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Original Article

ORIGINAL ARTICLE

The validity of pathology codes for biopsy-confirmed kidney disease in the Danish National Patobank

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ABSTRACT

Background. This study validates the application of Systematized Nomenclature of Medicine second edition (SNOMED II) codes used to describe medical kidney biopsies in Denmark in encoded form, aiming to support robust epidemiological research on the causes, treatments and prognosis of kidney diseases.

Methods. Kidney biopsy reports from 1 January 1998 to 31 December 2018 were randomly extracted from the Danish National Patobank, using SNOMED codes. A 5% sample was selected, and nephrologists assessed the corresponding medical records, assigning each case the applied clinical diagnoses. Sensitivity, specificity, positive predictive values (PPV), negative predictive values and Cohen's kappa coefficient for the retrieved SNOMED codes were calculated.

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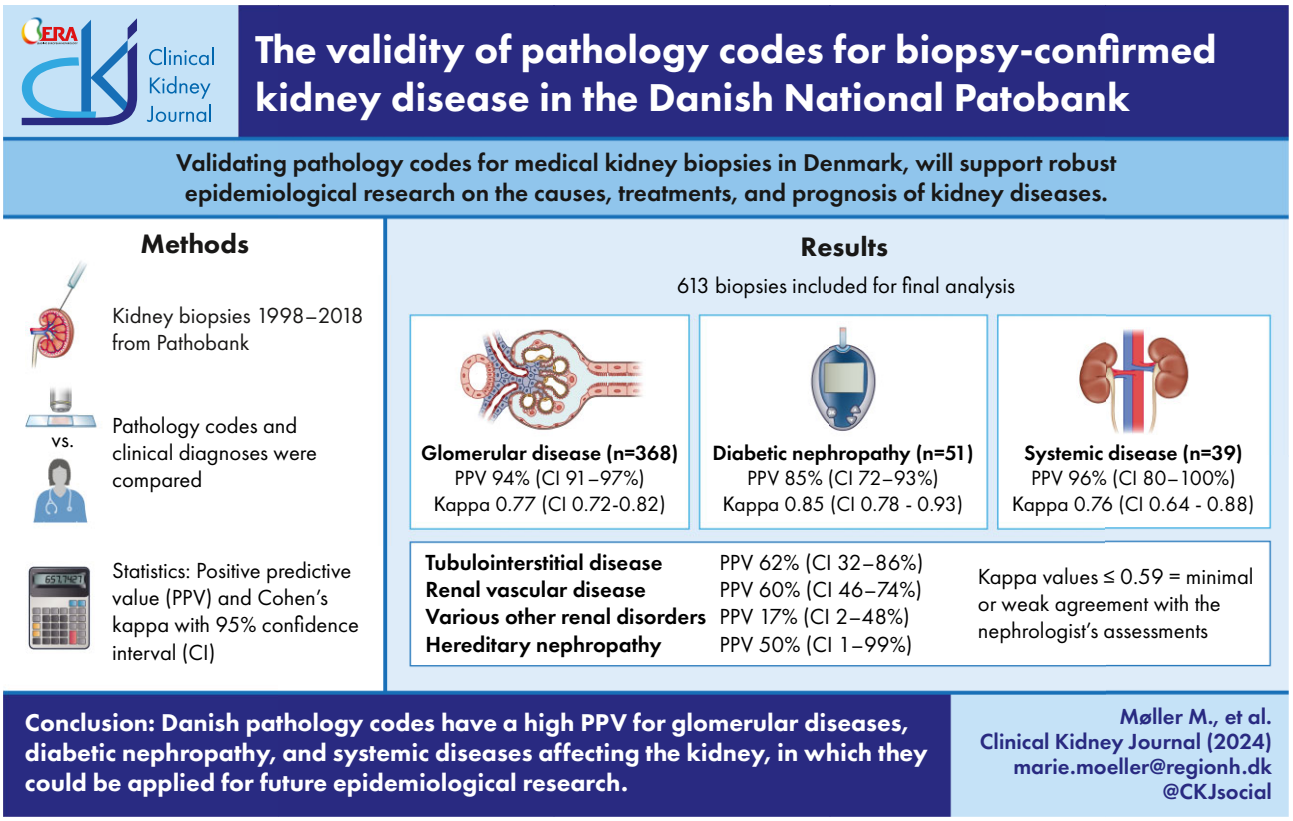
Results. A total of 613 kidney biopsies were included. The primary clinical disease groups were glomerular disease ($n = 368$), tubulointerstitial disease ($n = 67$), renal vascular disease ($n = 51$), diabetic nephropathy ($n = 51$) and various renal disorders ($n = 40$). Several SNOMED codes were used to describe each clinical disease group and PPV for the combined SNOMED codes were high for glomerular disease (94%), diabetic nephropathy (85%) and systemic diseases affecting the kidney (96%). Conversely, tubulointerstitial disease (62%), renal vascular disease (60%) and other renal disorders (17%) showed lower PPV.

