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Original Research

# Survival trends in patients diagnosed with colon and rectal cancer in the nordic countries 1990–2016: The NORDCAN survival studies



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## KEYWORDS

colon cancer;  
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Survival;  
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registries;  
NORDCAN;  
Colonic neoplasms;  
Rectal neoplasms

**Abstract Background:** Survival of patients with colon and rectal cancer has improved in all Nordic countries during the past decades. The aim of this study was to further assess survival trends in patients with colon and rectal cancer in the Nordic countries by age at diagnosis and to present additional survival measures.

**Methods:** Data on colon and rectal cancer cases diagnosed in the Nordic countries between 1990 and 2016 were obtained from the NORDCAN database. Relative survival was estimated using flexible parametric models. Both age-standardized and age-specific measures for women and men were estimated from the models, as well as reference-adjusted crude probabilities of death and life-years lost.

**Results:** The five-year age-standardized relative survival of colon and rectal cancer patients continued to improve for women and men in all Nordic countries, from around 50% in 1990 to about 70% at the end of the study period. In general, survival was similar across

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age and sex. The largest improvement was seen for Danish men and women with rectal cancer, from 41% to 69% and from 43% to 71%, respectively. The age-standardized and reference-adjusted five-year crude probability of death in colon cancer ranged from 30% to 36% across countries, and for rectal cancer from 20% to 33%. The average number of age-standardized and reference-adjusted life-years lost ranged between six and nine years.

**Conclusion:** There were substantial improvements in colon and rectal cancer survival in all Nordic countries 1990–2016. Of special note is that the previously observed survival disadvantage in Denmark is no longer present.

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## 1. Introduction

Colon and rectal cancer accounts for a tenth of newly diagnosed cancers globally [1] and in the Nordic countries (Denmark, Finland, Iceland, Norway, and Sweden) [2]. With approximately 12% of all cancer deaths due to colon and rectal cancer in the Nordic countries, it is second only to lung cancer as the main cause of cancer death [2]. Although survival for patients with colon and rectal cancer improved in all Nordic countries during the period 1968–2003, the survival has historically been lower in Denmark [3]. We have reported improvements in survival for a range of cancer sites during recent decades, including colon and rectum, with the largest improvements observed in Denmark [4].

The Nordic countries have a long-standing history of high-quality population-based standardized cancer registration and they cooperate closely, aiming at improvements and research through the Association of the Nordic Cancer Registries [5].

By the use of population-based registers and a range of measures of cancer survival, the aim of this study was to, in detail, assess survival trends in colon and rectal cancer by age and sex in the Nordic countries.

## 2. Methods

### 2.1. Data

Individual-level data on colon and rectal cancer in Denmark, Finland, Iceland, Norway, and Sweden were obtained from the NORDCAN database, which includes information from the national cancer registries in each country [6]. All individuals diagnosed with cancers of the colon (including appendix; International Classification of Diseases version 10 [ICD10]: C18) and rectum (C19–C20) between 1990 and 2016 were included. Follow-up for death and emigration was to the end of 2017 for all countries, with the exception of Finland, where follow-up ended in 2016. Emigration information was unavailable for Iceland. Cases diagnosed on the basis of a death certificate only (DCO) or through incidental autopsy findings were excluded, as

well as childhood cancers (patients aged <18 years at diagnosis) and subsequent primary tumors at the same site in the same patient (Appendix A.1). Population-based mortality rates were obtained from each country's national statistics office.

Information on stage according to the tumor-node-metastasis (TNM) classification (tumor size, lymph node involvement, and distant metastases) was available from Denmark, Iceland, Norway, and Sweden for years 2004–2016. TNM was registered according to the UICC Manual of Clinical Oncology editions 5, 6, and 7, and the countries adopted the new editions at different time points. In Denmark, the highest values of T, N, and M from clinical and pathological reports were used. Sweden, Norway, and Iceland also reported a combination of clinical and pathological TNM. Owing to differences in coding and proportions of missing data between the countries (Appendix A.2, Appendix A.3), stage distributions were not included in survival analyses.

### 2.2. Statistical analysis

The survival of patients with colon and rectal cancer was assessed using several measures based on predictions from flexible parametric relative survival models [7,8]. To investigate temporal trends in survival, separate models were fitted to the data from each country and for each cancer site, with models including age, calendar year, and sex. Age and calendar year at diagnosis were included by using restricted cubic splines with three degrees of freedom (DF). Two-way interactions between age and calendar year, age and sex, and calendar year and sex were included. The proportional excess hazards assumption was relaxed by incorporating time-dependent effects for calendar year, age, sex, and their interaction terms (three-way interactions), with 3 DF for each time-dependent effect, and 5 DF were used to model the log cumulative baseline excess hazard. To improve model stability, 96% of the age distribution was modeled continuously while individuals outside the 2nd and 98th percentile of age had their age reassigned to those percentile limits and were assumed to have the same relative survival (i.e., winsorizing) [9]. Owing to the small population size, simpler models were used for Iceland excluding the three-way interactions and

