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REVIEW

The Danish National Patient Registry: a review of content, data quality, and research potential

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Background: The Danish National Patient Registry (DNPR) is one of the world's oldest nationwide hospital registries and is used extensively for research. Many studies have validated algorithms for identifying health events in the DNPR, but the reports are fragmented and no overview exists.

Objectives: To review the content, data quality, and research potential of the DNPR.

Methods: We examined the setting, history, aims, content, and classification systems of the DNPR. We searched PubMed and the *Danish Medical Journal* to create a bibliography of validation studies. We included also studies that were referenced in retrieved papers or known to us beforehand. Methodological considerations related to DNPR data were reviewed.

Results: During 1977–2012, the DNPR registered 8,085,603 persons, accounting for 7,268,857 inpatient, 5,953,405 outpatient, and 5,097,300 emergency department contacts. The DNPR provides nationwide longitudinal registration of detailed administrative and clinical data. It has recorded information on all patients discharged from Danish nonpsychiatric hospitals since 1977 and on psychiatric inpatients and emergency department and outpatient specialty clinic contacts since 1995. For each patient contact, one primary and optional secondary diagnoses are recorded according to the International Classification of Diseases. The DNPR provides a data source to identify diseases, examinations, certain in-hospital medical treatments, and surgical procedures. Long-term temporal trends in hospitalization and treatment rates can be studied. The positive predictive values of diseases and treatments vary widely (<15%–100%). The DNPR data are linkable at the patient level with data from other Danish administrative registries, clinical registries, randomized controlled trials, population surveys, and epidemiologic field studies – enabling researchers to reconstruct individual life and health trajectories for an entire population.

Conclusion: The DNPR is a valuable tool for epidemiological research. However, both its strengths and limitations must be considered when interpreting research results, and continuous validation of its clinical data is essential.

Keywords: epidemiological methods, medical record linkage, registries, research design, validation studies

Introduction

As the role of routine computerized health data in epidemiological research is growing,[1] there is a need to examine their strengths and limitations.[2,3] Typical shortcomings of such data include limited linkage possibilities, incomplete temporal or geographic coverage, restriction to selected patient groups, and lack of systematic follow-up.[4–7] Among the examples, the Dutch nationwide hospital registry has been in operation since 1963, but personal records are anonymized, and therefore not linkable to other

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data sources.[4] Also, the United Kingdom's Clinical Practice Research Datalink has recorded detailed information on both diagnoses and prescriptions in primary care since 1987 but covers only part of the population and lacks information on patients who leave participating practices.[8] In the United States, the collection of routine health data is restricted to specific age groups (eg, Medicare beneficiaries),[6] income groups (eg, Medicaid beneficiaries),[6] professions (eg, the Veterans Affairs),[7] or members of private insurance plans (eg, Kaiser Permanente),[9] often without the possibility of linkage or long-term follow-up.

In the Nordic countries, government-funded universal health care, combined with the tradition of record-keeping and individual-level linkage, has led to establishment of extensive networks of interlinkable longitudinal population-based registries covering entire nations.[10,11] Patient registries with complete nationwide coverage and individual-level linkage potential have existed in Finland since 1969,[12] in Sweden since 1987,[13] in Iceland since 1999,[14] and in Norway since 2008.[15,16]

The Danish National Patient Registry (DNPR) is one such population-based administrative registry, which has collected data from all Danish hospitals since 1977 with complete nationwide coverage since 1978.[17–19] An epidemiologist setting out to use the DNPR must be familiar with the strengths and limitations of its data. Many studies have validated algorithms for identifying health events in the DNPR, but the reports are fragmented and no overview exists. Herein, we review the content and data quality of the DNPR and its potential as a research tool in epidemiology.

Setting

Denmark had 5,580,516 inhabitants in 2012, excluding inhabitants of Greenland and the Faroe Islands.[20] Although these areas are part of the Kingdom of Denmark, they are not covered by the DNPR. Since 2007, the Danish healthcare system has had three administrative levels:[10,21] 1) the state, responsible for legislation, national guidelines, surveillance, and health financing through the Ministry of Health; 2) the regions (n=5), responsible for delivery of primary and hospital-based care; and 3) the municipalities (n=98), responsible for a broad range of welfare services, including school health, child dental treatment, home care, primary disease prevention, and rehabilitation.

The Danish National Health Service provides tax-supported health care for the entire Danish population.[10,21] Redistributionist taxation finances ~85% of overall health care costs, including access to general practitioners (GPs), hospitals, outpatient specialty clinics, and partial reimbursement of prescribed medications.[21] Of note, outpatient specialty clinics include contacts from hospital-based (ambulatory) specialty clinics but not from private practice specialists or GPs. Patients' out-of-pocket expenditures cover the remaining costs of medication and dental care.[21] Except in emergencies, GPs (including on-call GPs) provide referrals to hospitals and specialists.[21] Approximately 4,100 GPs and 4,600 dentists, as well as physiotherapists, chiropractors, and home nurses, work in the primary health care sector.[21]

The Danish Civil Registration System is a key tool for epidemiological research in Denmark.[20,22] This nationwide registry of administrative information was established on April 2, 1968.[20] It assigns a unique ten-digit Civil Personal Register (CPR) number to all persons residing in Denmark, allowing for technically easy, cost-effective, and exact individual-level record linkage of all Danish registries.[20] The Danish Civil Registration System, which tracks and continuously updates information on migrations and vital status, permits long-term follow-up with accurate censoring at emigration or death.[20]

DNPR overview

History

In the early 1970s, most nonpsychiatric hospitals in Denmark established computerized Patient Administrative Systems (PASs).[1] Initially, individual hospitals collected varying information. To ensure standardized data collection, the Danish Health and Medicines Authority developed a protocol for data collection, in which the unit of observation was the hospital discharge record of an individual patient.[23] In 1976, all Danish counties (formerly the main administrative level, replaced by regions in 2007) were requested to submit these data to a central national hospital registry, which formed the basis for the DNPR (Danish, Landspatientregisteret).[23] This registry was established in 1977 and achieved complete nationwide coverage in 1978.[24]

Since its establishment, different names have been used in the literature for the DNPR. Commonly used English terms include the Danish National Hospital Register,[18] Danish National Health Registry,[19] Danish National Patient Register,[17] Danish Hospital Discharge Registry,[25] and Danish National Registry of Patients.[1] The official English name, as it appears in the registry declaration by the Danish Health and Medicines Authority, is the Danish National Patient Registry, DNPR. This term therefore will be used in this review.

Aims

The official aims of the DNPR are presented in Table 1.[26] The primary aim is continuous monitoring of hospital

Table 1 Aims of the Danish National Patient Registry

1. Form the basis for the Danish Health and Medicines Authority's hospital statistics
2. Form the basis for health economic calculations
3. Provide the Danish authorities with data to support hospital planning
4. Provide data to support the authorities responsible for hospital inspection
5. Monitor the frequency of various diseases and treatments
6. Provide a sampling frame for longitudinal population-based and clinical research
7. Facilitate quality assurance of Danish health care services
8. Provide hospital physicians with access to patient's hospitalization histories

and health services utilization for the Danish Health and Medicines Authority, thus providing a tool for health care planning.[26] The registry is also increasingly used to monitor the occurrence of diseases and use of treatments,[27] for quality assurance in the hospital sector,[28] and for medical research. Since 2002, the DNPR has served as the basis for paying public and private hospitals via the Diagnosis-Related Group system.[29,30] The registry also collects data for other health registries, including the Danish Psychiatric Central Research Register since 1995,[31] the Register of Legally Induced Abortions since 1995,[32] the Medical Birth Registry since 1997,[33] and the Danish Cancer Registry since 2004.[34]

Updates

DNPR data are updated continuously.[35] Each regional PAS is required by law to submit standardized data to the DNPR at least monthly, but in practice does so weekly or, for some hospitals, daily. As regional PASs may collect more information than is reportable to the DNPR, the contents of the PASs and the DNPR are overlapping but not identical. The overlapping data are referred to as the common content. The Danish Health and Medicines Authority reports all changes in the common content in its annual report – *Common content for basic registration of hospital patients* – which includes separate sections for users[36] and developers.[37] An overview of the registry's content and structure is also available online.[26]

Reporting to the DNPR became compulsory in 2003 for private hospitals and private outpatient specialty clinics, excluding private practice specialists and GPs.[38,39] Private practice specialists are only obliged to report activities that are not covered by the health insurance scheme (Danish, Sygesikringen). Despite their increasing share in the health sector, the 249 private hospitals and clinics in Denmark generated only 2.2% of the total hospital activity in 2010.[40] Registration of care provided by the private sector is mandatory, regardless of whether the referring hospital is public or private, whether out-of-pocket payments are involved, or whether patients are covered by a private health insurance.[38,39] However, the reporting from private hospitals and clinics is generally considered incomplete.[17,41]

DNPR content

Type of data

The content of the DNPR is structured, with each variable having a finite number of possible values.[36,37] Information reported to the DNPR includes administrative data, diagnoses, treatments, and examinations (Table 2).[26]

Administrative data include personal and admission data. The personal data include patients' CPR numbers and municipality and region of residence. The admission data include hospital and department codes, admission type (acute or nonacute), patient contact type (inpatient, outpatient, or emergency department [ED]), referral information, contact reason, and dates of admission and discharge.

Diagnoses associated with each hospital contact are registered in the DNPR as one primary diagnosis and, when relevant, secondary diagnoses.[36] The primary diagnosis is the main reason for the hospital contact. Secondary diagnoses supplement the primary diagnosis by identifying other relevant diseases related to the current hospital contact, eg, underlying chronic diseases.[26,36] An exception (since 2009) is brain death (code: R991), which is registered as a diagnosis secondary to the primary underlying condition leading to brain death.[36] In addition to primary and secondary diagnoses, the registry records referral, temporary, procedure-related, and supplementary diagnoses (Table 2). The discharging physician registers all diagnoses at the time of hospital discharge or at the end of an outpatient contact. However, outpatient and inpatient psychiatric contacts with long-term attendance are reported at least monthly.[36] ED contacts are registered as completed hospital contacts, regardless of whether patients are transferred to another hospital department.[36]

Treatments include information on surgery, other treatments (eg, invasive procedures, mechanical ventilation, dialysis, cancer treatments, and psychotherapy), anesthesia, and intensive care (Table 2).

Examinations include radiological procedures and other examinations (Table 2). The attending physician/surgeon registers treatment and examination codes immediately following their completion. Thus, each treatment and examination is assigned to its own exact date, independent of the dates of admission and discharge.

Table 2 Content of the Danish National Patient Registry

Administrative data	
CPR number	Unique ten-digit personal identification number assigned at birth or upon emigration
Residence	Municipality and region of residence
Hospital and department	Hospital and department admitting the patient
Patient contact	Inpatient, outpatient (ambulatory), or emergency department contacts
Admission type	Acute or nonacute
Referred from/referred to	General practitioner, outpatient (ambulatory) clinic, other hospital departments, foreign hospital, no referral (eg, acute admission via ambulance), or death (only applies to "referred to" if death is declared during admission)
Referral period	Period from referral date to start date for hospital contact
Waiting time	Period from referral date to start date for treatment
Contact reason	Reason for the hospital contact: diagnosis, accident, act of violence, suicide attempt, late complications, unknown (eg, unconscious patient), or other (rarely used)
Accident	Accident description, when an accident is the contact reason
Time specifications	Date and time of inpatient admission/discharge, start/end date for outpatient treatment, date of arrival to/discharge from emergency department, and date of referral (if relevant)
Other administrative data	Home visit (AAF6) or out-of-home visit (eg, drop-in center or prison service; AAF7) Treatment status of cancers covered by national treatment guaranties: referred, examined, or under treatment
Diagnoses	
Primary diagnosis	Main reason for hospitalization. When a patient is being examined and a diagnosis is not yet confirmed, a tentative "obs pro" (observation for) diagnosis may be used (the ICD-10 "Z-codes")
Secondary diagnoses	Optional diagnoses supplementing the primary diagnosis by, eg, describing the underlying chronic disease that is related to the current patient contact
Referral diagnosis	Diagnosis given by referring unit as the reason for referral
Temporary diagnoses	Diagnoses used only for ongoing nonpsychiatric outpatient contacts and never for completed contacts or for psychiatric contacts
Complications	Procedure-related complications, eg, perioperative bleeding or postoperative infections
Supplementary codes	Up to 50 codes supplementing the primary diagnosis, typically tentative diagnoses (eg, adding meningitis examination to the primary diagnosis disease of the central nervous system), drug abuse (eg, adding heroin to acute opioid intoxication), drug side effects (eg, adding acetylsalicylic acid to peptic ulcer disease), or cancer stage (eg, adding TNM stage to primary tumor diagnosis)
Treatments	
Surgery (K)	For example, surgery on the thyroid gland (KBA), lung (KGD), or coronary arteries (KFN)
Other treatments (B)	Patient care: eg, dress a wound with sterile bandage (BNPA40) or supra pubic catheter change (BJAZ14) Invasive procedures: eg, implantation of pacemaker (BFCA0)/cardioverter-defibrillator (BFCB0) or radiofrequency ablation (BFFB) Mechanical ventilation: invasive (BGDA0) or noninvasive (BGDA1) Cancer/immune-modulating treatments: antibody or immune-modulating therapy (BOHJ), radiation therapy (BWG), stem cell or bone marrow transplantation (BOQE and BOQF), cytostatic treatment (BWHA), and biological therapies (BWHB) Other medical treatment: eg, fibrinolysis (BOHA1) or initiation of parturition with prostaglandin (BKHD20) Telemedicine: eg, patient counseling by phone (BVAA33A), email (BVAA33B), or video (BVAA33D) Systemic psychotherapy: individual (BRSP1), couple (BRSP2), or family (BRSP3) Physiotherapy or occupational therapy (BVD) Other treatment examples: dialysis (BJFD), medical abortion (BKHD4), electroconvulsive therapy (BRXA1), total parenteral nutrition (BUAL1), and acupuncture (BAFA80)
Anesthesia and intensive care (N)	For example, during intensive care (NABB)
Examinations	
Radiological procedures (U)	For example, angiography (UXA), computed tomography (UXC), magnetic resonance imaging (UXM), X-ray (UXR), and ultrasound scan (UXU)
Temporary examinations (W)	Temporary classification of examinations
Other examinations (ZZ)	For example, planning rehabilitation (ZZ0175X), distortion product otoacoustic emission (ZZ7307), and cardiotocography (ZZ4233) For example, psychological evaluation (ZZ4991), semistructured diagnostic interview (ZZ4992), writing medical certificate (ZZ0182), providing preoperative antibiotic prophylaxis (ZPL0C), and procedure cancellation due to nonappearance of the patient (ZPP30)

Abbreviations: CPR, Civil Personal Register; TNM, Classification of malignant tumours based on tumor size (T), lymph node involvement (N) and distant metastasis (M).

Changes in content over time

Initially, the DNPR recorded information on all inpatient contacts only at nonpsychiatric (somatic) Danish departments,[23] whereas psychiatric inpatient contacts were recorded in the Psychiatric Central Research Register from 1969 to 1995, after which it was merged with the DNPR.[31] Registration of somatic outpatient contacts started in 1994 but was not complete (including the counties of Ribe, Ringkøbing, and Copenhagen) until 1995. Thus, since 1995, all psychiatric inpatient, psychiatric and somatic outpatient, and ED contacts in Denmark have also been reported to the DNPR.[23]

The personal data reported to the DNPR have remained unchanged since the registry's establishment in 1977,[36] but over time changes have been made to the admission data, diagnoses, treatments, and examinations.[35]

For the admission data, the first change occurred in 1987, whereby registration of patient contacts, referral information, and type of discharge was simplified (Table 3). Changes have been made almost annually thereafter, gradually expanding the registry's content as shown in Figure 1. The most recent changes to the admission data concerned type of admission and patient contact (Table 3). As of January 1, 2014, ED patients are no longer registered separately as "patient contact type 3" but instead as acute outpatients (ie, "admission type 1" and "patient contact type 2"), whereas other outpatients are registered as nonacute outpatients (ie, "admission type 2" and patient contact type 2). Thus, a patient contact in the DNPR was defined as an inpatient contact from 1977 through 1994; an inpatient, outpatient, or ED contact from 1995 through 2013; and as an inpatient or outpatient contact thereafter.

For diagnoses, it was originally possible to register up to 19 secondary diagnoses (ie, a maximum of 20 diagnoses per contact). Since 1995, the maximum number of recordable secondary diagnoses has increased to 99 in 1995–1998, 999 in 1999–2002, and 9,999 thereafter. Although in practice this means that there is no upper limit to the number of recordable secondary diagnoses, only the first 18 secondary diagnoses are subject to reimbursement by the Danish National Health Service.[42] Since the adaption of the tenth revision of the International Classification of Diseases (ICD-10) in 1994, 23% of hospital contacts have had one or more secondary diagnoses recorded. The median number of secondary diagnoses per contact in this period was 1 (interquartile range: 1–2 diagnoses).

Surgeries have been reported to the DNPR since 1977. Starting in 1999, diagnostic examinations and treatments were included.[26,35] It became mandatory to report on many medical treatments in 2001 (including cardiac, respiratory, kidney, and cancer treatments) and on radiological examinations in 2002. The results of examinations are not included in the DNPR (Table 2). Thus, the DNPR records when a patient undergoes magnetic resonance imaging, colonoscopy, biopsy, etc, but the findings are not registered explicitly. In some cases, however, findings may implicitly be inferred from the recorded diagnoses (eg, when an ulcer diagnosis follows procedure coding for gastroscopy).

