

USE OF DANISH PRESCRIPTION, PATHOLOGY, AND LABORATORY DATABASES IN CANCER RESEARCH

DENMARK: THE RIGHT CONSTELLATION

Universal tax-funded, income-independent healthcare

Extensive long-term record-keeping

Individual-level linkage, including primary data collection

Lifetime follow-up

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Science 11 July 2003:
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NEWS FOCUS

EPIDEMIOLOGY

The Epidemiologist's Dream: Denmark

Lone Frank

< Pr

EPIDEMIOLOGY

When an Entire Country Is a Cohort

Denmark has gathered more data on its citizens than any other country. Now scientists are pushing to make this vast array of statistics even more useful

For years, any woman who got an abortion had to accept more than the loss of her fetus: For some unknown reason, she also faced an elevated risk for breast cancer. At least that was what several small case-control studies had suggested before Mads Melbye, an epidemiologist at the Statens Serum Institute in Copenhagen, undertook the largest effort ever to explore the link. He and his colleagues obtained records on 400,000 women in Denmark's national Abortion Register, then checked how many of the same women were listed in the Danish Cancer Register. Their foray into the two databases led to a surprising result: As they reported in *The New England Journal of Medicine* in 1997, there appears to be no connection between abortion and breast cancer.

Their success underscores the value of a trove of data the Danish government has accumulated on its citizenry, which today totals about 5 million people. Other Scandinavian countries have created powerful database systems, but Denmark has earned a preeminent reputation for possessing the most complete and interwoven collection of statistics touching on almost every aspect of life. The Danish government has compiled nearly 200 databases, some begun in the 1930s, on everything from medical records to socioeconomic data on jobs and salaries. What makes the databases a plum research tool is the fact that they can all be linked by a 10-

digit personal identification number, called the CPR, that follows each Dane from cradle to grave. According to Melbye, "our registers allow for instant, large cohort studies that are impossible in most countries."



Beauty in numbers. These Danish twins starred in a variety show at the turn of the 20th century; now it's their medical records, part of a database, that are in demand.

But Melbye and other scientists think they can extract even more from this data gold mine. They argue that not enough money is being spent on maintaining and expanding existing databases, and they say that red tape is hampering studies that require correlation of health and demographic data. The problem is that, while they have unfettered access to more than 80 medical databases maintained

by the Danish Board of Health and public hospitals, their use of 120 demographic databases overseen by the agency Statistics Denmark is tightly restricted. Statistics Denmark won't allow researchers to remove from its premises data coded by CPR, and the procedures for accessing information at all are unwieldy and expensive.

Statistics Denmark officials are reluctant to release data tied to CPRs, citing privacy concerns. "The public should have confidence that information identifying them as individuals does not reside outside of this institution," says the agency's Otto Andersen.

Last month, Danish research minister Birte Weiss formed a committee to break the impasse. Denmark's databases are "a resource which can be used more optimally," she told *Science*. "This should be a scientific flagship."

Working the health databases can yield powerful results. For years the U.S. National Institutes of Health has supported a study following twins, hoping to tease out the relative contributions of genes and lifestyle to aging. Led by University of Southern Denmark gerontologist Kaare Christensen, the project has tapped the Danish Twin Register, which includes 110,000 pairs of twins born since 1870. After following more than 2000 pairs of twins aged 70 or older, Christensen's group has so far tied to genes about a quarter of the variation in human longevity. "The project is made possible by the unmatched age and completeness of the Danish Twin Register," he says.

The health databases have proven invaluable for probing contradictions raised by smaller studies and following disease pro-

CREDIT PHOTO COURTESY OF THE DANISH TWIN REGISTER, UNIVERSITY OF SOUTHERN DENMARK



Danish National Prescription Database

Key variables

CPR NUMBER

Date of dispensation

Active substance

Amount dispensed

Route of administration

Defined daily dose

(Since 1995)

Danish
Medical Birth

Danish Cancer
Registry
(since 1943)

Registry of
Causes of
Death
(since 1943)

Danish Civil
Registration
System
(since 1968)

Danish
National
Patient
Registry
(since 1977)

Danish Breast
Cancer
Cooperative
Group
Registry
(since 1977)

Keywords: melanoma; phosphodiesterase inhibitors; sildenafil; pharmacoepidemiology; cancer; Denmark; USA

Use of sildenafil or other phosphodiesterase inhibitors and risk of melanoma

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Background: Phosphodiesterase 5A inhibitors (PDEIs), a common treatment for erectile dysfunction, were recently linked to an increased risk of melanoma.

