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Disparities in colorectal cancer between Northern and Southern Sweden – a report from the new RISK North database

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ABSTRACT

Background: Geographic cancer health disparities have been reported in Sweden. The disparities are not fully understood, but may be attributed to differences in exposure to risk factors as well as differences in health care, socioeconomic and demography. The aim of this study was to describe the new nationwide population based RISK North database and its potential by analysing health disparities in colorectal cancer between Northern and Southern Sweden.

Methods: Cancer-specific data from the National Cancer Quality Registers for colorectal, gastric and oesophageal cancer and brain tumours were linked to several nationwide registers hereby creating a new database – RISK North. To exemplify the potential of RISK North, we analyzed differences in colorectal cancer incidence, mortality and survival in relation to gender, age, cohabitation and education between Northern and Southern Sweden 2007–2013.

Results: In colon cancer, the age-adjusted incidence per 100.000 was lower in Northern than Southern Sweden, 35.9 in the North vs. 41.1 in the South (p < 0.01). For rectal cancer, incidence rates were 12.6 vs. 19.7 (p < 0.01) and mortality rates 5.33 vs. 5.89 (p = 0.07), respectively. The largest difference in incidence was demonstrated for colon cancer among individuals ≥79 years old (190. vs. 237, i.e., ~20%). Survival in colon cancer was higher in Southern Sweden, HR 0.92 (0.87–0.98) adjusted for age, gender, co-habiting, education and m-stage at diagnosis. No difference in survival was seen for rectal cancer.

Conclusions: The new RISK North database enabled analysis of cancer disparities between Northern and Southern Sweden. The incidence of colorectal cancer were lower in the North of Sweden whereas colon cancer survival was higher in the South. These differences can be further analysed utilising the RISK North database.

Introduction

Overall cancer incidence is increasing in Sweden but incidence and mortality rates vary between geographical regions. A lower incidence of several cancers is found in the northern parts of Sweden, while overall cancer-specific survival is better in the southern parts [1]. The Northern Health Care Region (from here on designated Northern Sweden or the North), which consists of the four northernmost counties in Sweden differs from the rest of Sweden (Southern Sweden/the South) in some general aspects (Figure 1); most obvious in terms of lower population density and longer distances to health care, but among other also in lower socioeconomic status (SES) [2].

The underlying causes of regional cancer disparities between Northern and Southern Sweden are not fully understood, but health care, socioeconomic, demographic and life-style factors may contribute [3–6].

We here present a new database (RISK North) in order to study the multifactorial background to some of the cancer disparities. RISK North is a nationwide, population based database with close to complete follow-up.

RISK North uses the unique personal identity number of all Swedish citizens to link records from several nationwide demographic and health care registers with data emanating from the National Cancer Quality Registers for colorectal, gastric- and oesophageal cancers and brain tumours (Figure 2).

The linkage of the different types of registers enables to investigate regional differences regarding cancer incidence, mortality and outcome in relation to individual tumour-specific factors and management, as well as co-morbidity; demography and socioeconomic, within the same public health care system. The multi-register design of RISK North reflects the diverse ethology of cancer disparities and could help to identify risk groups and unequal cancer treatment.
Aims

The aims of this first study from RISK North are to describe the new database and to exemplify Risk North’s potential for research by analysing disparities in colorectal cancer between Northern and Southern Sweden.

Material and methods

Database RISK North – structure and design

The RISK North database uses data from the National Cancer Quality Registers for colorectal, gastric- and oesophageal cancer and brain tumours as the primary resource and linkage is made to several other registers (Figure 2). Individual data for every cancer reported to the Cancer Quality Registers in Sweden over the years 2007–2013 (colorectal cancer), 2009–2013 (brain tumours), 2006–2012 (gastric and oesophageal cancers) was sent to Statistics Sweden where an individual code key and a serial number was constructed for each case on the basis of the personal identity number. Using this code key, information from registers managed by Statistics Sweden was added and the code key was delivered to the Swedish Board of Health and Welfare for linkage with their registers. This includes registers from the Social Insurance Agency, Swedeheart and the Swedish quality register for cardiovascular disease. Statistics Sweden also provided a control cohort of five persons for each reported cancer diagnosis, matched for age (year of birth), gender and county. Furthermore, information on cancer, heart disease and death of first-degree relatives was added for every cancer case.