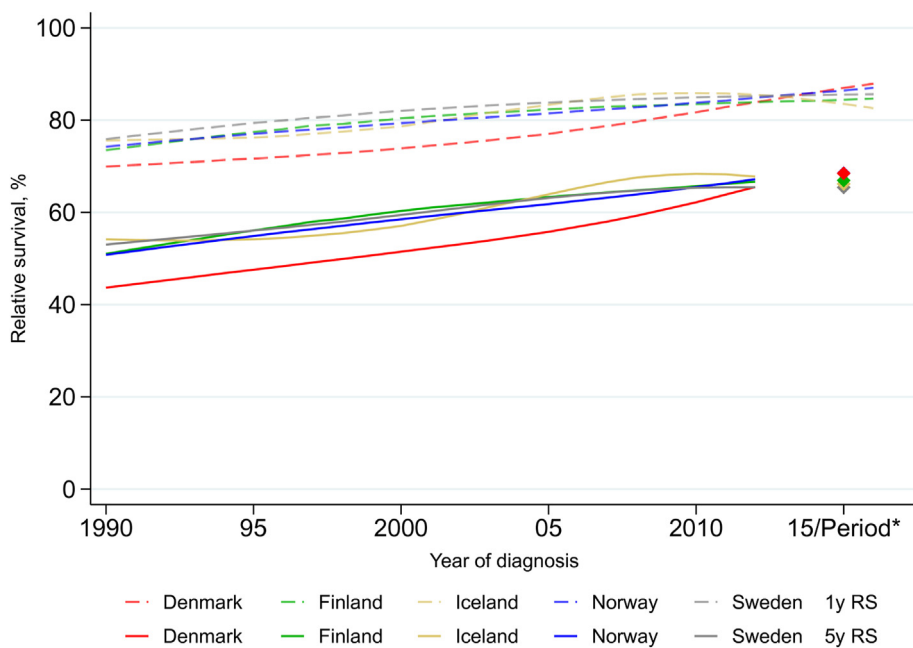


Fig. 1. Age-standardized one- and five-year relative survival in colon and rectal cancer, women and men combined, a comparison of time trends in the Nordic countries.