Table 3 Time line for patient contact and admission types in the Danish National Patient Registry

	Code	Registration period
Patient contact type		
Inpatient	0	Jan 1, 2002–ongoing
24 hour patient	0	Jan 1, 1977–Dec 31, 2001
Daytime patient	1	Jan 1, 1977–Dec 31, 1986
Half-day patient	1	Jan 1, 1987–2001
Outpatient	2	Jan 1, 1987–ongoing
Overnight patient	2	Jan 1, 1977–Dec 31, 1986
Emergency department patient	3	Jan 1, 1987–Dec 31, 2013
Admission type		
Acute	1	Jan 1, 1987–ongoing
Nonacute	2	Jan 1, 1987–ongoing

Number of patient contacts

During 1977–2012, the cumulative Danish population numbered 8,342,199 persons. During this period, 8,085,603 distinct persons were registered in the DNPR at least once. Among these, 7,268,857 (90%) persons were registered with an inpatient contact, 5,953,405 (74%) persons with an outpatient contact, and 5,097,300 (63%) persons with an ED contact. When excluding the unspecific Z-codes (factors influencing health status and contact with health services), the numbers of persons registered with inpatient, outpatient, and ED contacts were 4,610,123, 4,995,365, and 4,792,298, respectively. The distribution of all hospital contacts according to ICD category and patient contact type is shown in Table 4. The 25 most common ICD-10 diagnoses for each patient contact type are provided in Table 5.

Classification systems

The SKS browser

The classifications used in the DNPR are provided in the Health Care Classification System (Danish, Sundhedsvæsenets Klassifikations System [SKS]).[43] The SKS is a collection of international, Nordic, and Danish classifications.[43] SKS codes contain up to ten alphanumeric characters, the first being a letter representing a primary group, following a monohierarchical classification system.[43] Thus, diagnoses are registered under "D", surgery under "K", other treatments

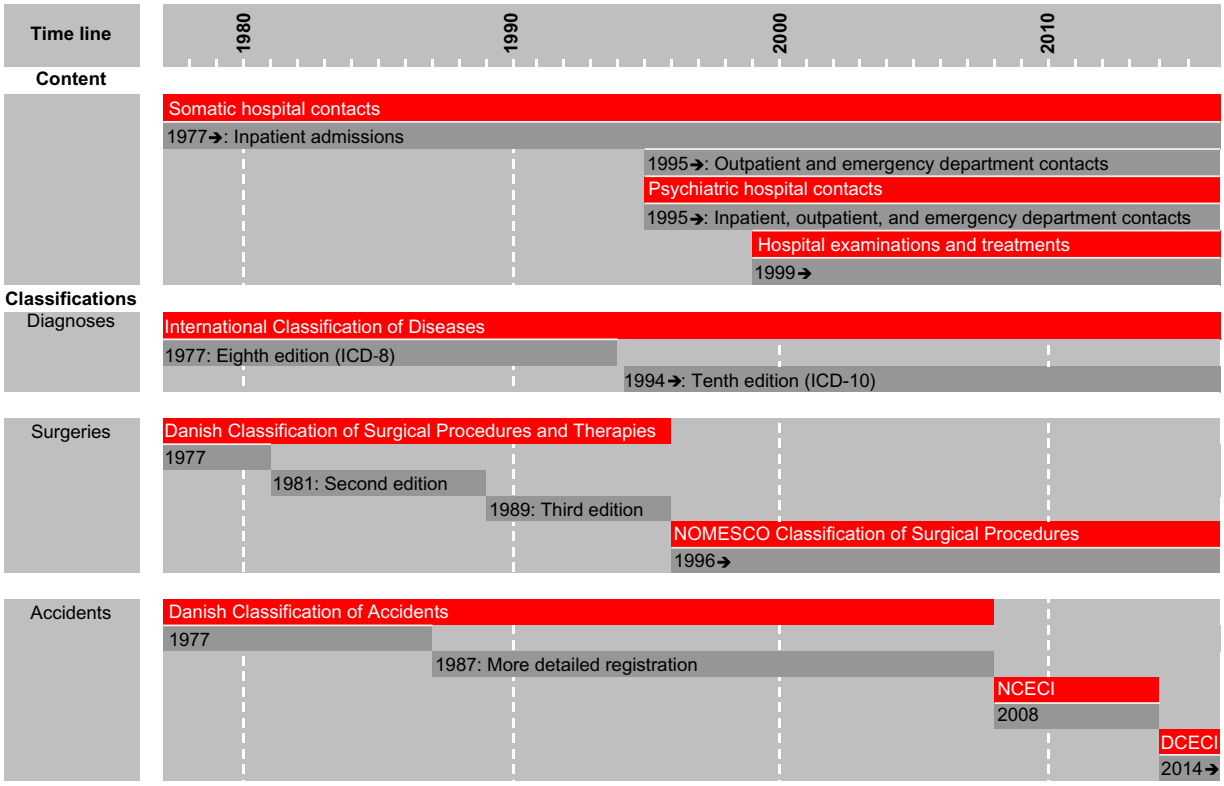

Figure 1 Timeline for the content and classification systems in the Danish National Patient Registry.
Abbreviations: DCECI, Danish Classification of External Causes of Injury; ed, edition; ICD, International Classification of Diseases; NCECI, Nordic Classification of External Causes of Injury; NOMESCO, Nordic Medico-Statistical Committee.

under "B", anesthesia under "N", and examinations under "U" or "ZZ" (Table 2).[36]

To facilitate the search for SKS codes, the Danish National Health and Medicines Authority maintains a user-friendly SKS browser (Figure 2),[44] searchable by code, by free text, or by browsing. Searching for acute myocardial infarction codes can be done by entering "DI21" or by typing the Danish or Latin term in a full phrase (akut myokardieinfarkt) or a partial phrase (eg, infarctus myo).[44] Manual browsing requires clicking the main group "Classification of diseases" (group D), then "Diseases of the cardiovascular system" (I), then "Ischemic heart disease" (I20–I25), and finally "Acute myocardial infarction" (I21). The SKS browser does not include historical codes,[44] but these are available online elsewhere.[45]

Changes over time

Over time, the DNPR has adopted different classification systems for diagnoses, surgeries, and accidents (Figure 1), whereas the classification systems for radiological procedures and in-hospital medications have remained unchanged since their introduction into the DNPR.[26,36]

Diagnoses were classified according to the ICD-8 until the end of 1993 and the ICD-10 thereafter. The three-digit ICD-8 codes were used in a modified Danish version (with two supplementary digits), which explains in part why ICD-9 coding was never introduced in Denmark. Coding granularity improved in 1994 through introduction of the five-digit ICD-10 codes. Although the DNPR follows the current international standards for disease classification, the ICD-10 version used in Denmark often does not allow for identification of certain clinical details, such as disease severity. Supplementary codes (eg, the so-called "TUL" codes) sometimes allow for anatomical precision, eg, to identify location of a thrombosis or surgery site in right/left or upper/lower extremity, but these codes are used inconsistently. Sometimes, ABC extensions are added to specific diagnostic codes, eg, atrial fibrillation (I489B) and flutter (I489A), making the Danish version of the ICD-10 more detailed than the international ICD-10 but less detailed than the clinical modification of the ICD-10 (ICD-10-CM), which is not used in Denmark.[46]

Surgeries were coded according to the three consecutive editions of the Danish Classification of Surgical Procedures and Therapies, from 1977 to 1995.[47] Since 1996, surgical procedures have been coded according to the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures.[48]

Table 4 Number of patients registered in the Danish National Patient Registry according to disease categories and patient contacts, 1977–2012[a]

ICD-8	ICD-10	Disease categories	Inpatient contact, n (%)	Outpatient contact, n (%)	Emergency department contact, n (%)	Any patient contact, n (%)
All	All	All diseases	7,268,857 (100)	5,953,405 (100)	5,097,300 (100)	8,085,603 (100)
0–139	A00–B99	Certain infectious and parasitic diseases	801,471 (11.0)	232,080 (3.9)	104,089 (2.0)	975,286 (12.1)
140–239	C00–D48	Neoplasms	1,308,247 (18.0)	910,226 (15.3)	18,619 (0.4)	1,599,930 (19.8)
280–289	D50–D89	Diseases of the blood and blood-forming organs	351,455 (4.8)	146,420 (2.5)	13,779 (0.3)	416,132 (5.1)
240–279	E00–E90	Endocrine, nutritional, and metabolic diseases	972,238 (13.4)	653,091 (11.0)	69,610 (1.4)	1,232,964 (15.2)
290–319	F00–F99	Mental and behavioral disorders	575,514 (7.9)	218,086 (3.7)	137,711 (2.7)	743,981 (9.2)
320–359	G00–G99	Diseases of the nervous system	514,425 (7.1)	504,543 (8.5)	90,232 (1.8)	840,500 (10.4)
360–379	H00–H59	Diseases of the eye and adnexa	295,631 (4.1)	738,413 (12.4)	126,565 (2.5)	997,947 (12.3)
380–389	H60–H95	Diseases of the ear and mastoid process	271,495 (3.7)	547,612 (9.2)	42,307 (0.8)	750,109 (9.3)
390–459	I00–I99	Diseases of the circulatory system	1,971,447 (27.1)	1,106,198 (18.6)	311,333 (6.1)	2,312,646 (28.6)
460–519	J00–J99	Diseases of the respiratory system	1,738,535 (23.9)	713,021 (12.0)	204,853 (4.0)	2,018,882 (25.0)
520–579	K00–K93	Diseases of the digestive system	1,717,940 (23.6)	1,116,975 (18.8)	174,675 (3.4)	2,229,186 (27.6)
680–709	L00–L99	Diseases of the skin and subcutaneous tissue	421,034 (5.8)	434,280 (7.3)	190,607 (3.7)	824,052 (10.2)
710–739	M00–M99	Musculoskeletal and connective tissue disease	1,178,743 (16.2)	1,747,207 (29.3)	440,731 (8.6)	2,387,728 (29.5)
580–629	N00–N99	Diseases of the genitourinary system	1,527,088 (21.0)	1,132,468 (19.0)	123,847 (2.4)	2,066,692 (25.6)
630–679	O00–O99	Pregnancy, childbirth, and the puerperium	1,287,919 (17.7)	429,432 (7.2)	44,587 (0.9)	1,321,981 (16.3)
760–779	P00–P96	Conditions originating in the perinatal period	468,787 (6.4)	75,901 (1.3)	1,867 (0.0)	490,506 (6.1)
740–759	Q00–Q99	Congenital malformations and deformations	274,586 (3.8)	235,560 (4.0)	4,116 (0.1)	412,386 (5.1)
780–799	R00–R99	Symptoms, signs, and findings not classified elsewhere	1,952,537 (26.9)	1,214,203 (20.4)	655,075 (12.9)	2,784,868 (34.4)
800–999	S00–T98	External causes of injury and poisoning	2,184,899 (30.1)	1,751,282 (29.4)	4,252,799 (83.4)	5,056,701 (62.5)
E00–E99	X01–Y98	External causes of morbidity and mortality	669,066 (9.2)	756 (0.0)	27,230 (0.5)	692,424 (8.6)
Y00–Y99	Z00–Z99	Factors influencing health and contact with health services	4,162,984 (57.3)	4,890,778 (82.2)	1,894,891 (37.2)	6,104,084 (75.5)

Notes: [a]The disease categories are ordered according to the ICD-10. Both primary and secondary diagnoses were included. A person (ie, one Civil Personal Register number) can contribute in several diseases categories, but only once in each cell.
Abbreviation: ICD, International Classification of Diseases.

Accidents have been coded using the Danish Classification of Accidents. A detailed registration was introduced in 1987. The latest version of the classification, the Nordic Classification of External Causes of Injury, also included suicide attempts and violence.[26] It was adopted in 2008 and used until a new Danish Classification of External Causes of Injury was incorporated in the SKS, in 2014.[36,37] Although closely related to the Nordic classification in structure, the new Danish classification facilitates a simpler registration of external causes of injury.

Radiological procedures (without results) are coded according to the Danish Classification of Radiological Procedures (UX codes). This classification system follows the general principles used for registration of treatments in the SKS.[36]

In-hospital medication use (without dispensed dose or route of administration) is registered using different modules consistent with the Anatomical Therapeutic Chemical (ATC) classification system. Data on in-hospital medical treatment are not commonly used in research, except for drugs exclusively administered at hospitals, eg, fibrinolysis or cancer/immune-modulating treatments such as antibody, radiation, cytostatic, and biological therapies (Table 2). These drugs are primarily registered with a SKS treatment code, but their ATC codes can also be used as supplemental

Table 5 The 25 most common ICD-10 diagnoses at the four-digit level in the Danish National Patient Registry, according to patient contact type, 1994–2012[a]

Inpatient contact		Outpatient contact		Emergency department contact	
Diagnosis (ICD-10 code)	**n (%)**	**Diagnosis (ICD-10 code)**	**n (%)**	**Diagnosis (ICD-10 code)**	**n (%)**
Any	**4,610,123 (100)**	**Any**	**4,995,365 (100)**	**Any**	**4,792,298 (100)**
1. Spontaneous vertex delivery (O800)	466,723 (10.1)	Senile cataract, unspecified (H259)	287,008 (5.7)	Fracture of lower end of radius (S934)	590,608 (12.3)
2. Pneumonia, unspecified (J189)	260,815 (5.7)	Presbycusis (H911)	193,200 (3.9)	Open wound of finger(s) without damage to nail (S610)	554,305 (11.6)
3. Abdominal pain, unspecified (R108)	159,390 (3.5)	Unilateral or unspecified inguinal hernia (K409)	178,811 (3.6)	Contusion of finger(s) without damage to nail (S600)	301,454 (6.3)
4. Angina pectoris, unspecified (I209)	147,605 (3.2)	Meniscus derangement due to tear or injury (M232)	157,750 (3.2)	Contusion of wrist and hand, exclusion fingers (S602)	263,753 (5.5)
5. Acute abdomen (R100)	146,264 (3.2)	Essential hypertension (I109)	132,992 (2.7)	Fracture of lower end of radius (S525)	250,339 (5.2)
6. Atrial fibrillation and flutter (I489)	142,849 (3.1)	Hearing loss, unspecified (H919)	126,037 (2.5)	Contusion of knee (S800)	243,863 (5.1)
7. Concussion (S060)	129,704 (2.8)	Fracture of lower end of radius (S525)	123,682 (2.5)	Open wound of head, part unspecified (S019)	242,506 (5.1)
8. Syncope and collapse (R559)	114,942 (2.5)	Complete or unspecified medical abortion (O049)	121,821 (2.4)	Open wound of scalp (S010)	241,943 (5.0)
9. Stroke, unspecified (I649)	112,366 (2.4)	Angina pectoris, unspecified (I209)	120,765 (2.4)	Contusion of other and unspecified parts of foot (S903)	204,344 (4.3)
10. Gastroenteritis of unspecified origin (A099)	107,339 (2.3)	Tear of meniscus (S832)	117,493 (2.4)	Sprain and strain of finger(s) (S636)	199,784 (4.2)
11. Unilateral or unspecified inguinal hernia (K409)	98,996 (2.1)	Abdominal pain, unspecified (R108)	117,381 (2.3)	Fracture of other finger (S626)	171,706 (3.6)
12. Delivery by emergency cesarean section (O821)	97,505 (2.1)	Varicose veins of lower extremities (I839)	116,957 (2.3)	Contusion of shoulder and upper arm (S400)	169,022 (3.5)
13. Volume depletion (E869)	95,031 (2.1)	Disc disorders with radiculopathy (M511)	113,217 (2.3)	Sprain and strain of unspecified parts of knee (S836)	163,976 (3.4)
14. Fracture of neck of femur (S720)	94,372 (2.0)	Asthma, unspecified (J459)	106,652 (2.1)	Concussion (S060)	162,564 (3.4)
15. Calculus of gallbladder, no cholecystitis (K802)	87,351 (1.9)	Hyperplasia of prostate (N409)	106,459 (2.1)	Injury of conjunctiva and corneal abrasion (S050)	155,675 (3.2)
16. Spontaneous breech delivery (O802)	86,451 (1.9)	Atrial fibrillation and flutter (I489)	105,710 (2.1)	Open wound of eyelid and periocular area (S011)	150,449 (3.1)
17. Acute myocardial infarction, unspecified (I219)	84,800 (1.8)	Unspecified hematuria (R319)	105,548 (2.1)	Contusion of thorax (S202)	149,719 (3.1)
18. Cerebral infarction, unspecified (I639)	84,001 (1.8)	Internal derangement of knee, unspecified (M239)	104,986 (2.1)	Contusion of elbow (S500)	147,950 (3.1)
19. Complete or unspecified medical abortion (O049)	80,284 (1.7)	Carpal tunnel syndrome (G560)	96,247 (1.9)	Contusion of toe(s) without damage to nail (S901)	133,673 (2.8)
20. Heart failure, unspecified (I509)	79,877 (1.7)	Calculus of gallbladder, no cholecystitis (K802)	94,599 (1.9)	Sprain and strain of wrist (S635)	133,174 (2.8)
21. Acute appendicitis, unspecified (K359)	74,769 (1.6)	Impingement syndrome of shoulder (M754)	91,306 (1.8)	Superficial injury of head, part unspecified (S009)	117,495 (2.5)
22. Constipation (K590)	73,162 (1.6)	COPD, unspecified (J449)	89,555 (1.8)	Superficial injury of scalp (S000)	117,118 (2.4)
23. Acute cystitis (N300)	72,768 (1.6)	Other primary gonarthrosis (M171)	89,528 (1.8)	Open wound of other parts of wrist and hand (S618)	116,600 (2.4)
24. Vacuum extractor delivery (O814)	69,842 (1.5)	Pain in limb (M796)	86,225 (1.7)	Foreign body in cornea (T150)	115,715 (2.4)
25. Essential hypertension (I109)	68,799 (1.5)	Low back pain (M545)	85,920 (1.7)	Sprain and strain of cervical spine (S134)	114,419 (2.4)

Notes: [a]Both primary and secondary diagnoses are included. Factors influencing health status and contact with health services (Z-codes) are not included.
Abbreviation: ICD, International Classification of Diseases; COPD, chronic obstructive pulmonary disease.

