DMCG.dk Benchmarking Consortium
Rapport om canceroverlevelse i Danmark 1995-2012

Danske Multidisciplinære Cancer Grupper (DMCG.dk)
Danish Breast Cancer Cooperative Group (DBCG)
Dansk Lunge Cancer Gruppe (DLCG)
Danish Colorectal Cancer Group (DCCG)
Dansk Gynækologisk Cancer Gruppe (DGCG)

DMCG.dk

databasernes fællessekretariat
regionernes kliniske kvalitetsudviklingsprogram

Definition

Benchmark
noun\ˈbench-ˌmärk\
: something that can be used as a way to judge the quality or level of other, similar things
- Merriam-Webster English Dictionary

Benchmarking
verb\ˈbench-ˌmärk-ˌing\
: Evaluate (something) by comparison with a standard
-Oxford English Dictionary

Members of the DMCG.dk Benchmarking Consortium (2014)

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Indhold

I. Forord

Den aktuelle rapport er den første af sin slags og repræsenterer naturtro klinisk funderede danske overlevelsestal for fire store kræftsygdomme – bryst-, lunge-, tyktarm/endetarm- og æggestokkræft. Dansk kræftbehandling har i to årtier været lettere stigmatiseret ved sammenligning af behandlingsresultater fra lande, som vi normalt finder os ligeværdige med. Et forhold som har ledt til store nationale behandlingsforbedrende tiltag. Der er således i dette tidsrum udarbejdet og implementeret hele tre kræftplaner, foretaget milliardinvesteringer i syghusvæsenet, gennemført behandlingscentralisering og screeningstiltag på udvalgte sygdomme. Desuden er de sygdomsspecifikke Danske Multidisciplinære Cancer Grupper - DMCG'erne etableret, hvilket har ledt til en lang række tiltag. Her i blandt udarbejdelse af nationale kliniske retningslinjer og kvalitets- og forskningsdatabaser for de enkelte kræftsygdomme, klinisk forskning og tusindvise afviklede MDT-konferencer samt udarbejdelse af kræftpakkeforløbsbeskrivelser og opfølgningsprogrammer for hele sygdomsspekteret. Dette til trods får Dansk kræftbehandling i internationale sammenlignende registerundersøgelser fortsat klaret sig yderst dårligt.

Det er derfor en meget stor glæde på baggrund af denne DMCG rapports naturtro kliniske data at kunne dokumentere ikke kun gode men også til stadighed forbedrede behandlingsresultater inden for de fire valgte store kræftsygdomme. Imidlertid giver disse data ikke mulighed for en direkte sammenligning med omverdenen, da disse sammenligninger hidtil og fortsat vil være præget af en grundlæggende forskel i datakomplethed og definitioner. Desuden vil en gunstig påvirkning af "den danske livsstil" udgøre en oplagt genvej i bestræbelserne på en forbedret kræftoverlevelse hertillands.

Rapportens forfattere skal have stor ros for et stykke flot og yderst veldisciplineret arbejde, som på kort tid har resulteret i udarbejdelse af dette vigtige dokument. Processen har været dygtigt koordineret af DMCG.dk's akademiske sekretær Mary Nguyen Nielsen og finansieret af Regionernes Kliniske Kvalitetsudviklingsprogram (RKKP).

Dansk kræftbehandling kan med reference til rapporten atter med rank ryg arbejde videre på fortsat forbedrede resultater i kræftbehandling – mod det højeste internationale niveau.

Michael Borre
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DMCG.dk

Århus, oktober 2014

II. Indledning og baggrund

Den foreliggende DMCG-rapport udspringer af det årlige møde mellem Danske Regioner, DMCG.dk's forretningsudvalg og RKKP-ledelsen i december 2013. På baggrund af OECD-rapporten "*Cancer Care: Assuring quality to improve survival*" blev der fra de regionale repræsentanter udtrykt undren over, at kræftbehandlingem i Danmark, på trods af implementering af kræftplaner, synes at halte bagefter de lande, vi sædvanligvis sammenligner os med.

På mødet gjorde flere af de tilstedeværende DMCG-repræsentanter gældende, at netop de seneste 5-10 års udvikling på området har betydet, at tidligere tiders dystre billede, som videreføres i OECD-rapporten, ikke længere kan betragtes som retvisende.