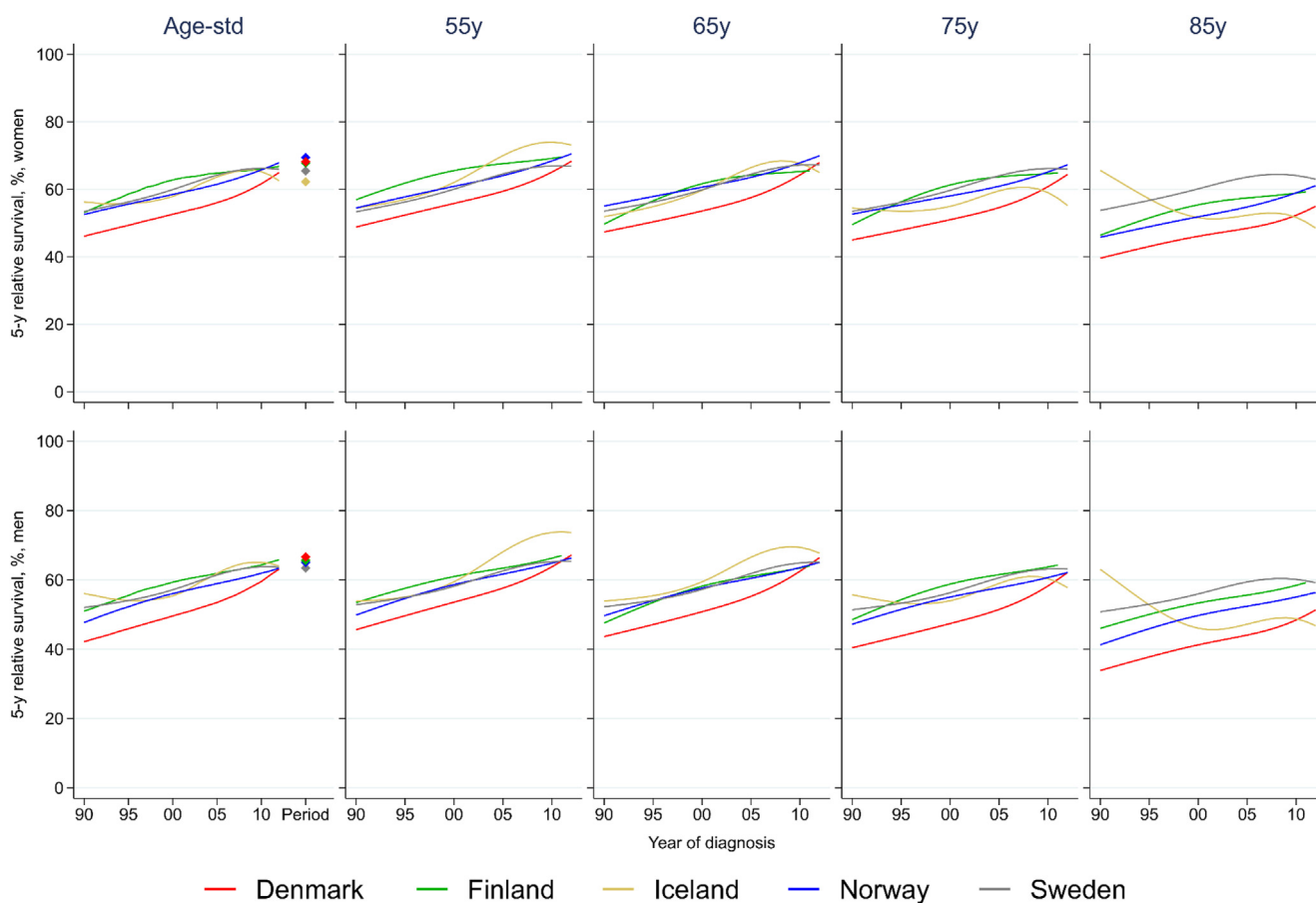


Fig. 2. Age-standardized and age-specific five-year relative survival in colon cancer, a comparison of time trends in the Nordic countries; women (top panel) and men (bottom panel). Estimates with 95% confidence intervals in [Appendix A.6](#) and [Appendix A.7](#).

using 2 DF for time-dependent effects. Within the models, country-specific population mortality rates stratified by age, sex, and calendar year were used to obtain expected mortality rates.

Based on these models, one- and five-year relative survival was estimated by sex for each calendar year and selected ages at diagnosis (55, 65, 75, 85). Age-standardized estimates of relative survival were also obtained, using regression standardization stratified by calendar year and sex [7]. We used an adapted version of the International Cancer Survival Standard 1 (ICSS1) age-standard weights ([Appendix A.4](#)).

To obtain estimates for patients diagnosed in the last years of data for which five years of follow-up is not available, a period approach was used [10]. The period window was 2013–2017 for Denmark, Norway, and Sweden; 2012–2017 for Iceland; and 2013–2016 for Finland. Flexible parametric models that were essentially the same as above, without the need to incorporate calendar year, were fitted separately for each country and cancer site.

The crude probability of all-cause death and death due to cancer five years after diagnosis [11], and the average number of life-years lost per individual diagnosed [12]

were estimated from the period models. Crude probabilities of cancer death are probabilities where death due to other causes are taken into account in comparison with the complement of relative survival (one minus relative survival) which can be interpreted as the probability of dying due to cancer in the hypothetical scenario that there were no other possible causes of death [13]. The number of life-years lost provides an estimate of the reduction in life expectancy in cancer patients compared to the life expectancy in the general population. To make the estimates of crude probabilities and life-years lost directly comparable across countries, the estimates were age-standardized, and the average background mortality in the Nordic countries was used for predictions rather than country-specific mortality rates (“reference adjusted”) [14]. Age-specific estimates of life-years lost were also estimated using the average background mortality in the Nordic countries.

Incidence and mortality rates were estimated by sex in five age groups using five-year diagnosis windows. Age-standardized rates were also estimated with three-year diagnosis windows and using the Nordic population distribution in the year 2000 for standardization ([Appendix A.4](#)).