Figure 2 User interface of the Danish Health Care Classification System (SKS browser).

Notes: Available at http://www.medinfo.dk/sks/brows.php. English translation (consecutive line order): administrative data/classifications of treatment and care/classification of diseases/classifications of external causes of injury/International Classification of Functioning (ICF)/classification of surgery/Anatomical Therapeutic Chemical (ATC) classification system/anesthesia, intensive care, prehospital care/classification of examinations/temporary classification of examinations/specifications/supplementary codes/ZZ-procedure codes/ZZK, ZZP, ZZV, and ZPP codes and pseudo procedure codes (cancer, cancelled, discontinued)/classification of hospitals and departments.

Abbreviation: SKS, Sundhedsvæsenets Klassifikations System.

codes (eg, fibrinolysis is covered by SKS code BOHA1 and ATC code B01AD).

Data quality

Measurements of data quality

The two most common measures of data quality are validity and completeness.[49] By validity we refer to the extent to which a variable measures the intended construct.[49] The positive predictive value (PPV) of registration is the most frequently reported measure of the validity of records in the DNPR. It is defined as the proportion of patients registered with a disease who truly have the disease and is usually estimated using medical record review as the reference standard to confirm the presence of disease.[49] The term reference standard is used here, as medical record is not always considered the gold standard in validation studies, although one must assume that it is a better representation of the truth than the registry record.

Completeness refers to the proportion of true cases of a disease that is correctly captured by the registry.[49] Completeness can be measured in relation to either all individuals in the general population with a specific disease or all patients admitted/treated for the specific disease. Completeness is largely determined by the registry's sensitivity and depends on the amount of missing data.[49] Since no complete reference source exists, it is difficult to estimate the overall completeness of registry data relative to the general population. Data completeness depends on hospitalization patterns and diagnostic accuracy. Thus, conditions such as nonfatal myocardial infarction or hip fracture, which should always lead to a hospital encounter, are registered consistently in the DNPR. In contrast, lifestyle risk factors (overweight, smoking, excessive alcohol consumption, and physical inactivity) and conditions as hypertension or uncomplicated diabetes are often treated by GPs and are thus not completely registered.

Overall data quality

After receiving data from the hospitals, the DNPR automatically checks for missing codes, incorrect digits, errors in CPR numbers, and inconsistencies between diagnoses and sex.[24] In case of errors, the records are returned to the source hospital for correction.[24]

The Danish Health and Medicines Authority has examined the PPVs of personal data, admission data, and diagnoses in the DNPR three times, using medical record review as the reference standard.[24,50,51] The first such validation was performed in 1980 as a pilot study of 1,000 randomly sampled discharges from a single hospital (Hillerød Hospital).[50] The study concluded that the validity of primary diagnoses in the DNPR was not sufficient for research.[50] The secondary study validated 1,094 random discharges from a 1990 nationwide sample and found high overall correlation between admission and discharge data in the DNPR and medical records.[24] The proportion of incorrect registrations was 1.4% for admission type, 8.1% for contact reason, 0.8%–8.7% for accident registration (lowest for work-related accidents), 14.8% for the "referral to" variable, and 1.5% for date of discharge. The "referral from" data were incorrect among 11.5% of nonacute patients. However, due to differing guidelines for reporting this variable, there was considerable regional variation in its validity. In the study, diagnoses and surgical procedures were categorized according to five clinical specialties covering 85% of all nonpsychiatric discharges (Table 6). A comparison of various primary diagnoses showed correct categorization at the five-digit level for 73% of all cases, increasing to 83% when alternative diagnoses were accepted. Substantial variation was observed between different clinical specialties, with the lowest PPV for medical diagnoses (66%) and the highest PPV for diagnoses associated with orthopedic surgery (83%). For all specialties, the proportion of correct diagnoses increased substantially when the comparison was made at the three-digit rather than at the five-digit level. It increased

Table 6 Summary results from the Danish Health and Medicines Authority's evaluation of diagnoses in the Danish National Patient Registry in 1990 according to clinical specialties

Clinical specialty	Positive predictive value of correct primary diagnoses			
	Five-digit diagnosis codes		Three-digit diagnosis codes	
	Primary diagnosis alone (%)	Primary + two secondary diagnoses (%)	Primary diagnosis alone (%)	Primary + two secondary diagnoses (%)
Medicine	66	72	73	81
Pediatrics	74	80	82	89
General surgery	77	82	84	89
Gynecology/obstetrics	77	88	83	94
Orthopedic surgery	83	85	89	91
Overall	73	80	81	88

even further when secondary diagnoses were also included (Table 6). The third validation study included 420 random discharges from a nationwide sample in 2003 and focused only on admission and discharge data.[51] The proportion of incorrect registrations in this sample was 3% for admission type and 8% for referral type. Data on admission/discharge dates, hospital/department codes, and CPR numbers were accurate.[51]

Systematic review of validated variables

The data quality of individual variables in the DNPR has been examined on an ad hoc basis.[25,52–164] To provide researchers with an overview of such studies, we performed a systematic review, aiming to create a bibliography of validated administrative data, diagnoses, treatments, and examinations in the DNPR.

Figure S1 shows a flowchart for the review process, including the search strategy. We searched MEDLINE (PubMed) and the *Danish Medical Journal* (http://ugeskriftet.dk/udgivelser) using the Danish and the various English names for the DNPR. One author (MS) screened titles and abstracts, and when necessary the full-text papers, for inclusion in the bibliography. Because validation is often a secondary study aim and therefore not highlighted in titles, abstracts, or keywords of papers, even a comprehensive systematic search cannot identify all relevant papers. We therefore also searched the reference lists of the retrieved papers for potentially relevant articles. Finally, we included additional studies known to us beforehand. We included all studies written in English or Danish, regardless of characteristics, such as publication status or year.

Two authors (MS and SAJS) independently extracted the following data from all included papers: patient contact type (inpatient, outpatient, or ED), diagnosis type (primary vs secondary), codes/algorithms used, measure of validity (PPV/negative predictive value), measure of completeness (sensitivity/specificity), the reference standard used, and results (absolute numbers, proportions, and confidence intervals [CIs]). Any disagreements were resolved by consensus. When patient contact, diagnosis type, or codes were not specified, we contacted the corresponding authors for this information. Unspecified patient type included most often both in- and outpatient diagnoses. Unspecified diagnosis type included most often both primary and secondary diagnoses. Unconfirmed data were categorized as not available (n/a). We used extracted information as well as more detailed information from selected studies to illustrate the use of various algorithms over time and to discuss methodological considerations, in particular information bias.

Our review showed that several different methods had been used to calculate CIs for proportions. Moreover, studies varied with respect to the number of decimal points reported for CIs, while some studies failed to report CIs. To permit direct comparisons among study results, we recalculated all proportions based on the absolute numbers provided in the papers. We used Wilson's score methods to calculate CIs with one decimal point precision.[165] When lack of absolute numbers precluded recalculations, we presented the results as reported in the original reference.

We identified 114 papers, validating 1–40 codes/algorithms each and 253 in total. The bibliography of validated variables is provided in Table S1. The variables are listed in the table according to the SKS coding (ie, ICD-10 codes for diagnoses and Nordic Medico-Statistical Committee codes for surgeries) and within each variable according to study period. Recalculation of all proportions reported was possible for 89% (102/114) of all studies.

We found that the PPVs of the reported diagnoses in the DNPR ranged from below 15%[137] to 100%.[58,97] Some of this variation (both intervariable and intravariable variation) may result from different reference standards used. The majority

of variables were examined in cross-sectional studies using medical record review as the reference standard. However, several other reference standards have also been used, including patient interviews,[84,146] clinical registries,[32,57,78,89,142] the Danish Cancer Registry,[59,60,64,67] a military conscription research database,[116] the Clinical Laboratory Information System Database,[72,73,114] the Danish National Pathology Registry and Data Bank,[120] the hospital pharmacy systems,[160] the Danish prescription registries,[79,83] GP verification,[75] radiology reports,[111,118] and autopsy reports.[110,141] Our review revealed variation in study settings and calendar year. The study setting is important to consider, as the PPV depends on the prevalence of disease and therefore on the data's department of origin. Thus, restriction to specialized departments, eg, rheumatology departments when examining the validity of a rheumatoid arthritis diagnosis, likely results in higher PPVs.[126] Similarly, the calendar year may affect the quality of variables, given the continuous improvement in diagnostic criteria and procedures used. As examples, the validation studies indicate a temporal increase in the PPV of ulcer disease (from 84% during 1997–2001[119] to 98% during 1998–2007[58]) and of myocardial infarction (from 92% during 1979–1980,[100] 94% during 1982–1991,[99] to almost 100% during 1996–2009[97]). Improvements in variable completeness over time have also been documented for, eg, bacteremia (from 4.4% in 1994,[25] 25.1% in 2000,[55] to 35.1% in 2011[55]).

We found that the definition of a disease in registry data is not always based on ICD codes alone but may require algorithms that combine a diagnosis with admission data (eg, admission type, patient contact, and department specialty), other diagnostic specification (such as primary vs secondary diagnoses), procedures, in-hospital medical treatment (eg, chemotherapy), prescription use, previous medical history (to identify incident events), time since first diagnosis or metastasis (to identify recurrent events), pathology data (for tumor genotypes),[166] or other registry data (eg, laboratory[167] and cancer data[34]). As an example, a validation study of recurrent venous thromboembolism tested different algorithms based on the inpatient vs outpatient diagnoses, presence or absence of an ultrasound or computed tomography (CT) scan during admission, and postdischarge anticoagulant drug use.[112] Based on the results of that study, a case of venous thromboembolism recurrence was defined as an inpatient diagnosis of deep venous thrombosis or pulmonary embolism recorded >3 months after the incident venous thromboembolism event among patients with an ultrasound or CT scan performed during admission (PPV =79%).[112] An algorithm for colorectal cancer recurrences combines metastasis and chemotherapy codes in the DNPR with cancer recurrence codes in the Danish National Pathology Registry (PPV =86%; sensitivity =95%).[61]

Lack of completeness of the DNPR in capturing certain conditions can sometimes be compensated by data linkage to other routine registries. Diabetes can be identified from at least one outpatient dispensation record for insulin or an oral antidiabetic drug (in the Danish prescription registries[168]) and/or by an inpatient or outpatient hospital diagnosis of type 1 or type 2 diabetes in the DNPR.[76] Recent studies have supplemented the algorithm with data on glycosylated hemoglobin A_{1c} level of ≥6.5% from the Clinical Laboratory Information System Database, increased specificity by excluding metformin-treated patients with polycystic ovarian syndrome,[169] and differentiated type 1 and type 2 diabetes using information on age at diagnosis combined with insulin monotherapy.[76]

The large variation in data validity found in our review underscores the need to validate diagnoses and treatments before using DNPR data for research. Furthermore, validation studies may need updates, as newer diagnostic criteria and procedures may differ from those used in older validation studies.

DNPR as a research tool

Health events

Potential uses of the DNPR, according to study design, are presented in Table 7. Patient cohorts of interest may be identified, along with their medical history and outcomes. Thus, the DNPR may provide data on diseases,[170,171] treatments,[172] and diagnostic examinations as exposures. Seasonal variation as an exposure has also been examined.[173]

Furthermore, the DNPR allows for identification of disease occurrence in the general population (risk studies),[174] where the exposure information could originate from other data sources involving primary or secondary data collection, eg, military conscription cohorts[175] or population-based health surveys such as the Danish Health Examination Survey,[176] the "How Are You?" study,[177] the Danish Diet, Cancer and Health study,[178] the Soon Parents cohort,[179] the Glostrup Population Studies,[180] and the Copenhagen City Heart study.[181] Extraordinary long-term follow-up (>35 years) for lifestyle-associated diseases is feasible.[175]

Using techniques similar to that in risk studies, the DNPR can be used to study outcomes in well-defined patient groups

Table 7 Use of the Danish National Patient Registry according to study design

Cohort studies	Identifying study cohorts from hospitalized patients, the general population (assessed from registries or in combination with primary data collection), and family cohorts (constructed through linkage to the Danish Civil Registration System) Identifying study exposures related to diseases, treatments, examinations, and seasonality Identifying disease occurrence in the general population (eg, associated with lifestyle factors identified from health surveys) or family cohorts Identifying disease outcome (recurrence or complications) in patients identified from the DNPR itself, clinical registries, or randomized trials Identifying health care utilization rates through counting frequency of inpatient/outpatient and planned/unplanned contacts Identifying temporal trends in disease incidence and use of treatments and diagnostic procedures
Case–control studies	Identifying cases (and exposure from the DNPR, other registries, health surveys, or primary data collection). Risk-set sampling is possible through linkage to the Danish Civil Registration System
Cross-sectional studies	Identifying patient's medical history at study entry according to diagnoses (index disease and comorbidities), treatments (in-hospital medical treatment, surgical procedures, anesthesia, and intensive care), and diagnostic procedures
Ecological studies	Identifying variations in health care and outcomes at the population level

Abbreviation: DNPR, Danish National Patient Registry.

(eg, diagnostic examinations,[182] recurrence,[112] and complications[183]) and prognostic factors.[170] These patient groups may be identified from the DNPR itself, other registries, or surveys. Most recently, the DNPR has also been used to gather long-term follow-up data for randomized controlled trials using clinically driven outcome detection.[184] The automated event-detection feature of the DNPR allows for large, low-cost randomized trials that reflect daily clinical practice, cover a broad range of patients and end points, and include lifelong follow-up.[183,185–187] As with cohort studies, DNPR data may be used to identify exposures and cases/outcomes in case–control studies[112,188,189] and ecological studies[182] (Table 7).

Health care planning

The administrative data related to each patient contact allow for studies of health care utilization and how health care planning may affect patient outcomes. As an example, admission rates for the most common medical conditions in Denmark have been found to be higher during the regular office hours than during the weekend hours.[190] However, admissions during the weekend hours have been associated with higher mortality rates (weekend nighttime hours > weekend daytime hours > weekday out-of-hours > weekday office hours).[190]

Record linkage

The availability of patient-identifiable data in the DNPR makes it technically easy to link to other Danish data sources using the CPR number.[20] Because Denmark's registries are numerous and far reaching even by the high standards of the Nordic countries,[22,191] additional information on, eg, cancer staging,[34] laboratory test results,[167] general practice utilization,[192] socioeconomic data,[193–196] prescription use,[197] all-cause mortality,[20] and cause-specific mortality[198] can easily be obtained to supplement the DNPR. Figure 3 shows the time line for the DNPR relative to selected administrative and clinical registries in Denmark, illustrating the potential for record linkage by calendar year. As shown, nationwide data can be obtained on, eg, all twins in Denmark since 1870 (the Danish Twin Registry),[199] specific causes of death since 1943 (the Danish Register of Causes of Death),[198] detailed cancer diagnoses since 1943 (the Danish Cancer Registry),[34] migration and vital status since 1968 (the Danish Civil Registration System),[20] personal income since 1970 (the Income Statistics Registry),[195] labor market statistics and health services since 1980 (the Integrated Database for Labour Market Research[193] and Danish National Health Service Register),[192] education since 1981 (the Population's Education Register),[194] prescribed medications since 1995 (the Danish National Prescription Registry),[168] and patient tissue samples and blood transfusions since 1997 (the Danish National Pathology Registry and Blood Transfusion Databases).[166] The Danish clinical registries constitute the infrastructure of the National Clinical Quality Databases and the Danish Multidisciplinary Cancer Groups.[200] The clinical registries contain information about individual patients used for quality improvement, research, and surveillance purposes.[200] Linkage to one or more of the current 69 clinical registries thus provides detailed information on a range of procedures (eg, hip arthroplasty and hysterectomy) and diseases (eg, heart failure, stroke, diabetes, and various malignant diseases; Figure 3).[200,201] Finally, individual-level linkage to data from randomized controlled trials, population surveys, and epidemiologic field studies is possible as previously described.

Methodological considerations

Methodological considerations related to the internal validity of cohort studies conducted within the DNPR are summarized

Figure 3 Timeline for the initiation of selected Danish registries linkable to the Danish National Patient Registry.
Abbreviations: ADHD, attention deficit hyperactivity disorder; ICD, International Classification of Diseases; GP, general practitioner; COPD, chronic obstructive pulmonary disease.

subsequently and in Table 8. We also address the special methodological problems that relate to studies of temporal health trends.

Precision

The nationwide coverage since 1978 provides sample sizes that permit studies of rare diseases, disease complications, and effects in subgroups of patients (effect modification and interactions). Of note, very rare diseases may still be difficult to study because of the relatively small size of the Danish population.[202]

Selection bias

Appropriate population-based study designs can reduce selection biases in cohort studies for three reasons. First, the Danish population has a relatively stable and homogeneous demography with regard to race and religion. Second, the universal health care system (and small private hospital sector)[40] prevents selection bias arising from selective inclusion of specific hospitals, health insurance systems, income levels, or age groups. Third, virtually complete follow-up of all patients (with no unrecorded dropouts) is possible because the Danish Civil Registration System records vital status and migrations on a daily basis.[20] Still, the cohort represented in the DNPR is only unselected for diseases that always require hospital treatment. For diseases that can be treated in general practice, cases included in the DNPR to some degree represent a selected patient group, with either high severity of the disease in question (eg, herpes zoster infections, obesity, diabetes, and hypertension) or severe comorbidity leading

Table 8 Methodological considerations related to the internal validity of cohort studies conducted with data from the Danish National Patient Registry

Precision	The large nationwide sample permits studies of rare diseases, disease complications, and treatment effects in subgroups of patients
Selection bias	The population-based coverage, within a universal health care system with virtually complete follow-up of all patients owing to the Danish Civil Registration System, reduces the risk of selection biases
Information bias	The risk of misclassification warrants validation of all variables used for research
Confounding	The registrations of diagnoses, treatments, and examinations for all hospital contacts may provide data on potential confounding factors. Seasonality may be controlled in the studies of infectious disease

to a lower threshold for hospital admission compared with patients without comorbidity (eg, pneumonia in transplant patients vs in young otherwise healthy adults).