Methods: We conducted two parallel case–control studies, using the Danish Nationwide Health Registries (DNHR) and the Kaiser Permanente Northern California (KPNC) electronic health records. Identifying men with histologically verified melanoma (cases) matched on birth year to 10 cancer-free controls, we estimated odds ratios (OR) for melanoma associated with high use of PDEIs (≥ 100 tablets filled), adjusting for available confounders.

RESEARCH ARTICLE

Open Access



Use of prescription drugs and risk of postoperative red blood cell transfusion in breast cancer patients: a Danish

The 14-day risk of transfusion was 3.5% among users of aspirin versus 1.1% among non-users (adjusted OR of 1.9 (95% CI: 1.4-2.7))
This difference was not explained by age stage and comorbidity level

Abstract

Background: Several frequently used prescription drugs may affect bleeding risk. We investigated use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), and statins and risk of postoperative red blood cell transfusion in breast cancer patients.

Methods: Using Danish population-based registries, we identified a cohort of women who underwent surgery for primary breast cancer ($n = 22,238$) during 2005–2012 and ascertained their use of aspirin, NSAIDs, SSRIs, and statins. For each drug, patients were categorized as users if they filled ≥ 1 prescription in the 60 days prior to surgery. We calculated the 14-day risk of red blood cell transfusion and relative risks (RRs) with 95% confidence intervals (CIs), comparing users with nonusers for each drug and adjusting for age, cancer stage, and Charlson Comorbidity Index score.

Postdiagnosis Statin Use and Mortality in Danish Patients With Prostate Cancer

Signe Benzon Larsen, Christian Dehrendorff, Charlotte Skriver, Susanne Oksbjerg Dalton, Christina Gade

Postdiagnosis statin use was associated with adjusted HRs of 0.83 (95% CI, 0.77 to 0.89) for prostate cancer mortality and 0.81 (95% CI, 0.76 to 0.85) for all-cause mortality.

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work, we examined whether postdiagnosis statin use was associated with reduced cancer-specific mortality or all-cause mortality among patients with prostate cancer in Denmark.

Material and Methods

From nationwide Danish registries, we identified all patients with incident prostate adenocarcinoma from 1998 to 2011 and retrieved data on tumor and patient characteristics, drug use, and primary treatment. We defined postdiagnosis use (two or more prescriptions) of statins as a time-varying covariate with 1-year lag. Cox proportional hazards regression models used to compute hazard ratios (HRs) for prostate cancer-specific mortality and all-cause mortality through 2012 associated with

Danish National Pathology Registry

Key variables

CPR NUMBER

Dates of request, reception & sign out

Specimen type

Procedures performed

Diagnoses as SNOMED codes

Conclusion/free text diagnoses

(Since 1995)

Danish

Danish Cancer Registry
(since 1943)

Registry of Causes of Death
(since 1943)

Danish Civil Registration System
(since 1968)

Danish National Patient Registry
(since 1977)

Danish Breast Cancer Cooperative Group Registry
(since 1977)

Danish National Pathology Registry

Key variables

CPR NUMBER

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(since 1968)

Danish National Patient Registry
(since 1977)

Danish Breast Cancer Cooperative Group Registry
(since 1977)

Existing data sources for clinical epidemiology: the Danish National Pathology Registry and Data Bank

This article was published in the following Dove Press journal:

Clinical Epidemiology

27 March 2010

[Number of times this article has been viewed](#)

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Lars Pedersen¹

Abstract: Diagnostic histological and cytological specimens are routinely stored in pathology department archives. These biobanks are a valuable research resource for many diseases, particularly if they can be linked to high quality population-based health registries, allowing large retrospective epidemiological studies to be carried out. Such studies are of significant importance, for example in the search for novel prognostic and predictive biomarkers in the era of personalized medicine. Denmark has a wealth of highly-regarded population-based registries that are ideally suited to conduct this type of epidemiological research. We describe

THE NATIONAL PATHOLOGY REGISTRY

Among 40,526 patients with prostate cancer (1989-2011)

- 34,660 (86%) had adenocarcinoma
- 5,866 had nonadenocarcinomas, unspecified histology, or no histology verification
- 16% had unknown gleason score

Among RCC patients who underwent nephrectomy or partial nephrectomy in 2016-17

- 88% had a leibovich score coded
- 96% had tumor size coded (versus 39% in 2010)

