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ARTICLE

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The renal cell cancer database Sweden (RCCBaSe) – a new register-based resource for renal cell carcinoma research

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ABSTRACT

Introduction: In 2005, the National Swedish Kidney Cancer Register (NSKCR) was set up to collect data on newly diagnosed patients with renal cell carcinoma (RCC). In 2015, the NSKCR was linked to a number of national healthcare and demographic registers to construct the Renal Cell Cancer Database Sweden (RCCBaSe). The aim was to facilitate research on trends in incidence, effects of treatment and survival, with detailed data on tumour characteristics, treatment, pharmaceutical prescriptions, socioeconomic factors and comorbidity.

Material and methods: All patients registered in the NSKCR between 2005 and 2014 were included. For each case, ten controls and first-degree relatives for cases and controls were identified. The RCCBaSe was created linking all cases, controls and first-degree relatives to a number of national registers with information on co-morbidity, socioeconomic factors and pharmaceutical prescriptions.

Results: Between 2005 and 2014, a total of 9,416 patients with RCC were reported to the NSKCR. 94,159 controls and a total cohort of 575,007 individuals including cases, controls and first-degree relatives were identified. Linkage to the Swedish cancer register resulted in 106,772 matches. When linked to the National patient register, 432,677 out-patient and 471,359 in-patient matches were generated. When linked to the Swedish renal registry 1,778 matches were generated. Linkage to the Prescribed drug register resulted in 448,084 matches and linkage to the The Longitudinal integration database for health insurance and labour market studies database resulted in 450,017 matches.

Conclusion: By linking the NSKCR to several Swedish national databases, a unique database for RCC research has been created.

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Renal cell carcinoma;
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Introduction

The National Swedish Kidney Cancer Register (NSKCR) was initiated in 2004 as an extensive complement to the Swedish Cancer Registry to gather more detailed information about the disease and to measure and improve the quality of care for patients with renal cell carcinoma (RCC). The NSKCR is administered by the regional cancer center in each of the six healthcare regions in Sweden, and report annually to the national register. Since the start of the register, registered data has included detailed information on diagnosis, tumour characteristics and treatment. The registration expanded in 2012 to include data from a 5-year follow-up of patients without metastatic disease at diagnosis. Since 2015 the register also includes detailed information on surgical procedures with pre-, peri- and post-operative data, including complications up to 90 days after surgery.

In 2015, the NSKCR was linked to a number of national healthcare and demographic registers to construct the Renal Cell Carcinoma Database Sweden (RCCBaSe). The aim was to create a comprehensive cohort of patients with RCC in order to study trends in incidence, effects of treatment, and overall as well as disease-specific survival, with detailed data on patient and tumour characteristics, treatment, comorbidity and socioeconomic factors. The database provides a unique resource for further research.

Material and methods

The National Swedish Kidney Cancer Register

In Sweden, all newly diagnosed patients with cancer are mandated by law to be reported to the national Swedish Cancer Registry according to the National Board of Health and Welfarés regulations [1]. Sweden is divided into six

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Table 1. Data currently collected in the standardized forms in the National Swedish Kidney Cancer Register (NSKCR).

Form	Data recorded
Diagnostics and primary treatment	Tumour information: imaging, biopsy, symptomatic tumour, bilateral, multifocal, tumour size, morphology, malignancy grade (Fuhrman), TNM stage, CT abdomen, preoperative CT thorax, localisation of metastases Treatment information: type of treatment (surgery, surveillance, oncologic treatment, supportive care), type of surgical treatment (nephrectomy, partial nephrectomy, radiofrequency ablation, cryotherapy or renal transplantectomy), surgical technique (open, laparoscopic, robotic, percutaneous), transabdominal or intraperitoneal approach, intention of treatment Dates of: referral, diagnosis, radiology, first visit to specialist, biopsy, treatment decision, surgery Other: smoking status (reported since 2018), if the patient was discussed in a multidisciplinary conference, if the patient had access to individual nurse, had a written health care plan or was included in a study.
Surgical treatment and complications up to 90 days after surgery	Preoperative data: Eastern Cooperative Oncology Group performance status, American Society of Anestesiologists score, Nephrometry score, length, weight, creatinine (pre- and post operative), Intraoperative data: Type of surgical treatment (nephrectomy, partial nephrectomy, radiofrequency ablation, cryotherapy or renal transplantectomy), surgical technique (open, laparoscopic, robotic, percutaneous), surgical approach (transabdominal or intraperitoneal), duration of surgery (min), bleeding (ml), if converted to open surgery, vascular clamping, renal ischemic time, radical surgery, intraoperative complications according to Uro-Clavien-Dindo. Postoperative data: Readmission, complications according to Uro-Clavien-Dindo
Five-year follow up of M0 patients	Recurrence, localisation of recurrence, type of treatment