Information bias

Although it is obvious that registration and retrieval of patient information from the DNPR must be based on correct SKS codes, this task is not always easy. The SKS includes many codes that might not be mutually exclusive from a clinical point of view. For many diagnoses, it is thus necessary to be aware of potential differences in registration practice among hospital departments[24] and over time.[122,170,203]

Before engaging in extensive retrieval and analysis of data, it is therefore important to consult clinicians from the relevant specialty to learn about current and previous coding practices. As an example, atrial fibrillation and atrial flutter have separate codes at the four-digit level. However, a large proportion of all diagnoses for atrial fibrillation or flutter are registered as "not elsewhere specified" (Danish, uden nærmere specifikation). Since ~95% of all I48 codes correspond to atrial fibrillation and only 5% to atrial flutter,[104] use of the unspecified code will increase the sensitivity of the DNPR-based definition of atrial fibrillation but reduce its specificity. Hence, DNPR studies on risk of atrial fibrillation are often limited by considering atrial fibrillation and flutter as one disease entity.[174] Another example is ICD-10 diagnoses of stroke (I60–I64). Approximately one-third of the cases are registered as unspecified stroke (I64),[204] and among these, two-thirds are ischemic strokes.[91] Inclusion of unspecified diagnoses will increase sensitivity but reduce specificity of stroke subtypes.

The introduction of the Diagnosis-Related Group system in 2002[29,30] regarding payment to public hospitals may have resulted in more complete registration. However, it may also have affected coding practices for some diseases and certain types of treatments. Private hospitals and clinics are potential sources of underreporting.[40] Although it has been mandatory for private health care providers to report all activities since 2003, and the Danish Health and Medicines Authority runs information campaigns to promote registration,[38] registration from private hospitals and clinics remains incomplete.[17,41] Private hospitals offer services paid by taxes due to the rules of "free hospital choice" or as part of an agreement with a region, as well as services paid privately either by insurance companies or private parties.[21,40] Services paid for by private parties have the highest degree of incomplete registration.

In contrast to validity, the completeness of diagnoses is often higher in the DNPR than in the clinical registries.[89,100,164,205,206] This higher completeness is expected since many clinical registries receive data from the DNPR. Another reason is that the law requires the national clinical registries to cover only 90% of patients with a given condition.[207] Moreover, the degree of completeness varies among and within clinical registries over time.[164,208]

Confounding

Nonrandomized studies are susceptible to confounding by known and unknown factors.[209] Therefore – irrespective of data source – the potential for confounding always needs to be addressed in the study design or analysis. The DNPR provides an opportunity to obtain information on many potential confounders, particularly comorbidities.[58,210] The possibility of identifying such covariables from patients' history of hospital encounters (back to 1977) rather than short-fixed historical windows may also result in less biased estimates.[211] Still, it should be kept in mind that incomplete registration of some diagnoses and missing data on other characteristics (eg, lifestyle risk factors[212]) may leave substantial residual and unmeasured confounding.

Temporal health trends

As data in the DNPR currently span almost four past decades, the registry is a unique data source to monitor long-term temporal trends in use of diagnostic procedures (eg, cardiac CT angiography),[164] treatments (eg, use of implantable cardioverter-defibrillators),[213] and disease incidence (eg, myocardial infarction).[27,170] Related particularly to disease incidence, however, a number of methodological problems must be considered.

First, the DNPR only covers patients with disease episodes associated with hospital contact and thus not necessarily the total number of patients with a given disease (as described previously).

Second, lack of information on deaths occurring outside the hospital among persons with no previous hospital contact for a given disease may lead to underestimation of both the disease incidence and the disease-specific mortality. This problem is particularly important for acute critical events such as myocardial infarction.[170] Still, it should be noted that a person is not considered legally dead in Denmark before a physician has confirmed clear signs of death. Thus, all patients dying in an ambulance or otherwise arriving at a hospital with no signs of life are also admitted and registered in the DNPR (even when no resuscitation is attempted at the hospital). Data linkage to the Danish Register of Causes of Death[198] may help to provide a more complete picture of the incidence of acute fatal events not included in the DNPR.[170]

Third, it may be difficult – or even impossible – to identify incident diagnoses of chronic diseases in older patients because of immigration or the lack of hospital data before 1977. Thus, events occurring prior to 1977 are left censored if individuals are enrolled in a study and left truncated if they are not.[214] On the other hand, the DNPR enables reconstruction of individual life and health trajectories of persons born in 1977 or later.

Fourth, defining incidence by "the first occurrence of the disease in the registry" leads to overestimation of incidence in the period immediately following the initiation of the DNPR, after initiation of a screening program, or after introduction of new registry codes, due to misclassification of "backlogged" prevalent cases as incident cases. Because this problem decreases with the passage of time after 1977 or with the number of screening rounds, a "washout period" before identification of incident cases may reduce the error. This source of error is less important when examining diseases of short duration, such as infections. The transition from ICD-8 to ICD-10 in 1994 and inclusion of outpatients and ED diagnoses in 1995 may similarly introduce artifacts in long-term incidence trends. Exemplifying this problem, the incidence of alcoholic cirrhosis showed no clear trend for men or women of any age from 1988 to 1993 but apparently increased by 32% in 1994 and by an additional 10% when including outpatient and ED visits.[122]

Fifth, changes in classification systems and diagnostic criteria and use of more sensitive diagnostic methods over time (diagnostic drift) may hamper the interpretation of secular trends in incidence. As an example, a transient increase in the observed rate of hospitalization with myocardial infarction in Denmark between 2000 and 2004 was likely attributable not to the true increase of occurrence but to new diagnostic criteria introduced in 2000, which included troponin as the main diagnostic biomarker.[170,215] Similar time-trend biases have been observed for the incidence of primary liver cancer[203] and advanced stages of lung cancer, the latter leading to an apparent improvement over time in stage-specific prognosis.[216]

Data access

The Danish Health and Medicines Authority has established guidelines for releasing data from the DNPR. Implementing the European Union Data Protection Directive (Directive 95/46/EC) on the protection of individuals with regard to the processing of personal data and on the free movement of such data, the Danish Act on Processing of Personal Data provides the legal basis for private and public institutions to obtain individually identifiable health data for research purposes.[217] This Act protects against abuse of such data and thus balances the privacy rights of individuals and the society's need for quality research. In order to access data from the DNPR, researchers have to apply to Research Service (Danish, Forskerservice).[26,218] Use of any health data also requires project-specific permission from the Danish Data Protection Agency,[217] and, in many cases, additional permission from the Danish Health and Medicines Authority to link data from various registries.[26] The Danish Data Protection Agency specifies safety precautions for data processing and also sets cancellation deadlines, ensuring that data traceable to individuals will not be stored longer than required to complete a project. As well, it is necessary to obtain permission from the Danish Health and Medicines Authority and the chief physician from relevant hospital departments to retrieve medical record files for validation of DNPR data.[219]

Conclusion

The DNPR is a valuable tool for epidemiological research, providing longitudinal registration of diagnoses, treatments, and examinations, with complete nationwide coverage since 1978. Denmark's constellation of universal health care, routine and long-standing registration of life and health events, and the possibility of exact individual-level linkage impart virtually unlimited research possibilities onto the DNPR. At the same time, varying completeness and validity of the individual variables underscore the need for validation of its clinical data before using the registry for research.

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Author contributions

MS conceived the study idea, designed the study, and wrote the initial draft. MS reviewed the literature on the registry content together with JLS; study examples together with HTS; and previous validation studies together with SAJS. HTS obtained data permissions and LP collected the data and carried out the descriptive analyses. All authors contributed to data analysis, drafting and critical revision of the paper, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

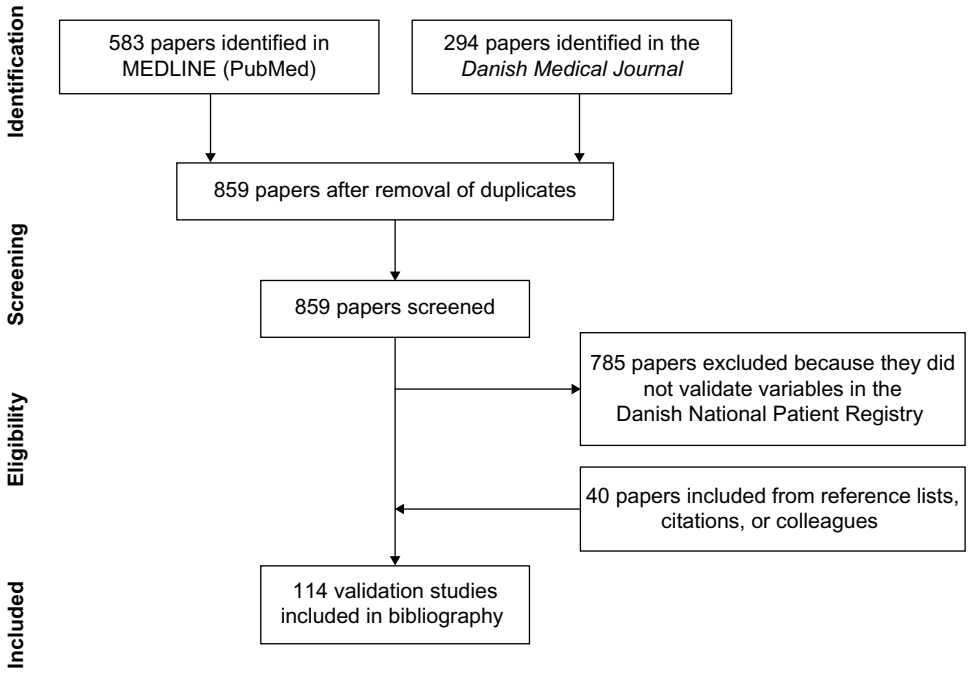

Figure S1 Flowchart for the systematic review of validation studies.
Notes: The literature search was performed on July 20, 2015 using the following search string in 1) PubMed: "Danish National Patient Registry" OR "Danish National Registry of Patients" OR "Danish National Hospital Register" OR "Danish National Health Registry" OR "Danish National Patient Register" OR "Danish Hospital Discharge Registry" OR "Danish National Hospital Registry" OR "Danish Hospital Registers"; and 2) the Danish Medical Journal: "Landspatientregisteret".

Table S1 Bibliography of validated administrative data, diagnoses, treatments, and examinations in the Danish National Patient Registry

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
Administrative data							
	Acute medical admission	2009 (IN)	Acute	127	PPV =97.6 (93.3–99.2); NPV =90.3 (75.1–96.7); Se =97.6 (93.3–99.2); Sp =90.3 (75.1–96.7)	MR	Vest-Hansen B et al. Clin Epidemiol. 2013[52]
	Nonacute medical admission	2009 (IN)	Nonacute	31	PPV =90.3 (75.1–96.7); NPV =97.6 (93.3–99.2); Se =90.3 (75.1–96.7); Sp =97.6 (93.3–99.2)	MR	Vest-Hansen B et al. Clin Epidemiol. 2013[52]
Diagnoses							
A00–B99: Certain infectious and parasitic diseases							
A02	Infections among patients diagnosed with cancer within previous 5 y (excl non-melanoma skin cancer)	2006–2010 (IN; A)	A02.1, A02.2C, A15–A19, A20.3, A22.7, A26.7, A42.7, A28.2B, A31, A32.1, A32.7, A39.0, A40–41, A46, A49.9, A54.8D, A54.8G, A87, B00.3, B01.0, B02.1, B26.1, B35–B49, B05.1, G00–G05, H01.0, H03, H60.0, H60.1–H60.3, H62, I33, I39.8, J12–J18, K12.2, K13.0, K61, L01, L03, L08, M00, M01.1, M01.3, M72.6, M86, N10–N12, N15.1, N15.9, N30, N34, N39.0	266	PPV =98.1 (95.7–99.2) overall, 80.1 (75.0–84.5) for agreement of specific infection type, 79.0 (63.7–88.9) for skin infection, 92.5 (85.3–96.3) for pneumonia, 84.4 (71.2–92.3) for sepsis	MR	Holland-Bill L et al. Ann Epidemiol. 2014[53]
A39	Meningococcal disease	1980–1993 (IN; A/B[e])	036.09, 036.10, 036.11, 036.12, 036.18, 036.19, 036.89, 036.99	296	PPV =85.8 (81.4–89.3); Se =89.8 (85.7–92.8)	MR (ref for PPV); Notification system for communicable diseases and DNPR (ref for Se)	Sørensen HT et al. Int J Risk Saf Med. 1995[54]
A40	Septicemia	1994 (IN; A/B[e])	A02.1, A28.2, A40–41, A42.7, A54.8, O08.0, O75.3, O85.9, P36	83	PPV =21.7 (14.2–31.7); Se =4.4 (2.8–6.9)	MR; Bacteremia database	Madsen KM et al. Infect Control Hosp Epidemiol. 1998[25]
	Bacteremia	2000–2011 (IN; A/B[e])	Definite (A02.1, A28.2B, A32.7, A39.2–4, A40–1, A42.7, A49.9A, B37.7, B49.9A) or possible (predominantly, A01.0, A39.0, A41.9, A46.9, I38.9, P36, P37.5, N10.9, N30.0, N39.0, O08.0U, O08.0V, KTJA40, KTJWC00, KTJL10)	37,740	$Se_{Definite/possible}$ =64.9 (64.5–65.3) $Se_{Definite}$ =32.3 (31.9–32.7)	Microbiology results recorded in electronic laboratory information system	Gradel KO et al. Plos One. 2015[55]
A41	Gram-negative bacteremia	1994–2012 (IN; A/B)	A41.5, A41.9B (septicemia/sepsis due to other Gram-negative organisms or urosepsis)	100	PPV_{All} =72.0 (62.5–79.9); $PPV_{A41.5}$ =85.7 (74.3–92.6); $PPV_{A41.9B}$ =54.6 (40.1–68.3)	Microbiology results recorded in electronic laboratory information system	Søgaard KK et al. Clin Epidemiol. 2014[56]
B18.0	HBV in HIV patients	1995–2004 (IN/OUT; A/B[e])	B18.0–B18.1	47	PPV =63.8 (49.5–76.0); Se =23.3 (16.8–31.3)	Danish HIV Cohort Study	Obel N et al. BMC Med Res Methodol. 2008[57]

(*Continued*)

Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
B18.2	HCV in HIV patients	1995–2004 (IN/OUT; A/B[e])	B18.2	134	PPV =94.0 (88.7–96.9); Se =47.7 (41.8–53.7)	Danish HIV Cohort Study	Obel N et al. BMC Med Res Methodol. 2008[57]
B20	HIV	1995–2004 (IN/OUT; A/B[e])	B20–B24	n/a (≥2006)	Se =98.7 (98.1–99.1)	Danish HIV Cohort Study	Obel N et al. BMC Med Res Methodol. 2008[57]
B21	AIDS	1998–2007 (IN/OUT; A)	B21–B24	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
C00–D48: Neoplasms							
C00–C75	Any tumor	1998–2007 (IN/OUT; A)	C00–C75	50	PPV =98.0 (89.4–99.9)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
		1977 (IN; A/B)	140–239 (excl brain tumors and non-melanoma skin cancer)	17,956	PPV =91.7 (91.3–92.1); Se =75.8 (75.2–76.3)	DCR	Osterlind A et al. Ugeskr Laeger. 1985[59]
C18	Colorectal cancer	2001–2006 (IN/OUT;[e] A/B[e])	C18–20	24,153	PPV =88.9 (88.5–89.3); Se =93.4 (93.1–93.7)	DCR	Helqvist L et al. Eur J Cancer Care. 2012[60]
	Colorectal cancer recurrences	2001–2011 (IN/OUT/ED;[e] A/B[e])	C76–C80, C18.9X, C20.9X, BWHA1–2, BOHJ17, BOHJ19B1 (algorithm combining metastasis and chemotherapy codes in the DNPR with cancer recurrence codes in the PD)	70	PPV =85.7 (75.7–92.1); NPV =99.0 (97.0–100); Se =95.2 (86.9–98.4); Sp =96.6 (93.8–98.1)	Actively followed cohort	Lash TL et al. Int J Cancer. 2014[61]
C51–58	Gynecological cancers	1977–1988 (IN; A/B[e])	180, 182.0, 183 (among women undergoing gynecological surgery)	614	PPV =89.9 (87.3–92.0); Se =94.7 (92.6–96.2)	MR	Kjaergaard J et al. J Epidemiol Biostat. 2001[62]
C53	Cervical cancer	1977–1988 (IN; A/B[e])	180 (among women undergoing gynecological surgery)	148	PPV =88.5 (82.4–92.7); Se =94.2 (89.1–97.1)	MR	Kjaergaard J et al. J Epidemiol Biostat. 2001[62]
C54–55	Uterus cancer	1977–1988 (IN; A/B[e])	182.00–182.09 (among women undergoing gynecological surgery)	261	PPV =90.4 (86.2–93.4); Se =92.9 (89.1–95.5)	MR	Kjaergaard J et al. J Epidemiol Biostat. 2001[62]
C56	Ovarian cancer	1977–1988 (IN; A/B[e])	183	205	PPV =90.2 (85.4–93.6); Se =97.4 (94.0–98.9)	MR	Kjaergaard J et al. J Epidemiol Biostat. 2001[62]
C61	Prostate cancer	1995–2012 (IN/OUT; A/B)	C61	240	PPV =98.3 (95.8–99.4)	MR (histologically-/biopsy-verified)	Drljevic A et al. Clin Epidemiol 2014[63]
C64	Urological cancer	2004–2009 (IN/OUT; A/B[e])	C64–68, D09.0–D09.1, D30.1–D30.9, D41.1–D41.9	41,129	PPV =86.6 (86.3–86.9); Se =94.9 (94.7–95.2)	DCR	Gammelager H et al. Eur J Cancer Prev 2012[64]
C76–80	Metastatic solid tumor	1998–2007 (IN/OUT; A)	C76–C80	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
C79.5	Bone metastases or skeletal-related events in patients with prostate (P) or breast (B) cancer	2000–2005 (n/a; n/a)	C79.5, BWGC1, M80.0, M84.4, M90.7, M43.9, 48.5, M54.5, M54.6, M54.9, G95.2, G95.8, KNAG (+ C61.9/C50)	27 P; 15 B	PPV_P =92.6 (76.6–97.9); NPV_P =71.2 (60.0–80.4); PPV_B =73.3 (48.1–89.1); NPV_B =90.6 (82.5–95.2); Se_P =54.4 (40.2–67.9); Sp_P =96.3 (87.5–99.0); Se_B =57.9 (36.3–76.9); Sp_B =95.1 (88.0–98.1)	MR	Jensen AØ et al. Clin Epidemiol. 2009[65]

