BMJ open

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|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2014-004956 |
| Article Type: | Research |
| Date Submitted by the Author: | 29-Jan-2014 |
| Complete List of Authors: | Holland-Bill, Louise; Aarhus University Hospital, Department of Clinical Epidemiology<br>Christiansen, Christian F; Aarhus University Hospital, Dept. of Clinical Epidemiology; Aarhus University Hospital, Department of Clinical Epidemiology<br>Ulrichsen, Sinna; Aarhus University Hospital, Department of Clinical Epidemiology<br>Ring, Troels; Aalborg University Hospital, Department of Nephrology<br>Jørgensen, Jens Otto; Aarhus University Hospital, Department of Endocrinology and Internal Medicine<br>Toft Sørensen, Henrik; Aarhus University Hospital, Department of Clinical Epidemiology |
| Primary Subject Heading: | Epidemiology |
| Secondary Subject Heading: | Research methods, Renal medicine, Diabetes and endocrinology |
| Keywords: | EPIDEMIOLOGY, Diabetes & endocrinology < INTERNAL MEDICINE, Nephrology < INTERNAL MEDICINE, GENERAL MEDICINE (see Internal Medicine) |

# Validity of the International Classification of Diseases, 10th revision (ICD-10) discharge diagnosis codes for hyponatremia in the Danish National Registry of Patients

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**Keywords:** validation study; ICD 10; hyponatremia; diagnosis; population register; clinical laboratory information system

**Word count:** 2,829

## ABSTRACT

**OBJECTIVE:** To examine the validity of the *International Classification of Diseases*, 10th revision (ICD-10) codes for hyponatremia in the nationwide population-based Danish National Registry of Patients (DNRP) among inpatients of all ages.

**DESIGN:** Population-based validation study.

**SETTING:** All somatic hospitals in the North and Central Denmark Regions from 2006 through 2011.

**PARTICIPANTS:** Patients of all ages admitted hospital (n=819,701 individual patients) during the study period. Patient could be included in the study more than once, and we did not restrict to patients with serum sodium measurements (total of n=2,186,642 hospitalization).

**MAIN OUTCOME MEASURE:** We validated ICD-10 discharge diagnoses of hyponatremia recorded in the DNRP, using serum sodium measurements obtained from the laboratory information systems (LABKA) research database as gold standard. One sodium value <135 mmol/l measured at any time during hospitalization confirmed the diagnosis. We estimated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for ICD-10 codes for hyponatremia overall and for cut-off points for increasing hyponatremia severity.

**RESULT:** An ICD-10 code for hyponatremia was recorded in the DNRP in 5,850 of the 2,186,642 hospitalizations identified. According to laboratory measurements, however, hyponatremia was present in 306,418 (14%) hospitalizations. Sensitivity of hyponatremia diagnoses was 1.8% (95% confidence interval (CI): 1.7%-1.8%). For sodium values <115mmol/l, sensitivity was 34.3% (95% CI: 32.6%-35.9%). Overall PPV was 92.5% (95% CI: 91.8%-93.1%), and decreased with increasing hyponatremia severity. Specificity and NPV were high for all cut-off points (≥99.8% and ≥86.2% respectively). Hyponatremic patients without a corresponding ICD-10 discharge diagnosis were younger and had higher Charlson Comorbidity Index scores than hyponatremic patients with a hyponatremia code in the DNRP.

**CONCLUSION:** ICD-10 codes for hyponatremia in the DNRP have high specificity, but very low sensitivity. Laboratory test results, not discharge diagnoses, should be used to ascertain hyponatremia.

# Article summery

### Article focus

- Hospital discharge diagnoses for hyponatremia recorded in the Danish National Registry of Patients (DNRP) may constitute valuable data sources for epidemiologic studies, however the validity of data must be established.

### Key Message

- ICD-10 coding of hyponatremia in the Danish National Registry of Patients (DNRP) is highly specific but greatly incomplete.
- Epidemiological studies relying on discharge diagnoses of hyponatremia may be susceptible to differential misclassification.

