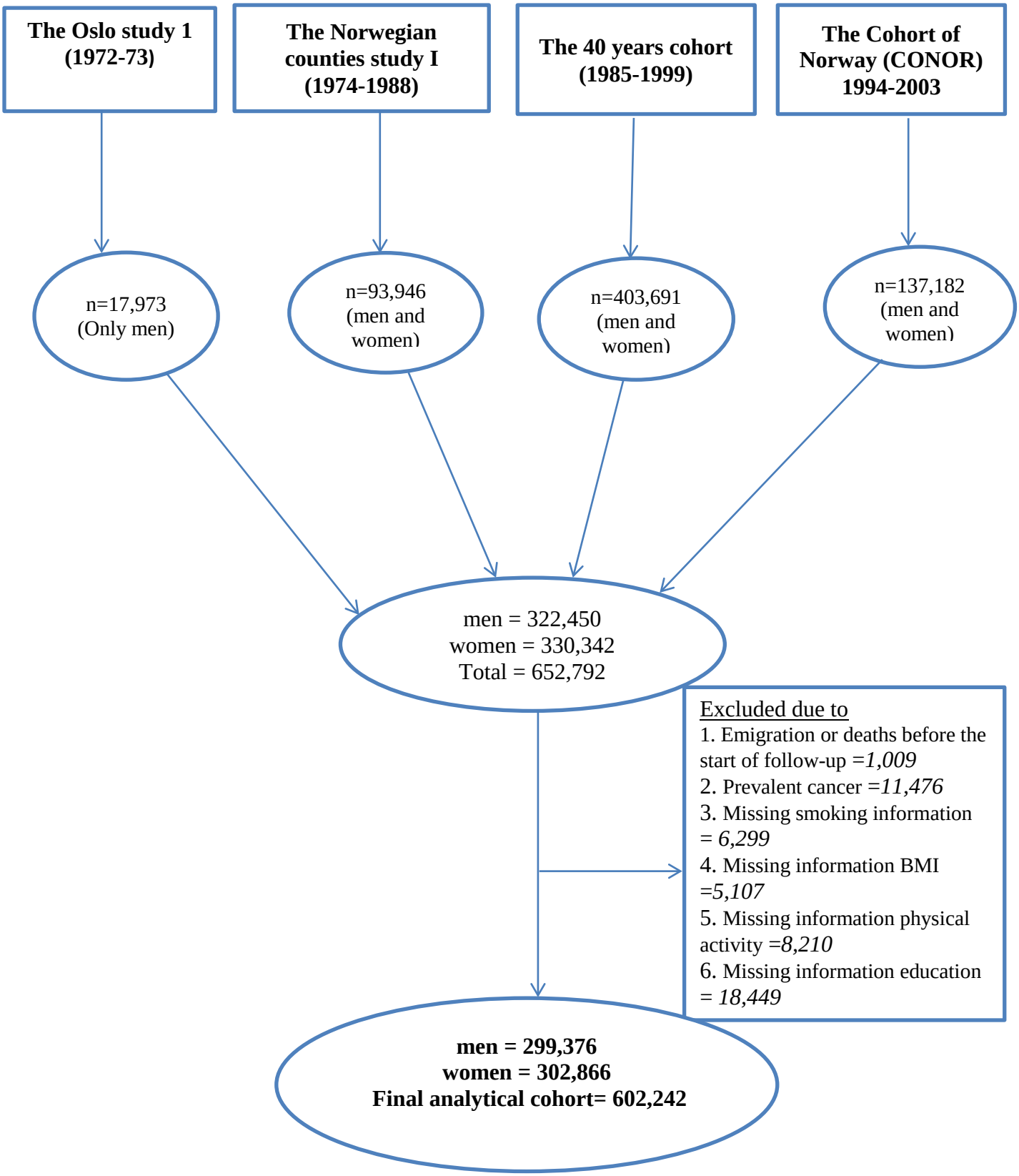

Figure 11: Detailed flowchart of participants from the different surveys

3.1 Pooling Datasets

After obtaining specified variables from each survey's primary data using the unique key identifier for each participant, we created a standardized data base for the pooled analyses. There were total 833,871 registered observations including 181,079 doubles or more. For participants who took part in more than one survey, only the earliest survey was included. Variables common to all surveys were transformed to the same format. The variables in the CONOR study were adequately structured and this was taken as a reference for standardizing the questionnaires. All surveys had a baseline questionnaire, which included detailed assessments of smoking habits, physical activity, and other lifestyle factors. At the screening facility height and weight were measured in a standardized way by a trained person, which allowed us to calculate body mass index (BMI, kg/m^2). Question on smoking habits were similar but not identical across all surveys. The questions asked about current and former daily smoking habits, smoking duration, average number of cigarettes smoked per day and in few surveys former smokers were asked about time since cigarette quitting. Only the CONOR study asked about age at smoking initiation. In the other surveys, this variable was estimated for both current (age at enrolment minus duration of smoking in years) and former (age at enrolment minus years since quitting and duration of smoking) smokers. We also found common formats for other variables such as menopause, menarche, HRT and alcohol consumption which were available only in the latest surveys such as 40 years III and IV and CONOR. Due to large missing in these variables which reached more than 50%, we were not able to use them in our main analysis. Detailed information on how the files were merged into single database is included in the appendix section (Appendix 3).

3.3 Exposure information

Participants who smoked daily were categorized as current smokers, and those who answered that they had smoked previously but not currently or if they answered the year since quitting smoking were categorized as former smokers. Current and former smokers were then combined into a single category called ever smokers. In Paper I, we further categorized ever smokers according to: age at smoking initiation (≤16, 17-19, 20-24, ≥25), numbers of cigarettes smoked per day (1-9, 10-19, ≥20), smoking duration in years (1-19, 20-29, 30-39, ≥40) and number of pack-years smoked (i.e., number of cigarettes smoked per day, divided by 20, multiplied by the duration of smoking in years) (0-9, 10-19, ≥20) . In Paper II and III, we categorized ever smokers by different measures of smoking exposure: age at smoking initiation (≤19, 20-24, ≥25), numbers of cigarettes smoked per day (1-9, 10-19, ≥20), smoking duration in years (1-19, 20-29, ≥30) and number of pack-years smoked (0-9, 10-19, ≥20). In all three papers, participants who were neither current nor former smokers were classified as never smokers. Participants were categorized into three groups based on their level of physical activity at enrolment: sedentary (reading, watching television, sedentary activity, or walking, bicycling <4 hours per week), moderate (walking, bicycling, and/or similar activities ≥4 hours per week), and heavy (light sports or heavy gardening ≥4 hours per week, heavy exercise or daily competitive sports). The most recent information regarding duration of education was obtained from Statistics Norway and was used to assign subjects to one of three categories of duration of education (<10, 10-12, ≥13 years).

3.4 Follow-up and endpoints

The study population comprised individuals who participated in of one of the four health surveys included in our thesis. We excluded participants who had emigrated or died before the start of follow-up n = 1,009 (50% women) and those with prevalent cancer n = 11,476 (62% women). We also excluded participants with missing information on either smoking exposure n = 6,299 (45% women) or on any of the co-variates [BMI, physical activity, education n = 31,766 (50% women)]. Altogether 50,550 (48% women) participants were excluded leaving 602,242 subjects (51% women) in the analytical cohort for all papers.

We followed all participants aged 19–67 years at enrolment through a linkage to the Cancer Registry of Norway and the Central Population Register, utilizing the unique 11-digit personal identification number to identify all cancer cases, emigrations and deaths. The participants were linked to the Cancer Registry of Norway, the Norwegian Cause of Death Registry and the Central Population Register. The national registries have accurate and detail information regarding cancer incidence and mortality (98). The national registries are both accurate and virtually complete (98;99). The start of follow-up was set at 1 January of the year after the baseline questionnaire was completed. In Paper I, person-years were calculated from the start of follow-up to the date of colon cancer diagnosis, the date of any incident cancer diagnosis (except skin basal cell carcinoma), emigration, death, or the end of follow-up, i.e., December 31, 2007, whichever occurred first. In Paper II, person-years was calculated from the start of follow-up to the date of rectal cancer diagnosis, the date of any incident cancer diagnosis (except skin basal cell carcinoma), emigration, death, or the end of follow-up, i.e. December 31, 2007, whichever occurred first. In paper III, follow-up ended at the time of death from primary CRC cancer, death from any other cancer (except basal cell carcinoma of the skin), emigration, death from other causes, or the end of follow up (December 31, 2007), whichever occurred first.

Colon and rectal cancer were classified according to the Seventh Revision of the International Statistical Classification of Diseases (ICD-7) (codes 153 and 154 respectively), and colon cancer was further categorized according to tumor location, i.e., proximal (codes 153.0/153.1) and distal (codes 153.2/153.3). Tumors that were overlapping (code 153.4), were specified as appendix (code 153.6), or were unspecified (code 153.9) were classified as "others" and were included in the analyses for the whole colon only. CRC mortality was classified according to ICD-9 and ICD-10.

3.5 Statistical analyses

We performed all analyses separately by gender. We used the t-test and χ^2 test for investigating differences in the distribution of selected characteristics between cases and non-cases and between ever and never smokers. The Cox proportional hazards model was used with age as the underlying time scale to estimate multivariate-adjusted hazard ratios (HR) with 95% confidence intervals (CIs) for the associations between different measures of smoking exposure age at smoking initiation, numbers of cigarettes smoked per day, smoking duration in years and number of pack-years smoked and colon cancer overall, and according to tumor location (Paper I), rectal cancer (Paper II) and CRC mortality (Paper III) with never smokers as the reference group. In Paper I, entry time was defined as age at enrolment and exit time was age at diagnosis of colon cancer, the date of any incident cancer diagnosis (except basal cell carcinoma), emigration, death, or the end of follow-up (31 December, 2007), whichever occurred first.

In Paper II, entry time was defined as age at enrolment and exit time was age at diagnosis of rectal cancer, the date of any incident cancer diagnosis (except basal cell carcinoma), emigration, death, or the end of follow-up (31 December, 2007), whichever occurred first.

In Paper III, entry time was defined as age at enrolment and exit time was age at death, emigration, or end of follow-up (31 December, 2007), whichever occurred first.

The possible confounders included in the final models in Paper I, II and III, selected a priori, were age at enrolment (continuous), level of physical activity (sedentary, moderate and heavy), BMI (continuous), all at enrolment and duration of education in years (<10, 10-12, ≥13). Tests for linear trends were obtained by creating an ordinal exposure variable with equally spaced scores and including it in the models with never smokers as the reference group. Test of heterogeneity by gender and its effect on the association between smoking and the risk of colon cancer overall, and by location, rectal cancer and CRC mortality were tested using Wald χ^2 statistics in Paper I, II and III, respectively. Two-sided p-values <0.05 were considered statistically significant. All analyses were conducted using STATA version 12.0 (Stata Corp., College Station, TX, USA).

In all the papers, the same methods of statistical analysis were used; only the outcome variable differed. Outcome for Paper I was colon cancer, Paper II was rectal cancer and Paper III was CRC mortality.

In all the papers, we re-analyzed the data excluding the 8,151 (99% men) participants who reported smoking only cigars or pipes. We had information on alcohol consumption for 37% (n = 221,748) of the participants. We did sensitivity analyses by gender for the main outcomes based on this population (49% men) with and without adjustment for alcohol consumption in all papers.

3.6 Ethical aspects

Oral or written informed consent was obtained from participants in the different surveys. Surveys carried out in 1995 and after had written consent. We also obtained approval from the respective steering committees to all the health surveys included. We obtained approvals from

the National Data Inspection Board, the Regional Committee for Medical Research Ethics (REK), the Norwegian Directorate of Health, Norwegian Tax Administration and Norwegian Public Health Institute. The data was handled in accordance with the permissions taken from the above mentioned governmental bodies.

4 Results – summary of papers

4.1 Paper I

The increased risk of colon cancer due to cigarette smoking may be greater in women than men.

In Paper I, we investigated the association between smoking and colon cancer overall, by location and gender. The study followed 602,242 Norwegian men and women and 3,998 colon cancer cases (46% of cases in women). Women ever smokers had a 19% (HR = 1.19, 95% CI = 1.09-1.32) and men ever smokers had 8% (HR = 1.08, 95% CI = 0.97-1.19) increased risk of colon cancer compared with gender specific never smokers. For all four dose-response variables examined, women ever smokers in the most exposed category of age at smoking initiation, (HR = 1.48, 95% CI = 1.21-1.81), number of cigarettes smoked per day (HR = 1.28, 95% CI = 1.06-1.55), smoking duration (HR = 1.47, 95% CI = 1.11-1.95), and pack-years smoked (HR = 1.33, 95% CI = 1.11-1.57) had a significantly increased risk of more than 20% for colon cancer overall and of more than 40% for proximal colon cancer compared with never smokers. Women ever smokers had a higher risk of proximal colon cancer compared to men ever smokers (Wald χ^2, p = 0.02).

Sensitivity analyses were carried out for participants with information on alcohol consumption which mainly included participants enrolled after 1995 (37% of total analytical cohort, n = 221,748). The corresponding risk estimates for women ever smokers were 16% (HR = 1.16, 95% CI = 0.86-1.74), 27% (HR = 1.27%, 95% CI = 0.82-1.51) and 11% (HR= 1.11, 95% CI = 0.78-1.59) for colon, proximal colon and distal colon cancer, respectively. However, among men ever smokers risk estimates were (HR = 0.99, 95% CI = 0.78-1.25), (HR = 0.97, 95% CI = 0.75-1.64), (HR = 0.82, 95% CI = 0.68-1.15) for colon, proximal colon

and distal colon cancer, respectively. Risk estimates with and without alcohol adjustment did not differ significantly.

The conclusion was that women smokers may be more susceptible to colon cancer and especially to proximal colon cancer than men smokers.

4.2 Paper II

Smoking increases rectal cancer risk to the same extent in women as in men: Results from a Norwegian cohort study.

In Paper II, we examined the association between smoking and rectal cancer incidence by gender among 602,242 Norwegian men and women. During a mean follow-up of 14 years, 2,176 cases (61% cases in men) were diagnosed with invasive rectal cancer. Both men and women ever smokers had a significantly increased risk of rectal cancer of more than 25% for men (HR = 1.27, 95% CI = 1.11-1.45) and women (HR = 1.28, 95% CI = 1.11-1.48) compared with gender specific never smokers. Men smoking ≥20 pack-years had an increased risk of rectal cancer of 35% (HR = 1.35, 95% CI = 1.14-1.58), whereas women showed an increased risk of 47% (HR = 1.47, 95% CI = 1.13-1.91) compared with gender specific never smokers. For both men and women, we observed significant dose-response associations with rectal cancer risk when looking at age at smoking initiation, number of cigarettes smoked per day, smoking duration and number of pack-years smoked and using never smokers as the reference group (p-trend<0.05). The test for heterogeneity by gender was not significant between smoking status and the risk of rectal cancer (Wald χ^2, p value; current smokers = 0.85; former smokers = 0.87 and ever smokers = 1.00).

In the sensitivity analyses for participants, mainly enrolled after 1995, with information on alcohol consumption, the risk estimate of rectal cancer incidence was 13% (HR = 1.13, 95%

CI = 0.83-1.55) with alcohol adjustment and 12% (HR = 1.12, 95% CI = 0.82-1.54) without alcohol adjustment among men ever compared with men never smokers. The risk estimate was 37% (HR = 1.37, 95% CI = 0.99-1.92) with alcohol adjustment and 39% (HR = 1.39, 95% CI = 1.00-1.94) without alcohol adjustment among women ever compared with women never smokers.

In conclusion, increased risk of rectal cancer due to smoking is similar in women as in men.

4.3 Paper III

Cigarette smoking and colorectal cancer mortality among 602,242 Norwegian men and women.

In Paper III, we examined the association between different measures of smoking exposure and CRC mortality overall and by subsites among 602,242 Norwegian men and women and 2,333 CRC deaths (60% in men). There were 1,607 (57% in men) colon cancer and 726 (67% in men) rectal cancer deaths. Women ever smokers had a 22% (HR = 1.22, 95% CI = 1.06-1.40) increased risk CRC mortality compared with women never smokers. Men ever smokers had a CRC mortality risk of 23% (HR = 1.23, 95% CI = 1.08-1.40) when compared with men never smokers. Women ever smokers had an almost 50% (HR = 1.49, 95% CI = 1.20-1.87) increased risk of mortality from proximal colon cancer compared with women never smokers.

A test for heterogeneity by gender showed an increased risk of mortality from proximal colon cancer among women, which was statistically significant for ever smokers and former smokers (Wald χ^2 = 0.02 and 0.04, respectively). It was also significant for former smokers and the risk of rectal cancer showing increased risk among men (Wald χ^2 = 0.02).

In the sensitivity analyses among participants with information on alcohol consumption (37% of total analytical cohort), the risk estimates of CRC mortality was (HR = 0.84, 95% CI =

0.60–1.18) and (HR = 1.25, 95% CI = 0.89–1.74) among men and women ever smokers respectively. Risk estimates with and without alcohol adjustment did not differ significantly.

In conclusion, smoking is associated with increased CRC mortality both among men and women. The risk of rectal and proximal colon cancer mortality was more pronounced among men and women smokers, respectively.

5 Discussion

5.1 Methodological issues

A detailed discussion of the findings is presented separately in each paper. In the following chapter, discussions of those aspects which are applicable to this thesis in general are presented. Epidemiological studies primarily provide important information regarding the general population. The main purpose of such studies is to generalize the results to another target population and to establish the association between a risk factor and an outcome. In this regard, validity of the study is a very important issue. The validity of an epidemiological study can be divided into two groups: internal validity and external validity.

5.1.1 Internal Validity

Internal validity is defined as the true measure of the variable obtained for the study subjects and refers to the logical conclusions drawn from them. It deals mostly with the accuracy of observed results of the study. Internal validity is evaluated by determining whether the observed changes or outcomes can be attributed to the main exposure and not to other causes. Several factors can influence the validity of observed association between an exposure and an outcome (100;101). A major threat to internal validity could be lack of representativeness of the study population. The two major errors that can occur in epidemiological studies are random and systematic errors. Internal validity depends both on random error as well as systematic errors such as bias and confounding (100;101). Figure 12 shows the diagrammatic view of error and its classification which are often encountered in a large epidemiological study.

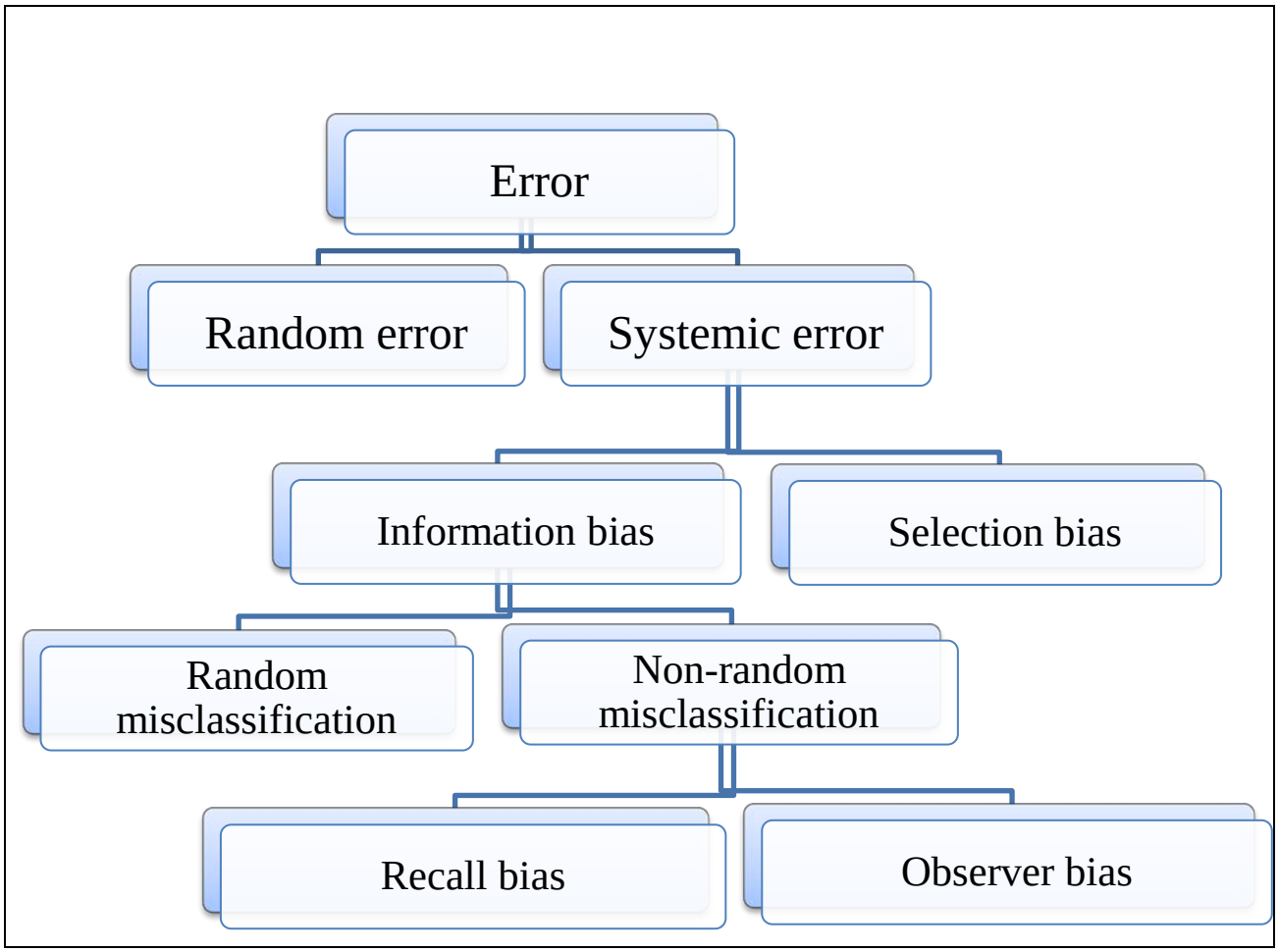

Figure 12: A systematic approach to bias
(Source: Appraising the evidence: what is selection bias? Henderson M et al: Reprinted with permission)

Random error can arises due to sampling variability and can be addressed by appropriate statistical hypothesis testing. Random error may lead to non-reproducibility of study results which in turn could weaken or restrict the association between an exposure and an outcome (100). A large sample size gives more precision to a study. In our study, the large sample size minimized the sampling error and thus increased the precision (100). We have also addressed the issue of random error by applying the appropriate statistical procedures. Our hypothesis was tested at the 5% alpha level and 95% confidence intervals were calculated. The null hypothesis was rejected at a less than 5% level. Another error encountered in epidemiological studies is systematic error. Epidemiological studies with a minimal systematic error have a high accuracy. These errors are independent of the size of the study and statistical significance

does not suggest the absence of any bias (102;103). We consider the discussion of selection and measurement bias relevant in relation to our study.

Selection bias (Paper I-III)

Selection bias in cohort studies results from the process of selecting study participants and can arise due to systematic differences in selection criteria (100). The possibility of this bias arises when a study sample is not representative of the source population (104). However, it is also true that selection bias is less probable in cohort studies than other epidemiological studies as the outcome is not known at the time of enrolment (105). In our study, we had no possibility to control for differences between responders and non-responders as there was no information available for the non-responders.

In all of the surveys included in our study, age was a major criterion for enrolling participants. Most of the men and women enrolled were between 40-45 years of age and a large group of participants were included from the 40 years cohort. The detail description of the study participants categorized by age group during the time of enrolment in different surveys is shown in table 2. The overall participation rate ranged from 56-88%. The attendance rate in CONOR was 56% (range 30-76%) whereas in the Oslo study I, it was approximately 60%. The participation rate for the Norwegian counties study remained between 78-90%. In 40 years cohort, the overall response rate was 69% but during 1994-99, the participation rate went down to 62%.

Table 2: Age at enrolment of participants included in different health surveys

Age at enrolment	Oslo study I	Norwegian counties study	40 years cohort	CONOR study	Total (%)
16-30	869	9,778	740	9,492	20,879 (3.5)
31-39	689	20,216	652	23,873	45,430 (7.5)
40-44	4,782	29,282	364,285	25,583	423,932(70.4)
45-50	9,506	23,458	5,281	16,675	54,920 (9.1)
≥50	1,100	752	13,809	41,420	57,081 (9.5)
Total	**16,946(3)**	**83,486(14)**	**384,767(64)**	**117,043(19)**	**602,242**

Non-response bias is always a major issue in large longitudinal epidemiological studies like ours and declining participation rate is one of the major problems. However, low participation rates do not always indicate a high level of bias. Indeed, there has been very little evidence of substantial bias as a result of non-response and non-response introduces less influence on exposure-disease associations (106-108). Furthermore, we had a similar proportion of men and women participants in our study. A total of 50,550 participants excluded, 48% of which were women due to missing covariates. Thus, our study had a same proportion of men and women excluded due to the missing data. Those excluded group were similar to the analytical cohort in regards to their level of education and physical activity. Incidence rates for colon and rectal cancer among excluded group were also similar to the analytical cohort**.** Furthermore, smoking prevalence among participants from different health surveys in our cohort was comparable to the Norwegian general population during the same period (Fig 13 and 14).