health care regions, where every region has its own regional cancer centre. The health care providers report newly diagnosed patients with RCC to the NSKCR through their respective regional cancer centre. The regional cancer centre cross check the coverage of the NSKCR with the Swedish Cancer Registry to ensure completeness. The coverage of the NSKCR between 2005 and 2014 was 99% compared to the Swedish Cancer Register [2].

The content of the NSKCR has previously been described [3,4]. Data is collected using standardized forms covering diagnostics and primary treatment, details of surgical treatment including 90-days follow up after surgical treatment, and a 5-year follow up of patients without metastatic disease at diagnosis. More detailed information of data collected in each form is available in Table 1. In the current version (1.0) of RCCBaSe, only data from the diagnostics and primary treatment form is available.

Data recorded in the diagnostics and primary treatment form includes information on tumour characteristics, histological RCC sub-type, nuclear grade and tumour size and stage. Histopathologic classification of grade was registered according to Fuhrman nuclear grade [5] and RCC sub-type was registered according to the World Health Organization (WHO) 2004 classification [6]. Information about the tumour, node and metastasis (TNM) classification was registered according to the 6th edition of the Union for International Cancer Control (UICC) until December 2011 [7]. Since January 2012 the UICC 7th edition from 2009 has been used. In the 2009 version, T2 tumours are registered as T2a or T2b and M-status can no longer be registered as MX.

The form also gives information regarding preoperative diagnostic work-up and primary treatment. Tumour size was measured by computed tomography (CT) or magnetic resonance imaging (MRI) to avoid the shrinking effect of fixation [8]. The lymph-node category was based on CT and/or MRI examinations of the abdomen or findings at surgery. If surgical treatment was chosen, type of surgical method and technique was registered. Since 2016 the localization of metastases has been recorded.

In future versions of the RCCBaSe the other forms will be included which will add even more detailed data on each patient with RCC. For example, the forms include ECOG (Eastern Cooperative Oncology Group) performance status, ASA (American Society of Anaesthesiologists) score, the R.E.N.A.L nephrometry score [9], pre- and postoperative creatinine, surgical and general complications from date of surgery until 90 days post-operatively according to Uro-Clavien-Dindo [10] and data on localization and treatment of recurrent disease.

The Renal Cell Cancer Database Sweden

In 2015, data of patients registered in the NSKCR from 2005 to 2014 was linked to a number of population-based registers in order to create the RCCBaSe (Figure 1). The linkage was performed using the Personal Identity Number (PIN), a 10-digit number assigned to each individual registered in the Swedish Population Register [11]. Ten controls for every RCC patient were retrieved. The controls were free of RCC at the end of the year of diagnosis of the index case and matched on gender, year of birth and county of residence. A control was allowed to become a case if RCC was diagnosed after the date of diagnosis of the index case.

For all cases and controls, first-degree relatives were identified using the Multi-Generation Register. The RCCBaSe was created linking all cases, controls and first generation relatives to the following Swedish national registers: the Swedish Renal Registry, the Swedish Cancer Register (including the Basal Cell Cancer Register), the Prescribed Drug Register, the