### Strengths and limitation of this study

- This is the first study to validate the International Classification of Diseases, 10th Revision code for hyponatremia in hospitalized patients of all ages.
- We used a population-based design with unambiguous individual-level linkage between registries containing complete data on all hospitalizations and laboratory, ensuring a large sample size and virtually eliminating the risk of selection bias.
- We did not consider the duration of hyponatremia. Sensitivity may have been higher if presence of hyponatremia required, that it was detected in more than one laboratory measurement during hospitalization.

## INTRODUCTION

Hyponatremia, defined as a serum sodium value <135mmol/l, is the most common electrolyte abnormality encountered in clinical practice.[1] It can be caused by a large variety of conditions, such as heart failure, kidney failure, cirrhosis, syndrome of inappropriate antidiuretic hormone, vomiting, and diarrhea, and can also be a side effect of several medications.[2] Results of recent studies have indicated that even a mild to moderate level of hyponatremia may be an important predictor of poor prognosis in patients with cardiovascular disease, kidney and liver disease, and cancer.[3-8] However, key aspects of the etiology and prognosis of hyponatremia remain unknown.

The Danish population-based medical registries may offer a unique opportunity for studies of the epidemiology of hyponatremia, if data are valid. However, as symptoms of mild and moderate hyponatremia may be vague, and concealed by or construed as symptoms of an underlying disease, it is likely that the condition will not be reported.[9,10] Thus, use of only inpatient discharge diagnoses of hyponatremia in epidemiologic studies may cause bias that can affect the validity of study results.[11]

To date, only one study has investigated the validity of *International Classification of Diseases* (ICD), 10$^{th}$ revision (ICD-10) codes for hyponatremia. This Canadian study was restricted to patients 66 years of age or older presenting with a hyponatremic serum sodium value at time of emergency department contact or at admission.[12] The sensitivity of hyponatremia coding was found to be as low as 7%. For inpatients younger than 66 years, knowledge of the validity hyponatremia diagnoses is limited to a study performed in a single hospital in the Netherlands using ICD-9 codes for hyponatremia. In this study, sensitivity was found to be just below 2%, using hospital laboratory data as the reference standard.[3] Similar results were found in a study examining the validity of outpatient professional ICD-9 claims for hyponatremia in the US.[14]

We therefore conducted the first population-based study examining the validity of ICD-10 inpatient discharge diagnoses of hyponatremia in the Danish National Registry of Patients (DNRP), in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), including patients of all ages.

## METHODS

### Setting and data collection

We used the DNRP to identify all admissions to hospitals in the North and Central Denmark Regions (2.1 million inhabitants in the study period) from 1 January 2006 to 31 December 2011. The DNRP contains information, including date of admission and discharge, department code and discharge diagnoses, on all admissions to Danish non-psychiatric hospitals since 1977.[15,16]

By use of the unique 10-digit civil registration number, assigned to all Danish residents since 1968,[17] we linked each patient's DNRP data to the clinical laboratory information system (LABKA) research database. For patients living in the North and Central Denmark Regions, data on virtually all specimens analyzed in clinical laboratories by hospitals and medical practitioners are entered into a computer-based clinical laboratory information system, which functions as a routine diagnostic tool for medical personnel.[18] Data are transferred electronically to the LABKA research database, managed by Aarhus University. Analyses are coded according to the NPU (Nomenclature, Properties and Units) system. The LABKA research database contains the civil registration number, time and date of blood sampling, and identification code of the requesting physician or hospital department.[18] We used the LABKA research database to retrieve information on all serum sodium measurements recorded during each of the identified hospitalizations.

### Hyponatremia diagnosis (ICD-10 code algorithm)

At hospital discharge, the attending physician assigns one primary diagnosis, reflecting the main reason for hospitalization and treatment and up to 19 secondary diagnoses regarding additional clinically relevant conditions, including underlying diseases, complications and symptoms.[19] Diagnoses recorded in the DNRP have been coded according to the *International Classification of Diseases* (ICD), 10th revision (ICD-10) since 1994.[16]

We developed an algorithm based on ICD-10 codes to identify discharge diagnoses of hyponatremia recorded in the DNRP for each hospitalization. The following ICD-10 codes were included in the algorithm: E87.1 (Hypo-osmolality and hyponatremia), E87.1A (Hyponatremia) and P74.2B (Hyponatremia in newborns [Danish version of ICD-10]).