THE NATION

PATHOLOGY

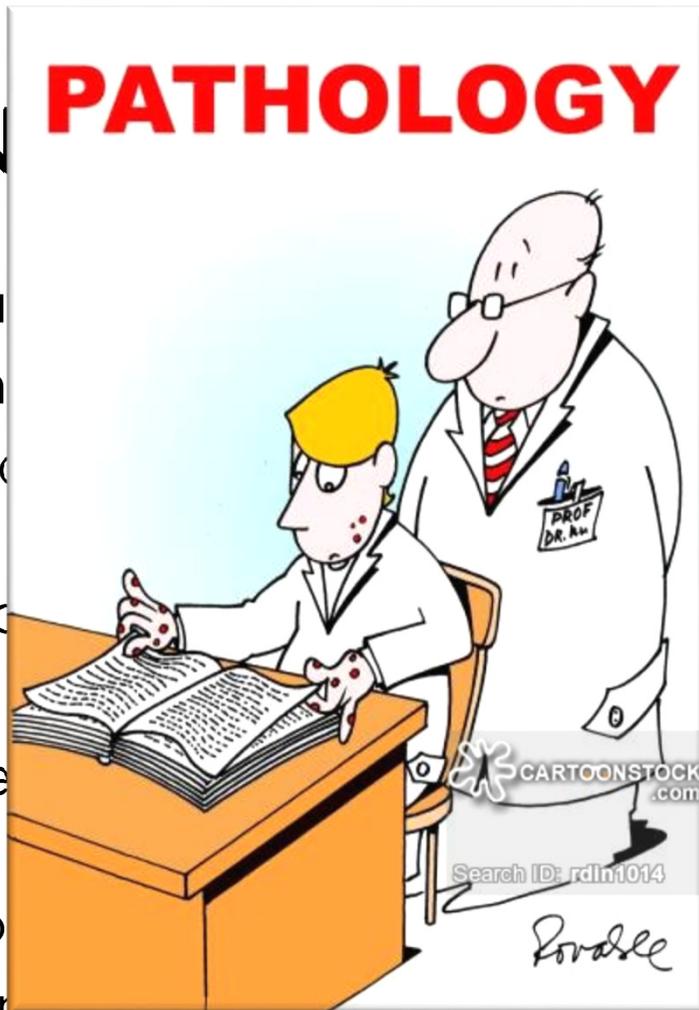
BY REGISTRY

Among 40,526 patients

- 34,660 (86%) had histology
- 5,866 had non-verified histology
- 16% had unknown histology

Among RCC patients in 2016-17

- 88% had a leiomyoma
- 96% had tumor



(1989-2011)

with histology, or no histology

with total or partial nephrectomy

(2010)

Consult a pathologist when working with this registry

PARAFFIN BLOCK ARCHIVE, INSTITUTE OF PATHOLOGY AARHUS UNIVERSITY HOSPITAL



Part of Denmark's largest biobank!

Routine diagnostic specimens from ~ 1960
Stored indefinitely
Millions of paraffin blocks

"A treasure chest for researchers"



Retrospective analysis of *KRAS* status in metastatic colorectal cancer patients: a single-center feasibility study

Table 1 *KRAS* mutations in metastatic colorectal cancer patients included in this study

	Female (%)	Male (%)	All (%)
Total number of patients	38 (35.9)	68 (64.2)	106 (100)
<i>KRAS</i>			
Wild type	17 (44.7)	31 (45.6)	48 (45.3)
Mutations overall	21 (55.3)	37 (54.4)	58 (54.7)
Gly12Asp	2 (5.3)	13 (19.1)	15 (14.1)
Gly12Ala	3 (7.9)	3 (4.4)	6 (5.7)
Gly12Val	8 (21.1)	8 (11.8)	16 (15.1)
Gly12Ser	2 (5.3)	1 (1.5)	3 (2.8)
Gly12Arg	0 (0.0)	3 (4.4)	3 (2.8)
Gly12Cys	2 (5.3)	2 (2.9)	4 (3.8)
Gly13Asp	2 (5.3)	6 (8.8)	8 (7.6)
Gly12Ala/12Ser	2 (5.3)	1 (1.5)	3 (2.8)

This article was published in the following Dove Press journal:
Clinical and Experimental Gastroenterology
17 September 2012
[Number of times this article has been viewed](#)