DMCG.dk og RKKP valgte at tage udfordringen op ved afrapportering af canceroverlevelse fra kliniske databaser, der dækker 4 store cancerområder. Vi kan i RKKP med stor glæde konstatere, at opgaven er løst på et højt, både kritisk og selvkritisk, niveau. Der er produceret et nuanceret billede af den danske kræftbehandlings kvalitet, hvor hovedindtrykket er ganske positivt, men hvor eksisterende – løsbare problemer samtidig fremhæves i de enkelte områders afrapportering.

Det er bemærkelsesværdigt, at afrapporteringen har kunnet foregå indenfor et så begrænset tidsrum og med så begrænset tilførsel af ekstra ressourcer. Dette skyldes entydigt eksistensen af DMCG-organisationen, hvor sammenhængen mellem kliniske retningslinjer, kvalitetsmåling og forskningsinfrastruktur på kræftområdet giver et helt enestående fagligt beredskab. Det er væsentligt, at dette beredskab også i fremtiden understøttes og udvikles.

Dernæst understreger rapporten et væsentligt paradoks i dansk sundhedspolitik: Det er utvivlsomt nødvendigt med international orientering og benchmark, hvis vi skal fastholde kvaliteten i sundhedsvæsenet. På den anden side viser rapporten klart begrænsningerne og meningsløsheden i anvendelse af rangstillingstabeller fra internationale, ikke klinisk funderede agenturer som grundlag for overordnet sundhedspolitik.

Slutteligt repræsenterer arbejdet et eksempel for de øvrige kliniske kvalitetsdatabaser med henblik på fremtidig anvendelse.

Derfor stor tak til rapportens forfattere og ikke mindst DMCG.dk's forretningsudvalg.

Paul D. Bartels
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III. Executive Summary

The Danish Multidisciplinary Cancer Groups (DMCG.dk) is a national network of physicians, other health care professionals, scientists, and government officials committed to improving cancer care in Denmark. DMCG.dk and the national cancer clinical databases are under the administration of the Joint Secretariat for the Danish Clinical Quality Improvement Program (Databasernes Fællessekretariat, Regionernes Kliniske Kvalitetsudviklingsprogram, RKKP).

Previous OECD reports[1] on cancer survival have repeatedly shown that Denmark performs worse when compared to our Scandinavian counterparts and other nations of comparable size and demographics. In this report on cancer survival in Denmark from 1995-2012, we linked individual level data from the national cancer clinical databases to compute age-standardized[2] 1-year and 5-year mortality rates, survival proportions, and relative survival for breast, lung, colorectal, and ovarian cancers. A defining feature of the Danish cancer clinical databases is high data completeness, clinically-based prospective data capture, and an organisational infrastructure (i.e., DMCG.dk) led by clinical experts working closely with their respective patient population.

We provide evidence that cancer survival in Denmark has steadily improved over the past 20 years, and that Danish cancer survival, especially in the most recent years, is higher than what has been previously reported elsewhere. It is important to note that the results presented in this report are based on clinical (i.e., hospital-based) data, in contrast to survival estimates from the OECD and other multinational collaborations such as NORDCAN, which are based on population-based cancer registry data. Thus, although our data analyses cannot be directly compared to results from the OECD 2013 reports, they nevertheless provide insight on temporal trends and developments in cancer survival in Denmark.

Summary of main findings and conclusions by cancer type

Breast cancer

Data from the Danish Breast Cancer Cooperative Group (DBCG) showed that the 5-year relative survival for Danish breast cancer patients was 88% for the period 2005-2009. Data analyses presented here also showed that breast cancer mortality rates have significantly decreased in Denmark during the period 1995-2012, and that stage-for-stage, Danish breast cancer patients have the same prognosis as patients in other Nordic and European Countries of comparable size and demographics. However, elderly breast cancer patients and those with major comorbidity are subgroups that were identified with poorer prognosis.

[1] OECD (2013), *Cancer Care: Assuring Quality to Improve Survival*, OECD Health Policy Studies, OECD Publishing. Available at: http://dx.doi.org/10.1787/9789264181052-en.See also OECD *Health at a Glance 2011*. Available at: http://dx.doi.org/10.1787/health_glance-2011-en.

[2] ICSS Cancer Population. See Corazziari I, Quinn M, Capocaccia R. Standard cancer patient population for age standardising survival ratios. *Eur J Cancer.* 2004;40(15):2307-2316.

