Adverse lifestyle effects of colorectal cancer screening

Does the incidence of selected lifestyle-related comorbidities change dependent upon a screening outcome?

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Abstract

Background: Mass-screening programs are necessary to prevent or even cure colorectal cancer. A criticism of screening however has been the risk of patient misinterpretation of the result, specifically the Health Certificate Effect. The study's aim is to examine whether a screening result could change the amount of health care services used in six different lifestyle related diseases.

Method: A sample of 100,116 patients from the NORCCAP trial was studied from 1998 to 2003. Each patient with one of the six lifestyle related disease groups was identified and tracked over the six years. A logistic panel regression method was used to see if health care usage in each of the six lifestyle-related disease groups changed following the screening outcome. Changes in disease related health care usage was compared to a control group.

Results: Screening results did appear to change the incidence of lifestyle related diseases, however not all of the results could be explained by a Health Certificate Effect. Participants who had a negative test result did appear to be at an increased risk for required outpatient care for complications relating to Diabetes Mellitus and Hypertension.

Conclusion: Attention must be paid to the effects of screening outcomes when evaluating a mass-screening program. This study has demonstrated that screening results can change the risk of requiring care for other lifestyle-related diseases.

Acknowledgements

I was first introduced to the premise behind this thesis project in November 2009 after a discussion with Eline Aas and Inger-Kristin Larsen. It was encouraging to see the excitement that they both showed upon discussing the topic and the possible directions. The potential value-added benefit of this project was a prerequisite for me and this soon became the main motivating factor on days when my motivation was at an all time low.

Throughout the thesis process, I went from having little-to-no knowledge of colorectal cancer to now, at its conclusion, firmly believing that it is the single most important health policy issue. But we all think this way about our projects right? If there is one central message to take from this project it is that colorectal cancer is a largely preventable cancer when mass screening programs are in place. While much has been said about the adverse events and costs associated with mass screening, I sincerely hope that this project can build on or even add a new framework for better predicting these indirect costs.

I will be forever grateful to my advisors Eline Aas and Inger-Kristin Larsen. They went over and above my expectations, and it was very reassuring to know that assistance was only an email, phone call or 'a look to my left' away. There were many ups and downs in these last few months, and their patience and continued positive outlook was the difference between me finishing and not finishing. Thank you for entrusting me with this project.

Lastly, but no less importantly, I would like to thank my fellow students who were there each and every day. You each played a vital role in every imaginable capacity, and provided me the incentive to wake up early and drag myself to school. I am proud of you all and I wish you all the best in the future. This is a major accomplishment and I could not think of a better group to study with.

Thank you all,

Jordan James Richard Sauer

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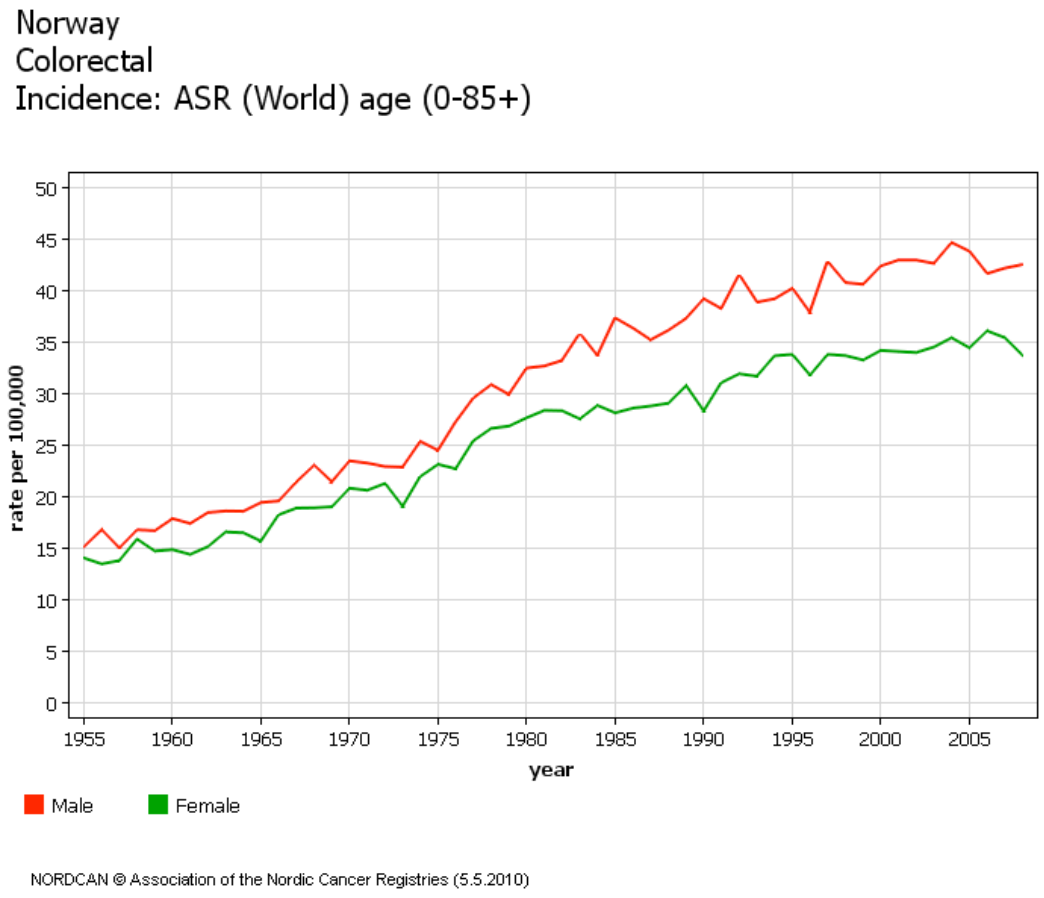
List of Abbreviations

AMI	Acute Myocardial Infarction
AP	Angina Pectoris
CEA	Cost-Effectiveness Analysis
COPD	Chronic Obstructive Pulmonary Disease
CRC	Colorectal Cancer
DM	Diabetes Mellitus
FOBT	Fecal Occult Blood Test
FS	Flexible Sigmoidoscopy
HBM	Health Belief Model
HCE	Health Certificate Effect
ICD-9 / ICD-10	International Classification of Disease
IHD	Ischemic Heart Disease
ITT	Intention to Treat
NCR	Norwegian Cancer Registry
NOK	Norwegian Kroner (Currency)
NORCCAP	Norwegian Colorectal Cancer Prevention Trial
NPR	Norwegian Patient Registry
SSB	Statistisk sentralbyrå
TPS	Telemark Polyp Study

1 Introduction

Colorectal cancer is one of the most common of cancers in the Nordic countries behind breast and prostate cancer (Hakama et. al. 2005). The 50-74 years old incidence rates of CRC within the Nordic countries' population varies from 70 to 130 per 100 000 people in females and more than 150 per 100 000 people in males (Hakama et. al. 2005). It is the present belief that the majority of CRCs occur due to a malignant transformation of an adenomatous polyp (McPhee & Papadakis 2008), however research points to any polyp of any size in the distal or proximal colon as being at risk for cancer (Imperiale et. al. 2000). Adenomatous polyps are lesions within the colon wall and are identified by their size, shape and general characteristics under a microscope. While not all of these polyps are cancerous, it is believed that they most commonly develop into malignant cancers. If left untreated, 50% of all cases of CRC will be fatal (McPhee & Papadakis 2008). Slightly less than 50% of cancerous adenomatous polyps are found in the distal to splenic flexure of the colon (McPhee & Papadakis 2008).

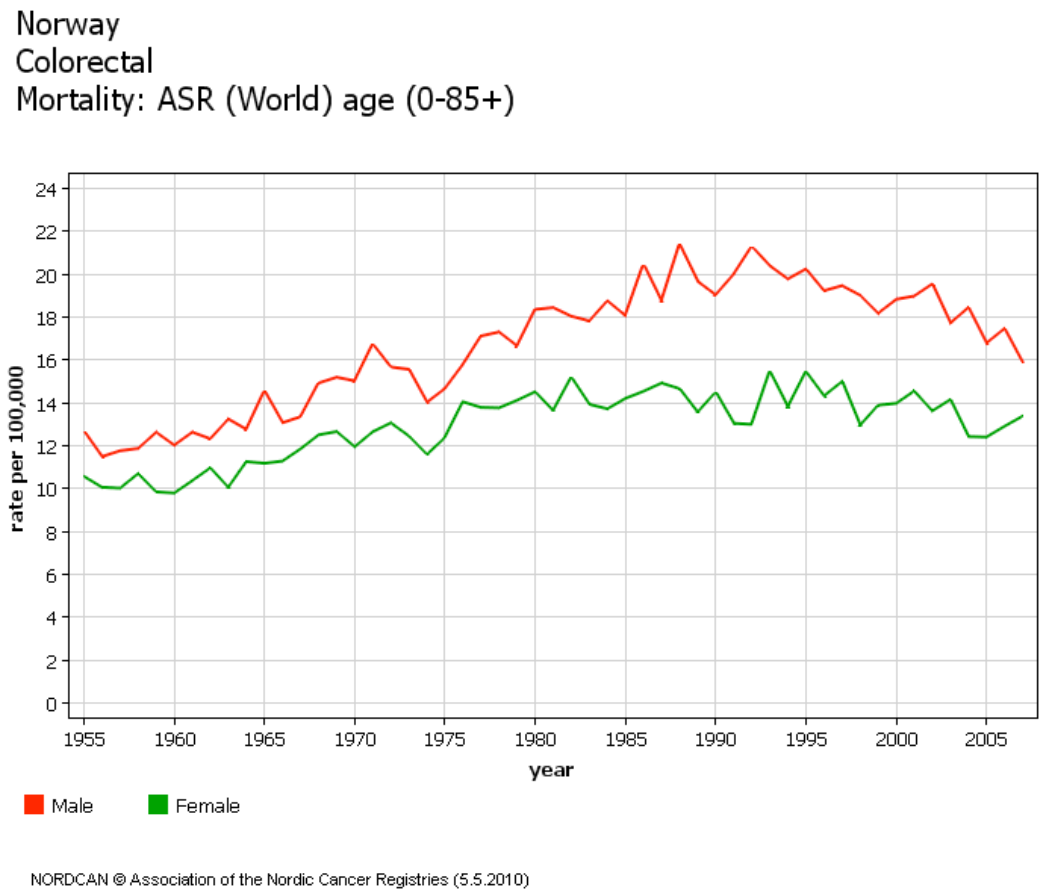
Figure 1: Norwegian Colorectal Cancer Incidence Age-Standardized Rate.



The incidence of CRC has been growing in Norway steadily in both males and females as reported in Figure 1. The increase does appear to be leveling off and in fact may be decreasing amongst the female population.

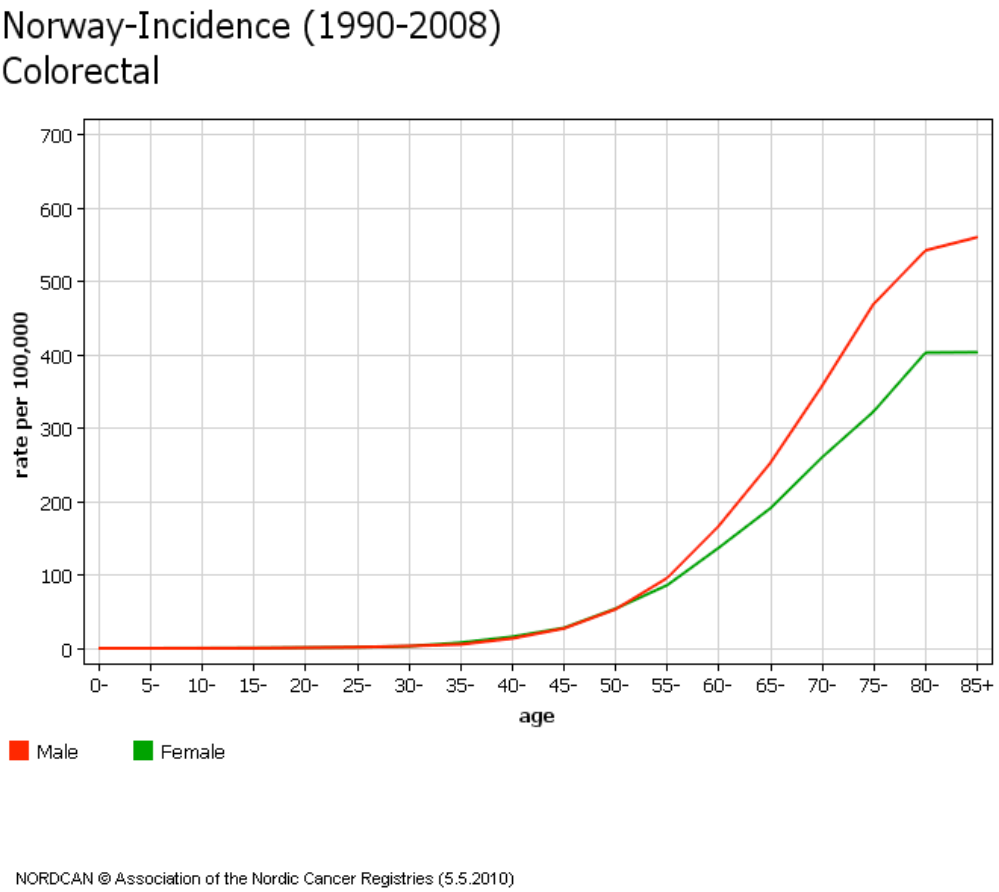
While there has been an increase in CRC incidence in Norway, there is fortunately a reduction in mortality as presented below in Figure 2. This could be due to further awareness of the risk factors for CRC over time, specifically people with a family history who choose to participate in screening.

Figure 2: Norwegian Mortality from Colorectal Cancer – Age Standardized Rate



The risk of CRC incidence appears to increase with age in Norway as presented in Figure 3. Cases are reported as early as 30 years of age and level off at the age of 85. The curve is steepest between the ages of 45 and 70 years, this indicates the age at which most CRC cases are reported in Norway.

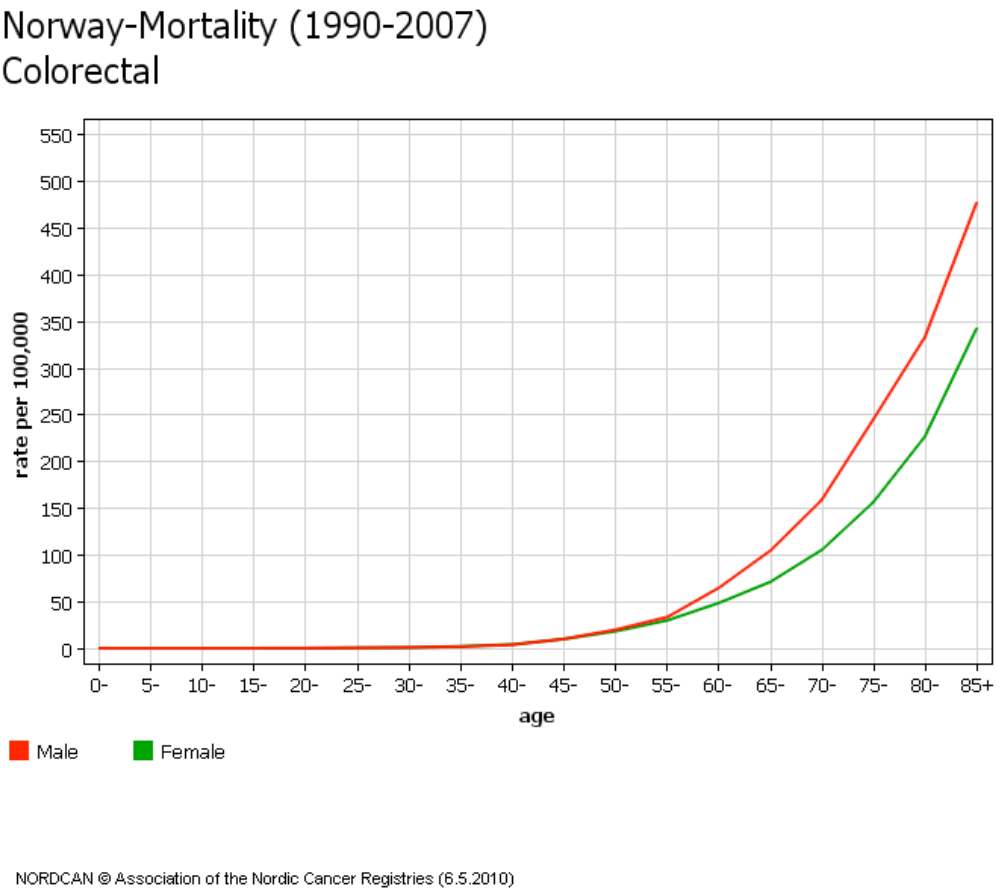
Figure 3: Norwegian Incidence Rate of Colorectal Cancer from 1990 to 2008 by Age.



