

# Accuracy of the hypospadias diagnoses and surgical treatment registrations in the Danish National Patient Register

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**Purpose:** The Danish National Health registers provide a valuable data source that offers unique opportunities for observational research, including studies on the congenital anomaly hypospadias. The accuracy of the diagnosis and surgical treatment registration of hypospadias in the Danish National Patient Register (DNPR) remains unknown.

**Patients and methods:** We randomly sampled 500 patients diagnosed with hypospadias in the DNPR from January 1, 1995 to December 31, 2012. Among these, 384 patients were also registered with surgical treatment for hypospadias. Medical records were collected and reviewed independently by two investigators. Any classification disagreements were resolved by consensus. Using the medical records as the gold standard, we estimated positive predictive values (PPVs) with 95% confidence intervals (CIs) for the hypospadias diagnoses and surgical treatment registrations overall, as well as for the clinical subtypes.

**Results:** We were able to retrieve medical records for 463 (92.6%) patients with hypospadias diagnoses and for 329 (85.7%) patients registered with surgical treatment. Presence of hypospadias was confirmed in 450 of 463 patients, yielding an overall PPV (95% CI) of 97.6% (95.8%–98.7%). For subtypes of hypospadias, the PPVs ranged between 37.5% and 72.7%. For surgical treatment of hypospadias, the overall PPV was 99.7% (97.9%–99.9%).

**Conclusion:** The validity of the registration of hypospadias diagnoses as well as surgical treatment for hypospadias in the DNPR is overall very high. For the specific subtypes of hypospadias diagnoses codes and the specific surgical treatment codes, the PPVs are lower and cautious use is warranted. However, the DNPR remains a valuable tool for future observational research on hypospadias.

**Keywords:** data quality, epidemiology, hospital register diagnoses, ICD-10, positive predictive value

## Introduction

The Nordic national health registers provide a highly valuable population-based data resource for observational research. For five decades, the Danish Civil Registration System has assigned a unique personal identification number to all Danish residents,<sup>1,2</sup> enabling individual level linkage of data from registers, medical databases, and birth cohorts. The Danish National Patient Register (DNPR) holds information on all hospital contacts with complete nationwide coverage since 1978.<sup>3,4</sup> It is among the most commonly used health-care register in Denmark and enables researchers to perform nationwide, population-based observational studies within various research fields. Research on rare conditions such as congenital abnormalities also benefits from these long-term follow-up data.

Hypospadias is a congenital anomaly of the male genitalia with an estimated prevalence of 0.5%–0.8% in Denmark.<sup>5</sup> It is recognizable by incomplete closure of the urethra leading to various degrees of displacement of the external urethral orifice along the ventral side of the penis, scrotum or perineum, often accompanied by abnormal foreskin and ventral penile shaft deviation.<sup>6</sup> In recent years, there has been a large research focus on temporal trends, etiology, and risk factors for hypospadias as well as long-term consequences for the affected boys.<sup>7</sup> Danish register-based research has contributed substantially to the current knowledge in this area.<sup>5,8–14</sup> Yet, many etiological aspects and research questions remain unanswered and register-based data will continuously serve as an important tool in answering these questions in the future.

Although the overall validity of the DNPR is considered high, not all diagnoses have been shown to be accurate.<sup>15</sup> The accuracy of the hypospadias diagnosis and surgical treatment in the DNPR remains unknown.

## Material and methods

### Setting and data collection

In this nationwide, population-based validation study, we assessed the accuracy of the International Classification of Diseases (ICD-10) discharge diagnosis codes and surgical treatment codes for hypospadias in the DNPR between January 1, 1995 and December 31, 2012. The DNPR was established in 1977<sup>3,4</sup> and provides complete nationwide information on all inpatient contacts to Danish hospitals since 1978 and on outpatient contacts since 1995. From 1977 to 1995, diseases were classified according to the ICD-8 and from 1995 and onward, the ICD-10 has been used.