C79.5	Bone metastases in patients with prostate cancer	2005–2010 (IN/OUT;[e] A/B[e])	C61 (from DCR) with prespecified PSA values, antiresorptive therapy, and bone scintigraphy, but without C77–C79	212	$PPV_{PSA>50\ \mu g/L}$=9.6 (4.7–18.5) and $NPV_{PSA<50\ \mu g/L}$=98.6 (94.9–99.6) regardless of receipt of antiresorptive therapy or presence of bone scintigraphy	MR	Ehrenstein V et al. Clin Epidemiol. 2015[66]
C81.0–96.9	Hematological cancer	1994–1999 (IN;[e] A[e])	C81.0–C96.9	1,075	PPV =84.5 (82.2–86.5); Se =91.5 (89.6–93.1)	DCR	Nørgaard M et al. Eur J Cancer Prev. 2005[67]
C81	Lymphoma	1998–2007 (IN/OUT; A)	C81–C85, C88, C90, C96	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
C81	Hodgkin's disease	1994–1999 (IN;[e] A[e])	C81.0–9	77	PPV =71.4 (60.5–80.3); Se =88.7 (78.5–94.4)	DCR	Nørgaard M et al. Eur J Cancer Prev. 2005[67]
C82	Non-Hodgkin's lymphoma or chronic lymphocytic leukemia	1994–1999 (IN;[e] A[e])	C82.0–85.9, C88.0–9, C91.1, C96.0–9	613	PPV =85.3 (82.3–87.9); Se =88.2 (85.3–90.6)	DCR	Nørgaard M et al. Eur J Cancer Prev. 2005[67]
C90	Multiple myeloma and other malignant plasma cell neoplasms	1994–1999 (IN;[e] A[e])	C90.0–2	158	PPV =82.3 (75.6–87.4); Se =90.9 (85.1–94.6)	DCR	Nørgaard M et al. Eur J Cancer Prev. 2005[67]
C91	Leukemia	1998–2007 (IN/OUT; A)	C91–C95	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
C92	Acute myeloid leukemia	1994–1999 (IN;[e] A[e])	C92.0	108	PPV =67.6 (58.3–75.7); Se =89.0 (80.4–94.1)	DCR	Nørgaard M et al. Eur J Cancer Prev. 2005[67]
D25	Uterine fibroma	1977–1988 (IN; A/B)	218.99 (among women undergoing gynecological surgery)	1,430	PPV =92.9 (91.4–94.1); NPV =88.9 (87.8–89.9); Se =77.4 (75.4–79.4); Sp =96.8 (96.2–97.4)	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
D27	Benign ovarian neoplasms	1977–1988 (IN; A/B)	220.99 (among women undergoing gynecological surgery)	743	PPV =78.2 (75.1–81.0); NPV =90.0 (89.1–90.9); Se =58.3 (55.2–61.3); Sp =95.9 (95.2–96.5)	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
D35.3	Craniopharyngioma	1985–2004 (IN/OUT;[e] A/B[e])	194.39, 226.21, 226.29, 253.99; D35.3, D44.4, C75.2	607	PPV =30.5 (27.0–34.3); Se =95.2 (77.3–99.2)	MR (for PPV)/Se with ref to North Jutland County registry and registries of a Danish neuroendocrine center	Nielsen EH et al. J Clin Epidemiol. 2011[69]
D47.2	Monoclonal gammopathy	2001–2011 (IN/OUT;[e] A/B[e])	D47.2	327	PPV =82.3 (77.8–86.0); Se =16.8 (14.4–19.6)	MR (for PPV); Se with ref to Regional monoclonal gammopathy database	Gregersen H et al. Clin Epidemiol. 2013[70]
D50–D89: Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism							
D35.0A	Pheochromocytoma	1977–1981 (IN; A/B)	255.29	230	PPV =19.1 (14.6–24.7)	MR	Andersen GS et al. Ugeskr Laeger. 1986[71]
D50.0	Anemia caused by bleeding	2000–2009 (IN/OUT; A/B[e])	D50.0, D62.6	3,391	PPV =95.4 (94.6–96.0)	LABKA	Zalfani J et al. Clin Epidemiol. 2012[72]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
D51	Anemia caused by B12 deficiency	2000–2009 (IN/OUT; A/B[e])	D51	1,089	PPV =36.8 (34.0–39.7)	LABKA	Ghezala IB et al. Clin Epidemiol. 2012[73]
D69	Chronic idiopathic thrombocytopenic purpura	1996–2007 (IN/OUT;[e] A/B[e])	D69 (>1 diagnosis >6 mo)	439	PPV =93.4 (90.7–95.4)	MR	Heden KEK et al. Clin Epidemiol. 2009[74]
E00–E90: Endocrine, nutritional and metabolic diseases							
E10	Diabetes mellitus	1998–2007 (IN/OUT; A)	E10.0, E10.1, E10.9, E11.0, E11.1, E11.9	50	PPV =96.0 (86.5–98.9)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
		1999–2003 (IN/OUT;[e] A/B[e])	E10–13, H36.0, O24, except O24.4	n/a	PPV =64;[f] Se =97[f]	GP verification	Kristensen JK et al. Ugeskr Laeger. 2007[75]
		1992–2001 (IN/OUT/ED;[e] A/B[e])	249–250, E10–E11 (and/or a prescription for insulin or an oral antidiabetes drug)	65	PPV =96.9 (89.5–99.2)	MR, LABKA	Thomsen RW et al. Diabetes Care. 2004[76]
	Diabetes in women	1977–2006[e] (IN/OUT;[e] A[e])	249; E10	40	PPV =95.0 (83.5–98.6)[e]	MR	Atladottir HO et al. Pediatrics. 2009[77]
	Diabetes in children	1996–2002 (A;[e] A/B)	E10–14 (age ≤15 y)	1,479	PPV =95.9 (94.8–96.8); NPV =100 (100–100);[g] Se =97.9 (97.1–98.6); Sp =100 (100–100)[g]	MR; Danish registry for child and adolescent diabetes	Svensson J et al. Ugeskr laeger. 2007[78]
	Type 1 diabetes mellitus	1996–2002 (IN;[e] A/B)	E10–14	1,479	PPV =94.3 (93.0–95.4); NPV =100 (100–100);[g] Se =98.0 (97.1–98.6); Sp =100 (100–100)[g]	MR; Danish registry for child and adolescent diabetes	Svensson J et al. Ugeskr laeger. 2007[78]
		1987–1993 (IN; A/B)	249	1,722	PPV =96.3 (95.4–97.1); Se =91.0 (89.6–92.2)	MR; PR	Nielsen GL et al. J Med Syst. 1996[79]
E10.2	Diabetes mellitus with chronic complications	1998–2007 (IN/OUT; A)	E10.2–E10.8, E11.2–E11.8	50	PPV =82.0 (69.2–90.2)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
E22.0	Acromegaly	1991–2009 (IN/OUT/ED;[e] A/B[e])	253.00, 253.01; E22.0	275	PPV =54.2 (48.3–60.0); $PPV_{Dep\ of\ endocrinology}$=66.7 (60.0–72.7)	MR	Dal J et al. Clin Epidemiol. 2014[80]
E282	Polycystic ovarian syndrome	1977–1988 (IN; A/B)	256.90 (among women undergoing gynecological surgery)	14	PPV =85.7 (60.1–96.0); NPV =99.9 (99.8–100); Se =70.6 (46.9–86.7); Sp =100 (99.9–100)	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
E26.0	Primary hyperaldosteronism	1977–1981 (IN; A/B)	255.00 (Conn's syndrome)	85	PPV =22.4 (14.8–32.3)	MR	Lund JO et al. Ugeskr Laeger. 1986[81]
E41	Undernutrition	2002–2011 (IN;[e] A/B[e])	E12, E41–44, E46–47, E64, Z03.8F (age ≥15 y)	172	$PPV_{Definite}$=11.1 (7.2–16.6) $PPV_{Definite/probable}$=70.9 (63.8–77.2)	MR	Rasmussen NH et al. *Clin Nutr*. 2015[82]
E87	Hyponatremia	2006–2011 (IN; A/B)	E87.1, E87.1A, P74.2B	5,850	PPV =92.5 (91.8–93.1); NPV =86.2 (86.2–86.2); Se =1.8 (1.7–1.8); Sp =100 (100–100)[g]	LABKA	Holland-Bill L et al. BMJ Open. 2014[83]

F00–F99: Mental and behavioral disorders							
F00	Dementia	1998–2007 (IN/OUT; A)	F00–F03, F05.1, G30	50	PPV =98.0 (89.5–99.7)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
		2003 (IN/OUT; A/B)	F00.0–F00.2, F00.9, G30.0–G30.1, G30.8–G30.9, F01.0–F01.3, F01.8–F01.9, F02.0, F03.9	197	PPV =85.8 (80.2–90.0) overall, 81.0 (69.2–89.1) for Alzheimer dementia, 18.5 (8.2–36.7) for vascular dementia	MR; patient interview	Phung TKT et al. Dement Geriatr Cogn Disord. 2007[84]
G00–G99: Diseases of the nervous system							
G12.2	Amyotrophic lateral sclerosis	1982–2009 (IN/OUT;[e] A/B[e])	348.0, G12.2 (age >19 y)	173	$PPV_{definite}$ =69.9 (62.7–76.3); $PPV_{definite/probable}$ =77.5 (70.7–83.1); $PPV_{definite/probable/suspected}$ =92.5 (87.6–95.6)	MR	Kioumourtzoglou MA et al. Amyotroph Lateral Scler Frontotemporal Degener. 2015[85]
G20	Parkinson's disease	1996–2006 (IN/OUT; A)	342, G20	1,040	PPV =82.4 (80.0–84.6)	MR	Wermuth L et al. Dan Med J 2012[86]
		2002–2006 (IN/OUT;[e] A[e])	G20 (age ≥35 y)	2,572	PPV =91.5 (90.3–92.5)	PR	Rugbjerg K et al. BMJ. 2008[87]
	Parkinson's disease (women)	1996–2009 (IN/OUT;[e] A[e])	G20[e] (neurology wards only)	923	PPV =80.5 (77.8–82.9)	MR	Greene N et al. Eur J Neurol. 2014[88]
G35.9	Multiple sclerosis treated at Department of Neurology or MS rehabilitation center	1994–2004 (IN/OUT; A/B)	G35.9	4,185	PPV =95.1 (94.3–95.8);[f] $PPV_{neurol\ dep}$ =96.3 (95.7–96.9); Se =92.8 (91.9–93.6);[f] $Se_{neurol\ dep}$ =86.9 (85.7–88.0)	Danish Multiple Sclerosis Registry	Mason K et al. Acta Neurol Scand. 2012[89]
G40	Epilepsy	1977–2002 (IN/OUT; A/B[e])	345, G40–41	188	PPV =81.4 (75.2–86.3)	MR	Christensen J et al. Epilepsy Res. 2007[90]
G45	Transient ischemic attack	1998–1999 (IN;[e] A/B[e])	G45	38	PPV =57.9 (42.2–72.2) to 68.4 (52.5–80.9)	MR; DS; CT/MRI; autopsy reports; angiography reports	Krarup LH. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	G45	134	PPV =60.5 (52.0–68.3)	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]
G81	Hemiplegia	1998–2007 (IN/OUT; A)	G81, G82	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
H00–H95: Diseases of the eye, adnexa, ear, and mastoid process							
H71	Cholesteatoma	1977–2007 (IN; A)	387.09; H71, H95.0, Q16.4A + surgery codes (see these below under KDC)	262	PPV =89.3 (85.0–92.5); Se =89.3 (84.7–92.6)	Surgical records	Djurhuus BD et al. Dan Med Bull. 2010[93]
I00–I99: Diseases of the circulatory system							
I10.9	Essential hypertension in males	1977–2010 (IN/OUT; A/B)	400–404; I10–I15	524	PPV =88.2 (85.4–90.9)	PR	Schmidt M et al. BMJ Open. 2013[94]
	Essential hypertension	1983–1990 (IN; A)	401.99	310	PPV =40 (26–55) to 60 (49–70)[f]	MR	Nielsen HW et al. Ugeskr Læger. 1996[95]
I20.0	Acute coronary syndrome	1993–2003 (IN/OUT/ED; A/B[e])	410, 427.27; I20.0, I21, I46	1,558	$PPV_{IN/OUT/ED}$ =65.5 (63.1–67.9); PPV_{IN} =80.1 (77.7–82.3)	MR; DS; blood tests, ECG	Joensen AM et al. J Clin Epidemiol. 2009[96]
I20.0	Unstable angina	1993–2003 (IN/OUT/ED; A/B[e])	I20.0	444	$PPV_{IN/OUT/ED}$ =27.5 (23.5–31.8); PPV_{IN} =42.0 (36.0–48.0)	MR; DS; blood tests, ECG	Joensen AM et al. J Clin Epidemiol. 2009[96]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
I21	Acute myocardial infarction	1996–2009 (IN;[e] A)	I21	148	PPV =100 (97.5–100)	MR	Coloma PM et al. BMJ Open. 2013[97]
		1998–2007 (IN/OUT; A)	I21, I22, I23	50	PPV =98.0 (89.5–99.7)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
		1993–2003 (IN/OUT/ED; A/B[e])	410; I21	1,072	$PPV_{IN/OUT/ED}$ =81.9 (79.5–84.1); $PPV_{IN; A/B}$ =92.4 (90.4–93.9); $PPV_{IN; A}$ =94.4 (92.6–95.7)	MR; DS; blood tests, ECG	Joensen AM et al. J Clin Epidemiol. 2009[96,98]
		1982–1991 (IN; A/B)	410, 427.24, 427.27, 427.91, 427.97	5,022	PPV_A =94.3 (93.6–94.9); PPV_{A+B} =93.4 (92.6–94.0); Se_A =62.8 (61.7–64.0); Se_{A+B} =69.5 (68.4–70.6)	DANMONICA definite or possible cases incl cardiac arrest	Madsen M et al. J Clin Epidemiol. 2003[99]
		1979–1980 (IN; A/B)	410–414	527	PPV =92.4 (89.8–94.4)	DS	Madsen M et al. Ugeskr laeger. 1990[100]
I26	PE	1994–2006 (IN/OUT/ED; A/B)	450.99; I26	353	PPV_{All} =67.4 (62.4–72.1); $PPV_{IN/OUT}$ =82.1 (77.2–86.1); PPV_{ED} =29.6 (22.0–38.5); PPV_A =87.0 (81.9–90.9)	MR; DS; blood tests; ultrasound; venography; echo; V-P lung scan; CT scan	Severinsen MT et al. J Clin Epidemiol. 2010[101]
	PE during pregnancy and postpartum	1980–2001 (IN;[e] A[e])	450.00–450.99; I26.0–I26.9 + (650–666; O80–84)	22	$PPV_{preg+postpartum}$ =81.8 (59.7–94.8);[f] PPV_{preg} =63.6 (40.7–82.8)[f]	MR	Larsen TB et al. J Clin Epidemiol. 2005[102]
	PE after stroke	2003–2006 (IN; A/B)	I26 (after admission to stroke units and age ≥18 y)	11	PPV =90.9 (62.3–98.4); NPV =97.4 (95.8–98.4); Se =0.0 (0.0–32–4); Sp =100 (99.3–100)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
I46	Cardiac arrest	1993–2003 (IN/OUT/ED; A/B[e])	427.27; I46	42	$PPV_{IN/OUT/ED}$ =50.0 (35.5–64.5); PPV_{IN} =53.1 (36.5–69.1)	MR; DS; blood tests, ECG	Joensen AM et al. J Clin Epidemiol. 2009[96]
I48	Atrial fibrillation or flutter	1993–2009 (IN/OUT/ED; A/B)	427.93, 427.94; I48	284	PPV_{All} =92.3 (88.6–94.8); $PPV_{IN/OUT}$ =94.0 (90.5–96.3) (independent of diagnosis type and department specialty); PPV_{ED} =64.7 (41.3–82.7)	MR + heart rhythm documentation	Rix TA et al. Scand Cardiovasc J. 2012[104]
		1980–2002 (n/a; n/a)	427.93, 427.94; I48	174	PPV =98.9 (95.9–99.7)	MR + heart rhythm documentation	Frost L et al. Am J Med. 2007[105]
		1980–2002 (n/a; n/a)	427.93, 427.94; I48	116	PPV =96.6 (91.5–98.7)	MR + heart rhythm documentation	Frost L et al. Arch Intern Med. 2004[106]
I48.9A	Atrial flutter	1977–1999 (IN/OUT/ED; A/B)	427.94; I48.9A	108	PPV =50.0 (40.7–59.3)	MR + heart rhythm documentation	Rix TA et al. Scand Cardiovasc J. 2012[104]
I50	Heart failure	1998–2007 (IN/OUT; A)	I50, I11.0, I13.0, I13.2	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]