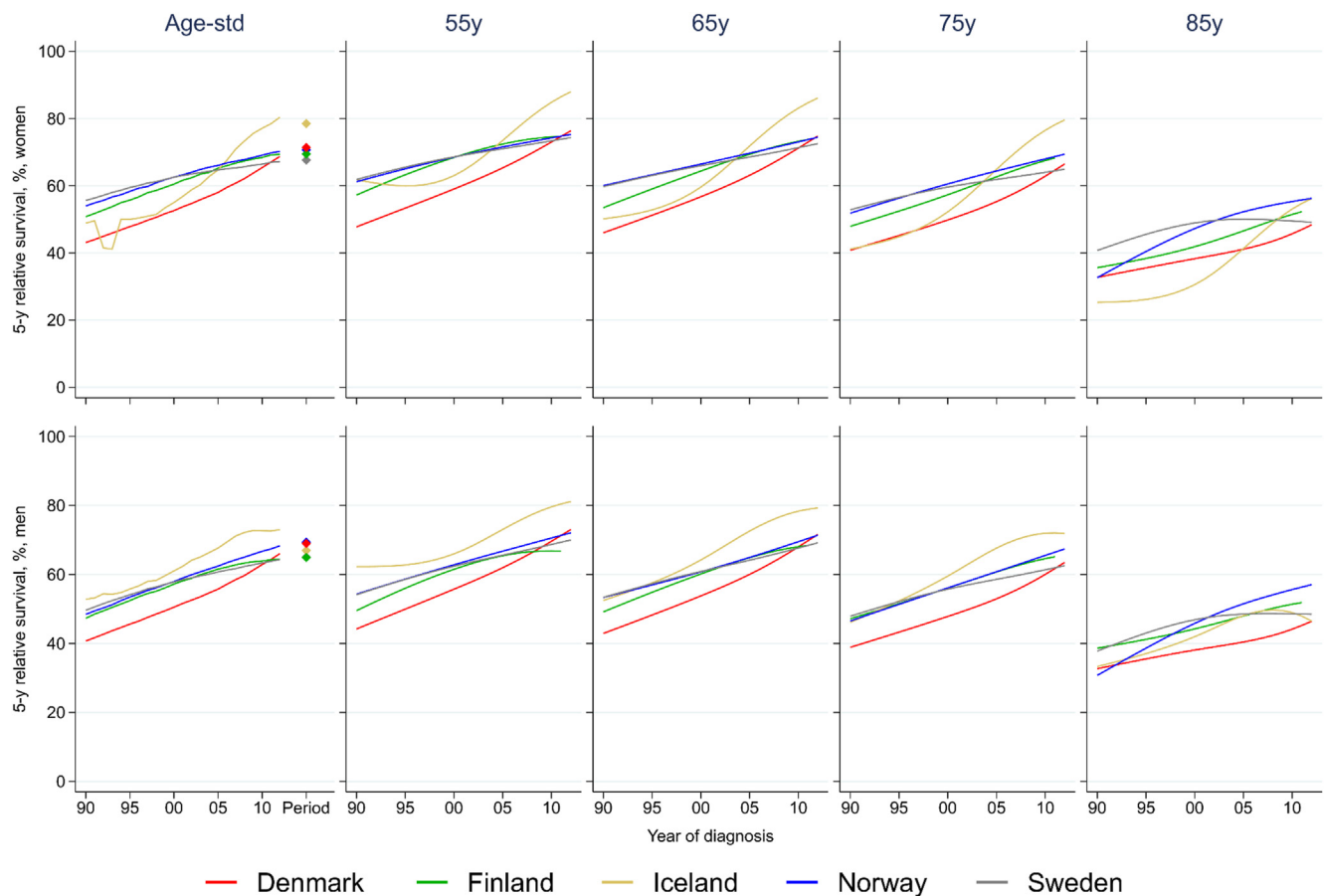


Fig. 3. Age-standardized and age-specific five-year relative survival in rectal cancer, a comparison of time trends in the Nordic countries; women (top panel) and men (bottom panel). Estimates with 95% confidence intervals in [Appendix A.6](#) and [Appendix A.7](#).

All analyses were performed in Stata [15]. The commands `stpm2` and `standsurv` were used for estimation [7].

Ethical approval for this study was granted by the Swedish Ethical Review Authority (approval 2017/641–31/1, amendment 2019–01913) and study permission from the National Institute of Health and Welfare in Finland (approval THL/870/5.05.00/2014, amendment 2019).

### 3. Results

Temporal trends in one- and five-year age-standardized relative survival in women and men, with colon and rectal cancer combined, showed an improvement over time in all five Nordic countries (Fig. 1). The survival improved most markedly in Denmark, and at the end of the study period, survival was similar across the countries with estimates of five-year survival close to 70%. This trend of improvement was observed for patients with both colon and rectal cancer (Fig. 2, Fig. 3, Appendix A.5, Appendix A.6). The five-year relative survival for patients with colon cancer improved over time both in women and men in all ages shown, with the possible exception of Icelandic patients aged 85 (Fig. 2, Appendix A.7). The largest improvement was observed in Denmark, where

survival was significantly lower during the first two decades of the study period, but from 2010 and onwards, the survival was more similar to the other Nordic countries except for the oldest age group with colon cancer, where the survival in Denmark and Iceland was somewhat lower than in the other Nordic countries. Survival for patients with rectal cancer also improved over time in all ages shown in both women and men also showing the largest improvement for the Danish patients (Fig. 3, Appendix A.7).

The reference-adjusted and age-standardized crude probability of cancer death and average number of life-years lost for colon and rectal cancer patients are presented in Table 1. The five-year crude probability of death in colon cancer ranged from 29.9% in Norway to 36.4% in Iceland for women, and from 32.0% in Denmark to 35.0% in Sweden for men. Crude probabilities of cancer death, i.e., probabilities accounting for death due to other causes, were approximately 1 percentage point lower than net probabilities of cancer death (one minus relative survival). The average number of life-years lost due to colon cancer ranged from 6.6 years in Icelandic men to 8.4 years in Swedish women. For rectal cancer, the reference-adjusted and age-standardized crude probability of cancer death at five years ranged from 20.4% in Iceland to 30.8% in Sweden for women, and from 29.1% in Norway to 33.4% in Finland for men. In Iceland, the average number of life-years lost due to rectal cancer was 5.9 years

Table 1

Age-standardized and reference-adjusted\* period estimates of five-year net and crude probability of cancer, other-cause, and all-cause death in addition to an estimate of life-years lost due to colon and rectal cancer. Comparison between the Nordic countries in men and women separately with 95% confidence intervals presented in parenthesis.