All patients registered with a main inpatient or outpatient hospital discharge ICD-10 code of hypospadias (Q54; hypospadias glandis [Q540], hypospadias coronalis [Q540A], hypospadias corporis penis [Q541], hypospadias penoscrotalis [Q542], hypospadias perinealis [Q543], other specified hypospadias [Q548], and hypospadias without specifications [Q549]) between January 1, 1995 and December 31, 2012 were identified. Among all registered in the DNPR, the Danish Statens Serum Institut randomly selected a representative sample of 500 patients. From the DNPR, we obtained information on the unique civil registration number, date of admission, date of operation, date of discharge, hospital code, departmental code, diagnostic specialty, all main and secondary diagnoses codes for hypospadias and other congenital anomalies or genetic syndromes (ICD-10: Q00–Q99) as well as surgical treatment codes for hypospadias; operation for hypospadias (KGH60), glandular hypospadias (KGH60A), corporal hypospadias (KGH60B), penoscrotal hypospadias

(KGH60C), and perineal hypospadias (KGH60D) for the randomly selected study population of 500 patients. Thus, we studied the accuracy of registration of surgical treatment among those registered with a hypospadias diagnosis.

Medical records were collected from June 2015 to September 2016. Copies of the medical records were requested by mail directed to the department responsible for the first hypospadias registration, as well as to the hospital performing the surgical treatment for hypospadias. Reminders were mailed to the non-responding departments after approximately 3 months and, finally, the remaining departments were contacted by phone and/or personal visits.

### Medical record review

From October 2016 to February 2017, two investigators independently reviewed each medical record, blinded to the diagnoses and surgical treatment codes registered in the DNPR. Data were extracted using scoring protocols developed in collaboration with experts within pediatric urology and then entered in the Research Electronic Data Capture (REDCap) software.<sup>16</sup> The physicians' descriptions in the medical records served as the gold standard. When discrepancies related to the location of the external urethral orifice existed, the description of urethral orifice according to the surgical operation report was superior. If the patient did not receive surgical treatment or if the description was missing, the description from the outpatient clinic was used. In the ICD-10, the condition penis arcuatus (Q544) is registered as a subtype of hypospadias. However, as isolated penile shaft deviation without urethral meatus displacement mainly originates due to various reasons other than hypospadias, penis arcuatus is not considered as a hypospadias subtype in pediatric urology. Therefore, penis arcuatus was not validated nor regarded as a hypospadias subtype in the medical record review. The independent reviews from the two investigators were compared, typing errors were corrected, and disagreements were resolved by consensus decision-making. Subsequently, data were exported for the statistical analyses performed in Stata 13.1.

### Statistical analyses

The accuracy of hypospadias diagnoses and surgical treatment codes was calculated as positive predictive values (PPVs) with 95% confidence intervals (CIs) overall for diagnosis of hypospadias and surgical treatment of hypospadias, as well as for every specific sub-diagnosis or -surgical treatment code. All PPVs were calculated as the proportion of diagnoses from the DNPR that were confirmed during the medical record review. When assessing the accuracy of the specific subtypes of hypospadias, we used different

approaches. A total of 440 (88%) patients were registered with more than one hypospadias diagnosis during the study period, which corresponds well with the clinical practice for diagnosing hypospadias in Denmark. Typically, the patients first have outpatient hospital contact and then, inpatient contact with surgical treatment. Subsequently, there will be at least one – and often many – follow-up outpatient hospital contacts. Therefore, we validated both the first diagnosis and the most severe diagnosis defined as the most proximal location of the external urethral orifice.

We further estimated PPVs stratified by calendar year of first diagnosis (1995–1998, 1999–2003, 2004–2008, and 2009–2012), region of Denmark (North, Central, Southern, Sealand, and Capital), hospital type (university and referral) and department type deciding the location of the external urethral orifice (pediatric urology or pediatric surgery, plastic surgery and general surgery or urology), number of ICD-10 hypospadias diagnoses in the DNPR (1 and  $\geq 2$ ), response time to our contact (fast if the departments responded after the first contact and slow if they responded after reminders were sent out) and presence of genetic syndromes or other congenital abnormalities.