To make it possible to analyse if the patterns in cancer health disparities between the North and South for colorectal, gastric and oesophageal cancer and brain tumours studied in RISK North are present for other cancer types as well the RISK North database also includes data from the Swedish cancer register for all Swedish cancer cases, regardless of type of cancer, in 1958–2013 linked to registers from the Social Insurance Agency.

The data was delivered to the Department of Radiations sciences at Umeå University and is kept within RISK North database. Thanks to the serial number and code key, anonymity for each individual is ensured.

Registers contributing to RISK North

National cancer quality registers

In Sweden, cancer-specific National Cancer Quality Registers have been designed to collect individual data on diagnoses, treatment and outcome for the major cancers. All new cases of cancer should be reported to these registers, and the registers are monitored and driven by steering committees. Throughout Sweden, Regional Cancer Centre’s (RCC) have the responsibility to maintain the registers and to help with statistical work and support. The decentralized responsibility for the National Cancer Quality Registers enables high completeness and continuous validation of cancer care.

Swedish colorectal cancer register (SCRCSR)

The national registers for invasive rectal and colon cancer were established in 1995 (rectal cancer) and 2007 (colon cancer) respectively. The completeness of the registers is very high, more than 98% of all colorectal cancer cases diagnosed in Sweden over the last ten years have been reported [7,8]. Individual data on tumour characteristics, initial management, treatment; outcome and several other variables are reported. Several studies have used information from these registers to describe differences in management and outcome of CRC in Sweden [9,10]. Variables in the Swedish colorectal cancer register (SCRCSR) have been shown to have good validity [11].

The Swedish national register for oesophageal and gastric cancer (NREV)

The register started in 2006 and includes newly diagnosed cases of cancer in the oesophagus or stomach in Sweden. The national register for oesophageal and gastric cancer (NREV) contains data on date, stage at diagnosis and planned treatment for all patients. For patient undergoing tumour resection, treatment data is recorded including follow-up and definitive staging. According to the latest
published validity study, the completeness was over 95% and the accuracy of the recorded variables was over 90% [12].

**National quality register for brain tumours**
The register was launched in 1999 with the aim to include all adults in Sweden with newly diagnosed primary brain tumours, including benign lesions such as meningiomas and neurinomas. The register has data on histopathology, tumour stage, treatment and outcome. Since the start of the register the completeness has varied depending on health care region. In three out of Sweden’s six health care regions the completeness has been almost complete (98–100%) [13]. Data for all years and all regions is included in RISK North but only data on malignant lesions from years and regions with high completeness will be used for analysis.

**Statistics Sweden**
Statistics Sweden (SCB) is a governmental agency responsible for several national registers. We included data from four registers held at SCB in RISK North:

- **The total population register (TPR)** Since 1968 information on all inhabitants in Sweden is reported to the total population register. The recorded variables include personal identity number, age, sex, marital status, citizenship and migration within, to, and from Sweden. The register was extended in 1998 with information regarding e.g. close relations and birth country of parents. Individuals are excluded from the register in case of death or emigration more than one year. The completeness over time is almost 100%, but there is an excess of up to 4–8% due to unreported emigration, especially among citizen born outside the Nordic countries [14].

- **The multi-generation register**
The multi-generation register is part of the total population register (TPR), containing personal identity of parents to every inhabitant of Sweden since 1961 with a birthdate of 1932 or later. Information on biological parents for adopted persons is also included. The register enables assessment of kinship between Swedish citizens, and thus family history among cancer patients [15].

- **Longitudinal integration database for health insurance and labour market studies (LISA by Swedish acronym)**
The longitudinal integration database for health insurance and labour market studies started in 1990 as a merge of several other registers in order to study health insurance and the labour market. The database includes all individuals residing in Sweden from 16 years of age and is annually updated. Our database RISK North uses information from LISA on socioeconomic factors from the year prior of the diagnosis; such as place of birth, income, mode and place of employment and highest level of education. Information...
from the LISA database has earlier been used to build a database (PCBase) for clinical epidemiological prostate cancer research [16].

**Geography database (GD)**

The geography database (GD) links personal identity numbers to GPS coordinates of residence with a precision of 250 × 250 m in urban areas, and 1000 × 1000 m in the countryside, respectively.

**Swedish social insurance agency**

**MIDAS-database (micro-data for analysis of the social insurance.)**

The Social Insurance Agency is the government agency for providing social insurance in Sweden. In 2004–2005 the agency started a database – MIDAS – containing individual information on sick leave, sickness benefit and rehabilitation allowance.

**The national board of health and welfare**

Data from four registers at the Swedish government agency National Board of Health and Welfare contributes to RISK North.

