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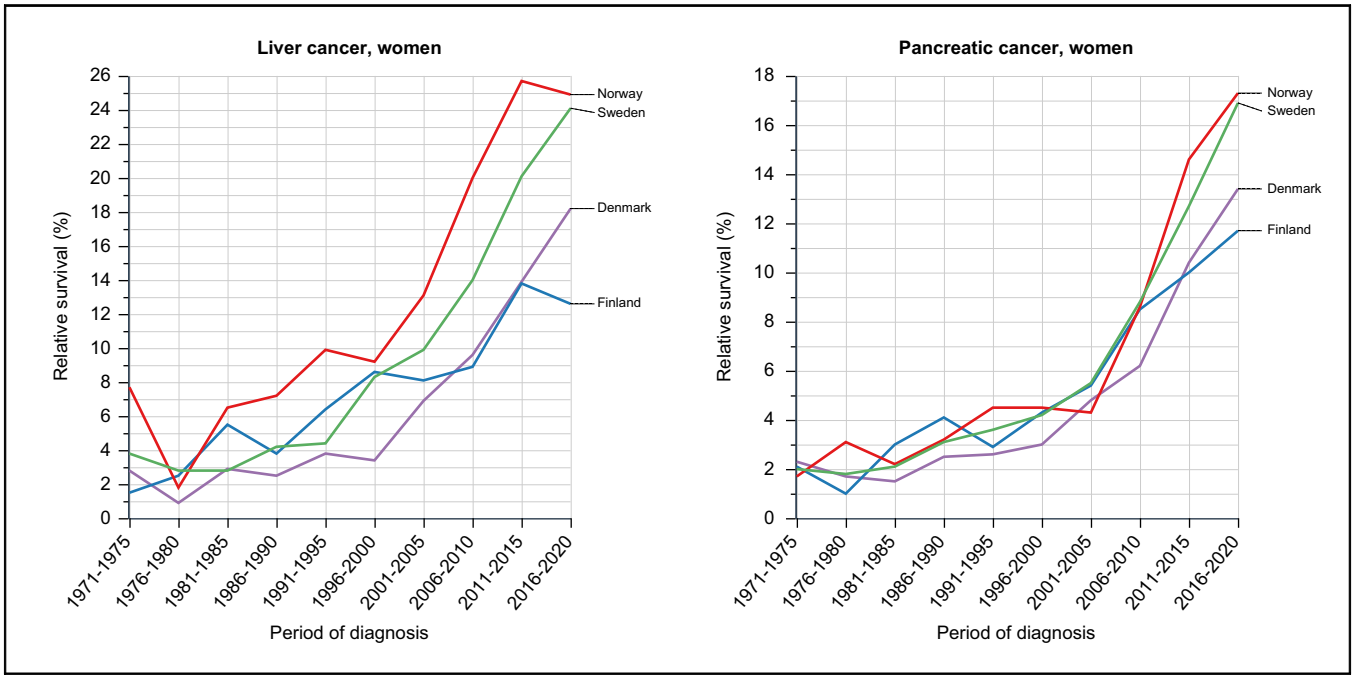
Graphical abstract



Highlights

- Five-year relative survival in liver and pancreatic cancer increased slowly until the year 2000, after which a steep increase in survival was observed.
- For liver cancer, survival in Sweden and Norway exceeded 20%, in Denmark reached 15%, and in Finnish men remained at 10%.
- In pancreatic cancer, survival exceeded 15% in Sweden and Norway but remained at 10% in Danish and Finnish males.
- Survival in both these cancers depended on age, and survival in those diagnosed at age over 80 years was very poor.

Lay summary
Liver and pancreatic cancers are among the most lethal of all cancers. In 50 years, survival in these cancers has slowly improved, and in the past 20 years, the development has been increasingly favourable. Widespread adoption of healthy lifestyles will be key to reducing the risk of these cancers.

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Long-term survival trends for primary liver and pancreatic cancers in the Nordic countries