The mortality from CRC in Norway is presented below in Figure 4. The starting age at which mortality is recorded appears to be slightly less the five years later than the age when reported cases of CRC incidence begin in Figure 3; this could demonstrate that the 5-year survival rate is quite poor. The steepness of the two curves in Figure 4 is also similar to those in Figure 3 but do not peak as high. One interesting observation of note is that incidence curves peak at between 400 and 550 per 100,000 people while mortality peaks at between 340 and 475 per 100,000 people, this suggests that the survival rates of CRC in Norway are low.

Screening has been introduced as a means to improve the survival time of CRC by locating potentially cancerous adenomatous polyps before they turn malignant. Even if there is evidence of cancerous lesions within the colon and rectum, early intervention can still remove the cancerous areas prior to it potentially metastasizing to other regions of the body.

Figure 4: Norwegian Mortality Rate of Colorectal Cancer from 1990 to 2007 by Age



1.1 Aim

The prevalence and incidence of CRC has been largely linked to a country's affluence and trends in lifestyle (Hakama et. al. 2005). For this reason, affluence could be an explanation for increasing trends in CRC within the Nordic countries. Similarly, this problem can be exacerbated by inadequate screening that is not backed up by educational programs involving information on lifestyle choices in relation to disease. With criticisms of mass screening programs leading to adverse events and patient misunderstanding of the results, there is an ever-increasing need to identify the areas of weakness in screening programs and remedy the persistent problems.

There has been frequent talk about a 'Health Certificate Effect' as a possible reason for results that appear to be skewed, unexplainable or against the hypothesis. These unintended effects have also been linked to increased costs being incurred that could inaccurately be transferred to mass screening for CRC. This paper intends to explore the way that individuals perceive their health and the use of health services. The principle of the Health Certificate Effect will

be explored through the patterns exhibited by individuals participating in the NORCCAP trial and how their results relate to other lifestyle-related comorbidities. The main aim for this thesis project is to evaluate the incidence of selected lifestyle-related comorbidities and whether there is a change following a mass-screening program for colorectal cancer.

This thesis will be organised as follows: a brief introduction to CRC, a discussion about screening aims and methods, the theories of health usage used to frame the research aims of this thesis, a description of the Health Certificate Effect, an introduction to the selected lifestyle-related disease groups, a brief discussion of the NORCCAP trial, a presentation of the data, an explanation of the methods used in the statistical analysis, the study's results and, a brief discussion of the results and their implications.

2 Background

2.1 Risk Factors

CRC has a number of risk factors. The incidence of CRC increases with age starting at 45 years and approximately 90% of all cases occur in individuals over the age of 50 years (McPhee & Papadakis 2008, Lieberman et. al. 2000, Imperiale et. al. 2000). Similar to other cancers, CRC does have links to family history of neoplasia that accounts for roughly 20%-30% of all cases; it should be noted that the genes leading to the cause of these cancers have yet to be identified (McPhee & Papadakis 2008). There is also a proportionate link to the age of the affected first-degree family member. Individuals with a first-degree family member having CRC have an approximately two times greater risk than the general population (McPhee & Papadakis 2008). This relative risk is increased however if the family member was diagnosed with CRC at less than 45 years of age by 3.8 times, was between the ages of 45 and 59 years of age by 2.2 times and was diagnosed above the age of 59 years by 1.8 times (McPhee & Papadakis 2008). Another risk factor is whether the individual has inflammatory bowel disease, this can increase the likelihood of an adenocarcinoma in the colon within seven to ten years following the onset of the patient's Ulcerative Colitis or Crohn's Disease. The cumulative risk further increases by 5% to 10% after twenty years and 20% after thirty years (McPhee & Papadakis 2008). Some epidemiological studies have pointed to diets that are rich in fats and red meats as causes for increases in the risk of CRC adenomas. Other risk factors include: sugar consumption, personal history of breast cancer, uterine cancer, ovarian cancer, physical inactivity, Diabetes Mellitus, obesity, smoking, alcohol in excess, abdominal radiotherapy, and ureterosigmoidostomy (Kumar & Clark 2009, Vatn & Hoff 1989). Diets that are high in fruits, vegetables and fibre have been shown to decrease the risk of CRC (McPhee & Papadakis 2008), as well as exercise (colon cancer only), aspirin and other NSAIDs, and combined oestrogen/progesterone hormone replacement therapy (Kumar & Clark 2009). Males are also more likely to suffer from colon cancer while more women tend to suffer from rectal cancer (Imperiale et. al. 2000), however some studies noted that polyp size and dysplasia are greater in women (Hoff et. al. 1984, Hoff et. al. 1985, Hoff 1987).

2.2 Symptoms

There is strong support of the ademonatous polyp to CRC sequence (Hakama et. al. 2005) and due to the fact that adenocarcinomas are rather slow growing, it may take up to several years before symptoms may appear. In most cases, the characteristics of the symptoms are dependent upon the location of the carcinoma, however most symptoms of CRC are found for reasons other than polyps (Vatn & Hoff 1989). Common symptoms include chronic blood loss form the carcinoma location, iron-deficiency anemia (due to blood loss), obstructions in the colon (although this is rare), lesions causing bowel pain, changes in bowel habits, constipation or alternating frequencies between loose stools, blood in the stool, and in some rare cases, weight loss (McPhee & Papadakis 2008).

2.3 Diagnosis

Since CRC is a slow growing disease and largely asymptomatic, most tumours are detected with the use of a FOBT, Flexible Sigmoidoscopy or Colonoscopy through screening. In some rare cases where the colon is obstructed or sigmoidoscope/colonoscope cannot reach an area further in the colon such as in the cecum, a barium enema or a CT colonography would be used (McPhee & Papadakis 2008).

2.4 Treatment

The most common form of treatment is the resection of the primary colonic or rectal cancer; about 80% of patients undergo surgery, although fewer than half in this group survive more than 5 years (Kumar & Clark 2009). The use of chemotherapy and radiation therapy (adjuvant therapy) is also used as a treatment option, however it is largely dependent upon the tumour staging of the CRC (Robinson et. al. 1999). Due to the largely unclear understanding of CRC development, a large emphasis must then be placed on secondary diagnostics tools such as screening methods and awareness in order to make treatment choices possible (Vatn & Hoff 1989). Below is a representation of CRC staging and its treatment implications based upon staging descriptions from McPhee & Papadakis (2008).

1. Stage 1 (Early): Has a high 5-year survival rate of between 90% and 100%, therefore chemotherapy or radiation treatment is not needed (McPhee & Papadakis 2008).

2. Stage 2 (Middle): The 5-year survival rate is roughly 80%, treatment such as chemotherapy or radiation is generally not needed, however patients with a higher risk of CRC recurrence (perforation, poor differentiation on histology) are suggested to receive adjuvant treatment (McPhee & Papadakis 2008).

3. Stage 3 (Late): Even with surgical resection, the 5-year survival rate is 20-30%, it is therefore recommended to provide post-surgical adjuvant therapy, which can significantly increase the survival rate (McPhee & Papadakis 2008).

4. Stage 4 (Fatal): By this stage, nearly 20% of patients have the CRC metastasize to other regions namely the liver and lung; the 5-year survival rate is as low as 5%. Resection of the new metastasized areas can increase the survival rate in 35%-55% of cases. Approximately 20% of patients in this group respond to chemotherapy regiments (McPhee & Papadakis 2008).

2.5 Method of Early Detection: Screening

The goals of CRC screening are to reduce the incidence of mortality through early detection and treatment interventions, and to detect the presence of potentially malignant adenomatous polyps and removing them (Janz et. al. 2003, Hakama et. al. 2005). The slow development of CRC taking an average of 10 years from the initial discovery of an adenoma to malignancy makes screening for this cancer ideal (Atkin 2002). When screened patients are compared to controls for survival rates of CRC, the screened group demonstrates a significantly higher survival rate, while those in the control group and unscreened individuals showed similar survival rates (Mandel et. al. 1993). It is then crucial that an early screening diagnosis is made in order for the CRC prognosis to improve through surgery (resection), which if caught early enough is considered curative (Hoff 2004). This ability to 'cure' and the generally slow development of malignancy is why polyp and CRC screening have been identified as being a necessary cancer to screen for (Hakama et. al. 2005).

2.5.1 Fecal Occult Blood Test

Of all the available screening tests, FOBT is the only method that has been tested in an adequately-sized Randomized Control Trial setting (Hoff 2004), the best known trials are the Newcastle Trial (Hardcastle et. al. 1996), The Minnesota Colon Cancer Control Study (Mandel et. al. 1993) and the Funen Trial (Kronborg et. al. 1996). Most CRC cancers and

some large adenomas result in increased chronic blood loss that may be detectable. A variety of FOBT tests are available to test for fecal occult blood in the stool that is linked to adenomatous polyps in the colon. To reduce the likelihood of false-positive tests the patient is asked to abstain from aspirin, NSAIDs, red meat, poultry, fish, and vegetables with peroxide activity (turnips, horseradish) for 72 hours; vitamin C may also give a false-positive test (McPhee & Papadakis 2008). The sensitivity (the ability to detect adenomatous polyps) of FOBT is estimated to be approximately 30% to 92% for a single screening round when testing for asymptomatic CRC (Hoff 2004, Towler et. al. 1998). When given to a general population, 2%-6% of tests are positive. It is recommended that patients with a positive test should then undergo a colonoscopy accompanied by the removal of any potentially malignant polyps. Of the total positive tests, 5%-18% will have CRC and adenomatous polyps are generally identified in 25%-50% of patients with a positive test (McPhee & Papadakis 2008). The low sensitivity of FOBT for advanced neoplasia makes them a less attractive choice for population-based screening than endoscopic (FS or colonoscopy) or radioscopic tests (CT colonography). They are more suitable in settings where health care resources are limited or in patients who desire non-invasive methods of screening. (McPhee & Papadakis 2008).

Table 1: Predicted Effectiveness of FOBT - Female

	Predicted Number of Deaths			**Predicted Mortality Rates**		
Period	Without Screening	With Screening	Difference	Without Screening	With Screening	Difference
Denmark						
1993-1997	5661	5661	-	17.0	17.0	-
1998-2002	5879	5434	445	17.1	15.5	1.7
2003-2007	5962	5206	756	17.0	14.7	2.4
2008-2012	5964	4928	1036	16.7	14.0	2.7
2013-2017	6097	5038	1059	16.5	13.8	2.7
Finland						
1993-1997	2880	2880	-	8.8	8.8	-
1998-2002	3019	2793	226	8.7	7.9	0.8
2003-2007	3123	2727	396	8.6	7.7	1.4
2008-2012	3254	2686	568	8.4	7.0	1.4
2013-2017	3335	2752	583	8.2	6.8	1.7
Norway						
1993-1997	3877	3877	-	14.0	14.0	-
1998-2002	4174	3855	319	14.3	12.8	1.5
2003-2007	4397	3850	547	14.2	12.1	2.1
2008-2012	4540	3673	867	13.9	11.5	2.4
Sweden						
1993-1997	6472	6472	-	10.4	10.4	-
1998-2002	6557	6071	486	10.0	9.0	1.0
2003-2007	6531	5732	799	9.4	8.1	1.4
2008-2012	6388	5270	1118	8.7	7.3	1.5
2013-2017	6101	5029	1072	7.9	6.6	1.3

(Adapted from Hrsitova & Hakama 1997).

The use of this method for screening is highly sensitive to attendance which is required every second year, as attendance decreases its cost-effective advantage over the other tests is weakened; at 50% compliance the cost-per-death prevented is similar to FS, and Colonoscopy (Lieberman 1995). An overall reduction in mortality of CRC using this method has been estimated to be between 7% and 33% (Towler et. al. 1998, Mandel et. al. 1993). The main benefit to the use of FOBT is the fact that is relatively easy to administer (in the comforts of home), it shows to have high individual compliance and it is inexpensive (Hardcastle et. al. 1996).

Table 2: Predicted Effectiveness of FOBT - Male

	Predicted Number of Deaths			**Predicted Mortality Rates**		
Period	Without Screening	With Screening	Difference	Without Screening	With Screening	Difference
Denmark						
1993-1997	5070	5070	-	22.1	22.1	-
1998-2002	5099	4622	477	21.5	19.3	2.2
2003-2007	5147	4406	741	20.9	17.9	3.0
2008-2012	5194	4290	904	20.2	16.9	3.4
2013-2017	5296	4373	923	19.8	16.5	3.3
Finland						
1993-1997	2354	2354	-	12.9	12.9	-
1998-2002	2634	2383	251	13.0	11.8	1.2
2003-2007	2948	2516	432	13.1	11.3	1.8
2008-2012	3267	2689	578	12.9	10.7	2.2
2013-2017	3595	2956	639	12.8	10.6	2.2
Norway						
1993-1997	4174	4174	-	21.8	21.8	-
1998-2002	4602	4187	415	23.6	21.2	2.4
2003-2007	5075	4367	708	25.4	21.7	3.6
2008-2012	5686	4718	968	27.4	22.9	4.5
Sweden						
1993-1997	6490	6490	-	14.4	14.4	-
1998-2002	6647	6045	602	14.1	12.6	1.5
2003-2007	6723	5758	965	13.6	11.5	2.0
2008-2012	6744	5528	1216	12.8	10.6	2.2
2013-2017	6709	5495	1214	11.8	9.8	2.0

(Adapted from Hrsitova & Hakama 1997).

Research by Hrsitova and Hakama has attempted to predict the gains of screening using a FOBT with a predicted 20% effectiveness for detecting CRC as presented in Table 1 and Table 2. The assumption in this model is that the screening program is started in the mid-1990s. The numbers are predicted and are a measurement of CRC related deaths in screened and non-screened individuals set against an age-adjusted 'world standard mortality' rate (Hristova & Hakama 1997). In all countries there is an expected mortality rate drop in CRC of between 0.8 and 3.4, which is not large but has a better result than mammography, which

already has a mandatory screening program in place in all four countries. There is also a trend (with exception for Norway which isn't present) that in the final year category of 2013-2017 that the mortality reduction slows, this is related to expected decrease in the number of people having CRC as the years progress through the positive effects of screening.

2.5.2 Flexible Sigmoidoscopy (FS)

The use of a 60 cm flexible sigmoidoscope permits visualization of the rectosigmoid and descending colon where approximately 50% of all CRCs are located (McPhee & Papadakis 2008, Hakama et. al. 2005). This screening method can be performed within a physician's office or clinic, it requires an easy to follow bowel preparation prior to the test and is a relative short test to administer (Hakama et. al. 2005). The use of FS has a sensitivity of 70% for detecting adenomatous polyps and advanced neoplasia (Hoff 2004). The long-term follow-up findings of the Telemark Polyp Study demonstrated an 80% reduction in CRC incidence (Hoff 2004). Adenomatous polyps are identified in 10%-20% of patients and CRC is detected in 1% of patients. Case-control studies suggest that screening sigmoidoscopy programs lead to a 60% to 80% reduction in CRC mortality (McPhee & Papadakis 2008). The risk of serious complications (perforation) associated with FS is less than 1 in 10 000 patients, however approximately 50% of advanced neoplasms (cancer, adenomas ≥ 1cm, polyps with villous histology or high-grade dysplasias) are proximal to the splenic flexure and are therefore above the reach of a FS examination (McPhee & Papadakis 2008). A frequent barrier to compliance using this screening method is the complaint of some degree of discomfort, although the procedure itself can take between 5 and 10 minutes (Segnan et. al. 2002, Gondal et. al. 2003). In the SCORE trial, 60.4% of patients experienced mild discomfort and 2% described the pain as being severe (Segnan et. al. 2002). This screening method also does not require as frequent screening as with FOBT, in fact follow-up intervals with removed adenomatous polyps in 'average-risk' individuals will not likely effect the incidence of CRC (Thiis-Evensen et. al. 2001). There is also a risk of perforation using this method that can cause infection, bleeding or further aggravation of any existing lesions (Hakama et. al. 2005).

2.5.3 Colonoscopy

The Colonoscopy screening method permits examination of the entire colon, for this reason this is the gold standard in screening of patients, it has an estimated sensitivity for detecting CRC of greater than 90% (Hoff 2004). This screening method is largely reserved for those

deemed to be at high risk due to a positive familial history of CRC or a positive test for lesions in a less sensitive test such as FOBT or FS because of the time costs of the test, the risk of perforation, and the use of sedation (Lieberman et. al. 2000, Hakama et. al. 2005). In asymptomatic individuals between 50 and 75 years of age undergoing screening colonoscopy, the prevalence of advanced neoplasia is 6-11% and of cancer is 1%. However there have yet to be Randomized Control Trials on the use of colonoscopy as a screening tool in regards to CRC mortality or incidence (Hoff 2004). The incidence of serious complications is close to 0.1% (Lieberman et. al. 2000). This method of screening in one study was demonstrated to detect the risk of potential CRC in 73.3% of patients prior to distal spread and nodal involvement (Lieberman et. al. 2000). Although it is the most sensitive test, polyps that are behind folds, or that are small and flat can be easily missed, therefore this should be done after optimal bowel preparation (McPhee & Papadakis 2008, Imperiale et. al. 2000); this optimal bowel preparation required has also been identified as being a major barrier to screening attendance (Hakama et. al. 2005). Similar to FS, Colonoscopy does carry a risk of perforations, while it is rare, some episodes are described as hazardous (Robinson et. al. 1999); the review of the literature within this project did not find any link of colonoscopy to a fatality.