Colon cancer	Denmark	Finland	Iceland	Norway	Sweden
<b>Women</b>					
5y net prob. of cancer death, %	31.8 (30.5–33.1)	32.2 (30.4–33.9)	37.8 (31.9–43.1)	30.5 (29.2–31.9)	34.5 (33.4–35.7)
5y crude prob. of cancer death, %	30.9 (29.7–32.2)	31.6 (29.9–33.3)	36.4 (31.4–42.3)	29.9 (28.6–31.2)	33.6 (32.5–34.8)
5y crude prob. of other-cause death, %	7.4 (7.2–7.5)	7.5 (7.3–7.7)	6.9 (6.3–7.6)	7.8 (7.6–7.9)	7.9 (7.7–8.0)
5y crude prob. of all-cause death, %	38.3 (37.1–39.4)	39.1 (37.5–40.7)	43.3 (38.2–48.5)	37.6 (36.4–38.9)	41.5 (40.4–42.5)
Life-years lost	7.7 (7.2–8.2)	7.3 (6.7–7.8)	8.1 (6.0–9.9)	7.2 (6.7–7.7)	8.4 (8.0–8.8)
<b>Men</b>					
5y net prob. of cancer death, %	33.4 (32.0–34.7)	34.4 (32.4–36.3)	34.1 (28.3–39.5)	35.0 (33.5–36.4)	36.6 (35.4–37.7)
5y crude prob. of cancer death, %	32.0 (30.8–33.3)	33.4 (31.6–35.3)	32.5 (27.6–38.3)	33.7 (32.4–35.1)	35.0 (33.9–36.1)
5y crude prob. of other-cause death, %	9.9 (9.7–10.1)	10.0 (9.7–10.3)	10.1 (9.0–11.2)	9.9 (9.6–10.1)	10.2 (10.1–10.4)
5y crude prob. of all-cause death, %	41.9 (40.8–43.1)	43.4 (41.8–45.1)	42.6 (37.9–47.2)	43.6 (42.3–44.8)	45.2 (44.2–46.2)
Life-years lost	7.1 (6.6–7.5)	6.8 (6.2–7.3)	6.6 (4.8–8.1)	7.0 (6.6–7.4)	7.4 (7.1–7.8)
Rectal cancer	Denmark	Finland	Iceland	Norway	Sweden
<b>Women</b>					
5y net prob. of cancer death, %	28.6 (26.7–30.5)	30.5 (28.0–33.0)	21.5 (12.3–29.7)	29.3 (27.3–31.3)	32.4 (30.7–34.0)
5y crude prob. of cancer death, %	27.4 (25.7–29.2)	29.5 (27.2–32.0)	20.4 (13.6–30.6)	28.1 (26.3–30.1)	30.8 (29.3–32.4)
5y crude prob. of other-cause death, %	7.5 (7.2–7.8)	7.5 (7.2–7.9)	7.5 (6.3–8.9)	7.6 (7.3–7.9)	7.5 (7.3–7.7)
5y crude prob. of all-cause death, %	34.9 (33.3–36.6)	37.0 (34.8–39.3)	27.9 (20.4–35.5)	35.7 (34.0–37.5)	38.3 (36.8–39.8)
Life-years lost	7.5 (6.7–8.2)	7.5 (6.7–8.3)	5.9 (2.6–8.6)	7.0 (6.2–7.8)	7.3 (6.7–7.8)
<b>Men</b>					
5y net prob. of cancer death, %	31.0 (29.4–32.6)	35.1 (32.7–37.4)	33.1 (24.3–40.8)	30.6 (28.8–32.4)	34.9 (33.5–36.4)
5y crude prob. of cancer death, %	29.2 (27.7–30.7)	33.4 (31.3–35.7)	30.9 (24.0–39.8)	29.1 (27.5–30.9)	33.0 (31.6–34.3)
5y crude prob. of other-cause death, %	10.1 (9.8–10.3)	9.8 (9.5–10.2)	9.2 (7.8–10.9)	10.5 (10.2–10.9)	10.0 (9.7–10.2)
5y crude prob. of all-cause death, %	39.2 (37.8–40.6)	43.3 (41.3–45.2)	40.1 (33.3–47.0)	39.7 (38.2–41.1)	42.9 (41.7–44.1)
Life-years lost	7.1 (6.5–7.7)	7.2 (6.5–7.9)	8.8 (6.0–10.9)	7.0 (6.4–7.6)	7.4 (6.9–7.9)

Period window 2013–2017 (2012–2017 for Iceland, 2013–2016 for Finland). \*Crude probabilities of death and life-years lost based on average background mortality in the Nordic countries.

in women and 8.8 years in men. In the other countries, the corresponding estimates ranged from 7.0 to 7.5 years in both women and men. Crude probabilities of death and life-years lost that are not reference-adjusted or age-standardized are presented in [Appendix A.8](#).