**Gold Standard (laboratory serum sodium measurements)**

We used serum sodium measurements recorded in the LABKA research database as the gold standard to confirm or disconfirm a diagnosis of hyponatremia identified by the ICD-10 algorithm. Hyponatremia was defined as serum sodium values <135 mmol/l for patients older than 30 days and <133 mmol/l for infants 30 days of age or younger.[20] Patients were considered to have hyponatremia if at least one hyponatremic serum sodium value was recorded during their hospitalization. If no serum sodium measurement was available, the patient was assumed to have a non-hyponatremic serum sodium value (135-145mmol/l). The following cut-off points for increasing severity of hyponatremia were chosen: 135 mmol/l, 130mmol/l, 125mmol/l, 120mmol/l and 115mmol/l.[13] The corresponding levels for infants less than 31 days of age were 133mmol/l, 128mmol/l, 123mmol/l, 118mmol/l and 113mmol/l.

**Other Variables**

For each patient, we assessed comorbidity by information retrieved from the DNRP on the conditions included in the Charlson Comorbidity Index (CCI). The CCI includes 19 medical conditions, each

assigned a weighted score between one and six. The sum of these individual scores is used as a measure of a patient's comorbidity burden.[21, 22] We calculated CCI scores for each patient and defined three comorbidity levels: low (CCI score 0), medium (CCI score 1-2) and high (CCI score of 3 or above). We included morbidities recorded within 10 years prior to the current hospitalization, as conditions requiring hospital treatment within this timeframe would likely influence the attending physician's diagnostic approach and evaluation during the current hospitalization.

Furthermore, we obtained information on department of admission and year of admission from the DNRP. Departments were categorized in the following five groups: internal medicine, surgery, gynecology/obstetrics, pediatrics, and other.

**Statistical analysis**

Patients with a hyponatremic serum sodium value recorded in the LABKA research database were divided into two categories: Those with an ICD-10 code for hyponatremia in the DNRP and those without. We described both groups of patients in terms of gender, age (median and associated interquartile range (IQR)), department of admission, CCI score and specific comorbidities.

We estimated the sensitivity, specificity, PPV, and NPV (see Figure 1) for ICD-10 codes for hyponatremia in the DNRP with corresponding 95% confidence intervals (CI), using the exact method for binomial proportions. We defined sensitivity as the probability an ICD-10 code for hyponatremia being registered in the DNRP, when the laboratory test result identified presence of hyponatremia. Specificity was defined as the probability of an ICD-10 code for hyponatremia not being registered in the DNRP, when hyponatremia was not identified in laboratory test results. We estimated the PPV as the proportion of patients for whom an ICD-10 code for hyponatremia recorded in the DNRP could be confirmed by a serum sodium measurement, and NPV as the proportion of patients with no ICD-10 code for hyponatremia in the DNRP, for whom non-hyponatremic, or no serum sodium values were

recorded in the LABKA research database. The analyses were repeated for all hyponatremia cut-off points and after stratification by department of admission and admission year.

Finally, we conducted three sensitivity analyses. First, we performed a complete case analysis, a method for dealing with missing data considering only subjects with recorded values for all covariates,[23] meaning that only patients with at least one serum sodium measurement during their hospitalization were included in the analysis. We did so, in order to evaluate the assumption that patients without a serum sodium measurement were normonatremic. In the second sensitivity analysis, we included only patients with more than one serum sodium measurement during their hospitalization. In the third sensitivity analysis, we included only the ICD-10 codes E87.1A (hyponatremia) and P74.2B (hyponatremia in newborns).

Data analyses were performed using the statistical software package STATA (version 12; Stata Corp, College Station, TX, USA).

The study was approved by the Danish Data Protection Agency (record number 2006-53-1396).

## RESULTS

### Characteristics

We identified 2,186,642 hospitalizations (819,701 individual patients) within the study period. For 1,308,740 (60%) hospitalizations, at least one serum sodium measurement was recorded in the LABKA research database, and for 1,037,647 (47%) subsequent measurements were recorded. According to the recorded serum sodium value, hyponatremia was present in 306,418 hospitalizations (14%). In the DNRP, we identified 5,850 hospitalizations with an ICD-10 code of hyponatremia (hypo-osmolality and hyponatremia= 3,722, hyponatremia=2,124, hyponatremia in newborns=4) among all 2,186,642 hospitalizations. Of these, 440 did not have a hyponatremic serum sodium value recorded in the LABKA research database.