Finally, in a sensitivity analysis, we assumed a worst-case scenario where all patients with unavailable medical records were classified as not having hypospadias.

## Ethical approval

The study was approved by the Danish Data Protection Agency (Ref. no: 2013-41-1964), the Danish National Board of Health (Ref. no: 3-3013-580/1), and the State Serum Institute (Ref. no: FSEID-00001380). In accordance with Danish legislation, approval from the Danish Ethics Committee was not required.

## Results

In the study period, 3,700 males were registered with a hypospadias diagnosis and among them 2,956 were registered with a surgical treatment code for hypospadias. We randomly sampled 500 of the 3,700 diagnosed males for this study and among these, 384 were registered with a surgical treatment code for hypospadias.

We successfully retrieved medical records for 463 (92.6%) out of the 500 patients from a total of 42 clinical departments in Denmark. Among the 384 patients registered with surgical treatment, we obtained descriptions from surgical treatment of hypospadias on 329 (85.7%) patients. No departments refused to participate.

Table 1 shows baseline characteristics from the DNPR of the 500 patients stratified by medical record availability. Only for 37 (7.4%) patients, medical records were unavailable,

and these were more often diagnosed in the early years of the study period and at referral hospitals.

We confirmed the hypospadias diagnosis for 450 of the 463 patients and found an overall PPV for the hypospadias diagnoses of 97.6% (95.8%–98.7%) (Table 2). Assuming a worst-case scenario where all 37 patients with unavailable medical records were misclassified, the PPV would be 90.0% (87.0%–92.3%).

Figure 1 shows the percentage distribution of the hypospadias subtypes registered in the DNPR (Figure 1A) as well as the subtype of hypospadias according to the medical record review (Figure 1B). We found glandular or coronal hypospadias in 47.2%, corporal hypospadias in 31.8%, penoscrotal hypospadias in 5.0%, and perineal hypospadias in 0.6%. The PPVs differed according to the specific subtypes; in case of glandular and coronal hypospadias, the PPV was 64.7% when validating the first hypospadias diagnosis and the PPV for the more severe subtypes ranged from 50.0% to 72.7% (Table 2).

**Table 1** Medical record availability according to characteristics among 500 patients diagnosed with hypospadias in the Danish National Patient Register, 1995–2012

	Medical record availability	
	Available n=463 (92.6%)	Not available n=37 (7.4%)
Year at first diagnosis, n (%)		
1995–1998	131 (28.3)	28 (75.7)
1999–2003	122 (26.4)	4 (10.8)
2004–2008	125 (27.0)	5 (13.5)
2009–2012	85 (18.4)	0 (0.0)
Region of Denmark, n (%)		
North	34 (7.3)	0 (0.0)
Central	167 (36.1)	8 (21.6)
Southern	84 (18.1)	8 (21.6)
Sealand	28 (6.1)	2 (5.4)
Capital	150 (32.4)	19 (51.4)
Hospital type, n (%)		
University	341 (73.7)	13 (35.1)
Referral	112 (26.3)	24 (64.9)
Department type, n (%)		
Pediatric urology or surgery	324 (70.0)	6 (16.2)
Plastic surgery	118 (25.5)	17 (46.0)
General surgery or urology	21 (4.5)	7 (18.9)
Other	0 (0.0)	7 (18.9)
Number of ICD-10 hypospadias diagnoses in DNPR, n (%)		
1	53 (11.5)	7 (18.9)
$\geq 2$	410 (88.5)	30 (81.1)
Genetic syndromes or other congenital abnormalities, <sup>a</sup> n (%)		
Yes	130 (28.1)	6 (16.2)
No	333 (71.9)	31 (83.8)

**Note:** <sup>a</sup>Genetic syndromes or congenital abnormalities (Q00–Q99) other than hypospadias (Q54, Q540, Q540A, Q541, Q542, Q543, Q548, and Q549).