Conclusions. SNOMED codes have a high PPV for glomerular diseases, diabetic nephropathy and systemic diseases affecting the kidney, in which they could be applied for future epidemiological research.

GRAPHICAL ABSTRACT



Keywords: Danish National Patient Registry, kidney biopsy, nephrology, SNOMED codes, validation

KEY LEARNING POINTS

What was known:

- Systematized Nomenclature of Medicine (SNOMED) codes are used to encode histological findings observed in kidney biopsies, providing a standardized method to describe such data.
- In countries with national registries and medical databases, linking SNOMED codes, registries and databases enables invaluable epidemiological research.
- Hence, validating nephrological SNOMED codes against corresponding clinical diagnoses will optimize the future utility of these codes for epidemiological research in kidney diseases.

This study adds:

- A total of 613 kidney biopsies from the Danish National Patobank were assigned clinical diagnoses by nephrologists and aligned with SNOMED codes.
- Multiple SNOMED codes were utilized to describe each clinical disease group, with high positive predictive values observed for glomerular diseases (94%), diabetic nephropathy (85%) and systemic diseases affecting the kidney (96%).

Potential impact:

- This study demonstrates the effectiveness of SNOMED codes in accurately classifying specific kidney diseases, underscoring their potential for epidemiological research.
- These findings hold significant implications for reducing variability and improving data reliability within the Danish Patobank registry.
- A national or even better an international harmonization of coding practices will further improve agreement between SNOMED codes and clinical disease groups.

INTRODUCTION

Kidney disease affects approximately 10% of adults, posing significant societal and personal burden [1]. A kidney biopsy is often needed to determine the underlying cause of kidney disease, offering crucial insights into cause, prognosis and treatment [2]. Registry codes describing the histological findings in the kidney biopsies hold potential for epidemiological research, enabling the exploration of associations between exposures, comorbidity, treatment and prognosis across different diagnoses of kidney diseases.

Patobank is a Danish nationwide database containing data from pathoanatomical examinations. All data from Patobank are transferred to The Danish Pathology Register, which is operated and financed by The Danish Health Data Authority [3]. Denmark initiated electronic histological descriptions in 1972, and since 1990 all departments of pathology have used electronic registration [4]. The early information consisted mainly of patient data and pathology diagnoses using a simple version of the Systematized Nomenclature of Medicine second edition (SNOMED II) coding system [5]. In 1997, The Danish National Board of Health published the Danish Codebook for Pathological-Anatomical Examinations, thereby systematizing the use of SNOMED codes [6]. This initiative expanded the number of SNOMED codes and standardized data registration in Patobank across all Danish pathology departments, accompanied by a legal obligation for Danish pathologists to consistently report pathology data [5, 6]. Today, the coding system remains based on SNOMED II, distinguishing Denmark from most countries utilizing SNOMED Clinical Terms (CT) [7]. Danish SNOMED II codes have continuously been expanded and maintained.

In Denmark, it is possible to extract SNOMED codes from Patobank for use in research projects. Information from Danish national registries can be linked at person-level to cohorts including patients with biopsy-confirmed kidney disease by using the unique Danish social security number. This allows the study of causes, long-term clinical course and effect of treatment in patients with different kinds of biopsy-confirmed kidney diseases [8].

While the Danish Pathology Registry ensures completeness and validity of data, limitations in histopathology reporting exist due to the potential coding variability between departments and personnel, and changes in practice over time [5, 9]. If investigations are to be conducted on the histopathologic material in Patobank, it is important to clarify the validity of the applied SNOMED codes. This study aims to validate the SNOMED codes against the corresponding clinical diagnosis provided by the clinicians. Validation of the SNOMED codes may facilitate the future use of these codes for epidemiological research and health surveillance.

MATERIALS AND METHODS

SNOMED operates on a multiaxial hierarchy, comprising Topography (T-codes), Procedure or histopathological technique (P-codes), Morphology (M-codes), Disease (S-codes), Function (F-codes) and Aetiology (Æ-codes) [9, 10]. It is mandatory for Danish pathologists to report at least one T- and one M-code. In Patobank, we retrieved kidney biopsy reports from adults with a kidney biopsy performed between 1 January 1998 and 31 December 2018. The biopsy reports were retrieved from all Danish departments of pathology. Presently, five pathology departments routinely describe medical kidney biopsies. Ninety-eight percent of the biopsies included in this study originated from these departments (26% from Odense University Hospital, 24% from Herlev Hospital, 21% from Rigshospitalet, 21% from Aarhus University Hospital and 8% from Aalborg University Hospital), whereas 2% were described by five other pathology departments during the study period. Inclusion criteria focused on specific SNOMED T- and P-codes defining the kidney biopsy (Table 1) and exclusion criteria focused on SNOMED codes for malignant diseases and biopsies from kidney transplants (Table 2).

Given the unpredictable distribution of diagnoses within the retrieved biopsies, conducting a power calculation prior to the study was not possible. To ensure statistical robustness, a minimum of 500 biopsies was deemed necessary. We estimated that approximately 500 annual native kidney biopsies were

Table 1: Inclusion criteria.