Table 1 shows the distribution of hospitalizations by presence/absence of an ICD-10 diagnosis of hyponatremia recorded in the DNRP, by gender, age and comorbidity variables, for patients with hyponatremic serum sodium values. Patients who had an ICD-10 code of hyponatremia recorded in the DNRP and a corresponding hyponatremic serum sodium measurement, were on average older, more often female, more likely admitted to an internal medicine department, and characterized by lower comorbidity levels than patients with no hyponatremia diagnosis in the DNRP, but hyponatremic serum sodium values recorded in the LABKA research database. Cerebrovascular disease, dementia, and ulcer disease were the only comorbidities more frequently found in patients with an ICD-10 code for hyponatremia and corresponding hyponatremic serum sodium value, compared to hyponatremic patients without a hyponatremia diagnosis in the DNRP. (Table 1)

**Table 1.**

Characteristics of hospitalizations identified in the DNRP from 2006 to 2011

| | Hospitalizations with at least on serum sodium value <135 mmol/l recorded in the LABKA research database | | All hospitalizations (n=2,186,642) n (%) |
|---|---|---|---|
| | ICD-10 code of hyponatremia in the DNRP* (n=5,410) n (%) | No ICD-10 code of hyponatremia in the DNRP* (n=301,008) n (%) | |
| **Sex** | | | |
| Female | 3,643 (67.3) | 148,120 (49.3) | 1,168,803 (53.5) |
| Male | 1,767 (32.7) | 152,588 (50.7) | 1,017,839 (46.5) |
| **Age, years** | | | |
| Median (IQR) | 77.3 (65.7-84.9) | 67.4 (54.2-78.2) | 54.7 (29.3-71.1) |
| **Department of admission** | | | |
| Internal medicine | 5,173 (95.6) | 184,848 (61.6) | 943,121 (43.1) |
| Surgical | 184 (3.4) | 88,378 (29.4) | 630,525 (28.8) |
| Gynaecologic/obstetric | 10 (0.2) | 7,104 (2.4) | 347,365 (15.9) |
| Pediatric | 29 (0.5) | 15,830 (5.3) | 165,289 (7.6) |
| Other | 14 (0.3) | 4,848 (1.6) | 100,342 (4.6) |
| **CCI level (score)** | | | |
| Low (0) | 2,075 (38.4) | 100,398 (33.4) | 1,232,762 (56.4) |
| Medium (1-2) | 2,182 (40.3) | 106,874 (35.5) | 588,783 (26.9) |
| High (≥3) | 1,153 (21.3) | 93,736 (31.1) | 365,097 (16.7) |

| | | | |
|---|---|---|---|
| **Specific comorbidities** | | | |
| Myocardial infarction | 312 (5.8) | 23,269 (7.7) | 108,373 (5.0) |
| Congestive heart failure | 460 (8.5) | 31,236 (10.4) | 121,429 (5.6) |
| Peripheral vascular disease | 464 (8.6) | 29,356 (9.8) | 115,620 (5.3) |
| Cerebrovascular disease | 1,017 (18.8) | 39,466 (13.1) | 182,304 (8.3) |
| Dementia | 107 (3.1) | 4,247 (1.4) | 20,711 (1.0) |
| Chronic pulmonary disease | 870 (16.1) | 48,726 (16.2) | 231,121 (10.6) |
| Connective tissue disease | 291 (5.4) | 13,990 (4.7) | 73,299 (3.4) |
| Ulcer disease | 450 (8.3) | 20,645 (6.9) | 79,050 (3.6) |
| Mild liver disease | 189 (3.5) | 13,413 (4.5) | 37,698 (1.7) |
| Moderate to severe liver disease | 66 (1.2) | 6,279 (2.1) | 14,999 (0.7) |
| Diabetes I and II | 521 (9.6) | 39,995 (13.3) | 150,205 (6.9) |
| Diabetes with complications | 269 (5.0) | 25,083 (8.3) | 85,035 (3.9) |
| Hemiplegia | 35 (0.7) | 2,462 (0.8) | 16,060 (0.7) |
| Moderate to severe renal disease | 143 (2.6) | 20,123 (6.7) | 75,441 (3.5) |
| Malignant tumor | 781 (14.4) | 64,882 (21.6) | 312,845 (14.3) |
| Leukemia | 22 (0.4) | 4,636 (1.5) | 17,190 (0.8) |
| Lymphoma | 51 (0.9) | 7,096 (2.4) | 25,348 (1.2) |
| Metastatic cancer | 183 (3.4) | 23,948 (8.0) | 105,512 (4.8) |
| AIDS | 3 (0.1) | 475 (0.2) | 2,014 (0.1) |