**The Swedish cancer register**

The Swedish cancer register was founded in 1958. Every new diagnosis of cancer and some selected premalignant lesions are reported consecutively, resulting in currently 60,000 new reports every year. Reporting data is mandatory by law for both clinicians and pathologists and the completeness is about 96%. Unreported cases are mainly clinical diagnoses in situations of advanced disease [17]. The Swedish Cancer Register contains data on ICD code, age at diagnosis, gender, reporting hospital, date of death and histopathology. From 2004, classification on TNM-stage is included in the register.

**The cause of death register (CDR)**

In Sweden every death is reported to the National Board of Health and Welfare. Cause of death is registered, as well as contributing underlying disease; place where death occurred and whether an autopsy was performed. Cause of death is registered according to the international ICD system. The register has been running consecutively since 1961 and is updated yearly. Initially, only Swedish residents were included, but since 2012 every person diseased in Sweden, regardless of nationality, is added to the register. The completeness is high, only 1% of all death certificates are not linked to a cause of death certificate. Information on these deaths is still included in the causes of death register but without any medical information. The main weaknesses in the cause of death register (CDR) is the reliability of the underlying causes of death certificates and an autopsy rate under 10%. Over the last years, 2.3–2.8% of all certificates are deemed inadequate and validation studies indicate the correct cause of death is given in about 50–90% of cases when matching against the Swedish Inpatient Register (IPR). The reliability is highest among patients with malignant diseases, 90% [18].

**The Swedish inpatient register**

The Swedish inpatient register (also called The Hospital Discharge Register) is the largest register regarding public health in Sweden and was established in 1964. It covers all public and private hospitalizations and has 100% completeness since 1987. Information regarding every in-patient medical care event is reported as well as outpatient consultation to hospital receptions. There is information regarding time and length of hospitalization, diagnoses, surgery, if care was voluntary and information on injuries. The register makes it possible to compare health care between different parts of Sweden and between private and public health facilities. Primary care visits are not reported to the IPR. For in-patient medical care the validity of the register data is about 85–95% [19].

**The Swedish prescribed drug register**

Since 2005 every prescribed medicine for every person in Sweden is reported to the prescribed drug register. The register only covers prescribed drugs, medicines given in hospitals or medicines not covered by prescriptions, e.g. cytotoxic agents are not included [20].

**Additional registers**

**VIP – västerbotten intervention program**

Information from the VIP project can provide data on individuals in RISK North residing in the county of Västerbotten in the Northern region of Sweden. The county of Västerbotten has 266,000 inhabitants constituting 29.9% of the Northern health region’s population. The VIP project was initiated due to an observed high mortality from cardiovascular disease in the county. The aim of the project is to reduce mortality and morbidity from cardiovascular disease and diabetes and includes health-promoting activities in a variety of fields e.g., schools, elderly care, industries etc. As for public health care, inhabitants of the county of Västerbotten are invited to a health survey at the age of 40, 50 and 60 years of age at their local general practitioner. At the health survey hypertension, diabetes and hypercholesterolemia are assessed. Weight and height are measured and a structured interview is performed to identify risk behaviour regarding physical activity, tobacco- and alcohol use, diet, social support, and mental. If indicated, a general practitioner appointment or motivating interviews are offered. Thorough information regarding health and behaviour can be obtained from the VIP-data and compliance within the county is more than 65% [21].
Sweden (the Swedish web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies)

In 2009, four clinical quality registers reporting cardiovascular disease in different settings were merged to form Swedeheart, a national quality register for heart disease in Sweden. This register contains data from all cardiac care units in Sweden on patients with acute cardiovascular syndromes since 1995. It also covers secondary prevention after cardiac events and thoracic heart surgery. The Swedeheart register has 100% completeness of all Swedish patients undergoing angiography, angioplasty or heart surgery. The register however captures only 60% of all patients with acute myocardial infarction, since many of those patients are admitted to non-coronary care units [22].

Data from the RISK North database utilized to study disparities in colorectal cancer.

In order to study disparities in colorectal cancer in the present study, we used data in RISK North originating from the Swedish Colorectal Cancer Register (SCRCR) on all patients in Sweden diagnosed with colorectal cancer 2007–2013. The data was linked with information from CDR, LISA. TPR and GD.

Incidence and mortality rates were based on data from the SCRCR, TPR and CDR. Age, gender and whether distant metastases were present (M0 or M1) at diagnosis were also obtained from the SCRCR. Data from the GD was used to determine where the patient was living at time of diagnosis, including allocation to Northern or Southern Sweden.