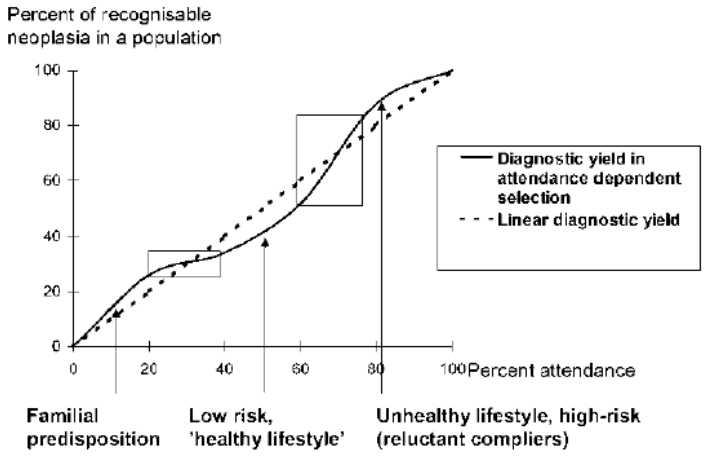
2.5.4 Concerns of Screening Catchment

A large concern in deciding which CRC screening method to use is concerned with desire to use a test with a high degree of sensitivity, a low cost to administer, a maximum convenience for health provider and patient alike, and an ability to collect a high number of individuals (Hakama et. al. 2005). There is continual conflict between all the above factors and Figure 5 demonstrates a model of this concern. Screening studies are sensitive to attendance rates, which are reliant upon an individual's response to knowledge about the program or the method in question (Hoff 2004).

The broken line in the model demonstrates an ideal situation where a test was able to detect 100% of lesions and CRC; such a test does not yet exist (Hoff 2004). Due to the fact that there is no 'perfect test', a combination of methods would be required in order to achieve the desired 100% in the model. However, with each test added, there is a risk of decreasing the attendance rate. The solid line demonstrates the actual diagnostic yield where those with a familial predisposition which would give the test initially high pick-up rates for lesions (Hoff 2004). At the other end of the model are those individuals within the high lifestyle risk group

who ‘reluctantly comply’ (Hoff 2004), and would be the last to join the screening and most likely to be the most sensitive to attendance rates (Whynes et. al. 2003). It is thus imperative to catch those who are highest risk to reduce CRC incidence. A further concern related to catchment is the detection of polyps and appropriate action following the finding of adenomatous polyps. It has been found that in general, greater than 90% of adenomatous polyps do not progress to malignancy (Hakama et. al. 2005). The high number of non-cancerous adenomatous polyps has created challenges in finding an appropriate test with high efficacy that will still catch the maximum number of at-risk individuals but not produce unnecessary resource cost.

Figure 5: Hoff’s Theoretical Catchment Attendance Patterns Based on Patient Risk



(Figure from: Hoff 2004)

2.6 Cost Component

The necessity to screen presents a cost component as well for health care services. While much emphasis has been placed on the test costs, there is further the cost associated with treating cancer when compared to screening. For a health program to be put into place, such as a mass screening for CRC, the program must be demonstrated to be cost-effective. The associated costs must first be known; this may include the financial cost but also the potential consequences of the program (Drummond et. al. 2005). There must also be a weighing of various options, for example, ‘what are the costs of action (screening) vs. inaction (treatment)?’ It is known that a large share of medical costs are incurred in the final months of the patient’s life, it is thus important to use screening as a tool to reduce cancer costs which could be incurred within end-of-life care (Howard et. al. 2009). Therefore patients who do not attend screening programs can incur a massive cost and resource burden on the health system.

Patients who have their potentially malignant polyps discovered at an early stage incur lower lifetime medical costs when compared to those with undetected polyps (Howard et. al. 2009). Thus for screening to accurately be evaluated, one would need to have the information of various courses of action available in terms of their costs and consequences (Drummond et. al. 2005).

3 Theoretical Framework

An underlying principle surrounding participation and non-participation in a screening program surrounds the belief of the study's invitees. These frameworks have been used as an explanation to determine reasons for certain health behaviours among the sample used in this thesis. To explain this phenomenon this thesis will combine tenets of the 'Health Belief Model' by Janz and Becker, and Rosenstock's 'Use of Health Services Model'.

3.1 Rosenstock's Determinants of Health Behaviour

Rosenstock examines the use of health services in terms of groups with certain characteristics. In general, it is concluded that people who most often use preventative or detection services (such as a screening) are younger to middle-aged, female, are highly educated, and earning a high income (Rosenstock 2005). A similar trend is seen in the use of diagnostic and treatment services such as a visit to the dentist or physician. This trend is explained through what Rosenstock describes as 'motivation for perception and action' in that if one is unconcerned with a particular aspect of their health, they are unlikely to take any action that could have some bearing on that aspect (Rosenstock 2005). For example, if one believes that they are unlikely to come into contact with a given disease, they would then not see it as being justifiable to take measures to prevent it or act upon it. This draws onto Rosenstock's three components of his 'Determinants of Health Behaviour' in terms of potential cancer screening and detection program barriers.

3.1.1 The health motive or threat

This component comprises two dimensions. The first dimension is whether the individual believes that they are susceptible to the given disease and the second is whether the threat from the given disease would have serious implications on the individual (Rosenstock 1963). Therefore, the individual most believe that they are at risk for the given disease and that by not acting there could be serious implications. The higher the perceived susceptibility and the higher the perceived threat, the more likely the individual will act.

3.1.2 Belief about the utility of various courses of action in reducing the health threat

In this component the motive and threat are established, however the individual must also believe that the course of action available to solve this threat can reduce the likelihood of it occurring and also reduces the potential seriousness of the problem (Rosenstock 1963). The individual must further believe that undertaking these actions will not increase or lead to further threats (Rosenstock 1963), in other words the individual must believe that the course of action is safe and will lead to positive outcomes. With respect to a screening test for cancer, the individual must first believe that they are suffering from cancer regardless of whether symptoms are present (Rosenstock 1963). Building upon this assumption, the individual must believe that existing methods available can detect cancer (both symptomatic and asymptomatic) and that by having the cancer detected earlier, there will be a better cancer prognosis (Rosenstock 1963). Lastly, the individual must also believe that the facilities, personnel and methods available are competent to both employ and administer these tests (Rosenstock 1963).

3.1.3 Conflicts among motives and courses of action

This is described as when motives, their beliefs and the proposed courses of action of these motives are in conflict with each other. These must then be resolved in order for a behaviour or response to emerge (Rosenstock 1963). An example of this is if the individual is motivated to take a certain response to improve their health well-being but may be drawn away on acting upon it by unpleasant factors (embarrassment), potential pain, inconvenience, emotionally upsetting experiences or an unwanted expense (Rosenstock 1963). The individual could also believe that the health professional would be unable to reconcile these fears; the risk in this belief is that the individual could then believe that the motive for action is no longer important enough. Thus for the individual to act in this case, the perceived benefit must outweigh the perceived ‘cost’. The individual must then also be convinced that the need for action is necessary as delaying the action risks decreasing the level of motivation.

3.1.4 Inducing Behavioural Change

Rosenstock claims that there is a rather large error that public health officials have failed to rectify, in that in the context of screening programs for chronic disease, individuals are asked to recognize signs and factors of various diseases in differing ways (Rosenstock 1963). This

poses a number of problems in that it assumes or demands that the lay public has a knowledge of human physiology and medicine, it places the lay person in position where they must decide which tests are needed or which specialist to see, and lastly that each screening program appeal will lose its message among those who are not concerned with it so program appeals will then have to often be repeated.

If barriers to action are based upon individual responses to readiness to behave, determined beliefs, psychological barriers, interpersonal influences and critical incidents, it would thus be in the public's interest to simply minimize the barriers to action (Rosenstock 2005). This can be done through increasing the chances to act and providing better cues for trigger responses, this can be done through reducing financial costs (publicly funded screening), distances to travel to screening (mobile screening programs) or setting hours of operation that are convenient (scheduling an appointment) (Rosenstock 2005). Similarly trigger responses (cues to action) can be as simple as reminders from physicians to patients or announcements and stories in the mass media (Rosenstock 2005).

Therefore Rosenstock concludes that three conditions must be met for an individual to act in a prevention or detection program:

1. The individual must be ready to take action relative to a particular health condition, based on susceptibility and serious consequences

2. The individual believes that the test or preventative method in question is feasible and appropriate to the desired outcomes; thus reducing susceptibility and threat

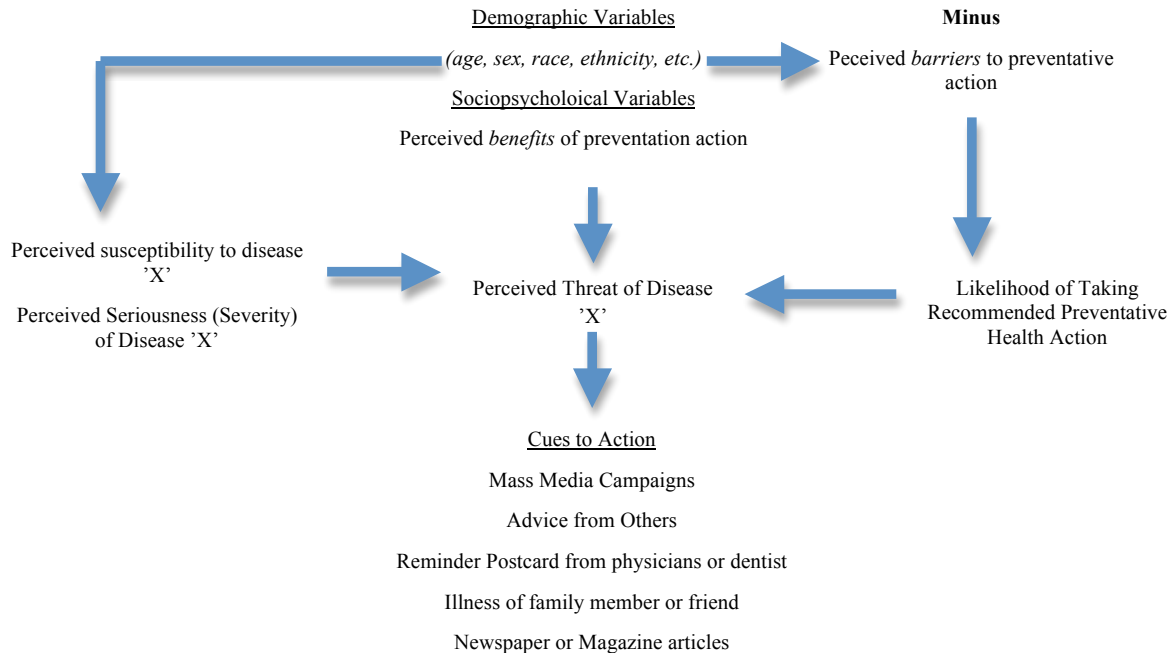
3. There must be a cue or stimulus to trigger the response.

While efforts to minimize barriers and maximize convenience to the public are keys to screening acceptance, there will always be a group that remains that is either not psychologically ready to act or will not respond to cues to seek various health services no matter how they are presented (Rosenstock 2005). In the context of the NORCCAP study, one could expect that those who were invited to screening but did not attend would be in this group where they lacked a trigger or cue to act. It would then be expected that these Non-Attendee people could be the most at risk for lifestyle related diseases.

3.2 The Health Belief Model (HBM)

The HBM was designed as a means to explain reasons behind the failure of individuals to accept preventative and screening initiatives as a means of early disease detection for asymptomatic disease (Janz & Becker 1984). The HBM consists of four principle tenets described below in Figure 6:

Figure 6: Janz and Becker's 'Health Belief Model'



(Figure adapted from Janz & Becker 1984)

1. Perceived Susceptibility: This describes how vulnerable an individual may feel towards a particular disease and how great of a risk may be felt of contracting the particular disease
2. Perceived Severity: This is a personal measure of the individual in regards to the seriousness of the disease. This measure includes medical consequences (death, pain, disability) and social consequences (inability to work, social relations, family life).
3. Perceived Benefits: This highlights the fact that while an individual may acknowledge the seriousness and susceptibility of disease there must also be an available course of action to reduce the threat of the specific disease. The course of action must also prove to be beneficial (feasible and efficacious) to the individual in order for them to accept the action available.

4. Perceived Barriers: Some health actions may have potentially negative aspects associated with it, and these negative aspects act as barriers to intended health behaviours. The individual prior to undertaking a health action will weigh the costs and benefits of their actions, and should the potential 'costs' outweigh the benefits, the individual may choose not to act. Identified barriers could be the financial expense, pain, embarrassment caused by the procedure, inconvenience or unwanted side effects.

The final tenet of 'Perceived Barriers' appears to be the strongest barrier to CRC screening compliance using this framework. In a study carried out by Janz et. al. the opinions and attitudes of individuals towards screening and CRC were collected through a series of telephone interviews (2003). The primary reason for respondents not participating in screening was the barrier of 'embarrassment' of undertaking FOBT, FS and Colonoscopy. The degree to which respondents saw the various preventative measure to CRC in terms of everyday life was a strong predictor of screening participation (Janz et. al. 2003). Similar to the conclusions presented by Rosenstock (2005), the authors conclude that more must be done to inform all sectors of screening and health effects in CRC awareness campaigns. It is through education campaigns and 'physician-guided' promotion that perceived barriers to CRC screening will be removed (Janz et. al. 2003: 633).

3.2.1 **Behaviours**

In the screening context, it is of utmost importance to have a high degree of participation in order to both increase the possibilities of identifying asymptomatic patients with a certain disease and to increase the efficacy of a particular test. However, using the HBM framework the majority of participants are those who are already of the opinion that they are at particular risk of the disease being screened. This theory has been demonstrated by the general trend that the vast majority of participants in screening are those who view themselves as being at risk or have been identified as being at risk; more specifically risk due to a family member having a similar ailment (Janz & Becker 1984). Similarly, research in this area has demonstrated that those who are married (or common law relationship) tend to view 'susceptibility' and 'severity' more strongly and act upon these beliefs through higher screening participation (Janz & Becker 1984).

The study of HBM also extends to ones view of healthy lifestyle behaviour, a common example of this would be views on smoking. With countless links and media campaigns

demonstrating the effects of smoking upon ones life expectancy and overall health well-being, it is very apparent that a HBM is in effect in this case as well. Those who do not see a link between smoking habits and various acute and chronic disease risks are more likely smokers themselves while those who identify themselves as 'non-smokers' link smoking to disease. Therefore in the HBM context, one could conclude that a smoker would view the barriers of smoke cessation as being greater than the susceptibility and seriousness of diseases related to smoking (Janz & Becker 1984).

Due to the fact that HBM is largely associated with psychological behaviour it is important to identify limitations of the model: some behaviours are habitual which could hinder health related behaviour, many health behaviours are undertaken for non-health reasons (for example appearance), economic/environmental factor could prevent an individual from a health behaviour although they may believe it to be beneficial, and the model assumes that health is important to individuals and that cues to action are widely available; in some instances that is not the case (Janz & Becker 1984).

3.3 Summary

Both the 'trigger' model presented by Rosenstock and the HBM model presented by Janz & Becker demonstrate the psychological processes behind screening programs and the health of individuals. Similarly, there is a challenge in trying to bring in individuals who are of lower-socioeconomic status who are traditionally least likely to attend a screening (Hardcastle et. al.1986); this emphasizes the need to maximize 'uptake from all sections of the community' (Atkins 2002: 1298). Both models acknowledge that for an individual to act, they first must believe that their action is necessary for the well-being of themselves. The models further demonstrate that for these actions to occur various opportunities to remedy these concerns must be available and must be demonstrated to be effective. Lastly, both models emphasize the necessity that education through means of physicians, health professionals, mass media and screening programs must provide opportunities for individuals to take an active role in their own health decisions by presenting clear facts to individuals (Janz et. al. 2003, Hoff 2004). It is within this 'lack of necessary education' that adverse events can occur within a mass-screening program, leading to what is described in the following section as the Health Certificate Effect.

4 The Health Certificate Effect (HCE)

The 'Health Certificate Effect' is a concept that is concerned with the interpretation of a health result by an individual and is identified as a major obstacle within screening programs (Robinson et. al. 1999, Thiis-Evensen et. al. 2006). The primary concern with this effect is that in the context of a screening program for a specific disease, a negative test could be wrongly interpreted as meaning that the individual is 'healthy'. Further, the screening result could be misunderstood that the negative result is a clean bill of health and risky lifestyles choices such as smoking or intake of unhealthy foods could 'justifiably' continue (Tymstra & Bieleman 1987). While there is emphasis on the need to screen for preventable or manageable disease, the practice of mass screening risks presenting unintended consequences such as the HCE which can hinder the effectiveness of a mass screening program.