* DNRP = Danish National Registry of Patients

### Sensitivity, specificity, PPV and NPV

For 440 (7.5%) of the 5,850 hospitalizations with an ICD-10 code for hyponatremia recorded in the DNRP, no hyponatremic serum sodium measurement was recorded in the LABKA research database during the hospitalization (for 178, no measurement was recorded at all). This corresponds to a PPV of an ICD-10 code for hyponatremia of 92.5% (95% CI: 91.8%–93.1%) for serum sodium values <135 mmol/l (<133 mmol/l for infants 30 days of age or younger). As expected, PPV decreased with lower serum sodium cut-off points. A total of 5,410 hospitalizations had both an ICD-10 code recorded in the DNRP and a corresponding hyponatremic laboratory measurement, resulting in a sensitivity of the ICD-10 codes of 1.8% (95% CI: 1.7%–1.8%). Sensitivity increased with lower cut-off points for serum sodium, reaching 34.3% (95% CI: 32.6%–35.9%) for serum sodium <115 mmol/l. Specificity and NPV

for serum sodium <135 mmol/l were 100% (97.5% CI: 100%) and 86.2% (95% CI: 86.2%–86.2%), respectively. Specificity and NPV remained high for all serum sodium cut-off points (Table 2).

**Table 2.**

Validity of ICD-10 codes for hyponatremia recorded in the DNRP*, using serum sodium measurements in the LABKA research database as gold standard.

| Hyponatremic serum sodium value recorded in LABKA research database (mmol/l) | | ICD-10 code for hyponatremia recorded in the DNRP* Yes | No | Total | Primary Analysis Validity Measures | % (95% CI) | Sensitivity Analyses Requiring at least one serum sodium measurement during hospitalization % (95% CI)\] | Requiring >1 serum sodium measurement during hospitalization % (95% CI) | ICD-10 algorithm restricted to code E87.1A and P74.2B % (95% CI) |
|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | | | | | | | | |
| Na<135[¤] | Yes | 5,410 | 301,008 | 306,418 | Sensitivity | 1.8 (1.7-1.8) | 1.8 (1.7-1.8) | 1.9 (1.8-2.0) | 0.7 (0.6-0.7) |
| | No | 440 | 1,879,784 | 1,880,224 | Specificity | 100 (100-100) | 100 (100-100) | 100 (100-100) | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 92.5 (91.8-93.1) | 95.4 (94.8-95.9) | 95.8 (95.2-96.3) | 94.6 (93.6-95.6) |
| | | | | | NPV | 86.2 (86.2-86.2) | 76.9 (76.8-77.0) | 74.7 (74.6-74.8) | 86.1 (86.0-86.1) |
| **Cut-off points for increasing severity of hyponatremia** | | | | | | | | | |
| Na<130l[§] | Yes | 4,528 | 80,605 | 85,133 | Sensitivity | 5.3 (5.2-5.5) | 5.3 (5.2-5.5) | 5.6 (5.4-5.7) | 2.1 (2.0-2.2) |
| | No | 1,322 | 2,100,187 | 2,101,509 | Specificity | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 77.4 (76.3-78.5) | 79.8 (78.7-80.9) | 80.5 (79.4-81.6) | 83.0 (81.4-84.6) |
| | | | | | NPV | 96.3 (96.3-96.3) | 93.8 (93.8-93.9) | 93.0 (93.0-93.1) | 96.2 (96.2-96.2) |
| Na<125l[#] | Yes | 3,261 | 21,544 | 24,805 | Sensitivity | 13.1 (12.7-13.6) | 13.1 (12.7-13.6) | 13.6 (13.1-14.0) | 5.4 (5.1-5.7) |
| | No | 2,589 | 2,159,248 | 2,161,837 | Specificity | 99.9 (99.9-99.9) | 99.8 (99.8-99.8) | 99.8 (99.8-99.8) | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 55.7 (54.5-57.0) | 57.5 (56.2-58.8) | 57.9 (56.5-59.2) | 62.5 (60.4-64.5) |
| | | | | | NPV | 99.0 (99.0-99.0) | 98.3 (98.3-98.4) | 98.1 (98.1-98.1) | 98.9 (98.9-98.9) |
| Na<120l[£] | Yes | 2,061 | 6,219 | 8,280 | Sensitivity | 24.9 (24.0-25.9) | 24.9 (24.0-25.8) | 25.4 (24.5-26.4) | 6.3 (5.8-6.9) |
| | No | 3,789 | 2,174,573 | 2,178,362 | Specificity | 99.8 (99.8-99.8) | 99.7 (99.7-99.7) | 99.7 (99.7-99.7) | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 35.2 (34.0-36.5) | 36.3 (35.1-37.6) | 36.3 (35.0-37.6) | 50.6 (47.5-53.7) |
| | | | | | NPV | 99.7 (99.7-99.7) | 99.5 (99.5-99.5) | 99.5 (99.4-99.5) | 99.6 (99.6-99.7) |
| Na<115l[$] | Yes | 1,107 | 2,127 | 3,234 | Sensitivity | 34.3 (32.6-35.9) | 34.2 (32.6-35.9) | 34.9 (33.1-36.6) | 9.3 (8.3-10.3) |
| | No | 4,743 | 2,178,665 | 2,183,408 | Specificity | 99.8 (99.8-99.8) | 99.7 (99.6-99.7) | 99.6 (99.6-99.6) | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 18.9 (17.9-20.0) | 19.5 (18.5-20.6) | 19.5 (18.4-20.6) | 28.8 (26.1-31.7) |
| | | | | | NPV | 99.9 (99.9-99.9) | 99.8 (99.8-99.8) | 99.8 (99.8-99.8) | 99.9 (99.9-99.9) |