SNOMED-codes		
T71XXX (All T-codes corresponding to kidney tissue)	AND	P30990 (needle biopsy) and/or P30610 (biopsy) and/or P30993 (biopsy, medical indication)
AND period: 1 January 1998 to 31 December 2018 AND only biopsies from adult patients		

The table illustrates the inclusion criteria employed for retrieving biopsies from Patobank. A kidney biopsy was defined using SNOMED codes corresponding to both kidney topography and biopsy procedures. Only biopsies from adults between 1998 and 2018 were included.

Table 2: Exclusion criteria.

SNOMED codes	
Code	Code text
• M8XXXX	• Malignant diseases
• M9XXXX	• Lymphoid neoplasia
• M15600	• Transplant
• P3061X	• Donor biopsy
• M09450	• No signs of malignancy
Doublettes (multiple biopsies from one person)	
EM descriptions created on a separate requisition number	

The table illustrates the exclusion criteria used to retrieve biopsies from Patobank. None of the SNOMED codes was permitted in the dataset. Additionally, biopsies were excluded if they were duplicates or if the EM description was not accompanied by an LM description.

performed in Denmark, and with a study duration of 20 years, we sampled all biopsies from three preselected weeks, representing approximately 5% of the total biopsy pool. The three 1-week periods in the years 1998–2018 were 1 February to 7 February, 1 June to 7 June, and 1 October to 7 October (Fig. 1). For each kidney biopsy retrieved from Patobank, we received comprehensive information, including the department of pathology performing the histopathological examination, the date of arrival of the biopsy to the department, the department who ordered the biopsy, the patient's social security number, the utilized SNOMED codes and the conclusion of the pathology report. Medical records associated with these biopsies were retrieved and underwent review by a local nephrologist from the 12 corresponding departments of nephrology in Denmark. The local nephrologist labelled each patient with a clinical diagnosis based on the review of the medical file including the full pathology report and the pathologist conclusive remarks. The nephrologist chose between the following clinical disease groups: 'Glomerular disease', 'Tubulointerstitial disease', 'Diabetic nephropathy', 'Renal vascular disease', 'Systemic disease affecting the kidney', 'Hereditary nephropathies', 'Various acute and chronic renal disorders', 'Should be omitted', 'Normal disease group' and 'Other disease groups'. The chosen clinical disease group could be specified further as defined in Appendix 1. For instance, glomerular diseases could be specified as immunoglobulin A (IgA) nephropathy, membranous nephropathy, etc. The clinical disease groups, along with their subgroups and specified conditions, were defined based on the European Renal Association (ERA) Registry's primary renal diagnosis set [11]. This pairing aimed to enhance comparability with studies investigating biopsy-proven kidney diseases. For the final validation, the clinical diagnoses were aligned with the applied SNOMED codes, facilitating a systematic code review for each clinical disease group.

Prior to the retrieval of the clinical diagnosis from the medical records, the procedure was piloted. Nephrologists from all 12 participating departments of nephrology independently assessed 14 challenging cases with, for example, an atypical clinical presentation compared with the pathology findings. Using Light's Kappa, the interrater reliability demonstrated a substantial agreement with a Kappa value of 0.65, albeit with some uncertainty (P-value = .99) [12, 13]. Unclear cases prompted explanatory comments. The pilot prompted a refinement of the standard operation procedure for the process. The refinement resulted in the addition of the disease group termed 'Hereditary nephropathies'. Anti-neutrophil cytoplasmic antibody (ANCA) vasculitis were classified by the nephrologists in two different groups ('Glomerular disease' and 'Systemic disease affecting the kidney'). This was solved by alignment with ERA coding, accomplished by relocating five codes from one disease group to another.

Two nephrologists and one pathologist categorized the used SNOMED codes into disease-specific groups or an 'undefining code'-group, denoting SNOMED codes lacking specificity and applicable across all clinical disease groups. For a detailed grouping of the SNOMED codes, see Appendix 2.

Statistics

Concordance between the clinical diagnoses retrieved from the medical records (reference) and SNOMED codes from Patobank was described by sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV) and Cohen's kappa coefficient (κ) of agreement. Data are presented with 95% confidence interval (95% CI) using a binomial exact model for PPV, NPV, sensitivity and specificity, and the normal approximation method for κ. The level of agreement for κ values were: $<$0.20, none; 0.20–0.39, minimal; 0.40–0.59, weak; 0.60–0.79, moderate; 0.80–0.90, strong; and $>$90, almost perfect [14]. Statistical analyses were conducted using R version 4.1.0 (2021-05-18) [15].

Ethics

The Danish Data Protection Agency (no. P-2020-23) and the Danish Patient Safety Authority (no. 3-3013-3271/1) approved the study.