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Background & Aims: Liver cancer (LC) and pancreatic cancer (PC) are often diagnosed at an advanced stage resulting in high mortality. High-quality survival data are rarely available for trend analyses over a long period.
Methods: The Danish, Finnish, Norwegian, and Swedish cancer data were accessed at the NORDCAN database. We analysed relative 1- and 5-year survival trends in LC and PC between years 1970 and 2019.
Results: Relative 1-year survival in LC for Nordic men and women was about 10% in the period between 1970 and 1974, and it increased moderately by year 2000 and steeply thereafter, eventually reaching 40–50%. The patterns in 5-year survival were similar, but after the year 2000, survival in Norway and Sweden increased steeply to 23%, whereas survival in Denmark and Finland lagged behind, reaching 10% to 15%. The patterns for PC also showed rapid improvement after the year 2000, with 1-year survival reaching 30% to 40% and 5-year survival reaching 10% for Finland and 15% for Norway and Sweden. Survival was best for patients diagnosed before age 50 years, and it was worst for older patients. For both cancers the difference between 1- and 5-year survival increased with time.
Conclusions: Survival in LC and PC improved first modestly and then steeply over the 50-year period covered. The increase in 5-year survival was less than that of 1-year survival. The survival gains were most likely the result of earlier diagnosis, improved treatment, and better organised supportive care. The challenges are to keep up these positive trends, to extend survival benefits past Year 1, and to obtain similar results in elderly patients. Primary prevention through avoidance of risk factors would reduce case numbers.
Lay summary: Liver and pancreatic cancers are among the most lethal of all cancers. In 50 years, survival in these cancers has slowly improved, and in the past 20 years, the development has been increasingly favourable. Widespread adoption of healthy lifestyles will be key to reducing the risk of these cancers.

Introduction

Liver cancer (LC) and pancreatic cancer (PC) have remained among the most fatal cancers in the world, and particularly for PC, progress has been slow.[1–3] Presentation and risk factors of these cancers differ in many ways. The incidence for LC is highest in some developing countries of Asia and Africa, whereas PC is most common in developed countries.[1] The modifiable risk factors of the two cancers are better known for LC for which the population attributable fraction (PAF) in the UK and Australia was estimated at 50% to 70% for men and 40% to 57% for women, whereas the estimates for PC were about 30% for both sexes. Only tobacco smoking and obesity were the shared risk factors.[4,5] Incidence trends in LC were recently analysed for the Nordic countries, with a likely historical influence of the contrast medium Thorotrast, and a more recent increase in incidence ascribed to life-style factors, such as alcohol, particularly in Finland and Denmark, and infections by HBV and HCV, particularly in Sweden.[6] The underlying carcinogenic mechanisms in LC, specifically for hepatocellular carcinoma, are thought to involve chronic inflammation, associated with many of the risk factors.[7] Inflammation causes necrosis (necroinflammation) and immune disturbances that further lead to cirrhosis and progression to cancer; chronic inflammation is estimated to be associated with 90% of hepatocellular cancers.[8,9] Pancreatic intraepithelial neoplasia is the most common precursor for pancreatic ductal adenocarcinoma, and particularly, cystic intraductal papillary mucinous neoplasms (IPMNs) often colocalise with ductal adenocarcinoma.[10] Inflammation is also a risk factor for PC, as chronic pancreatitis, and particularly its hereditary form, causes a high risk.[10] However, oncogenic pathways play a major role as somatic mutations occur in practically all tumours and usually

Keywords: Hepatocellular carcinoma; Relative survival; Mortality; Risk factors; Treatment.
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include KRAS or CDKN2A, TP53, and SMAD4.[10,11] A few signalling pathways are known to be activated in most PCs, and these contribute to the rapid progression of the disease.[11]

The only curative treatment for LC and pancreatic ductal adenocarcinoma is surgery.[10,12] According to the Swedish national registry for hepatocellular carcinoma, current treatments include resection, ablation, transarterial chemoembolization, and sorafenib, combined accounting for more than half the patients, and best supportive care was offered to 35% of patients; some 5% were recipients of a liver transplantation.[13] According to the Swedish national registry on PC patient data, about one-third of the patients underwent resection, and there was an increase in this trend.[14] According to a national Norwegian study on pancreatic ductal adenocarcinoma, resection rates, median age of those resected, and perioperative chemotherapy increased over the 10-year period, resulting in an increase in overall survival after resection from 16.0 to 25.1 months.[15] Median survival for patients who did not undergo resection (some 85% of all) was 4.2 months.

Reliable long-term data from LC and PC are not available from many sources because of diagnostic uncertainties. The Cancer Incidence in Five Continents (CI5) by the International Agency for Research on Cancer (IARC) volume V, covering years 1978–1982, reported quality indicators, such as proportion of histologically verified cancers.[16] Few European cancer registries showed histological verification of >50% for LC or PC, but all the Nordic registries showed high verification rates, 85–93% for LC and 61–82% for PC.[16] Using this type of reliable cancer data, we wanted to analyse long-term survival trends in LC and PC from Denmark (DK), Finland (FI), Norway (NO), and Sweden (SE), where survival data are available at the national level from 1970 to 2019. In these countries, healthcare has traditionally been offered to the population with minimal direct costs to patients, and the results should thus depict the 'real-world' survival experience through a half century. In addition, we calculated survival differences between Years 1 and 5 over time, allowing insights into changing diagnostic and treatment paradigms.