Jonathan Montomoli¹
Stephen Jacques
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Trine Frøslev¹
Aliko Taylor³
Rune Erichsen¹

Background: The occurrence of *KRAS* mutations and in metastatic colorectal cancer patients is not well documented.
Objectives: To examine the feasibility of identifying *KRAS* mutations and their association with c
Methods: We used the Danish Pathology Database to identify (or in some cases secondary) tumor specimens from selected

Functional Polymorphisms in UDP-Glucuronosyl Transferases and Recurrence in Tamoxifen-Treated Breast Cancer Survivors

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Abstract

Background: Tamoxifen is oxidized by cytochrome-P450 enzymes (e.g., *CYP2D6*) to two active metabolites, which are eliminated via glucuronidation by UDP-glucuronosyl transferases (*UGT*). We measured the association between functional polymorphisms in key *UGTs* (*UGT2B15*2*, *UGT2B7*2*, and *UGT1A8*3*) and the recurrence rate among breast cancer survivors.

Methods: We used the Danish Breast Cancer Cooperative Group registry to identify 541 cases of recurrent breast cancer among women with estrogen receptor-positive tumors treated with tamoxifen for at least 1 year (ER^+/TAM^+), and 300 cases of recurrent breast cancer among women with estrogen receptor-negative tumors who were not treated with tamoxifen (ER^-/TAM^-). We matched one control to each case on ER status, menopausal status, stage, calendar period, and county. *UGT* polymorphisms were genotyped from archived

The clinical laboratory information system (LABKA)

Key variables

CPR NUMBER

Results of all analyzed blood samples from patients at hospital departments and medical practices

Standard classification (NPU codes)

Date of blood sample analysis

(Since mid 1990)

Danish

Danish Cancer Registry
(since 1943)

Registry of Causes of Death
(since 1943)

Danish Civil Registration System
(since 1968)

Danish National Patient Registry
(since 1977)

Danish Breast Cancer Cooperative Group Registry
(since 1977)

Existing data sources for clinical epidemiology: The clinical laboratory information system (LABKA) research database at Aarhus University, Denmark

This article was published in the following Dove Press journal:

Clinical Epidemiology

31 March 2011

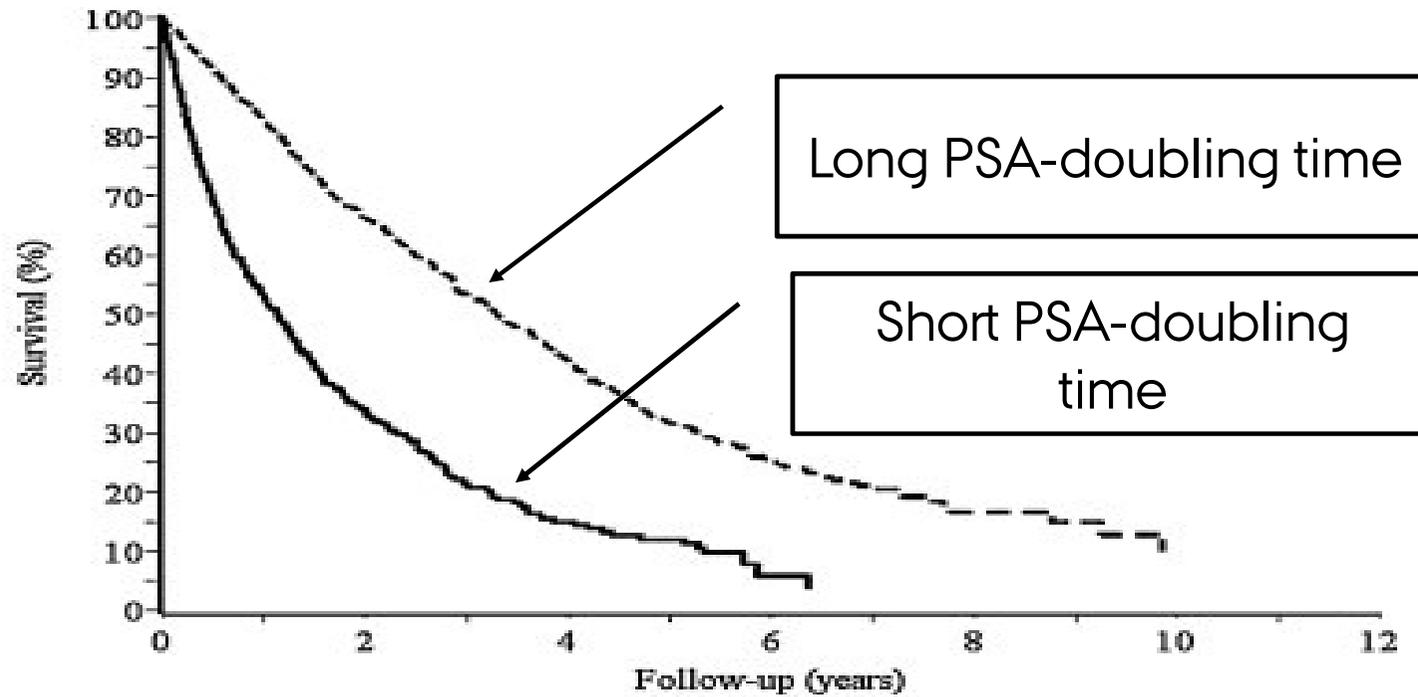
Number of times this article has been viewed