Cohabiting status and educational level were obtained from the TPR and LISA.

Educational level was used as a proxy for SES, which has been shown to be an adequate marker [19] Three levels of education; low (up to nine years of compulsory school), middle (secondary education two to three years) and high (university or college) were used. Individuals <18 years were not included in calculations for educational level. Cohabiting status was defined as living at the same address as another person (living alone vs. not living alone).

All patients reported in the SCRCR between 2007 and 2013 with colorectal cancer were included in the study. In the survival analyses patients were followed until death or end of follow-up in 2014-12-31.

Statistical methods to examine disparities in colorectal cancer

Incidence and mortality rates in Northern and Southern Sweden for colon and rectal cancer, in total and for subgroups based on sex, age, level of education and cohabitation status were calculated. Rates were age-adjusted based on the Swedish population 2000 and are presented as number of cancer cases and cancer deaths per 100,000 person-years. Chi-square tests ($\chi^2 = 0.05$) were used for all comparisons of categorical data.

For survival analysis we estimated the hazard ratio between Northern and Southern Sweden using Cox proportional hazard regression analysis stratifying over age (10-year groups), sex and M-stage and controlling for education level and cohabiting status. In the stratified Cox proportional hazard analysis, hazard ratios are assumed to be the same in all strata and no hazard ratios are estimated for the covariates that are stratified over.

All statistical analysis were performed in R version 3.2.3. [23].

Approvals

The regional Board of Ethics in Umeå approved the creation of the RISK North database and the overall aim of the study. Delivery and linking of data has also been approved from the steering committees and authorities at each included register.

Results

The RISK North database

The RISK North database comprises 371,505 colorectal, gastric- and oesophageal cancer and brain tumour cases, 1,857,080 matched controls and 1,654,747 relatives. Additionally there are 1,031,123 cases of other cancer types in the database. In total there are 4,914,455 individuals and 1917 different variables in the RISK North database.

Baseline demographics of Northern and Southern Sweden’s populations

During the study period 2003–2013 the mean population of the Northern Health Care Region (i.e., The North) was 877670, representing 9% of Sweden’s total population. In the South 91% of the population resided. The population density was 3.9 people per square kilometre in the North compared to 38.4 in the South. The population in the North was older and a lower proportion had a high level of education (Table 1).

Colon cancer

During the study period 2561 cases of invasive colon cancer were reported in the North and 25,259 in the South of Sweden respectively. This corresponds to a 12.7% lower overall age-standardized incidence rate in the North (35.9 vs. 41.1, $p < .01$). In subgroup analysis, the lower incidence of colon cancer in Northern Sweden was demonstrated in both sexes, in individuals >69 years old and was not associated with cohabiting status, level of education or metastatic disease at diagnosis (Table 2). The largest difference in incidence was among individuals >79 years old, 190 vs. 236, corresponding to a relative difference of 19.6%.

Median age at diagnosis for colon cancer was 73 years in the North and 72 years in the South.
The overall age-adjusted, mortality in colon cancer was 10.0% lower in Northern compared to Southern Sweden (11.0/100,000 person-years vs. 12.2/100,000 person-years, \( p = 0.01 \)) (Table 2). Differences in mortality between the North and South were noted for: individuals of age 80+, males, individuals living with partners and those with middle education level (Table 2).

Survival was significantly higher in Southern than Northern Sweden, when stratified for age, gender and advanced disease at diagnosis (M1) and adjusting for level of education and cohabiting status, HR 0.92 (CI 0.87–0.98). (Table 3)

Rectal cancer
A total of 13,505 cases of invasive rectal cancer were reported during the study period –1264 cases in Northern and 12,241 in Southern Sweden. This corresponds to an age-standardized overall 10.5% lower incidence in the North compared to the South (17.6 vs. 19.7, \( p < 0.01 \)) (Table 4). The significantly lower incidence for rectal cancer in the North was also demonstrated in subgroup analysis for: both sexes, in individuals >69 years age, individuals living with partner

<table>
<thead>
<tr>
<th>Table 1. Demographic differences between the population in the North vs. the rest of Sweden 2007–2013.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Northern Sweden</strong></td>
</tr>
<tr>
<td>Mean population</td>
</tr>
<tr>
<td>Mean age</td>
</tr>
<tr>
<td>Population by age group</td>
</tr>
<tr>
<td>0–9</td>
</tr>
<tr>
<td>60–69</td>
</tr>
<tr>
<td>70–79</td>
</tr>
<tr>
<td>80+</td>
</tr>
<tr>
<td>Cohabiting status</td>
</tr>
<tr>
<td>Living alone</td>
</tr>
<tr>
<td>Not living alone</td>
</tr>
<tr>
<td>870,434</td>
</tr>
<tr>
<td>Education</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Medium</td>
</tr>
<tr>
<td>High</td>
</tr>
<tr>
<td>721,297</td>
</tr>
</tbody>
</table>

Sums for different subgroups do not match the totals due to missing values.