Lung cancer

Data from the Danish Lung Cancer Registry (DLCR) showed that survival of Danish lung cancer patients is on par with other countries traditionally used for benchmarking comparison. The 5-year relative survival for the period 2005-2009 was 15% overall, and 13% and 16% for males and females, respectively. For the period 2000-2004, the overall 5-year relative survival for Denmark was 12%. Furthermore, mortality rates for Danish lung cancer patients, for both males and females, have been decreasing significantly since the year 2000. However, incidence rates have increased during this same period, especially for females. A high prevalence of comorbidity and delay in primary diagnosis in Danish lung cancer patients continues to contribute to poor survival.

Colorectal cancer

Data from the Danish Colorectal Cancer Group and Database (DCCG) showed that the 5-year relative survival was 63% for colon cancer and 65% for rectal cancer for the period 2009-2012. From 2005-2008, the 5-year relative survival was 61% for colon cancer and 64% for rectal cancer. Significant improvements have been made in the care and treatment of Danish colorectal cancer patients in the period 2001-2012. Since 2000, several important initiatives have taken place in Denmark. Notable areas of improvement include major and thorough revision of rectal cancer care and the implementation of laparoscopic surgery for colorectal cancer, which may have had a particular impact on improving colon cancer prognosis.

Ovarian cancer

Data from the Danish Gynaecological Cancer Group and Database (DGCG) showed that the 5-year survival for ovarian cancer patients was 37% for the period 2005-2009. Data analyses presented here also showed that mortality rates for ovarian cancer have been decreasing in Denmark since 1995. The estimates reported here, especially over the most recent years, indicate that Denmark is on par with some, but not all, of the countries that we traditionally compare us to. Survival trends have been gradually increasing since the year 2000 and the greatest improvement in ovarian cancer survival has occurred within the most recent years. Further improvements, with increased acceleration are expected, both in the 5-year survival and in the short-term, 1-year survival, as a result of treatment initiatives such as the implementation of lymph node resection.

IV. Methods

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Setting and source population
Denmark (with a population of 5.6 million residents) is a small and relatively homogenous country located in Northern Europe. All residents have equal-access to tax-financed, national healthcare and only a small fraction of health care services and medications are paid out-of-pocket.[1] Furthermore, linkage of data from all national health registers at the individual patient-level allows for real-time population tracking and virtually complete follow-up of all residents.[2,3]

Data sources and organizational infrastructure
Denmark has more than 70 national clinical databases that prospectively collect data on health care monitoring indicators for the purpose of quality improvement and research infrastructure.[4] The Danish Multidisciplinary Cancer Groups (DMCG.dk) is a national network of physicians and other health care professionals, scientists, and government officials committed to improving cancer care in Denmark.[5] DMCG.dk is under the administration of the Joint Secretariat for the Danish Clinical Quality Improvement Program (Databasernes Fællessekretariat, Regionernes Kliniske Kvalitetsudviklingsprogram, RKKP).[6] Each DMCG cancer group has a corresponding national clinical database and data from these clinical databases can be further linked to numerous national registries and databases (see below) via the unique person-identification number assigned to all residents upon birth or immigration.

There are currently 23 cancer clinical databases under the auspices of DMCG.dk and RKKP.dk (with the 24th cancer database recently approved). Data on breast, colorectal, lung and ovarian cancer were obtained from the following national clinical databases and, where relevant, patient histories were also supplemented with data from the Danish National Patient Register,[7] the Danish Civil Registration System,[8] the Danish Pathology Register[9] and the Danish Cancer Registry.[10]

i. Danish Breast Cancer Cooperative Group (DBCG)[11]
DBCG has prospectively collected data on Danish breast cancer patients since 1977 to present day. Demographic data and data pertaining to the diagnosis, treatment and long-term follow-up of Danish breast cancer patients are systematically registered by relevant pathology, surgery and oncology departments in Denmark. The collected data includes detailed information on primary surgery, pathology, disease stage and adjuvant treatment (endocrine, chemotherapy, biological treatment and radiotherapy), recurrence (local, regional, distant, and contralateral breast cancer) and survival.

ii. Danish Lung Cancer Registry (DLCR)[12]

DLCR has prospectively collected data on Danish lung cancer patients since 01-January 2000 to present day. Data parameters, which are registered by participating hospital departments in Denmark, include (amongst other variables) survival, morbidity, cancer stage, resection/operation rates, and time-to-diagnosis and treatment. Since 2012, the DLCR has been incorporated into the National Clinical Cancer Database (Den Nationale Kliniske Kræftdatabase, DNKK), which is an umbrella clinical database platform currently under development.[6]

iii. Danish Colorectal Cancer Group (DCCG) and Database[13]