Materials and methods

Nordic cancer registries and NORDCAN

In year 2000, the national populations covered 11.7 million men (2.6 in DK, 2.5 in FI, 2.2 in NO, and 4.4 in SE) and 12.2 million women (2.7 in DK, 2.7 in FI, 2.3 in NO, and 4.5 in SE). Cancer registration started early in the Nordic countries, 1943 in DK, 1953 in FI and NO, and 1958 in SE. These registries have been considered of high quality because of diagnostic accuracy, high national coverage, and minimal loss to follow-up, all important features in survival studies.[16,17] Another quality indicator reported by CI5 was a low proportion of cases identified from death certificates only, which was <4% for LC and PC in the Nordic registries.[16]

The NORDCAN database was created by the Nordic cancer registries, which transferred epidemiologically relevant individual-level data to the publicly accessible database.[18] However, NORDCAN does not contain pathological details of the patients or tumours, nor does it contain data on risk factors or comorbidities. The database was subsequently moved to the IARC website (https://nordcan.iarc.fr/en/database#bloc2).

Diagnostic codes and the related cancers

NORDCAN defines LC by the International Classification of Diseases (ICD) version 10 code C22, which includes hepatocellular carcinoma, intrahepatic bile duct carcinoma, and some rare entities such as unspecific liver cancers. The proportion of hepatocellular carcinoma to intrahepatic bile duct carcinoma is about 2 to 1, and survival is somewhat better for hepatocellular carcinoma.[19] The childhood tumour, hepatoblastoma, is one of the rare entities. In the current database (1970–2019), individuals with LC diagnosed before age 50 years accounted for 5.5% of male and 5.3% of female patients, and those diagnosed before age 10 years accounted for 0.6% of all patients.

For PC, the ICD version 10 code is C25, which covers ductal adenocarcinoma and rare neuroendocrine tumours, such as insulinoma, which may be of relatively early onset. In the Swedish national PC registry, neuroendocrine tumours account for less than 10% of ductal adenocarcinoma.[14] For PC, patients diagnosed before age 50 years accounted for 4.8% of male and 3.6% of female patients (1970–2019).

Survival analysis

We carried out survival analyses in retrospective cohorts collected by the Nordic cancer registries. Survival tools at the NORDCAN website enable analysis of 1- and 5-year relative survival, which was applied for LC and PC between years 1970 and 2019 in 5-year periods. The analysis was based on the cohort survival method for periods from 1970 to 2014 and a hybrid analysis combining period and cohort survival in the last period 2015–2019, as detailed.[18] Age-standardised relative survival was assessed using the Pohar Perme estimator.[20] Age standardisation was performed by weighting individual observations using external weights as defined by the International Cancer Survival Standard (ICSS).[18,21] National general population life tables stratified by sex, year, and age were used in the calculation of expected survival.

As exclusion and inclusion criteria, only first diagnosed cancers were included, and cases with death certificates only or patients 90 years or older were excluded. Groups were analysed if a minimum of 30 patients were alive at the start.

We derived relative survival rates (and 95% CIs) in 5- or 10-year periods directly using the database tool. When 95% CIs between two consecutive periods did not overlap, we considered this difference in the relative survival to be 'statistically significant'. We also calculated a difference in survival percentage between Years 1 and 5 as a measure on how well survival was maintained between Years 1 and 5.[22] A small difference indicates favourable survival between Years 1 and 5 after diagnosis.

Age-specific survival was available from an earlier version of NORDCAN in which follow-up started in 1967 and ended in 2016 (https://www-dep.iarc.fr/NORDCAN/english/frame.asp).

Results

The cohorts subjected to survival analysis are shown in Table 1. Over 41,000 male and 25,000 female participants with LC were included. The age-adjusted incidence in women was approximately half of the male rates, and the NO rates were half of the other rates. LC was diagnosed at age over 70 years in men and at age a few years higher in women. For PC, patient numbers were much higher than those for LC, and hence, the incidence rates

Table 1. Numbers of incident cases, age-standardised rates, and median ages of onset (years) in male and female liver and pancreatic cancers in the Nordic countries, 1970 to 2019.