In a study by Tymstra and Bieleman to assess the effects of mass screening for cardiovascular disease, they introduce a practical example of potential mass screening consequences (1987). For the most part, patients with a positive test result for cardiovascular disease were induced to change certain risky health behaviours such as smoking cessation, partaking in physical activity or improving dietary choices. However, there was a group of patients with a favourable test result (negative test) who led particularly unhealthy lifestyles yet it did not affect their results (Tymstra & Bieleman 1987). Unfortunately these results did not induce lifestyle change and was in most part regarded as meaning that the results of the screening were a 'justification of their unhealthy behaviour' (Tymstra & Bieleman 1987: 290).

Similar results were observed in the Telemark Polyp Study where the leading cause of death in both their sample group and control group was coronary heart disease (Hoff et. al. 2000). In the NORCCAP study (which followed the Telemark Polyp Study), a HCE was also suspected and the authors pointed out a possible circumstance where patients had a sense of 'being taken care of' through screening services leading to a situation where detrimental lifestyle choices will continue and efforts to increase awareness of possible unhealthy practices will be largely ignored; specifically smoking habits (Larsen et. al. 2007: 477, Hoff et. al. 2000). Those who were invited to the CRC screening had a reduced intake of fruits and vegetables, did not increase their frequency of physical activity, had a higher weight gain and demonstrated no improvement in their smoking habits when compared to the study's control group (Larsen et. al. 2007, Hoff 1987, Hoff et. al. 2000). A similar HCE was also discovered in findings from

the Telemark Polyp Study in their 13-year follow up which demonstrated a general sense of well-being amongst the screenees with negative findings which lasted for approximately 1 year following the study (Hoff et. al. 2001).

Smoking has also been shown to significantly increase the number of colorectal polyps when compared to those who do not smoke (Hoff et. al. 1987). For this reason smoking and obesity were primary risk factors used in seeking to identify and explain a presence of a 'Health Certificate Effect'. To continue on with this analysis, a selection of lifestyle related conditions were selected in the following section. Observations in the rates of reported incidents in the various disease groups were observed in those who were invitees who attended the NORCCAP trial (positive and negative test), those who declined to attend, the control group and the group of excluded individuals. The selected lifestyle-related disease groups all have strong relations to diet, smoking status, exercise and obesity, which are all similar lifestyle factors studied in the post-NORCCAP analyses. Links have also been drawn between one's intake of fat, protein and low intake of fibre to the development of polyps (Vatn & Hoff 1989), which could share some similar characteristics to other disease groups. Similarly, the follow-up study of Larsen et. al. also made the observation that participants in the trial with advanced neoplasia had a poorer lifestyle than those in the control group (2006a, 2006b), it could then be explored if these same risk factors also showed increased frequency in also disease groups listed in the proceeding section compared between screenees and controls.

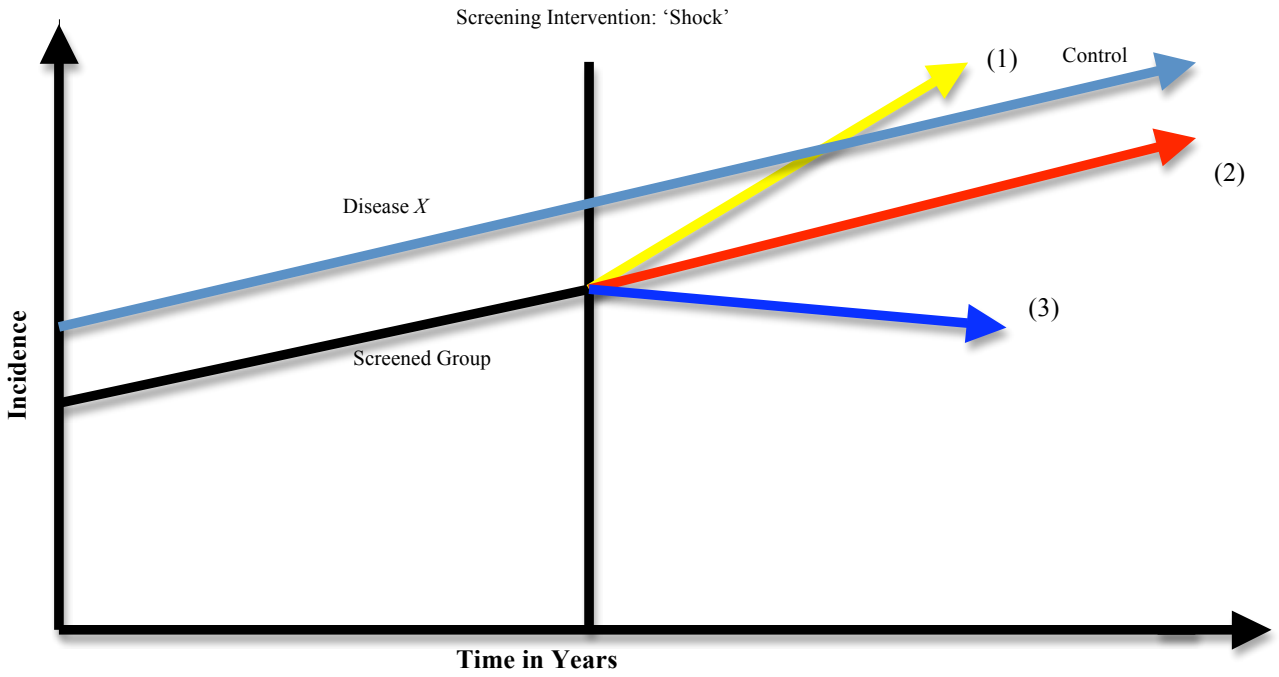
4.1 Expected Model

If a Health Certificate Effect were present, the method used in this study should be able to accurately demonstrate whether or not adverse effects of screening could be explained by the results. An illustration of the potential hypothetical result is given below in Figure 7.

Figure 7 demonstrates the purpose of the statistical model. Given the incidence path of disease *X*, it would be expected that the control would be a constant rate for the given disease since they would not be affected by a screening result 'shock'. Those who were screened, should an adverse screening effect be present, would be expected to have a change in incidence of disease differing from the constant. The intervention may either 'shock' the individual into adopting a negative or positive lifestyle change. A positive lifestyle change following the screening intervention would be expected to lead to a decrease in incidence illustrated by the royal blue (3) arrow. A negative lifestyle change, would be associated with

an increase in the incidence of disease *X* at a higher rate than that of the constant as illustrated by the yellow (1) arrow.

Figure 7: Model of the Health Certificate Effect



In the context of this study, it would be predicted that those within the Negative Findings and Non-Attendee groups would be at risk of being affected by the Health Certificate Effect as illustrated by the yellow arrow (1). This would mean that the invitees who had a Negative Finding or Non-Attendee would deem themselves as being healthy, but could in fact be suffering from another medical condition; this could be known or unknown to the participant.

5 Lifestyle-Related Disease Groups

5.1 Diabetes Mellitus (DM)

Diabetes Mellitus is a chronic syndrome of hyperglycaemia (when an excess of glucose is circulating around the body), which is due to the inability to break down glucose because of insulin deficiency, resistance or a combination of both factors (Kumar & Clark 2009). Effects of this disease are irreversible and its late effects can lead to the onset of coronary heart disease, peripheral vascular disease and stroke, hypertension and neuropathy (Kumar & Clark 2009, McPhee & Papadakis 2008). The disease is divided into two groups, Type 1 and Type 2. Type 1 is a disease of insulin deficiency where glucose cannot be broken down; this disease is more commonly referred to as 'Juvenile Diabetes' as it will manifest itself between early childhood and puberty.

Type 2 is common in populations of more affluent societies. Circulating insulin is sufficient to prevent ketoacidosis but increasingly becomes unable to prevent hyperglycaemia; over time this trend leads to insulin resistance within the body (McPhee & Papadakis 2008). This disease can remain subclinical or undiagnosed for many years before diagnosis, with 25% to 50% of patients already showing signs of vascular complications at the time of diagnosis (Kumar & Clark 2009). Obesity can increase the risk of diabetes by 80-100 times (Kumar & Clark 2009) with present waist-to-hip ratios greater than 0.9 in men and 0.8 in women also being associated with increased risk of diabetes in obese subjects (McPhee & Papadakis 2008). When diabetes is diagnosed in a man between the ages of 40 and 59, their life expectancy will be reduced by 5-10 years (Kumar & Clark 2009). This form of diabetes is preventable through a proper diet and physical activity, and in some cases the effects can even be reversed (Kumar & Clark 2009).

5.2 Hypertension & Secondary Hypertension

Hypertension or as it is more commonly referred to as 'High Blood Pressure' is identified as an elevated arterial systolic blood pressure that is $\geq$ 140 mm Hg or a diastolic blood pressure of $\geq$ 90 mm Hg (McPhee & Papadakis 2008). Hypertension is present in roughly 20% to 30% of the population (Kumar & Clark 2009) and if left untreated can dramatically increase the risk of stroke, coronary heart disease, peripheral vascular disease, end-stage renal disease, and

heart failure (McPhee & Papadakis 2008). As blood pressure rises, there is in increased risk of mortality and morbidity, for example isolated systolic hypertension can lead to a 2 to 3 -fold increase in cardiac mortality (Kumar & Clark 2009). Hypertension is divided into two categories, Primary and Secondary. The onset of Primary Hypertension occurs between 25 and 50 years of age and can be due to a number of genetic and environmental factors such as; sympathetic nervous system hyperactivity, abnormal cardiovascular or renal development, rennin-angiotensin system activity, defect in natriuresis, intracellular sodium and calcium, and certain exacerbating factors such as obesity, intake of sodium in ones diet, alcohol consumption, cigarette smoking, stress and amount of exercise (Kumar & Clark 2009, McPhee & Papadakis 2008).

The smaller group of Secondary Hypertension is identifiable in those showing signs of hypertension prior to 25 years of age, those showing sudden symptoms after 50 years of age or those suddenly not responding to earlier hypertension treatments (McPhee & Papadakis 2008). Secondary Hypertension is largely due to other conditions that can increase blood pressure in the body for example, renal diseases alone account of 80% of all Secondary Hypertension cases (Kumar & Clark 2009).

Identifiable signs of hypertension include a high blood pressure or a different pressure between different extremities (arms and legs), narrowing of the retinas, a left ventricular heave, and a weak or delayed pulse (McPhee & Papadakis 2008).

5.3 Chronic Obstructive Pulmonary Disease (COPD)

COPD is the combination of syndromes (emphysema, asthma and bronchitis) that cause permanent destruction to the lung and obstruction to airflow (Kumar & Clark 2009). The presence of Chronic Bronchitis or Emphysema is most often link to the progression of obstruction in COPD (McPhee & Papadakis 2008). Long-term exposure to toxic particles and gases are the leading causes for the onset of COPD; cigarette smoke accounts of 90% of these cases in developed countries (Kumar & Clark 2009). It is predicted by 2020 that COPD will account for the fifth most cause of disability worldwide and the third leading cause of death (Kumar & Clark 2009). Similarly, infections related to the lower respiratory tract, such as COPD, accounts for 10% of the worldwide burden of morbidity and mortality and 75% of the worldwide antibiotic usage (Kumar & Clark 2009).

COPD is most often identified by a persistent cough with white or clear spitum, as well as wheezing and breathlessness; these symptoms can be further worsened by cold weather, atmospheric pollution and foggy weather (Kumar & Clark 2009). Symptoms are usually present for ten years or more and are diagnosed in patients between the ages of 50 and 60 (McPhee & Papadakis 2008). The disease can further progress to where everyday day activities such as walking or getting dressed leads to breathlessness. When these factors are combined they can lead to or further progress other diseases such as hypertension, osteoporosis, depression, and metabolic problems (weight-loss, loss of muscle mass) (Kumar & Clark 2009).

There are a number of drug therapy treatments to manage the symptoms of COPD however it is imperative that smoking be ceased as it can slow down the rate of lung and bronchial deterioration, therefore prolonging death (Kumar & Clark 2009, McPhee & Papadakis 2008).

5.4 Ischemic Heart Disease (IHD)

This group is characterized by a group of diseases most commonly referred to as 'coronary heart disease' in the heart that are due to an imbalance of oxygen and other nutrients and the demand for these substance (Kumar & Clark 2009). This could be due to factors that could reduce coronary flow to the heart such as: atheroma, thrombosis, spasm, embolus, coronary ostial stenosis, coronary arteritis and hypotension (Kumar & Clark 2009). They are a result of prolonged atherosclerotic plaque causing blood and nutrients to improperly circulate to certain parts of the heart; leading to permanent damage (McPhee & Papadakis 2008, Kumar & Clark 2009). The disease can be classified as being with ST or without ST elevation; diagnosed using an Electrocardiogram (ECG). Patients with ST elevation require immediate reperfusion therapy that is meant to remove a blockage through the use of a stent. Patients without ST elevations are predominantly older, already have a pre-existing vessel disease, and have a pre-existing vascular disease; this group is of high risk of death following hospital discharge (McPhee & Papadakis 2008). This group of heart diseases is the number one cause of death worldwide.

Symptoms include an intense building pain, sudden weakness, cold sweats, light-headedness, and sudden death (this occurs in 50% of patients prior to arriving at the hospital due to ventricular fibrillation) (McPhee & Papadakis 2008). It should be noted however, that up to

one-third of patients with IHD do not have an episode detected until they undergo an ECG (McPhee & Papadakis 2008).

Traditional risk factors include increased age, gender as men have a higher incidence, family history, smoking, diet, obesity, hypertension, Diabetes Mellitus and a sedentary lifestyle (Kumar & Clark 2009).

5.4.1 Angina Pectoris (AP)

The onset of Angina Pectoris is due to atherosclerotic (thicken of artery walls) heart disease and is largely characterized as darting, gripping, heavy, tight or knife-like pains (McPhee & Papadakis 2008, Kumar & Clark 2009). The pain is central/retrosternal but may also be felt in the jaw and arm, this pain can range from mild discomfort to severe pain (Kumar & Clark 2009). This pain can be brought on by physical exertion, anger, vivid stress-inducing dreams, or in some instances, even at rest (Kumar & Clark 2009).

Signs following an attack usually indicate elevated systolic and diastolic blood pressure, a gallop heart rhythm, and ventricular/supra-ventricular arrhythmias (McPhee & Papadakis 2008), however diagnosis is largely based on patient history (Kumar & Clark 2009). AP can be a result of or a cause of other disease such as Diabetes Mellitus, Hypertension, or peripheral vascular disease (McPhee & Papadakis 2008). Treatment of AP includes the management of other pre-existing conditions such as Diabetes and Hypertension, smoking cessation, weight loss, treatment for high cholesterol, and regular exercise (Kumar & Clark 2009). Prognosis of Angina Pectoris is very good as annual mortality is < 2% (Kumar & Clark 2009).

5.4.2 Acute Myocardial Infarction (AMI)

Acute Myocardial Infarction is similar to the symptoms and signs of AP, however while AP is largely stress related, a myocardial infarction is a sudden attack that can occur at any time. Many incidents of AMI occur at rest and may only be picked up by patterns on an ECG. This sudden ‘attack’ is more commonly referred to a ‘Heart Attack’ where a portion of the heart has died because of atherosclerotic heart disease (Kumar & Clark 2009). Further, 1 in every 6 attacks ends in sudden death as the first, last and only symptom (Kumar & Clark 2009).

6 Data

6.1 Norwegian Colorectal Cancer Prevention (NORCCAP) Trial

This study provided the sample of participants and controls used in this thesis. The results from this trial became the bulk of the focus for this thesis, specifically the finding groups. A brief description of the trial is described below.

The Norwegian Colorectal Cancer Prevention (NORCCAP) screening study was a prospective controlled study with the aim of undertaking a large scale screening to gain information about the prevalence, attendance rates, and distribution of colonic neoplasms in the age-risk population of individuals 50 to 64 years of age (Bretthauer et. al. 2002, Gondal et. al. 2003). A sample of 20,780 men and women with a ratio of 1:1 were drawn from populations in the urban Oslo area and the mixed rural/urban county of Telemark[1] were placed into the intervention group; a control group of 79,808 people was also established from these counties and were not invited to participate in screening but shared similar characteristics are the invited for screening group. Both screening and control groups were selected at random from the Norwegian Patient Registry. Those in the intervention group were randomized to either a once-only FS or a combination of a once-only FS and a FOBT screening test. Intervention group members were also informed of the study background, the aim of the research, the benefits of the trial, the various risks associated with participation in the trial and the procedures involved in the examinations (Bretthauer et. al. 2002). The sampling from the FOBT arms was done no earlier than 10 days prior to the FS appointment and was collected from three stool samples (Bretthauer et. al. 2002). Exclusion for this trial included those who had previous colorectal surgery, ongoing radiation or cytotoxic therapy for malignant disease, severe chronic cardiopulmonary disease, life-long anticoagulant therapy, a coronary episode or cerebrovascular incident within the last 3 months, disabled, unable to give written informed consent, resident abroad, unknown address or deceased (Bretthauer et. al. 2003).