DCCG has prospectively collected data on Danish colon and rectal cancer patients from 01-May-2001 to 31-December-2012, including information on demographic data, staging, acute/elective surgery, other treatments received, and postoperative complications. All incident colorectal cancer in persons 18 years or older, diagnosed and/or treated at a surgical department, are registered. See Chapter 3 for further details on DCCG.

iv. Danish Gynaecology Cancer Group (DGCG) and Database[14]

DGCG has prospectively collected data on Danish ovarian cancer patients since 01-January 2005 to present day. The database covers data on ovarian cancer (including borderline-type), peritoneal cancer, tuba cancer, corpus cancer (including hyperplasia med atypical), cervix cancer and trophoblastic disease. In 2014, the database was expanded to include vulvar cancer. Data parameters are registered on-line by participating Gynaecology, pathology, and oncology departments in Denmark. In addition, data on nurse-related care and activities were also registered.

Inclusion and exclusion criteria

All incident cancer registered in the above clinical databases were included in the survival analyses. A defining feature of the Danish cancer clinical databases is high data completeness with regard to registration of incident cancer (i.e., minimum requirement of > 90% coverage of the specific cancer population) and great efforts and resources are spent on data validation to ensure data correctness and periodic evaluation of the clinical databases, i.e., medical audit and annual indicator reports. Patients who emigrated outside of Denmark or who were registered as lost-to-follow up were excluded from the analyses for lung and colorectal cancers, whereas for breast and ovarian cancers, patients who were registered as lost-to-follow-up were right-censored. See Appendix 1 algorithm ICD-codes for cancer diagnosis.

It should be briefly noted that the OECD Cancer Care and Health-at-a-Glance reports are based on data from the Danish Cancer Registry, whereas this report is primarily based on data from the Danish national clinical databases. The quality of the data, as well as data on patient and tumor characteristics, can greatly affect the measured survival estimate. Patients included in the national clinical databases have "clinical-only diagnoses,"[15], whereas patients whose cancer diagnoses are registered at-time-of death or just shortly prior to death will not be routinely included in the clinical databases. This is a distinguishing feature of the national clinical databases. Inclusion of this sub-group of patients (e.g. death-certificate-only diagnosis) is controversial and can greatly impact survival estimates, as was illustrated in the UK Thames Cancer Registry, where 5-year relative survival decreased from 9.2 to 5.6 months when including an additional 15% of cases with death-certificate-only cancer diagnoses.[15] Nevertheless, regardless of the Danish data source, survival

estimates from all Danish data sources provide evidence for the same pattern/trend over time, i.e. improved cancer survival in Denmark.

Covariates (other prognostic factors)
Data on comorbidities, cancer stage, and surgery status/history were also included in the analyses.[15] History of comorbidities were identified using ICD-8 and ICD-10 codes corresponding to the Charlson Comorbidities Index[16,17] and using data-linkage to the Danish National Patient Register for patient histories up to 10 years prior to the cancer diagnosis date. See Appendix 2 for the ICD codes for the 19 Charlson comorbidity diseases and for further algorithm specifications.

Cancer stage and surgery status were queried from either the respective clinical database alone (breast, colorectal), or in combination with supplemental data from the Danish Cancer Registry (lung), the Danish Pathology Register (ovarian, including borderline-type), and the Danish National Patient Register (ovarian, lung).

Outcome measures and statistical analyses
For each cancer type, we computed 3 outcome measures relating to the first-year and the first five-year period after diagnosis, and additionally the first ten-year period after diagnosis for breast cancer:

i. Absolute all-cause mortality rate per 100 person-years
ii. Absolute (overall) survival proportion
iii. Relative survival

All estimates were then age-standardized according to the ICSS cancer population weights (cluster 1).[18] For colorectal and lung cancer, estimates were also gender-standardized to reflect the gender distributions in real-world patient populations. Thus, for colon cancer and lung cancer, the male and female subpopulations were weighted equally, whereas for rectal cancer the overall male:female ratio was fixed at 60:40. Finally, the mortality and survival measurements reported here reflect all-cause mortality and all-cause survival (in contrast to the OECD Cancer Care 2013 report which reports cancer-specific mortality). Cancer-specific mortality/survival was not investigated because coding in the Danish Register of Causes of Death is known to have less than optimal data quality and likely to yield biased estimates.[19,20] Poor data validity on the causes-of-death in cancer patients[21] is not unique to Denmark.