Country	Male			Female		
	No. of cases	ASR	Age of onset (years)	No. of cases	ASR	Age of onset (years)
Liver cancer						
Denmark	9,354	4.2	69	5,316	1.9	73
Finland	9,266	4.7	71	6,065	2.1	75
Norway	4,327	2.4	73	2,623	1.2	73
Sweden	18,184	4.4	72	11,513	2.3	74
Pancreatic cancer						
Denmark	19,833	8.8	70	19,736	6.8	72
Finland	19,343	8.8	70	21,409	7.1	75
Norway	15,242	8.0	71	14,893	5.9	75
Sweden	28,757	6.9	71	28,435	5.5	74

ASR, age-standardised rate per 100,000 (world standard).

were some two times higher in men and three times higher in women than those for LC; for NO, the differences were even higher.

Relative 1-year survival for Nordic men and women in LC is shown in Fig. 1 for the 50-year period. Survival was between 5% and 15% in the period 1970–1974, and it increased to over 50% for SE men and women, and to 40% for FI men and women; survival for the other Nordic populations was between SE and FI. All survival curves deviate from linearity and are characterised by strong upward bends from about year 2000 onwards.

The underlying survival data are shown in Table 2 in 10-year intervals. Significant improvements (*i.e.* nonoverlapping 95% CIs) in survival are marked by an asterisk. Consistent with Fig. 1, most significant improvements were achieved towards the end of the follow-up.

LC 5-year survival is plotted in Fig. 2; it shows a steep improvement after year 2000 and deviation of development

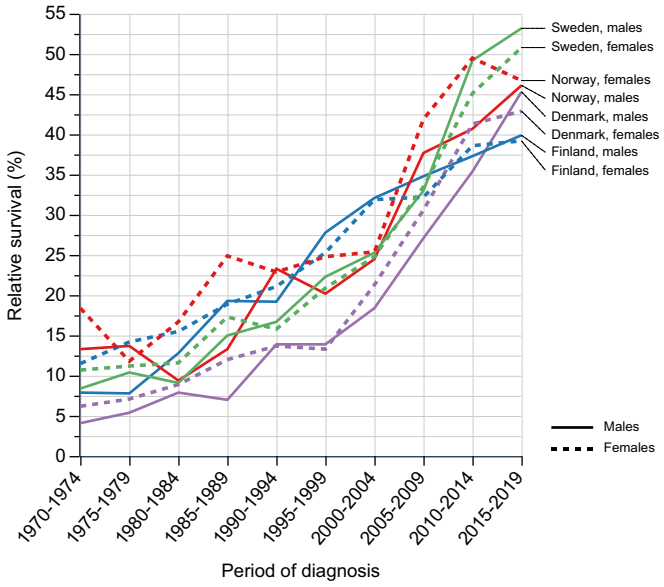

Fig. 1. Relative 1-year survival in liver cancer among Nordic men and women between 1970 and 2019.

Table 2. Relative 1- and 5-year survival rate (%, 95% CI) and their difference for liver cancer in the Nordic countries. *The 95% CIs were nonoverlapping for survival between this and the previous period. Diff, difference between 1- and 5-year survival in % units.