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Abstract: This paper provides an introduction to the clinical laboratory information system (LABKA) research database in Northern and Central Denmark. The database contains millions of stored laboratory test results for patients living in the two Danish regions, encompassing 1.8 million residents, or one-third of the country's population. More than 1700 different types of blood test analyses are available. Therefore, the LABKA research database represents an incredible source for studies involving blood test analyses. By record linkage of different Danish registries with the LABKA research database, it is possible to examine a large number of biomarkers as predictors of disease risk and prognosis and as markers of disease severity, and to evaluate medical treatments regarding effectiveness and possible side effects. Large epidemiological studies using routinely stored blood test results for individual patients can be performed because it is possible to link the laboratory data to high-quality individual clinical patient data in Denmark.

Keywords: biochemistry, laboratory procedures, diagnosis, therapeutic drug monitoring, epidemiological methods, registries



Bone metastasis-free survival (BMFS) among men in a castration-resistant prostate cancer (CRPC) cohort stratified by PSA doubling time at CRPC index date.

PSA=prostate specific antigen

Cancer Epidemiol 2015



Validity of the recorded International Classification of Diseases, 10th edition diagnoses codes of bone metastases and skeletal-related events in breast and prostate cancer patients in the Danish National Registry of Patients

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20 July 2009
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Objective: The clinical history of bone metastases and skeletal-related events (SREs) secondary to cancers is not well understood. In support of studies of the natural history of bone metastases and SREs in Danish prostate and breast cancer patients, we estimated the sensitivity and specificity of hospital diagnoses for bone metastases and SREs (ie, radiation therapy to the bone, pathological or osteoporotic fractures, spinal cord compression and surgery to the bone) in a nationwide medical registry in Denmark.

Study design and setting: In North Jutland County, Denmark, we randomly sampled 100 patients with primary prostate cancer and 100 patients with primary breast cancer diagnoses from the National Registry of Patients (NRP), during the period January 1st, 2000 to December 31st, 2000 and followed them for up to five years after their cancer diagnosis. We used information from medical chart reviews as the reference for estimating sensitivity, and specificity of the NRP International Classification of Diseases, 10th edition (ICD-10) coding for bone metastases and SRE diagnoses.

VALIDITY OF DIAGNOSIS CODES OF BONE METASTASES AND SRE'S

Bone metastases:

- Sensitivity: 44%
- Specificity: 100%
- Positive predictive value: 100%

Any SRE:

- Sensitivity: 55%
- Specificity: 94%
- Positive predictive value: 80%

- Validation of algorithms to detect distant metastases in men with prostate cancer using routine registry data in Denmark

This article was published in the following Dove Press journal:

Clinical Epidemiology

10 April 2015

[Number of times this article has been viewed](#)

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Objective: Among patients with prostate cancer, diagnostic codes for bone metastases in the Danish National Registry of Patients have a sensitivity of 44%. In an attempt to improve the sensitivity of registry-based identification of metastases from prostate cancer, we tested a series of algorithms, combining elevated prostate-specific antigen (PSA) levels, use of antiresorptive therapy, and performed bone scintigraphy.