Results from the period analysis show that the five-year relative survival for colon cancer was fairly stable across ages 45–75 in all countries with a slight decrease between ages 80 and 85 ([Fig. 4](#), [Appendix A.7](#), [Appendix A.9](#)). Although the five-year relative survival was similar across age, the reference-adjusted number of life-years lost decreased across age since younger patients have a longer remaining lifespan. For example, a patient diagnosed at age 55 lost on average around 11 years, which decreased to around 2.5 years in age 85 in both women and men. For rectal cancer patients, the five-year relative survival was stable across ages below 70 in all countries after which they declined at similar rates ([Fig. 5](#), [Appendix A.7](#), [Appendix A.9](#)). The average number of reference-adjusted life-years lost was very similar across countries and by sex, ranging from around 10 years in patients aged 55 to around three years in patients aged 85.

The incidence rates of colon cancer increased over time in both women and men aged 70 and above, with larger increases in Norway and Denmark ([Appendix A.10](#)). The mortality rate was mostly stable over time, with a slight decrease in Norwegian and Danish men aged 60 and above. For rectal cancer, the incidence rate was fairly stable over time in both women and men aged 40–79 years ([Appendix A.11](#)). The incidence of rectal cancer was higher in Denmark and Norway over the whole period under study in both women and men. The rectal cancer mortality rate decreased over time in both women and men, with the largest decrease found in Danish and Norwegian men above 80 years at diagnosis.

#### 4. Discussion

In this up-to-date analysis on colon and rectal cancer in the Nordic countries, survival improved continuously between 1990 and 2017. The age-standardized five-year relative survival is now close to 70% in all Nordic countries. These improvements were seen in both sexes and across ages. While colon and rectal cancer survival in the