Period	Liver, 1 year, male								Liver, 1 year, female							
	Denmark	Diff	Finland	Diff	Norway	Diff	Sweden	Diff	Denmark	Diff	Finland	Diff	Norway	Diff	Sweden	Diff
1970–1979	4.7 (3.4–6.2)		7.7 (5.7–10.2)		14.0 (10.8–17.5)		9.2 (7.8–10.6)		6.7 (5.0–8.7)		13.1 (10.2–16.4)		14.3 (10.1–19.2)		10.7 (9.1–12.4)	
1980–1989	7.1 (5.6–8.7)		16.1 (13.7–18.6)*		11.7 (9.0–14.8)		11.9 (10.5–13.5)		10.0 (8.1–12.2)		17.0 (14.3–20.0)		20.5 (16.3–25.0)		14.2 (12.5–16.1)*	
1990–1999	13.8 (11.9–15.9)*		23.9 (21.4–26.5)*		22.5 (19.0–26.1)*		19.2 (17.6–20.9)*		13.5 (11.3–16.0)		22.7 (19.8–25.8)		24.6 (20.3–29.2)		17.9 (16.1–19.8)	
2000–2009	22.2 (20.3–24.3)*		33.1 (30.9–35.4)*		31.7 (28.3–35.1)*		29.4 (27.6–31.2)*		25.5 (22.5–28.7)*		31.4 (28.5–34.4)*		35.2 (30.5–40.0)*		28.8 (26.4–31.1)*	
2010–2019	40.3 (38.4–42.2)*		38.9 (36.9–40.9)*		44.0 (41.3–46.8)*		51.7 (50.2–53.2)*		41.9 (38.9–44.8)*		37.8 (35.0–40.6)*		46.7 (43.0–50.4)*		48.2 (46.0–50.4)*	
	Liver, 5 years, male								Liver, 5 years, female							
1970–1979	0.8 (0.30–1.7)	3.9	1.5 (0.60–3.4)	6.2	3.8 (2.2–6.1)	10.2	2.2 (1.5–3.1)	8	1.3 (0.60–2.6)	5.4	2.1 (1.0–3.9)	11	4.4 (2.2–7.8)	9.9	3.4 (2.5–4.6)	7.3
1980–1989	1.7 (1.0–2.8)	5.4	4.4 (3.0–6.1)	11.7	2.2 (1.1–3.9)	9.5	2.6 (1.9–3.5)	9.3	2.4 (1.4–3.7)	7.6	4.7 (3.2–6.6)	12.3	7.1 (4.5–10.5)	13.4	3.3 (2.4–4.3)	10.9
1990–1999	3.8 (2.7–5.2)	10	6.4 (5.0–8.2)	17.5	5.9 (4.0–8.3)*	16.6	5.8 (4.8–6.8)*	13.4	3.3 (2.1–4.8)	10.2	6.2 (4.5–8.2)	16.5	10.1 (7.1–13.7)	14.5	5.5 (4.4–6.7)*	12.4
2000–2009	4.8 (3.8–6.0)	17.4	9.2 (7.8–10.7)	23.9	10.9 (8.6–13.5)*	20.8	11.2 (9.9–12.5)*	18.2	7.2 (5.4–9.4)*	18.3	8.0 (6.3–10.0)	23.4	16.3 (12.6–20.4)	18.9	11.1 (9.5–12.9)*	17.7
2010–2019	11.4 (9.8–13.1)*	28.9	9.9 (8.4–11.5)	29	20.6 (17.9–23.4)*	23.4	21.0 (19.5–22.6)*	30.7	14.6 (12.0–17.4)*	27.3	11.5 (9.3–13.8)	26.3	23.4 (19.8–27.1)	23.3	20.6 (18.5–22.9)*	24.9

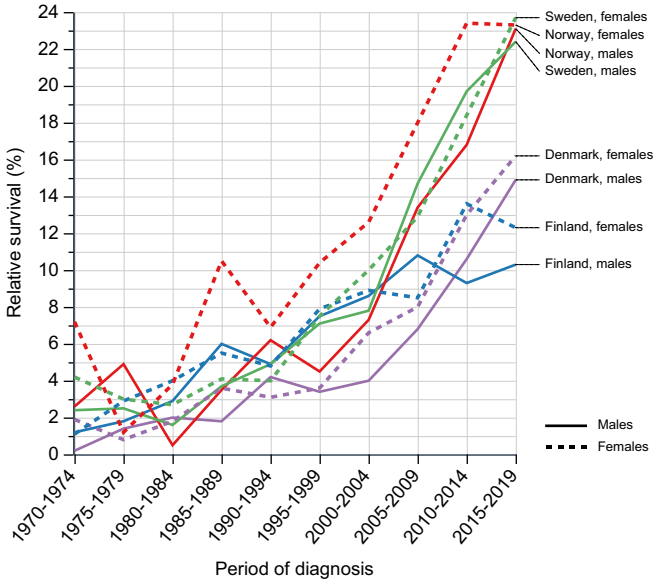

Fig. 2. Relative 5-year survival in liver cancer among Nordic men and women between 1970 and 2019.

between the countries, NO and SE reaching over 20% final survival and less successful countries DK and FI finishing at 10% to 16%.

The 5-year survival figures are shown in Table 2, with significant differences in final survival between NO and SE *vs*. DK and FI. Column 'Diff' shows the difference between Year 1 and 5 survival, which markedly increased with time. No sex differences were noted for 1- or 5-year survival.

Relative 1-year survival for PC is shown in Fig. 3. Survival between 1970 and 1974 was somewhat over 10%, and after a modest increase, survival increased sharply, reaching over 40% for NO and SE women but only 33% for FI men. The actual survival data in Table 3 confirm the significantly increasing trends