	Heart failure at University Hospital cardiac care unit	2005–2007 (IN/OUT; A/B)	I11.0, I13.0, I13.2, I42.0, I42.6–9, I50.0–I50.1, I50.9	758	$PPV_{Overall}$= 84.0 (81.3–86.5); $PPV_{First\text{-}time\ events}$= 77.9 (74.1–81.6)[f]	MR	Mard S et al. Clin Epidemiol. 2010[107]
		1998–1999 (IN; A/B)	I50	156	PPV =80.8 (73.9–86.2); NPV =90.1 (88.9–91.2); Sp =98.9 (98.5–99.2); Se =29.4 (25.3–33.9)	Clinical examination	Kümler T et al. Eur J Heart Fail. 2008[108]
I60–I69	Cerebrovascular disease	1998–2007 (IN/OUT; A)	I60–I69, G45–G46	50	PPV =94.0 (83.8–97.9)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
		1998–1999 (IN;[e] A/B[e])	I60–I69, G45	236	PPV =78.4 (72.7–83.2) to 80.1 (74.5–84.7)	MR; DS	Krarup LH et al. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	I60–I69.8, G45	565	PPV =68.5 (64.6–72.2)	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]
I60–I64	Stroke	1980–2002 (n/a; A/B)	430–434, 436; I60–I64 following a diagnosis of atrial fibrillation/flutter	164	PPV =97.0 (93.1–98.7)	MR	Frost L et al. Am J Med. 2007[105]
		2010 (IN; A)	I61, I63–I64 admitted to neurologic wards	46	PPV =93.5 (82.5–97.8); NPV =71.8 (62.8–79.4); Se =58.1 (46.7–68.7); Sp =96.3 (89.8–98.8)	MR including MRI and CT scan (for PPV). Other neurologic disorders were included to assess Se, Sp, and NPV	Wildenschild K et al. Clin Epidemiol. 2013[109]
		1998–1999 (IN;[e] A/B[e])	I60–I64	164	PPV =80.5 (73.8–85.8) to 86.0 (79.8–90.5)	MR; DS	Krarup LH et al. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	I60–I64	377	PPV =79.3 (74.9–83.1)	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]
	Stroke complications	2003–2006 (IN; A/B)	J12–J18, N30.0, N30.8, N30.9, N10, L899, R297, EUHE, I82.9A-E, I26, K590 (after admission to stroke units and age ≥18 y)	88	PPV =76.1 (66.3–83.8); NPV =85.1 (83.9–86.1); Se =7.7 (5.8–10.3); Sp =99.5 (99.2–99.7)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
I60	Subarachnoid hemorrhage	1998–1999 (IN;[e] A/B[e])	I61	3	PPV =66.7 (20.8–93.9)	MR; DS	Krarup LH et al. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	I61	29	PPV =48.3 (31.4–65.6)	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]
		1977–1995 (IN;[e] A/B[e])	430; I60	191	$PPV_{neurosurgery\ wards}$=93 (85–98);[f] $PPV_{neurology\ wards}$=75 (60–87);[f] $PPV_{non\text{-}specialty\ wards}$=47 (36–59)[f]	MR; DS; autopsy reports	Gaist D et al. BMJ. 2000[110]
I61	Intracerebral hemorrhage	1998–1999 (IN;[e] A/B[e])	I60	23	PPV =73.9 (53.5–87.5)	MR; DS	Krarup LH et al. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	I60	35	PPV =65.7 (49.2–79.2)	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
I63	Ischemic stroke	1998–1999 (IN;[e] A/B[e])	I63	33	PPV =97.0 (84.7–99.5) to 100 (89.6–100)	MR; DS	Krarup LH et al. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	I63	113	PPV =87.6 (80.3–92.5)	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]
	Pediatric arterial thrombosis (0–18 y)	1994–2006 (IN/OUT/ED;[e] A/B)	I63–I64, H34.1–H34.2, I74, N28.0A, N28.0D, I21	472	PPV_{all}=53.6 (49.1–58.1); PPV_{ED}=7.3 (2.5–19.4); PPV_{ward}=58.0 (53.3–62.6); $PPV_{neonates}$=75.3 (64.9–83.4)	MR; lab tests; ECG; radiology reports	Tuckuviene R et al. Clin Epidemiol. 2010[111]
I64	Unspecified stroke	1998–1999 (IN;[e] A/B[e])	I64	105	PPV =72.4 (63.2–80.0) to 80.0 (71.4–86.5) for unspecified stroke confirmed as being any stroke	MR; DS	Krarup LH et al. Neuroepidemiology. 2007[91]
		1994–1999[e] (IN/OUT/ED; A/B[e])	I64	200	PPV =76.0 (69.6–81.4) for unspecified stroke confirmed as being any stroke	MR; DS	Johnsen SP et al. J Clin Epidemiol. 2002[92]
I70	Peripheral vascular disease	1998–2007 (IN/OUT; A)	I70–I74, I77	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
I80.0	Superficial thrombophlebitis during pregnancy/d postpartum	1980–2001 (IN;[e] A[e])	451.01, 451.91; I800 + (650–666; O80–84)	125	$PPV_{preg+postpartum}$=89.6 (84.3–95.0);[f] PPV_{preg}= 88.0 (81.0–82.8)[f]	MR	Larsen TB et al. J Clin Epidemiol. 2005[102]
I80.1–3	DVT	1994–2006 (IN/OUT/ED; A/B)	451.00, 451.08, 451.09, 451.99; I80.1–I80.9	742	PPV_{All}=54.6 (51.0–58.1); $PPV_{IN/OUT}$=71.3 (67.4–74.9); PPV_{ED}=31.9 (27.1–37.0); PPV_{A}=72.4 (68.2–76.2)	MR; DS; blood tests; ultrasound; venography; echo; V-P lung scan; CT scan	Severinsen MT et al. J Clin Epidemiol. 2010[101]
	DVT during pregnancy and postpartum	1980–2001 (IN;[e] A[e])	451.00, 451.08–451.09, 451.90, 451.92, 451.99; I80.1–I80.9 + (650–666; O80–84)	153	$PPV_{preg+postpartum}$=86.3 (79.8–91.3);[f] PPV_{preg}=74.5 (66.8–81.2)[f]	MR	Larsen TB et al. J Clin Epidemiol. 2005[102]
	DVT after stroke	2003–2006 (IN; A/B)	I82.9 (after admission to stroke units and age ≥18 y)	8	PPV =87.5 (52.9–97.8); NPV =97.1 (95.4–98.2); Se =16.7 (3.0–56.4); Sp =100 (99.3–100)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
I80.1–3+ I26	VTE	1994–2006 (IN/OUT/ED; A/B)	450.99, 451.00, 451.08, 451.09, 451.99; I26, I80.1–I80.9	1,100	PPV_{All}=58.5 (55.5–61.3); $PPV_{IN/OUT}$=75.0 (71.9–77.8); PPV_{ED}=31.3 (27.2–35.7); PPV_{A}=77.0 (73.7–80.0)	MR; DS; blood tests; ultrasound; venography; echo; V-P lung scan; CT scan	Severinsen MT et al. J Clin Epidemiol. 2010[101]
		2004–2012 (IN/OUT; A/B)	I80.1–3, I26 + AC prescription ≤30 d after	20	PPV =90.0 (69.9–97.2)	MR	Schmidt M et al. J Thromb Haemost. 2014[112]

	Pediatric VTE (0–18 y)	1994–2006 (IN/OUT/ED;[e] A/B)	I67.6, I63.6, G0.8, H34.8, I26, I80.1–I80.9, I81–I82, O22.5A, O87.3, O22.3, O22.8–O22.9, O87A–O87F, O87.1	640	PPV_{all} =53.9 (50.0–57.7); PPV_{ED} =7.4 (4.1–13.1); PPV_{ward} =66.3 (62.1–70.3); $PPV_{neonates}$ =82.4 (66.5–91.7)	MR	Tuckuviene R et al. Clin Epidemiol. 2010[111]
	VTE in non-pregnant women 15–49 y	2001–2009 (IN/OUT;[e] A/B[e])	438, 450, 451.00, 451.08, 451.99, 453.02; I26, I67.6, I80.1–I80.3, I82.2–I82.3, I82.8–I82.9	200	PPV =76.0 (69.6–81.4); PPV_{+AC} =99[f]	MR; ultrasound; phlebography; CT; scintigraphy	Lidegaard O et al. BMJ. 2011[113]
	VTE during pregnancy and postpartum	1980–2001 (IN;[e] A[e])	450.00–450.99, 451.00–451.99; I26.0–I26.9, I80.0–I80.9 + (650–666, O80–84)	304	$PPV_{preg+postpartum}$ =87.3 (83.0–90.9);[f] PPV_{preg} =79.3 (74.3–83.8)[f]	MR	Larsen TB et al. J Clin Epidemiol. 2005[102]
	VTE recurrence	2004–2012 (IN/OUT; A/B)	I80.1–3, I26 (>3 mo after first–time diagnosis) + ultrasound/CT scan during admission or AC prescription ≤30 d after	90	$PPV_{IN/OUT, A/B, scan}$ =27.5 (16.1–42.8); $PPV_{IN/OUT,A/B,AC\ use}$ =30.2 (18.6–45.1); $PPV_{IN, A/B, scan}$ =79.0 (56.7–91.5); $PPV_{IN, A/B, AC\ use}$ =56.5 (36.8–74.4)	MR	Schmidt M et al. J Thromb Haemost. 2014[112]
	VTE in prostate cancer patients	1995–2012 (IN/OUT; A/B)	I26, I80.1–3 (+ C61)	115	PPV =86.1 (78.6–91.3); NPV =98.3 (94.0–99.5); Se =98.0 (93.1–99.5); Sp =87.8 (81.1–92.3)	MR; VTE diagnostics	Drljevic A et al. Clin Epidemiol 2014[63]
J00–J99: Diseases of the respiratory system							
J12	Respiratory syncytial virus infections	1996–2003 (IN; A/B)	J12.1, J20.5, J21.0, B97.4	10,983	PPV =92.1 (91.5–92.6); NPV =83.8 (83.4–94.2); Se =67.9 (67.1–68.6); Sp =96.6 (96.4–96.8)	MR; RSV Laboratory database	Stensballe LG et al. Scand J Infect Dis. 2005[114]
J12	Pneumonia after stroke	2003–2006 (IN; A/B)	J12–J18 after (admission to stroke unit and age ≥18 y)	14	PPV =92.9 (68.5–98.7); NPV =63.3 (59.3–67.1); Se =6.0 (3.5–10.1); Sp =99.7 (98.5–100)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
J40	Chronic pulmonary disease	1998–2007 (IN/OUT; A)	J40–J47, J60–J67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
J44	COPD exacerbation	2008 (IN; A/B)	$J44_A$, $J96_A$, $J13_A$–$J18_A$ + $J44_B$ (age ≥30 y)	1,581	PPV =92.1 (90.7–93.3); NPV_{COPD} for related respiratory conditions =80.6 (78.5–82.5)	MR; 1,546 acute hospitalizations for J96 or J13–18 without J44 as B-diagnosis used to obtain NPV	Thomsen RW et al. Respir Med. 2011[115]
J45	Asthma history reported by male conscripts	1977–2003 (IN/OUT/ED; A/B[e])	493; J45	925	PPV =65.3 (62.2–68.3); NPV =96.5 (96.2–96.7); Se =44.5 (41.9–47.1); Sp =98.5 (98.3–98.6)	Conscription database	Jensen AO et al. Clin Epidemiol. 2010[116]
J45	Asthma in children	2002 (IN; A)	J45, J46.9 (age 6–14 y)	319	PPV =84.6 (80.3–88.2); NPV =99.4 (99.1–99.6); Se =90.0 (86.1–92.9); Sp =99.4 (99.1–99.6)	MR; All acute admissions were assessed to yield Se, Sp, and NPV	Moth G et al. Acta Paediatr. 2007[117]
J86.0	Pleural empyema	1995–2009 (IN; A/B)	510; J86.0, J86.9	224	PPV =90.6 (86.1–93.8)	MR; lab tests; radiology reports	Søgaard M et al. Clin Epidemiol 2011[118]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
K00–K93: Diseases of the digestive system							
K25	Ulcer disease	1998–2007 (IN/OUT; A)	K22.1, K25–K28	50	PPV =98.0 (89.5–99.7)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
		1997–2001 (n/a; n/a)	531–534, K25–K28	200	$PPV_{Overall}$ =84.5 (78.8–88.7); $PPV_{bleeding\ ulcer}$ =93.0 (84.6–97.0); $PPV_{uncomplicated\ ulcer}$ =72.7 (64.4–79.6)	MR	Lassen A et al. Am J Gastroenterol. 2006[119]
K50	Crohn's disease	1988–1992 (IN; A/B[e])	563.01	281	PPV =97.2 (94.5–98.6); Se =94.4 (89.4–97.1)	MR and PD for PPV; PD for Se	Fonager K et al. Scand J Gastroenterol. 1996[120]
K51	Ulcerative colitis	1988–1992 (IN; A/B[e])	563.19, 569.04	506	PPV =90.3 (87.4–92.6); Se =93.7 (90.2–96.0)	MR and PD for PPV; PD for Se	Fonager K et al. Scand J Gastroenterol. 1996[120]
K59.0	Constipation after stroke	2003–2006 (IN; A/B)	K59.0 (after admission to stroke units and age ≥18 y)	7	PPV =42.9 (15.8–75.0); NPV =84.7 (81.6–87.4); Se =3.9 (1.3–10.8); Sp =99.4 (98.2–99.8)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
K70	Mild liver disease	1998–2007 (IN/OUT; A)	B18, K70.0–K70.3, K70.9, K71, K73–K74, K76.0	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
K70	Liver cirrhosis	1985–1989 (IN; A/B[e])	571.09, 571.90–571.92, 571.99	198	PPV =85.4 (79.8–89.6); Se =93.2 (85.9–96.8)	MR and PD for PPV; PD for Se only	Vestberg K. J Med Syst. 1997[121]
K70.3	Alcoholic cirrhosis	1997–2005 (IN/OUT/ED;[e] A/B)[e]	571.09; K70.3 (+ a liver biopsy during that hospital contact: SNOMED codes T56xxx)	516	PPV =77.7 (73.9–81.1)	PD	Jepsen P et al. BMC Gastroenterol. 2008[122]
K72	Moderate/severe liver disease	1998–2007 (IN/OUT; A)	B15.0, B16.0, B16.2, B19.0, K70.4, K72, K76.6, I85	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
K572–K579	Diverticular disease	1999–2008 (IN/OUT; A/B[e])	K572–K579	100	PPV =98.0 (93.0–99.5)	Discharge summary/ outpatient notes	Erichsen R et al. Clin Exp Gastroenterol. 2010[123]
K859	Acute pancreatitis	1981–2000 (IN;[e] A/B[e])	577.00–577.09; K85.9	99	$PPV_{1981–2000}$ =82 (72.8–88.9)[f] $PPV_{1997–1999}$ =91 (83.0–96.0)[f]	MR	Floyd A et al. Scand J Gastroenterol. 2002[124]
L00–L99: Diseases of the skin and subcutaneous tissue							
L89.9	Decubitus after stroke	2003–2006 (IN; A/B)	L89.9 (after admission to stroke units and age ≥18 y)	8	PPV =50.0 (21.5–78.5); NPV =96.6 (94.7–97.8); Se =18.2 (5.1–47–7); Sp =99.5 (98.4–99.8)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
M00–M99: Diseases of the musculoskeletal system and connective tissue							
M00	Septic arthritis after knee arthroscopy	1998–2000 or 2003–2005 (IN; n/a)	M00, T81.4, T81.8–T81.9 (+ KNGA, KNGD, KNGE, KNGF, or KNGH)	450	Se =66.9 (59.2–73.8)	Danish Patient Insurance Association	Majholm B et al. Dan Med J. 2012[125]
M05	Rheumatoid arthritis (women)	1977–2006[e] (IN/OUT;[e] A[e])	712.19, 712.39, 712.59; M05, M06	40	PPV =75.0 (59.8–85.8)[e]	MR	Atladottir HO et al. Pediatrics. 2009[77]