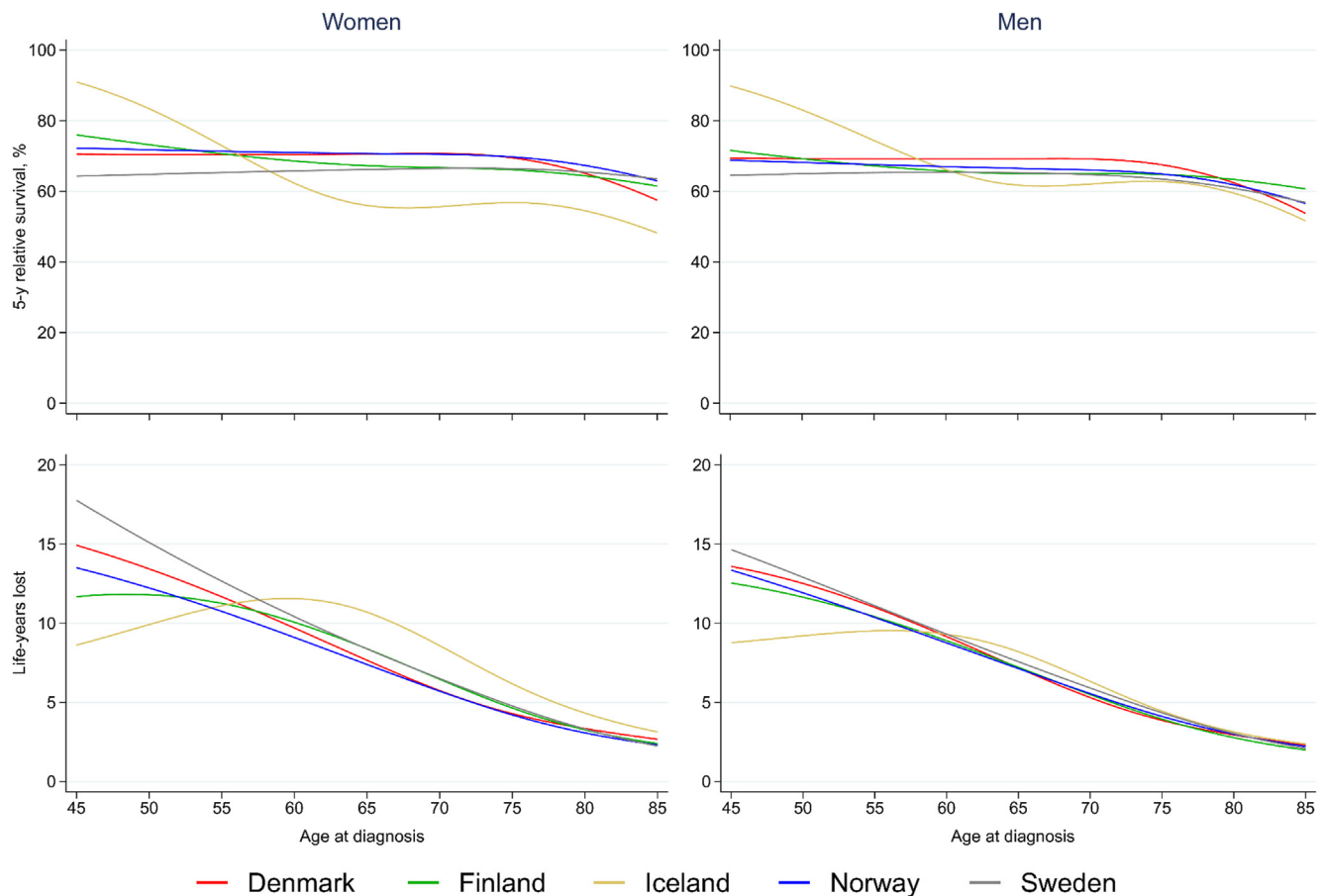


Fig. 4. Period estimates of five-year relative survival (top panel) and life-years lost (bottom panel) by age at diagnosis, colon cancer. Period window 2013–2017 (2012–2017 for Iceland, 2013–2016 for Finland). Estimates with 95% confidence intervals in [Appendix A.7](#) and [Appendix A.9](#).

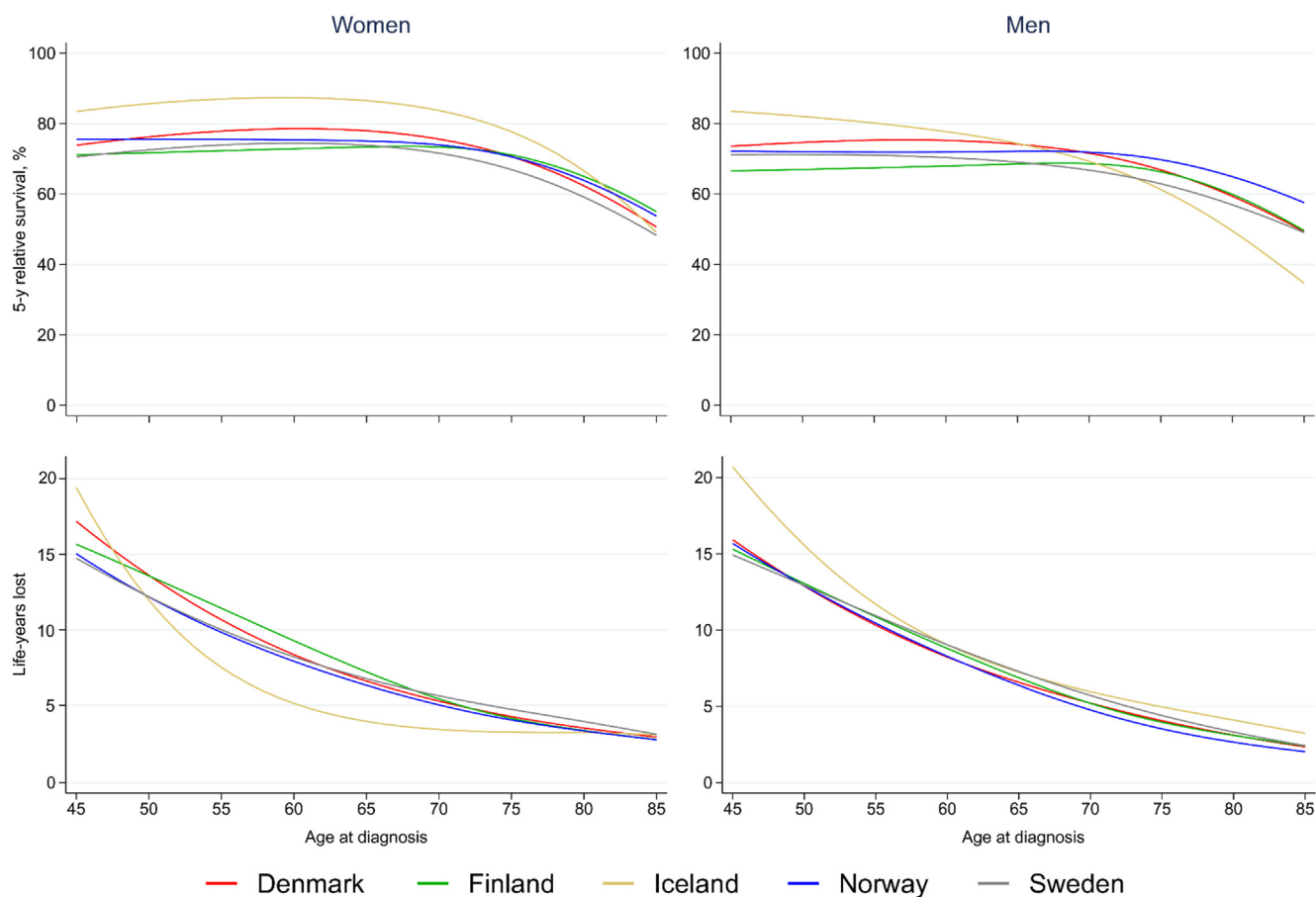


Fig. 5. Period estimates of five-year relative survival (top panel) and life-years lost (bottom panel) by age at diagnosis, rectal cancer. Period window 2013–2017 (2012–2017 for Iceland, 2013–2016 for Finland). Estimates with 95% confidence intervals in [Appendix A.7](#) and [Appendix A.9](#).