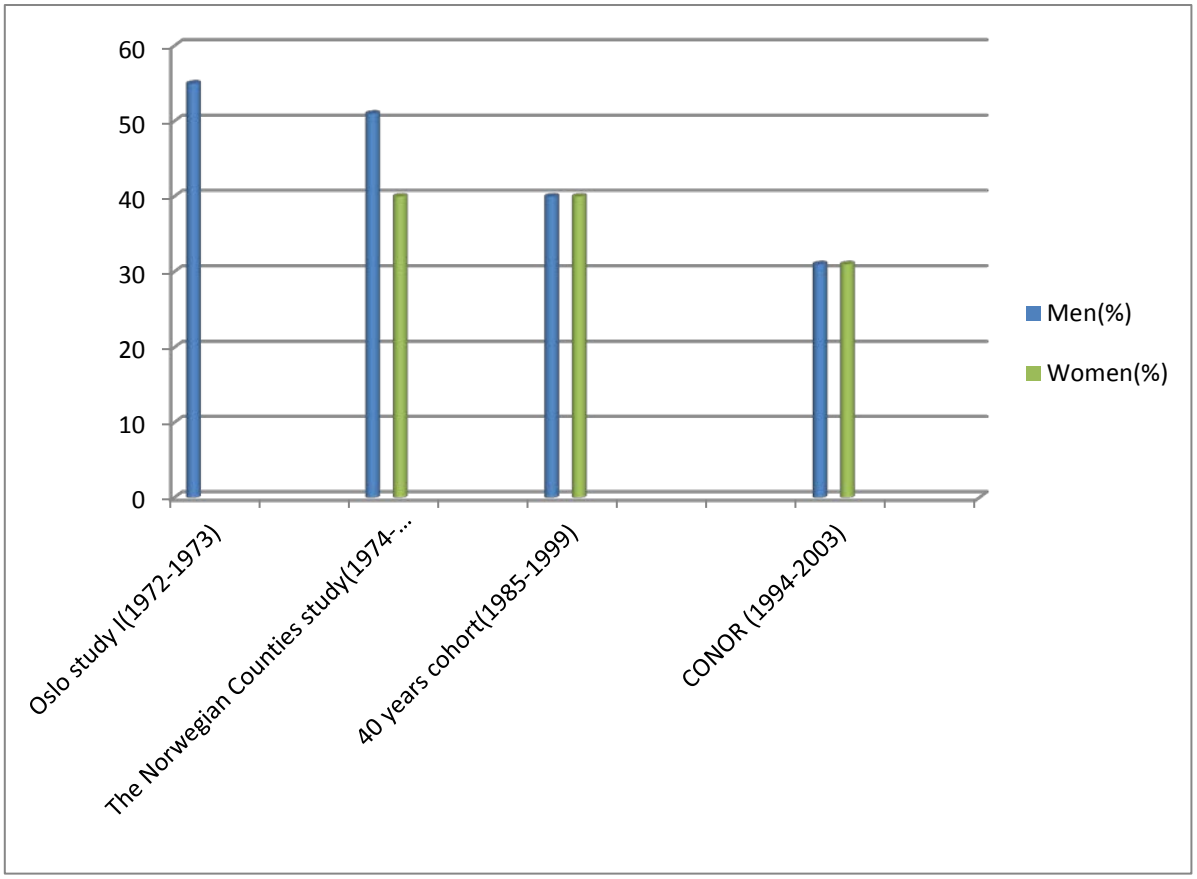

Figure 13: The prevalence of current smokers included in surveys by gender

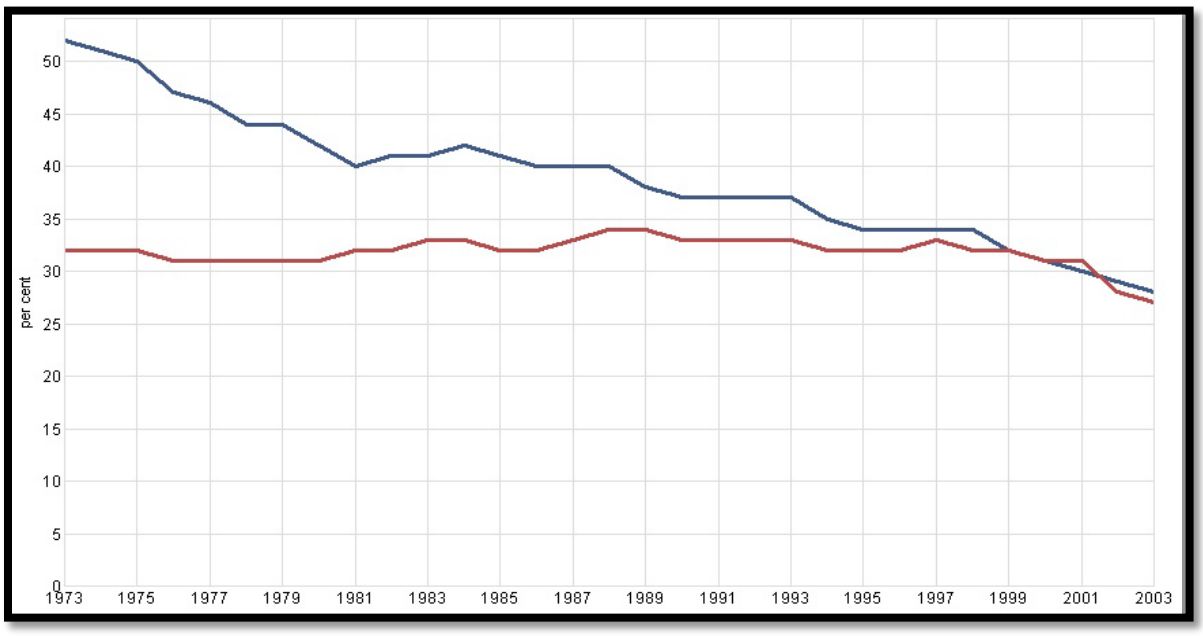

Figure 14: The prevalence of current smokers aged 16-74 years from 1973-2003 in Norway by gender

Information bias (Paper I-III)

Information bias is also known as observation, classification or measurement bias and arises from incorrect determination of an exposure, an outcome, or both (109). Measurements bias occurs when exposures and outcome variables are incorrectly measured (100). In the different surveys included in our study, height and weight were measured according to the standard procedure to minimize the measurement errors. There were some differences in the measurement of exposures variable but we minimized these differences by finding a common format during the merging of the datasets. Smoking history was obtained at study enrolment, and so was not subject to recall bias. Furthermore, smoking habits change; current smokers could have stopped smoking whereas never smokers may have started smoking. Our analysis was based on ever and never smokers, thus only the status of never smokers could have changed during follow-up. In addition to this, very few Norwegians start to smoke after the age of 30, and the mean age at enrolment for our study is more than 40 years, thus minimizing this type of bias. We assume that the possibility of information bias in our study is limited.

Confounding and statistical analyses (Paper I-III)

Confounder is defined as a variable which is associated with main exposure variable but at the same time an independent risk factor for the dependent variable (100;101). As a confounding variable is associated with the exposure and also with outcome but does not stand in the intermediate pathway in the chain of causation between an exposure and an outcome (109), it leads to the mixing or blurring of effects. This is one of the major challenges of an observational study as it can either attenuate or inflate an association between an exposure and an outcome. In a way, confounder is similar to bias but it can be controlled by stratification and adjustment in multivariate models. The magnitude of confounding can be evaluated by comparing crude and adjusted effect measure. Age and gender are almost always potential confounders (100;101). Our analyses were stratified by gender and hazard ratios

(HRs) and 95% CI were estimated by fitting Cox proportional hazard models where age was the primary time variable. In Papers I, II and III, age, BMI, physical activity at enrolment and duration of education were the confounders based on a priori, and were controlled for when estimating the association between smoking and colon and rectal cancer incidence and CRC mortality. The other important covariates that are established risk factors for CRC, such as alcohol consumption, HRT, diet such as red meat and COX inhibitors such as aspirin could not be adjusted for in the main analyses. Information on alcohol consumption was missing on more than 60% of the total participants whereas information on HRT was missing in more than 70% of total women. It has been reported that women could have protective hormonal effects until menopause from HRT which delay or protect them from development of CRC (76). The use of HRT declined after there was growing evidence that it could be risk factor for breast cancer and other cardiovascular disease (110). Similarly, we lacked information on molecular data and CRC screening, as it was not common in Norway when the surveys included in our study were conducted. In addition to this, the information on staging of CRC was also not available. Cigar and pipe smoking may have less potential to be confounders and this could be the reason our sensitivity analyses excluding those smoking only cigar and pipe did not materially change the estimates (33). We also performed the sensitivity analyses among participants who had information on alcohol consumption, with and without alcohol adjustment. Only 37% of the total cohort (48% men) had information on alcohol consumption. Our sensitivity analyses including only those with information on alcohol consumption, risk estimates increased among women and but decreased among men ever smokers for rectal cancer incidence as well as for CRC mortality compared to risk estimates for the main cohort. For colon cancer, the estimates were more or less similar for women but decreased among men compared to risk estimates for the main cohort. However, the results did not change materially with and without alcohol adjustment in this sub cohort either among

men or women indicating that the lack of alcohol intake in the main cohort might not be a major limitation. However, the interpretation of our sensitivity analyses should be done with caution as they included fewer cases, younger participants with less follow-up time than in the main cohort. We should be very cautious to interpret the results of our sensitivity analyses as we lost a large number of cases and follow up time period (>75%). The studies such as Oslo study I, the Norwegian counties study and earlier rounds of 40 years cohort did not have the information on alcohol consumption. It is also true that the alcohol consumption is higher among men than women in Norway (111). Thus, the lack of adjustments of alcohol consumption in our main cohort analyses is likely to have inflated the estimates among men more than women and thus attenuated the gender difference.

The statistical approach to use Cox proportional hazards analysis with age as primary time variable to examine the association between smoking and CRC incidence and mortality was considered appropriate to answer the research questions in Papers I, II and III. Modelling the events using a proportional hazards model with age as the time scale has been recommended as an appropriate method in large health surveys with disease or death as outcome. Furthermore, it has been suggested that using age as a primary time variable is more meaningful and less restrictive than using time on study as the time scale (112).

5.1.2 External validity

External validity is the probability of generalizing the study results to a wider population. This can be also referred as the possibility, or the degree to which the results of the study is applicable to different population in other places and at different time periods (100;101;113). Internal validity is always a pre-requisite for external validity. Although, we had some issues with internal validity, we are convinced that it did not distort our results. Our study includes

very large participants from all over Norway. The separate health surveys included in our study have well-validated datasets. In general, it is difficult to generalize the study results to a wider population but we assume our study conclusion could be generalized to the Caucasian and Western population.

5.2 Discussion of the main results

The main findings are discussed in the respective papers (Papers I-III) in detail. Despite some methodological limitations in the three papers, they have contributed to further support the fact that smoking increases CRC incidence and mortality among both men and women. The discussion below is focused on the main messages of the three papers regarding the association between smoking and CRC.

5.2.1 Gender differences in smoking related colon cancer

The findings from Paper I is in agreement with IARC and United States Surgeon General's recent conclusion that cigarette smoking is associated with colon cancer (15;33). Incidence rates are more important and reliable indicator of trends in disease occurrence than mortality rates as incidence is not influenced by changes in treatment and survival (6). The main difference in CRC in general observed by gender is due to the higher incidence of rectal cancer in men than women. There is not much difference in incidence rates of colon cancer between men and women in Norway.

There are gender reported differences in incidence of colon cancer by location (i.e. proximal vs. distal colon cancer). Some studies have concluded in general that the risk of distal colon cancer is lower among women than in men (114-116). Previous knowledge regarding smoking and colon cancer incidence in general varies by gender. Some studies reported that

the association between smoking and colon cancer may be stronger in men as compared to women (75;117;118). However, these reports could be attributed to the low prevalence of ever smoking women. On the other hand, the results of the studies among women only (119-122) reported findings which were more or less comparable to men for both colon as well as rectal cancer. A recent study from Europe which included men and women from ten European countries reported the risk estimates by subsites and indicated that the ever smokers have an increased risk of colon cancer, which was especially pronounced in the proximal than in the distal colon (123). However, this study did not report the risk estimates by gender. Another study of Norwegian women reported an increased risk of proximal than distal colon cancer among women ever smokers (119). A study among postmenopausal women in the United States aged 55-69 years at baseline also reported an increased risk of proximal than distal colon cancer (120). Furthermore, smoking has been shown to be associated with a higher incidence proximal colon cancer among Caucasian women in the United States as compared with distal colon cancer (124). A study from Japan which was conducted both among men and women and included around 400 colon cancer, reported the risk estimates by gender and the findings were insignificant increase risk of colon cancer among both men and women ever smokers (125). Increased risk of proximal colon cancer among women smokers has been reported to be related with epigenetic changes which are induced by tobacco related carcinogens (120). It has also been suggested that gender-related differences in hormonal factors (126) or susceptibility to tobacco related carcinogens (127) could have influenced the observed different associations for proximal and distal colon cancer by gender (120) which might explain the reason for increased risk of proximal colon cancer among women smokers compared to men smokers. There are not many prospective cohort studies examining the association between smoking and colon cancer by location and gender in detail. Our study is among the very few studies with a very large numbers of incidence cases as well as a large

proportions of ever and never smokers that examined the association between smoking and colon cancer incidence by location and gender. The findings from our study suggested that women smokers maybe more prone to colon cancer especially for proximal colon cancer than men smokers. Our findings could be a strong warning for the women smokers who could be more vulnerable to smoking related colon cancer than men. This may have important clinical and research implications if further confirmed by other large population based epidemiological studies.

5.2.2 Smoking related risk of rectal cancer among women is same as in men

The epidemiologic evidence supports that it takes decades before the increased risk of rectal cancer appears and that smoking plays an important role in early carcinogenesis both among men and women (15;86;87). The incidence rate of rectal cancer is higher among Norwegian men compared to Norwegian women and as mentioned earlier this is the main reason for gender difference in CRC incidence rate in general. The difference in rectal cancer incidence rate was almost 1.5 fold higher among Norwegian men in the beginning of our study period and the situation remained similar until the end of our study period. In the latest report from Norwegian Cancer Registry, this difference is also valid for the present time period (10). Risk patterns were shown to be generally consistent for colon and rectal cancer (73;75). However, some studies reported a stronger dose response association between smoking and rectal rather than colon cancer (8;118;121;122;128). Recent meta-analyses also concluded that the ever smokers are in increased risk of rectal cancer (70;83-85), however these studies did not present the risk estimates by gender. Our findings are in accordance with findings of these meta-analyses regarding higher risk estimates for rectal than colon cancer. In a study done among women in the United States, an increased risk of rectal cancer but not colon cancer was observed among ever smokers (121). Another study done among Norwegian women

reported the higher risk for colon than rectal cancer among smokers (119). Furthermore, two recent studies, one from 10 European countries including almost half a million men and women and 950 rectal cancer cases (123) and another from Asia including 329 rectal cancer cases (64) are the largest cohort study done before ours examining the association between smoking and rectal cancer. The study from 10 European countries found a non-significant increase in rectal cancer; however the later study found a significant increased risk of rectal cancer among ever smokers. These studies did not report the risk estimates by gender. A few studies from Japan examined the association between smoking and rectal cancer, however they included 200 or less cases (73;74). Furthermore, these studies showed an insignificant increased risk of rectal cancer among men and women ever smokers. Our study is one of the few to examine the association between smoking and rectal cancer by gender in detail. Our findings indicated that there is a significant increased risk for rectal cancer among men and women ever smokers. Furthermore, the findings also concluded that the risk was similar for women as in men. This could be a very important finding as the impact of cigarette smoking could be reflected in future rectal cancer incidence among women as the smoking epidemic among women began later than men, and as for colon cancer, rectal cancer also has a long latent period.

5.2.3 Smoking increases the risk of CRC Mortality

In Paper III, we found increased risk of CRC mortality both among men and women ever smokers. We concluded that the risk of rectal cancer mortality was higher among men smokers and risk of proximal colon cancer mortality was higher among women smokers. Similarly, the increased mortality risk by subsites was slightly more pronounced among current smokers compared with the former smokers both among men and women. The higher risk of rectal cancer mortality among men ever smokers and increased proximal colon cancer mortality risk among women ever smokers could be a mere reflection of the colon and rectal

cancer incidence in our cohort. As mentioned earlier, smoking is one of the major preventable causes of death worldwide. Mortality from different diseases has been decreased in last decades due to early diagnosis and treatment; however current smokers have an increased risk of mortality compared to never smokers. Recently, two meta-analyses also reported that the risk of CRC mortality was higher among current than former smokers (83;84). Long term smoking is associated with an increased risk of CRC mortality both among men and women (15). Furthermore, increased mortality among current smokers could be due to possible differences in health behaviours. A recent report from the United States Surgeon General concluded that there is a sufficient evidence to infer a causal relationship between cigarette smoking and increased all-cause and cancer-specific mortality (15). Quitting smoking can decrease the mortality burden and CRC patients should be encouraged to quit smoking as smoking can lead to poorer response to cancer treatment (129). Furthermore, the relationship between smoking and mortality is stronger than before and recommendations encouraging smokers to quit is very important.

6 Conclusions

The main aim of this thesis was to examine the association between smoking and CRC incidence and mortality overall and by subsites and gender.

The conclusions to be drawn from the studies are:

1. Smoking increased the risk of colon cancer among both men and women. The increased risk of colon cancer especially proximal colon cancer due, to smoking may be greater in women than men.

2. Smoking increased the risk of rectal cancer among both men and women. The risk was similar for women as for men.

3. Smoking increased the risk of CRC mortality among both men and women. The risk of rectal and proximal colon cancer mortality was most pronounced among men and women ever smokers, respectively.

4. The observed smoking related increased risk in colon and rectal cancer was dependent on different smoking exposures such as age at smoking initiation, number of cigarettes smoked per day, duration of smoking and pack years smoked both among men and women.

5. The observed smoking related increased risk in CRC mortality was dependent on different smoking exposures such as age at smoking initiation, number of cigarettes smoked per day, duration of smoking and pack years smoked both among men and women.

7 Implications for public health practice and further perspectives

CRC is one of the major public health problems in Norway. Our findings are consistent with the latest report from the IARC (1) and the United States Surgeon General (15) regarding the association between smoking and CRC. Smoking is possibly the most important modifiable risk factor of CRC. Detailed knowledge about the adverse harmful effects of smoking is important for general public health and future strategy planning. Additional strict rules against tobacco companies and tobacco sales should be implemented. The general population should be made aware of the possible harmful effects of smoking on the risk of CRC and younger age groups should be given special attention regarding smoking cessation and encouraged not to start smoking. Since women may be more vulnerable to the carcinogenic effects of smoking in relation to CRC, women-oriented awareness of harmful effects of smoking should be initiated. Current smokers should be encouraged to quit since the comorbid situation is increased among current smokers. More emphasis should be placed on taxes and price policies in the control of tobacco use to improve public health. Furthermore, CRC screening programme could be very helpful for early diagnosis and treatment.

As there is a long latent period between smoking and risk of CRC, an investigation with a longer follow up period could reveal more exact risk estimates. Future studies should focus on the replication of the present findings and it will be very important to conduct these studies with detailed information on most available covariates in relation to smoking and CRC.

8 Erratum

In Paper I:

For the excluded men and women, the overall incidence of colon cancer was 53 and 59 per 100, 000 person-years, respectively.

The overall incidence of colon cancer among men and women was 49 and 44 per 100, 000 person-years, respectively.

Above presented overall incidence rates were for CRC and not only for colon cancer.

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PAPER I

Parajuli R, Bjerkaas E, Tverdal A, Selmer R, Le Marchand L, Weiderpass E, Gram IT

The increased risk of colon cancer due to cigarette smoking may be greater in women than men

Cancer Epidemiol Biomarkers Prev.2013; 22(5), 862-71

PubMED: PMID 23632818

PAPER II

Parajuli R, Bjerkaas E, Tverdal A, Le Marchand L, Weiderpass E, Gram IT

Smoking increases rectal cancer risk to the same extent in women as in men: Results from a Norwegian cohort study

(Submitted to BMC Cancer)

PAPER III

Parajuli R, Bjerkaas E, Tverdal A, Le Marchand L, Weiderpass E, Gram IT

Cigarette smoking and colorectal cancer mortality among 602,242 Norwegian males and females

Clinical Epidemiology, Dovepress (Online)

Appendices

1. Surveys questionnaires
2. Description of methodology
3. Variable description
4. Summary of some of the prospective studies examining the association between smoking and colorectal cancer published between 2002-2013

Appendix 1

QUESTIONAIRE OSLO HEALTH STUDY I

HJERTE - KARSYKDOMMER

SPØRRESKJEMA

	JA	NEI
Har De, eller har De hatt:		
Hjerteinfarkt?	13	
Angina pectoris (hjertekrampe)?	14	
Annen hjertesykdom?	15	
Åreforkalkning i bena?	16	
Hjerneslag?	17	
Sukkersyke?	18	
Er De under behandling for:		
Høyt blodtrykk?	19	
Bruker De:		
Nitroglyserin?	20	

	JA
Bevegelse og kroppslig anstrengelse i Deres arbeid. Spørsmålet gjelder bare det siste året. Sett kryss i den ruten hvor „JA" passer best.	
Har De:	
Overveiende stillesittende arbeid? (f.eks. skrivebordsarbeid, urmakerarbeid, montering)	21
Arbeid som krever at De går mye? (f.eks. ekspeditørarb., lett industriarb., undervisning)	22
Arbeid hvor De går og løfter mye? (f.eks. postbud, tyngre industriarb., bygningsarbeid)	23
Tungt kroppsarbeid? (f.eks. skogsarbeid, tungt jordbruksarb., tungt bygn.arb.)	24

	JA
Bevegelse og kroppslig anstrengelse i Deres fritid. Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året. Sett kryss i den ruten hvor „JA" passer best.	
Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse?	25
Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? (Heri medregnes også gang eller sykling til arbeidsstedet, søndagsturer m.m.)	26
Driver mosjonsidrett tyngre hagearbeid a.l.? (Merk at virksomheten skal være minst 4 timer i uken.)	27
Trener hardt eller driver konkurranseidrett, regelmessig og flere ganger i uken?	28

	JA	NEI
Har De i det siste året følt Dem merkbart mere anspent eller irritabel enn før?	29	
Regner De Dem selv for å være en person som presser Dem selv og ofte velger et høyt tempo?	30	
Eller regner De Dem selv for en person som gir avkall på slik innsats, for heller å ha ro og fredelige dager?	31	
Mener De at det er mere enn vanlig press på tidsfrister i Deres arbeidssituasjon?	32	

72 Ø

	JA	NEI
Røker De daglig for tiden?	33	
Hvis svaret var „JA" på forrige spørsmål, besvar da:		
Inhalerer De?	34	
Røker De sigaretter daglig? (håndrullede eller fabrikkframstilte)	35	
Bruker De mest filtersigaretter?	36	
Hvis De ikke røker daglig nå, besvar da:		
Har De røkt sigaretter daglig tidligere?	37	
Hvis De svarte „JA", hvor lenge er det siden De sluttet?		
Mindre enn 3 måneder?	38	
3 måneder – 1 år?	39	
1 – 5 år?	40	
Mere enn 5 år?	41	
Hvor mange sigaretter røker eller røkte De daglig? (håndrullede + fabrikkframstilte)		
1 – 4?	42	
5 – 9?	43	
10 – 14?	44	
15 – 19?	45	
20 – 24?	46	
25 eller flere?	47	
Røker De noe annet enn sigaretter daglig?		
Sigarer eller serutter/cigarillos?	48	
Pipe?	49	
Hvis De røker pipe, hvor mange pakker pipetobakk (50 gram) bruker De pr. uke?		
½ pakke eller mindre pr. uke?	50	
½ – 2 pakker pr. uke?	51	
Mere enn 2 pakker pr. uke?	52	

	JA	NEI
Får De smerter eller ubehag i brystet når De:		
Går i bakker, trapper eller fort på flat mark?	53	
Går i vanlig takt på flat mark?	54	
Hvis De får smerter eller ubehag i brystet ved gange, pleier De da å:		
Stanse?	55	
Saktne farten?	56	
Fortsette i samme takt?	57	
Hvis De stanser eller saktner farten, forsvinner smertene da:		
Etter mindre enn 10 minutter?	58	
Etter mere enn 10 minutter?	59	
Får De smerter i tykkleggen når De:		
Går?	60	
Er i ro?	61	
Hvis De får leggsmerter, besvar da:		
Forverres smertene ved raskere tempo eller i bakker?	62	
Gir smertene seg når De stopper?	63	

RØKT I ANTALL ÅR: 64

TID SIDEN SISTE MÅLTID: 65

BLODTRYKK: 66 68 69 71

QUESTIONAIRE THREE COUNTIES
FINNMARK COUNTY, ROUND 1 AND 2
NORWEGIAN

A

Har De, eller har De hatt:	JA	NEI
Hjerteinfarkt? 33		
Angina pectoris (hjertekrampe)? 34		
Annen hjertesykdom? 35		
Åreforkalkning i bena? 36		
Hjerneslag? 37		
Sukkersyke? 38		
Er De under behandling for:		
Høyt blodtrykk? 39		
Bruker De:		
Nitroglycerin? 40		

B

Får De smerter eller ubehag i brystet når De:	JA	NEI
Går i bakker, trapper eller fort på flat mark? 41		
Går i vanlig takt på flat mark? 42		
Hvis De får smerter eller ubehag i brystet ved gange, pleier De da å:		
1 Stanse? 43		
2 Saktne farten?		
3 Fortsette i samme takt?		
Hvis De stanser eller saktner farten, forsvinner smertene da:		
1 Etter mindre enn 10 minutter? 44		
2 Etter mer enn 10 minutter?		
Får De smerter i tykkleggen når De:		
Går? 45		
Er i ro? 46		
Hvis De får leggsmerter, besvar da:		
Forverres smertene ved raskere tempo eller i bakker? 47		
Gir smertene seg når De stopper? . . 48		
Har De vanligvis:		
Hoste om morgenen? 49		
Oppspytt fra brystet om morgenen? . . 50		

C

Bevegelse og kroppslig anstrengelse i Deres **fritid.**
Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter så ta et gjennomsnitt.

Spørsmålet gjelder bare det siste året.

Sett kryss i den ruten hvor „JA" passer best.

	JA
1 Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 51	
2 Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? . . (Heri medregnes også gang eller sykling til arbeidsstedet, søndagsturer m.m.)	
3 Driver mosjonsidrett, tyngre hagearbeid e.l.? . . . . . (Merk at yirksomheten skal være minst 4 timer i uken.	
4 Trener hardt eller driver konkurranseidrett, regelmessig og flere ganger i uken?	

G

Har noen i Deres husstand (utenom Dem selv) vært innkalt til nærmere undersøkelse hos distriktslegen etter forrige hjerte-kar undersøkelse? 80	JA	NEI

D

Røyker De daglig for tiden? 52	JA	NEI
Hvis svaret var „JA" på forrige spørsmål, besvar da:		
Røyker De sigaretter daglig? . . . . . 53 (håndrullede eller fabrikkframstilte)		
Hvis De ikke røyker sigaretter nå, besvar da:		
Har De røykt sigaretter daglig tidligere? . 54		
Hvis De svarte „JA", hvor lenge er det siden De sluttet?		
1 Mindre enn 3 måneder? 55		
2 3 måneder - 1 år?		
3 1 - 5 år?		
4 Mer enn 5 år?		
Besvares av dem som røyker nå eller har røykt tidligere:		
Hvor mange år tilsammen har De røykt daglig? 56-57 — Antall år:		
Hvor mange sigaretter røyker eller røykte De daglig? Oppgi antall pr. dag 58-61 (håndrullede + fabrikkframstilte) — Ant. sigaretter:		
Røyker De noe annet enn sigaretter daglig?		
Sigarer eller serutter/cigarillos? . . . 62		
Pipe? 63		
Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke?		
Oppgi gjennomsnittlig antall pakker pr. uke. 64-66 — Ant. tobakk pk.		

E

Har De vanligvis skiftarbeid eller nattarbeid? 67	JA	NEI
Kan De vanligvis komme hjem fra arbeidet:		
Hver dag? 68		
Hver helg? 69		
Har De i perioder lengre arbeidsdager enn vanlig? . . . . . 70 (f.eks. under sesongfiske, onnearbeid)		
Har De i løpet av siste året hatt:		
Sett kryss i den ruten hvor „JA" passer best.		
1 Overveiende stillesittende arbeid? . . 71 (f.eks. skrivebordsarb., urmakerarb., montering)		
2 Arbeid som krever at De går mye? . . (f.eks. ekspeditørarb., lett industriarb., undervisn.)		
3 Arbeid hvor De går og løfter mye? . . (f.eks. postbud, tyngre industriarb, bygningsarb)		
4 Tungt kroppsarbeid? . . . . . (f.eks. skogsarbeid, tungt jordbruksarb tungt bygningsarb)		
Har De i løpet av de siste 12 mnd måttet flytte fra hjemstedet på grunn av forandring i arbeidssituasjonen? 72		
Er husmorarbeid Deres hovedyrke? 73		
Har De i løpet av de siste 12 mnd fått arbeidsledighetstrygd? 74		
Er De for tiden sykmeldt, eller får De attføringspenger? 75		
Har De full eller delvis uførepensjon? . . 76		

F

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? . 77	JA	NEI	VET IKKE
Er to eller flere av Deres besteforeldre av finsk ætt? 78			
Er to eller flere av Deres besteforeldre av samisk ætt? 79			

MELDING OM SKJERMBILDEFOTOGRAFERING OG HJERTE-KARUNDERSØKELSE

(Gjelder bare den person brevet er adressert til)

Skjermbildefotograferingen kommer nå til Deres distrikt.

Tid og sted for Deres frammøte vil De finne nedenfor.

Også denne gangen vil en del av befolkningen få tilbud om hjerte-karundersøkelse. De tilhører denne gruppe. En orientering om undersøkelsen er gitt i vedlagte brosjyre.

Vennligst fyll ut spørreskjemaet på baksiden og ta det med til undersøkelsen. Ta også med tuberkulinkort eller helsebok, om De har.

Fravær bes eventuelt meldt på vedlagte seddel.

Med hilsen

HELSERÅDET FYLKESLEGEN
STATENS SKJERMBILDEFOTOGRAFERING

Født dato Personnr. Kommune Kretsnr.

Møtested Kjønn Første bokstav etternavn Dag og dato Klokkeslett

SKRIV IKKE HER!