*DNRP = Danish National Registry of Patients
[¤] Corresponding to <133 mmol/l for infants of 30 day or less of age
[§] Corresponding to <128 mmol/l for infants of 30 day or less of age
[#] Corresponding to <123 mmol/l for infants of 30 day or less of age
[£] Corresponding to <118 mmol/l for infants of 30 day or less of age
[$] Corresponding to <113 mmol/l for infants of 30 day or less of age

Sensitivity was higher among admissions to internal medicine departments than among admissions to surgical, gynecologic/obstetric, pediatric, and "other" departments (Table 3). The validity measures were virtually unchanged across strata of admission year.

**Table 3.**

Validity of ICD-10 codes for hyponatremia recorded in the DNRP, stratified by year and department of admission, for serum sodium values <135mmol/l[¤] and <125mmol/l[#]

| | Sensitivity % (95% CI) | | Specificity % (95% CI) | | PPV % (95% CI) | | NPV % (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | 135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l |
| **Admission Year** | | | | | | | | |
| 2006 | 1.5 (1.4-1.7) | 12.5 (11.5-13.5) | 100 (100-100) | 99.9 (99.9-99.9) | 92.8 (90.8-94.5) | 66.6 (63.2-69.9) | 86.8 (86.6-86.9) | 99.0 (98.9-99.0) |
| 2007 | 1.4 (1.3-1.5) | 12.0 (11.0-13.1) | 100 (100-100) | 99.9 (99.9-99.9) | 94.4 ( 92.4-96.0) | 65.3 (61.6-68.8) | 87.0 (86.9-87.1) | 99.0 (99.0-99.1) |
| 2008 | 1.7 (1.6-1.8) | 12.3 (11.3-13.3) | 100 (100-100) | 99.9 (99.9-99.9) | 91.1 (89.1-92.8) | 53.6 (50.4-56.8) | 85.9 (85.8-86.1) | 99.0 (98.9-99.0) |
| 2009 | 1.8 (1.7-1.9) | 12.6 (11.6-13.6) | 100 (100-100) | 99.9 (99.8-99.9) | 93.4 (91.7-94.8) | 51.4 ( 48.4-54.5) | 85.5 (85.3-85.6) | 99.0 (98.9-99.0) |
| 2010 | 1.9 (1.8-2.0) | 14.2 (13.2-15.4) | 100 (100-100) | 99.9 (99.9-99.9) | 91.6 (89.8-93.2) | 54.4 (51.4-57.4) | 86.3 (86.2-86.4) | 99.1 (99.0-99.1) |
| 2011 | 2.2 (2.0-2.3) | 15.2 (14.1-16.4) | 100 (100-100) | 99.9 (99.9-99.9) | 92.2 (90.6-93.6) | 49.8 (47.0-52.7) | 85.8 (85.7-85.9) | 99.1 (99.0-99.1) |
| **Department** | | | | | | | | |
| Internal medicine | 2.7 (2.7-2.8) | 16.5 (16.0-17.0) | 99.9 (99.9-100) | 99.7 (99.7-99.7) | 92.8 (92.1-93.4) | 56.0 (54.7-57.3) | 80.3 (80.2-80.4) | 98.3 (98.3-98.3) |
| Surgical | 0.2 (0.2-0.2) | 2.3 (1.9-2.8) | 100 (100-100) | 100 (100-100) | 90.6 (85.8-94.3) | 57.6 (50.5-64.5) | 86.0 (85.9-86.1) | 99.2 (99.2-99.2) |
| Gynecologic/ Obstetric | 0.1 (0.1-0.3) | 3.1 (1.2-6.7) | 100 (100-100) | 100 (100-100) | 76.9 (46.2-95.0) | 46.2 (19.2-74.9) | 98.0 (97.9-98.0) | 99.9 (99.9 -100) |
| Pediatric | 0.2 (0.1-0.3) | 3.4 (1.7-5.8) | 100 (100-100) | 100 (100-100) | 85.3 (68.9-95.0) | 35.3 (19.7-53.5) | 90.4 (90.3-90.6) | 99.8 (99.8-99.8) |