Nordic countries is among the highest in the world, similar trends of improvements have also been reported in other regions of Europe [16] as well as in other high-income countries [17,18]. In general, the relative survival was similar across ages and in men and women.

While colon and rectal cancer survival improved in all Nordic countries, the most marked change was observed in Denmark. The result from several earlier studies has shown poorer survival in patients with colon and rectal cancer in Denmark [3,16], findings which at least partly have been attributed to differences in the proportion of patients receiving curative surgery [19]. Changes in Denmark that may explain recent improvements include the launch of national cancer plans in 2000 with earmarked funding for cancer care, introduction of accelerated cancer patient pathways in 2007, improved access to endoscopic investigations, centralization of cancer surgery, and improvements in post-operative care [20,21].

Moreover, Denmark was the first Nordic country to introduce a national screening program for colon and rectal cancer for ages 50–74 in 2014–2018, based on a pilot project in 2005–2006 [22]. Sweden started implementing a national screening program in 2020, Norway

and Finland are planning to start in 2022, while Iceland does not yet have a national screening program. An increase in colon cancer incidence was observed in Denmark for all ages, possibly due to increased awareness of symptoms or the gradual implementation of screening [23]. However, it is unlikely that organized screening has had a detectable effect on overall colon and rectal cancer survival during the period under study.

In all Nordic countries, there have been gradual changes in Consensus Guidelines for management of colon and rectal cancer [24], improved quality registration of diagnosis and treatment [25], introduction of multidisciplinary team meetings [26], nationwide audits [27,28], efforts to centralize treatment, and decrease waiting times [29,30]. Changes in treatment guidelines include a shift toward more selective use of preoperative radiotherapy and radiochemotherapy for rectal cancer, a higher proportion of patients receiving treatment with curative intent, intensified treatment of metastatic disease, and increased use of laparoscopic surgery for colon and rectal cancer [20,31–34]. General improvements in health care in the Nordic countries during the time period have likely also had a positive effect on the observed relative survival for patients with colon and



rectal cancer. Other factors affecting survival may include changes in lifestyle, comorbidity burden, and public awareness of early signs and symptoms [35].

Although information on stage at diagnosis was available, the stage was recorded differently across countries, e.g., using clinical or pathological information, varying numbers of cases with missing information, and no data available from Finland in this study. Future efforts are needed to harmonize the collection and reporting of disease stage in the Nordic cancer registries, as differences in stage distribution as well as stage-specific survival are essential in understanding the differences in outcomes across countries. This will be of special importance for the evaluation and comparisons of the effects of national screening programs [36].

A major strength of our study was the use of the population-based NORDCAN database, which includes individual-level data on virtually all cancer patients in the Nordic countries. Record linkages to the Total Population Registers in each country provided complete follow-up information on death and migration, except in Iceland where migration data are unavailable. In the Nordic countries, all residents have access to similar tax-funded healthcare systems at low out-of-pocket costs. Death certificate-initiated cancers are included in the cancer registers of all Nordic countries except Sweden [37]. Including these cases has been shown to lead to a slight underestimation of survival, while not including them might instead overestimate survival [38]. This may explain the higher survival in Swedish patients aged 85 years at diagnosis. The small numbers of cancer cases in Iceland caused less reliable estimates, and possible differences in survival between Iceland and the other Nordic countries should, therefore, be interpreted with caution. Other limitations included one year less follow-up in Finland. Collectively, these limitations could bias the comparisons of survival between countries.

## 5. Conclusions

There were substantial improvements in the survival of patients with colon and rectal cancer in all Nordic countries. Of special note is that the previously observed survival disadvantage in Denmark is no longer present.

## Credit author statement

**Frida E Lundberg:** conceptualization, methodology, formal analysis, visualization, writing-original draft preparation. **Helgi Birgisson:** writing-original draft preparation. **Tom Børge Johannesen:** writing-original draft preparation. **Gerda Engholm:** data curation, writing-reviewing and editing. **Anni Virtanen:** writing-reviewing and editing. **David Pettersson:** writing-reviewing and editing. **Elinborg J Ólafsdóttir:** writing-reviewing and editing. **Mats Lambe:** writing-reviewing and editing. **Paul C Lambert:** conceptualization,

methodology, funding acquisition, supervision, writing-reviewing and editing. **Lina Steinrud Mørch:** writing-reviewing and editing. **Anna LV Johansson:** conceptualization, methodology, writing-reviewing and editing. **Therese M-L Andersson:** conceptualization, methodology, writing-original draft preparation.

## Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejca.2022.05.032>.

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