Absolute all-cause mortality rate (reported per 100 person-years) is calculated as the number of deaths divided by the sum of the patient-time at risk during the period concerned. This method of measurement takes into account "patient-time at risk" by accounting for the length of time each cancer patient contributes while being in the patient population at risk.[22] It is important to note that the mortality rate per 100 person-years is different from the measure of taking the number of deaths caused by a given cancer divided by the total general population (conventionally expressed per 100,000 population as seen in the OECD Cancer Care 2013 report). Taking into accounting the actual "time-at-risk of death" among cancer patients is an appropriate and robust method when 'benchmarking' clinical outcomes within the context of assessing quality of care.[22] In the present report, mortality rates are presented for the first year and the first five years after diagnosis, and

additionally, the first ten years with respect to breast cancer. These rates have been calculated from observations in closed cohorts followed from diagnosis and onwards. If a disease has a particularly high short-term mortality it is likely to observe that the 5-years mortality rate is *lower* than the 1-year mortality. This is so, because the long-term survivors accumulate patient-time at risk in the denominator of the 5-years mortality rate, whereas the contribution of the risk-time for long-term survivors is limited to a maximum of 1 year in the denominator of the 1-year rate. Thus, the 1-year mortality rate is controlled by the high short-term mortality, whereas the 5-year mortality rate also includes the contributions from long-term survivorship. Conversely, for a disease with low initial excess mortality, the 5-year mortality rate may be higher than the 1-year mortality rate, due to ageing of the patient and/or accumulating harmful effects related to the disease.

Absolute survival proportion (reported as percentages) is defined as the proportion of a closed population that survives throughout a given period of time.[22] The measurement is estimated using the Kaplan-Meier Method (ovarian), the actuarial method (breast), or using simple calculations of proportions (colorectal, lung). The latter alternative yields identical estimates to those obtained by the Kaplan-Meier method, because of the exclusion of the (very few) patients lost to follow-up before completing 5 years of follow-up.

Relative survival is estimated as the ratio of the observed survival of the patients (all deaths considered events) to the expected survival. The expected survival is estimated from the general Danish population (i.e., reference population), matched by gender, age and calendar time, and using the Ederer II method (breast), Ederer I (ovarian), or a case-mix matrix method (lung, colorectal). Data on the reference (cancer-free) population was queried from the national bureau of statistics, Statistics Denmark.[23]

All estimates are presented with 95% confidence intervals. For the analyses for lung and colorectal, confidence intervals were derived on the basis of Poisson distribution,[24] with scaling of the unadjusted point-estimates to the age/gender standardized point-estimates, and with respect to relative survival, with compensation for the expected number of deaths (assumed to occur without variance). Also, Chi-squared (χ^2) test statistics were used to evaluate for heterogeneity between the diagnosis calendar periods (for lung, colon and rectal cancers, respectively). With respect to the analyses for breast and ovarian cancers, the standard error of the observed survival proportion was estimated using Greenwood's method and the variance of the expected survival was assumed constant. Also, the standard error of the relative survival was estimated as the standard error of the observed survival divided by the expected survival.

Statistical analyses were performed using SAS and STATA (breast), SAS and SPSS (ovarian), and MS Excel programming software (lung and colorectal cancer).

Appendices

Appendix 1. ICD codes for identification of incident breast, colorectal, ovarian and lung cancers
Appendix 2. ICD codes for identification of the 19 Charlson comorbidity diseases

Appendix 1. ICD codes for identification of incident breast, colorectal, ovarian and lung cancers

Danish Cancer Clinical Database	Study Period	ICD-10 Diagnose Code	Total Number of Patients (N)	Notes
DBCG (breast cancer)	1995-2012	DC50	68,842	--
DCCG (colorectal cancer)	2001 -2012	DC18 (colon), but excluding DC 18.1 appendix DC20 (rectum)	29,385 colon 15,213 rectal 44,598 total	--
DGCG (ovarian cancer)	1995* -2012	DC56 (ovary)	9,972	*Data from 1995-2004 is from the Danish National Patient Register (NPR). Incident ovarian cancer was defined as first-time registration of ICD-10 code DC56 and with a histologically verified ovarian cancer in the Danish Pathology Register. Data for 2005-2012 is linked from the NPR, the Danish Pathology Register and the DGCG database. For all patients, data was linked to the Danish Pathology Register for data on histology, which was of particular significance when identifying borderline-type cancer.
DLCG (lung cancer)	2000** -2012	DC34 (lung) and DC33 (trachea)	52,435	**DLCR covers the period 2003-2012. Patients with diagnosis in the period 2000-2002 were identified in the Danish Cancer Registry (ICD-10 C33 and C34) and supplemented with data on staging and surgical resections from the Danish National Patient Register.