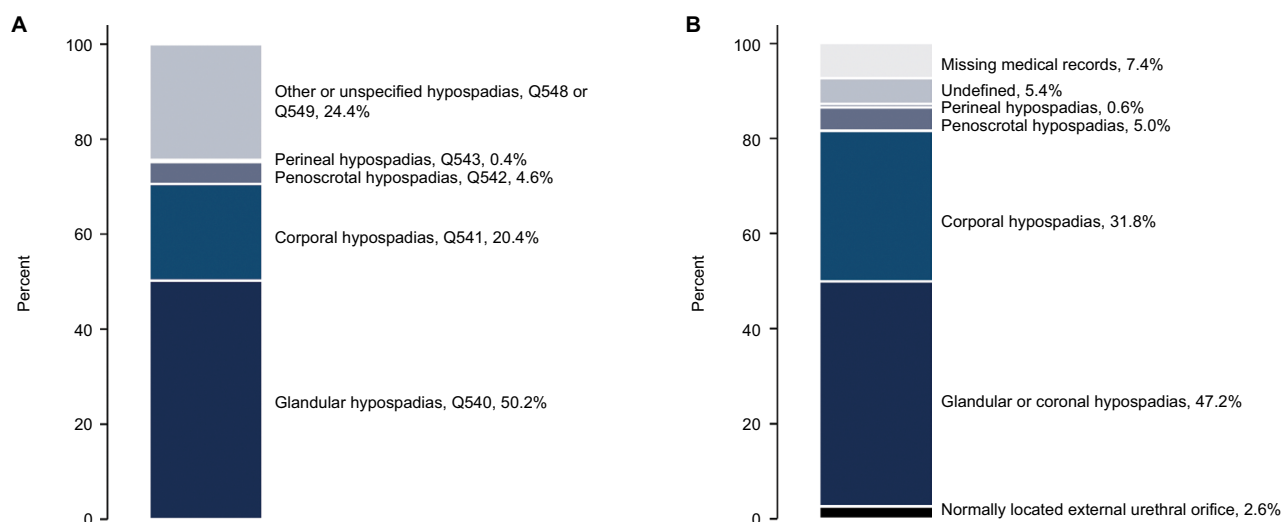
**Abbreviation:** DNPR, Danish National Patient Register; ICD, International Classification of Diseases.

**Table 2** Positive predictive values of the hypospadias diagnoses among 463 patients in the Danish National Patient Register, 1995–2012

	ICD-10	Accuracy of the first diagnosis <sup>a</sup>				Accuracy of the most severe diagnosis <sup>b</sup>			
		Sample	Ratio <sup>c</sup>	PPV (%)	95% CI (%)	Sample	Ratio <sup>c</sup>	PPV (%)	95% CI (%)
Overall hypospadias <sup>d</sup>	Q54 <sup>d</sup>	463	450/463	97.6	95.8–98.7	463	450/463	97.6	95.8–98.7
Glandular or coronal hypospadias	Q540	235	152/235	64.7	58.3–70.6	208	150/208	72.1	65.6–77.8
	Q540A								
Corporal hypospadias	Q541	92	50/92	54.3	43.9–64.4	173	98/173	56.6	49.1–63.9
Penoscrotal hypospadias	Q542	22	16/22	72.7	49.0–88.1	33	18/33	54.5	36.8–71.2
Perineal hypospadias	Q543	2	1/2	50.0	–	8	3/8	37.5	8.7–79.1
Other or unspecified hypospadias <sup>e</sup>	Q548	112	110/112	98.2	93.1–99.6	41	39/41	95.1	82.2–98.8
	Q549								