T. S. M.: (17) M: (18) (19–24) / (25–30) (31–32)

QUESTIONNAIRE THREE COUNTIES STUDY, SOGN OG FJORDANE AND OPPLAND COUNTIES, ROUND 1 AND 2

A

	JA	NEI
Har De, eller har De hatt:		
Hjerteinfarkt? 33		
Angina pectoris (hjertekrampe)? 34		
Annen hjertesykdom? 35		
Åreforkalkning i bena? 36		
Hjerneslag? 37		
Sukkersyke? 38		
Er De under behandling for:		
Høyt blodtrykk? 39		
Bruker De:		
Nitroglycerin? 40		

B

	JA	NEI
Får De smerter eller ubehag i brystet når De:		
Går i bakker, trapper eller fort på flat mark? 41		
Går i vanlig takt på flat mark? 42		
Hvis De får smerter eller ubehag i brystet ved gange, pleier De da å:		
1 Stanse? 43		
2 Saktne farten?		
3 Fortsette i samme takt?		
Hvis De stanser eller saktner farten, forsvinner smertene da:		
1 Etter mindre enn 10 minutter? 44		
2 Etter mer enn 10 minutter?		
Får De smerter i tykkleggen når De:		
Går? 45		
Er i ro? 46		
Hvis De får leggsmerter, besvar da:		
Forverres smertene ved raskere tempo eller i bakker? 47		
Gir smertene seg når De stopper? 48		
Har De vanligvis:		
Hoste om morgenen? 49		
Oppspytt fra brystet om morgenen? 50		

C

	JA
Bevegelse og kroppslig anstrengelse i Deres **fritid**. Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter så ta et gjennomsnitt.	
Spørsmålet gjelder bare det siste året.	
Sett kryss i den ruten hvor „JA" passer best.	
1 Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 51	
2 Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? (Heri medregnes også gang eller sykling til arbeidestedet, søndagsturer m.m.)	
3 Driver mosjonsidrett, tyngre hagearbeid e.l.? (Merk at yrksomheten skal være minst 4 timer i uken.	
4 Trener hardt eller driver konkurranseidrett, regelmessig og flere ganger i uken?	

D

	JA	NEI
Røyker De daglig for tiden? 52		
Hvis svaret var „JA" på forrige spørsmål, besvar da:		
Røyker De sigaretter daglig? (håndrullede eller fabrikkframstilte) 53		
Hvis De ikke røyker sigaretter nå, besvar da:		
Har De røykt sigaretter daglig tidligere? 54		
Hvis De svarte „JA", hvor lenge er det siden De sluttet?		
1 Mindre enn 3 måneder? 55		
2 3 måneder - 1 år?		
3 1 - 5 år?		
4 Mer enn 5 år?		
Besvares av dem som røyker nå eller har røykt tidligere:		
Hvor mange år tilsammen har De røykt daglig? 56-57 — Antall år:		
Hvor mange sigaretter røyker eller røykte De daglig? Oppgi antall pr. dag 58-61 (håndrullede + fabrikkframstilte) — Ant. sigaretter:		
Røyker De noe annet enn sigaretter daglig?		
Sigarer eller serutter/cigarillos? 62		
Pipe? 63		
Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke?		
Oppgi gjennomsnittlig antall pakker pr. uke. 64-66 — Ant. tobakkpk.		

E

	JA	NEI
Har De vanligvis skiftarbeid eller nattarbeid? 67		
Kan De vanligvis komme hjem fra arbeidet:		
Hver dag? 68		
Hver helg? 69		
Har De i perioder lengre arbeidsdager enn vanlig? 70		
(f.eks. under sesongfiske, onnearbeid)		
Har De i løpet av siste året hatt:		
Sett kryss i den ruten hvor „JA" passer best.		
1 Overveiende stillesittende arbeid? 71 (f.eks. skrivebordsarb., urmakerarb., montering)		
2 Arbeid som krever at De går mye? (f.eks. ekspeditørarb., lett industriarb., undervisn.)		
3 Arbeid hvor De går og løfter mye? (f.eks. postbud, tyngre industriarb., bygningsarb.)		
4 Tungt kroppsarbeid? (f.eks. skogsarbeid, tungt jordbruksarb. tungt bygningsarb.)		
Har De i løpet av de siste 12 mnd måttet flytte fra hjemstedet på grunn av forandring i arbeidssituasjonen? 72		
Er husmorarbeid Deres hovedyrke? 73		
Har De i løpet av de siste 12 mnd fått arbeidsledighetstrygd? 74		
Er De for tiden sykmeldt, eller får De attføringspenger? 75		
Har De full eller delvis uførepensjon? 76		

F

	JA	NEI	VET IKKE
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 77			

G

	JA	NEI
Har noen i Deres husstand (utenom Dem selv) vært innkalt til nærmere undersøkelse hos distriktslegen etter forrige hjerte-kar undersøkelse? 80		

MELDING OM SKJERMBILDEFOTOGRAFERING OG HJERTE-KARUNDERSØKELSE

(Gjelder bare den person brevet er adressert til)

Skjermbildefotograferingen kommer nå til Deres distrikt.

Tid og sted for Deres frammøte vil De finne nedenfor.

Også denne gangen vil en del av befolkningen få tilbud om hjerte-karundersøkelse. De tilhører denne gruppe. En orientering om undersøkelsen er gitt i vedlagte brosjyre.

Vennligst fyll ut spørreskjemaet på baksiden og ta det med til undersøkelsen. Ta også med tuberkulinkort eller helsebok, om De har.

Fravær bes eventuelt meldt på vedlagte seddel.

Med hilsen

HELSERÅDET FYLKESLEGEN
STATENS SKJERMBILDEFOTOGRAFERING

Født dato Personnr. Kommune Kretsnr.

Møtested Kjønn Første bokstav etternavn Dag og dato Klokkeslett

SKRIV IKKE HER!

T. S. M.: (17) M: (18) (19–24) / (25–30) (31–32)

QUESTIONNAIRE THREE COUNTIES STUDY,
ALL COUNTIES COUNTY,
ROUND 3
NORWEGIAN

A FAMILIE

	JA	NEI	VET IKKE
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 12			

B EGEN SYKDOM

	JA	NEI
Har De, eller har De hatt:		
Hjerteinfarkt? 13		
Angina pectoris (hjertekrampe)? 14		
Hjerneslag? 15		
Sukkersyke? 16		
Er De under behandling for:		
Høyt blodtrykk? 17		
Bruker De:		
Nitroglycerin? 18		

C SYMPTOMER

	JA	NEI	
Får De smerter eller ubehag i brystet når De:			
Går i bakker, trapper eller fort på flat mark? 19			
Går i vanlig takt på flat mark? 20			
Dersom De får smerter eller vondt i brystet ved gange, pleier De da å:			
Stoppe? 21			1
Saktne farten?			2
Fortsette i samme takt?			3
Dersom De stopper eller saktner farten, forsvinner smertene da:			
Etter mindre enn 10 minutter? 22			1
Etter mer enn 10 minutter?			2
Har De vanligvis:	JA	NEI	
Hoste om morgenen? 23			
Oppspytt fra brystet om morgenen? 24			

D MOSJON

Bevegelse og kroppslig anstrengelse i Deres fritid. Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året.

Sett kryss i den ruta hvor «JA» passer best

Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 25	1
Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uka? ..... (Her skal De også regne med gang eller sykling til arbeidsstedet, søndagsturer m.m.)	2
Driver mosjonsidrett, tyngre hagearbeid e.l.? .. (Merk at aktiviteten skal vare minst 4 timer i uka).	3
Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka?	4

E SALT/FETT

Hvor ofte bruker De salt kjøtt eller salt fisk til middag?

Sett kryss i den ruta hvor «JA» passer best

Aldri eller sjeldnere enn en gang i måneden 26	1
Opptil en gang i uka	2
Opptil to ganger i uka	3
Mer enn to ganger i uka	4

Hvor ofte pleier De strø ekstra salt på middagsmaten?

Sett kryss i den ruta hvor «JA» passer best

Sjelden eller aldri 27	1
Av og til eller ofte	2
Alltid eller nesten alltid	3

Hva slags margarin eller smør bruker De til vanlig på brød?

Sett kryss i den ruta hvor «JA» passer best

Bruker ikke smør eller margarin på brød 28	1
Smør	2
Hard margarin	3
Myk (Soft) margarin	4
Smør/margarin blanding	5

Hva slags fett blir til vanlig brukt til matlaging i Deres husholdning?

Sett kryss i den ruta hvor «JA» passer best

Smør eller hard margarin 29	1
Myk (Soft) margarin eller olje	2
Smør/margarin blanding	3

F RØYKING

	JA	NEI	
Røyker De daglig for tiden? 30			
Hvis svaret er «JA», svar da på dette:			
Røyker De sigaretter daglig? ..... 31 (håndrullet eller fabrikkframstilte)			
Hvis De ikke røyker sigaretter nå, besvar da:			
Har De røykt sigaretter daglig tidligere? 32			
Hvis De svarte «JA», hvor lenge er det siden De sluttet?			
Mindre enn 3 måneder? 33			1
3 måneder – 1 år?			2
1–5 år?			3
Mer enn 5 år?			4
Besvares av dem som røyker nå eller som har røykt tidligere:			
Hvor mange år tilsammen har De røykt daglig? 34			Antall år
Hvor mange sigaretter røyker eller røykte De daglig? Oppgi tallet på sigaretter daglig ..... 36 (håndrullet + fabrikkframstilte)			Antall sigaretter
Røyker De noe annet enn sigaretter daglig?	JA	NEI	
Sigarer eller serutter/sigarillos? 40			
Pipe? 41			
Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke?			
Oppgi gjennomsnittlig antall pakker pr. uke 42			Ant. tobakk pk.

G KAFFE

Hvor mange kopper kaffe drikker De vanligvis daglig?

Sett kryss i den ruta hvor «JA» passer best

Drikker ikke kaffe, eller mindre enn en kopp 45	1
1 – 4 kopper	2
5 – 8 kopper	3
9 eller flere kopper	4

Hva slags kaffe drikker De vanligvis daglig?

Kokekaffe 46	
Filterkaffe 47	
Pulverkaffe 48	
Koffeinfri kaffe 49	
Drikker ikke kaffe 50	

H ARBEID

	JA	NEI
Har De i løpet av de siste 12 måneder fått arbeidsledighetstrygd? 51		
Er De for tiden sykmeldt, eller får De attføringspenger? 52		
Har De full eller delvis uførepensjon? 53		
Har De vanligvis skiftarbeid eller nattarbeid 54		
Har De i det siste året hatt:		
Sett kryss i den ruta hvor «JA» passer best		
For det meste stillesittende arbeid? ..... 55 (f.eks. skrivebordsarb., urmakerarb., montering)		1
Arbeid som krever at De går mye? ..... (f.eks. ekspeditørarb., lett industriarb., undervisn.)		2
Arbeid hvor De går og løfter mye? ..... (f.eks. postbud, tyngre industriarb., bygningsarb.)		3
Tungt kroppsarbeid? ..... (f.eks. skogsarb., tungt jordbruksarb., tungt bygn.arb.)		4
Er husmorarbeid hovedyrket Deres? 56	JA	NEI

I ETTERUNDERSØKELSE

Hvis denne helseundersøkelsen viser at De bør undersøkes nærmere: Hvilken almenpraktiserende lege ønsker De da å bli henvist til?

Skriv navnet på legen her

..... 57

Ingen spesiell lege 60

Ikke skriv her

Ikke skriv her

QUESTIONNAIRE 40 YEARS STUDY, ROUND 1

A FAMILIE

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 12

JA | NEI | VET IKKE

B EGEN SYKDOM

Har De, eller har De hatt:

JA | NEI

Hjerteinfarkt? 13
Angina pectoris (hjertekrampe)? 14
Hjerneslag? 15
Sukkersyke? 16

Er De under behandling for:

Høyt blodtrykk? 17

Bruker De:

Nitroglycerin? 18

C SYMPTOMER

Får De smerter eller ubehag i brystet når De:

JA | NEI

Går i bakker, trapper eller fort på flat mark? 19
Går i vanlig takt på flat mark? 20

Dersom De får smerter eller vondt i brystet ved gange, pleier De da å:

Stoppe? 21
Saktne farten? .....
Fortsette i samme takt? .....

1 2 3

Dersom De stopper eller saktner farten, forsvinner smertene da:

Etter mindre enn 10 minutter? 22
Etter mer enn 10 minutter? .....

1 2

Har De vanligvis:

JA | NEI

Hoste om morgenen? 23
Oppspytt fra brystet om morgenen? 24

D MOSJON

Bevegelse og kroppslig anstrengelse i Deres fritid. Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året.

Sett kryss i den ruta hvor «JA» passer best

Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? ..... 25 — 1

Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uka? ..... — 2
(Her skal De også regne med gang eller sykling til arbeidsstedet, søndagsturer m.m.)

Driver mosjonsidrett, tyngre hagearbeid e.l.? .. — 3
(Merk at aktiviteten skal vare minst 4 timer i uka).

Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka? ..... — 4

E SALT/FETT

Hvor ofte bruker De salt kjøtt eller salt fisk til middag?

Sett kryss i den ruta hvor «JA» passer best

Aldri eller sjeldnere enn en gang i måneden ..... 26 — 1
Opptil en gang i uka ..... — 2
Opptil to ganger i uka ..... — 3
Mer enn to ganger i uka ..... — 4

Hvor ofte pleier De strø ekstra salt på middagsmaten?

Sett kryss i den ruta hvor «JA» passer best

Sjelden eller aldri ..... 27 — 1
Av og til eller ofte ..... — 2
Alltid eller nesten alltid ..... — 3

Hva slags margarin eller smør bruker De til vanlig på brød?

Sett kryss i den ruta hvor «JA» passer best

Bruker ikke smør eller margarin på brød ..... 28 — 1
Smør ..... — 2
Hard margarin ..... — 3
Myk (Soft) margarin ..... — 4
Smør/margarin blanding ..... — 5

Hva slags fett blir til vanlig brukt til matlaging i Deres husholdning?

Sett kryss i den ruta hvor «JA» passer best

Smør eller hard margarin ..... 29 — 1
Myk (Soft) margarin eller olje ..... — 2
Smør/margarin blanding ..... — 3

F RØYKING

JA | NEI

Røyker De daglig for tiden? 30

Hvis svaret er «JA», svar da på dette:

Røyker De sigaretter daglig? 31
(håndrullet eller fabrikkframstilte)

Hvis De ikke røyker sigaretter nå, besvar da:

Har De røykt sigaretter daglig tidligere? 32

Hvis De svarte «JA», hvor lenge er det siden De sluttet?

Mindre enn 3 måneder? ..... 33 — 1
3 måneder – 1 år? ..... — 2
1–5 år? ..... — 3
Mer enn 5 år? ..... — 4

Besvares av dem som røyker nå eller som har røykt tidligere:

Hvor mange år tilsammen har De røykt daglig? ..... 34 — Antall år

Hvor mange sigaretter røyker eller røykte De daglig?
Oppgi tallet på sigaretter daglig ..... 36 — Antall sigaretter
(håndrullet + fabrikkframstilte)

Røyker De noe annet enn sigaretter daglig?

JA | NEI

Sigarer eller serutter/sigarillos? 40
Pipe? 41

Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke?

Oppgi gjennomsnittlig antall pakker pr. uke ..... 42 — Ant. tobakk pk.

G KAFFE

Hvor mange kopper kaffe drikker De vanligvis daglig?

Sett kryss i den ruta hvor «JA» passer best

Drikker ikke kaffe, eller mindre enn en kopp ..... 45 — 1
1 – 4 kopper ..... — 2
5 – 8 kopper ..... — 3
9 eller flere kopper ..... — 4

Hva slags kaffe drikker De vanligvis daglig?

Kokekaffe 46
Filterkaffe 47
Pulverkaffe 48
Koffeinfri kaffe 49
Drikker ikke kaffe 50

H ARBEID

JA | NEI

Har De i løpet av de siste 12 måneder fått arbeidsledighetstrygd? 51

Er De for tiden sykmeldt, eller får De attføringspenger? 52

Har De full eller delvis uførepensjon? 53

Har De vanligvis skiftarbeid eller nattarbeid 54

Har De i det siste året hatt:

Sett kryss i den ruta hvor «JA» passer best

For det meste stillesittende arbeid? ..... 55 — 1
(f.eks. skrivebordsarb., urmakerarb., montering)
Arbeid som krever at De går mye? ..... — 2
(f.eks. ekspeditørarb., lett industriarb., undervisn.)
Arbeid hvor De går og løfter mye? ..... — 3
(f.eks. postbud, tyngre industriarb., bygningsarb.)
Tungt kroppsarbeid? ..... — 4
(f.eks. skogsarb., tungt jordbruksarb., tungt bygn.arb.)

JA | NEI

Er husmorarbeid hovedyrket Deres? 56

I ETTERUNDERSØKELSE

Hvis denne helseundersøkelsen viser at De bør undersøkes nærmere: Hvilken almenpraktiserende lege ønsker De da å bli henvist til?

Skriv navnet på legen her

..... 57

Ingen spesiell lege 60

Ikke skriv her

Ikke skriv her

QUESTIONNAIRE 40 YEARS STUDY, ROUND 2

A FAMILIE

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 12

JA	NEI	VET IKKE

B EGEN SYKDOM

Har De, eller har De hatt:

	JA	NEI
Hjerteinfarkt? 13		
Angina pectoris(hjertekrampe)? 14		
Hjerneslag? 15		
Sukkersyke? 16		

Hvis De har sukkersyke, i hvilket år ble diagnosen stillet? ..... 17 — 19____

Er De under medikamentell behandling for høyt blodtrykk? 19

JA	NEI

C SYMPTOMER

Får De smerter eller ubehag i brystet når De:

	JA	NEI
Går i bakker, trapper eller fort på flat mark? 20		
Går i vanlig takt på flat mark? 21		

Dersom De får smerter eller vondt i brystet ved gange, pleier De da å:

Stoppe? 22	1
Saktne farten?	2
Fortsette i samme takt?	3

Dersom De stopper eller saktner farten, forsvinner smertene da:

Etter mindre enn 10 minutter? 23	1
Etter mer enn 10 minutter?	2

Har De vanligvis:

	JA	NEI
Hoste om morgenen? 24		
Oppspytt fra brystet om morgenen? 25		

D MOSJON

Bevegelse og kroppslig anstrengelse i Deres fritid. Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året.
Sett kryss i den ruta hvor «JA» passer best

Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 26	1
Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uka? ..... (Her skal De også regne med gang eller sykling til arbeidsstedet, søndagsturer m.m.)	2
Driver mosjonsidrett, tyngre hagearbeid e.l.? . (Merk at aktiviteten skal vare minst 4 timer i uka.)	3
Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka?	4

E SALT/FETT

Hvor ofte bruker De salt kjøtt eller salt fisk til middag?
Sett kryss i den ruta hvor «JA» passer best

Aldri eller sjeldnere enn en gang i måneden 27	1
Opptil en gang i uka	2
Opptil to ganger i uka	3
Mer enn to ganger i uka	4

Hvor ofte pleier De strø ekstra salt på middagsmaten?
Sett kryss i den ruta hvor «JA» passer best

Sjelden eller aldri 28	1
Av og til eller ofte	2
Alltid eller nesten alltid	3

Hva slags margarin eller smør bruker De til vanlig på brød?
Sett kryss i den ruta hvor «JA» passer best

Bruker ikke smør eller margarin på brød 29	1
Smør	2
Hard margarin	3
Myk (Soft) margarin	4
Smør/margarin blanding	5

Hva slags fett blir til vanlig brukt til matlaging i Deres husholdning?
Sett kryss i den ruta hvor «JA» passer best

Smør eller hard margarin 30	1
Myk (Soft) margarin eller olje	2
Smør/margarin blanding	3

F RØYKING

Røyker De

	JA	NEI
Sigaretter daglig? (håndrullet eller fabrikkframstilte) 31		
Sigarer eller serutter/sigarillos daglig? 32		
Pipe daglig? 33		

Hvis De ikke røyker daglig nå, besvar da:

Har De røykt daglig tidligere? 34	

Hvis De svarte «JA», hvor lenge er det siden De sluttet?

Mindre enn 1 år? 35	1
Mer enn 1 år?	2

Besvares av dem som røyker nå eller som har røykt tidligere:
Hvor mange år tilsammen har De røykt daglig? ..... 36 — Antall år

Hvor mange sigaretter røyker eller røykte De daglig?
Oppgi tallet på sigaretter daglig ..... 38 (håndrullet + fabrikkframstilte) — Antall sigaretter

G KAFFE

Hvor mange kopper kaffe drikker De vanligvis daglig?
Sett kryss i den ruta hvor «JA» passer best

Drikker ikke kaffe, eller mindre enn en kopp 42	1
1 – 4 kopper	2
5 – 8 kopper	3
9 eller flere kopper	4

Hva slags kaffe drikker De vanligvis daglig?

Kokekaffe 43	
Filterkaffe 44	
Pulverkaffe 45	
Koffeinfri kaffe 46	
Drikker ikke kaffe 47	

H ARBEID

Har De i det siste året hatt:
Sett kryss i den ruta hvor «JA» passer best

For det meste stillesittende arbeid? ..... 48 (f.eks. skrivebordsarbeid, urmakerarbeid, montering)	1
Arbeid som krever at De går mye? ..... (f.eks. ekspediterarb., lett industriarb., undervisning)	2
Arbeid hvor De går og løfter mye? ..... (f.eks. postbud, tyngre industriarb., bygningsarbeid)	3
Tungt kroppsarbeid? ..... (f.eks. skogsarb., tungt jordbruksarb., tungt bygn.arb.)	4

Har De i Deres arbeid noen gang vært i kontakt med:

	JA	NEI	VET IKKE
Asbeststøv? 49			
Kvartsstøv? 50			

	JA	NEI
Har De vanligvis skiftarbeid eller nattarbeid? 51		
Er husarbeid i hjemmet hovedyrket Deres? ..... 52 (Svar: «NEI» hvis lønnet arbeid utenom husarbeid er 18 timer eller mer pr. uke)		
Har De daglig omsorg for syke eller funksjonshemmede i familien? 53		
Har De i løpet av de siste 12 måneder fått arbeidsledighetstrygd? 54		
Er De for tiden sykmeldt, eller får De attføringspenger? 55		
Har De full eller delvis uførepensjon? 56		

I ETTERUNDERSØKELSE

	JA	NEI	VET IKKE
Er to eller flere av dine besteforeldre av finsk ætt? 57			
Er to eller flere av dine besteforeldre av samisk ætt? 58			

Hvis denne helseundersøkelsen viser at du bør undersøkes nærmere:
Hvilken almenpraktiserende lege/kommunelege ønsker du da å bli henvist til?

Skriv navnet på legen her →

..... 59

Ingen spesiell lege 62

Ikke skriv her

Ikke skriv her

QUESTIONNAIRE 40 YEARS STUDY, ROUND 3

EGEN HELSE

Hvordan er helsen din nå? *Sett bare ett kryss.*

Dårlig	12	1
Ikke helt god		2
God		3
Svært god		4

Har du, eller har du hatt:

	JA	NEI	Alder første gang
Hjerteinfarkt 13			år
Angina pectoris (hjertekrampe) 16			år
Hjerneslag/hjerneblødning 19			år
Astma 22			år
Diabetes (sukkersyke) 25			år

Bruker du medisin mot høyt blodtrykk?

Nå	28	1
Før, men ikke nå		2
Aldri brukt		3

Hvis ja, hvilket merke bruker du nå?

Ikke skriv her

Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende? 33 — JA / NEI

Har du de siste to ukene følt deg:

	Nei	Litt	En god del	Svært mye
Nervøs og urolig? 34				
Plaget av angst? 35				
Trygg og rolig? 36				
Irritabel? 37				
Glad og optimistisk? 38				
Nedfor/deprimert? 39				
Ensom? 40	1	2	3	4

Får du smerter eller ubehag i brystet når du: — JA / NEI

Går i bakker, trapper eller fort på flat mark? 41

Hvis du får slike smerter, pleier du da å:

Stoppe? 42	1
Saktne farten?	2
Fortsette i samme takt?	3

	JA	NEI
Dersom du stopper, forsvinner smertene da etter mindre enn 10 minutter? 43		
Kan slike smerter like gjerne opptre mens du er i ro? 44		

Mottar du nå noen av følgende ytelser?

Syketrygd (sykmeldt) 45	
Attføringspenger 46	
Uførepensjon (hel eller delvis) 47	
Arbeidsledighetstrygd 48	

ENDRING AV HELSEVANER

Dette gjelder din interesse for å endre helsevaner. Røykespørsmålet besvares bare av dem som røyker.

	Spise sunnere JA	Spise sunnere NEI	Trimme mer JA	Trimme mer NEI	Slutte å røyke JA	Slutte å røyke NEI
Har du de siste 12 mnd. forsøkt å: 49						
Om 5 år, tror du at du har endret vaner på noen av disse områdene? 52						

Anslå din høyeste og laveste vekt i løpet av de siste 5 år. *(Se bort fra vekt under svangerskap)* 55

Høyeste vekt:	Laveste vekt:
kg	kg

SYKDOM I FAMILIEN

	JA	NEI	VET IKKE
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 61			

Har én eller flere foreldre/søsken hatt:

	JA	NEI
Hjerteinfarkt *før* de fylte 60 år? 62		
Hjerneslag *før* de fylte 70 år? 63		

RØYKING

Hvor lenge er du vanligvis daglig til stede i røykfylt rom? 64 — Antall timer

Sett 0 hvis du ikke oppholder deg i røykfylt rom.

Røyker du selv?

	JA	NEI
Sigaretter daglig? 66		
Sigarer/sigarillos daglig? 67		
Pipe daglig? 68		

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? 69 — Antall år

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? 71	Antall sigaretter
Hvor gammel var du da du begynte å røyke daglig? 75	Alder år
Hvor mange år tilsammen har du røykt daglig? 77	Antall år

MOSJON

Hvordan har din fysiske aktivitet i fritiden vært det siste året? *Tenk deg et ukentlig gjennomsnitt for året. Arbeidsvei regnes som fritid.*

	Timer pr. uke: Ingen	Under 1	1-2	3 og mer
Lett aktivitet *(ikke svett/andpusten)* 79				
Hard fysisk aktivitet *(svett/andpusten)* 80	1	2	3	4

KAFFE/TE/ALKOHOL

Hvor mange kopper kaffe/te drikker du daglig? *Sett 0 hvis du ikke drikker kaffe/te daglig.*

Kokekaffe 81	Antall kopper
Annen kaffe 83	Antall kopper
Te 85	Antall kopper

Er du total avholdsmann/-kvinne? 87 — JA / NEI

Hvor mange ganger i måneden drikker du vanligvis alkohol? *Regn ikke med lettøl. Sett 0 hvis mindre enn 1 gang i mnd.* 88 — Antall ganger

Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av to uker? 90

Regn ikke med lettøl.

Sett 0 hvis du ikke drikker alkohol.

Øl	Vin	Brennevin
glass	glass	glass

FETT

Hva slags margarin eller smør bruker du vanligvis på brødet? *Sett ett kryss.*

Bruker ikke smør/margarin 96	1
Meierismør	2
Hard margarin	3
Bløt (soft) margarin	4
Smør/margarin blanding	5
Lettmargarin	6

UTDANNING

Hvilken utdanning er den høyeste du har fullført?

Grunnskole 7-10 år, framhaldsskole, folkehøgskole 97	1
Realskole, middelskole, yrkesskole, 1-2 årig videregående skole	2
Artium, øk.gymnas, allmennfaglig retning i videregående skole	3
Høgskole/universitet, mindre enn 4 år	4
Høgskole/universitet, 4 år eller mer	5

ETTERUNDERSØKELSE

Hvis denne helseundersøkelsen viser at du bør undersøkes nærmere, hvilken allmennpraktiserende lege/kommunelege ønsker du da å bli henvist til? Oppgi legens navn:

Ikke skriv her

QUESTIONNAIRE 40 YEARS STUDY, ROUND 4

Spørreskjemaet er en viktig del av helseundersøkelsen. Vennligst fyll ut skjemaet på forhånd og ta det med til helseunder søkelsen. Dersom enkelte spørsmål er uklare, lar du dem stå ubesvart til du møter fram, og drøfter dem med personalet som gjennomfører undersøkelsen. *Alle svar vil bli behandlet strengt fortrolig.*

Det utfylte skjemaet vil bli lest av en maskin. Bruk blå eller sort farge ved utfylling. Det er viktig at du går fram slik:

- i de små boksene setter du kryss for det svaret som passer best for deg
- i de store boksene skriver du tall eller blokkbokstaver – NB! innenfor rammen for boksen.