RESULTS

A total of 19 901 kidney biopsies were retrieved. Out of these, 1173 biopsies (5.9%) occurred during the three specified 1-week sampling periods. A thorough examination of the retrieved data from Patobank by an experienced pathologist and nephrologist led to the removal of 432 biopsies (Fig. 1), leaving 741 biopsies for further analysis. Subsequent chart reviews by the local

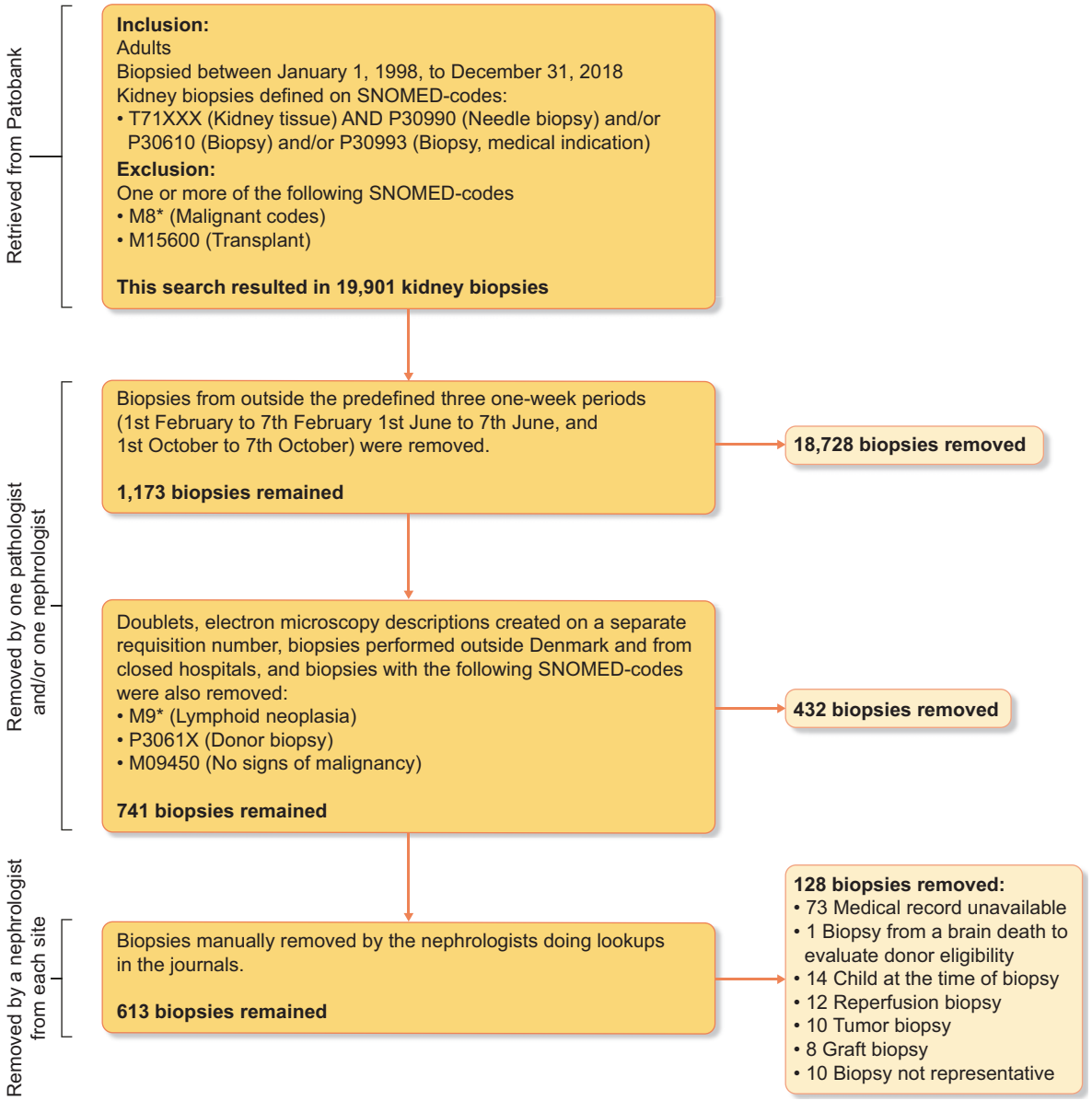


Figure 1: Flowchart describing inclusion and exclusion criteria and steps in the process.

nephrologists resulted in the manual removal of an additional 128 biopsies, ultimately yielding a dataset comprising 613 biopsies. Among the included biopsies, 227 were obtained between 1998 and 2008, while 386 biopsies were obtained from 2009 to 2018 (Supplementary data, Table S1).

Of the 128 removed biopsies, 14 were excluded due to patient age at the time of biopsy, attributed to a retrieval error from Patobank. Thirty (30/741; 4%) graft biopsies and tumour biopsies were manually excluded from the study, facilitated by access to medical records. This exclusion process may not be applicable in other epidemiological studies unless graft/tumour biopsies are appropriately coded in Patobank. An evaluation of the SNOMED codes for these 30 biopsies revealed great similarity to those typically assigned to native medical kidney biopsies, except for one case where the SNOMED code 'Chronic graft nephropathy' (F44450) was applied. Further review of all SNOMED codes from 'The Danish Health Data Authority official SNOMED classification' [16] identified 22 additional SNOMED codes relating to kidney transplant rejection or failure, which would be suitable for future exclusion criteria, namely F44000–F44460, S46900 and F06071.