	Rheumatoid arthritis	1977–2001 (IN/OUT; A/B)	712.19, 712.39, 712.59; M05–M06 (except M06.1) (age >15 y)	217	PPV =59.0 (52.3–65.3), higher for rheumatology departments and inpatient admissions; Se =26.4 (17.6–37.6)	PPV using MR/Se using MR-confirmed self-reported cases in the Danish Nationwide Twin Population cohort	Pedersen M et al. Eur J Epidemiol 2004[126]
M05	Connective tissue disease	1998–2007 (IN/OUT; A)	M05–M06, M08–M09, M30–M36, D86	50	PPV =98.0 (89.5–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
	Connective tissue disease following breast implant	1977–1993 (IN; A/B)	712.09–712.39, 712.59, 716.09, 716.19, 734.00–734.09, 734.19, 734.90	35	$PPV_{Definite}$ =82.9 (67.3–91.9)	MR	Friis S et al. Ann Plast Surg. 1997[127]
M510	Lumbar disc prolapse	1990–1991 (IN; A)	725.11	98	PPV =90[f]	MR	Jensen MV et al. Ugeskr laeger. 1995[128]
M87	Osteonecrosis of the jaw in postmenopausal osteoporosis	2005–2010 (IN/OUT;[e] A/B[e])	K04.6, K10.2, K10.3, M87	60	PPV =31.7 (21.3–44.2)	MR	Gammelager H et al. Clin Epidemiol. 2013[129]
	Osteonecrosis of the jaw among cancer patients	2005–2009 (IN/OUT;[e] A/B[e])	K04.6, K10.2–K10.3 (except K10.2E–F), M87 + prior C00–C97 (except C44)	91	PPV =19.8 (12.9–29.1)	MR	Gammelager H et al. Cancer Epidemiol. 2012[130]
	Osteonecrosis of the jaw in patients with cancer diagnosed within 5 y	2005–2010[e] (IN/OUT;[e] A/B[e])	K04.6, K10.2, K10.3, M87 + prior C15–C29, C33–C43, C45–C97 (excl head and neck cancers and non-melanoma skin cancer) + departments of oral and maxillofacial surgeries	197	PPV =42.1 (35.5–49.1); Se =73.3 (63.9–80.9)	MR	Ehrenstein V et al. Pharmacoepidemiol Drug Saf. 2014[131]
N00–N99: Diseases of the genitourinary system							
N00	Moderate to severe renal Disease	1998–2007 (IN/OUT; A)	112, 113, N00–N05, N07, N11, N14, N17–N19, Q61	50	PPV =100 (92.9–100)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
N30.0	Urinary infection after stroke	2003–2006 (IN; A/B)	N30.0, N30.8, N30.9, N10 (after admission to stroke units and age ≥18 y)	39	PPV =76.9 (61.7–87.4); NPV =70.9 (67.0–74.6); Se =14.3 (9.8–20.4); Sp =98.0 (96.1–99.0)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
N80	Endometriosis	1977–1988 (IN; A/B)	625.3 (among women undergoing gynecological surgery)	427	PPV =95.1 (92.6–96.8); NPV =89.3 (88.4–90.2); Se =45.8 (42.6–49.1); Sp =99.5 (99.2–99.7)	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
N830–N832	Ovarian cysts	1977–1988 (IN; A/B)	615.2	601	PPV =75.5 (72.0–78.8); NPV =87.2 (86.2–88.2); Se =45.1 (42.1–48.2); Sp =96.2 (95.6–96.8)	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
N91–N94	Bleeding disorders	1977–1988 (IN; A/B)	626 (among women undergoing gynecological surgery)	986	PPV =93.9 (92.3–95.2); NPV =95.2 (94.5–95.8); Se =83.0 (80.7–85.1); Sp =98.4 (98.0–98.8)	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
O00–O99: Pregnancy, childbirth and puerperium							
O021–03	Abortion	1984 (IN; A/B[e])	642, 644, and 631, 643, 645 if also registered in Register of Legally Induced Abortions within +/− 90 days	359	PPV =46–69 for confirmation on four-digit level	DS	Schmidt L et al. Ugeskr laeger. 1989[132]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
	Spontaneous abortion	1980–2008 (IN/OUT/ED;[e] A[e])	634.6, 645.1, 643.8, 643.9; O02.1A, O03	117	PPV_{All} =97.4 (92.7–99.1)	DS	Lohse SR et al. Clin Epidemiol. 2010[133]
O04–06	Provoked abortion	1994 (IN;[e] A/B[e])	O04–06	17,764	PPV =93.5 (93.2–93.9); Se =97.0 (96.8–97.3)	Register of Legally Induced Abortions	Krebs L et al. Ugeskr laeger. 1997[32]
O139	Gestational hypertension	1998–2000 (IN/OUT; A/B[e])	O13.9	3,039	PPV =56.3 (33.2–76.9); NPV =97.3 (96.7–97.8); Se =10.0 (5.4–17.9); Sp =99.8 (99.5–99.9)	MR	Klemmensen ÅK et al. Am J Epidemiol. 2007[134]
O139	Hypertensive disorders of pregnancy	1998–2000 (IN/OUT; A/B[e])	O13.9–O14.1–O14.2, O14.9–O15.0	3,039	PPV =88.8 (81.0–93.6); NPV =96.9 (96.2–97.5); Se =48.9 (41.6–56.2); Sp =99.6 (99.3–99.8)	MR	Klemmensen ÅK et al. Am J Epidemiol. 2007[134]
		1982–1987 (IN; A/B[e])	n/a	112	PPV =70;[f] NPV =98;[f] Se =75[f]	MR	Kristensen J et al. J Clin Epidemiol 1996[135]
O14	Preeclampsia	1998–2000 (IN/OUT; A/B[e])	O14.0–O14.2, O14.9–O15.0	3,039	PPV =74.4 (64.0–82.6); NPV =99.1 (98.7–99.4); Se =69.3 (59.0–78.0); Sp =99.3 (98.9–99.5)	MR	Klemmensen ÅK et al. Am J Epidemiol. 2007[134]
		2001 (IN; A/B[e])	O13–14	39	PPV =69.2 (53.6–81.4); NPV =98.6 (97.7–99.2); Se =64.3 (49.2–77.0); Sp =98.9 (98.1–99.4)	MR	Langhoff-Ross J et al. 2003[136]
O24	Gestational diabetes	2001 (IN; A/B[e])	O24	21	PPV =100 (84.5–100); NPV =99.7 (99.2–99.9); Se =87.5 (69.0–95.7); Sp =100 (99.7–100)	MR	Langhoff-Ross J et al. 2003[136]
O32	Malpresentation of fetus	2001 (IN; A/B[e])	O32	37	PPV =48.7 (33.5–64.1); NPV =99.3 (98.6–99.6); Se =69.2 (50.0–83.5); Sp =98.3 (97.3–98.9)	MR	Langhoff-Ross J et al. 2003[136]
O342	Previous cesarean section	2001 (IN; A/B[e])	O34.2, Z35.8E	84	PPV =90.5 (82.3–95.1); NPV =97.7 (96.6–98.5); Se =76.0 (66.8–83.3); Sp =99.2 (98.5–99.6)	MR	Langhoff-Ross J et al. 2003[136]
O365	Small for gestational age	2001 (IN; A/B[e])	O36.5	25	PPV =56.0 (37.1–73.3); NPV =99.5 (98.8–99.8); Se =70.0 (48.1–85.5); Sp =99.0 (98.2–99.4)	MR	Langhoff-Ross J et al. 2003[136]
O409	Polyhydramnios	1982–1987 (IN; A/B[e])	n/a	19	PPV =74;[f] NPV =100;[f] Se =82[f]	MR	Kristensen J et al. J Clin Epidemiol 1996[135]
O42	Premature rupture of membranes	2001 (IN; A/B[e])	O42.3	50	PPV =64.0 (50.1–75.9); NPV =98.5 (97.6–99.1); Se =66.7 (52.5–78.3); Sp =98.3 (97.4–98.9)	MR	Langhoff-Ross J et al. 2003[136]
O44	Placenta previa	1982–1987 (IN; A/B[e])	n/a	53	PPV =70;[f] NPV =99;[f] Se =68[f]	MR	Kristensen J et al. J Clin Epidemiol 1996[135]
O45	Abruptio placenta	1982–1987 (IN; A/B[e])	n/a	172	PPV =69;[f] NPV =97;[f] Se =70[f]	MR	Kristensen J et al. J Clin Epidemiol 1996[135]

O489	Prolonged pregnancy	2001 (IN; A/B[e])	O48.9	53	PPV =67.9 (54.5–78.9); NPV =99.4 (98.7–99.7); Se =83.7 (70.0–91.9); Sp =98.4 (97.5–99.0)	MR	Langhoff-Ross J et al. 2003[136]
O62	Abnormalities of forces of labor	2001 (IN; A/B[e])	O62.2	317	PPV =85.5 (81.2–88.9); NPV =88.2 (85.7–90.2); Se =73.8 (69.1–78.1); Sp =94.0 (92.0–95.4)	MR	Langhoff-Ross J et al. 2003[136]
O641	Obstructed labor due to breech presentation	2001 (IN; A/B[e])	O64.1, O32	46	PPV =76.1 (62.1–86.1); NPV =99.4 (98.7–99.7); Se =83.3 (69.4–91.7); Sp =99.0 (98.2–99.4)	MR	Langhoff-Ross J et al. 2003[136]
O654	Obstructed labor due to fetopelvic disproportion	2001 (IN; A/B[e])	O65.4	21	PPV =85.7 (65.4–95.0); NPV =98.6 (97.8–99.2); Se =54.6 (38.0–70.2); Sp =99.7 (99.2–99.9)	MR	Langhoff-Ross J et al. 2003[136]
O68	Fetal distress	2001 (IN; A/B[e])	O68	166	PPV =63.3 (55.7–70.2); NPV =97.4 (96.2–98.2); Se =80.8 (73.2–86.6); Sp =93.9 (92.2–95.2)	MR	Langhoff-Ross J et al. 2003[136]
O700	First degree perineal laceration	2001 (IN; A/B[e])	O70.0	174	PPV =50.6 (43.2–57.9); NPV =90.5 (88.4–92.2); Se =49.2 (41.9–56.4); Sp =90.9 (88.9–92.6)	MR	Langhoff-Ross J et al. 2003[136]
O701	Second degree perineal laceration	2001 (IN; A/B[e])	O70.1	91	PPV =46.2 (36.3–56.3); NPV =96.3 (95.0–97.3); Se =52.5 (41.7–63.1); Sp =95.3 (93.9–96.4)	MR	Langhoff-Ross J et al. 2003[136]
O710	Rupture of uterus	1980–1987 (IN; A/B[e])	O71.0–O71.1	956	PPV =13.5 (11.5–15.8)	MR	Devantier A et al. Ugeskr Læger 1991[137]
O714	Vaginal laceration	2001 (IN; A/B[e])	O71.4	56	PPV =8.9 (3.9–19.3); NPV =99.7 (99.2–99.9); Se =62.5 (30.6–86.3); Sp =95.4 (94.1–96.5)	MR	Langhoff-Ross J et al. 2003[136]
O72	Postpartum hemorrhage	2001 (IN; A/B[e])	O72	57	PPV =52.6 (39.9–65.0); NPV =98.6 (97.7–99.2); Se =66.7 (52.1–78.6); Sp =97.5 (96.4–98.3)	MR	Langhoff-Ross J et al. 2003[136]
P00–P96: Certain conditions originating in the perinatal period							
P22	Infant respiratory distress syndrome	1977–2008 (IN;[e] A/B[e])	776.19; P22.0	90	$PPV_{Overall}$ =81.1 (71.8–87.9); PPV =89.2 (79.4–94.7) for preterm infants born <37 wks	MR	Thygesen SK et al. Clin Epidemiol. 2013[138]
P57.0	Kernicterus	1994–2003 (IN; A/B[e])	P57.0, P57.7, P57.9 (+ gestational age ≥35 y)	15	PPV =40.0 (19.8–64.3)	MR	Maimburg RD et al. Acta Obstet Gynecol Scand. 2009[139]
Q00–Q99: Congenital malformations, deformations and chromosomal abnormalities							
Q20	Congenital cardiac malformations	2000–2008 (IN/OUT/ED;[e] A/B[e])	Q20–25, except Q20.9, Q21.9, Q22.9, Q23.9, Q24.9, Q25.9	3,536	PPV =98.4 (98.0–99.8)	MR	Agergaard P et al. Clin Epidemiol. 2011[140]
		1994–2002 (IN/OUT;[e] A/B[e])	Q20–26	418	PPV =89.0 (85.6–91.7)	MR; echo, autopsy	Jepsen B et al. Int J Risk Saf Med. 2006[141]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
		1991–1994 (IN; A/B[e])	740–759; Q00–99 (except 755.69, 752.10–752.19, Q53, Q65)	744	PPV =88.2 (85.7–90.3); Se =89.9 (87.5–91.9)	MR; Medical Birth Registry; National Registry of Congenital Abnormalities	Larsen H et al. Scand J Public Health. 2003[142]
Q53	Cryptorchidism	1995–2009 (n/a; A)	Q53	452	PPV =80.3 (76.4–83.7)	MR	Jensen MS et al. J Urol. 2012[143]
Q54	Hypospadias	1989–2003 (IN;[e] A/B[e])	752.20–752.29; Q54	43	PPV =93.0 (81.4–97.6)	MR	Pedersen L et al. Int J Med Sci. 2006[144]
Q96	Turner syndrome	1984–1993 (IN; A/B)	310.54, 311.54, 312.54, 313.54, 314.54, 315.54, 759.50[e]	237	PPV =68.8 (62.6–74.3)	MR; Cytogenetic Central Register	Gravholt CH et al. J Clin Epidemiol. 1998[145]
R00–R99: Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified							
R29.7	Falls after stroke	2003–2006 (IN; A/B)	R29.7, EUHE (after admission to stroke units and age ≥18 y)	1	PPV =0.0 (0.0–79.4); NPV =84.5 (81.4–87.2); Se =0 (0–5.1); Sp =99.8 (98.9–100)	MR	Ingeman A et al. Clin Epidemiol. 2010[103]
R56	Febrile seizures	1990–2001 (IN/OUT; A/B[e])	780.21; R56.0	249	PPV =92.8 (88.8–95.4); NPV =98.6 (98.2–98.8); Se =71.5 (66.4–76.2); Sp =99.7 (99.6–99.8)	MR/telephone interviews	Vestergaard M et al. J Clin Epidemiol. 2006[146]
R570	Shock overall	2005–2012 (IN; A/B)	R57.0–R57.2, A41.9A (+BFHC92, BFHC93 excl BFHC93E-H, BFHC95)	158	PPV =86.1 (79.8–90.6); $PPV_{+\ Inotrope/vasopressor}$ =93.1 (84.8–97.0)	MR	Lauridsen MD et al. BMC Med Res Methodol. 2015[147]
R570	Cardiogenic shock	2005–2012 (IN; A/B)	R570 (+ BFHC92, BFHC93 excl BFHC93E-H, BFHC95)	46	PPV =93.5 (82.5–97.8); $PPV_{+\ Inotrope/vasopressor}$ =96.0 (80.5–99.3)	MR	Lauridsen MD et al. BMC Med Res Methodol. 2015[147]
R571	Hypovolemic shock	2005–2012 (IN; A/B)	R571 (+ BFHC92, BFHC93 excl BFHC93E-H, BFHC95)	34	PPV =70.6 (53.8–83.2); $PPV_{+\ Inotrope/vasopressor}$ =69.2 (42.4–87.3)	MR	Lauridsen MD et al. BMC Med Res Methodol. 2015[147]
R572	Septic shock	2005–2012 (IN; A/B)	R572, A41.9A (+ BFHC92, BFHC93 excl BFHC93E-H, BFHC95)	78	PPV =69.2 (58.3–78.4); $PPV_{+\ Inotrope/vasopressor}$ =82.4 (66.5–91.7)	MR	Lauridsen MD et al. BMC Med Res Methodol. 2015[147]
S00–T98: Injury, poisoning and certain other consequences of external causes							
S02	Head injury	1982–1985[e] (IN; n/a)[e]	800–803, 850–854[e]	>50[e]	PPV =90[f]	MR	Sørensen HT et al. Ugeskr Laeger. 1987[148]
S73	Traumatic hip dislocation	1989–1990 (IN; n/a)	835.99	755	PPV =16.0 (13.6–18.8)	MR; X-rays	Hougaard K et al. Ugeskr Laeger 1992[149]
T634F	Anaphylactic shock after bee sting	1973–1985 (IN; A/B[e])	999.49	n/a	Se =60.0 (38.7–78.1)	MR	Sørensen HT et al. Allergy. 1989[150]