Table 2. Age-adjusted incidence and mortality per 100,000 person-years from colon cancer 2007–2013, in Northern and Southern Sweden, respectively.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subgroup</th>
<th>HR a</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td>Northern Sweden (ref)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Southern Sweden</td>
<td>0.92</td>
<td>0.87–0.98</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Lower (ref)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>0.90</td>
<td>0.87–0.94</td>
<td></td>
</tr>
<tr>
<td>Higher</td>
<td>0.82</td>
<td>0.77–0.86</td>
<td></td>
</tr>
<tr>
<td>Cohabitation status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living alone (ref)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not living alone</td>
<td>0.79</td>
<td>0.76–0.83</td>
<td></td>
</tr>
</tbody>
</table>

aHazard ratios optimized of all strata (each strata has its own baseline hazards).

The overall age-adjusted, mortality in colon cancer was 10.0% lower in Northern compared to Southern Sweden (11.0/100,000 person-years vs. 12.2/100,000 person-years, \( p = 0.01 \)) (Table 2). Differences in mortality between the North and South were noted for: individuals of age 80+, males, individuals living with partners and those with middle education level (Table 2).

Survival was significantly higher in Southern than Northern Sweden, when stratified for age, gender and advanced disease at diagnosis (M1) and adjusting for level of education and cohabiting status, HR 0.92 (CI 0.87–0.98). (Table 3)
(cohabiting) and high education. The most pronounced difference was found among individuals >79 years old, 72.4 vs. 88.0 corresponding to a relative difference of 17.7%.

For rectal cancer, median age at diagnosis was 69 years in the North vs. 70 years in the South.

A numerical but statistically non-significant 9.51% lower mortality in rectal cancer in the North was noted, (5.33 vs. 5.89, \(p = .07\)). In sub-group analyses a significantly lower mortality for rectal cancer in the North was noted in individuals aged 70–79 (19.9 vs. 25.4, \(p = .02\)) (Table 4).

No difference in overall survival between Northern and Southern Sweden in rectal cancer was noted when stratified for age, gender and advanced disease at diagnosis (M1) and adjusting for level of education and cohabitation status (Table 5).

### Discussion

In this study, we present the RISK North database, a national database where data from National Cancer Quality Registers for 371,505 individuals with brain tumours, colorectal-, gastric- or oesophageal cancer matched with controls and relatives are linked to 14 other registers. The linkage enables research on individual and regional differences in demography, socioeconomic and comorbidity in association with tumour-specific data. This type of database can be used for many different types of studies e.g., national studies; our focus is on cancer care in the North. In the present study, the RISK North database was used to assess differences in incidence, mortality and survival for colorectal cancer between Northern and Southern Sweden.

A lower incidence of colorectal cancer was noted in Northern Sweden, with the most pronounced difference among elderly patients with colon cancer. For patients with colon cancer the survival was worse in Northern Sweden – adjusted for the risk factors age, gender, metastatic disease, SES and cohabitation status.

### The RISK North database – strengths and limitations

The main strength of the RISK North database is the possibility to analyse matched data on an individual level from different sources (registers), while protecting the identity and integrity of the study subjects. It is a nationwide, population based database with close to complete follow-up.

The linking of data enables unique studies on the multifactorial background to disparities in cancer. The RISK North database, as any database, can however only demonstrate associations between factors and not exact mechanisms.

The validity of our results is depending on the quality of the underlying registers where the data was retrieved to build the RISK North database. For the data used in this study, the quality and the completeness of the register data is very high, with the exception of the CDR. Prior validation studies of the CDR indicate incorrect cause of death in about 10% of patients with cancer [18,24]. This can affect the exact mortality rates for colorectal cancer given in our study, but probably not the relation between mortality rates in Northern vs. Southern Sweden.