Eksempler:
Avkryssing: [X] Tall: 1 2 3 4 5 6 7 8 9 0 Bokstaver: A B C

Med vennlig hilsen

Statens helseundersøkelser ♥ Kommunehelsetjenesten

1. EGEN HELSE

Hvordan er helsen din nå? *(Sett bare ett kryss)*

Dårlig	Ikke helt god	God	Svært god
☐ 1	☐ 2	☐ 3	☐ 4

Har du, eller har du hatt:	JA	NEI	Alder første gang	
Hjerteinfarkt	☐	☐		år
Angina pectoris (hjertekrampe)	☐	☐		år
«Hjerneslag/hjerneblødning («drypp»)	☐	☐		år
Astma	☐	☐		år
Diabetes (sukkersyke)	☐	☐		år

Får du smerter eller ubehag i brystet når du:	JA	NEI
Går i bakker, trapper eller fort på flat mark?	☐	☐

Hvis du får slike smerter, pleier du da å:

Stoppe?	Saktne farten?	Fortsette i samme takt?
☐ 1	☐ 2	☐ 3

	JA	NEI
Dersom du stopper, forsvinner smertene da etter mindre enn 10 minutter?	☐	☐
Kan slike smerter like gjerne opptre mens du er i ro?	☐	☐

2. HVORLEDES FØLER DU DEG?

Har du de siste to ukene følt deg:

	Nei	Litt	En god del	Svært mye
Nervøs og urolig?	☐	☐	☐	☐
Plaget av angst?	☐	☐	☐	☐
Trygg og rolig?	☐	☐	☐	☐
Irritabel?	☐	☐	☐	☐
Glad og optimistisk?	☐	☐	☐	☐
Nedfor/deprimert?	☐	☐	☐	☐
Ensom?	☐	☐	☐	☐
	1	2	3	4

3. SYKDOM I FAMILIEN

	JA	NEI	VET IKKE
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)?	☐	☐	☐
Har en eller flere foreldre/søsken hatt:			
Hjerteinfarkt *før* de fylte 60 år?	☐	☐	☐
Hjerneslag/hjerneblødning *før* de fylte 70 år?	☐	☐	☐

4. MUSKEL/SKJELETT-PLAGER

	JA	NEI
Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende?	☐	☐

Hvis NEI, gå til avsnitt 5. SOSIALE FORHOLD.
Hvis JA, svar på følgende:

Hvor har du hatt disse plagene?	JA	NEI
Nakke	☐	☐
Skuldre (aksler)	☐	☐
Albuer	☐	☐
Håndledd/hender	☐	☐
Bryst, mage	☐	☐
Øvre del av ryggen	☐	☐
Korsryggen	☐	☐
Hofter	☐	☐
Knær	☐	☐
Ankler, føtter	☐	☐

Hvor lenge har plagene vart sammenhengende?
Svar for det området hvor plagene har vart lengst.

Hvis under 1 år, oppgi antall mnd. ..... *Antall mnd.*

Hvis 1 år eller mer, oppgi antall år ..... *Antall år*

Har plagene redusert din arbeidsevne det siste året?
Gjelder også hjemmearbeidende. Sett bare ett kryss.

Nei/ubetydelig	I noen grad	I betydelig grad	Vet ikke
☐ 1	☐ 2	☐ 3	☐ 4

	JA	NEI	Ikke i arbeid
Har du vært sykmeldt pga. disse plagene det siste året?	☐	☐	☐
Har plagene ført til redusert aktivitet i fritida?	☐	☐	

5. SOSIALE FORHOLD

Mottar du nå noen av følgende ytelser?	JA	NEI
Syketrygd (sykmeldt)	☐	☐
Attføringspenger	☐	☐
Uførepensjon (hel eller delvis)	☐	☐
Arbeidsledighetstrygd	☐	☐

Er husarbeid i hjemmet hovedyrket ditt? *(Svar NEI hvis lønnet arbeid utenom husarbeid er 18 timer eller mer pr. uke)*	JA	NEI
	☐	☐

6. UTDANNING

Hvilken utdanning er den høyeste du har fullført?
Sett bare ett kryss.

- Mindre enn 7 år grunnskole ☐
- Grunnskole 7-10 år, framhaldsskole, folkehøgskole ☐ 1
- Realskole, middelskole, yrkesskole, 1-2 årig videregående skole ☐ 2
- Artium, øk.gymnas, allmennfaglig retning i videregående skole ☐ 3
- Høgskole/universitet, mindre enn 4 år ☐ 4
- Høgskole/universitet, 4 år eller mer ☐ 5

7. KOST

Hvor ofte bruker du disse matvarene?
Sett kryss i de rutene som beskriver ditt forbruk best.

	Flere g. daglig	Daglig	1-6 g. pr uke	1-3 g. pr mnd	Sjelden eller aldri
Fisk (middag, pålegg)	☐	☐	☐	☐	☐
Frukt/grønt	☐	☐	☐	☐	☐
Helmelk, kefir, yoghurt	☐	☐	☐	☐	☐
Lettmelk, lettyoghurt	☐	☐	☐	☐	☐
Skummet melk (sur/søt)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Hva slags smør eller margarin bruker du vanligvis PÅ BRØDET?
Sett kryss i den ruta som passer best.

- Bruker ikke smør/margarin ☐ 1
- Meierismør ☐ 2
- Hard margarin ☐ 3
- Bløt (soft) margarin ☐ 4
- Smør/margarin blanding ☐ 5
- Lettmargarin/lettsmør (Brelett) ☐ 6

Hva slags fett bruker du/dere vanligvis TIL MATLAGING?
Sett kryss i den ruta som passer best.

- Smør/margarin ☐ 1
- Myk (soft) margarin/olje ☐ 2
- Bare olje ☐ 3
- Vet ikke ☐ 4

8. KAFFE / TE / ALKOHOL

Hvor mange kopper kaffe/te drikker du daglig?
Sett 0 hvis du ikke drikker kaffe/te daglig.

Antall kopper daglig

Kokekaffe	Annen kaffe	Te
☐☐	☐☐	☐☐

	JA	NEI
Er du total avholdsmann/-kvinne?	☐	☐

Hvor mange ganger i måneden drikker du vanligvis alkohol? *Regn ikke med lettøl.*
Sett 0 hvis mindre enn 1 gang i mnd. ..... *Antall ganger* ☐☐

Hvor mange glass øl, vin eller brennevin drikker du VANLIGVIS i løpet av to uker?
Regn ikke med lettøl. Sett 0 hvis du ikke drikker alkohol.

Glass øl	Glass vin	Glass brennevin
☐☐	☐☐	☐☐

9. RØYKING

Hvor lenge er du vanligvis daglig tilstede i røykfylt rom? ..... *Antall hele timer* ☐☐
Sett 0 hvis du ikke oppholder deg i røykfylt rom.

Røyker du selv:

	JA	NEI
Sigaretter daglig?	☐	☐
Sigarer/sigarillos daglig?	☐	☐
Pipe daglig?	☐	☐

Aldri røykt daglig ..... (Sett kryss) ☐

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? ..... *Antall år* ☐☐

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? ..... *Antall sigaretter* ☐☐

Hvor gammel var du da du begynte å røyke daglig? ..... *Alder i år* ☐☐

Hvor mange år til sammen har du røykt daglig? ..... *Antall år* ☐☐

10. MOSJON

Hvordan har din fysiske aktivitet i fritiden vært det siste året?
Tenk deg et ukentlig gjennomsnitt for året.
Arbeidsvei regnes som fritid. Besvar begge spørsmålene.

	Timer pr. uke: Ingen	Under 1	1-2	3 og mer
Lett aktivitet *(ikke svett/andpusten)*	☐	☐	☐	☐
Hard fysisk aktivitet *(svett/andpusten)*	☐ 1	☐ 2	☐ 3	☐ 4

Bevegelse og kroppslig anstrengelse i din fritid. Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året.
Sett kryss i den ruta som passer best.

- Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? ☐ 1
- Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uka? ☐ 2
  (Her skal du også regne med gang eller sykling til arbeidsstedet, søndagsturer m.m.)
- Driver mosjonsidrett, tyngre hagearbeid e.l.? ☐ 3
  (Merk at aktiviteten skal vare minst 4 timer i uka)
- Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka? ☐ 4

11. ENDRING AV HELSEVANER

Dette gjelder din interesse for å endre helsevaner. Røykespørsmålet besvares bare av dem som røyker.

	Spise sunnere		Trimme mer		Slutte å røyke	
	JA	NEI	JA	NEI	JA	NEI
Har du de siste 12 mnd. forsøkt å:	☐	☐	☐	☐	☐	☐
Om 5 år, tror du at du har endret vaner på noen av disse områdene?	☐	☐	☐	☐	☐	☐

	Høyeste vekt	Laveste vekt
Anslå din høyeste og laveste vekt i løpet av de siste 5 år. *(Hele kg)* *(Se bort fra vekt under svangerskap)*	☐☐☐	☐☐☐

VEND!

12. MEDISIN MOT HØYT BLODTRYKK

Bruker du medisin mot høyt blodtrykk?

Nå	Før, men ikke nå	Aldri brukt
☐ 1	☐ 2	☐ 3

Hvis du bruker medisin nå, hvilke(t) merke(r) bruker du?

Ikke skriv i disse rutene

13. MEDISIN MOT HØYT KOLESTEROL

	JA	NEI
Bruker du kolesterolsenkende medisiner NÅ?	☐	☐

Hvis NEI, gå til 14. ETTERUNDERSØKELSE.

Hvor gammel var du da du begynte med kolesterolsenkende medisiner? ..... *Alder i år*

Hvis du bruker kolesterolsenkende medisiner, hva var grunnen til at du begynte med slik medisin?
(Sett kryss i de rutene som passer for deg.)

	JA	NEI
Hjerteinfarkt	☐	☐
Angina pectoris (hjertekrampe, brystkrampe)	☐	☐
Høyt innhold av kolesterol i blodet	☐	☐
Hjertesykdom i familien (foreldre, søsken)	☐	☐
Hjerneslag/hjerneblødning/ «drypp»	☐	☐
Dårlig blodsirkulasjon i bena (åreforkalkning, «røykeben»)	☐	☐
Andre årsaker	☐	☐

Skriv hvilke årsaker her:

Ikke skriv i disse rutene

	JA	NEI
Jeg er usikker på årsaken	☐	☐

Hvilke kolesterolsenkende medisiner bruker du NÅ og hvilken dose bruker du?

Hvilke(t) merke(r) bruker du? — Samlet dose på ett døgn

mg

mg

mg

Ikke skriv i disse rutene

14. ETTERUNDERSØKELSE

Hvis denne helseundersøkelsen viser at du bør undersøkes nærmere, hvilken allmennpraktiserende lege/kommunelege ønsker du da å bli henvist til?
Oppgi legens navn:

Ikke skriv i disse rutene

15. TIL KVINNER SOM DELTAR I HELSE-UNDERSØKELSEN

Hvor gammel var du da du fikk menstruasjon aller første gang? ..... *Alder i år*

	JA	NEI
Har du for tiden regelmessig menstruasjon? *Regn den for regelmessig hvis den ikke har vært borte mer enn 3 mnd. sammenhengende siste år.*	☐	☐

Til deg som svarte JA: Omtrent hvor mange dager etter starten på siste menstruasjon skjer helseundersøkelsen? *(Sett bare ett kryss)*

Under 8 ☐ 8-14 ☐ 15-21 ☐ Mer enn 21 dager ☐

Hvis du for tiden ikke har regelmessig menstruasjon, ber vi deg fylle ut nedenfor *(Sett bare ett kryss)*

Menstruasjonen sluttet av seg selv for minst 6 mnd. siden (overgangsalder)	☐ 1
Menstruasjonen sluttet etter underlivs-operasjon, strålebehandling eller cellegift	☐ 2
Usikker på om menstruasjonen har sluttet (mulig overgangsalder)	☐ 3
Gravid i mindre enn 6 måneder	☐ 4
Gravid i 6 måneder eller mer	☐ 5
Har nylig født eller ammer, og har ikke fått menstruasjonen tilbake	☐ 6
Helt uregelmessige menstruasjoner, med svært korte eller svært lange pauser	☐ 7
Ingen eller uregelmessig menstruasjon på grunn av hormonbehandling	☐ 8
Har aldri hatt menstruasjoner	☐ 9

Hvis du ikke lenger har menstruasjon, hvor gammel var du da den sluttet? ..... *Alder i år*

Hvor mange barn (levende barn) **har du født?** *Antall barn*

Hvor lenge har du ammet dine barn til sammen?
(f.eks. 3 barn: 1 + 6 + 10 = 17 måneder) ..... *Antall mnd.*

Bruker du nå, eller har du tidligere brukt	Nå	Før, men ikke nå	Aldri
P-pille (*også minipille*) eller p-sprøyte	☐	☐	☐
Vanlig spiral	☐	☐	☐
Hormonspiral (pris ca. kr. 1000)	☐	☐	☐
Østrogen/progesteron *(tabletter, plaster, sprøyte)*	☐	☐	☐
Østrogen *(krem eller stikkpiller)*	☐	☐	☐

Til deg som bruker p-pille, hormonspiral (ikke vanlig spiral) eller hormoner i overgangsalderen NÅ:
Hvilke(t) merke(r) bruker du?

Ikke skriv i disse rutene

Omtrent hvor lenge har du brukt det du bruker nå?

Antall år *Hvis mindre enn ett år: .....Måneder*

Takk for utfyllingen!
Nok en gang:
Velkommen til undersøkelsen!

IE 3213201 - 30.000 - Beyer-Hecos 11/98 (ID.NR. 1/98)

CONOR STUDY QUESTIONS NORWEGIAN

VARIABEL/ VARIABLE	SPØRRESKJEMA NORSK (NORWEGIAN)
	EGEN HELSE
a1	**1. Hvordan er helsen din nå?** *Sett bare ett kryss* Dårlig Ikke helt god God Svært god
a2_1 to a2_10	**2. Har du eller har du hatt?** Ja Nei Alder 1.gang Hjerteinfarkt Angina pectoris (hjertekrampe) Hjerneslag/ Hjerneblødning Astma Diabetes (sukkersyke)
a4	**3. Har du i løpet av siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende?** Ja Nei
a5_1 to a5_7	**4. Har du de to siste ukene følt deg:** Nei Litt En god del Svært mye Nervøs og urolig Plaget av angst Trygg og rolig Irritabel Glad/optimistisk Nedfor/deprimert Ensom
	FYSISK AKTIVITET
a6_1 to a6_2	**5a. Hvordan har din fysiske aktivitet i fritiden vært det siste året?** *Tenk deg et ukentlig gjennomsnitt for året. Arbeidsvei regnes som fritid.* Timer per uke i gjennomsnitt Ingen Under 1 1-2 3 el mer Lett aktivitet (*ikke*

	svett/andpusten) Hard fysisk aktivitet *(svett/andpusten)*
a6_3	**5 b. Angi bevegelse og kroppslig anstrengelse i din fritid. Hvis aktiviteten varierer meget f.eks mellom sommer og vinter, så ta et gjennomsnitt.** **Spørsmålet gjelder bare det siste året.** *(Sett ett kryss i den ruta som passer best)* Lese, ser på fjernsyn eller annen stillesittende beskjeftigelse? Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uka? *(Her skal du regne med gang eller sykling til arbeidsstedet, søndagsturer m.m)* Driver mosjonsidrett, tyngre hagearbeid e.l? *(Merk at aktiviteten skal vare minst 4 timer i uka)* Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka
	RØYKING
a7_2	**6 . Hvor lenge er du vanligvis daglig til stede i røykfylt rom?** *Sett 0 hvis du ikke oppholder deg i røykfylt rom.* Antall timer……..
a7_3	**7. Røkte noen av de voksne hjemme da du vokste opp?** Ja Nei
a7_4	**8. Bor du/har du bodd sammen med noen daglig-røykere etter fylte 20 år?** Ja Nei
a8_0 to a8_3	**9. Røyker du selv ?** Ja Nei Sigaretter daglig Sigarer/sigarillos daglig Pipe daglig
a9	**10. Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet?** ……år
a10	**11. Hvis du røker daglig nå eller har røykt tidligere:** **Hvor mange sigaretter røyker eller røykte du vanligvis daglig?** Antall sigaretter…….
a11	**12. Hvor gammel var du da du begynte å røyke?** ……..år
a12_1	**13. Hvor mange år til sammen har du røykt daglig ?**

	……..år
	KAFFE, TE OG ALKOHOL
a13_1 to a13_2 **a13_4**	**14.a Hvor mange kopper kaffe drikker du daglig?** *Sett 0 hvis du ikke drikker kaffe daglig* Kokekaffe, antall kopper……. Annen kaffe, antall kopper……..
a13_5 to a13_8	**14.b Hva slags kaffe drikke du vanligvis?** *Sett kryss* Filter-/pulverkaffe Kokekaffe/trykkanne Annen kaffe (espresso og lignende) Drikker ikke kaffe
a13_9 to a13_10	**14c. Hvor mange kopper kaffe/te drikker du daglig?** *Sett 0 hvis du ikke drikker kaffe/te daglig* Antall kopper kaffe……. Antall kopper te……
a14_1 and a14_1_2 **(a14_1 made of 14_1_1** **and 14_1_2)**	**15 a. Hvor mange ganger i måneden drikker du vanligvis alkohol?** Regn ikke med lettøl. Sett 0 hvis mindre enn 1 gang i måneden. Antall ganger…….
a14_1 and a14_1_1 **(a14_1 made of 14_1_1** **and 14_1_2)**	**15 b. Omtrent hvor ofte har du i løpet av det siste året drukket alkohol?** *(Lettøl og alkoholfritt øl regnes ikke med)* 4-7 ganger i uka 2-3 ganger i uka Ca 1.gang i uka 2-3 ganger pr måned Omtrent1 gang i mnd. Noen få ganger siste år Har ikke drukket alkohol siste år Har aldri drukket alkohol
a14_4_1, a14_5_1	**16 a. Hvor mange glass øl, vin eller brennevin** **drikker du vanligvis i løpet av to uker?** *Regn ikke med lettøl. Sett 0 hvis du ikke drikker alkohol.* Øl…..glass Vin…..glass Brennevin…..glass
a14_2	*Til dem som har drukket siste år* **16 b. Når du har drukket alkohol, hvor mange glass/og eller drinker** **har du vanligvis drukket?** Antall…….
a14_3	**16 c. Omtrent hvor mange ganger i løpet av det siste året har du drukket så mye** **som minst 5 glass og/eller drinker i løpet av et døgn?** Antall ganger……..

a14_4, a14_5, **a14_6, a14_6_1**	**16 d. Når du drikker alkohol, drikker du da vanligvis:** *(Sett ett eller flere kryss).* Øl Vin Brennevin
a14_7	**17. Er du total avholdsmann/-kvinne?** Ja Nei
	SKOLEGANG
a15, a15_2 **(made of a15_1 and a15_2)**	**18 a. Hvilken utdanning er den høyeste du har fullført?** Mindre enn 7 år grunnskole Grunnskole 7-10 år, framhaldsskole, folkehøyskole Realskole, middelskole, yrkesskole, 1-2 årig videregående skole Artium, økonomisk gymnas, allmennfaglig retning i videregående skole Høgskole/universitet, mindre enn 4 år Høgskole/universitet, 4 år eller mer
a15, a15_1 **(made of a15_1 and a15_2)**	**18 b. Hvor mange års skolegang har du gjennomført?** *(Ta med alle år du har gått på skole eller studert)* Antall år……
	SYKDOM I FAMILIEN
a16	**19. Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet)** **eller angina pectoris (hjertekrampe)?** Ja Nei Vet ikke
b15_1 to b15_30	**20. Kryss for de slektninger som har eller har hatt noen av sykdommene:** Mor Far Bror Søster Barn Hjerneslag eller hjerneblødning Hjerteinfarkt før 60 års alder Astma Kreftsykdom Sukkersyke (diabetes) Alder da de fikk sukkersyke
	LOKALMILJØ OG BOLIG
b1	**21. I hvilken kommune bodde du da du fylte 1 år?** ***Hvis du ikke bodde i Norge, oppgi hvilket land i stedet for fylke.*** **……..**
b2	**22. Hvilken type bolig bor du i?** Enebolig/ villa Gårdsbruk Blokk/terrasseleilighet

	Rekkehus/2-4mannsbolig Annen bolig/institusjon/omsorgsbolig
b3	**23. Hvor stor er din boenhet?** **……**m2
b29	**24. Er det heldekkende tepper i stua?** Ja Nei
b30	**25. Er det katt i boligen?** Ja Nei
	FAMILIE OG VENNER
Sjekke	**26a. Hvem bor du sammen med?** *Sett ett kryss for hvert spørsmål og angi antall.* Ja Nei Antall Ektefelle/samboer Andre personer over 18 år Personer under 18 år
b4_1 to b4_6	**26 b. Bor du sammen med noen?** Ja Nei *Hvis JA:* Ja Nei Antall Ektefelle/samboer Andre personer, 18 år og eldre Personer under 18 år
b4_7 and b4_8	**26 c (kun på eldreskjema)** **Bor du ?** *Sett kryss* Hjemme Institusjon/bofellesskap **Bor du sammen med?** Ja Nei Ektefelle/samboer? Andre personer?
b31	**27. Hvor mange av barna har plass i barnehage?** ……..
b5	**28. Hvor mange gode venner har du? Regn med de du kan snakke fortrolig med og som kan gi deg hjelp når du trenger det?** *(Tell ikke med de du bor sammen med, men ta med andre slektninger)* **……**
b6	**29. Føler du at du har nok gode venner?** Ja

	Nei
b7	**30. Hvor ofte tar du vanligvis del i foreningsvirksomhet som for eksempel syklubb, idrettslag, politiske lag, religiøse eller andre foreninger?** Aldri, eller noen få ganger i året 1-2 ganger i måneden (før år 1996), 1-3 ganger i måneden (etter år 1996) Omtrent 1 gang i uken Mer enn en gang i uken
	ARBEID
b8_1 to b8_4	**31. Hva slags arbeidssituasjon har du nå?** Lønnet arbeid Heltids husarbeid Utdanning, militærtjeneste Arbeidsledig, permittert
b9 and b9_1	**32a. Hvor mange timer lønnet arbeid har du i uka?** …….timer
b9	**32 b. Er du i inntektsgivende arbeid?** Ja, full tid Ja, deltid Nei
b10_1, b10_2, b10_3 **b10_4, b10_5, b10_6** **b10_7**	**33. Mottar du noen av følgende ytelser?** Sykepenger (er sykemeldt) Alderstrygd, førtidspensjon (AFP) eller etterlattepensjon Rehabiliterings-/attføringspenger Uførepensjon (helt eller delvis) Dagpenger under arbeidsledighet So1sialhjelp/stønad Overgangsstønad for enslige forsørgere
b11	**34. Har du skiftarbeid, nattarbeid eller går vakter?** Ja Nei
b12	**35. Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive arbeidet ditt?** For det meste stillesittende arbeid? *(f.eks1 skrivebordsarbeid, montering)* Arbeid som krever at du går mye? *(f.eks ekspeditørarbeid, lett industriarbeid, undervisning)* Arbeid der du går og løfter mye? *(f.eks postbud, pleier, bygningsarbeider)* Tungt kroppsarbeid?*(f.eks skogsarbeid, tungt jordbruksarbeid, tungt bygningsarbeid)*
b32	**36. Kan du <u>selv</u> bestemme hvordan arbeidet ditt skal legges opp?** *(Sett bare ett kryss)*

	Nei, ikke i det hele tatt I liten grad Ja, stort sett Ja, det bestemmer jeg selv
b33_1, b33_2, b33_3	**37a. Har du noen av følgende yrker ?** **(heltid eller deltid)** *Sett kryss for hvert spørsmål* Ja Nei Sjåfør Bonde/gårdbruker Fisker
b33_4, b33_5	**37b. Hvilket yrke/tittel har eller hadde du på dette arbeidsstedet?** (spørsmålet henviser til et mellomliggende spørsmål (ikke CONOR)om den virksomhet man har arbeidet i lengst tid siste 12 mnd) *(For eksempel; sekretær, lærer, industriarbeider, barnepleier, møbelsnekker,* avdelingsleder, selger sjåfør e.l) Yrke……
	SYKDOM OG SKADER
b13_1, b13_2, b13_3 **b13_4, b13_5, b13_6** **b13_7, b13_8**	**38. Har du noen gang hatt**: *Sett et kryss for hvert spørsmål. Oppgi også alder ved hendelsen.* *Hvis det har skjedd flere ganger, hvor gammel var du siste gang.* Ja Nei Aldersiste gang Lårhalsbrudd Brudd ved håndledd/underarm Nakkesleng (whiplash) Skade som førte til syke- husinnleggelse
b14_1, b14_2, b14_3 **b14_4, b14_5**	**39. Har du eller har du hatt?** *Kryss av ja eller nei for hvert spørsmål* Ja Nei Høysnue Kronisk bronkitt/emfysem Benskjørhet (osteoporose) Fibromyalgi/fibrositt/kronisk)smertesykdom Psykiske plager som du har søkt hjelp for
b17	**40. Hoster du omtrent daglig i perioder av året?** Ja Nei
b18	**41.** *Hvis ja:* **Er hosten vanligvis ledsaget av oppspytt?** Ja Nei
b19	**42. Har du hatt slik hoste så lenge som i en 3 måneders periode i** **begge de to siste år?** Ja Nei

b20	**43. Hvor ofte er du plaget av søvnløshet?** Aldri, eller noen få ganger i året 1-2 ganger i måneden (før år 2000), 1-3 ganger i måneden (etter år 2000) Omtrent 1 gang i uken Mer enn 1 gang i uken
b21	**44. Har du siste året vært plaget av søvnløshet som har gått utover arbeidsevnen?** Ja Nei
	BRUK AV MEDISINER
b16_1, b16_2	**45. Bruker du?** Nå / Før, men ikke nå / Aldri brukt Kolesterolsenkende medisin Medisin mot høyt blodtrykk
b16_19 to b16_24	**46a. Har du i løpet av det siste året brukt noen av følgende midler daglig eller nesten daglig?** *Angi hvor mange måneder du brukte dem. Sett 0 hvis du ikke har brukt noen av midlene.* **Legemidler** Smertestillende ……mnd. Sovemedisin ……mnd. Beroligende midler ……mnd. Midler mot depresjon ……mnd. Allergimedisin ……mnd. Astmamedisin ……mnd. *Med medisiner mener vi her medisiner som er kjøpt på apotek.* *Kosttilskudd og vitaminer regnes ikke med.*
b16_3 to b16_8	**46 b. Hvor ofte har du i løpet av <u>de siste 4 ukene</u> brukt følgende medisiner?** *(Sett ett kryss per linje)* Daglig / Hver uke, men ikke daglig / Sjeldnere enn hver uke / Har ikke brukt siste 4 uker Smertestillende uten resept Smertestillende på resept Sovemedisin Beroligende medisin Antidepressiva Annen medisin på resept
b16_9_1 to b16_18_3	**46c. Fyll inn navn på medisin, årsak til bruk og tiden den ble brukt fra sp 46b** **Navn på medisin / Grunn til bruk / Hvor lenge brukt Inntil et år/ett år eller mer** 1.