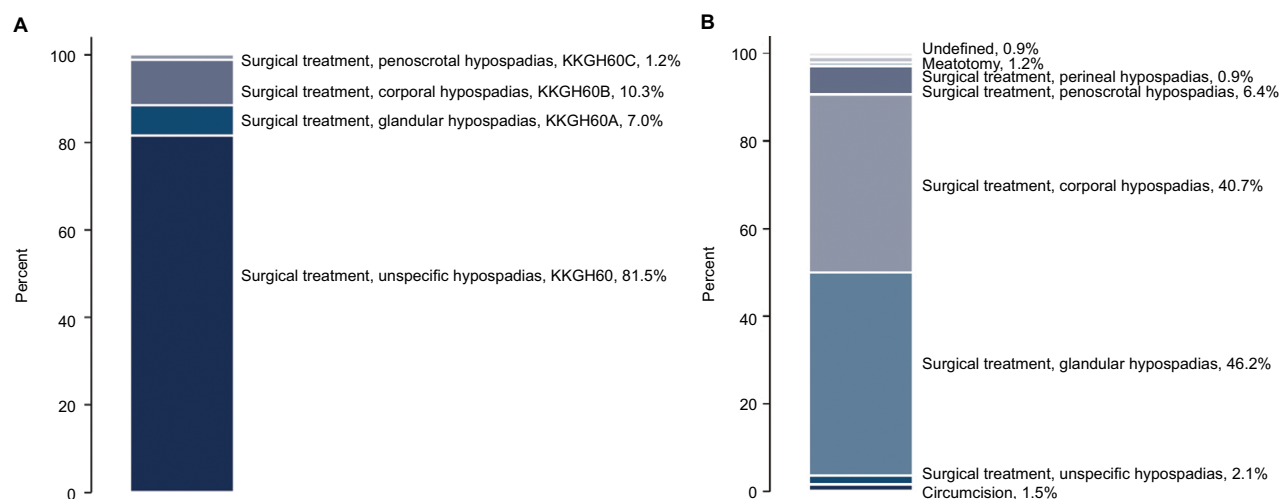
**Notes:** <sup>a</sup>Accuracy of the first ICD-10 diagnosis of hypospadias registered in the DNPR from 1995 to 2012. <sup>b</sup>Accuracy of the most severe ICD-10 diagnosis of hypospadias registered in the DNPR from 1995 to 2012. <sup>c</sup>Ratio denotes confirmed diagnoses/available records. <sup>d</sup>Overall PPV for all ICD-10 codes for hypospadias, Q54, Q540, Q540A, Q541, Q542, Q543, Q548, and Q549. <sup>e</sup>Accuracy of other (Q548) or unspecified hypospadias (Q549) registration in regard to the number of diagnoses that could be confirmed as any form of hypospadias in the medical record review.

**Abbreviations:** DNPR, Danish National Patient Register; ICD, International Classification of Diseases; PPV, positive predictive value.



**Figure 1** Percentage distribution of the ICD-10 diagnoses codes for subtypes of hypospadias registered in the Danish National Patient Register (A) and subtype of hypospadias based on medical record review (B).

**Abbreviation:** ICD, International Classification of Diseases.



**Figure 2** Percentage distribution of the operation codes for surgical treatment of hypospadias registered in the Danish National Patient Register (A) and surgical treatment of hypospadias based on medical record review (B).

Figure 2 presents the percentage distribution of the operation codes for surgical treatment of hypospadias registered in the DNPR (Figure 2A) and the surgical treatment of hypospadias retrieved from the medical record review (Figure 2B). In total, 81.5% was registered in the DNPR with the unspecific hypospadias operation code KGH60. Table 3 presents the PPVs of surgical treatment of hypospadias. The medical records confirmed 328 of the 329 registered surgical treatments, yielding an overall PPV of 99.7% (97.9%–99.9%). As for the diagnoses, the PPVs of subtypes of surgical treatment were lower than the PPV for overall surgical treatment, decreasing stepwise according to severity (Table 3).