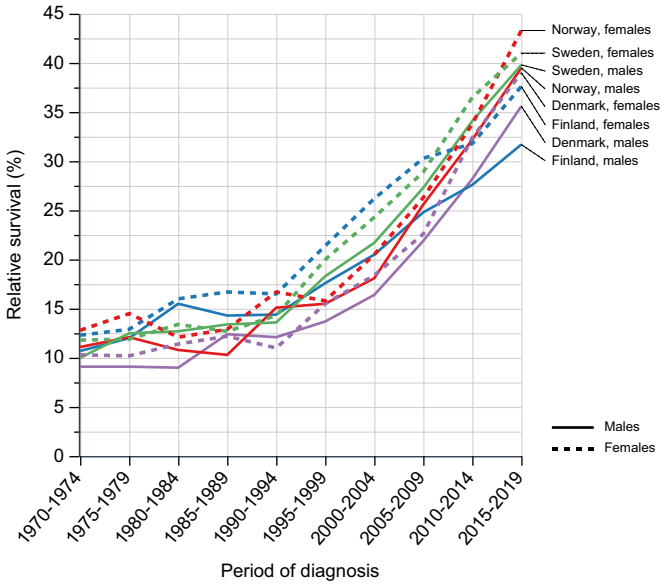

Fig. 3. Relative 1-year survival in pancreatic cancer among Nordic men and women between 1970 and 2019.

Table 3. Relative 1- and 5-year survival rate (%, with 95% CI) and their difference for pancreatic cancer in the Nordic countries. *The 95% CIs were nonoverlapping for survival between this and the previous period. Diff, difference between 1- and 5-year survival in % units.

Period	Pancreas, 1 year, male							Pancreas, 1 year, female						
	Denmark	Diff	Finland	Diff	Norway	Diff	Sweden	Denmark	Diff	Finland	Diff	Norway	Diff	Sweden
1970–1979	9.1 (8.1–10.1)	7.4	1.3 (0.80–2.0)	9.9	1.6 (1.1–2.3)	9.7	2.5 (2.0–3.0)	8.7	1.7 (1.2–2.3)	8.3	1.6 (1.0–2.3)	11.1	1.8 (1.2–2.7)	11.4	1.9 (1.5–2.5)	9.6
1980–1989	10.7 (9.6–11.8)	8.3	2.5 (1.9–3.3)	12.3	1.6 (1.1–2.3)	8.0	2.6 (2.1–3.2)	10.3	1.8 (1.4–2.4)	9.6	3.0 (2.3–3.9)	12.8	2.7 (2.0–3.5)	9.8	2.3 (1.9–2.9)	10.7
1990–1999	12.8 (11.6–14.1)	10.1	2.7 (2.1–3.4)	13.3	2.9 (2.2–3.8)	12.0	2.8 (2.3–3.4)	13	2.5 (1.9–3.2)	10.5	3.3 (2.6–4.1)	15.5	3.8 (2.9–4.8)	12.1	3.5 (2.9–4.2)	13.3
2000–2009	19.4 (18.1–20.7)*	14.9	5.0 (4.3–5.7)*	15.5	4.6 (3.8–5.6)	17.0	5.7 (5.0–6.6)*	18.1	4.4 (3.7–5.2)*	15.5	5.8 (5.0–6.7)*	21.3	5.4 (4.5–6.5)	17.4	5.8 (5.1–6.7)*	19.8
2010–2019	32.1 (30.7–33.5)*	22.8	7.5 (6.6–8.5)*	20.9	12.8 (11.4–14.4)*	23.3	11.8 (10.7–12.9)*	25.3	10.5 (9.3–11.8)*	24.8	8.9 (7.8–10.1)*	24.4	13.4 (11.9–15.1)*	23.9	12.8 (11.7–13.9)*	26.1
	Pancreas, 5 years, male							**Pancreas, 5 years, female**						
1970–1979	1.7 (1.2–2.3)													
1980–1989	2.4 (1.8–3.0)													
1990–1999	2.7 (2.1–3.4)													
2000–2009	4.5 (3.8–5.2)*													
2010–2019	9.3 (8.3–10.5)*													

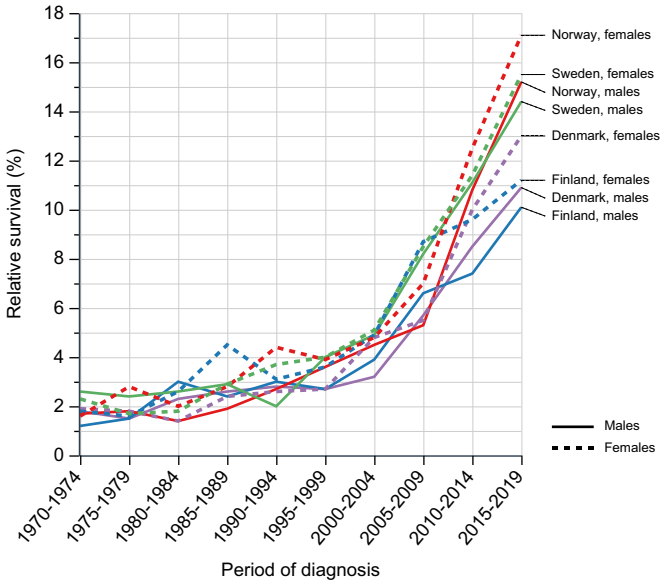

Fig. 4. Relative 5-year survival in pancreatic cancer among Nordic men and women between 1970 and 2019.

towards the end of the follow-up. The survival figures of DK and FI men in 2015–2019 were significantly below those for NO and SE men.