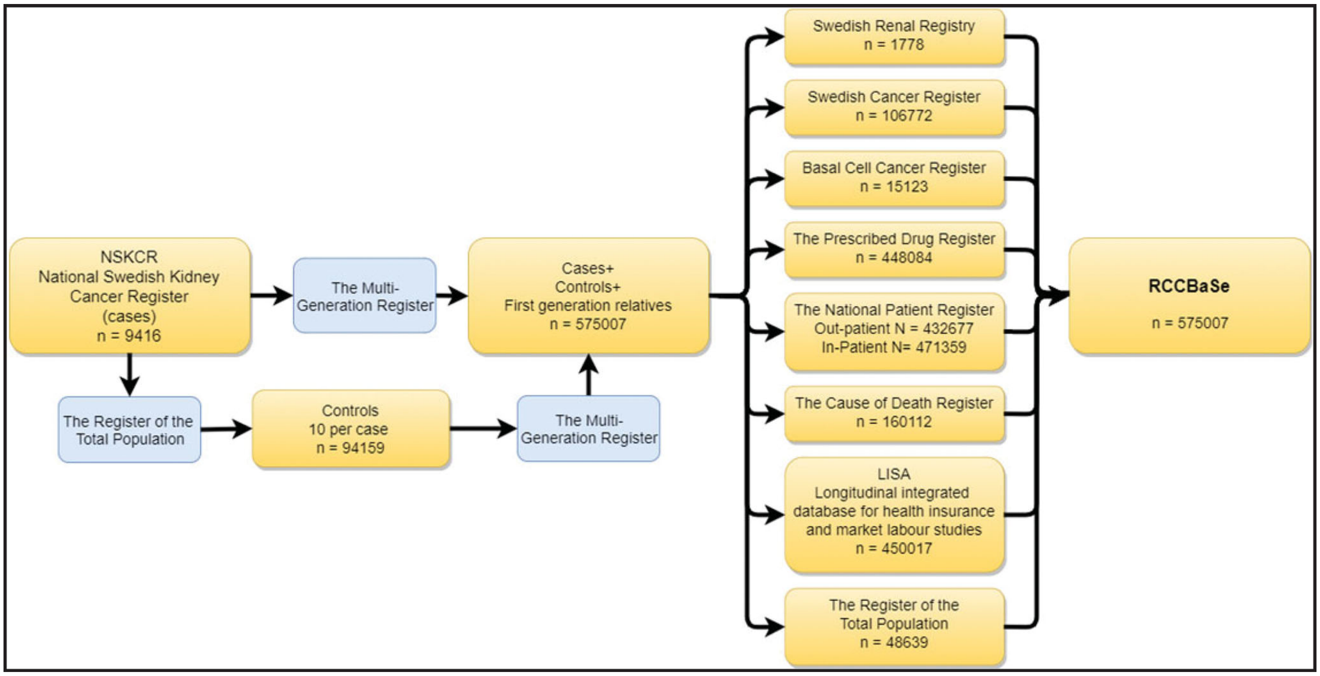

Figure 1. Flowchart for the creation of the Renal Cell Cancer Database Sweden (RCCBaSe).

National Patient Register, the Cause of Death Register, the Longitudinal integrated database for health insurance and labor market studies (LISA), and the Register of the Total Population (Figure 1).

Follow-up of cases started at the time of diagnosis of case/index case and ended at time of death, emigration or study closing date (December 31, 2014), whichever came first. The follow up of controls started at the time of RCC diagnosis of the index case and ended at the time of RCC diagnosis, death, emigration or study closing date.

The RCCBaSe project was approved by the central research ethics committee and the research ethics committee at Umeå University.

Swedish national registers

The Swedish Cancer Register was founded in 1958 and covers the entire Swedish population [12]. It is compulsory by law for every health care provider to report newly detected cancer cases to the register and completeness of the register is high [13]. For all patients registered in RCCBaSe, all other cancer diagnoses and date of diagnosis for each patient were retrieved. *The Basal Cell Cancer Register* is linked to the Swedish Cancer Register and has been available since 2004 [14].

The Swedish Renal Registry is a quality register for patients with chronic kidney failure and kidney function of less than 30% of normal kidney function. More than 30,000 patients have been registered since the start of the register in 1991. The coverage rate is >97% for kidney transplant patients and >95% for patients undergoing hemodialysis [15].

The National Patient Register was set up in the 1960s by the National Board of Health and Welfare and contains information about in-patient care. Reporting to the register has been mandatory since 1984. Since 2001 the register also covers outpatient visits including day surgery and psychiatric care from both private and public caregivers. Primary care is not covered. Information available includes length of stay, type of department, main and secondary diagnosis, external cause of injury and procedures coded to the ICD-9 or ICD-10 [16].

By using data from the National Patient Register, the Charlson Comorbidity Index (CCI) was calculated for all included patients and controls to estimate concomitant disease burden [17]. The CCI is a scoring system that takes into account the number and the seriousness of comorbid disease by assigning a specific weight to different diseases that are summed to a score representing different comorbidity levels (0 points = no comorbidity, 1 point = mild comorbidity, 2 points = intermediate comorbidity, >3 points severe comorbidity). Data for comorbidity was collected from 10 years before diagnosis to 30 days before RCC diagnosis.