[1] Telemark Polyp Study results and trial described in Hoff et. al. 2000.

Table 3: Screening Method – Patient Characteristics

		FS Only	FS & FOBT
Total		6,694	6,266
Gender			
	Male	3,256	3,043
	Female	3,438	3,233
Age			
	50 – 54 years	2,308	2,099
	55 – 59 years	2,705	2,479
	60 – 64 years	1,681	1,688
Area			
	Telemark	3,740	3,484
	Oslo	2,954	2,782

(Figure adapted from Gondal et. al. 2003)

In the FS arm of the trial, all visualized lesions within the colon were biopsied but not removed. For this reason, a diagnosis of an adenoma was only made after a histopathological examination of the biopsied lesion. The study assumed that all polyps that were ≥ 10 mm were defined as being positive as well as any biopsied specimen identified as being a neoplasia; these positive findings were referred for a colonoscopy. In the FOBT arm of the trial, a test must have more than 3 windows used to be valid and one positive test window was referred for colonoscopy (Gondal et. al. 2003). Individuals who did not have a plausible reason for a positive result were asked to repeat their test and if the results continued, and were then referred to a specialist in gastroenterology.

The total population of the screened group is shown in Table: 3 (Gondal et. al. 2003). The breakdown between gender, age, and screening type (FS or FS/FOBT) are fairly similar, however there were more participants from Telemark (71%) than from Oslo (58%). A total of 20,780 individuals were invited however 777 were excluded according to the study's exclusion criteria which left 20,003 individuals eligible, however only a total of 12,290 invitees took part (Bretthauer et. al. 2003). There were n = 2639 participants who had a

positive on either the FS or FOBT, and of that group n = 2524 attended a follow-up colonoscopy (Larsen et. al. 2006b).

6.2 Description of the Data

Data for use in this project was collected in conjunction with NPR data of patients within the NORCCAP trial consisting of both controls and invitees. Further patient information was also provided by the Norwegian Cancer Registry and SSB. This data encompassed 6 years of information between the years of 1998 and 2003. The various data sources were then combined and identified using assigned patient numbers. This data included information concerning patient CRC screening outcomes, socioeconomic status, education, year of admission to hospital, ICD 9 and 10 coding, hospital code, county location of screening, civil status, age, birth country, and type of care received (inpatient or outpatient). Due to the fact that multiple data sources were combined, there was a risk of duplicate patients presented in the data set. The data was then cleaned to remove duplicate patient records and patients were then divided between the type of care received either outpatient and inpatient hospital care.

To study the aims of this thesis, patients were then identified using ICD-9 and ICD-10 code grouping on the basis of disease selected for study that were identified as being associated with patient lifestyle. The data set was narrowed to 6 disease groups that were selected based upon their ICD-9 or 10 coding, these diseases included Diabetes Mellitus, COPD, Hypertension, Angina Pectoris, Acute Myocardial Infarction and Ischemic Heart Disease. A patient had to have either a main diagnosis and/or a maximum of three secondary diagnoses of within the selected ICD-9 or 10 codes to remain in the data sample. For example, a patient may have a main diagnosis of Diabetes Mellitus, and only a third secondary diagnosis with a relevant ICD-9 or 10 codes. Should a patient have multiple diagnoses of the same coding within the same year, it was only recorded once for that year. However, having a COPD coding for example, in one year would be recorded again and counted again if it appeared following the initial diagnosis in the following year. All patients who did not fulfill the ICD-9 or 10 disease coding requirements were removed from the sample. A list of the disease groups and their coding are included in the Appendix I.

Variables used within this analysis are listed and described below in Table 4 and observations were used from NPR data between the years of 1998 and 2003.

Table 4: Description of the Data Variables

Variable	Description	Observation Year
Age 1999	*The age of the patient corresponding to their age in 1999.*	*1999*
Age Squared	*The age in 1999 variable was squared in order to determine the steepness of the change in age and the shape of the curve*	
lnssb	*The assigned patient number identifier; it does not correspond to their real national number*	
Income	*Patient income is listed in both a figure in Norwegian Kroner (NOK) and divided into groupings from (1) 0 – 99 999, (2) 100 000 – 199 999, (3) 200 000 – 299 999, (4) 300 000 – 399 999, (5) 400 000 – 599 000, and (6) 600 000 +*	*1999*
Education	*The level of education attained at 1999, divided by low <10 years, intermediate < 14 years, and high > years.*	*1999*
Birth Country	*Patients were recorded as either being born in Norway or being born abroad*	*1999*
County	*There were two principle counties in the study of either Oslo or Telemark, however a third 'Other' group was established for those residing in a different county.*	
Intention to Treat	*This group was divided into controls and those invited to the screening*	*1999,2000,2001*
Findings Group	*This group includes controls, attendance to screening with a positive test for CRC, a positive test for adenomatous polyps or a negative test, those who did not attend, those with returned mail or died, and those who were excluded due to the exclusion criteria of the NORCCAP study.*	*1999,2000,2001*
Civil Status	*This group was divided into single, married, common-law, widow, separated and divorced*	*1999*
Gender	*Male or Female.*	
Year	*The time dimension within the statistical model*	*1998-2003*

Below in Table: 5 are the descriptive figures of the data used in this study. There were identical characteristics observed between the outpatient and inpatient group. The percentages are listed in proportion to the total sample in the outpatient and inpatient groups. With regards to the disease proportions, there were differences within the two treatment care categories; it was for this reason that a separation of inpatient and outpatient groups was made. While there is evidence of patients requiring care within both the inpatient and outpatient setting, the majority of treatments for Diabetes Mellitus and COPD were handled in the outpatient setting.

This separation is important to maintain should further work study a cost component of screening outcomes.

Table 5: Individual Patient Characteristic of the Data Sample

Data Characteristics		Outpatient	Inpatient
Age 1999			
	50 - 54 years	51.6%	51.6%
	55 - 64 years	48.4%	48.4%
Education	**Low**	24.2%	24.2%
	Intermediate	47.1%	47.1%
	High	28.7%	28.7%
Income	**Level 1**	13.5%	13.5%
	Level 2	25.3%	25.3%
	Level 3	32.4%	32.4%
	Level 4	14.2%	14.2%
	Level 5	8.7%	8.7%
	Level 6	5.1%	5.1%
Civil Status	**Single**	11.4%	11.4%
	Married	59.8%	59.8%
	Common-law	3.8%	3.8%
	Widow	20.4%	20.4%
	Separated	3.7%	3.7%
	Divorced	0.2%	0.2%
Birth Place	**Norway**	88%	88%
	Other	12%	12%
Gender	**Female**	50.1%	50.1%
	Male	49.9%	49.9%
Intention to Treat	**Control**	79.4%	79.4%
	Invited	20.6%	20.6%
Findings Groups	**Control**	79.4%	79.4
	Attended - CRC	0.004%	0.004%
	Attended - POS	2.2%	2.2%
	Attended - NEG	10.6%	10.6%
	Non-Attendee	7%	7%
	Returned / Dead	0.4%	0.4%
	Excluded	0.4%	0.4%
County	**Oslo**	72.7%	72.7%
	Telemark	25.5%	25.5%
	Other	0.9%	0.9%
Average Number of Cases per Year			
	Diabetes Mellitus	732	436
	Hypertension	686	800
	COPD	429	353
	Angine Pectoris	332	510
	AMI	40	242
	IHD	532	620
Total Number of Patients in Sample		100,116	100,106

A detailed breakdown of the proportion of patients within the two different screening age groups is located in Appendix II. Each table is arranged according to the lifestyle-related disease group and all figures are measured as ‘proportion of cases per 1000 people’.

7 Methods

The dataset was prepared for statistical analysis using a method called Logistic Panel Regression. Using Logistic Panel Regression allows changes within the six disease groups to be studied over time. Each patient number, given by 'lnrssb' in the dataset, is repeated 6 times representing the six years of data provided (1998-2003) for each year. This required changing each variable category of finding group, civil status, education, income and disease diagnosis by year into individual binary outcomes. It was assumed throughout the analysis that zero was to represent 'not present' and one was to represent 'present'. This statistical analysis was used because of its ability to easily measure the probability of changes over time in a variety of independent variables on the given dependent variable of Disease Group '*x*'. The goal of this study was to measure survival time following a treatment within the NORCCAP trial patients, over intervals given by *t* = time in years (Hosmer & Lemeshow 1989). The formula for the fitting of the independent variables is given as (1) below. The following formula demonstrated the fitting of the variables when specifying for random effects. This formula represents the probability of being at a hospital department (inpatient or outpatient) given by *h* with a specific disease given by *d* for the given independent variables given by *i* at time interval *t* with parameters β given *x* characteristics dependent upon the disease group *y*.

$$\Pr(y_{it}^{hd} \neq 0 | x_{it}) = P(x_{it}\beta + v_i) \quad (1)$$

The second formula (2) measures the goodness of fit or the predictability of *y* within the model. Where R^2 represents the deviance within the random effect panel regression model. The fitting of the model is found using the log likelihood from the output of the constant represented by $\log_e L_1$ is compared to $\log_e L_1$ the measures of the full model (Fox 1997).

$$R^2 = 1 - \frac{G_1^2}{G_0^2} = 1 - \frac{\log_e L_1}{\log_e L_0} \quad (2)$$

The third (3) formula defines rho (given by ρ) is an additional panel-level variance component which explains the total proportion of the total variance contributed to by the panel-level variance. This formula is done by taking the log of the variance $\ln(\sigma_v^2)$, the standard deviation σ_v is included in the output from the regressions. When $\rho = 0$, the panel-level data

component is not important and the panel estimator is the same as the pooled estimator, called the logit (Stata 2007).

$$\rho = \frac{\sigma_v^2}{\sigma_v^2 + \sigma_\varepsilon^2} \quad (3)$$

The variable 'Year' in the dataset corresponds to the time dimension within the Logit Regression Model. Regressions were run assuming normal distribution and the separation of outpatient and inpatient data was maintained.

There were two regressions run for each disease group in each inpatient group and outpatient group. A new variable was created in order to measure the time dimension of disease between years within the same patient dependent upon being screened or not screened. This new variable was labeled as "interaction" and corresponded to the seven possible screening findings outcomes divided by those who had their screenings in 1999, 2000 and 2001. The 'interaction' variable was calculated by multiplying the 'findings group' variable by the patients who had a screening. The interaction variable was created as a means to demonstrate whether the screening result would result in a change in disease incidence for the given disease groups dependent upon the finding outcomes.

8 Results

There were a total of four regressions done for each of the six lifestyle-related disease groups. The intention to treat group did not have an analysis using the interaction variable because the intention to treat variable was already accounted for in the interaction variable groups. The Coefficients are written in normal text and the Standard Errors are written in parenthesis in each of the tables. A calculation to determine the log likelihood of each regression result given by formula (2) in the Methods section will be written in the description of each disease group result as well as the 'rho' from formula (3) given by ρ.

8.1 Diabetes Mellitus (DM)

Results of the logistic panel regressions are given below in Table: 6. In all four of the regressions, ρ is greater than zero therefore the variance between the panel levels is important.

In regards to group findings, those in the Non-Attendee group show a significantly higher risk of being treated for DM than the control group within the inpatient treatment side at the 1% level. Those who are in the invited group with a negative screening result, show a decreased risk of being treated for DM at the 10% significance level in the inpatient sample group when compared to controls. The lone significant result in the outpatient group were those who occupied the returned mail or died group, which demonstrated a decreased risk of DM than controls; this group was a small sample.

In the interaction category of the results, those who attended screening and had a positive or negative result showed 10% significance on the inpatient side; both results showed a decrease in incidence when compared to the control group. The non-attendee group demonstrated an increased risk of incidence with significance at the 10% level. The outpatient side showed highly significant results for increases in incidence for those who received a negative result and those who failed to attend the screening at the 1% level.

The risk of incidence of being treated for DM increases with each passing year within the study sample, and this holds significant at the 1% level in both inpatient and outpatient categories. Similarly, this same trend applies to one's increasing age, however the

significance levels are different between inpatient at 10% significance and outpatient at 1%. The difference is partly due to the majority of treatment associated with DM being undertaken at the outpatient level.

Table 6: Regression Output – Diabetes Mellitus

Diabetes Mellitus					
		Inpatient		**Outpatient**	
Variable	**Category**	**Findings Group**	**Intention to Treat**	**Findings Group**	**Intention to Treat**
Age	Age in 1999	0.393 (.206) *	0.382 (.206) *	0.679 (.237) ***	0.633 (.234) ***
	Age Squared	-0.003 (002)	-0.003 (.002)	-0.006 (.002) ***	-0.005 (.002) ***
Year	Time Measure	0.127 (.013) ***	0.127 (.013) ***	0.245 (.012) ***	0.237 (.012) ***
Education	Low <10 yrs.		*Reference*		
	Intermediate <14 yrs.	-0.335 (.076) ***	-0.349 (.076) ***	-0.193 (.092) **	-0.194 (.091) **
	High > 14 yrs.	-1.062 (.108) ***	-1.079 (.108) ***	-0.450 (.115) ***	-0.454 (.114) ***
Income	0 - 99,999		*Reference*		
	100,000 - 199,999	0.132 (.099)	0.126 (.098)	-0.149 (.118)	-0.141 (.117)
	200,000 - 299,999	-0.701 (.108) ***	-0.723 (.108) ***	-0.588 (.123) ***	-0.582 (.122) ***
	300,000 - 399,999	-0.945 (.140) ***	-0.973 (.140) ***	-0.887 (.156) ***	-0.883 (.155) ***
	400,000 - 599,999	-1.165 (.175)***	-1.193 (.175) ***	-0.980 (.184) ***	-0.973 (.182) ***
	600,000+	-1.002 (.208) ***	-1.028 (.208) ***	-0.814 (.211) ***	-0.807 (.210) ***
Civil Status	Single		*Reference*		
	Married	-0.192 (.106) *	-0.214 (.106) **	-0.040 (.123)	-0.041 (.122)
	Cohabitation	0.573 (.176) ***	0.554 (.176) ***	0.540 (.213) **	0.538 (.211) **
	Widowed	-0.147 (.120)	-0.159 (.120)	-0.165 (.141)	-0.170 (.140)
	Separated	-0.246 (.200)	-0.259 (.200)	0.067 (.220)	0.062 (.218)
	Divorced	-1.452 (1.254)	-1.476 (1.257)	-1.001 (1.237)	-1.001 (1.228)
Birth Country	Norway		*Reference*		
	Other	0.786 (.093) ***	0.799 (.093) ***	0.967 (.108) ***	0.966 (.106) ***
Gender	Male		Reference		
	Female	-1.115 (.075) ***	-1.128 (.075) ***	-1.020 (.086) ***	-1.018 (.085) ***
County	Oslo		*Reference*		
	Telemark	-0.077 (.083)	-0.093 (.082)	-0.097 (.094)	-0.095 (.093)
	Other	-1.197 (.547) **	-1.199 (.549) **	-2.457 (1.291) *	-2.428 (1.266) *
Groups: Findings	Control		*Reference*		
	Attended - CRC	0.958 (1.334)		0.153 (1.785)	
	Attended - Positive	-0.195 (.244)		-0.130 (.263)	
	Attended - Negative	-0.230 (.126) *		-0.117 (.133)	
	Non-Attendee	0.330 (.119) ***		-0.008 (.146)	
	Returned Mail or Died	-0.255 (.507)		-1.477 (.831) *	
	Excluded	1.635 (.357) ***		0.572 (.514)	
Intention to Treat	Control		*Reference*		
	Invited		0.079 (.084)		0.026 (.095)
Interaction: Time	Control		*Reference*		
	Attended - CRC	-20.201 (31598.79)		-20.386 (154458.2)	
	Attended - Positive	-1.111 (.636) *		0.173 (.440)	
	Attended - Negative	-0.420 (.241) *		0.825 (.192) ***	
	Non-Attendee	0.294 (.170) *		1.047 (.197) ***	
	Returned Mail or Died	0.134 (.843)		0.461 (1.250)	
	Excluded	0.845 (.426) **		-0.295 (1.297)	
R^2 = Log Likelihood		0.133	0.134	0.310	0.310
ρ = rho		0.733	0.735	0.891	0.888

*** significant at a 1% level, ** significant at a 5% level, * significant at a 10% level

Socioeconomic factors also play a major role in incidence with intermediate and high education, as well as income above 200,000 NOK showing a decreased chance in being treated for DM with significance at the 1% and 5% levels. Those who are not born in Norway show an increased risk of DM incidence than those born in Norway. Men have a higher risk in incidence than women; both variables are at the highest significance level. In the Civil Status category, only those occupying the Cohabitation variable showed an increased risk of being treated for DM at the 5% level. However, married people on the inpatient side appeared to have their risk of DM reduced at the 10% level. While those living in a county other than Oslo or Telemark do show a lower incidence of being treated for DM, the sample is too small of draw any conclusions and their home county is unknown.