Curves for 5-year survival in PC increased slowly from about 2% without large differences between the sexes or the countries until about year 2000; survival steeply improved thereafter distinguishing NO and SE with strong gains (15%) and DK and FI men with lowest gains (10%) (Fig. 4). Table 3 confirms the significant differences in survival between NO and SE *vs*. DK and FI during 2015–2019. The difference between 1- and 5-year survival increased with time, and it reached >20% units in the final period, which is compatible with effects of earlier diagnosis and improved but not curative treatment.

Age-specific survival data were generated from an earlier version of NORDCAN, and results for LC in SE are shown in Fig. S1. Survival decreased with increasing age and was best for patients diagnosed before age 50 years (both 1- and 5-year survival). Although survival in other age groups was initially quite similar, after year 1990 differences became apparent, and age groups from 70 to 89 years lagged behind. In Table S1, we compared 5-year survival between all patients and those aged 80–89 years in 2012–2016. For SE men, survival was 18%, but among the older aged patients, it was 7%, with an equal drop in women from 17% to 10%. For the old DK and FI patients, survival was at 2–4%.

Age-specific data for PC in SE are shown in Fig. S2. Survival in age group 80-89 years did not improve over time, and 5-year survival in this age group remained at 4% for men and 3% for women. These data for all countries are found in Table S2. Among 80–89-year-old patients, 3% of NO men and women were alive in 5 years in 2012-2016. In DK and FI the survival in this age group was a miserable 1% or 0%.

Discussion

Novel findings of the present study include demonstration of a modest development in 1- and 5-year survival for LC and PC by year 2000 and a strong positive development thereafter by year 2019. Female survival was generally better than male survival in each country, but the differences were not significant. Although survival in the early period did not show country-specific differences, these emerged over time, and the development in DK and FI dragged behind NO and SE. In 2015–2019, FI male and female survival in LC and PC was significantly below the rates for NO and SE; for 5-year survival in LC, the FI rate was only 50% of those for NO and SE. We can speculate about the slower improvement in survival in DK and FI than that in NO and SE. During the 1980s, the proportion of healthcare expenditure of the gross national product markedly dropped in DK. In the 1990s, FI was in deep economic crisis, and healthcare expenditure was severely cut. Economic realities may influence the decisions about treatment intensity and judgement about fitness of patients for surgery or other treatments. A closer look into these differential trends among the Nordic countries may teach a lesson about the interplay of health economics and health outcomes.

NORDCAN supports analysis of relative survival, which is the comparison of survival in the defined cancer population with the matched national reference population. The method is well selected for comparison of survival rates between the Nordic countries or any other countries because there is no need to ascertain the cause of death or competing risks; the availability of such data or their definitions may be absent or ambiguous.[23,24] This is the reason why international comparisons use relative survival as shown below with some examples. Our 5-year survival data for LC in the last period (2010–2019) ranged from 9.9% to 20.4% and that for PC from 7.5% to 13.4%. As a comparison, a European study covering data up to 2007, reported 5-year relative survival at 12% for LC and 7% for PC.[25] In the global Concord-3 study, 5-year survival for LC ranged between 5–30% during 2010–2014, being highest for Japan and in the range of 10–19% in many European and North American countries.[26] In the same study, for patients diagnosed with PC, survival was in the range 10–15% for many European and North American countries. In an LC study covering seven countries in years 1995–2014, survival increased in all countries, and the best survival was in Australia.[19] In a recent UK study (1997 to 2014) on primary LC, 5-year survival reached 14.3% in the last period.[27]