Analyses stratified by year at first diagnosis, region of Denmark, hospital type, response time, and presence of genetic syndromes or other congenital abnormalities closely agreed with our main findings (Table 4). However, the PPVs varied according to department type as well as number of hypospadias diagnoses in the DNPR. For general surgery or urology, the PPV was lower than for pediatric surgery and urology and for plastic surgery. For those registered with  $\geq 2$  diagnoses, the PPV was 98.0 (96.1%–99.0%) compared to 90.6% (79.1%–96.1%) for those who had only one diagnosis in the DNPR (Table 4). In total, 28.1% of the boys were also registered in the DNPR with other congenital abnormalities or genetic syndromes. It is well known that boys born with hypospadias more often have additional congenital abnormalities or that the hypospadias is part of a genetic syndrome.<sup>1,2</sup> In particular, cryptorchidism and other urogenital anomalies are frequent.<sup>3,4</sup> Yet, the PPV did not vary between those with isolated hypospadias and those also registered with other congenital abnormalities.

## Discussion

This nationwide, population-based validation study showed that the ICD-10 hypospadias diagnoses and surgical treatments in the DNPR have an overall high PPV.

This study is the first to validate and provide PPVs of hypospadias diagnosis and surgical treatment registrations. A former Danish case–control study by Pedersen et al. indicated a similarly high accuracy.<sup>17</sup> Their main objective was to examine the risk of hypospadias among boys exposed to anti-histamines during pregnancy using data from the DNPR from 1989 to 2003.<sup>17</sup> As a secondary aim, they investigated the potential misclassification by reviewing medical records for 43 of the 227 hypospadias cases. They did not estimate PPVs, but found that three out of the 43 cases were misclassified.

Later, in a large systematic review of the content in the DNPR, Schmidt et al. recalculated the proportions and found a PPV of 93.0% (81.4%–97.6%).<sup>15</sup> However, the study was performed only on data from the North and Central regions in Denmark (i.e., not a random sample of the registry content) and covered an earlier time period.

A major strength of our study was the nationwide population-based design. We were able to study a random sample of all patients recorded with an ICD-10 diagnosis of hypospadias, and successfully retrieved 92.6% of the requested medical records, thus, limiting the risk of selection bias. Comparison of characteristics among available and unavailable medical records showed that older records were less available and that unavailability was associated with geographical region and type of hospital. In stratified analyses, we found very similar PPVs when we compared PPVs between departments who responded fast versus those who responded slowly to our medical record request. Further, in a rather unlikely worst-case scenario, assuming that all patients with missing information were incorrectly registered, the PPV was still 90.0% (87.0%–92.3%). We are therefore quite confident that the presented PPV is not substantially overestimated.

In contrast, the PPVs for subtypes of hypospadias were rather low ranging from 37.5% to 72.7%, and although the PPVs for surgical treatments were generally higher, they never reached the level of the overall PPVs. However, the sample sizes for penoscrotal and perineal hypospadias were small, rendering uncertain PPVs. Thus, in general, cautious interpretation of research on specific subtypes of hypospadias is warranted. Further, it is important to emphasize that we did not validate the ICD-8 codes, which were used from 1977 to 1994. Often, register-based studies cover the whole registration period for the DNPR, but our results cannot be extrapolated to the period before 1995.

Further, it should be noted that we present PPV as the validity measure. The PPVs are influenced by the prevalence of hypospadias in the sample. If one had randomly sampled boys from the entire population, where the prevalence of hypospadias is lower than in this study, the PPVs may also have been lower. However, as this would require a very large sample, such a study seems rather unfeasible. Thus, in this study, we have assessed the validity of the hypospadias diagnoses and surgical treatment codes registered in the DNPR.