Abbreviations: ICD-10, International Classification of Diseases, 10th Revision

Appendix 2. ICD codes for identification of the 19 Charlson diseases and Charlson Comorbidity Index Score[16]

Disease	ICD-8 Code	ICD-10 Code	Score
Myocardial Infarction	410	I21; I22; I23	1
Congestive Heart Failure	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	I50; I11.0; I13.0; I13.2	1
Peripheral Vascular Disease	440; 441; 442; 443; 444; 445	I70; I71; I72; I73; I74; I77	1
Cerebrovascular Disease	430-438	I60-I69; G45; G46	1
Dementia	290.09-290.19; 293.09	F00-F03; F05.1; G30	1
Chronic Pulmonary Disease	490-493; 515-518	J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3	1
Connective Tissue Disease	712; 716; 734; 446; 135.99	M05; M06; M08; M09; M30; M31; M32; M33; M34; M35; M36; D86	1
Ulcer Disease	530.91; 530.98; 531-534	K22.1; K25-K28	1
Mild Liver Disease	571; 573.01; 573.04	B18; K70.0 – K70.3; K70.9; K71; K73; K74; K76.0	1
Diabetes Mellitus Insulin dependent Non-Insulin dependent Unspecified type	 249.00; 249.06; 249.07; 249.09 250.00; 250.06; 250.07; 250.09	 E10.0; E10.1; E10.9 E11.0; E11.1; E11.9 E14.0; E14.1; E14.9	1
Hemiplegia	344	G81; G82	2
Moderate-Severe Renal Disease	403; 404; 580-583; 584; 590.09; 593.19; 753.10-753.19; 792	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61	2
Diabetes Mellitus with End Organ Damage Insulin dependent Non-Insulin dependent Unspecified type	 249.01-249.05; 249.08 250.01-250.05; 250.08	 E10.2 – E10.8 E11.2 – E11.8 E14.2 – E14.8	2
Any Tumor	140-194 EXCLUDING: 173 Other malignant neoplasm of skin AND EXCLUDING THE SPECIFIC CANCER TYPE under investigation: 183 Malignant neoplasm of ovary, Fallopian tube and broad ligament 153 Malignant neoplasm of large intestine, except rectum 154 Malignant neoplasm of rectum and rectosigmoid junction 174 Malignant neoplasm of breast 162 Malignant neoplasm of trachea, bronchus and lung	C00-C75: EXCLUDING: C44 (superficial skin cancers BCC/SCC) AND EXCLUDING THE SPECIFIC CANCER TYPE under investigation: C56x ovarian cancer C50x breast cancer C33x and C34x cancer of trachea, bronchus and lung C18x colon cancer C20x rectal cancer	2
Leukemia	204-207	C91-C95	2
Lymphoma	200-203; 275.59	C81-C85; C88; C90; C96	2
Moderate-Severe Liver Disease	070.00; 070.02; 070.04; 070.06; 070.08; 573.00; 456.00-456.09	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85	3
Metastatic Solid Tumor	195-198; 199	C76-C80	6
AIDS	079.83	B21-B24	6

Abbreviations: ICD, International Classification of Diseases; CCI, Charlson Comorbidity Index

Appendix 2 (continued). ICD codes for identification of the 19 Charlson diseases and Charlson Comorbidity Index Score[16]

1. Data on comorbidities supplemented from the Danish National Patient Register.

2. 3-month exclusion window: Any cancer registration occurring up to 90 days before the cancer index date is to be excluded from the CCI scoring (in order to eliminate unspecific cancer registrations, which are likely to be related to the incident cancer diagnosis).

3. Overrule to avoid double counting: If a subject has a record of both mild and moderate-severe liver disease, scoring is only to be given for the moderate-severe liver disease. Likewise for diabetes and diabetes with end organ damage.

4. 10-year look-back period for history of comorbidities from index date (i.e. cancer diagnosis date).

5. Four Charlson comorbidity categories based on following CCI scores: 0, 1, 2, ≥3

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