	2. 3. 4. 5. 6.
	KOSTTILSKUDD
b16_25 to b16_27	**47 a. Har du i løpet av det siste året brukt noen av følgende midler daglig eller nesten daglig?** *Angi hvor mange måneder du brukte dem. Sett 0 hvis du ikke har brukt noen av midlene.* Jerntabletter ……mnd. Vitamin D-tilskudd ……mnd. Andre vitamintilskudd ……mnd. Tran ……mnd.
b16_28, b16_29	**47 b. Bruker du følgende kosttilskudd?** Ja, daglig Iblant Nei Tran, trankapsler, Fiskeoljekapsler Vitamin- og/eller mineraltilskudd
	RESTEN AV SKJEMAET SKAL BARE BESVARES AV KVINNER
b22	**48. Hvor gammel var du da du fikk menstruasjon første gang?** ……..år
b23	**49. Hvis du ikke lenger har menstruasjon, hvor gammel var du da den sluttet?** ……..år
b24	**50. Er du gravid nå?** Ja Nei Usikker Over fruktbar alder
b25	**51. Hvor mange barn har du født tidligere?** ……barn
b26_1 to b26_12	**52. Hvis du har født, fyll ut for hvert barn barnets fødselsår og omtrent antall måneder du ammet hvert barn.** Barn Fødselsår Antall måneder med amming 1. 2. 3. 4. 5. 6.
b27_1 to b27_4	**53. Bruker du eller har du brukt:**

		Nå	Før	Aldri
	P-pille (også minipille)			
	P-sprøyte			
	Hormonspiral (ikke vanlig spiral)			
	Østrogen (tabletter eller plaster)			
	Østrogen (krem eller stikkpiller)			
b28_1to b28_5	**54. Hvis du brukte p-pille, minipille, p-sprøyte, hormonspiral eller østrogen, hvilket merke bruker du?** ……			

CONOR STUDY QUESTIONS ENGLISH

QUESTIONNAIRE IN ENGLISH

YOUR OWN HEALTH

1. What is your current health status? *Tick one only*

Poor
Not so good
Good
Very good

2. Do you have, or have you had?

	Yes	No	Age first time
Heart attack			
Angina pectoris (heart cramp)			
Cerebral stroke/ Brain haemorrhage			
Asthma			
Diabetes			

3. Have you during the last year suffered from pain and/or stiffness in muscles and joints that have lasted for at least 3 months ?

Yes
No

4. Have you in the last two weeks felt :

	No	A little	A lot	Very much
Nervous or worried				
Anxious				
Confident and calm				
Irritable				
Happy/Optimistic				
Down/Depressed				
Lonely				

PHYSICAL ACTIVIYY

5a. How has your physical activity during leisure time been over the last year ?

Think of your weekly average for the year. Time spent going to or fromworkk counts as leisure time

Hours per week

	None	Less than 1	1-2	3 or more
Light activity				

(*not sweating or out of breath* **)**

Hard physical activity
(*sweating/out of breath*)

5 b. Please note physical activity during the past year in your spare time.
If **activity varies between summer and wintertime,**
note a mean value.
(Tick one only)
Reading, watching TV or any other sedentary activity?

Walking, cycling, or other activity, other for at least 4 hours a week?
(Count also walking back and forth from work)

Light sports, heavy gardening?
(At least 4 thours perweek)

Hard exercise, competitive sports? *Regularly and several times a week*

SMOKING

6 . How many hours a day do you normally spend in smoke-filled rooms?
Write 0 if you don`t spend time in smoke-filled rooms
Number of hours……..

7. Did any of the adults smoke at home when you grew up?
Yes
No

8. Do you now, or have you ever lived together with a daily smoker after the age of 20 years?
Yes
No

9. Do you smoke ?
Yes No
Cigarettes daily
Cigars/cigarillos daily
Pipe daily

10. If you previously smoked daily, how long is it since you quit?
……number of years

11. If you smoke daily now or previously:
How many cigarettes do you,or did you usually smoke per day?
Number of cigarettes……..

12. How old were you when you began smoking?
……..year

13. How many years in all have you smoked daily ?

……..years

COFFEE, TEA AND ALCOHOL

14.a How many cups of coffee do you usually drink daily ?
Write 0 if you do not drink coffee daily
Boiled coffee (coarsely ground), number……
Coffee other, number……..

14.b What type of coffee do you usually drink?
Please tick
Filter/instant coffee
Boiled coffee (coarsely ground)
Other (espresso etc)
Do not drink coffee

14c. How many cups of coffee/tea do you usually drink daily?
Write 0 if you do not drink coffee/tea daily
Number of cups with coffee…….
Number of cups with tea……

15 a. How many times a month do you usually drink alcohol?
Do not count low-alcohol beer. Put 0 if less than once a month.
Number of times…….

15 b. Approximately how often during the past 12 months have you consumed alcohol?
(Do not count low-alcohol beer)
4-7 times a week
2-3 times a week
App. 1 time a week
2-3 times a month
Appr. 1 time a month
A few times last year
Have not drunk alcohol the last year
Have never drunk alcohol

16 a. How many glasses of beer, wine or spirits
do you usually drink during a two-weeks period?
Do not count low-alcohol beer. Put 0 if you do not drink alcohol.

Beer…..glasses Wine…..glasses Spirits…..glasses

For those who have consumed alcohol during the past year
16 b. When you drank alcohol, how many glasses
did you usually drink ?
Number of glasses…….

16 c. Approximately how often during the past 12 months have you consumed alcohol
corresponding to at least 5 glasses of spirits in 24 hours?
Number of times……..

16 d. When you drink alcohol, do you usually drink: *(Tick one or more).*

Beer Wine Spirits (hard liquor)

17. Are you a total abstainer from alcohol ?

Yes

No

EDUCATION

18 a. What is the highest level of education you have completed?

Less than 7 year of primary school

7-10 years primary/secondary school

Technical school, middle school, vocational school, 1-2 years senior high school

High school diploma (3-4 years)

College/university, less than 4 years

College/university, 4 or more years

18 b. How many years education have you completed all together?

(Count every year you went to school)

Number of years…….

ILLNESS IN THE FAMILY

19. Have one or more of your parents or siblings had a heart attack or angina pectoris?

Yes

No

Don't know

20. Tick for those relatives who have or have had:

	Mother	Father	Brother	Sister	Child
Cerebral stroke or brain haemorrhage					
Myocardial infarction before age 60					
Asthma					
Cancer					
Diabetes					
Age when diabetes was first diagnosed					

RESIDENLY

21. In which muncipality did you live at the age of 1 year*?*

If you did not live in Norway, give country of residence instead of municipality.

……..

22. What type of dwelling do you live in?

Villa/detached house

Farm

Flat/apartment

Terraced/semi-detached house
Other/institution/care home

23. How large is your home?
……m2

24. Do you have wall-to-wall carpets in the living-room?
Yes No

25. Is there a cat in your home?
Yes No

FAMILY AND FRIENDS

26 a. With whom do you live? *Tick one for each question and write the number*

	Yes	No	Number
Spouse/Partner			
Other persons older than 18 years			
Persons younger than 18 years			

26 b. Do you live with anyone?
Yes
No

If YES:

	Yes	No	Number
Spouse/Partner			
Other persons older than 18 years			
Persons younger than 18 years			

26 c (only at the questionary for the elderly)
Where do you live ? *Please tick*
Home
Institution

Do you live with?

	Yes	No
Spouse/Partner?		
Other persones?		

27. How many of the children attend day care/kindergarten/nursery school?
……..

28. How many good friends do you have with whom you can talk confidentially and who can provide help if you need it?
(Do not count people you live with, but do include other relatives)
…….

29. Do you feel that you have enough good friends?
Yes

No

30. How often do you usually take part in organised activities, e.g.
sewing circles, sports clubs, political meetings, religious or other organizations?
Never, or just a few times a year
1-2 times a month (before year 1996), 1-3 times a month (after year 1996)
Approximately once a week
More than once a week

WORK

31. What is your current work situation?
Paid work
Full-time housework
Under education, military service
Unemployed, on leave without payment

32 a. How many hours of paid work do you have per week?
…….number of hours

32 b. What is your current work situation – paid work?
Yes, full-time
Yes, part time
No

33. Do you receive any of the following?
Sickness benefit?
Old-age pension?
Rehabilitation benefit?
Disability pension?
Unemployment benefits?
Social welfare benefits?
Social benefit-single parent?

34. Do you work shifts or nights?
Yes
No

35. If you have paid or unpaid work, which statement describes your work best?
Mostly sedentary work?
(e.g. office work, mounting)

Work that requires a lot of walking?
(e.g. shop assistant, light industrial work, teaching)

Work that requires a lot of walking and lifting?
(e.g. postman, nursing, construction)

Heavy manual labour? *(e.g. forestry, heavy farmwork, heavy construction*)

36. Do you decide yourself how your work will be done? *(Tick one only)*

Not at all
Very little
Yes, sometimes
Yes, my own decision

37 a. Do you have any of the following occupations ?
(full time or part time) *Tick one for each question*

	Yes	No
Driver		
Farmer		
Fisherman		

37 b. What occupation/title did you have at this work?
(the question refers to another question (not CONOR) about the occupation where they worked the longest period during the past year)
Ex secretary, teacher, industrial worker, nursing, carpenter, l eader, salesman, driver etc)
Occupation:……

YOUR OWN ILLNESS and INJURIES

38. Have you ever had:
Tick one for each question. State age at event.
If it has happened several times, write age at the last event.

	Yes	No	Age at last time
Hip fracture			
Wrist/forearm fracture			
Whiplash			
Injury requiring hospital admission			

39. Do you have or have you ever had?
Tick yes or no for each question

	Yes	No
Hay fever		
Chronic bronchitis/emphysema		
Osteoporosis		
Fibromyalgia/fibrositis/chronic pain syndrome		
Psychological problems for which you have sought help		

40. Do you cough almost daily for some periods of the year?
Yes No

41. If yes,
do you bring up phlegm?
Yes No

42. If you cough almost daily for some periods of the year, have you had this kind of cough for as long as 3 months in each of the last two years?
Yes No

43. How often do you suffer from sleeplessness?
Never, or just a few times a year
1-2 times a month (before year 2000), 1-3 times a month (after year 2000)
Approximately once a week
More than once a week

44. Have you in the last twelve months suffered from sleeplessness to the extent that it has affected your ability to work ? Yes No

USE OF MEDICATION

45. Do you take?

	Currently	Previously	Never
Lipid lowering drugs			
Medications for high blood pressure			

46 a. Have you for any length of time in the past year used any of the following medications every day or almost daily?
Indicate how many months you have used the medication. Write 0 if you did not take the medication.

Medications:
Painkillers ……months.
Sleeping pills ……months.
Tranquilizers ……months.
Antidepressants ……months.
Allergy pills ……months.
Asthma medication ……months.
Only medication bought at pharmacy .
Do not include dietary supplements

46 b. How often during the last 4 weeks have you taken any of the following medication?
Tick one per line

	Daily	Weekly but not daily	Less than weekly	Not taken last 4 weeks
Painkillers without prescription				
Painkillers on prescription				
Sleeping pills				
Tranquilizers				
Antidepressants				
Other medication on prescription				

46.c Fill in name of medication, reason for use and time used from q 46.b

Brand name	**Reason for use**	**For how long up to 1 year/1 year or more**
1.		

2.
3.
4.
5.
6.

DIETARY SUPPLEMENTS

47 a. Have you for any length of time in the past year taken any of the *following daily or almost daily?*
Indicate how many months you have used them. Write 0 if you did not take any.
Iron tablets ……..months
Vitamin D supplements ……..months
Other vitamin supplements ……..months
Cod liver oil ……..months

47 b. Do you take any of the following?

	Yes, daily	Sometimes	No
Cod liver oil, capsules			
Fish oil capsules			
Vitamin and or mineral supplements			

THE REST OF THE FORM SHOULD ONLY BE FILLED IN BY WOMEN

48. How old were you when you started menstruating?
……..year

49. If you no longer menstruate, how old were you when you stopped menstruating?
……..year

50. Are you pregnant at the moment?
Yes No Unsure Postmenopausal

51. How many children have you given birth to?
……children

52. If you have given birth, what year was the child born and how many months did you breastfeed each child

Child	Year born	Number of months with breastfeeding
1.		
2.		
3.		
4.		
5.		
6.		

53. Do you use or have you ever used:

	Now	Previously	Never
Contraceptive pills (OC) (incl. minipill)			
Contraceptive injections			
Hormonal intrauterine device			
Estrogen (tablets or patches)			
Estrogen (cream or suppositories)			

54. If you use contraceptive pills, hormonal intrauterine device, or estrogen, what brand do you currently use?

……

Nå

Appendix 2

METHODS DESCRIPTION
NORWEGIAN HELATH STUDIES

Randi Selmer 30 Nov 2007. Updated 23 June 2008.
Measurements in Health Surveys 1972-2003.

Blood pressure

1. 1972-84: Systolic and diastolic blood pressure were measured twice with a standard mercury sphygmomanometer after 4 minutes rest. The second measurement has usually been used in follow up studies. The interval between first and second measurement was 1 minute. Diastolic blood pressure was recorded at the disappearance of the Korotkoff sounds (phase V). When phase V was absent, phase IV was used. Standard size cuffs were used throughout. The blood pressure was measured on the right upper arm with the person sitting on a chair.
2. 1985-2003: Pulse recordings, systolic and diastolic blood pressures were measured by an automatic device (DINAMAP, Criticon, Tampa, USA), which measured the blood pressure in mm Hg automatically by an oscillometric method. After 2 minutes preceding rest, three recordings were made at one-minute intervals. The values of the mean of the second and third systolic blood pressure measurements were used in calculating the cardiovascular risk score (CVD risk score). Arm circumference of right upper arm was measured 10 cm above fossa cubiti. From these measurements small, medium or large cuff was chosen. The blood pressure was measured on the right upper arm with the person sitting on a chair.

The two methods have been compared (PG Lund-Larsen: Blodtrykk målt med kvikksølvmanometer og med Dinamap under feltforhold- en sammenligning. Norsk epidemiologi 1997; 7 (2): 235-41)

Serum analyses

Sera from the screenings were sent to the Department of Clinical Chemistry, Ullevål University Hospital, Oslo, Norway

Serum lipids

Non-enzymatic methods: Total cholesterol and triglycerides

Non enzymatic methods were used in Oslo 1972-73, first screening in Finnmark, Oppland and Sogn og Fjordane 1974-78 and second screening in Finnmark 1977-78. Enzymatic methods were used from second screening in Sogn og Fjordane 1980.

Stensvold et al. BMJ 1993:

"A blood sample was taken from non-fasting subjects and analysed for serum concentrations of total cholesterol and triglycerides, both components being measured non-enzymatically on a Tchnicon AutoAnalyzer. On later comparison with enzymatic methods, the non-enzymatic methods used gave on average 10% higher triglyceride values and 8% higher cholesterol values. The participants reported the time since last meal."

The triglyceride values included in the data set are corrected values compatible with enzymatic methods according to the formula:

(New method) = 0.90 x (Old method) - 0.11

The cholesterol values included in the data set are corrected values compatible with enzymatic methods according to the formula:

(New method) = 0.92 x (Old method) + 0.03

The formula was evolved after extensive test program comparing new and old method.

Enzymatic methods:
All measurements of HDL cholesterol were enzymatic. (Stensvold I, Urdal P, Thürmer H, Tverdal A, Lund-Larsen PG, Foss OP. High-density lipoprotein cholesterol and coronary, cardiovascular and all cause mortality among middle-aged Norwegian men and women.Eur Heart J. 1992 Sep;13(9):1155-63.)

Non-fasting serum total cholesterol, serum HDL cholesterol, glucose and serum triglycerides were measured directly by an enzymatic method (Technicon or Hitachi autoanalyzer). Seronorm Lipoprotein was used as internal quality control material for the lipid analyses and Autonorm Human Liquid for the glucose. The control material was done at the start and for every 30^{th} sample.

Stability of cholesterol measurements from 1972 has been documented (OP Foss and P Urdal: Kolesterol gjennom mer enn 25 år: kan svarene sammenliknes over så lang tid? Norsk epidemiologi 2003; 13 (1): 85-88))

Glucose
Serum glucose was measured in first screening in Finnmark, Oppland and Sogn og Fjordane 1974-78 and second screening in Finnmark 1977-78 and in a sample in second screening in Oppland 1981-83 by a non enzymatic method by Brown (ME Brown: Ultra-micro sugar determinations using 2, 9-dimethyl-1, 10-phenanthroline hydrochloride (Neocuproine). Diebetes 10:60, 1961.) The same method was used in Oslo 1972-73. The results obtained with this method were about 0.8-1.1 mmol/l higher than the true concentration defined as the value found with a specific enzymatic method.

From 1994 non fasting serum glucose was measured by enzymatic method described above. The old glucose values have not been adjusted to levels comparable with enzymatic methods.

Weight and height
Body weight (in kilograms, one decimal) and height (in centimetres, one decimal) was measured according to standard protocol with the participants wearing light clothing without shoes (manually recorded until 2000 and after that with an electronic Height and Weight scale)

Waist and hip
Waist and hip were measured from Finnmark and Akershus 1996/97 and onwards. Waist circumference was measured at the umbilicus to the nearest cm with the subject standing and breathing normally. In obese individuals, waist circumference was defined as the midpoint between the iliac crest and lower margin of ribs. Hip circumference was measured as the maximum circumference around the buttocks. Both waist and hip were measured with a measuring tape of steel – which was emphasized to be horizontal. Waist and hip circumference were used to calculate the waist-hip ratio using the formula waist (cm)/ hip circumference (cm).

Measurements of lipids in three counties 1974-1988			
	Finnmark	**Sogn og Fjordane**	**Oppland**
Name			
Screening 1			
u1kol_mg	total cholesterol mg/dl old method	total cholesterol mg/dl old method	total cholesterol mg/dl old method
u1kolest	total cholesterol old method converted to mmol/l by factor 0.02586	total cholesterol old method converted to mmol/l by factor 0.02586	total cholesterol old method converted to mmol/l by factor 0.02586
u1kolenz	total cholesterol mmol/l converted to enzymatic values from u1kolest by formulae	total cholesterol mmol/l converted to enzymatic values from u1kolest by formulae	total cholesterol mmol/l converted to enzymatic values from u1kolest by formulae
No HDL measurements			
u1trigly	triglycerides mmol/l old method	triglycerides mmol/l old method	triglycerides mmol/l old method
u1trienz	triglycerides mmol/l converted to enzymatic values from u1trigly by formulae	triglycerides mmol/l converted to enzymatic values from u1trigly by formulae	triglycerides mmol/l converted to enzymatic values from u1trigly by formulae
Screening 2			
u2kol_mg	total cholesterol mg/dl old method	total cholesterol mg/dl enzymatic method	total cholesterol mg/dl enzymatic method
u2kolest	total cholesterol old method converted to mmol/l by factor 0.02586	total cholesterol enzymatic method converted to mmol/l by factor 0.02586	total cholesterol enzymatic method converted to mmol/l by factor 0.02586
u2kolenz	total cholesterol mmol/l converted to enzymatic values from u2kolest by formulae	u2kolenz=u2kolest	u2kolenz=u2kolest
u2hdlkol	mg/dl, enzymatic*	mg/dl, enzymatic*	mg/dl, enzymatic*
u2hdlkl	converted to mmol/l by factor 0.02586	converted to mmol/l by factor 0.02586	converted to mmol/l by factor 0.02586
u2trigly	triglycerides mmol/l old method	triglycerides mmol/l enzymatic method	triglycerides mmol/l enzymatic method
u2trienz	triglycerides mmol/l converted to enzymatic values from u1trigly by formulae	u2trienz=u2trigly	u2trienz=u2trigly
Screening 3			
u3kolest/u3kolenz	All values enzymatic mmol/l . Sometimes renamed u3kolest to u3kolenz to indicate that these are enzymatic values.		
u3hdlkl	No measurements	All values enzymatic mmol/l*	All values enzymatic mmol/l*
u3trigly/u3trienz	All values enzymatic mmol/l . Sometimes renamed u3trigly to u3trienz to indicate that these are enzymatic values.		

*Eur Heart J. 1992 Sep; 13(9):1155-63.

High-density lipoprotein cholesterol and coronary, cardiovascular and all-cause mortality among middle-aged Norwegian men and women. Stensvold I, Urdal P, Thürmer H, Tverdal A, Lund-Larsen PG, Foss OP.

SUMMARY THREE COUNTIES STUDY

The cardiovascular surveys in Finnmark, Sogn og Fjordane and Oppland 1974-78, 1977-83 and 1985-88. Sources: Final reports from each survey in each county

County	Period	Age groups invited	Number invited	Number attending	% attendance, fully invited ages
Finnmark	1974-75	All residents in age 35-49 by Dec 1974 (born 25-39). Age 20-34: 10% random samples	17401	14340	82.4 Men: 78.8, women: 86.2
	1977-78	All residents born 1925-42, samples in younger ages from 20 years.	20647	17145	83.0 Men: 79.2 women: 87.3
	1987-88	All residents in age 40-62 by Dec 1987 (born 1925-47) + those aged 30-39 and invited in 1977-78 + 10 % of non-invited in age 20-39. All residents 18 years or older in Bugøynes.	22994	17852	77.6 Men: 73.4, women: 82.6
Sogn og Fjordane	1975-76	All residents in age 35-49 by Dec 1975 (born 1926-40) + 10 % random sample in age 20-39.	16603	14966	90.1 Men: 87.4, women:93.1
	1980-81	All residents born 1926-40 + samples in younger ages from 17 years.	19506	17473	89.6 Men: 86.8, women:92.6
	1985-86	All residents in age 40-54 by Dec 31 1985 (born 1931-45) + those younger than 40 years and invited in 1980-81 + 5-% sample of those in age 20-39 not invited in 1980-81 +10 % sample of invited in 1980-81 in age 55-59. A few older subjects in a hypertension register.	21423	18669	87.1 Men: 83.9, women: 90.7
Oppland	1976-78	All in age 35-49 by Dec 1976 (born 1927-41) +10- % random sample in age 20-39.	31620	28399	89.8 Men: 87.8, women: 91.8
	1981-83	All residents born 1927-41 + samples in younger ages from 20 years.	31581	28437	90.0 Men: 88.1, women: 91.9
	1986-88	All residents aged 40-54 on Dec 1986 (born 1932-46) + all residents below 40 years and a 10 % sample in age 55-59 if invited in 1981-83 + 5-% of not invited in 1981-83 in age 20-39. A few older subjects in a hypertension register.	37270	32124	86.2 Men: 83.5, women: 88.9

CONOR STUDY
MATERIALS AND METHODS
DESCPRIPTION

Cohort Norway (CONOR): Materials and methods

Anne Johanne Søgaard, Norwegian Institute of Public Health, April 2006

CONOR (COhort NORway) is a large collaborative project between epidemiological centres at the University of Tromsø, the Norwegian University of Science and Technology in Trondheim, the University of Bergen, the University of Oslo, and the Norwegian Institute of Public Health.

Data from 10 regional studies

In CONOR, regional data from 10 different epidemiological studies have been merged into a national database, which is more representative of the Norwegian population than each of the individual sites.

The database consists of information obtained from questionnaires, a simple physical examination, analyses of blood samples, and frozen stored blood and/or DNA. The main purpose of CONOR is to study the aetiology of rare diseases by testing environmental, inheritable, cultural and social factors in order to describe the dispersion of diseases and risk factors by time, place and socio-demographic factors.

CONOR is particularly suitable for studying gene-environment interactions and for linkages to various national registers (eg. cancer-, cause of death-, hospital- and medical birth registers).

Invitation and procedures

Altogether 309,832 individuals were invited in the 10 studies based on addresses from the Population registry of Norway (Hammer, 2002). Some of the individual studies invited all subjects above a specific age (for example all above 19 years in HUNT II), whereas others invited all subjects in selected age groups (for example all 30-, 40-, 45-, 60 and 75 years in OPPHED and TROFINN). The web site for each study contains more detailed information (see Table 1).

In all CONOR surveys, the data collection followed a standard procedure. Letters of invitation were mailed about 2 weeks before the time of appointment and included a

questionnaire and a booklet with the aims of the study and information about the examinations and procedures. At the screening, the main questionnaire was collected from the attendees, they went through a physical examination and a non-fasting blood sample was drawn for analyses in fresh serum. Another sample was stored at minus 80 degrees. In most studies, the participants were given one or two supplementary questionnaires, which they were instructed to fill in at home and to return by mail in pre-addressed envelopes.

About four weeks after attending the examination, a letter with some results from the examination and blood tests was sent to all participants. Those with the highest scores of cardiovascular risk were offered a new clinical examination at the regional University Hospital - or, in some of the studies, were asked to visit their own general practitioner.

Measures

All surveys have been carried out in collaboration with the National Health Screening Service, Oslo (now Norwegian Institute of Public Health). Experienced and trained personnel conducted all procedures. Non-fasting serum total and HDL cholesterol, glucose and triglycerides were measured directly by an enzymatic method (Boehringer 148393, Boehringer-Mannheim, Federal Republic of Germany – from 2000 Hitachi 917 auto analyzer, Roche Diagnostic, Switzerland).

The Department of Clinical Chemistry, Ullevål University Hospital, Oslo, performed all laboratory assessments except for HUNT II where the analyses were performed at the Department of Clinical Chemistry, Innherad Hospital, Levanger. Comparisons of blood-samples were performed between the laboratories, and small differences were found (Tverdal A et al 1997). Calibration procedures were carried out between these laboratories in connection with the surveys (Dr. Lund-Larsen PG, National Health Screening Service, personal communication). An acceptable stability of the laboratory analyses over time in the population surveys has been reported (Foss & Urdal, 2003).

Heart rate, systolic and diastolic blood pressures were measured by an automatic device (DINAMAP, Criticon, Tampa, USA), which measured the blood pressure in

mm Hg automatically by an oscillometric method. After 2 minutes of preceding rest, three recordings were made at one-minute intervals. Mean values of the second and third systolic blood pressure measurements were used in calculating the cardiovascular risk score (CVD risk score) (Tverdal et al., 1989). The stability of the blood-pressure measures have been evaluated and deemed acceptable (Lund-Larsen, 1997).

Body weight (in kilograms, one decimal) and height (in cm, one decimal) was measured according to a standard protocol with the participants wearing light clothing without shoes (manually recorded until 2000 and after that with an electronic Height and Weight Scale). Body mass index (BMI) was calculated as kg/m^2. Waist circumference was measured at the umbilicus to the nearest cm and with the subject standing and breathing normally. In obese individuals, waist circumference was defined as the midpoint between the iliac crest and lower margin of ribs. Hip circumference was measured as the maximum circumference around the buttocks. Both waist and hip were measured with a measuring tape of steel – which was emphasized to be horizontal. Waist and hip circumference were used to calculate the waist-hip ratio using the formula waist (cm)/ hip circumference (cm).

Most of the studies consist of a central core and several supplementary projects – for example extra samples of blood, ECG, ultrasonographic examination of carotid artery and abdominal aorta, and bone mineral densitometry (BMD). The web site for each study contains more detailed information (see Table 1). Only a limited and mutual core of each study constitutes CONOR. Most of the studies have published reference papers with more detailed information about their own study (Table 2).

The CONOR-questions

All surveys used 50 common CONOR-questions agreed upon before the first CONOR survey in Tromsø in 1994. The exact wording of the questions is available at the CONOR web site (http://www.fhi.no/dav/CA11310499.doc). Some of these questions were placed on the second questionnaire handed out at the screening station – and thus have lower response rate.

The CONOR-questions cover the following main topics: Self-reported health and diseases such as diabetes, asthma, coronary heart disease, stroke and mental distress, musculo-skeletal pains, family history of disease, risk factors and lifestyle, environment while growing up, social network and social support, education, work and housing, some types of occupation, use of medications and reproductive history (women).

Several of these questions have been evaluated or validated previously and were deemed acceptable (Tretli et al., 1982; Jacobsen & Thelle, 1987; Løchen & Rasmussen, 1992; Thune et al., 1997, Joakimsen et al., 1998; Saltin & Grimsby, 1968; Derogatis et al., 1974; Ainsworth et al., 1996; Brugha et al., 1985; Strand et al., 2003; Søgaard et al 2003). The Population registry of Norway, which was used for invitation, contains information about gender, birth date, marital status, address and country of birth.

Participation in the CONOR studies

Altogether 181,891 subjects accepted to participate and provided a declaration of consent – 7,460 of these participated in more than one survey. The age distributing of these 174 430 participants is shown in table 3. The participation rate varied among the surveys. The participation was slightly reduced throughout the study-period 1994-2003 - and was higher in rural as compared to urban areas.