In the present study, the difference between 1- and 5-year survival was around 10% units in 1970–1974, but it steadily increased to more than 20% units, indicating that because of the vastly increasing 1-year survival, the gains in 5-year survival were contributed by gains in 1-year survival. In our previous studies on colorectal and urological cancers, the difference between 1- and 5-year survival either declined or modestly increased with time, in contrast to the present results.[22,28,29] The large increase in the difference may suggest that improvements in earlier diagnosis, treatments, and care helped, increasing numbers of patients survive past Year 1, but lack of curative treatment options resulted in death before 5 years. Also, increasing numbers of liver transplantations have first influenced 1-year survival and with aging patients will increase 5-year survival. According to the Swedish experience, most individuals with LC and PC are seen by multidisciplinary teams, active treatment was centralised, and supportive care was organised.[13,14] The median survival for hepatocellular carcinoma was 1.4 years, but in the patients who underwent resection, it was 4.6 years.[13] For PC, the median survival was less than 6 months (5-year survival 6%), and for individuals receiving

treatment with curative intent, it was 2 years.[14] The major challenge is to maintain the positive survival course and to extend survival benefits past Year 1, which would require methods for early detection and new treatment options.[10,12,30–32] For PC, imaging methods are continuously improving for cystic precursor lesions, including IPMN.[33]

Survival differed by age groups, and particularly young patients (diagnosis before age 50 years) had good survival. These patients accounted for 5% or less of all, and some caution is due when drawing conclusions about their survival advantage. The NORDCAN diagnostic classification for LC includes hepatoblastoma for which survival is good. Even if patients diagnosed before age 10 years accounted for 0.6% of all LC, they accounted for more than 10% of those diagnosed before age 50 years and thus boosted survival. For PC, neuroendocrine tumours (such as insulinoma) are included in ICD code C25, and most of the patients are diagnosed at a broad age range around 60 years, earlier than median age of onset for PC.[34,35] The incidence has been increasing in Sweden and the USA, probably because of increasing diagnostics.[36,37] These are rare entities (less than 10% of PC), but with excellent survival, they would bias survival, probably most in age group younger than 50 years.[14] The NORDCAN classification system does not allow removal of the rare entities.

The major concern in age group-specific survival was the poor survival in patients older than 80 years in LC and, particularly, in PC, for which only 0 or 1% of the DK and FI patients survived 5 years and the outcome was only marginally better in NO and SE. Poor survival among old LC and PC have been noted in previous studies, with association with low active treatment of the old.[30,38] In the national Norwegian study on pancreatic ductal adenocarcinoma, resection rates varied by age, and although 24% of patients younger than 60 years underwent resection, the proportion in those older than 75 years was 7%; however, in all age groups, the proportion was increasing.[15] According to a Dutch study, only less than 10% of individuals with PC older than 74 years were offered surgery or systemic therapy, and over 90% received supportive care.[39] LC and PC are cancers of the elderly and, as populations age, more elderly patients will be diagnosed, calling for improved treatment strategies.

The NORDCAN database lacks detailed diagnostic and clinical data. LC includes also intrahepatic bile duct cancer, and PC includes some relatively benign rare entities. As a compensation for such deficits, NORDCAN enables reliable country-wise survival analysis over a half century that cannot be conducted anywhere outside the Nordic countries. The recent update includes data until the end of 2019 and is therefore quite current.

In conclusion, the present follow-up documented LC and PC survival results until the end of 2019. Overall, survival increased over time, and its pace accelerated after year 2000. This is most likely a consequence of multiple factors including diagnostics, treatment, and supportive care.[30] Although immunotherapy with atezolizumab + bevacizumab is providing some valuable hope in metastatic/advanced hepatocellular carcinoma, similar developments have not yet been seen in the other tumour types discussed here.[40] As these cancers remain to be fatal, primary prevention is a valuable option; as for LC, many risk factors are known, and some of these also predispose to PC.[4,5] Increased physical activity, avoidance of obesity, control of type 2 diabetes, and non-smoking will help reduce risk of both these cancers, and moderation of alcohol consumption and avoidance and control of hepatitis virus infections would help reduce risk of LC.

Abbreviations

CI5, Cancer Incidence in Five Continents; DK, Denmark; FI, Finland; IARC, International Agency for Research on Cancer; ICD, International Classification of Diseases; ICSS, International Cancer Survival Standard; IPMN, intraductal papillary mucinous neoplasm; LC, liver cancer; NO, Norway; PAF, population attributable fraction; PC, pancreatic cancer; SE, Sweden.

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Conflicts of interest

AH is a shareholder in Targovax ASA. AH is an employee and shareholder in TILT Biotherapeutics Ltd. Other authors declare no conflict of interest.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Design: KH. Acquisition of data: KH. Statistical analysis and interpretation: KH, AF, AH, OH, VL. Manuscript writing: all authors. Approval of the final text: all authors.

Data availability statement

The NORDCAN database can be accessed by anyone.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhepr.2022.100602.

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