According to medical record reviews of the 613 patients' kidney biopsies, 368 had glomerular disease, 67 had tubulointerstitial disease, 51 had renal vascular disease, 51 had diabetic nephropathy, 40 had various other acute and chronic renal disorders, 39 had systemic diseases affecting the kidney, 16 showed no evidence of kidney disease, 12 had other diseases and 4 were identified with hereditary nephropathy. Thirty-three exhibited mixed diseases, indicating the co-occurrence of two or more clinical disease groups within their medical records. Twenty-five of these had glomerular disease and tubulointerstitial disease ($n = 7$) or glomerular disease or tubulointerstitial disease with either diabetic nephropathy ($n = 6$), renal vascular disease ($n = 8$), or various acute and chronic renal disorders ($n = 4$).

In total 124 M-, S- and F-SNOMED codes were used to describe the cohort (Appendix 2). The range of assigned M-, S- and F-SNOMED codes varied from 1 to 11, with a median of 3 (interquartile range 2–4). S-codes were utilized in 33% of all cases. Unfortunately, we lack the data necessary to explore potential variations across pathology departments. In the clinical disease groups 'No evidence of kidney disease' and 'Other diseases', no specific SNOMED codes were identified. For the clinical disease group 'Renal vascular disease', there were no specific SNOMED codes, therefore we decided to assess SNOMED codes suggestive for 'Renal vascular disease' and conditional on the absence of other disease-defining SNOMED codes.

Sensitivity, specificity, PPV, NPV and κ are presented for the SNOMED codes to determine the clinical diagnosis in Table 3.

The combined SNOMED codes showed high PPV for glomerular disease [94% (95% CI 91–97)], diabetic nephropathy [85% (95% CI 72–93)] and systemic diseases affecting the kidney [96% (95% CI 80–100)]. Tubulointerstitial disease had a PPV of 62% (95% CI 32–86), renal vascular disease 60% (95% CI 46–74), various other renal disorders 17% (95% CI 2–48) and hereditary nephropathy 50% (95% CI 1–99).

The combined SNOMED codes for clinical disease groups showed Cohen's κ: Glomerular disease $\kappa = 0.77$ (95% CI 0.72–0.82), Diabetic nephropathy $\kappa = 0.85$ (95% CI 0.78–0.93) and Systemic disease $\kappa = 0.76$ (95% CI 0.64–0.88). Other groups had κ values $\leq$0.59, indicating minimal or weak agreement with nephrologist's assessments.

Several subclassified diseases were well represented and therefore were further examined (Table 4). In the group with the clinical diagnosis hypertensive nephropathy, we did not find any specific SNOMED codes. Therefore, we decided to assess SNOMED codes suggestive of hypertensive nephropathy with the absence of other disease-defining SNOMED codes. This approach with exclusion of other disease-defining SNOMED codes increased the PPV for hypertensive nephropathy from 35 (95% CI 25–46) to 56 (95% CI 40–71) and κ from 0.42 (95% CI 0.29–0.55) to 0.52 (95% CI 0.38–0.67). Although sensitivity decreased due to more stringent SNOMED code demands, there were substantially fewer false positive observations (from 57 to 19 observations) (Table 4).

DISCUSSION

In this study of 613 patients, we observed high PPV for SNOMED codes associated with glomerular disease (94%), diabetic nephropathy (85%) and systemic diseases affecting the kidney (according to ERA's grouping of primary renal diagnoses) (96%), and κ values with substantial agreement. Other clinical disease groups displayed weaker PPV and κ agreements ($\kappa \leq 0.59$). Certain subclassified disease groups in our study warranted further investigation. We found a high PPV, sensitivity and κ when combining SNOMED codes for IgA nephropathy, lupus nephritis and renal amyloidosis, although not all individual codes were adequate for epidemiological purposes. Also, while certain other subclassified disease groups (e.g. ANCA-positive vasculitis and minimal change disease) exhibited a high PPV, their sensitivity and κ were low. Stricter SNOMED code criteria improved PPV for hypertensive nephropathy to 56% (from 35%) and κ to 0.52 (from 0.42), although with reduced sensitivity. Overall, glomerular diseases, diabetic nephropathy and the broad ERA registry definition of systemic kidney diseases are well-suited for future epidemiological research using SNOMED codes. However, research into specific systemic kidney diseases is not always adequately captured by SNOMED codes and a

Table 3: Statistics over the chosen disease group compared with one or more of the specific SNOMED codes within this disease (defined in Appendix 2).