8.2 Hypertension

The results of the regressions for Hypertension are described below in Table: 7. In all four regressions ρ was greater than zero, which means that the variance between panel levels is important.

The group findings showed that those in the inpatient wing who attended the screening with a negative test were less likely than controls to be treated for complications related to Hypertension than controls, this was at the highest significance level. When the interaction variable was added, results for those who attended the screening in the inpatient wing were all significant. Those who had a CRC result were at an increased risk than controls to have Hypertension complications, while those with positive or negative tests where shown to have a decreased risk of Hypertension complications. On the outpatient side, only those with a negative result at screening showed a decreased risk when compared to controls.

The risk of being treated for complications associated with Hypertension increases with age and the risk increases as years in the trial progress. Similar trends are observed for patients in both the inpatient and outpatient groups suggesting that various complications can be treated in both types of care within this disease group.

Socioeconomic factors are also present in this group and demonstrate that education and income levels are highly significant in the incidence of Hypertension. Education was highly significant in reducing the chances of being treated for Hypertension when compared to

controls at the 1% levels within the inpatient group; it did not prove to be significant at any level in the outpatient group. The results within the regression for income prove to be more

Table 7: Regression Output - Hypertension

Hypertension					
		Inpatient		**Outpatient**	
Variable	**Category**	**Findings Group**	**Intention to Treat**	**Findings Group**	**Intention to Treat**
Age	Age in 1999	0.325 (.117) ***	0.328 (.117) ***	0.610(.138) ***	0.594 (.138) ***
	Age Squared	-0.002 (.001) **	-0.002 (.001) **	-0.005 (.001) ***	-0.005 (.001) ***
Year	Time Measure	0.173 (.009) ***	0.175 (.009) ***	0.181 (.010) ***	0.178 (.010) ***
Education	Low <10 yrs.		*Reference*		
	Intermediate <14 yrs.	-0.186 (.045) ***	-0.191 (.045) ***	0.065 (.057)	0.069 (.057)
	High > 14 yrs.	-0.553 (.059) ***	-0.560 (.059) ***	-0.049 (.068)	-0.044 (.068)
Income	0 – 99,999		*Reference*		
	100,000 – 199,999	0.195 (.061) ***	0.196 (.061) ***	0.227 (.081) ***	0.236 (.081) ***
	200,000 – 299,999	-0.081 (.064)	-0.085 (.063)	0.315 (.080) ***	0.326 (.080) ***
	300,000 – 399,999	-0.180 (.079) **	-0.186 (.078) **	0.266 (.095) ***	0.277 (.095) ***
	400,000 – 599,999	-0.365 (.095) ***	-0.371 (.095) ***	0.288 (.107) ***	0.300 (.107) ***
	600,000+	-0.326 (.113) ***	-0.334 (.113) ***	0.450 (.121) ***	0.461 (.121) ***
Civil Status	Single		*Reference*		
	Married	0.113 (.064) *	0.109 (.064) *	0.118 (.074)	0.123 (.074) *
	Cohabitation	0.208 (.109) *	0.200 (.109) *	0.278 (.129) **	0.276 (.129) **
	Widowed	0.053 (.072)	0.049 (.072)	-0.093 (.085)	-0.095 (.085)
	Separated	0.117 (.114)	0.112 (.114)	0.149 (.131)	0.147 (.131)
	Divorced	0.452 (.418)	0.450 (.418)	0.125 (.506)	0.131 (.506)
Birth Country	Norway		*Reference*		
	Other	-0.117 (.063) *	-0.120 (.063) *	-0.218 (.077) ***	-0.227 (0.077) ***
Gender	Male		*Reference*		
	Female	-0.543 (.042) ***	-0.551 (.041) ***	-0.403 (.049) ***	-0.398 (.049) ***
County	Oslo		*Reference*		
	Telemark	0.114 (.046) **	0.112 (.045) **	-0.010 (.055)	0.0002 (0.055)
	Other	-0.480 (.270) *	-0.480 (.270) *	-0.334 (.280)	-0.348 (.281)
Groups: Findings	Control		*Reference*		
	Attended – CRC	-0.026 (.885)		-0.544 (1.253)	
	Attended – Positive	0.160 (.120)		-0.013 (.149)	
	Attended – Negative	-0.162 (.068) ***		-0.007 (.073)	
	Non-Attendee	-0.020 (.075)		-0.122 (.094)	
	Returned Mail or Died	-0.452 (.373)		-1.209(.622) *	
	Excluded	0.856 (.215) ***		0.652 (.285) **	
Intention to Treat	Control		*Reference*		
	Invited		-0.067 (.048)		-0.003 (0.057)
Interaction: Time	Control		*Reference*		
	Attended - CRC	2.599 (1.032) **		-21.994 (170068.6)	
	Attended - Positive	-0.700 (.325) **		0.158 (.364)	
	Attended - Negative	-0.621 (.173) ***		0.430 (.151) ***	
	Non-Attendee	0.081 (.148)		0.305 (.203)	
	Returned Mail or Died	0.609 (.684)		-20.751 (50457.12)	
	Excluded	1.103 (.307) ***		0.818 (.617)	
R^2 – Log Likelihood		0.040	0.040	0.070	0.070
ρ = rho		0.515	0.516	0.610	0.611

*** significant at a 1% level, ** significant at a 5% level, * significant at a 10% level

difficult to interpret. Within the inpatient group, the results would suggest that incidence of Hypertension would increase at the 100,000 to 199,999 NOK level, while a decrease in incidence would be expected for those in the sample with an income of 300,000 NOK and above. The polar opposite occurs within the outpatient group however, which showed that the risks of Hypertension increase at all income levels at the highest significance levels. Civil status was significant for those who were married and in cohabitation in both groups showing an increased risk of Hypertension complications on both treatment type sides. Gender was also highly significant with women having a significantly lower risk of Hypertension complications than men. Birth country also proved to be significant with the Norwegian born population showing a higher risk of Hypertension than foreign born populations.

8.3 Chronic Obstructive Pulmonary Disease (COPD)

The results of the regressions for COPD are described below in Table: 8. In all four of the regressions ρ was greater than zero, which means that the variance between panel levels is important.

In the findings group variable those who attended the screening with a negative result were significant on both treatment sides with a reduced risk of COPD than the control group. The invitees who did not attend were at increased risk of COPD on the inpatient side. The excluded group was highly significant on the inpatient and outpatient side within the findings group; this variable will be explained in further detail within the discussion.

Age did not appear to have any significance on the inpatient side, however it was significant at the 5% level on the outpatient side. The year variable was significant at the highest level and increased the risk of COPD with each passing trial year at both patient levels.

The socioeconomic variables showed highest significance on the inpatient side. Income above 200,000 NOK was attributed to a decreased risk of COPD, while income in the 100,000 to 199,999 NOK range showed an increased risk over the reference group. A similar trend was seen on the outpatient side for increased risk in the same income group, however only income of 400,000 NOK and above was shown to have a significant decrease. Education proved to be a significant factor in all 4 regressions at the highest significance level and led to a decreased risk in COPD over the low education group. Women were also less likely than men to have

Table 8: Regression Output – Chronic Obstructive Pulmonary Disorder

COPD		Inpatient		Outpatient	
Variable	**Category**	**Findings Group**	**Intention to Treat**	**Findings Group**	**Intention to Treat**
Age	Age in 1999	0.221 (.243)	0.225 (.244)	0.554 (.242)**	0.542 (.240) **
	Age Squared	-0.001 (.002)	-0.001 (.002)	-0.004 (.002) *	-0.004 (.002) *
Year	Time Measure	0.167 (.015) ***	0.165 (.015) ***	0.247 (.014) ***	0.244 (.014) ***
Education	Low <10 yrs.	*Reference*			
	Intermediate <14 yrs.	-0.687 (.085) ***	-0.705 (.085) ***	-0.462 (.086) ***	-0.466 (.085) ***
	High > 14 yrs.	-1.743 (.145) ***	-1.772 (.146) ***	-1.658 (.141) ***	-1.667 (.140) ***
Income	0 - 99,999	*Reference*			
	100,000 - 199,999	0.320 (.109) ***	0.313 (.109) ***	0.437 (.120) ***	0.441 (.119) ***
	200,000 - 299,999	-0.830 (.125) ***	-0.860 (.125) ***	-0.037 (.126)	-0.044 (.125)
	300,000 - 399,999	-1.110 (.175) ***	-1.145 (.176) ***	-0.220 (.163)	-0.232 (.162)
	400,000 - 599,999	-1.182 (.226) ***	-1.214 (.227) ***	-0.396 (.207) *	-0.397 (.205) *
	600,000+	-2.366 (.405) ***	-2.415 (.408) ***	-1.049 (.308) ***	-1.050 (.305) ***
Civil Status	Single	*Reference*			
	Married	-0.349 (.130) ***	-0.380 (.131) ***	0.035 (.134)	0.023 (.132)
	Cohabitation	0.581 (.198) ***	0.551 (.199) ***	0.572 (.210) ***	0.547 (.208) ***
	Widowed	0.585 (.137) ***	0.569 (.137) ***	0.711 (.142) ***	0.698 (.141) ***
	Separated	0.340 (.219)	0.322 (.219)	0.417 (.225) *	0.410 (.223) *
	Divorced	0.434 (.987)	0.417 (.994)	0.600 (.898)	0.591 (.895)
Birth Country	Norway	*Reference*			
	Other	-0.633 (.139) ***	-0.631 (.139) ***	-0.372 (.132) ***	-0.372 (.131) ***
Gender	Male	*Reference*			
	Female	-0.452 (.084) ***	-0.470 (.084) ***	-0.380 (.083) ***	-0.386 (.082) ***
County	Oslo	*Reference*			
	Telemark	0.231 (.092) **	0.226 (.092) **	-0.188 (.095) **	-0.185 (.094) **
	Other	-0.650 (.567)	-0.639 (.570)	-2.193 (.857) ***	-2.175 (.850) **
Groups: Findings	Control	*Reference*			
	Attended - CRC	-19.397 (11642.7)		-22.866 (38638.53)	
	Attended - Positive	-0.224 (.276)		-0.282 (.273)	
	Attended - Negative	-0.334 (.144) **		-0.408 (.143) ***	
	Non-Attendee	0.346 (.135) ***		0.044 (.144)	
	Returned Mail or Died	-0.707 (.694)		-1.708 (1.003)	
	Excluded	2.838 (.334) ***		2.488 (.430) ***	
Intention to Treat	Control		*Reference*		
	Invited		0.138 (.096)		-0.109 (.098)
Interaction: Time	Control	*Reference*			
	Attended - CRC	22.185 (11642.7)		0.431 (.136)	
	Attended - Positive	0.517 (.422)		0.570 (.519)	
	Attended - Negative	0.158 (.228)		0.173 (.284)	
	Non-Attendee	0.116 (.205)		-0.111 (.295)	
	Returned Mail or Died	1.583 (.844) *		1.975 (1.394)	
	Excluded	-0.524 (.453)		0.219 (.624)	
R^2 = Log Likelihood		0.160	0.160	0.195	0.197
ρ = rho		0.755	0.760	0.809	0.805

*** significant at a 1% level, ** significant at a 5% level, * significant at a 10% level

COPD complications at the highest significance level in both inpatient and outpatient. A similar result was also shown in the birth country variable, where those born outside of Norway had a decrease risk of being treated for COPD than those born in Norway. Those in the county of Telemark had an increased risk of suffering from COPD than those in Oslo on

the inpatient side, while the opposite was true on the outpatient side. The civil status variable showed increased risk of COPD complications in the cohabitation and widowed groups in both treatment groups at the highest significance level, however in the inpatient group it was observed that those who were married had a decreased risk of COPD at the highest significance level. Those who were separated showed an increased risk of COPD on the outpatient side at the 10% significance level.

8.4 Angina Pectoris (AP)

The results of the regressions for AP are discussed below in Table 9. In all four of the regressions ρ was greater than zero, which means that the variance between panel levels is important.

Those who were invited for screening appeared to have a decreased risk of requiring treatment for AP, this was only observed on the outpatient side and was at the lowest significance level; this observation did not occur in the inpatient group. There were no significant results on the inpatient side within the findings group and only those with a negative screening result and those who did not attend screening had significant results at the 10% level that resulted in a decrease on the outpatient side. When the interaction variable was included, only the excluded group had significant results at the 5% level in both treatment cases resulting in an increase in treatment for AP.

The age variable was only significant at the 10% level in the outpatient group, which resulted in an increase in the treatment for AP. The year variable was highly significant, but only on the outpatient side. Risks of AP appeared to only increase on the outpatient side but not the inpatient side, this may suggest that treatment is largely handled by outpatient care.

A strong effect was seen within the socioeconomic variables. Education was highly significant in both care groups, which resulted in a decrease in risk of requiring AP care as education increases when compared to the low education group. Those study members who occupied the income group of 100,000 to 199,999 NOK were highly significant on both sides of the treatment care and were at increased risk of requiring treatment for AP. Decreases in AP care were observed from 300,000 NOK above in the inpatient group, while decreases in AP were only observed starting at the 400,000 NOK and above income level. Those who were male, lived in Telemark and were born outside of Norway had a significantly increased risk of

requiring care in both the inpatient and outpatient group. Similarly, those who were married, in cohabitation, widowed and separated were all at a significantly higher risk of requiring care for AP than those who were single in both the inpatient and outpatient groups.

Table 9: Regression Output – Angina Pectoris

Angina Pectoris					
		Inpatient		**Outpatient**	
Variable	**Category**	**Findings Group**	**Intention to Treat**	**Findings Group**	**Intention to Treat**
Age	Age in 1999	0.082 (.167)	0.082 (.167)	0.327 (.180) *	0.315 (.180) *
	Age Squared	0.0001 (.001)	0.0001 (.002)	-0.002 (.002)	-0.002 (.002)
Year	Time Measure	-0.014 (.012)	-0.015 (.012)	0.106 (.014) ***	0.104 (.014) ***
Education	Low <10 yrs.		*Reference*		
	Intermediate <14 yrs.	-0.343 (.063) ***	-0.348 (.063) ***	-0.171 (.069) **	-0.173 (.069) **
	High > 14 yrs.	-0.854 (.086) ***	-0.858 (.086) ***	-0.533 (.091) ***	-0.531 (.091) ***
Income	0 - 99,999		*Reference*		
	100,000 - 199,999	0.334 (.090) ***	0.339 (.090) ***	0.391 (.099) ***	0.385 (.099) ***
	200,000 - 299,999	-0.111 (.094)	-0.114 (.094)	0.103 (.103)	0.095 (.102)
	300,000 - 399,999	-0.470 (.117) ***	-0.476 (.116) ***	-0.073 (.124)	-0.084 (.123)
	400,000 - 599,999	-0.579 (.137) ***	-0.584 (.137) ***	-0.377 (.151) **	-0.386 (.151) ***
	600,000+	-0.545 (.162) ***	-0.548 (.161) ***	-0.420 (.182) **	-0.427 (.181) **
Civil Status	Single		*Reference*		
	Married	0.583 (.102) ***	0.582 (.102) ***	0.459 (.109) ***	0.461 (.109) ***
	Cohabitation	1.003 (.162) ***	0.991 (.162) ***	0.406 (.187) **	0.397 (.187) **
	Widowed	0.573 (.112) ***	0.568 (.112) ***	0.495 (.119) ***	0.495 (.119) ***
	Separated	0.950 (.157) ***	0.945 (.157) ***	0.623 (.173) ***	0.628 (.173) ***
	Divorced	0.633 (.633)	0.634 (.634)	0.802 (.626)	0.804 (.626)
Birth Country	Norway		*Reference*		
	Other	0.267 (.082) ***	0.264 (.082) ***	0.212 (.090) **	0.207 (.090) **
Gender	Male		*Reference*		
	Female	-1.529 (.065) ***	-1.531 (.065) ***	-1.068 (.067) ***	-1.071 (.067) ***
County	Oslo		*Reference*		
	Telemark	0.139 (.065) **	0.143 (.065) **	0.513 (.068) ***	0.513 (.067) ***
	Other	-0.614 (.387)	-0.613 (.388)	-0.150 (.373)	-0.145 (.373)
Groups: Findings	Control		*Reference*		
	Attended - CRC	-17.559 (4624.384)		-28.280 (1170670)	
	Attended - Positive	-0.099 (.184)		-0.248 (.193)	
	Attended - Negative	-0.058 (.096)		-0.191 (.101) *	
	Non-Attendee	-0.003 (.106)		-0.222 (.118) *	
	Returned Mail or Died	-0.623 (.501)		0.169 (.440)	
	Excluded	1.605 (.270) ***		1.090 (.287) ***	
Intention to Treat	Control		*Reference*		
	Invited		0.020 (.068)		-0.125 (.073) *
Interaction: Time	Control		*Reference*		
	Attended - CRC	-0.011 (11323.17)		0.185 (.400)	
	Attended - Positive	-0.288 (.355)		0.460 (.429)	
	Attended - Negative	-0.098 (.167)		0.198 (.229)	
	Non-Attendee	0.254 (.167)		0.240 (.272)	
	Returned Mail or Died	-0.711 (1.136)		-28.245 (1169321)	
	Excluded	0.708 (.348) **		1.116 (.529) **	
R^2 = Log Likelihood		0.089	0.090	0.053	0.054
ρ = rho		0.649	0.651	0.589	0.590

*** significant at a 1% level, ** significant at a 5% level, * significant at a 10% level

8.5 Acute Myocardial Infarction (AMI)

The results of the regressions for AMI are discussed below in Table: 10. In all four of the regressions ρ was greater than zero, which means that the variance between panel levels is important.