Ethics and approvals

All participants of the studies included in CONOR, have given their written consent. The participant's names and personal ID numbers are omitted when data are used for research purposes. The Norwegian Data Inspectorate has approved - and the Regional Committees for Medical Research Ethics has evaluated each individual study. The studies have been conducted in full accordance with the World Medical Association Declaration of Helsinki.

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TABLE 1. Number of invited and participating subjects in Cohort Norway (CONOR) 1994-2003.

Name of the study	Year of survey	Number invited†	Invited age-groups in years‡	Number of participants *			Web address
				Men	Women	Total	
Tromsø IV (The fourth Tromsø Study)	1994-1995	37,558	25 +	12,797	14,128	26,925	http://uit.no/tromsoundersokelsen/tromso4/2
HUNT II (The second North-Trøndelag Health Study)	1995-1997	94,196	20 +	30,442	34,576	65,018	http://www.hunt.ntnu.no/
HUSK (The Hordaland Health Study)	1997-1999	38,587	40-44, 46-47, 70-72	11,678	13,852	25,530	http://www.uib.no/isf/husk/
Oslo II (The second Oslo Study)	2000	14,209§	48-77	6,919		6,919	http://www.fhi.no/artikler/?id=54685
HUBRO (The Oslo Health Study)	2000-2001	58,660#	30, 31, 40, 45, 46, 59/ 60, 75/ 76	9,751	12,264	22,015	http://www.fhi.no/artikler/?id=54464
OPPHED (The Oppland and Hedmark Health Study)	2000-2001	22,327	30, 40, 45, 60, 75	5,650	6,752	12,402	http://www.fhi.no/artikler/?id=28233
Tromsø V (The fifth Tromsø Study)	2001	10,353	30 +	3,491	4,586	8,077**	http://uit.no/tromsoundersokelsen/tromso5/2
I-HUBRO (The Oslo Immigrant Health Study)	2002	12,088††	20-60	1,915	1,768	3,683	http://www.fhi.no/artikler/?id=28217
TROFINN (The Troms and Finnmark Health Study)‡‡	2002	16,229	30-77	4,318	5,009	9,327	http://www.fhi.no/artikler/?id=28261
MoRo II (The second part of the Romsås in Motion Study)	2003	5,535	34-70	899	1,096	1,995	http://www.fhi.no/artikler/?id=28254
CONOR (Cohort Norway)	1994-2003	309,742	20-103	87,157	92,928	181,891*	http://www.fhi.no/artikler/?id=28138

* Number of participants equals those who attended the survey and/or answered at least one questionnaire and signed a written consent. 7,460 persons participated in a second CONOR survey and 1 person participated in a third. Thus, the total numbers of participants with consent were 174,430.

† The numbers include all individuals invited. The individual surveys could have published papers with slightly different total numbers.

‡ HUSK: All 40-44 years and those participating in a study in 1992-93 born 1950-51 and 1925-27; Oslo II: All those invited to the Oslo Study 1972-73, except those invited to HUBRO and MoRo I (Invited in 1972/73: all men born 1923-32 and 7% random sample of those born 1933-52); Tromsø V: All 30, 40, 45, 60, 75 years and all those participating in phase II in Tromsø IV - which included: all born 1920-1939, 5-10% sample of other age groups attending phase I, all women born 1940-44; I-HUBRO: 30% random sample of people born in Pakistan, all born in Turkey, Sri Lanka, Iran, Vietnam - except those invited to HUBRO; MoRo II: All those participating in a study in 2 local districts in Oslo in 2000 (MoRo

I) born 1933-1969 – except those participating in HUBRO; TROFINN: All 30, 40, 45, 60, 75 years and all those participating in three Finnmark studies in the period 1974-1988 – which included: All born 1925-1947, all born 1948-1968 invited to Finnmark I, II or III.
§ 2,515 more men who belonged to the Oslo II cohort, also belonged to the HUBRO cohort, and were only invited to HUBRO. Of these 1,320 men participated. They are only counted as invited to HUBRO. 50 more men belonged to the MoRo-cohort, and are only counted as invited there.
# Include 17,308 invitees (31 and 46 years – additional cohorts) who were not reminded. The attendance-rate of these was low.
** 7,166 of these participated also in Tromsø IV.
†† Include 4,116 persons (20-30 years – additional cohort) who were not reminded. The attendance-rate of these was very low.
‡‡ Include 18 of 25 municipalities in Troms and 10 of 19 municipalities in Finnmark. The other municipalities participated in Tromsø V and in SAMINOR, i.e. a health survey in communities with Sámi and Norwegian population, at the same time.

Table 2. Reference papers to the 10 participating CONOR studies.

Tromsø IV: Wilsgard T. Longitudinal analyses of cardiovascular risk factors. The Tromsø study 1974-1995. ISM skriftserie nr. 65. Tromsø, Norway: Institute of Community Medicine, University of Tromsø, 2002.

HUNT II: Holmen J, Midthjell K, Krüger Ø, Langhammer A, Lingaas Holmen T, Bratberg GH, Vatten L, Lund-Larsen PG. The Nord-Trøndelag Health Study 1995-97 (HUNT 2): Objectives, contents, methods and participation. Nor J Epidemiol 2003; 13: 19-32.

HUSK: Bjelland I, Tell GS, Vollset SE, Refsum H, Ueland PM. Folate, vitamin B12, homocysteine, and the MTHFR 677C->T polymorphism in anxiety and depression: the Hordaland Homocysteine Study. Arch Gen Psychiatry 2003 Jun;60(6):618-26 - and

Sanne B, Mykletun A, Dahl AA, Moen BE, Tell GS; Hordaland Health Study. Occupational differences in levels of anxiety and depression: the Hordaland Health Study. J Occup Environ Med 2003;45:628-38.

Oslo II: Lund Håheim L, Holme I, Hjermann I, Søgaard AJ, Lund-Larsen PG, Leren P. Resultater fra Oslo-undersøkelser blant de samme menn i 1972/3 og i år 2000. Endring i risikofaktorer for hjerte- og karsykdom. Tidskr Nor Laegefor (Cond accepted)

HUBRO: Søgaard AJ, Selmer R, Bjertness E, Thelle D. The Oslo Health Study. The impact of self-selection in a large, population-based survey. Int J Equity Health 2004:3: 1-24. Online: http://www.equityhealthj.com/content/3/1/3

OPPHED: Only web-site - http://www.fhi.no/artikler/?id=28233

Tromsø V: Johnsen SH, Fosse E, Joakimsen O, Mathiesen EB, Stensland-Bugge E, Njølstad I, Arnesen E. Monocyte count is a predictor of novel plaque formation: a 7-year follow-up study of 2610 persons without carotid plaque at baseline the Tromso Study. Stroke. 2005;36(4):715-9.

I-HUBRO: Holvik K, Meyer HE, Haug E, Brunvand L.Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Norway: the Oslo Immigrant Health Study. Eur J Clin Nutr. 2005;59:57-63.

TROFINN: Only web-site - http://www.fhi.no/artikler/?id=28260

MoRo II: Jenum AK,. Anderssen SA, Birkeland KI, Holme I, Graff-Iversen S, Lorentzen C, Ommundsen Y, Raastad T, Ødegaard AK, Bahr R. Promoting physical activity in a low-income multi-ethnic district: behavioural, psychological and biological effects of a pseudo-experimental community intervention study to reduce risk factors for diabetes and cardiovascular disease (submitted)

CONOR: Engeland A, Søgaard AJ. CONOR (Cohort NORway) – en oversikt over en unik forskningsdatabank. Nor J Epidemiol 2003;13:73-7 - and Magnus P, Arnesen E, Holmen J, Stoltenberg C, Søgaard AJ, Tell GS. CONOR (Cohort NORway): historie, formål og potensiale. Nor J Epidemiol 2003;13:79-82.

Table 3 Number of participants in Cohort Norway (1994-2003) according to gender and age-groups (at the time they attended the screening station). If participating in more than one study, only the last one is counted.

	Men	Women	Total
Age	N	N	N
<20	116	148	264
20-29	5 884	7 236	13 120
30-39	13 322	15 547	28 869
40-49	27 969	32 148	60 117
50-59	10 517	10 176	20 693
60-69	12 229	10 373	22 602
70-79	13 119	11 883	25 002
80+	1 460	2 303	3 763
Total	84 616	89 814	174 430

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COHORT PROFILE

Cohort Profile: Cohort of Norway (CONOR)

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How did the study come about?

A number of large population-based cardiovascular surveys have been conducted in Norway since the beginning of the 1970s. The surveys were carried out by the National Health Screening Service in cooperation with the universities and local health authorities. All surveys comprised a common set of questions, standardized anthropometric and blood pressure measurements and non-fasting blood samples that were analysed for serum lipids at the Ullevål Hospital Laboratory. These surveys provided considerable experience in conducting large-scale population-based surveys, thus an important background for the Cohort of Norway (CONOR). In the late 1980s the Research Council of Norway established a programme in epidemiology. This also gave stimulus to the idea of establishing a cohort including both core survey data and stored blood samples. In the early 1990s, all universities, the National Health Screening Service, The National Institute of Public Health and the Cancer Registry discussed the possibility of a national representative cohort.[1] The issue of storing blood samples for future analyses raised some concern and it was discussed in the parliament. In 1994, the Ministry of Health appointed the Steering Committee for the CONOR collaboration. In 1994–95, the fourth round of the Tromsø Study was conducted, and became the first survey to provide data and blood samples for CONOR. During the years 1994–2003, a number of health surveys that were carried out in other counties and cities also provided similar data for the network. So far, 10 different surveys have provided data and blood samples for CONOR (Figure 1). The administrative responsibility for CONOR was given to the Norwegian Institute of Public Health (NIPH) in 2002. The CONOR collaboration is currently a research collaboration between the NIPH and the Universities of Bergen, Oslo, Tromsø and Trondheim.

The purpose of CONOR

The CONOR cohort has not been established on the basis of any single hypothesis but is rather a multipurpose study. The ambition was to set up a sufficiently large enough cohort to study aetiological factors for a wide range of diseases. Additionally, this cohort should make it possible to describe Norwegian men and women in terms of distribution of exposures and health status according to time, place and socio-economic factors.

In 2002, CONOR and the Norwegian Mother and Child study (MoBa),[2] received a 5-year grant from the Norwegian Research Council to build a technology platform under the Functional Genomics programme (FUGE), called the Biobanks for Health in Norway (Biohealth) platform.[3] The overall aim was to investigate separate and combined effects of genes and environment on the risk of disease.

Who is in the sample?

Altogether 309 742 individuals were invited to the 10 surveys based on the 11-digit personal identifier and addresses from the Population Registry of Norway.[4] The goal is to include 200 000 participants. We defined those who attended the survey and/or answered at least one questionnaire and signed a written informed consent as participants. The numbers in Table 1 include individuals who participated and had given their written consent for research and linkage to health registries. A total of 7309 persons participated in two CONOR surveys, and one person participated in three. Thus, the total number of

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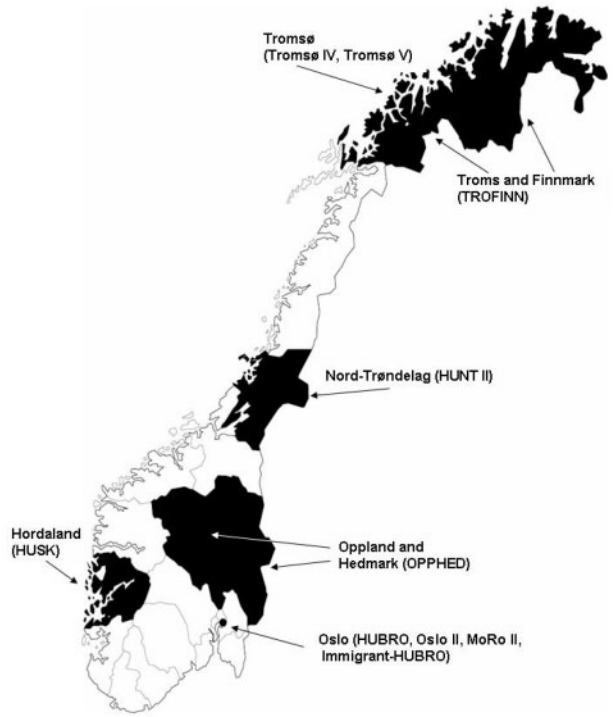

Figure 1 Map of Norwegian counties with location of each sub-study included in cohort of Norway (CONOR)

individuals in the CONOR cohort is 173 236. The distribution of age at the first examination and the number of deaths during follow-up through 2003 is given in Table 2. The individual surveys may have published papers with slightly different total numbers. Sampling procedures differed somewhat between the individual studies. The web site for each study contains more detailed information (Table 1).

What has been measured?

In all the CONOR surveys, the data collection followed a standard procedure. Letters of invitation were mailed about 2 weeks before the time of appointment and included a questionnaire and a brochure with the aims of the study and information about the examinations and procedures. At the screening, this initial questionnaire was collected from the attendees, participants underwent a physical examination and a non-fasting blood sample was drawn. In most studies, the participants were given one or two supplementary questionnaires, which they were instructed to fill in at home and return by mail in pre-addressed stamped envelopes.

About 4 weeks after attending the examination, a letter with selected results from the examination and blood tests was sent to all participants. Those with the highest scores of cardiovascular risk (a modified Framingham risk score based on multiplying the relative risks attributable to the subject's gender, serum cholesterol, systolic blood pressure the number of cigarettes currently smoked per day and family history of

Table 1 Number of invited and participating subjects in cohort of Norway (CONOR) 1994–2003

Name of the study	Year of survey	Number invited	Invited age-groups in years	Number of participants[a]			
				Men	Women	Total	Web address
Tromsø IV (The fourth Tromsø Study)	1994–1995	37 558	25+	12 797	14 128	26 925	http://uit.no/tromsoundersokelsen/tromso4/2
HUNT II (The second North-Trøndelag Study)	1995–1997	94 196	20+	30 441	34 576	65 017	http://www.hunt.ntnu.no/
HUSK (The Hordaland Health Study)	1997–1999	38 587	40–44, 46–47, 70–72	11 678	13 851	25 529	http://www.uib.no/isf/husk/
Oslo II (The second Oslo Study)	2000	14 209	48–77	6919		6919	http://www.fhi.no/artikler/?id=54685
HUBRO (The Oslo Health Study)	2000–2001	58 660	30, 31, 40, 45, 46, 59/60, 75/76	9509	11 852	21 361	http://www.fhi.no/artikler/?id=54464
OPPHED (The Oppland and Hedmark Health Study)	2000–2001	22 327	30, 40, 45, 60, 75	5602	6661	12 263	http://www.fhi.no/artikler/?id=28233
Tromsø V (The fifth Tromsø Study)	2001	10 353	30+	3440	4457	7897	http://uit.no/tromsoundersokelsen/tromso5/2
I-HUBRO (The Oslo Immigrant Health Study)	2002	12 088	20–60	1877	1737	3614	http://www.fhi.no/artikler/?id=28217
TROFINN (The Troms and Finnmark Health Study)	2002	16 229	30–77	4196	4836	9032	http://www.fhi.no/artikler/?id=28261
MoRo II (The second part of the Romsås in Motion Study)	2003	5535	34–70	896	1093	1989	http://www.fhi.no/artikler/?id=28254
CONOR (Cohort Norway)[a]	1994–2003	309 742	20–103				
Sum of participants				87 355	93 191	180 546	http://www.fhi.no/artikler/?id=28138
Sum of individuals				84 153	89 083	173 236	

[a]Number of participants equals those who attended the survey and agreed that information from the CONOR survey and blood samples can be linked to other registers and used in research. A total of 7310 individuals participated in more than one survey. Thus, the total number of individuals equals 173 236.

coronary heart disease) were advised to visit their own general practitioner, and in some cases offered a follow-up examination at the local hospital.[5]

Measures

Only a restricted core set of measurements and questionnaire responses constitute the CONOR data. Most individual studies that contribute to CONOR have more detailed measurements and questionnaire data. In the following section we describe the key core measurements that all studies contribute to CONOR; at the end we briefly describe some of the additional measurements that are in some of the contributing individual studies. All surveys were carried out in collaboration with the National Health Screening Service, Oslo (now the NIPH). Experienced and trained personnel conducted all procedures. Non-fasting serum total- and HDL-cholesterol, glucose and triglycerides were measured directly by an enzymatic method (Boehringer 148393, Boehringer-Mannheim, Federal Republic of Germany—from 2000 Hitachi 917 auto analyzer, Roche Diagnostic, Switzerland).

The Department of Clinical Chemistry, Ullevål University Hospital, Oslo, performed all laboratory assessments except for HUNT II (The second North-Trøndelag Study) where the analyses were performed at the Department of Clinical Chemistry, Levanger Hospital, Levanger. In Tromsø IV and V, cholesterol and triglycerides were measured at the Department of Clinical Chemistry, University Hospital North-Norway, Tromsø. Calibration procedures were carried out between these laboratories in connection with the surveys (Dr P.G. Lund-Larsen, National Health Screening Service, personal communication). An acceptable stability of the laboratory analyses over time in the population surveys has been reported.[6]

Heart rate, systolic and diastolic blood pressures were measured by an automatic device (DINAMAP, Criticon, Tampa, FL,USA). After 2 min of seated resting, three recordings were made at 1-min intervals. Mean values of the second and third systolic blood pressure measurements were used in calculating the cardiovascular risk score (CVD risk score) (Tverdal, 1989 5/id). The stability of the blood pressure measures has been evaluated and deemed acceptable.[7]

Body weight (in kilograms, one decimal) and height (in centimetres, one decimal) was measured according to a standard protocol with the participants wearing light clothing without shoes (manually recorded until 2000 and after that with an electronic Height and Weight Scale). Body mass index (BMI) was calculated as kilograms per square metre. Waist circumference was measured at the umbilicus to the nearest centimetre and with the subject standing and breathing normally. In obese individuals, waist circumference was defined as the midpoint between the iliac crest and lower margin of ribs. Hip circumference was measured as the maximum circumference around the buttocks. Both waist and hip were measured with a measuring tape of steel—which was emphasized to be placed horizontally. The waist–hip circumferences were used to calculate the waist–hip ratio.

Most individual studies that contribute to CONOR have several additional measurements—for example, extra samples of blood, ECG and ultrasonographic examination of carotid artery and abdominal aorta. Four of the study sites measured bone mineral density (DEXA and/or SXA) and have established a research group called Norwegian Epidemiologic Osteoporosis Studies (NOREPOS).[8] Altogether, around 28 000 individuals have had their bone mineral density measured and currently a number of collaborative studies are carried out.

The CONOR questions

All surveys used about 50 core CONOR questions agreed upon before the first CONOR survey in Tromsø in 1994. The exact wording of the questions is available at the CONOR website (http://www.fhi.no/dav/CA11310499.doc). Some questions have been slightly modified over the years.

The CONOR questions cover the following main topics: self-reported health and diseases such as diabetes, asthma, coronary heart disease, stroke and mental distress, musculo-skeletal pains, family history of disease, risk factors and lifestyle, social network and social support, education, work and housing, some types of occupation, use of medications and reproductive history (women).

Several of the questions have been evaluated or validated and deemed acceptable.[9–18] The Population Registry of Norway that was used to identify eligible subjects, contains information about gender, date of birth, marital status, address and country of birth.

Blood samples

Blood samples were drawn from the CONOR participants. EDTA blood for CONOR and the other sub-surveys have normally been collected in 7 or 5 ml vacutainers. These vacutainers were made by different manufacturers but were normally made of polypropylene. DNA has been extracted from more than 90 000 specimens to medio 2007, and Biohealth intends to extract DNA from all samples by Spring 2008. The extracted DNA and an additional sample of 1.25 ml EDTA-blood will be stored at a national biobank storage site at HUNT/NTNU biobank in Levanger (Mid-Norway).

What has been found?

Although a number of analyses from each participating study have been conducted, the CONOR file has only recently been compiled and made available for research. The first CONOR project was anchored in NOREPOS describing urban–rural differences in forearm fractures.[19] Other methodological and validation studies have been completed as described above.

What are the main strengths and weaknesses?

The CONOR database has several strengths: it is population based including populations from various parts of Norway, both rural and urban. The 11-digit personal identification number makes it possible to link cohort participants to national health registries. At present, several large linkages to other registers have been or are in the process of being conducted. These include linkages with census-based data for the whole population and the Medical Birth Registry of Norway, Disability Registry, Cancer Registry of Norway. Tables 2 and 3 present number of deaths and new cases of cancer in CONOR since date of examination by linkage to the death and cancer registries. Other large linkages include data from the Norwegian Drug Prescription Database and information from

Table 2 Number of participants (*n*) and number of deaths until December 31, 2003 in the cohort of Norway (CONOR) by age at inclusion in the surveys

	Men		Women	
Age (years)	*n*	Deaths	*n*	Deaths
<25	2037	15	2512	6
25–34	12 028	56	14 658	22
35–44	21 544	158	24 399	123
45–54	17 009	296	18 474	218
55–64	11 698	604	11 903	325
65–74	13 654	2008	9399	991
⩾75	6183	2138	7738	2141
Total	84 153	5279	89 083	3826

Table 3 Follow-up 1994–2006[a] of the CONOR cohort members. Number of cases of first cancer diagnosis in the Norwegian Cancer Registry after initial CONOR examination

	Men		Women	
	<70 years	⩾70 years	<70years	⩾70 years
Cancer site (ICD-7)				
Colorectal cancer (152-4)	582	631	528	476
Trachea, bronchus and lung (162)	191	300	133	110
Breast (170)	1	4	936	271
Prostate (177)	607	995	0	0
Bladder and other urinary organs (181)	102	235	33	51
Melanoma of skin (190)	170	89	238	82
All sites (including basal cell carcinoma of skin)	3180	3971	5411	2515

[a]Follow-up approximately through March 2006.

health surveys in several counties in the 1970s. There are also a number of disease registers that may be linked to the CONOR database. Earlier this year, the government passed a new legislation to make the national hospital discharge register personal identifiable, which would be possible to link to CONOR in the near future.

A major strength of CONOR is its sample size that means it would be able to make a unique contribution to establish main genetic effects and gene–environmental interactions, since precise and robust estimation of these effects requires very large sample sizes.[20,21] Our aim is to reach 200 000 individuals with blood samples and extracted DNA and we anticipate reaching this sample size by Spring 2008. For some hypotheses, it would be most efficient to employ a nested case control study design within CONOR, and we anticipate several such studies in the future. This comparatively large sample size means cases for a number of common and less common diseases may be identified from various sources.

There are some important weaknesses: the overall participation rate is 58% and is lowest in the surveys in Oslo and other urban areas and became lower throughout the study period. However, the overall participation rate is influenced by low participation rate in those aged ⩽30 years. The study population is somewhat heterogeneous as it includes sampling from 10 geographical areas with various age groups included over a 10-year period. The number of core variables is limited, and in some cases the wording of questions is slightly changed over the years.

Can I get hold of the data? Where can I find out more?

Guidelines have been developed for projects using data from CONOR (www.fhi.no). These shall ensure that projects will have a high scientific quality, facilitate quick publication of results from CONOR and make the data accessible for research. Research groups may apply for access. A project leader must be appointed. Researchers not residing in Norway are advised to seek contact with Norwegian counterparts. The study objectives should be within the broader aims of CONOR. Further details of these guidelines are provided at the CONOR website.

Applications and enquiries can be sent electronically to the Norwegian Public Health Institute (email: conor@fhi.no). Applications will be evaluated by the CONOR Steering Committee.

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Appendix 3

Project name	The role of smoking and socio-economy in explaining health disparities in breast cancer and colorectal cancer incidence and mortality
	Variables Description
Authors	Eivind Bjerkaas and Ranjan Parajuli
Finalized	
Date of masterfile	16 March 2012
Name of masterfile	master_sc_v_112.zip

Inclusions selected on survey from data manager:

3 Counties I	62 220
3 Counties II	9 188
3 Counties III	22 538
CONOR	137 182
40 Years (total)	403 691
Oslo I	17 973
Sum	652,792

Analytical cohort: 602, 242(m=299,376, f=302,866)

Cancer cases in cohort by smoking status

	Never-smokers	Former-smokers	Current-smokers	Total
Breast cancer	3,028	1,581	2,881	7,490*
Colon cancer	1,368	1,099	1,531	3,998
Rectal cancer|	648	602	926	2,176

*Only among women

Cancer Mortality in cohort by smoking

	Never-smokers	Former-smokers	Current-smokers	Total
Breast cancer	459	216	431	1,106*
Colon cancer	1,607	443	642	1,607
Rectal cancer|	202	181	343	726

*Only among women

Daily smokers

The daily-smokers variable in CONOR was based on question "Do you smoke daily?" (In CONOR, this question includes cigarettes, pipe and cigar daily smokers, according to CONOR documentation (variable a8_0)).

In Oslo health study I, the question "Do you smoke daily?" is used for current smokers. Answering "yes" to this question will be current smokers.

In the Norwegian counties study (I, II and III), this was based on the question "Do you smoke daily now?" A positive answer will give a categorization of daily smoker. (We do not consider other answers regarding smoking to classify the current smokers.)

40 years I was based on the question "Do you smoke daily now?" Answering "Yes" will be current smokers.

40 years II was based on the questions "Do you smoke cigarettes daily? Or "Do you smoke cigar daily?" "Do you smoke pipe daily?" answering "Yes" to any of these questions gives daily-smokers.

The 40 years III and IV was based on "Do you smoke cigarettes daily?" or "Do you smoke cigar daily?" or "Do you smoke pipe daily?" If participants have answered "Yes" on any of the above questions, then they are categorized as current smokers.

Former smokers

After we got all current smokers, then we categorized remaining participants in the former-smokers category as below:

In CONOR if participants have valid answer (greater than 0) in questions "How long time since quit smoking (a_9)?" or numbers of cigarettes smoking daily (a_10) or "How old were you when you start smoking (a_11)? or "How many years of smoking in total(a_12_1).?" ,then categorized as former- smokers.

Oslo study I: Those who answered "Yes" to the question "Have you smoked cigarettes daily previously" (tidlrok) in Oslo health study were classified as former smokers. In addition, we check if a valid value on (tidsidsl) "How long since quitting?!", if there is a valid value then we categorized them as former smokers.

In the Norwegian counties those answering "Yes" to the questions "Have you smoked cigarettes daily previously?" were categorized as former-smokers. If answering any value (except zero) to the question "How long since you quit smoking?", and "How many years have you smoked daily?" and "how many cigarettes do you or did you smoke daily?", and <u>not</u> a current smoker, then categorized as a former smoker.

40 years I and II is done similar as the Norwegian Counties. Those answering "Yes" to the questions "Have you smoked cigarettes daily previously?" were categorized as former-smokers. If answering any value (except zero) to the question "How long since you quit

smoking?", and "How many years have you smoked daily?" and "how many cigarettes do you or did you smoke daily?", and not a current smoker, then categorized as a former smoker.

(Please note the comment from Randi about classification this question in 40 years II.)

40 years III and IV: any answer more than zero in the question "if you have smoked previously, how long since you quit?" then a former smoker. (As answering option is in years, we might misclassify those answering zero because they have quit less than 1 year ago.) Also, answering any value more than zero to the questions "how many cigarettes do you smoke or did you smoke daily", "how old were you when you started to smoke daily?" or "how many years have you smoked daily?", then classified as former smoker, if not already classified as a current smoker.

After we have categorized current and former-smokers, from the remaining group of participants, we categorized never-smokers in the following ways:

Never smokers

CONOR: Answering "No" to the question "Do you smoke daily (a8_0)?" then never smokers.

In the Norwegian counties study, participants answering "No" in the questions "Do you smoke cigarettes daily?" or Do you smoke cigars daily?" or Do you smoke pipes daily?" and if answering "No" to the question "Have you smoked cigarettes daily previously?" were categorized as never smokers.

In the 40 years I and II we did the same in the Norwegian counties. Participants answering "No" in the questions "Do you smoke cigarettes daily?" or "Do you smoke cigars daily?" or "Do you smoke pipes daily?" and if answering "No" to the question "Have you smoked cigarettes daily previously?" were categorized as never smokers.