Disease group	Number of times the disease groups are chosen	Number of times the SNOMED codes are used	True positive	False positive	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Kappa (95% CI)
Glomerular disease	368	337	318	19	86 (82–90)	92 (88–95)	94 (91–97)	82 (77–86)	0.77 (0.72–0.82)
Tubulointerstitial disease	67	13	8	5	12 (5–22)	99 (98–100)	62 (32–86)	90 (87–92)	0.17 (−0.02 to 0.36)
Diabetic nephropathy	51	53	45	8	88 (76–96)	99 (97–99)	85 (72–93)	99 (98–100)	0.85 (0.78–0.93)
Renal vascular disease[a]	51	43	28	15	55 (40–67)	97 (96–99)	65 (49–79)	96 (94–97)	0.56 (0.43–0.7)
Various acute and chronic renal disorders	40	12	2	10	5 (0.6–17)	98 (97–99)	17 (2–48)	94 (91–95)	0.05 (−0.21 to 0.31)
Systemic disease affecting the kidney	39	26	25	1	64 (47–79)	100 (99–100)	96 (80–100)	98 (96–99)	0.76 (0.64–0.88)
Hereditary nephropathies	4	2	1	1	25 (0.6–81)	100 (99–100)	50 (1–99)	100 (99–100)	0.33 (−0.32 to 0.98)

[a]The results in this disease group include patients assigned one or more SNOMED codes for 'Renal vascular disease' without any other disease-defining SNOMED codes, as no specific SNOMED codes were identified for this disease group.

Table 4: Statistics of one of the chosen sub-classified disease groups compared with one or more of the specific SNOMED codes within this disease.

Disease group	SNOMED code (corresponding text)	Number of patients with the disease	Number of times the SNOMED codes are used	True positive	False positive	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Kappa (95% CI)
IgA nephropathy	IgA glomerulonephritis	61	57	45	12	74 (61–84)	98 (96–99)	79 (66–89)	97 (95–98)	0.74 (0.64–0.83)
ANCA-positive GN	Wegener's granulomatosis	62	13	11	2	18 (9–30)	100 (99–100)	85 (55–98)	92 (89–94)	0.27 (0.08–0.46)
MCD	Minimal change disease	43	28	25	3	58 (42–73)	99 (98–100)	89 (72–98)	97 (95–98)	0.69 (0.56–0.82)
FSGS[a]	Focal segmental glomerulosclerosis	61	68	47	21	77 (65–87)	96 (94–98)	69 (57–80)	97 (96–99)	0.7 (0.6–0.79)
Membranous nephropathy	Diffuse membranous glomerulonephritis	37	46	37	9	100 (91–100)	98 (97–99)	80 (66–91)	100 (99–100)	0.88 (0.81–0.96)
MPGN	Diffuse MPGN	20	21	16	5	80 (56–94)	99 (98–100)	76 (53–92)	99 (98–100)	0.77 (0.63–0.92)
Lupus nephritis	Disseminated lupus erythematosus	24	22	17	5	71 (49–87)	99 (98–100)	77 (55–92)	99 (98–100)	0.73 (0.58–0.88)
	Lupus erythematosus	24	5	4	1	17 (5–37)	100 (99–100)	80 (28–99)	97 (95–98)	0.27 (–0.04 to 0.57)
	One or more of the above codes	24	27	21	6	88 (68–97)	99 (98–100)	78 (58–91)	99 (99–100)	0.82 (0.7–0.94)
Henoch–Schoenlein	Henoch–Schoenlein purpura	8	6	3	3	38 (9–76)	100 (99–100)	50 (12–88)	99 (98–100)	0.42 (0.02–0.82)
Anti-GBM	Anti-GBM glomerulonephritis	5	5	5	0	100 (48–100)	100 (99–100)	100 (48–100)	100 (99–100)	1 (1–1)
Renal scleroderma	Scleroderma	4	3	3	0	75 (19–99)	100 (99– 100)	100 (29–100)	100 (99–100)	0.86 (0.57–1.14)
Renal amyloidosis	Amyloid deposition	21	16	16	0	76 (53–92)	100 (99–100)	100 (79–100)	99 (98–100)	0.86 (0.74–0.98)
	Amyloidosis	21	10	10	0	48 (26–70)	100 (99–100)	100 (69–100)	98 (97–99)	0.64 (0.42–0.85)
	Primary amyloidosis	21	1	1	0	5 (0.12–24)	100 (99–100)	100 (2–100)	97 (95–98)	0.09 (–0.31 to 0.48)
	One or more of the above codes	21	19	19	0	90 (70–99)	100 (99–100)	100 (82–100)	100 (99–100)	0.95 (0.88–1.02)
Chronic hypertensive nephropathy	Arteriolosclerosis	43	59	18	41	42 (27–58)	93 (90–95)	30.51 (19–44)	95 (93–97)	0.3 (0.14–0.46)
	Hypertension	43	5	5	0	12 (4–25)	100 (99–100)	100 (48–100)	94 (92–96)	0.2 (–0.05 to 0.44)
	Atherosclerosis	43	7	3	4	7 (1–19)	99 (98–100)	43 (10–82)	93 (91–95)	0.1 (–0.15 to 0.36)
	Arteriolosclerosis with fibrinoid necrosis	43	7	6	1	14 (5–28)	100 (99–100)	86 (42–100)	94 (92–96)	0.22 (–0.01 to 0.46)
	Arteriosclerosis	43	26	9	17	21 (10–36)	97 (95–98)	35 (17–56)	94 (92–96)	0.22 (0.01–0.42)
	One or more of the above codes	43	88	31	57	72 (56–85)	90 (87–92)	35 (25–46)	98 (96–99)	0.42 (0.29–0.55)
	One or more of the above codes AND absence of other disease defining codes[b]	43	43	24	19	56 (40–71)	97 (95–98)	56 (40–71)	97 (95–98)	0.52 (0.38–0.67)