T84.5	Periprosthetic hip joint infection	2003–2008 (IN; A/B[e])	T84.5 + hip-specific NCSP code + departments of orthopedic surgery. Infection-specific surgery: KNFS19, KNFS49, KNFU89, KNFW69	283	PPV =84.8 (80.2–88.5); $PPV_{+\text{ Infection-specific surgical code}}$ =86.1 (80.5–90.3)	MR	Lange J et al. Hip Int. 2015[151]
Z00–Z99: factors influencing health status and contact with health services							
Z131	Glucose tolerance test	2001 (IN; A/B[e])	Z13.1	111	PPV =57.7 (48.4–66.4); NPV =94.8 (93.2–96.0); Se =54.7 (45.7–63.4); Sp =95.4 (93.9–96.5)	MR	Langhoff-Ross et al. 2003[136]
Z358D	High-risk pregnancy due to previous complicated pregnancy/birth	2001 (IN; A/B[e])	Z35.8D	29	PPV =34.5 (19.9–52.7); NPV =97.5 (96.5–98.3); Se =27.0 (15.4–43.0); Sp =98.3 (97.3–98.9)	MR	Langhoff-Ross et al. 2003[136]
Z358E	High-risk pregnancy due to previous cesarean section	2001 (IN; A/B[e])	Z35.8E	77	PPV =88.3 (79.3–93.7); NPV =97.3 (96.1–98.1); Se =70.1 (60.4–78.3); Sp =99.1 (98.4–99.5)	MR	Langhoff-Ross et al. 2003[136]
Other conditions							
	Charlson Comorbidity Index conditions	1998–2007 (IN/OUT; A)	See individual diseases	950	PPV =98.0 (96.9–98.7)	DS	Thygesen SK et al. BMC Med Res Methodol. 2011[58]
Treatments							
Surgery (K)							
KDC	Surgery for cholesteatoma	1977–2007 (IN)	20380–20700, 20990, KDC, KDD, KDE, KDFD30 (except KDCA10, KDCA20, KDCW00, KDEE, KDEE00)	107	PPV =98.1 (93.4–95.5)	Surgical records	Djurhuus et al. Dan Med Bull. 2010[93]
KHAD10	Breast implant	1977–1992 (IN)	38500, 38540	2,576	PPV =100 (99.9–100)[g]	MR	Friis S et al. Ann Plast Surg. 1997[127]
		1977–1989 (IN; n/a)	3854	71	PPV =100 (94.9–100)[g]	MR	McLaughlin JK et al. J Natl Cancer Inst. 1995[152]
KHAD00	Breast augmentation	1977–1989 (IN; n/a)	3850	74	PPV =94.6 (86.9–97.9)	MR	McLaughlin JK et al. J Natl Cancer Inst. 1995[152]
KJAP	Intraperitoneal adhesiolysis	1977–1988 (IN)	40480	341	PPV =95.9 (93.2–97.5); NPV =99;[f] Se =87.0 (83.2–90.0); Sp =100[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KJBC00	Gastroesophageal antireflux operation	1997–1999 (IN)	KJBC00, KJBC01 (age ≥18 y + admission >3 days or readmission or in-hospital death)	243	PPV =100 (98.4–100)	MR	Holte K et al. Ugeskr Laeger. 2001[153]
KJEA	Appendectomy	1977–1988 (IN)	43000	899	PPV =99.0 (98.1–99.5); NPV =100;[f] Se =98.5 (97.4–99.1); Sp =100[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KJKA2	Cholecystectomy	2004–2005 (IN)	KJKA2	1,361	PPV =99.9 (99.6–100)	MR	Harboe KM et al. *Int J Qual Health Care. 2009*[154]
KKFC10	Orchiectomy in prostate cancer patients	2002–2008 (IN)	KKFC10, KKFC13, KKFC15	50	PPV =100 (92.9–100); NPV =100 (92.9–100)	MR	Jespersen CG et al. Clin Epidemiol. 2012[155]
KKFH00	Corrective surgery of cryptorchidism	1995–2009 (IN)	KKFH00–KKFH01, KKFH10	249	PPV =99.2 (97.1–99.8)	MR	Jensen MS et al. J Urol. 2012[143]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
KL	Operations for gynecological cancer	1977–1988 (IN)	Hysterectomy, oophorectomy, partial resection of the ovaries (unspecified codes)	n/a (≈10,182)	PPV =95[f]	MR	Kjaergaard J et al. J Epidemiol Biostat. 2001[62]
KLAD00A	Unilateral ovarian resection	1977–1988 (IN)	60040	1,128	PPV =96.2 (94.9–97.2); NPV =98;[f] Se =93.3 (91.7–94.6); Sp =99[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLAD00B	Bilateral ovarian resection	1977–1988 (IN)	60060	195	PPV =82.1 (76.1–86.8); NPV =100;[f] Se =91.4 (86.3–94.7); Sp =99[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLAE1	Unilateral oophorectomy	1977–1988 (IN)	60100	399	PPV =90.5 (87.2–93.0); NPV =99;[f] Se =93.5 (90.6–95.6); Sp =99[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLAE2	Bilateral oophorectomy	1977–1988 (IN)	60120	87	PPV =79.3 (69.7–86.5); NPV =100;[f] Se =79.3 (69.7–86.5); Sp =100[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLAF0	Unilateral salpingo-oophorectomy	1977–1988 (IN)	60320	925	PPV =95.8 (94.3–96.9); NPV =98;[f] Se =90.4 (88.4–92.1); Sp =99[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLAF1	Bilateral salpingo-oophorectomy	1977–1988 (IN)	60300	534	PPV =85.6 (82.4–88.3); NPV =99;[f] Se =89.6 (86.7–92.0); Sp =98[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLCD	Hysterectomy	1977–1988 (IN)	61020	3,162	PPV =99.1 (98.7–99.4); NPV =96;[f] Se =97.9 (97.3–98.3); Sp =98[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
		1998–2000 (IN)	KLCC10, KLCC11, KLCC20, KLCD00, KLCD01, KLCD04, KLCD10, KLCD11, KLCD96, KLCD97, KLEF13[e]	1,026	PPV =99.8 (99.3–100)	DS	Møller C et al. Ugeskr laeger. 2002[156]
KLCD10	Total vaginal hysterectomy	1977–1988 (IN)	61040	157	PPV =73.9 (66.5–80.1); NPV =100;[f] Se =93.6 (87.8–96.7); Sp =99[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLCD11	Supravaginal hysterectomy	1977–1988 (IN)	61000	184	PPV =91.3 (86.3–94.6); NPV =100;[f] Se =88.0 (82.6–91.8); Sp =100[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLCD30	Radical hysterectomy	1977–1988 (IN)	61100	91	PPV =90.1 (82.3–94.7); NPV =100;[f] Se =96.5 (90.1–98.8); Sp =100[f]	DS	Kjaergaard J et al. J Clin Epidemiol. 2002[68]
KLEF	Vaginal prolapse surgery	1996–1998 (IN)	KLCD10, KLDC10, KLEF00, KLEF03, KLEF10, KLEF13, KLEF40, KLEF53, KLFE20	296	PPV =69.3 (63.8–74.2)	MR	Ottesen M. Ugeskr Laeger 2009[157]
KMAA00A	Amniocentesis	2001 (IN)	KMAA00A	32	PPV =75.0 (57.9–86.8); NPV =96.8 (95.6–97.7); Se =40.7 (29.1–53.4); Sp =99.3 (98.5–99.6)	MR	Langhoff-Ross et al. 2003[136]

KMAC00	Labor induction with artificial rupture of membrane	2001 (IN)	KMAC00	38	PPV =55.3 (39.7–69.9); NPV =99.1 (98.3–99.5); Se =67.7 (50.1–81.4); Sp =98.5 (97.5–99.0)	MR	Langhoff-Ross et al. 2003[136]
KMAC05	Artificial rupture of membrane during labor	2001 (IN)	KMAC05	98	PPV =80.6 (71.7–87.2); NPV =79.9 (77.3–82.2); Se =27.6 (22.8–33.1); Sp =97.7 (96.5–98.6)	MR	Langhoff-Ross et al. 2003[136]
KMAE	Vacuum extraction	2001 (IN)	KMAE	105	PPV =97.1 (91.9–99.0); NPV =99.4 (98.7–99.7); Se =99.4 (88.4–97.4); Sp =99.7 (99.1–99.9)	MR	Langhoff-Ross et al. 2003[136]
KMBA	Removal of placenta	2001 (IN)	KMBA	33	PPV =81.8 (65.6–91.4); NPV =99.3 (98.6–99.6); Se =77.1 (61.0–87.9); Sp =99.5 (98.8–99.8)	MR	Langhoff-Ross et al. 2003[136]
KMBC10	Vaginal stitching	2001 (IN)	KMBC10	87	PPV =6.9 (3.2–14.2); NPV =99.8 (99.2–99.9); Se =75.0 (40.9–92.9); Sp =91.4 (89.4–93.0)	MR	Langhoff-Ross et al. 2003[136]
KMBC30	Perineal stitching (excl sphincter)	2001 (IN)	KMBC30	242	PPV =60.3 (54.1–66.3); NPV =85.0 (82.1–87.4); Se =57.9 (51.8–63.9); Sp =86.2 (83.4–88.6)	MR	Langhoff-Ross et al. 2003[136]
KMBC33	Perineal stitching (incl sphincter)	2001 (IN)	KMBC33	25	PPV =92.0 (75.0–97.8); NPV =98.5 (97.5–99.1); Se =62.2 (46.1–75.9); Sp =99.8 (99.2–99.9)	MR	Langhoff-Ross et al. 2003[136]
KMCA	Cesarean section	2001 (IN)	KMCA	185	PPV =97.8 (94.6–99.2); NPV =99.6 (98.9–99.8); Se =97.8 (94.6–99.2); Sp =99.6 (98.9–99.8)	MR	Langhoff-Ross et al. 2003[136]
KN	Orthopedic surgery	2004 (IN)	n/a	554	PPV =63.2 (59.1–67.1)	MR	Lass et al. Ugeskr laeger. 2006[158]
KPBE2–KPBE3	Upper limb embolectomy	1990–2002 (IN)	86823–86824, PBE20, PBE30	1,134	PPV =97.3 (96.2–98.1)	MR	Andersen LV et al. Clin Epidemiol. 2009[159]
KTMD00	Episiotomy (incl stitching)	2001 (IN)	KTMD00	130	PPV =96.9 (92.4–98.8); NPV =99.6 (98.9–99.9); Se =97.7 (93.4–99.2); Sp =99.5 (98.8–99.8)	MR	Langhoff-Ross et al. 2003[136]
Other treatments (B)							
BAFA7	Infiltration anesthesia	2001 (IN; A/B[e])	BAFA7	338	PPV =60.1 (54.8–65.1); NPV =85.9 (82.9–88.4); Se =70.2 (64.7–75.2); Sp =79.5 (76.2–82.4)	MR	Langhoff-Ross et al. 2003[136]
BAFA80	Acupuncture	2001 (IN; A/B[e])	BAFA80	36	PPV =75.0 (58.9–86.3); NPV =98.3 (97.3–98.9); Se =61.4 (46.6–74.3); Sp =99.1 (98.3–99.5)	MR	Langhoff-Ross et al. 2003[136]
BAFA81	Inhalation anesthesia with nitrous oxide	2001 (IN; A/B[e])	BAFA81	85	PPV =76.5 (66.4–84.2); NPV =80.6 (77.9–83.0); Se =25.9 (20.9–31.7); Sp =97.5 (96.1–98.4)	MR	Langhoff-Ross et al. 2003[136]

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Table S1 (*Continued*)

ICD codes[a]	Condition	Study period (contact type; diagnosis type)	ICD codes/algorithm[b]	n[c]	PPV; NPV; sensitivity; specificity[d]	Reference standard	Reference
BAFA87	Intracutaneous sterile water	2001 (IN; A/B[e])	BAFA87	20	PPV =85.0 (64.0–94.8); NPV =96.0 (94.6–97.0); Se =29.3 (19.2–42.0); Sp =99.7 (99.1–99.9)	MR	Langhoff-Ross et al. 2003[136]
BFHC92	Inotropes/vasopressors in shock patients	2005–2012 (IN)	BFHC92–BFHC93, BFHC95 (excl BFHC93E-H) (+ R570–R572, A41.9A)	72	PPV =88.9 (79.6–94.3)	MR	Lauridsen MD. BMC Med Res Methodol. 2015[147]
BGDA	Mechanical ventilation in ICU patients	2005–2010 (IN)	NABE/NABB + BGDA0	50	PPV =100 (92.9–100)	MR	Blichert-Hansen et al. Clin Epidemiol. 2013[160]
BJFD	Acute dialysis in ICU admitted patients	2005–2010 (IN)	NABE/NABB + BJFD00/BJFD02	50	PPV =98.0 (89.5–99.7)	MR	Blichert-Hansen et al. Clin Epidemiol. 2013[160]
BKHD0	Uterotonic drugs following birth	2001 (IN; A/B[e])	BKHD0	57	PPV =12.3 (6.1–23.3); NPV =98.8 (97.9–99.3); Se =35.0 (18.1–56.7); Sp =95.5 (94.1–96.6)	MR	Langhoff-Ross et al. 2003[136]
BKHD20	Induction with prostaglandins	2001 (IN; A/B[e])	BKHD20	51	PPV =98.0 (89.7–99.7); NPV =93.4 (91.8–94.7); Se =41.3 (33.0–50.2); Sp =99.9 (99.4–100)	MR	Langhoff-Ross et al. 2003[136]
BKHD3	Labor induction medication	2001 (IN; A/B[e])	BKHD3	298	PPV =83.6 (78.9–87.3); NPV =92.5 (90.5–94.1); Se =80.0 (75.3–84.1); Sp =94.0 (92.2–95.4)	MR	Langhoff-Ross et al. 2003[136]
BKQA0	Bath	2001 (IN; A/B[e])	BKQA0	67	PPV =85.1 (74.7–91.7); NPV =74.5 (71.6–77.1); Se =18.6 (14.7–23.4); Sp =98.6 (97.5–99.3)	MR	Langhoff-Ross et al. 2003[136]
BWGC1	Radiation therapy to the bone in patients with prostate (P) or breast (B) cancer	2000–2005	BWGC1 (+ C61.9/C50)	16 P; 10 B	PPV_P=75.0 (50.5–89.8); NPV_P=83.3 (74.0–89.8); PPV_B=60.0 (31.3–83.2); NPV_B=95.6 (89.1–98.3); Se_P=46.2 (28.8–64.5); Sp_P=94.6 (86.9–97.9); Se_B=60.0 (31.3–83.2); Sp_B=95.6 (89.1–98.3)	MR	Jensen AØ et al. Clin Epidemiol. 2009[65]
BWHA	Chemotherapy for colorectal cancer	2009–2010	BWHA1–BWHA2, BOHJ19B	35	PPV =97.1 (85.5–99.5); NPV =93.3 (70.2–98.8); Se =97.1 (85.5–99.5); Sp =93.3 (70.2–98.8)	MR; hospital pharmacy production systems	Lund JL et al. Clin Epidemiol. 2013[161]
BWHB40	Bisphosphonate therapy in cancer patients	2005–2009	BWHB40	60	PPV =98.3 (91.1–99.7)	MR	Nielsson MS et al. Clin Epidemiol 2012[162]
BWHC	Gonadotropin-releasing hormone agonist in prostate cancer patients	2002–2008	BWHC	100	PPV =93.0 (86.3–96.6); NPV =94.0 (87.5–97.2); Se =93.9 (87.4–97.2); Sp =93.1 (86.4–96.6)	MR	Jespersen CG et al. Clin Epidemiol. 2012[155]

ATC codes (M)							
MJ06BB16	Palivizumab	1999–2010	MJ06BB16	182	PPV_{MR} =91.7 (80.4–96.7); NPV_{MR} =59.0 (53.3–64.5); Se_{MR} =26.7 (20.5–33.9); Sp_{MR} =97.8 (94.4–99.1); PPV_{PR} =90.7 (85.6–94.1); NPV_{PR} =98.4 (97.9–98.9); Se_{PR} =79.7 (73.7–84.6); Sp_{PR} =99.4 (99.0–99.6)	MR; PR	Haerskjold A et al. Clin Epidemiol. 2015[163]
Anesthesia and intensive care (N)							
NAAC	General anesthesia	2001 (IN)	NAAC	20	PPV =40.0 (21.9–61.3); NPV =95.9 (94.6–97.0); Se =15.1 (7.9–27.1); Sp =98.9 (98.1–99.4)	MR	Langhoff-Ross et al. 2003[136]
NAAD0	Epidural nerve block	2001 (IN)	NAAD0	24	PPV =75.0 (55.1–88.0); NPV =91.8 (89.9–93.3); Se =17.7 (11.5–26.2); Sp =99.4 (98.6–99.7)	MR	Langhoff-Ross et al. 2003[136]
NAAD1	Spinal anesthesia	2001 (IN)	NAAD1	35	PPV =77.1 (61.0–87.9); NPV =91.6 (89.8–93.1); Se =22.7 (16.1–31.0); Sp =99.2 (98.4–99.6)	MR	Langhoff-Ross et al. 2003[136]
NAAD43	Pudendal nerve block	2001 (IN)	NAAD43	40	PPV =70.0 (54.6–81.9); NPV =95.9 (94.4–97.0); Se =43.1 (31.8–55.2); Sp =98.6 (97.6–99.2)	MR	Langhoff-Ross et al. 2003[136]
NABB	Intensive care unit admission	2005–2010 (IN)	NABB, NABE	47	PPV =87.2 (74.8–94.0)	MR	Blichert-Hansen et al. Clin Epidemiol. 2013[160]
Examinations (U)							
UXCC00A	Cardiac CT Angiography	2008–2012	UXCC00A	289	PPV =100 (98.7–100)	MR	Nielsen LH et al. Clin Epidemiol. 2014[164]
UXUD88A	Fetal umbilical artery flow velocity measurement	2001 (IN)	UXUD88A	63	PPV =77.8 (66.1–86.3); NPV =94.9 (93.4–96.1); Se =47.6 (38.2–57.1); Sp =98.6 (97.7–99.2)	MR	Langhoff-Ross et al. 2003[136]

Notes: [a]The ordering corresponds to the SKS browser, ie, ICD-10 for diagnoses and NOMESCO for surgery; [b]ICD codes without and with capital letters refer to ICD-8 and ICD-10 codes, respectively; [c]reflects the reviewed number of records in the DNPR (ie, the denominator in calculations of PPV). Among obstetric variables, we included only validation results based on >20 diagnoses; [d]confidence intervals were calculated using Wilson's score method; [e]information not specified in validation papers, but confirmed through correspondence with authors. Unspecified and unconfirmed data are listed as not available (n/a); [f]recalculation of confidence intervals using Wilson's score method not possible due to insufficient data; [g]confidence limit equals 100 due to rounding.

Abbreviations: A, primary diagnosis; AC, anticoagulant therapy; B, secondary diagnosis; COPD, chronic obstructive pulmonary disease; CT, computed tomography; d, day; DVT, deep venous thrombosis; DANMONICA, Danish Monitoring Trends and Determinants in Cardiovascular Disease project; DCR, Danish Cancer Registry; DNPR, Danish National Patient Registry; DS, discharge summaries; echo, echocardiography; ECG, electrocardiography; ED, emergency department; GP, general practitioner; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICD, International Classification of Diseases; ICU, intensive care unit; IN, inpatient contact; LABKA, Clinical Laboratory Information System Database; mo, month; MR, medical records; MRI, magnetic resonance imaging; MS, multiple sclerosis; n/a, not available; NPV, negative predictive value; OUT, outpatient contact; PD, Pathology Registry; PE, pulmonary embolism; PPV, positive predictive value; PR, Prescription Registry; PSA, prostate specific antigen; Se, study sample sensitivity; Sp, study sample specificity; ultrasound, ultrasonography; y, year(s); V-P, ventilation-perfusion; VTE, venous thromboembolism; NOMESCO, Nordic Medico-Statistical Committee; wks, weeks.