With respect to the findings group, those who attended the screening with a negative result were significant on both the inpatient and outpatient side resulting in a decrease in AMI risk. Those who were non-attendees had a lower risk of AMI on the outpatient side with significance at the 10% level. Those who were invited to screening (ITT) had a lower risk of AMI at the 5% level than controls, however the number of people in this group is small. When the interaction variable was included, the only significant groups were those who attended the screening with a positive test and those with a negative, their risk were both decreases on the inpatient side only.

The risk in suffering from an AMI is significant and increases with age in both inpatient and outpatient categories at the 5% and 10% level. In regards to the year variable, as the study progresses the risk of being treated for AMI decreases in the inpatient group, but increases in the outpatient group. This could be explained by the much lower sample group within the outpatient group compared to the inpatient; although the number of patients suffering from an AMI is low when compared to the other lifestyle-related diseases in this study.

Education at the intermediate and high levels resulted in significantly lower risk on the inpatient side with both variables have significance at the 1% level. On the outpatient side, only the high education group resulted in a decrease in the risk of AMI at the 5% level. Income was a contributing factor to a decrease in AMI on the inpatient side from 300,000 NOK and up, while income did not have any significance on the outpatient side. All the categories of civil status resulted in an increase in AMI when compared to those who were single on the inpatient side with exception to those who occupied the divorce group. Women were at a decreased risk than men on both the inpatient and outpatient side and those residing in Telemark were more likely to suffer from an AMI than those in Oslo at the 1% level.

Table 10: Regression Output – Acute Myocardial Infarction

Acute Myocardial Infarction					
		Inpatient		**Outpatient**	
Variable	**Category**	**Findings Group**	**Intention to Treat**	**Findings Group**	**Intention to Treat**
Age	Age in 1999	0.283 (.168) *	0.278 (.167) *	0.993 (.445) **	1.000 (.445) **
	Age Squared	-0.002 (.002)	-0.002 (.002)	-0.008 (.004) **	-0.008 (.004) **
Year	Time Measure	-0.039 (.016) **	-0.037 (.016) **	0.068 (.039) *	0.069 (.039) *
Education	Low <10 yrs.		*Reference*		
	Intermediate <14 yrs.	-0.256 (.062) ***	-0.264 (.062) ***	-0.034 (.169)	-0.030 (.169)
	High > 14 yrs.	-0.738 (.087) ***	-0.749 (.087) ***	-0.493 (.216) **	-0.488 (.216) **
Income	0 - 99,999		*Reference*		
	100,000 - 199,999	0.001 (.091)	0.002 (.091)	-0.208 (.246)	-0.190 (.246)
	200,000 - 299,999	-0.096 (.093)	-0.106 (.092)	-0.134 (.240)	-0.114 (.240)
	300,000 - 399,999	-0.290 (.113) ***	-0.303 (.112) ***	-0.368 (.290)	-0.348 (.290)
	400,000 - 599,999	-0.308 (.130) **	-0.317 (.130) **	-0.117 (.311)	-0.096 (.311)
	600,000+	-0.576 (.170) ***	-0.588 (.170) ***	0.287 (.329)	0.302 (.329)
Civil Status	Single		*Reference*		
	Married	0.240 (.097) **	0.230 (.097) **	0.305 (.253)	0.312 (.253)
	Cohabitation	0.654 (.159) ***	0.641 (.159) ***	0.594 (.432)	0.588 (.432)
	Widowed	0.364 (.106) ***	0.358 (.106) ***	0.405 (.277)	0.399 (.276)
	Separated	0.399 (.158) **	0.394 (.158) **	0.234 (.436)	0.231 (.436)
	Divorced	-0.690 (1.012)	-0.696 (1.012)	-19.889 (33659.08)	-22.041 (99192.8)
Birth Country	Norway		*Reference*		
	Other	-0.010 (.087)	-0.009 (.086)	0.214 (.208)	0.200 (.208)
Gender	Male		*Reference*		
	Female	-1.394 (.068) ***	-1.401 (.068) ***	-1.492 (.181) ***	-1.489 (.180) ***
County	Oslo		*Reference*		
	Telemark	0.306 (.063) ***	0.302 (.063) ***	-0.007 (.173)	0.011 (.172)
	Other	-0.001 (.325)	0.001 (.325)	0.206 (.744)	0.206 (.744)
Groups: Findings	Control		*Reference*		
	Attended - CRC	0.422 (1.034)		-20.392 (74389.88)	
	Attended - Positive	0.001 (.174)		-0.154 (.449)	
	Attended - Negative	-0.167 (.101) *		-0.586 (.292) **	
	Non-Attendee	0.078 (.103)		-0.638 (.341) *	
	Returned Mail or Died	-0.182 (.460)		-20.536 (26206.11)	
	Excluded	1.082 (.242) ***		1.003 (.637)	
Intention to Treat	Control		*Reference*		
	Invited		-0.046 (.067)		-0.502 (.197) **
Interaction: Time	Control		*Reference*		
	Attended - CRC	-18.725 (25435.11)		-0.011 (.276)	
	Attended - Positive	-2.048 (1.015) **		-20.039 (30558.27)	
	Attended - Negative	-0.504 (.275) *		0.698 (.644)	
	Non-Attendee	0.074 (.223)		-19.407 (16094.16)	
	Returned Mail or Died	-18.195 (8740.974)		0.006 (81873.9)	
	Excluded	0.203 (.510)		-21.139 (74786.77)	
R^2 = Log Likelihood		0.001	0.001	0.009	0.009
ρ = rho		0.228	0.232	0.524	0.526

*** significant at a 1% level, ** significant at a 5% level, * significant at a 10% level

8.6 Ischemic Heart Disease (IHD)

The results of the regressions for IHD are discussed below in Table: 11. In all four of the regressions ρ was greater than zero, which means that the variance between panel levels is important.

The findings group had only one significant result at the 10% level for those who had a negative screening test on the inpatient side with a reduced risk of IHD complications. A similar result was observed for the interaction variable, with only the negative screening test sample showing any significance at a 10% level with their risk of IHD complications reduced when compared to the control group.

Increases in the sample's age, as well as in the progression of the study's years resulted in an increased risk of IHD in both the inpatient and outpatient group at the 1% significance level; however the age variable in the outpatient side was only significant at the 10% level.

Education was a significant reducing factor of IHD at the intermediate and high levels on both treatment sides. In regards to income level, those in the 100,000 to 199,999 NOK group had an increased risk of IHD complications than the reference group at the 1% level for both the inpatient and outpatient treatment sides. The outpatient side also had significance at the 200,000 to 299,999 NOK income level with an increase in IHD risk at the 5% significance level. The risk of IHD was reduced among those with an income of 300,000 NOK and above with a 1% to 5% significance level, however this was only true for patients on the inpatient side. Those who were married, in cohabitation, widowed and separated all had an increased risk of IHD complications at the 1% significance level on both the inpatient and outpatient side. Men were also at an increased risk for IHD than women at the 1% significance level on both treatment sides. Those born outside of Norway were also at an increased risk of IHD complications at the 5% significance level, but this was only the case for those in the inpatient group. Those residing in Telemark were at a decreased risk for IHD complications when compared to the Oslo group at the 1% significance level, this was however only the case for the inpatient side.

Table 11: Regression Output – Ischemic Heart Disease

Ischemic Heart Disease					
		Inpatient		**Outpatient**	
Variable	**Category**	**Findings Group**	**Intention to Treat**	**Findings Group**	**Intention to Treat**
Age	Age in 1999	0.533 (.183) ***	0.530 (.183) ***	0.346 (.193) *	0.337 (.193) *
	Age Squared	-0.004 (.002) **	-0.004 (.002) **	-0.002 (.002)	-0.002 (.002)
Year	Time Measure	0.048 (.011) ***	0.048 (.011) ***	0.205 (.012) ***	0.204 (.012) ***
Education	Low <10 yrs.		*Reference*		
	Intermediate <14 yrs.	-0.259 (.070) ***	-0.267 (.070) ***	-0.166 (.075) **	-0.172 (.075) **
	High > 14 yrs.	-0.857 (.091) ***	-0.863 (.091) ***	-0.862 (.098) ***	-0.866 (.098) ***
Income	0 - 99,999		*Reference*		
	100,000 - 199,999	0.414 (.102) ***	0.422 (.102) ***	0.408 (.116) ***	0.423 (.116) ***
	200,000 - 299,999	-0.034 (.105)	-0.036 (.105)	0.259 (.116) **	0.266 (.116) **
	300,000 - 399,999	-0.262 (.124) **	-0.269 (.124) **	-0.044 (.135)	-0.042 (.135)
	400,000 - 599,999	-0.344 (.141) **	-0.348 (.141) **	-0.065 (.151)	-0.060 (.151)
	600,000+	-0.509 (.168) ***	-0.519 (.168) ***	-0.226 (.179)	-0.223 (.179)
Civil Status	Single		*Reference*		
	Married	0.592 (.106) ***	0.593 (.106) ***	0.617 (.112) ***	0.624 (.112) ***
	Cohabitation	1.025 (.178) ***	1.012 (.178) ***	0.775 (.203) ***	0.758 (.203) ***
	Widowed	0.627 (.116) ***	0.626 (.117) ***	0.561 (.124) ***	0.560 (.124) ***
	Separated	0.770 (.173) ***	0.771 (.173) ***	0.804 (.182) ***	0.802 (.182) ***
	Divorced	-0.294 (.813)	-0.290 (.817)	0.205 (.741)	0.218 (.744)
Birth Country	Norway		*Reference*		
	Other	0.218 (.089) **	0.214 (.089) **	-0.027 (.099)	-0.038 (.099)
Gender	Male		*Reference*		
	Female	-2.120 (.074) ***	-2.128 (.074) ***	-2.072 (.082) ***	-2.076 (.081) ***
County	Oslo		*Reference*		
	Telemark	-0.193 (.073) ***	-0.187 (.073) ***	-0.123 (.077)	-0.119 (.076)
	Other	-0.826 (.422) **	-0.806 (.421) *	-0.855 (.443) *	-0.870 (.446) *
Groups: Findings	Control		*Reference*		
	Attended - CRC	-18.741 (6406.406)		-20.716 (16359.33)	
	Attended - Positive	0.024 (.190)		-0.063 (.203)	
	Attended - Negative	-0.176 (.106) *		-0.179 (.111)	
	Non-Attendee	-0.014 (.115)		-0.082 (.124)	
	Returned Mail or Died	-0.643 (.519)		-1.077 (.662)	
	Excluded	2.158(.283) ***		2.420 (.291) ***	
Intention to Treat	Control		*Reference*		
	Invited		-0.008 (.074)		-0.006 (.079)
Interaction: Time	Control		*Reference*		
	Attended - CRC	0.043 (15718.26)		0.314 (56636.71)	
	Attended - Positive	-0.091 (.315)		-0.892 (.632)	
	Attended - Negative	-0.310 (.185) *		0.296 (.209)	
	Non-Attendee	0.191 (.169)		0.348 (.240)	
	Returned Mail or Died	-0.079 (889)		-19.756 (22602.52)	
	Excluded	0.745 (.325) **		0.666 (.466)	
R^2 = Log Likelihood		0.138	0.140	0.138	0.139
ρ = rho		0.714	0.717	0.730	0.733

*** significant at a 1% level, ** significant at a 5% level, * significant at a 10% level

9 Discussion

The aim of this study was to explore the behaviours of the Norwegian population towards a mass screening program for CRC and whether the outcomes have an effect on the lifestyle related diseases of Diabetes Mellitus, Hypertension, Chronic Obstructive Pulmonary Disease, Angina Pectoris, Acute Myocardial Infarction and Ischemic Heart Disease. The results indicated that when looking at the Findings Group and Interaction Group, the group that was most expected to experience the Heath Certificate Effect, the Negative Findings group, did have significant results. It was predicted at the start of the study that the Negative Findings group would be the group at most risk for increases in the six disease groups due to a HCE, however this group experienced a general decrease in incidence when compared to the control group. The described decrease occurred in all the disease groups with exception to Angina Pectoris. There was also significance found in the Non-Attendee group that resulted in an increased risk for Diabetes Mellitus, Hypertension and COPD, while there was a decreased risk in Acute Myocardial Infarction, Angina Pectoris and Ischemic Heart Disease.

Although the significant results did not always occur in the expected group, the Findings Group results may still exhibit a Health Certificate Effect. The increased risk of not attending for DM and COPD may correspond to the tenets behind the HBM and demonstrates a lack of a 'trigger' described by Rosenstock. The Non-Attendee members in the sample show an increased risk in two diseases that are highly correlated to lifestyle factors and demonstrates that this group is a health risk group. The Negative Findings group did show an increased risk of Hypertension on the outpatient side when the Interaction variable was included as well as for Diabetes Mellitus on the Outpatient side; these results were both at the highest significance level. One could expect that when tracking the risk of giving a screening, the Negative Results group and the Non-Attendee do present increased risk when the screening interaction with time is added for Diabetes Mellitus and Hypertension. If the time following the screening were increased, the trend could be better followed; there was only a 1 to 3-year follow-up from the screening 'shock'.

There is similarly another possibility that the Negative Findings group should not be the group of concern. These results may actually show that those in the Negative Findings group may in fact be the healthiest. It could quite possibly be that the Non-Attendee group should be the group requiring the most attention. Using tenets of the HBM and Rosenstock, one could

say that those in the Non-Attendee group may view themselves as being in good health. The results do show that the Non-Attendee group is at increased risk for DM and COPD complications, which are strongly correlated to lifestyle choices.

9.1 Limitations

The time length after screening presents a large challenge for accurately presenting the results and whether a Health Certificate Effect is present regardless of the significant results in the disease groups. A follow up of more years after the initial screening would enable a stronger and more accurate reporting of the time trends.

This study did not account for deaths, part of this reason was that the number of dead was so small and the primary concern in this study was the effect of the various independent variables on the dependent disease group variables. When one considers the relatively short 5-year survival rate of those diagnosed with CRC, there is a strong possibility that those with a CRC result from the screening trial would not as many as the initial 41 patients at the end of the data period. By not including death, the incidence of the various disease groups could appear higher than in reality or a death may be inaccurately reported as 'no disease' present for that year. However, because all the findings groups were measured the same way the risk of inflating or deflating the number of disease cases would be shared and most likely would not change the regression results a great deal. Similarly, the CRC-invited group, which would most likely have the most deaths did not have significant results.

The data was a combination of dataset from many sources. One challenge was how part of the data was written using the ICD-9 coding and some used the ICD-10 coding, while all was done to match the coding together there is some risk that corresponding codes could have been missed. All was done to stay consistent and the codes used are listed in Appendix I with the equivalents used throughout the study's progression. Further, as new diagnostic tools become available for detecting disease become available, the criteria for coding a disease risks changing as well. An example of this was in the diagnosis of Acute Myocardial Infarction that changed following the use of an ECG. The World Health Organisation has made amendments to the ICD-9 coding by providing supplements, however there was an additional code used in the ICD-9 called Old Myocardial Infarction, this was included and recorded as Acute Myocardial Infarction in this study; it is unclear how many patients this might have affected.

The selection of diseases related to the heart and circulatory system proved to be problematic. Both Angina Pectoris and Acute Myocardial Infarction are forms of Ischemic Heart Disease so it could be argued that diseases in this category could have been counted three times. All three diseases are a result of the building of plague in the main arteries and heart valves, however each of the three diseases manifested themselves differently and each has different treatment and health outcomes. For example, Angina Pectoris is non-fatal and is largely characterized by stress-induced pain, while an Acute Myocardial Infarction is a sudden and often fatal bout of pain caused by inadequate nutrients coming to the heart. It is also possible to have Ischemic Heart Disease and not experience an Acute Myocardial Infarction or have an Angina Pectoris episode. Since the three diseases were coded differently in the ICD-9 and 10 from each other, there were numerous instances where only one of the diseases was coded in the same patient and that the study was largely based upon reason for inpatient and outpatient care, this did not appear to be that great of a problem.

The Excluded findings group provided a challenge within this study in that the majority of disease groups selected for this study where conditions within the NORCCAP trial's exclusion criteria. For this reason, the Exclusion group had highly significant results in all lifestyle-related disease groups and their risk of complications where higher than controls. The conclusions to draw from this group are difficult to interpret since the exclusion group is small and their initial health issues led to them being excluded from the NORCCAP trial.