The Cause of Death Register was set up in 1961 and contains data about the cause of death in deceased persons who were registered residents in Sweden at the time of death. Data includes date of death, underlying and contributing causes of death, information weather autopsy was performed or not and if the patient had undergone surgery within four weeks before death [18].

The Longitudinal integration database for health insurance and labour market studies (LISA) was set up in 1990. It contains socioeconomic data on all individuals age 16 years and older who are Swedish residents. Information includes education level, income, place of employment, country of birth, year of immigration, place of residence, number of people in the household and socioeconomic classification [19].

Table 2. Descriptive statistics at the time of diagnosis for patients included in National Swedish Kidney Cancer Register (NSKCR).

	Male ($n = 5792$)	Female ($n = 3624$)
Age		
Mean (SD)	65.5 (11.6)	67.8 (11.5)
	N (%)	N (%)
Education level		
Low	2058 (35.5)	1441 (39.8)
Intermediate	2418 (41.7)	1420 (39.2)
High	1134 (19.6)	659 (18.2)
Missing	182 (3.1)	104 (2.9)
Marital status		
Married	3591 (62.0)	1887 (52.1)
Divorced	851 (14.7)	663 (18.3)
Unmarried	1044 (18.0)	378 (10.4)
Widowed	246 (4.2)	639 (17.6)
Missing	60 (1.0)	57 (1.6)
RCC type		
Clear cell	4204 (72.6)	2785 (76.8)
Papillary	794 (13.7)	269 (7.4)
Chromophobe	248 (4.3)	203 (5.6)
Collecting duct	20 (0.3)	17 (0.5)
Not possible to classify	113 (2.0)	65 (1.8)
Other kidney histopathology than above	112 (1.9)	60 (1.7)
Missing	301 (5.2)	225 (6.2)
Fuhrman grade		
G1	568 (9.8)	479 (13.2)
G2	2335 (40.3)	1512 (41.7)
G3	1518 (26.2)	781 (21.6)
G4	520 (9.0)	260 (7.2)
GX	458 (7.9)	298 (8.2)
Missing	393 (6.8)	294 (8.1)
T stage		
T0	1 (0.0)	2 (0.1)
T1a	1719 (29.7)	1111 (30.7)
T1b	1305 (22.5)	870 (24.0)
T2	702 (12.1)	458 (12.6)
T2a	168 (2.9)	107 (3.0)
T2b	116 (2.0)	68 (1.9)
T3a	886 (15.3)	485 (13.4)
T3b	513 (8.9)	299 (8.3)
T3c	29 (0.5)	19 (0.5)
T4	197 (3.4)	114 (3.1)
TX	149 (2.6)	85 (2.3)
Missing	7 (0.1)	6 (0.2)
N stage		
N0	3928 (67.8)	2543 (70.2)
N1	224 (3.9)	104 (2.9)
N2	420 (7.3)	211 (5.8)
NX	1203 (20.8)	756 (20.9)
Missing	17 (0.3)	10 (0.3)
M stage		
M0	3696 (63.8)	2362 (65.2)
M1	1151 (19.9)	635 (17.5)
MX	931 (16.1)	622 (17.2)
Missing	14 (0.2)	5 (0.1)
Charlson Comorbidity Index[a] (points)		
No comorbidity (0)	3201 (55.3)	2085 (57.5)
Mild comorbidity (1)	1293 (22.3)	791 (21.8)
Intermediate comorbidity (2)	398 (6.9)	226 (6.2)
Severe comorbidity (3)	356 (6.1)	197 (5.4)
Missing	544 (9.4)	325 (9.0)

[a] The Charlson Comorbidity Index was calculated from 10 years before date of Renal Cell Carcinoma (RCC) diagnosis to 30 days before date of RCC diagnosis.

The Register of the Total Population was created in 1968 and is administrated by Statistics Sweden (SCB). The register is updated on a daily basis and contains information about the population and its´ changes, mainly using the information from the Swedish Tax Agency. The register includes information on births, deaths, emigrated, immigrated and civil status changes [20].

The Prescribed Drug Register was set up in 2005 and contains data on all dispensed drugs dispensed at pharmacies in Sweden on an individual basis [21,22]. It includes information on gender and residence of the patient, dispensed item, date of prescription and dispensing, dispended amount, dosage, defined daily doses, prescribing practice and the prescriber's medical specialty. It does not include drugs used in hospitals, nursing homes or vaccines.

The Multi-Generation Register was created in 2000 and includes family information of persons (index persons) registered in Sweden since 1961, and born in 1932 or later. Information includes connections between index persons and their biological or adoptive parents. The register can also be used to link index persons to siblings, children and cousins [23].