[a]The subclassified disease group FSGS in this table consist of both primary and secondary FSGS.
[b]The subclassified disease group 'Chronic hypertensive nephropathy' in this row consists of patients with one or more of the presented SNOMED codes and absence of any other disease defining SNOMED codes.
FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; GN, glomerulonephritis; MCD, minimal change disease; MPGN, membranoproliferative glomerulonephritis.

combination of these codes will be necessary for research into these disease (e.g. lupus nephritis, ANCA-positive vasculitis and renal amyloidosis).

To our knowledge, this study represents the first validation of SNOMED codes for biopsy-confirmed kidney diseases, utilizing medical records as the reference standard. Currently, there is limited research validating kidney biopsy coding practices, hampering comparative analysis [17]. SNOMED codes from Patobank have been used in previous Danish registry studies, but there has been no prior validation of these codes [18–22]. Two studies from Sweden and Italy validated SNOMED codes for identifying individuals with serrated polyps and lung cancer. They used histopathology report free-text searches and manual review of health records, achieving PPV of 95% and 93%, respectively [23, 24].

In the group diagnosed with hypertensive nephropathy, we chose to examine SNOMED codes suggestive of hypertensive nephropathy. This approach could have been applied to other clinical disease groups, likely increasing the PPV and decreasing sensitivity. The decision to adopt this method in future studies depends on the researcher's priorities: favouring a smaller, more precise cohort or a larger cohort with a potential increase in false positives.

In Denmark, we have the opportunity to use International Classification of Diseases 10th revision (ICD-10) codes for epidemiological research. However, ICD-10 codes specific for types of kidney disease have not been validated for research in biopsy-confirmed kidney diseases. For both SNOMED and ICD-10 codes, there are interdepartmental and interpersonal differences in how clinicians use these codes. Nevertheless, there is a potential for combining ICD-10 codes with SNOMED codes to optimize the classification of kidney diseases as attempted in the study by Heaf *et al*. [25]. However, this method is not validated, and therefore investigation in a new validation study is warranted.

We excluded doublets and electron microscopy (EM) descriptions without accompanying light microscopy (LM) and immunofluorescence microscopy (IFM). Some departments used separate requisition numbers for LM, IFM and EM, while other merged them. We merged descriptions whenever feasible and excluded EM descriptions lacking LM and IFM. This consideration holds importance for future epidemiological investigations, as SNOMED codes alone may not consistently differentiate between LM and EM. Jensen *et al*. merged LM and IFM with EM for biopsies within 28 days, a strategy we endorse based on our findings [18]. Even if a patient undergoes two biopsies within 28 days, the lack of representativeness in the first biopsy is unlikely to impact disease classification significantly, as non-specific SNOMED codes would likely be assigned.

Clinicians' differing interpretations of clinical factors inevitably result in discrepancies in research studies. One example illustrating this discrepancy is provided by Marcussen *et al*. [26], who had four pathologists independently reanalyse 100 kidney biopsies initially diagnosed with glomerulonephritis. Their findings, showing an overall agreement of 0.67 and a Kappa value of 0.61 (95% CI 0.58–0.65), underscore the interpersonal variations in observations.

Strengths and limitations

This study has several strengths. This was a large cohort of 613 kidney biopsies with review of associated medical records by senior nephrologists. Before any data entry, all nephrologists collaborated to align their work by discussing challenging cases. We included biopsies from all Danish hospitals performing kidney biopsies, except two small centres, to address interdepartmental and interpersonal differences in coding practices. Given the changes in coding practices and referral patterns for biopsies over time, we investigated data variances between 1998–2008 and 2009–18 (Supplementary data, Table S1). We found no notable differences between the two time periods.

Additionally, the study benefits from Denmark's long-standing tradition of maintaining comprehensive national administrative registries and medical databases. Each resident is assigned a unique personal identification number. This system allows for the collection of data on the entire population. Follow-up limitations primarily arise from emigration or death, affecting roughly 8% of Denmark's population [27].