40 years III: Participants answering "No" to the question "Do you smoke cigarettes daily?" Do you smoke cigars daily?" or "Do you smoke pipes daily?" and not answering the question "if you have smoked previously, how long since you quit?", then categorized as never smoker.

40 years IV: Participants answering "No" to the questions "Do you smoke cigarettes daily?" or "Do you smoke cigars daily?" or "Do you smoke pipes daily ?" and not answering the question "if you have smoked previously, how long since you quit?", then they are categorized as a never smoker. In addition we include the question unique for IV: "Never smoked daily?", then a never smoker. (Brings any records from missing to never, not from daily or former.)

Oslo: Those answering "No" to the both questions "Do you smoke daily?" and answering "No" to the question "Have you smoked cigarettes daily previously?" were categorized as never-smokers.

Ever-smokers (daily+ former- smokers)

Duration of smoking

The duration of smoking variable was based on two questions. In the CONOR and the Oslo health study I, daily and former smokers answered the questions "Numbers of years smoked?" In the Norwegian counties study and the 40 years cohort, subjects answering that they were ever smokers were asked "How many years all together have you smoked daily?" Duration of smoking will be further categorized into three groups (1-29, 30-39 and >40)(Ref: Cigarette smoking and risk of colorectal cancer among Norwegian women). Suggestion: Look in EPIC article for different categories which can be appropriate to use in our cohort)

Age at smoking initiation

The age at smoking initiation variable in CONOR and 40 years III+IV was based on question "How old were you when you started smoking"?

In the Norwegian counties study, 40 years I and II cohort and Oslo health study I, this variable is constructed. We subtracted total years of smoking from age at enrollment to construct the age at smoking initiation. This variable was available for both daily and former smokers.

Numbers of cigarettes

The numbers of cigarettes variable was based on question "Numbers of cigarettes smoked daily?" in CONOR and Oslo health study I. In the Norwegian counties study(I, II and III) and 40 years cohort(I,II,III and IV) , ever-smokers were asked "How many cigarettes do you smoke/smoked daily?" to extract information on numbers of cigarettes. We will further categorized it into three groups (1-9, 10-14 and > 15) (Ref: Gram et al: Cigarette smoking and risk of colorectal cancer among Norwegian women). This can be modified during the analysis by other categorizations if more groups needed.

Time since quitting smoking (former smokers only)

The time since quitting smoking variable was based on question "How long since you have quit smoking?" in CONOR, 40 years III and IV.

Answering option in CONOR and 40 years III and IV was "time in years" continuous variable. (rokslutp3 roykslutp4)

In the Norwegian counties study, Oslo health study I and 40 years I there were four different answering options:

a. Quit since 3 months
b. Quit since 3 months to 1 year
c. Quit since 1 to 5 years
d. Quit for more than 5 years

In 40 years II the question was "If you have smoked previously, how long since you quit" with answering options "less than one year" and "more than one year". (roykslutp2)

Answers > 60 years is set to missing as outlier (n=4).

Conclusion:

- For *current* smokers "time since quitting smoking" can be handled ok.
- For former smokers it is a problem for 40 years II because we can only differ between <1 year and > 1 year.
- We decide that *former smokers* from Norwegian Counties, 40 years I and II and Oslo I will be called missing in the continuous variable, but can still be handled as categorical variable with four options.

Latency

We have used information from several variables (see below.). For current smokers the information is good. For former smokers, we have information from CONOR and 40 years III and IV. The others are set to missing.
Latency is a constructed variable
Latency for current smokers:

a. Years between smoking initiation and cohort enrollment(latency 1)
   or
b. Years between smoking initiation and censoring/failures(latency 2)

For former-smokers

a. Years between smoking initiation and time since quitting

In some of the surveys, like in the Norwegian counties study 40 years I+II and Oslo health study I, we have "time since quitting" variable which was used for constructing latency for former-smokers was available only in four different options as:

1. Less than three months
2. Three months to 1 year
3. 1 year to 5 years
4. 5 years to more

Our main goal was to create a continuous latency variable which was not possible for former-smokers in these surveys.

a. Latency
   Latency 1 (Total years from smoking initiation and quitting or cohort enrollment – current smokers only)

b. Latency 2 (Total years between smoking initiation to failure/censoring – current smokers only)

c. Latency 3 (Total years between smoking initiation and quitting or cohort enrollment- former smokers only)
   "Only for CONOR, 40 years III and IV"

   # missing here includes if participants are from other surveys rather than CONOR, 40 years III and IV".

d. Latency 4 (Total years between smoking initiation to failure/censuring – former smokers only)
   "Only for CONOR, 40 years III and IV"

Pack- years of smoking

This is calculated as number of cigarettes smoked per day, divided by 20 and multiplied by the number of years smoked.

Pipe smokers

The “pipe_smoker_sc” variable yes/no comes from all our surveys.

The amount of pipe smoking *(packs pr week)* will come from 3C I, II, III, 40Y I, II, and Oslo I. Variable name “number_pipetobacco_sc”.

In Oslo 1 they only ask about nr of packs in 3 categories. We have estimated that if answering 0-0,5 pack will be 0,25 pack, 1-2 packs will be 1,25 and 2 packs will be 2 packs. Then they are categorized in the variable “number_pipetobacco_sc”.

Further, if any answer then considered “yes”, if no answer then considered “no”, in the “pipe_smoker_sc” variable.

(For BC analysis pipe smokers are disregarded due to very low number of female pipe smokers.)

Alcohol Variables

The alcohol variables are from the CONOR and the 40 years study III and IV. The 40 years study I and II, the Oslo study and the Norwegian county study has no alcohol information.

Teetotalers

In CONOR and 40 years study III and IV the question was “are you a teetotaler?” and there was a “yes/no” answering option.
We have added the persons who are light/moderate/heavy drinker from the “alcohol frequency” variable into the non-teetotalers group, to increase the numbers of non-teetotallers.

Alcohol frequency

Our alcohol frequency variable is constructed to become a light, moderate and heavy (n=42, drinker as categorical variable. In general, we have considered a heavy drinker to drink more than once a week, a moderate drinker once a week, and a light drinker to drink less than once a week.

CONOR
In the CONOR study the variable “drinking pattern” is a 1 to 5 categorical variable: 1. Drinking more than once a week 2. Drinking once a week. 3. 2-3 times pr month 4. Once a month. 5. Less than once a month. The following categorization has been made: if answering 1 in CONOR, then categorized as heavy drinker. If answering 2 in Conor, then categorized as a moderate drinker. In answering 3,4 or 5 in CONOR, then categorized as a light drinker.

40 years
There is no information about alcohol consumption in 40 years I and II. In 40 years III and IV the question was “how many times pr month do you drink alcohol?”. If drinking 5 times or

more pr week, then categorized as a heavy drinker. If drinking 4 times pr month (once a week) then categorized as a moderate drinker. If drinking less, then categorized as a light drinker.

The Norwegian counties study and Oslo health study I
No information.

Alcohol grams pr day

This variable has been constructed from information about drinking frequency and type of drink. According to the (ref: www.fhi.no), one glass of wine equals 14,4 grams of pure alcohol, one glass of beer equals 11,9 grams of pure alcohol, and one glass of spirits equals 12,8 grams of pure alcohol. Values larger than 100 grams pr day has been considered extreme, and have been set to missing (n=12).

CONOR
In CONOR the question was "how many glasses of wine / beer / spirits do you drink in a two weeks period?" The calculated amount of grams was divided on 14, to get the alcohol consumption per day.

40 years
In 40 years III and IV the question was "how many glasses of wine / beer / spirits do you drink in a two weeks period?" (Calculation as above).

BMI

Height and weight were recorded at the health station for all participants, and body mass index (BMI) was calculated by standard formula (ref). Observations with extreme values for height and weight were set to missing as follows: height <100 or >250 cm, weight <35 or >250 kg, BMI <15 or >60 kg/m2.(Ref: T Stocks Me-Can Cohort Profile 2009).

BMI is categorized in 4 different groups according to WHO classifications in following order:

1. <18.5
2. 18.5-24.9
3. 25-29.9
4. >30

In the analysis we will collapse category 1 and 2 due to low number in category 1 (1.17%) giving BMI as a 1-3 category.

Other variables

Menopause assessment (women only)

Women were categorized as pre-, peri- or postmenopausal. Only 10 per cent of our cohort was equal to, or older than 48 years old at inclusion, therefore most in our cohort was premenopausal at inclusion.

Questions about menopause were present in CONOR and 40 years III and IV as a continuous variable "age at menopause". In the County Study and in 40 years I and II, this was a question with 6 options: "

1=Ja, menopause inntrådt

2=Nei, menopause ikke inntrådt

3=Usikker om menopause

4=Gravid

5=primær amenorrhoe

6=Hysterectomy

Answering 1 and 6 were classified as postmenopausal, 2 and 4 were premenopausal, 3 and 5 were uncertain and classified as the other missing according to age (see below):

If missing information, women were classified as premenopausal if they were less than 46 years of age. If they were older than 55 years of age, they were classified as postmenopausal. Women who were between 46 and 55 years of age were classified as perimenopausal / unknown. (Ref: EPIC).

Oral contraceptive use (woman only)

We made the variable "oral contraceptive use" a binary variable (ever / never). In CONOR it was reported in questionnaires as current, former or never user, and the current and former category were collapsed into ever user by us. There is no information about OC in the County Study.
In the 40 years study, this information was initially collected through interviews, later from questionnaires. Due to inconsistent information from several of these studies, we have only used information from 40 year III in our study. This is in accordance with advice from tex. Anders.

Post- menopausal hormonal therapy (PMHT) (women only)

Post-menopausal hormonal therapy (PMHT) in CONOR was 5 category options, with different answering options for never users, former users, and for users of PHT with or without prescriptions. In the 40 years study, the answering options were ever, former, never. There is no information about PHT in the Norwegian counties study.

Menarche (women only)

Age at menarche was categorized as a continuous variable. Information about menarche is in CONOR and 40 years III and IV.

Comment from Anders: use average age for menarche?

Women reporting menarche at age 6 years old or less (n=9), or 22 years old or more (n=31), were set to missing.

Parity (women only)

Information about parity was provided by the Statistics Norway, and is the reported number of live born children at 31. December 2001. This is the official data and is more updated than the questionnaire.

Age at first childbirth (women only)

Variable created from information provided by the SSB, which provided the year for the persons first child, and birth year.
Year first childbirth – year born = age at first childbirth

Smoking exposure before first childbirth (woman only)

Year at first childbirth was given by the SSB.
Age at smoking initiation is a continuous variable in CONOR and 40 years III and IV.

The age at smoking initiation variable in CONOR and 40 years III+IV was based on question "How old were you when you started smoking"?

In the Norwegian counties study, 4o years I and II cohort and Oslo health study I, this variable is constructed. We subtracted total years of smoking from age at enrollment to construct the age at smoking initiation. <u>This variable was available for both daily and former smokers.</u>

We therefore have good information about smoking exposure before first childbirth, for both former and current smokers.

Formulas:

1. Year of survey assessment – total years of smoking = year of smoking initiation
   Year of smoking initiation – year of birth = age at smoking initiation

2. Age at enrollment - total years of smoking = age at smoking initiation

<u>Total: Age at smoking intiation</u>

<u>Year first childbirth – year smoking initiation = years of smoking before first childbirth</u>

Excluded:

- Male sex
- Non-smokers

- Smokers initiating after first childbirth
- No parity

In the variable exposure_before_first_childbirth are those with negative number (ie those initiating *after* first childbirth) not included.

Physical activity

The physical activity variable was created as a 1 to 4 categorical variable, with the variable description from CONOR as a reference: 1. Reading, watch TV, other sedentary activity, etc. 2. Walking, bicycling, etc. 3. Light sports, heavy gardening > 4 hours pr week. 4. Hard exercise, competitive sports regularly. In all the included studies except 40 years III, there were a 1 to 4 categorical variable.

In the 40 years III, there were two questions for physical activity: "how much light activity do you do pr week?", and "how much heavy activity do you do pr week", with a 1 to 4 answering option for both questions.

If answering 1 or 2 to I aktiv then 1
3 or 4 to Iaktiv then 2
1 or 2 to h_aktiv then 3
3 or 4 to h_aktiv then 4

Group 1: Light physical
Group 2: Mild physical activity
Group 3: Moderate physical activity
Group 4: Hard physical activity

Education

We have information about education level from SSB, and the 1970, 1980 and 1990 census. By consensus, we decide to use the highest level of education from the 1980 or 1990 census. If the information is missing, then we use the 1970 census. If no information from any census, then real missing.

Educational level was given in 1-8 categorical variables from SSB. Value 9 is not answered or unknown level of education:

1. 7 years primary school
2. 9-10 years primary/secondary school
3. Technical school, middle school, vocational school, 1-2 years senior school
5. University or university college level 1
6. University or university college level 2
7. University or university college level 3

8. University researcher level

9. Not answered or unknown level of education

These were merged into four levels of education as follows:

1: 1 and 2 low education level
2: 3 and 4 low/medium education level
3: 5 and 6 medium/high education level
4: 7 and 8 high education level

This made four education categories (new_ses4groups_NEW).

Income

As for education, information provided by SSB from the 1970, 1980, 1990. Information about income was categorized in different ways in the different census, which makes it difficult to compare the different time periods.

Income was categorized as follows: Distribution of all incomes at one census was categorized in quartiles. The first quartile was given value 1, the second quartile was given value 2, the third quartile was given 3, and the fourth quartile was given 4. This was done for all three census independently.

The highest quartile registered at either census counted for that individual. The income files were organized by Knut Hansen in the master file (income_max_quart).

SES

To create four groups for socioeconomic status (SES), income and education categories were added. The sum classified the individuals as follows:

A) 2 score= SES group 1
B) 3 and 4 score = SES group 2
C) 5 and 6 score= SES group 3
D) 7 and 8 score= SES group 4

Comment: we suggest creating 3 SES groups instead of 4. The reason for this is that the groups 2 and 3 will be very homogenous, if we create 4 categories.

If we create 3 categories, we will have a low, middle and high SES category, which is a common way of classifying social groups. It probably gives a more correct picture of the data, as the most important issue about SES will be to differ between low and high SES. We therefor also create a variable (ses3groups_NEW), where the above group 2 and 3 is merged.

eb
rp

Appendix 4

Table: Prospective studies published in the period 2002-2013 examining the association between smoking and risk of colorectal cancer

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/ comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Terry et al. (2002), USA, Canadian National Breast Screening Study (NBSS)	Multicenter randomized controlled trial of mammography screening. 89835 women aged 40-59 years. Follow-up 1982-1993. Incident colorectal cancer or death was ascertained by computerized record linkage to the National Mortality Database and the Canadian Cancer Database. Participants completed a self-administered questionnaire.	363 colon, 164 rectal incident cases	Never smokers Ex-smokers Current smokers *Cigarettes/d* 1-9 10-19 20-29 30-39 40+ p trend *Years smoked* 1-9 10-19 20-29 30-39 40+ p trend *Years since smoking commended* 1-9 10-19 20-29 30-39 40+ p trend	274 145 108 56 78 93 12 8 42 53 83 61 12 12 24 85 105 22	1.0 1.03 (0.80-1.33) 0.93 (0.71-1.24) 0.89 (0.61-1.28) 0.94 (0.67-1.32) 1.16 (0.87-1.53) 0.87 (0.44-1.69) 0.63 (0.26-1.52) 0.99 0.93 (0.61-1.40) 0.90 (0.62-1.30) 1.04 (0.77-1.42) 1.16 (0.83-1.63) 0.68 (0.25-1.86) 0.66 1.50 (0.74-3.05) 0.84 (0.50-1.40) 0.91 (0.67-1.24) 1.05 (0.79-1.39 1.12 (0.62-2.04) 0.98	1.0 1.44 (1.00-2.06) 1.17 (0.78-1.75) 1.31 (0.80-2.14) 1.98 (1.32-2.96) 0.97 (0.61-1.56) 0.72 (0.23-2.29) 0.90 (0.28-2.85) 0.82 1.31 (0.75-2.28) 1.24 (0.75-2.05) 1.37 (0.89-2.11) 1.12 (0.65-1.94) 3.14 (1.33-7.42) 0.07 1.76 (0.64-4.82) 0.97 (0.47-2.02) 1.11 (0.72-1.73) 1.52 (1.01-1.26) 2.27 (1.06-4.87) 0.03		Adjusted for age (in 5-year age groups), BMI (quartiles), educational level, vigorous physical activity, hormone replacement therapy, menopausal status and alcohol intake
Tiemersma et al. (2002), Netherlands, Monitoring Project on Cardiovascular Disease Risk Factors	Nested case-control study, controls frequency matched for age and gender. Using data from the prospective	102 incident cases, 537 controls	Never smokers Former smokers Current smokers p trend	30 43 29			1.0 1.01.4 (08-2.5) 0.9 (0.5-1.7) 0.27	Adjusted for age, sex, center, coffee and alcohol consumption and body mass index.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/ comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Tiemersma et al. (2002), (contd)	Monitoring Project on Cardiovascular Disease Risk Factors conducted in Amsterdam, Maastricht and Doetinchen. Including persons aged 20-59 years. Follow-up 1987-1998. Incident cancer was obtained by record linkage with the Netherlands Cancer Registry and with the three regional cancer registries. Participants completed a self-administered questionnaire.		*Smoking duration (years)* *Former smokers* 1-15 16-30 >30 p trend *Current smokers* 1-15 16-30 >30 p trend *Cigarettes/d* *Former smokers* 1-10 11-20 >20 p trend *Current smokers* 1-10 11-20 >20 p trend *Time since quit smoking* >18 years 9-18 years 0-8 years p trend	 13 23 7 3 7 19 12 21 10 10 14 5 18 16 9			 1 (ref.) 2.7 (1.03-7.4) 3.2 (1.04-9.8) 0.04 1 (ref.) 0.4 (0.1-1.9) 1.9 (0.5-8.2) 0.28 1 (ref) 2.1 (0.9-5.0) 1.7 (0.6-4.6) 0.15 1 (ref.) 1.1 (0.4-2.8) 1.2 (0.3-4.0) 0.75 1 (ref.) 2.6 (1.0-6.5) 2.2 (0.8-5.5) 0.10	Adjusted for age, sex, center, coffee and alcohol consumption and body mass index.
Limburg et al. (2003); USA; Iowa Women's Health Study	Baseline questionnaire was mailed in January 1986 to randomly selected women aged 55-69 years, 41836 (42,7%) responded. Incident CRC cases	869 incident CRC cases and 249 fatal CRC cases	***CRC incidence*** Never smokers Current smokers Former smokers p trend	 558 122 189			 1.0 1.10 (0.89-1.37) 1.21 (1.01-1.45) 0.14	Adjusted for age, BMI, waist-hip ratio, physical activity level, hormone replacement therapy, alcohol consumption, intake of methionine, total calories, fat,

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/ comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Limburg et al. (2003); (cont)	were identified through the IOWA Cancer Registry, Follow-up continued through December 1999		*Age at initiation* ≤30 years >30 years p trend *Total duration (yrs)* 1-19 20-39 ≥40 p trend *Cigarettes/d* 1-19 20 >20 p trend Pack-years 1-19 20-39 ≥40 p trend ***CRC Mortality*** Never Current smokers Former smokers p trend *Age at initiation* ≤30 years >30 years p trend	 287 24 71 129 111 163 99 49 123 105 83 158 45 46 81 10			 1.20 (1.02-1.40) 0.90 (0.59-1.39) 0.03 1.16 (0.89-1.52) 1.08 (0.88-1.32) 1.30 (1.04-1.63) 0.03 1.15 (0.95-1.38) 1.23 (0.97-1.54) 1.12 (0.82-1.54) 0.08 1.15 (0.93-1.41) 1.16 (0.92-1.45) 1.21 (0.94-1.56) 0.06 1.0 1.58 (1.09-2.29) 1.14 (0.80-1.62) 0.02 1.34 (1.00-1.80) 1.04 (0.48-2.22) 0.14	sucrose, red meat, calcium, folate, and vitamin E.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/ comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Limburg et al. (2003); (cont)			*Total duration (yrs)* 1-19 20-39 ≥40 p trend *Cigarettes/d* 1-19 20 >20 p trend *Pack-years* 1-19 20-39 ≥40 p trend	 24 32 35 47 33 11 36 27 28			 1.53 (0.96-2.43) 1.02 (0.67-1.53) 1.55 (1.04-2.31) 0.07 1.27 (0.89-1.80) 1.50 (0.99-2.28) 1.07 (0.57-2.00) 0.14 1.30 (0.88-1.91) 1.08 (0.69-1.70) 1.63 (1.05-2.49) 0.05	Adjusted for age, BMI, waist-hip ratio, physical activity level, hormone replacement therapy, alcohol consumption, intake of methionine, total calories, fat, sucrose, red meat, calcium, folate, and vitamin E.

Reference, location, name of study	**Cohort description**	**No. of subjects**	**Smoking categories**	**No of cases**			**Relative risks (95%CI or *p* value)**			**Adjustment factors/comments**
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Otani et al. (2003), Japan, The Japan Public Health Center-based prospective study on cancer and cardiovascular disease (JPHC study)	Cohort I started 1990 in 5 areas in 5 prefectures (Iwate, Akita, Nagano, Okinawa, Tokyo) and covered all residents aged 40-59. Cohort II started 1993 in 6 areas in 6 prefectures (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa, Osaka) and covered all residents aged 40-69. 57591 men and 59103 women. Active follow-up 1990-1999, 1993- 1999 using data of Ministry of Health, Labor and Welfare for deaths and the JPHC cancer registry for incidence. Participants completed a self-administered questionnaire.	447 incident cases (299 colon cancers, 148 rectal cancers)	Never smokers Former smokers Current smokers *Pack years* <20 20-29 30-39 40+ p trend	53 86 160 17 31 55 54	25 38 85 16 19 18 29	78 124 245 33 50 73 83	1.0 1.4 (0.96-1.9) 1.4 (0.99-1.9) 0.9 (0.5-1.5) 1.2 (0.8-2.0) 1.7 (1.1-2.4) 1.3 (0.9-2.0) 0.16	1.0 1.2 (0.7-2.0) 1.4 (0.9-2.3) 1.6 (0.9-3.0) 1.5 (0.8-2.7) 1.0 (0.6-1.9) 1.4 (0.8-2.3) 0.48	1.0 1.3 (0.98-1.7) 1.4 (1.1-1.8) 1.1 (0.8-1.7) 1.3 (0.9-1.9) 1.4 (1.05-2.0) 1.4 (0.99-1.8) 0.47	Adjusted for age (5 year groups), family history of colorectal cancer, BMI, alcohol consumption, physical exercise and 9 Public Health Center areas