Results

Between 2005 and 2014, a total of 9,416 patients with RCC were reported to the NSKCR. Table 2 shows descriptive data at the date of diagnosis for patients registered in the NSKCR. Figure 2 shows the total number of RCC patients reported to the NSKCR per year. For each case, ten controls were identified ($n = 94,159$), and through the Multi-Generation register first generation relatives were identified for all cases and controls. When linked to the Swedish Cancer register and the Swedish Basal cell cancer register, 106,772 and 15,123 unique matches respectively were generated. When linked to the National Patient Register, 432,677 out-patient and 471,359 in-patient matches were generated. When linked to the Swedish Renal Registry 1,778 unique matches were generated. Linkage to the Prescribed Drug Register resulted in 448,084 unique matches. Linkage to the Cause of Death register resulted in 160,112 matches. Linkage to the LISA database and the Register of the Total population resulted in 450,017 and 48,639 unique matches respectively.

Discussion

By linking the NSKCR to several Swedish national databases, a unique research database for RCC has been created. Strengths include the detailed information on tumour characteristics and primary treatment, the large sample size and high coverage of almost the entire national cohort, and the high coverage in many of the used registers. This makes it possible to perform high quality longitudinal population based cohort studies. Limitations include a relatively short follow-up time. Also, the data from the prescribed drug register has only been available since July 2005.

Data from the NSKCR has previously been used to assess trends in incidence, pre-operative work up, treatment and survival for RCC patients. For example, data from the NSKCR has been used to evaluate the metastatic potential of RCCs ≤7 cm, RCC recurrence in primary non-metastatic patients, and to what extent nephron-sparing surgery was used for patients with stage T1. [3,4,24–27].

The RCCBaSe will be regularly be updated and information from the other forms described in Table 1 will be added.

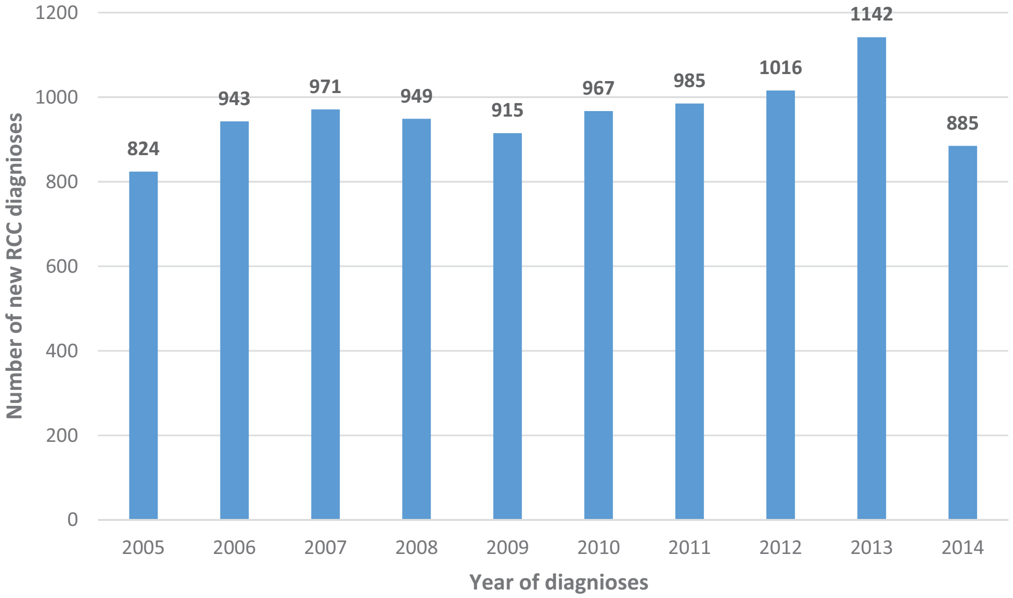

Figure 2. Total number of patients with renal cell carcinoma reported to the National Swedish Kidney Cancer Register (NSKCR) per year between 2005 and 2014.

This will enable access to more extensive information on surgical treatment, surgical and general complications and follow up of patients.

RCCBaSe thus includes almost 10,000 patients with information on tumour characteristics and cancer treatment, inpatient and out-patient care, use of prescribed drugs and socioeconomic status, making it possible to increase the knowledge in many areas of renal cell cancer research.

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Disclosure statement

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