Patients and methods: We randomly selected 212 men diagnosed with prostate cancer in 2005–2010 in the Central Denmark Region with prespecified PSA values, antiresorptive therapy, and bone scintigraphy who did not have a registry-based diagnostic code indicating presence of distant metastases. We defined three candidate algorithms for bone metastases: 1) PSA >50 µg/L and bone scintigraphy, 2) PSA >50 µg/L and antiresorptive therapy, and 3) PSA ≤50 µg/L with antiresorptive therapy or bone scintigraphy. An algorithm for distant metastasis site other than bone was defined as PSA >50 µg/L alone. Medical chart review was used as the reference standard to establish the presence or absence of metastases. Validity was expressed as a positive predictive value (PPV) or a negative predictive value, based on whether

RESULTS

Table 2 Positive predictive values of the potential algorithms to identify presence of distant metastases

Sampling algorithm	Total	Presence confirmed by medical record					
		Bone metastases		Nonbone metastases		Any metastases	
		n	PPV (95% CI)	n	PPV (95% CI)	n	PPV (95% CI)
30 days before or after the index date							
PSA >50 µg/L in the absence of ART or bone scintigraphy	37	1	0.03 (0.0007–0.14)	0	–	1	0.03 (0.0007–0.14)
PSA >50 µg/L and bone scintigraphy without ART	32	1	0.03 (0.0008–0.16)	3	0.09 (0.02–0.25)	4	0.12 (0.04–0.29)
PSA >50 µg/L and ART	4	0	–	0	–	0	–
PSA ≤50 µg/L and ART or bone scintigraphy	40	2	0.05 (0.006–0.17)	2	0.05 (0.006–0.17)	4	0.10 (0.03–0.24)
PSA >50 µg/L and bone scintigraphy without ART	32	3	0.09 (0.02–0.25)	6	0.19 (0.07–0.36)	9	0.28 (0.14–0.47)
PSA >50 µg/L and ART	4	0	–	0	–	0	–
PSA ≤50 µg/L and ART or bone scintigraphy	40	2	0.05 (0.01–0.17)	4	0.10 (0.03–0.24)	6	0.15 (0.06–0.30)

Abbreviations: ART, antiresorptive therapy; CI, confidence interval; PPV, positive predictive value; PSA, prostate-specific antigen.

Validity of the Danish National Registry of Patients for chemotherapy reporting among colorectal cancer patients is high

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Clinical Epidemiology

29 August 2013

[Number of times this article has been viewed](#)

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Background: The Danish National Registry of Patients (DNRP) is a potentially valuable resource for monitoring national trends in the use of chemotherapy and evaluating the benefits and harms of alternative treatments among colorectal cancer (CRC) patients in Denmark. However, the validity of chemotherapy reporting in the DNRP is unknown. In this study, we evaluated the validity of the DNRP for identifying the receipt of chemotherapy and specific treatments, and the timing and number of treatments among CRC patients, using medical records and pharmacy data as the reference standard.

Methods: We selected a random sample of CRC patients with lymph node involvement who were diagnosed at Aarhus University Hospital (n = 25) or Aalborg University Hospital (n = 25) from 2009 to 2010. Administration dates, specific treatments, and number of treatment courses were abstracted for the 180 days post diagnosis from the DNRP, medical records, and pharmacy production databases. The prevalence of chemotherapy, timing of first administration, and number of courses were described. DNRP data were compared with the reference standard for each hospital, and the kappa, sensitivity, specificity, positive and negative predictive values, and 95% confidence intervals were calculated for the receipt of any chemotherapy and specific treatments.

Results: The prevalence of chemotherapy was 72% and 68% among CRC patients treated in Aarhus and Aalborg, respectively, with >90% of patients without distant metastasis receiving treatment within 90 days from diagnosis. Patients received on average 4.6 and 4.7 treatment courses in Aarhus and Aalborg, respectively. Kappa, sensitivity, and specificity of chemotherapy reporting in the DNRP was high (≥ 0.88), but the sensitivity of individual chemotherapies varied by hospital.

Conclusion: The validity of chemotherapy reporting in the DNRP was high, although some variation by hospital exists. The DNRP represents a population-based nationwide resource that can be used to provide timely and accurate evaluations of chemotherapy use among CRC patients in Denmark.

Keywords: chemotherapy, colorectal cancer, administrative data

28. AUGUST 2018 | PROFESSOR

MULTIPLE MYELOMA DATA

Among 850 multiple myeloma patients who received Bortezomib based treatment in 2010-2015 according to the clinical database

- 76 % had a bortezomid treatment coded in DNPR
- 38 % had at least 1 code stating complex cytostatic treatment

→ it is difficult to identify treatment and particularly treatment lines

THANK YOU!





AARHUS
UNIVERSITET