#### Table 5. Hazard ratios of all causes of death among rectal cancer cases estimated in cox model stratified over m-stage, sex and age at diagnosis (10-year groups) and adjusted for region, education level and cohabitation status.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subgroup</th>
<th>HRa</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern Sweden (ref)</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Southern Sweden</td>
<td></td>
<td>1.01</td>
<td>0.92</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower (ref)</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td></td>
<td>0.90</td>
<td>0.84</td>
</tr>
<tr>
<td>Higher</td>
<td></td>
<td>0.82</td>
<td>0.75</td>
</tr>
<tr>
<td>Cohabitation status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living alone (ref)</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not living alone</td>
<td></td>
<td>0.79</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Hazard ratios optimized of all strata (each strata has its own baseline hazards).

\(a\)Hazard ratios optimized of all strata (each strata has its own baseline hazards).
In the present study, the definitions of North and South are rough, there is e.g., much variation within the South. In future RISK North studies more detailed geographical approaches will be possible.

Disparities in colorectal cancer

Incidence
Differences in colorectal cancer incidence have been demonstrated between countries in terms of higher rates in already economically developed countries in the “West” or in countries recently adapting a more western lifestyle [25,26]. Studies on disparities in colorectal cancer rates within countries has often focused on SES, associated to differences in lifestyle, co-morbidity and adherence to screening. Results in prior studies are inconsistent whether low SES is a risk factor for colorectal cancer [27–29].

In the present study the most marked difference in incidence rates of colorectal cancer between Northern and Southern Sweden was noted among patients over 70 years of age. The underlying causal relationship behind this regional difference cannot be determined by the data in RISK North. One explanation could be a difference in lifestyle between Northern and Southern Sweden, with a healthier lifestyle in the north, which however has decreased over time, explaining the greater difference in incidence among older individuals. Life-style differences between Northern and Southern Sweden are not known, but one prior study has reported trends to a more sedentary life-style and increasing use of alcohol in some parts of Northern Sweden in the recent years [24]. These are all known life-style risk factors for colorectal cancer [5].

Deeper analyses are necessary to understand what covariates are behind the connection between SES and cancer risk and outcome.

In the present study, individuals with low SES (educational level) in both Northern and Southern Sweden had a higher risk for colorectal cancer (Tables 2 and 4). On a population level however, the North has a lower proportion of highly educated people (Table 1) and still a lower risk for colorectal cancer compared to the population in the South. In subgroup analysis of individuals with the same educational level, the risk for colorectal cancer was lower in the North in most subgroups (Tables 2 and 3). It should be stated however, that educational level is not always the same as income level. In Sweden, some groups of blue-collar workers have higher incomes than defined academics. Hence, the exact impact of SES on the disparities in incidence in this study needs further investigation, taking into account differences in life-style and co-morbidity on an individual level.

Regarding screening for colorectal cancer, no program was running in Sweden during the study period, except for one region in the South. A further analysis excluding the region with screening showed persistent differences in incidence (data not shown).

Mortality and survival
The differences in mortality for colorectal cancer between Northern and Southern Sweden were less pronounced than the differences in incidence, indicating worse survival in Northern Sweden.

This was confirmed in survival analysis for colon cancer, showing worse outcome for patients in the North adjusted for the known risk factors age, gender, metastatic disease at diagnosis, low SES and living alone [30,31].

Consequently, the worse outcome in Northern Sweden raises questions regarding surgical and oncological management including the impact of travel distances and co-morbidity.

In earlier studies on cancer survival, the regional differences could not be explained by correlating differences in tumour stage, SES or comorbidity [3]. Lower SES, as in the North of Sweden, has however been correlated with higher co-morbidity [32]. Travel distance to health care has previously been shown to be associated with more advanced stages at diagnosis [33], less intensive treatment [34] and worse outcome for colorectal cancer [35].

For rectal cancer no difference in survival was demonstrated between Northern and Southern Sweden. The reasons could be related to a more standardised and centralized treatment of rectal compared to colon cancer.

Future studies with the RISK North database will enable in-depth analysis of the correlation between outcome and quality of colorectal cancer care, travel distances and other risk factors such as co-morbidity, SES and co-habiting status.

Conclusions
We here describe the RISK North database as a useful tool to assess cancer disparities between Northern and Southern Sweden, showing a lower incidence of colorectal cancer in the North, with most predominant difference among the elderly. We also found worse survival for colon cancer patients in Northern Sweden, a disparity that calls for further analysis. Future RISK North studies can examine the complex relationships between outcome, surgical and oncological management, SES, travel distances, co-morbidity and other risk factors.

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References