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Shimizu et al. (2003), Japan	Cohort study with 31152 residents in Takayama, Japan who were 35 years old or older. Follow up 1993- 2000. Participants completed a self-administered questionnaire.	198 colon and 97 rectal incident cases	*Men* Never ≤20 pack-years >20 pack-years p trend *Women* Never ≤10 pack-years >10 pack-years p trend	 16 41 47 68 4 5	 7 16 34 32 4 2		 1.0 1.36 (0.79-2.33) 1.37 (0.81-2.32) 0.19 1.0 0.59 (0.21-1.62) 0.77 (0.30-1.96) 0.54	 1.0 1.33 (0.57-3.12) 2.44 (1.12-5.30) 0.04 1.0 1.76 (0.60-5.14) 0.94 (0.21-4.16) 0.63		Adjusted for age, height, BMI, alcohol intake and years of education.
van der Hel et al. (2003), Netherlands, Diagnostisch Oderzoek Mammacarcinoom (DOM)	Nested case-control study in a population based screening program with 27722 women. Baseline assessment by questionnaire.	191 colon and 67 rectal cancer incident cases, 871 controls	Never Ever smoked	119 64	43 23	162 87	1.0 1.36 (0.97-1.92)	1.0 1.31 (0.76-2.25)	1.0 1.35 (0.99-1.83)	Adjusted for age and BMI.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases		Relative risks (95%CI or *p* value)			Adjustment factors/comments
						Colon cancer	Rectal cancer	Colorectal cancer	
Wakai et al. (2003), Japan, Japan Collaborative Cohort (JACC)	110792 inhabitants aged 40-79 completed a baseline questionnaire. They were enrolled from 45 study areas throughout Japan, total 59879 eligible subjects from 24 study areas with cancer registries Follow-up 1988-1997 by cancer registries.	408 colon cancer (219 men, 189 women) and 204 rectal cancer cases (147 men and 57 women)	*Men* Never smoker Former smokers Current smokers *Women* Never Former smokers Current smokers *Men* *Cigarettes/d* 0-19 20-39 40+ p trend *Age at starting smoking (yrs)* 26+ 23-25 20-22 <20 p trend *Years of smoking* 0-19 20-39 40+ p trend *Pack-years* 0-19 20-39 40-59 60+ p trend	 39 67 113 175 4 10 59 102 9 18 34 97 24 13 92 67 26 89 41 10 	 34 44 69 55 1 1 44 55 9 10 16 56 25 6 61 39 22 48 24 10 	 1.0 1.07 (072-159) 1.23 (085-178) 1.0 1.07 (0.39-2.92) 1.06 (055-2.02) 1.05 (0.70-1.58) 1.30 (0.89-1.89) 0.69 (0.33-1.43) 0.56 1.10 (0.62-1.93) 1.54 (0.97-2.44) 1.13(0.78_1.64) 1.04 (0.62-1.74) 0.76 0.99 (0.53-1.87) 1.31 (0.89-1.92) 1.07 (0.71-1.61) 0.52 0.92 (0.56-1.52) 1.43 (0.98-2.10) 1.11 (0.71-1.73) 0.68 (0.34-1.37) 0.90 	 1.0 0.88 (0.56-1.39) 0.83 (0.55-1.26) 1.0 1.05 (0.14-7.69) 0.36 (0.05-2.65) 0.95 (0.60-1.50) 0.79 (0.51-1.22) 0.80 (0.38-1.69) 0.26 0.73 (0.36-1.49) 0.84 (0.46-1.53) 0.77 (0.50-1.18) 1.18 (0.69-1.99) 0.91 0.58 (0.24-1.39) 1.01 (0.65-1.56) 0.72 (0.45-1.16) 0.35 0.96 (0.56-1.66) 0.89 (0.57-1.40) 0.72 (0.42-1.22) 0.78 (0.38-1.59) 0.23 		Adjusted for age, area, education, family history of colorectal cancer, BMI, alcohol drinking, walking time, sedentary work and consumption of green leafy vegetables and beef.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases		Relative risks (95%CI or *p* value)			Adjustment factors/comments
						Colon cancer	Rectal cancer	Colorectal cancer	
Wakai et al. (2003); (cont)			*Years since smoking cessation (yrs)* 0-9 10-19 20+ p trend	 31 23 12	 16 20 6	 1.09 (0.68-1.75) 1.29 (0.77-2.17) 0.79 (0.41-1.52) 0.29	 0.68 (0.37-1.24) 1.47 (0.84-2.57) 0.53 (0.22-1.28) 0.80		Adjusted for age, area, education, family history of colorectal cancer, BMI, alcohol drinking, walking time, sedentary work and consumption of green leafy vegetables and beef.
Colangelo et al. (2004), USA, The Chicago Heart Association Detection Project in Industry (CHA)	Screening program on cardiovascular disease. The CHA cohort was screened between 1967 and 1973. 39522 men and women from 84 cooperating companies and organizations in the Chicago area underwent baseline assessment. 22295 men and 17004 women remained for analyses. Active follow-up until 1979, after 1979 follow-up until 1997 by the National Death Index.	349 CRC deaths, 208 among men, 141 among women	*Men* Never smoked Past smoker *Cigarettes/d* 1-10 cigs/d 11-20 cigs/d >20 cigs/d p trend *Women* Never smoked Past smoker *Cigarettes/d* 1-10 cigs/d 11-20 cigs/d >20 cigs/d p trend	CRC 56 74 10 35 33 70 18 17 28 8				 1.0 0.96 (0.68-1.36) 0.75 (0.38-1.48) 1.09 (0.71-1.68) 1.36 (0.88-2.11) 0.19 1.0 0.91 (0.54-1.53) 1.23 (0.72-2.09) 1.43 (0.91-2.23) 1.25 (0.59-2.62) 0.13	Adjusted for age, race, categories of education, body mass index, gender, and height.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Jee et al. (2004), Korea, The Korean Cancer Prevention Study (KCPS)	1307275 Koreans from 30 to 95 years who received health insurance from the Korean Medical Insurance Corporation and who had biennial medical evaluations in 1992-1995. 1212209 participants were the final sample. For information on cancer mortality a Computerized search for death certificate data from the National Statistical Office in Korea was performed. Active follow up 1993-2001.	511 colon Cancer cases in men	*Men* Never smoker Former smokers Current smoker	Colon 91 139 281	 1.1 (0.9-1.4) 1.1 (0.8-1.4)			Adjusted for age.
Sanjoaquin et al. (2004), United Kingdom, The Oxford Vegetarian Study	11140 vegetarians and non-vegetarians who were recruited in the UK between 1980 and 1984 completed a questionnaire. Each participant was flagged at the UK National health Service central	95 incident colorectal cancer cases	 Never smoker Former smokers Current smokers	CRC 36 43 16			1.0 1.80 (1.13-2.85) 1.70 (0.92-3.15)	Adjusted for age, sex, and alcohol.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
							Colon cancer	Rectal cancer	Colorectal cancer	
Sanjoaquin et al. (2004); (cont)	register for information on cancer registration and death. A total of 10998 participants were included in the analysis. Follow up 1980-1999									Adjusted for age, sex, and alcohol.
Doll et al. (2005) United Kingdom	34439 male British doctors, who reported their smoking habits in November 1951 were follow-up periodically through mailed questionnaire; 50 year for mortality 1951-2001; 272 deaths from pancreatic cancer		Never smoker Cigarette smokers Former Current *Current cigarettes/d* 1-14 15-24 ≥25 Other smokers Former Current				1.0 1.43 1.33 1.39 1.13 1.52 1.54 1.27	1.0 1.55 2.39 1.44 1.76 4.73 1.62 2.25	1.0 1.45 1.56 1.39 1.29 2.22 1.55 1.48	Standardized indirectly for age and study year
Yun et al. (2005), Republic of Korea, National Health Insurance Corporation Study	733134 Korean men, 30 years old or older who were insured by the National Health Insurance Corporation and had a medical evaluation in 1996. Follow-up through 2000. Incident cancer cases were identified from the Korean Central Cancer Registry	417 colon, 453 rectum cancer cases	Never Former smokers Current smokers *Cigarettes/d* 1-9 10-19 ≥20 *Current smokers* *Years of smoking* 1-9 10-29 ≥30 p trend	C 99 148 170 36 102 32 59 45 66	R 106 131 216 38 131 47 62 76 78	CRC	1.0 1.37 (1.06-1.77) 0.81 (0.63-1.05) 0.97 (0.66-1.43) 0.78 (0.59-1.04) 0.76 (0.51-1.15) 0.87 (0.62-1.23) 0.61 (0.42-0.88) 0.96 (0.69-1.33)	1.0 1.17 (0.91-1.52) 0.97 (0.76-1.24) 0.95 (0.65-1.39) 0.95 (0.73-1.24) 1.05 (0.74-1.50) 0.80 (0.57-1.13) 1.00 (0.74-1.36) 1.12 (0.82-1.52) <0.01		Adjusted for age, place of residence, BMI, alcohol drinking, leisure time physical activity frequency, meat consumption, preference for vegetables and meats.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
							Colon cancer	Rectal cancer	Colorectal cancer	
Yun et al. (2005); (cont)	(KCCR) and six regional cancer registries (RCRs).		*Former smokers* *Years of smoking* 1-19 20-29 ≥30 p trend	 95 23 21	 89 24 6		 1.36 (1.02-1.80) 1.15 (0.72-1.83) 2.08 (1.29-3.37) 0.06	 1.21 (0.91-1.61) 1.23 (0.78-1.92) 0.61 (0.27-1.41)		Adjusted for age, place of residence, BMI, alcohol drinking, leisure time physical activity frequency, meat consumption, preference for vegetables and meats.
Lüchtenborg et al. (2005), Netherlands, The Netherlands Cohort Study on Diet and Cancer	A total of 58279 men and 62573 women between the ages of 55 and 69 years from 204 municipal population registries completed a self-administered questionnaire in 1986. Incident cancer cases are identified through annual record linkage to the Netherlands Cancer Registry and the Pathologisch Anatomisch Landelijk Geautomatiseerd Archief (PALGA). The vital status of a sub cohort of 3,500 men and women	2948 sub cohort members, 661 colorectal cancer cases		CRC						Adjusted for age (years), sex, family history of colorectal cancer, and BMI.
			Never smoked	206					1.0	
			Former smokers	298					1.30 (1.03-1.65)	
			Current smokers	146					0.91 (0.71-1.18)	
			Cigarettes/day							
			<5	47					1.02 (0.71-1.46)	
			5-<10	50					0.91 (0.59-1.30)	
			10-<15	84					1.10 (0.80-1.52)	
			15-<20	61					1.16 (0.82-1.64)	
			20-<25	76					1.15 (0.83-1.59)	
			≥25	95					1.59 (1.16-2.17)	
			p trend						0.01	
			Duration (yrs)							
			<10	17					1.02 (0.59-1.78)	
			10-<20	53					1.16 (0.81-1.64)	
			20-<30	92					1.15 (0.85-1.55)	
			30-<40	128					1.32 (1.00-1.73)	
			40-<50	109					0.90 (0.67-1.20)	
			≥50	38					1.45 (0.93-2.28)	
			p trend						0.49	

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Lüchtenborg et al. (2005); (cont)	was biannually examined. Follow up 1989-1994.		*Age at first exposure* <15 15-<17 17-<19 19-<21 21-<25 ≥25 p trend *Years since cessation* <1 1-<10 10-<20 20-<30 ≥30 p trend	 71 116 103 65 35 44 155 101 104 65 17 			 1.14 (0.81-1.62) 1.41 (1.04-1.92) 1.11 (0.83-1.50) 1.26 (0.90-1.77) 1.17 (0.78-1.77) 0.87 (0.61-1.25) 0.32 0.94 (0.73-1.22) 1.39 (1.03-1.86) 1.38 (1.03-1.86) 1.25 (0.88-1.77) 0.75 (0.43-1.29) 0.27	Adjusted for age (years), sex, family history of colorectal cancer, and BMI.
Kim et al (2006), Korea, Korea Elderly Phamacepidemiologic Cohort (KEPEC)	Population-based dynamic cohort with 14103 cohort members aged 65 years or more and living in Busan Metropolitan City from 1993-1998. The participants were beneficiaries of the Korean Medical Insurance Corporation (KIMIC). Baseline information was surveyed by a self-administered	100 incident colorectal cancer cases	 Non-smoker Former smokers Current smokers p trend *Daily smoking amount (packs)* ≤0.5 0.5-1 >1 p trend *Smoking duration* ≤20 pack-yrs 20-40 pack-yrs >40 pack-yrs p trend	CRC 57 14 26 4 20 16 6 32 2 			 1.0 2.03 (1.02-4.03) 1.36 (0.80-2.32) 0.26 1.56 (0.56-4.35) 1.77 (1.03-3.05) 0.95 (0.51-1.76) 0.28 1.29 (0.52-3.22) 1.63 (0.97-2.74) 0.96 (0.27-3.24) 0.15	Adjusted for age at baseline, gender precancerous lesion of CRC, medication history of NSAID & antibiotics, alcohol drinking and BMI.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/comments
				CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Kim et al (2006); (cont)	questionnaire. Follow up for a mean of 8.7 person years.		*Smoking duration* ≤ 45 yrs > 45 yrs P trend *Age started smoking* ≥ age 20 < age 20 p trend	 31 9 27 13			 1.51 (0.97-2.34) 2.35 (1.16-4.74) <0.01 1.03 (0.60-1.79) 2.15 (1.17-3.93) 0.06	Adjusted for age at baseline, gender precancerous lesion of CRC, medication history of NSAID & antibiotics, alcohol drinking and BMI.
Akhter et al. (2007), Japan	Prospective cohort study in 14 municipalities of Miyagi Prefecture in rural northern Japan. 47605 Participants aged 40-64 years (22836 men and 24769 women). Information was obtained by self-administered questionnaire. Follow-up 1990-1997. Record linkage with the Miyagi Prefectural Cancer Registry for information on incident cases. Analysis was limited to 21,695 men due to small	188 incident colorectal cancer cases	Never smoker Former smokers Current smokers *Cigarettes/d* 1-19 ≥20 p trend *Age started smoking* >22 19-22 ≤18 p trend *Smoking duration (yrs)* 1-29 30-39 ≥40 p trend	22 50 116 29 82 37 60 16 33 50 30			1.0 1.73 (1.04-2.87) 1.74 (0.93-2.34) 1.32 (0.75-2.31) 1.60 (0.99-2.58) 0.04 1.36 (0.80-2.32) 1.56 (0.95-2.55) 1.86 (0.97-3.58) 0.03 1.46 (0.82-2.60) 1.52 (0.91-2.53) 1.59 (0.89-2.86) 0.08	Adjusted for age in years, family history of colorectal cancer; education level, BMI, walking time, alcohol drinking and current drinkers, consumption frequencies of meat, green-yellow vegetables and fruits.

Reference, location, name of study	**Cohort description**	**No. of subjects**	**Smoking categories**	**No of cases**	**Relative risks (95%CI or *p* value)**			**Adjustment factors/comments**
				CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Akhter et al. (2007); (cont)	prevalence of smoking in women.		*Smoking duration* ≤ 45 yrs > 45 yrs P trend *Age started smoking* ≥ age 20 < age 20 p trend	 31 9 27 13			 1.51 (0.97-2.34) 2.35 (1.16-4.74) <0.01 1.03 (0.60-1.79) 2.15 (1.17-3.93) 0.06	Adjusted for age in years, family history of colorectal cancer; education level, BMI, walking time, alcohol drinking and current drinkers, consumption frequencies of meat, green-yellow vegetables and fruits
Huxley (2007) Asia Pacific Cohort Studies Collaboration, Asia Pacific Cohort Studies Collaboration (APCSC)	Collaboration of 33 cohort studies in the region. 539201 participants (35% female, 65% male). Studies were included if they had continued follow-up for at least 5000 person-years and had recorded vital status at the end of follow-up. Data on cigarette smoking were based on self-report.	751 colorectal cancers (454 men, 297 women)	Cigarette smoking (Yes/No) p value Cigarette smoking (5/day) p value				 1.43 (1.09-1.88) 0.01 1.00 (0.92-1.09) 0.99	Adjusted for diabetes, BMI, and alcohol.

Reference, location, name of study	**Cohort description**	**No. of subjects**	**Smoking categories**	**No of cases**	**Relative risks (95%CI or *p* value)**			**Adjustment factors/comments**
					Colon cancer	Rectal cancer	Colorectal cancer	
Paskett et al. (2007), USA, Women's Health Initiative (WHI)	The WHI includes an observational study and three clinical trials. 146877 women. Clinical outcomes were reported semiannually for the clinical files and annually for the observation study. Follow-up 1998-2005.	1075 colon, 176 rectal cancer cases (461 right-sided and 296 left-sided)	Former smokers Current smokers p trend *Age at smoking initiation* <20 ≥20 p value for trend *Cigarettes/d* <25 ≥25 p trend *Duration of smoking* <20 20-29 30-39 ≥20 p trend *Age at smoking cessation* <30 30-39 40-49 ≥50 Current smoker p trend *Time since cessation* Current smoker <10 10-19 20-29 30-39 ≥50 p trend		1.12 (0.97-1.29) 1.03 (0.77-1.38) 0.28 1.13 (0.96-1.33) 1.08 (0.91-1.29) 0.27 1.05 (0.90-1.21) 1.47 (1.16-1.85) 0.01 0.95 (0.79-1.15) 1.27 (1.02-1.58) 1.18 (0.93-1.50) 1.19 (0.93-1.54) 0.03 0.95 (0.72-1.27) 0.87 (0.67-1.14) 1.24 (0.98-1.56) 1.24 (1.02-1.52) 1.04 (0.78-1.39) 0.06 1.05 (0.78-1.40) 1.15 (0.76-1.75) 1.32 (1.06-1.64) 1.16 (0.92-1.46) 0.90 (0.70-1.17) 0.97 (0.73-1.29) 0.69	1.15 (0.80-1.67) 1.95 (1.10-3.47) 0.05 1.14 (0.75-1.75) 1.39 (0.91-2.10) 0.13 1.29 (0.90-1.86) 1.14 (0.59-2.18) 0.31 0.87 (0.52-1.43) 1.95 (1.20-3.17) 1.24 (0.68-2.27) 1.53 (0.83-2.83) 0.05 0.79 (0.36-1.73) 0.84 (0.42-1.70) 1.39 (0.78-2.46) 1.53 (0.93-2.52) 1.93 (1.08-3.44) 0.01 1.98 (1.11-3.52) 1.81 (0.77-4.26) 1.45 (0.84-2.50) 1.27 (0.71-2.28) 1.10 (0.59-2.06) 0.53 (0.19-1.46) 0.90		Adjusted for age ethnicity, study arm, family history of colorectal cancer, total physical activity metabolic equivalents, duration of nonsteroidal anti-inflammatory drug use, alcohol, hormone therapy use, colonoscopy, history of diabetes, total dietary calcium, total dietary fibre, percent energy from fat, hemoglobin, waist circumference, red meat intake, and stratified by study (observational study, clinical trial nonhormone trial, hormone trial treatment assignment).

Reference, location, name of study	**Cohort description**	**No. of subjects**	**Smoking categories**	**No of cases**			**Relative risks (95%CI or *p* value)**			**Adjustment factors/comments**
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Tsong et al. (2007), Singapore, Singapore Chinese Health Study	Citizens of Singapore who resided in government-built housing estates, 45-74 years old, Hokkiens and Cantonese. 61,321 subjects. Baseline information collection by in-person interview. Linkage with the Singapore Cancer Registry and Singapore Registry of Births and Deaths. Follow-up 1993-2004	845 incident cases (516 colon and 329 rectal)	Never smokers Former smokers Current smokers *Cigarettes/day* <13 13+ p trend *Age at starting to smoke* 15+ years <15 years p trend *Duration of smoking* <40 years 40+ years p trend	338 75 103 68 110 148 30 94 84	157 63 109 58 114 126 46 83 89		1.0 0.96 (0.73-1.27) 0.83 (0.64-1.06) 0.84 (0.64-1.11) 0.91 (0.71-1.17) 0.38 0.89 (0.71-1.12) 0.80 (0.54-1.18) 0.19 0.88 (0.68-1.14) 0.87 (0.66-1.14) 0.27	1.0 1.45 (1.04-2.01) 1.63 (1.23-2.17) 1.38 (0.99-1.90) 1.71 (1.28-2.28) 0.0003 1.40 (1.07-1.84) 2.34 (1.63-3.36) <0.0001 1.37 (1.01-1.84) 1.85 (1.36-2.52) <0.0001		Adjusted for age, gender, dialect group, year of recruitment, level of education, BMI, history of diabetes, family history of colorectal cancer, alcohol consumption, and physical exercise
Batty et al. (2008), UK, The Whitehall study	17322 London based government employees, aged 40-69 years, participated in a medical examination in the 1960s (response rate 74%). 74% response Cancer mortality ascertained by using procedures of the National Health Service Central Registry until 2005	52 colon cancer deaths, 16 rectum cancer deaths	Never Former smokers Current smokers *Former smokers* Effect per 10 cigarettes/d Effect per 10 years of smoking *Current smokers* Effect per 10 cigarettes/d Effect per 10 years of smoking	52 118 129	16 58 40		1.0 1.11 (0.80-1.55) 1.33 (0.96-1.86) 1.03 (0.88-1.22) 1.04 (0.88-1.23) 1.05 (0.87-1.27) 1.09 (0.83-1.43)	1.0 1.94 (1.11-3.39) 1.51 (0.84-2.74) 1.31 (1.08-1.38) 1.13 (0.87-1.45) 1.25 (0.93-1.70) 1.26 (0.77-2.05)		Adjusted for age, employment grade, physical activity, BMI, marital status, systolic and diastolic blood pressure, cholesterol forced expiratory volume in 1s, height, impaired glucose tolerance, diabetes and disease at entry.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases	Relative risks (95%CI or *p* value)			Adjustment factors/comments
					Colon cancer	Rectal cancer	Colorectal cancer	
Kenfield et al. (2008), USA, The Nurses Health Study	Established 1976, 121700 female US registered nurses aged 30 up to 55 years, residing in 11 states. Baseline information obtained by mailed questionnaire. Deaths were usually reported by families and deaths among nonrespondents were identified by searching the National Death Index. Follow up 1980-2004.	578 colorectal cancers deaths		CRC				Adjusted for age (months), follow-up period, history of hypertension, diabetes, high cholesterol levels, BMI, change in weight from age 18 years to baseline (1980), alcohol intake, physical activity, previous use of oral contraceptives, postmenopausal estrogen therapy use and menopausal status, parental history of myocardial infarction at age 65 years or younger and age at starting smoking, servings of beef, pork, lamb or processed meat, total calcium and folate intake, and duration of aspirin use.
			Never				1.0	
			Former smokers	238			1.23 (1.02-1.49)	
			Current smokers	214			1.63 (1.29-2.05)	
			Cigarettes/d smoked by current smokers	126				
			1-14				1.37 (0.95-1.96)	
			15-24	36			1.73 (1.27-2.35)	
			≥24	55			1.83 (1.26-2.64)	
			p trend				0.23	
			S*tarting age among current smokers*,					
			≤35				1.25 (0.77-2.02)	
			18-21	19			1.73 (1.32-2.27)	
			≥21	83			1.55 (1.01-2.39)	
			p trend	32			0.95	
			Y*ears since quitting in former smokers*,					
			<5				0.87 (0.59-1.29)	
			5-<10	32			0.64 (0.40-1.01)	
			10-<15	22			0.96 (0.65-1.43)	
			15-<20	32			0.93 (0.63-1.38)	
			≥26	33			0.70 (0.53-0.93)	
			p trend	95			0.40	

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Gram et al. (2009), Norway, The Norwegian Women and Cancer Study	68160 women aged 30- 69 years who completed a questionnaire in 1996 or 1998. Follow-up by linkages to national registers through 2005.	425 incident cases of histological confirmed primary invasive colorectal cancers, 284 colon (137 proximal, 108 distal) and 141 rectal cancer cases	Never Former smokers Current smokers Ever smokers *Smoking initiation* ≥20 <20 p trend *Cigarettes/d* 1-9 10-14 ≥ 15 p trend *Years smoked* 1-19 20-29 ≥30 p trend *Pack-years smoked* 0-9 10-19 ≥ 20 p trend *Time since quitting smoking (years)* ≥20 10-19 1-9 0 p trend	97 107 80 187 98 89 114 53 20 55 47 85 78 75 34 36 24 33 84 	53 40 48 88 42 46 51 28 9 23 19 46 35 28 25 16 5 13 4 		1.0 1.4 (1.1-1.9) 1.1 (0.8-1.6) 1.3 (1.0-1.7) 1.3 (1.0-1.7) 1.3 (1.0-1.8) 0.05 1.3 (1.0-1.7) 1.4 (1.0-1.9) 1.2 (0.7-2.0) 0.11 1.2 (0.9-1.7) 1.4 (1.0-2.0) 1.3 (1.0-1.8) 0.07 1.1 (0.8-1.5) 1.7 (1.2-2.3) 1.2 (0.8-1.8) 0.03 1.2 (0.8-1.7) 1.7 (1.2-2.6) 1.5 (1.0-2.4) 1.2 (0.9-1.6) 0.16	1.0 0.9 (0.6-1.4) 1.2 (0.8-1.8) 1.1 (0.7-1.5) 1.0 (0.6-1.5) 1.2 (0.8-1.8) 0.5 1.0 (0.7-1.5) 1.2 (0.8-2.0) 0.9 (0.4-1.9) 0.7 0.9 (0.5-1.5) 0.9 (0.5-1.6) 1.3 (0.8-1.9) 0.3 0.9 (0.6-1.3) 1.1 (0.7-1.7) 1.5 (0.9-2.5) 0.13 0.9 (0.5-1.6) 1.1 (0.6-2.1) 0.5 (0.2-1.3) 1.2 (0.8-1.8) 0.5		Adjusted for age, menopausal status, hormonal contraceptive and postmenopausal hormonal therapy use, BMI and alcohol consumption, all at enrolment.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Gram et al. (2009); (cont)			*Proximal colon canc.* Never Former smokers Current smokers Ever smokers *Distal colon cancer* Never Former smokers Current smokers Ever smokers	 44 53 40 93 36 46 26 72			 1.0 1.6 (1.1-2.4) 1.4 (0.9-2.1) 1.5 (1.0-2.2) 1.0 1.7 (1.1-2.7) 1.0 (0.6-1.6) 1.3 (0.9-2.0)			Adjusted for age, menopausal status, hormonal contraceptive and postmenopausal hormonal therapy use, BMI and alcohol consumption, all at enrolment.
Hannan et al. (2009), U.S.	Participants were drawn from the Cancer Prevention Study II Nutrition Cohort, a sub cohort of the CPS II mortality cohort, including residents in 21 states with population based state cancer registries and 50 to 74 years of age in 1992. Participants completed a mailed questionnaire. Follow-up questionnaires were sent in 1997, 1999, 2001, 2003, and 2005, with response rate among living	Self-reported cases were verified from medical records (n = 1227) or through linkage to state cancer registries (n = 422). Additional cases (n = 313) were identified through linkage with the National Death	Never smokers Former smokers Current smokers *Former smokers* *Age at cessation* Before age 40 40-49 yrs of age 50-59 yrs of age Age 60 or elder p trend *Years since cessation* ≥ 31 yrs ago 21-30 yrs ago 11-20 yrs ago 1-10 yrs ago p trend	CRC 813 993 156 261 242 260 160 239 238 232 214					1.0 1.23(1.11-1.36) 1.27(1.06-1.52) 1.05(0.91-1.22) 1.31(1.13-1.52) 1.44(1.24-1.66) 1.29(1.08-1.54) 0.0014 1.03(0.89-1.19) 1.28(1.10-1.49) 1.33(1.14-1.55) 1.48(1.27-1.73) 0.0003	Adjusted for age , BMI, education, family history of colorectal cancer, physical activity, race, aspirin use, alcohol intake, Vegetable consumption, fibre/whole grain consumption, red and processed meat consumption, history of endoscopy

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
				CRC			Colon cancer	Rectal cancer	Colorectal cancer	
Hannan et al. (2009); (cont)	participants at least 89%. The follow up period ended on June 30, 2005. 51365 men and 73386 women were included in the analysis. Incident cases of colorectal cancer were identified by ICD-9 codes 153-154.1 or by ICD 10 codes C18-C20	Index (NDI).	*Current smokers Duration of smoking* < 40 years 40-49 years 50+ years p trend	29 71 56					1.02(0.69-1.49) 1.32(1.02-1.72) 1.38(1.04-1.84) 0.052	Adjusted for age , BMI, education, family history of colorectal cancer, physical activity, race, aspirin use, alcohol intake, Vegetable consumption, fibre/whole grain consumption, red and processed meat consumption, history of endoscopy
Limsui et al.(2010) US	Among 37399 participants in a population-based cohort study (the Iowa Women's Health Study)	1233 CRC	Never smokers Former smokers Current smokers Ever smokers	C 	R 	CRC 			1.00 1.16(1.00-1.35) 1.23(1.04-1.46) 1.19(1.05-1.35)	Adjusted for age, BMI, waist-hip, physical activity, alcohol, exogenous estrogen, daily intake of total calories, fat, sucrose, red meat, calcium, vitamin E and methionine.
Leufkens et al.(2011), European Prospective Investigation into cancer and Nutrition (EPIC)	465,879 participants in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Mean follow-up time was 8.7 years	1,791 colon 766 proximal tumors 772 distal tumors 253 colon tumors unspecified in location. 950 rectum cancer. 2741 CRC	Never smokers Former smokers Current smokers Ever smokers *Proximal colon cancer* Never smokers Former smokers Current smokers Ever smokers	746 841 556 285 303 370 239 131	378 464 306 158	1124 1305 862 443	1.0 1.18(1.06-1.32) 1.21(1.08-1.36) 1.13(0.98-1.31) 1.0 1.27(1.08-1.50) 1.25(1.04-1.50) 1.31(1.06-1.64)	1.0 1.06(0.91-1.23) 1.10(0.94-1.30) 0.98(0.80-1.19)	1.0 1.06(0.91-1.23) 1.10(0.94-1.30) 0.98(0.80-1.19)	Adjusted for weight, height, physical activity, education, dietary intake of energy from fat, energy from non-fat, fiber, fruit, vegetables, red meat, processed meat, alcohol, and fish

Reference, location, name of study	**Cohort description**	**No. of subjects**	**Smoking categories**	**No of cases**			**Relative risks (95%CI or *p* value)**			**Adjustment factors/comments**
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Leufkens et al.(2011) (cont)		cases.	*Distal colon cancer* Never smokers Former smokers Current smokers Ever smokers	 323 358 243 115			 1.0 1.05(0.89-1.24) 1.13(0.95-1.36) 0.91(0.73-1.14)			Adjusted for weight, height, physical activity, education, dietary intake of energy from fat, energy from non-fat, fiber, fruit, vegetables, red meat, processed meat, alcohol, and fish
Parajuli et al. (2013), Norway	602, 242 men and women from four different Norwegian health surveys were followed. Mean follow up of 14 years.	3998 colon cancer (46% in women). 2072 proximal colon cancer (47% in women) and 1520 distal colon cancer (43% in women)	<u>*Men*</u> Never smokers Former smokers Current smokers Ever smokers *Proximal colon cancer* Never smokers Former smokers Current smokers Ever smokers *Distal colon cancer* Never smokers Former smokers Current smokers Ever smokers <u>*Women*</u> *Colon cancer* Never smokers Former smokers Current smokers Ever smokers	 834 355 657 1012			1.0 1.14(1.02-1.27) 1.03(0.92-1.15) 1.08(0.97-1.19) 1.0 1.06(0.90-1.24) 1.02(0.86-1.19) 1.03(0.90-1.19) 1.0 1.24(1.03-1.47) 0.95(0.79-1.13) 1.08(0.92-1.26) 1.0 1.16(1.02.1.31) 1.22(1.10-1.36) 1.19(1.09-1.32)			Adjusted for age, physical activity, BMI and education.

Reference, location, name of study	Cohort description	No. of subjects	Smoking categories	No of cases			Relative risks (95%CI or *p* value)			Adjustment factors/comments
				C	R	CRC	Colon cancer	Rectal cancer	Colorectal cancer	
Parajuli et al. (2013) (cont)			*Proximal colon cancer* Never smokers Former smokers Current smokers Ever smokers *Distal colon cancer* Never smokers Former smokers Current smokers Ever smokers *Men* *Colon cancer* Never smokers Former smokers Current smokers Ever smokers *Proximal colon cancer* Never smokers Former smokers Current smokers Ever smokers *Distal colon cancer* Never smokers Former smokers Current smokers Ever smokers	 438 186 362 548 295 132 227 359 534 744 874 1,618 267 350 431 781 217 323 326 649			 1.0 1.22(1.02-1.45) 1.37(1.18-1.59) 1.31(1.15-1.49) 1.0 1.15(0.94-1.41) 1.12(0.93-1.34) 1.13(0.96-1.32) 1.0 1.14(1.02-1.27) 1.03(0.92-1.15) 1.08(0.97-1.19) 1.0 1.06(0.90-1.24) 1.02(0.86-1.19) 1.03(0.90-1.19) 1.0 1.24(1.03-1.47) 0.95(0.79-1.13) 1.08(0.92-1.26)			Adjusted for age, physical activity, BMI and education

Source: International Agency on Research on Cancer (IARC) monograph 100 E 2012 for the cohorts until 2009