Due to the use of a Logistic Panel Regression, many of the categorical variables had to be changed into binary coding, for example, the Income Group had to change to each income level being separated and then coded as zero for 'not present' and 1 for 'present'. While this was a simple method to prepare the data, there was a risk of over-simplifying and increasing the size of outputs from the regression. A number of assumptions had to be made using this binary method, particular in the Interaction variables. A patient who was invited to screening was indentified by a '1', while the remaining controls where indentified using a '0'. An invited participant was assigned a '1' from the time of their screening through to the end of the sample year of 2003. While this would report changes between years within the same patient, there is of course a risk of patient having numerous cases of the diseases within the same year; this makes changes hard to report and difficult to track. A more dynamic model instead of a binary model may show different findings.

9.2 Strengths

This study presents a simple method to track and measure potential adverse effects of undertaking a mass-screening program for CRC. A great deal of literature has been presented about concerns about the Health Certificate Effect and for the most part it has been only discussed, no study has attempted to demonstrate it using statistical methods.

The methods in this study could be easily transferred and used to evaluate other screening programs, specifically in terms of tracking changes over the years with a given dependent variable of concern within a single patient. The use of a panel data method enables the times series to be easily tracked within each patient rather easily. Similarly, by isolating variables in a binary manner, changes were simple to see and the data was easy to prepare.

The interaction variable used to track a change in disease patterns within each patient following the results from the findings group is a strong method to determine whether unexpected effects could be seen in the given screening program studied. With a longer study period and a sample over a greater number of years, it would be a suitable model to investigate trends and a good method to test for the Health Certificate Effect.

The socioeconomic factors that were discussed in the Theoretical portion of this study were confirmed by the results in this study. There is overwhelming evidence drawn from the results of this study that those with education that is of 14 years and above is a highly significant variable in reducing risk in each of the six disease groups. There is also a strong correlation between income and complications associated with the disease groups. Those in the 100,000 to 199,999 NOK group were at a higher risk than controls in the Hypertension, COPD, Angina Pectoris, and Ischemic Heart Disease groups. Similarly, as income increases, the risk of disease decreases. These factors cannot be controlled, however it does demonstrate that even in a society with universal health care, these factors are still a highly significant variables within screening (Sreenivasan 2007) and lifestyle-related disease incidence.

These results also show that existing methods used to evaluate screening programs are at risk for missing all costs and consequences. In the scope of this study, areas of potential costs were demonstrated based upon a screening result alone. Changes in behaviour and risk do occur following screening. The work of Howard and colleagues has identified cost savings in lifetime treatment costs in those with detected polyps than undetected; one area that they were unable to analyze however was net cost of screening (2009). By adding the lifestyle related

disease component from this study, determining a better estimate for net CRC screening costs could be partly achieved.

9.3 Future Study and Implications

A common criticism from the literature concerning undertaking a mass screening program has to do with the adverse implications that could occur within the screened group. A professional and randomized standard to carrying-out a trial must be maintained which at times requires the necessity of determining the effectiveness of the method of the study and providing the educational information needed for the participants to understand the results. It is the misinterpretation of the results that can lead to adverse events following the screening results.

Studies by Tymstra and Bielemen (1987) and Larsen et. al. (2006a) have pointed to unintended consequences following mass screening. The solution advised by Rosenstock (2005) and the Health Belief Model (Janz & Becker 1984) has been to provide the necessary information needed for the screening participants to understand the results. There is of course a trade-off between the amount of information given before and after the trial by those running the screening program and the amount of resources available to do so while still controlling costs.

Future studies could explore the Cost-Effectiveness component further. To do so, one would need to identify the costs associated with undertaking a mass-screening program and then determine the amount of information needed in order for patients to fully understand their results with their associated costs. Further, the results of this study would be used to examine the DRG costs associated with the disease groups. By determining the costs to treat the adverse events, there would be evidence to demonstrate both the risk of requiring treatment for the disease groups in question and the additional health costs associated with treating the other disease groups based upon a screening result. The cost component could also be explored over the years of the trial and following the trial. The conclusions drawn from adding the cost component would provide a better estimate of what costs are associated with mass screening and the adverse event costs.

10 Conclusion

This thesis project aimed to determine whether outcomes of a mass screening could have an effect on life-style related diseases. In working to answer this question a methodology was created to track changes in disease related admissions to either inpatient or outpatient health care.

It was hypothesized that a potential Health Certificate Effect could be present where patients who had negative results in their CRC screening may interpret the result as meaning that they are healthy. The assumption was that patients who did not believe that they were unhealthy would continue their same lifestyle choices, as they had no 'shock' to make them think otherwise. In this study, it was hypothesized the patients who were invited to the screening but did not attend and those who had a negative test would be at increased risk for other life-style related diseases. The results did show that a Health Certificate Effect might be present in the Diabetes Mellitus, Hypertension and COPD disease groups. When compared to the Control group patients in the Negative Screening Result Group and the Non-Attendee group, required more health care for those conditions and the risks did change when following their screening test. However these results were not consistent between the Findings and Interaction group so there is the possibility, that in some cases those patients with a Negative Finding might in fact be in good health.

The statistical method used and the framework in this study could be a good tool to use when seeking to evaluate indirect costs associated with mass screening programs.

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Appendix I: *New Coding for ICD-9 and ICD-10*

Diabetes Mellitus – ICD-9 **250**, ICD-10 **E10-E14**.

Hypertension, Secondary Hypertension & Hypertensive Heart Disease – ICD-9 **401, 402, 405**, ICD-10 **I10, I11, I15**.

Chronic Obstructive Pulmonary Disease – ICD-9 **496 & 492**, ICD-10 **J43 & J44**.

Angina Pectoris – ICD-9 **413**, ICD-10 **I20**.

Acute Myocardial Infarction & Old Myocardial Infarction – ICD-9 **410 & 412**, ICD-10 **I21**.

Ischemic Heart Disease Acute and Chronic – ICD-9 **411 & 414**, ICD-10 **I25**.

Appendix II: Proportions per 1000 patients listed by Disease Group and Age Group

Diabetes Mellitus

Diabetes Mellitus												
	Outpatient						**Inpatient**					
Patients 50 - 54 Years												
	1998	1999	2000	2001	2002	2003	1998	1999	2000	2001	2002	2003
Control	0.091	0.684	0.919	1.137	0.572	0.814	0.214	0.244	0.374	0.340	0.298	0.512
Attended - CRC	0	0	0	0	0	0	0	0	0	0	8.333	8.333
Attended - Positive Findings	0	0.396	0.528	0.925	0.396	0.528	0	0	0.132	0	0.264	0.132
Attended - Negative Findings	0.045	0.608	0.653	0.923	0.765	0.833	0.158	0.180	0.158	0.135	0.315	0.360
Non-Attendee	0.031	0.628	0.691	0.910	0.816	0.910	0.377	0.282	0.628	0.408	0.502	0.753
Returned / Dead	0	0.667	0	0	0	0.667	0.667	0	0.667	0.667	0	1.333
Excluded	0.752	1.504	3.008	1.504	2.256	2.256	2.256	2.256	4.511	0.752	1.504	1.504
Patients 55 - 64 Years												
Control	0.104	0.795	1.036	1.137	0.704	0.762	0.397	0.436	0.603	0.595	0.471	0.625
Attended - CRC	0	0	0	0	3.448	0	0	0	0	0	0	0
Attended - Positive Findings	0	0.629	1.118	1.398	1.118	1.225	0.350	0.280	0.280	0.629	0.559	0.909
Attended - Negative Findings	0.016	0.845	0.975	1.154	0.829	0.796	0.211	0.276	0.374	0.455	0.585	0.569
Non-Attendee	0.235	1.543	1.517	1.413	1.177	1.020	0.785	0.811	1.230	1.047	0.916	0.785
Returned / Dead	0	0.470	0	0	0.939	0.470	1.409	1.409	0	0.939	0	0.470
Excluded	0	1.424	1.068	1.424	1.068	1.068	1.424	1.779	2.491	0.712	1.424	1.779

Hypertension

Hypertension												
	Outpatient						**Inpatient**					
Patients 50 - 54 Years												
	1998	1999	2000	2001	2002	2003	1998	1999	2000	2001	2002	2003
Control	0.035	0.649	0.698	0.712	0.579	0.698	0.351	0.400	0.537	0.621	0.574	0.946
Attended - CRC	0	0	0	0	8.333	0	0	0	0	8.333	8.333	8.333
Attended - Positive Findings	0	0.793	1.057	0.793	0.396	0.925	0	0.396	0.528	0.132	0.925	0.925
Attended - Negative Findings	0	0.653	0.630	0.765	0.968	0.743	0.315	0.203	0.270	0.495	0.608	0.945
Non-Attendee	0.031	0.408	0.659	0.753	0.722	0.596	0.377	0.439	0.659	0.628	0.722	0.973
Returned / Dead	0	0	0.667	0	0.667	0	2.000	0.667	0	1.333	0.667	1.333
Excluded	0	1.504	0	0.752	0.752	0	0.752	1.504	3.008	4.511	1.504	3.008
Patients 55 - 64 Years												
Control	0.069	0.958	0.987	1.313	0.850	0.792	0.669	0.858	1.030	1.091	1.091	1.455
Attended - CRC	0	0	0	0	0	0	0	3.448	3.448	0	0	0
Attended - Positive Findings	0.070	0.978	1.048	1.048	0.978	0.909	1.049	0.909	0.839	1.329	2.168	1.818
Attended - Negative Findings	0.049	0.894	1.154	1.040	0.894	0.959	0.439	0.439	0.683	1.138	1.203	1.446
Non-Attendee	0.105	0.654	0.628	1.125	0.994	0.759	0.680	0.994	1.361	1.439	1.151	1.439
Returned / Dead	0	0	0.470	0	0.470	0	0.939	1.409	0.470	0	0	0
Excluded	0	2.847	3.203	2.135	2.135	1.779	2.847	1.779	3.559	2.491	1.779	3.203

Chronic Obstructive Pulmonary Disorder

COPD												
	Outpatient						**Inpatient**					
Patients 50 - 54 Years												
	1998	1999	2000	2001	2002	2003	1998	1999	2000	2001	2002	2003
Control	0.030	0.281	0.354	0.456	0.305	0.430	0.126	0.156	0.226	0.235	0.202	0.319
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	0
Attended - Positive Findings	0	0.661	0.264	0.396	0.528	0	0	0.264	0	0.132	0.264	0.396
Attended - Negative Findings	0	0.248	0.180	0.180	0.225	0.248	0.023	0.180	0.135	0.135	0.113	0.315
Non-Attendee	0.031	0.408	0.471	0.188	0.471	0.502	0.126	1.157	0.282	0.314	0.408	0.659
Returned / Dead	0	0	0	0	0	0	0	0.667	0	0	0	0
Excluded	0	0.752	0.752	2.256	2.256	3.008	0	0.752	0.752	2.256	1.504	3.008
Patients 55 - 64 Years												
Control	0.049	0.608	0.740	0.850	0.562	0.663	0.291	0.428	0.540	0.452	0.425	0.644
Attended - CRC	0	0	0	0	0	0	0	0	3.448	0	0	0
Attended - Positive Findings	0	0.419	0.559	0.699	0.349	0.489	0.350	0.490	0.490	0.490	0.350	0.350
Attended - Negative Findings	0.016	0.390	0.406	0.487	0.552	0.422	0.130	0.341	0.406	0.471	0.536	0.439
Non-Attendee	0.052	0.680	0.732	0.654	0.785	0.759	0.497	0.863	0.680	0.837	0.837	0.968
Returned / Dead	0	0.470	0	0	0.470	0.939	0	1.409	0.939	0	0.470	0.470
Excluded	0	2.847	3.559	3.203	3.559	4.271	5.338	4.271	3.559	4.626	4.281	3.559

Angina Pectoris

Angina Pectoris												
	Outpatient						**Inpatient**					
Patients 50 - 54 Years												
	1998	1999	2000	2001	2002	2003	1998	1999	2000	2001	2002	2003
Control	0.037	0.263	0.326	0.321	0.267	0.244	0.254	0.405	0.470	0.395	0.270	0.344
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	0
Attended - Positive Findings	0	0.264	0.661	0.396	0.661	0.528	0.132	0.264	0.132	0.396	0.396	0.396
Attended - Negative Findings	0.023	0.113	0.383	0.338	0.203	0.405	0.225	0.248	0.315	0.405	0.225	0.338
Non-Attendee	0	0.314	0.314	0.534	0.251	0.251	0.188	0.408	0.408	0.251	0.251	0.377
Returned / Dead	0	0.667	0	0	1.333	0.667	0.667	0.667	0	0	0	0
Excluded	0	1.504	3.759	0.752	1.504	0.752	2.256	3.008	5.263	3.579	3.008	1.504
Patients 55 - 64 Years												
Control	0.080	0.532	0.584	0.573	0.356	0.332	0.488	0.762	0.855	0.677	0.504	0.537
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	0
Attended - Positive Findings	0	0.769	0.349	0.767	.0559	0.419	0.699	0.769	0.769	0.769	0.979	0.769
Attended - Negative Findings	0.033	0.422	0.487	0.552	0.552	0.341	0.455	0.634	0.601	0.959	0.618	0.667
Non-Attendee	0.105	0.392	0.680	0.523	0.471	0.392	0.890	1.204	1.020	1.073	0.654	0.811
Returned / Dead	0	0.939	0.470	0.470	0.470	0	0.470	0.470	1.409	0.939	0.470	0
Excluded	0	3.559	1.424	1.424	0.712	0.712	2.491	3.559	3.203	0.356	2.491	1.779

Acute Myocardial Infarction

Acute Myocardial Infarction												
	Outpatient						**Inpatient**					
Patients 50 - 54 Years												
	1998	1999	2000	2001	2002	2003	1998	1999	2000	2001	2002	2003
Control	0.016	0.030	0.019	0.042	0.033	0.028	0.293	0.100	0.186	0.205	0.130	0.219
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	8.333
Attended - Positive Findings	0	0	0	0	0	0	0.396	0	0.132	0	0.132	0.396
Attended - Negative Findings	0.023	0	0.023	0.068	0.023	0.045	0.135	0.045	0.135	0.225	0.113	0.293
Non-Attendee	0.031	0	0.063	0	0	0	0.188	0.157	0.188	0.157	0.188	0.157
Returned / Dead	0	0	0	0	0	0	0.667	0	0	0	0	0
Excluded	0.752	0	0.752	0	0	0	3.759	0	1.504	2.256	0	0.752
Patients 55 - 64 Years												
Control	0.044	0.047	0.063	0.104	0.052	0.028	0.471	0.200	0.271	0.304	0.219	0.299
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	0
Attended - Positive Findings	0	0	0.069	0	0.280	0.070	0.490	0.140	0.140	0.350	0.629	0.350
Attended - Negative Findings	0.016	0	0.016	0.065	0.016	0.033	0.228	0.081	0.244	0.195	0.341	0.439
Non-Attendee	0.026	0	0.026	0.078	0.026	0.026	0.706	0.340	0.419	0.314	0.445	0.550
Returned / Dead	0	0	0	0	0	0	1.409	0.939	0	0	0	0
Excluded	0	0	0	0.356	0	0	2.135	1.068	1.504	0.356	0.356	0

Ischemic Heart Disease

Ischemic Heart Disease												
	Outpatient						**Inpatient**					
Patients 50 - 54 Years												
	1998	1999	2000	2001	2002	2003	1998	1999	2000	2001	2002	2003
Control	0.047	0.330	0.619	0.553	0.437	0.572	0.405	0.319	0.549	0.381	0.372	0.512
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	0
Attended - Positive Findings	0	0.264	0.396	0.396	0.396	1.189	0	0.264	0.264	0.264	0.264	0.793
Attended - Negative Findings	0	0.225	0.473	0.450	0.405	0.585	0.270	0.225	0.293	0.338	0.248	0.428
Non-Attendee	0.094	0.408	0.722	0.596	0.345	0.659	0.251	0.282	0.502	0.282	0.408	0.502
Returned / Dead	0	0	0.667	0	0	0	0.667	0.667	0.667	0	0.667	0
Excluded	0	3.759	6.767	6.015	3.759	5.263	3.008	1.504	4.511	3.759	3.759	4.511
Patients 55 - 64 Years												
Control	0.115	0.614	0.962	0.830	0.551	0.767	0.789	0.641	1.061	0.806	0.773	0.874
Attended - CRC	0	0	0	0	0	0	0	0	0	0	0	0
Attended - Positive Findings	0.210	0.559	1.188	0.767	0.699	0.559	0.769	0.909	0.909	0.699	1.399	1.329
Attended - Negative Findings	0.033	0.471	0.845	0.650	0.536	0.764	0.455	0.471	0.585	0.666	0.748	0.910
Non-Attendee	0.105	0.706	1.046	0.706	0.445	0.602	0.916	0.942	1.073	0.890	1.047	1.282
Returned / Dead	0	0.470	0.470	0.470	0.470	0	0.939	1.409	0.939	0.470	0.470	0
Excluded	0.712	2.847	5.338	3.203	2.491	1.424	4.271	4.626	5.338	2.847	3.759	1.779