Moreover, because of the design, we were not able to study the completeness, e.g., the proportion of patients with hypospadias, who were not registered in the DNPR (false



**Table 3** Positive predictive values of surgical treatment of hypospadias among 329 patients in the Danish National Patient Register, 1995–2012

	ICD-10	Sample	Ratio <sup>a</sup>	PPV (%)	95% CI (%)
Overall surgical treatment for hypospadias <sup>b</sup>	KGH60 <sup>b</sup>	329	328/329	99.7	97.9–99.9
Hypospadias, unspecific <sup>c</sup>	KGH60	268	267/268	99.6	97.4–99.9
Glandular or coronal hypospadias	KGH60A	23	20/23	87.0	64.2–96.1
Corporal hypospadias	KGH60B	34	28/34	82.4	64.8–92.2
Penoscrotal hypospadias	KGH60C	4	3	75.0	4.1–99.5
Perineal hypospadias	KGH60D	0	–	–	–

**Notes:** <sup>a</sup>Ratio denotes confirmed diagnoses/available records. <sup>b</sup>The overall PPV for all surgical treatment codes (KGH60, KGH60A, KGH60B, KGH60C, and KGH60D) for hypospadias among the 329 patients with available descriptions from surgical treatment. <sup>c</sup>The PPV for the unspecific hypospadias operation code KGH60, calculated as the number of boys with a hypospadias operation verified in the medical records/number of boys registered with KGH60.

**Abbreviations:** ICD, International Classification of Diseases; PPV, positive predictive value.

**Table 4** Positive predictive values of the hypospadias diagnosis stratified by potentially modifying characteristics among 463 patients in the Danish National Patient Register, 1995–2012

	Overall hypospadias diagnoses		
	Ratio	PPV (%)	95% CI (%)
Year at first diagnosis			
1995–1998	127/131	96.9	92.1–98.9
1999–2003	117/122	95.9	90.5–98.3
2004–2008	122/125	97.6	92.8–99.2
2009–2012	84/85	98.8	92.0–99.8
Region of Denmark			
North	33/34	97.1	81.3–99.6
Central	164/176	98.2	94.5–99.9
Southern	81/84	96.4	89.4–98.9
Sealand	28/28	100.0	–
Capital	144/150	96.0	91.3–98.2
Hospital type			
University	336/341	98.5	96.5–99.4
Referral	114/122	93.4	87.4–96.7
Department type			
Pediatric urology or surgery	320/324	98.8	96.7–99.5
Plastic surgery	116/118	98.3	93.4–99.6
General surgery or urology	14/21	66.7	44.1–83.6
Number of ICD-10 hypospadias diagnoses in DNPR			
1	48/53	90.6	79.1–96.1
≥2	402/410	98.0	96.1–99.0
Response time			
Fast	372/382	97.4	95.2–98.6
Slow	78/81	96.4	89.0–98.8
Genetic syndromes or other congenital abnormalities <sup>b</sup>			
Yes	126/130	96.9	92.0–98.8
No	224/333	97.3	94.9–98.6

**Notes:** <sup>a</sup>Overall hypospadias diagnoses, any type; Q54, Q540, Q540A, Q541, Q542, Q543, Q548, and Q549. <sup>b</sup>Genetic syndromes or congenital abnormalities (Q00–Q99) other than hypospadias (Q54, Q540, Q540A, Q541, Q542, Q543, Q548, and Q549).

**Abbreviations:** DNPR, Danish National Patient Register; ICD, International Classification of Diseases; PPV, positive predictive value.

negative cases), as the study population was defined as patients registered with ICD-10 codes in the DNPR. This needs to be considered when using the ICD-10 codes for hypospadias ascertainment in register-based research.

## Conclusion

We found a very high overall PPV of hypospadias diagnosis and surgical treatment registrations. Thus, the DNPR is a valid tool for observational research on hypospadias. However, in future studies on specific subtypes of hypospadias, there should be awareness of the low PPVs.

## Disclosure

The authors report no conflicts of interest in this work.

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