Moreover, since 1997, the Danish National Board of Health has systemized the use of SNOMED codes, standardizing data registration in Patobank across all pathology departments. This initiative was accompanied by a legal obligation for Danish pathologists to consistently report pathology data, ensuring the completeness and validity of the Danish Pathology Registry [5, 6, 9].

Finally, we analysed the dataset including 57 of the excluded biopsies (Supplementary data, Table S2). This analysis, showed no notable differences from the initial findings, confirming the validity of the approach adopted in this study.

This study also has limitations. It investigated 9 clinical disease groups and 66 subclassified diseases using 124 SNOMED codes, resulting in numerous combinations. Despite a large cohort, several diseases were rarely or not at all represented in the study. Many kidney diseases have a low prevalence in the population and a low frequency in the biopsy cohort was expected. Therefore, we grouped diagnoses into nine broad clinical disease groups.

The methodology employed in this study cannot address kidney diseases with low prevalence. Previous studies validating medical codes for rare conditions often employ a hypothesis-driven approach, assessing code accuracy and calculating PPV [28, 29]. A similar strategy could be used to validate SNOMED codes for uncommon kidney diseases. However, it is not possible to calculate sensitivity and specificity without identifying true-negative and false-negative cases. This pose challenges for validation of rare conditions where limited number of cases are available.

As mentioned, Denmark's coding system relies on SNOMED II, differing from SNOMED CT which is widely used elsewhere [7]. Danish SNOMED II codes evolve uniquely, potentially making them incomparable globally. Additionally, kidney biopsy coding varies worldwide, with some using SNOMED or ERA codes, while others rely on proprietary systems [17].

Biopsies lacking accessible medical records ($n = 73$) were excluded. The digitization of patient records in Denmark from 2006 to 2012 reduced exclusions post-2006 (75% of unobtainable records dated from 1998–2006) [30]. Given the absence of major revisions to SNOMED coding practice since 1997, we believe that excluding cases with unobtainable records does not markedly impact the results, ensuring the validation spans the entire period. However, ongoing SNOMED maintenance may introduce code changes and new codes, potentially impacting consistency over time. The present results may only be applicable to SNOMED codes prescribed between 1998 and 2018.

Forty percent of biopsies, even those excluded due to unavailable records, occurred from 1998 to 2008, suggesting an increased frequency of kidney biopsies in the latter study phase. This may be due to an increased overall use of kidney biopsies in

patients with kidney disease, or an increased occurrence of kidney disease. The present study could not address this question.

Perspective

This study demonstrates strengths in classifying specific kidney diseases, underscoring the potential of SNOMED codes for accurate epidemiological research. The study addresses the limitations of the SNOMED codes and offer valuable guidance for future studies.

Certain kidney diseases lacked adequate categorization using SNOMED codes. We suggest a national or even better an international harmonization of coding practices to improve agreement between SNOMED codes and clinical disease groups. Integrating the ERA coding system into the Danish SNOMED system could potentially enhance existing S-codes, leading to improved accuracy and efficiency in disease coding. A contemporary requirement of the pathologists to apply an S-code/ERA code, would ensure standardization and international alignment of the Danish coding system with others.

CONCLUSION

This study highlights the high PPV of SNOMED codes in Denmark for glomerular diseases, diabetic nephropathy and other systemic kidney diseases. However, caution is advised for other clinical diagnoses. This validation study provides results that will enhance the accuracy of epidemiological research in biopsy-confirmed kidney diseases, ensuring the reliability of data from the Danish Patobank registry.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

M.M., D.H. and D.K. conceived and designed the study. M.M., R.B., H.D., J.W.G., H.H., K.H., M.H., P.I., K.H.J., M.B.J., T.K., F.H.M., K.E.O. and K.D.S. collected clinical data. M.M. drafted the manuscript. M.M. and D.H. had full access to and ensured the integrity and accuracy of the data. M.M. conducted the statistical analyses, while M.M., D.H. and I.B. interpreted the data. All authors contributed significantly to manuscript revision and intellectual input.

DATA AVAILABILITY STATEMENT

Data have not been made publicly available due to Research Ethics and Governance approvals. Requests to collaborate and share some of the data may be directed to the corresponding author.

CONFLICT OF INTEREST STATEMENT

No potential conflicts of interest were reported by M.M., I.B., H.D., J.W.G., H.H., K.H., P.I., K.H.R., M.B.J., D.K., F.H.M., P.R., K.E.O., F.P. and K.D.S. T.K. reports honoraria for education and consultancy from AstraZeneca. R.B. reports honoraria for education and consultancy from AstraZeneca, Bayer, Mundipharma, Vifor and Boehringer Ingelheim. M.H. reports honoraria for advisory boards for AstraZeneca, Bayer, Boeringer Ingelheim, Vifor, GSK and Novo Nordisk A/S, and education for AstraZeneca, Boeringer Ingelheim and Novo Nordisk A/S outside the scope of this manuscript. D.H. reports research grant from Vifor Pharma and Gedeon Richter, and consultancy fees and lecture fees from UCB Nordic, GSK and AstraZeneca.

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