| Other | 0.3 (0.2-0.5) | 1.5 (0.4-3.9) | 100 (100-100) | 100 (100-100) | 58.3 (36.6-77.9) | 16.7 (4.74-37.4) | 95.2 (95.0-95.3) | 99.7 (99.7-99.8) |

* DNRP = Danish National Registry of Patients

[¤]Corresponding to <133mmol/l for infants of 30 day or less of age

[#] Corresponding to <123mmol/l for infants of 30 day or less of age

## Sensitivity analyses

Compared to the primary analyses, we observed no changes in neither sensitivity nor specificity estimates when including only patients with at least one serum sodium measurement during their

hospitalization in the analysis. PPV increased slightly for all serum sodium cut-off points, while NPV decreased for the three highest cut-off points. Including only patients with more than one serum sodium measurement also yielded almost identical results (Table 2).

After restriction to the most specific ICD-10 codes for hyponatremia, PPV increased slightly and sensitivity decreased (94.6% (95% CI: 93.6%–95.6%) and 0.7% (95% CI: 0.6%–0.7%), respectively). Estimates of specificity and NPV were virtually unchanged (Table 2).

## DISCUSSION

This is the first study to report on the validity of ICD-10 coding of hyponatremia using comprehensive population-based medical registries, and including patients of all ages. A record of a hyponatremia diagnosis in the DNRP was found to be specific to and highly predictive of hyponatremia confirmed by laboratory values. However, the disorder was greatly underreported, though to a lesser extent in patients admitted to an internal medicine department compared to other departments. We found sensitivity to be low even for severe degrees of hyponatremia. These results were robust when we used a stricter definition of hyponatremia and complete case analysis.

Our findings correspond with those of Movig *et al*.'s single-center study conducted in The Netherlands, in which ICD-9-CM coding of hyponatremia in inpatient discharge records was compared with hospital laboratory data.[13] As in our study, sensitivity at the cut-off point of 135 mmol/l was 1.7%, and increased with decreasing serum sodium levels. Sensitivity thus reached 30.6% for values below 115 mmol/l. In addition, their estimates for PPV, NPV, and specificity were similar to our results (91.7%, 79.5% and <99.9%, respectively). A Canadian study by Gandhi *et al.* examined ICD-10 coding for hyponatremia and reported a sensitivity of 4.5% for the cut-off point of <135 mmol/l and 34.4% for the cut-off point of 125 mmol/l.[12] The study was, however, restricted to patients ≥66 years of age presenting with hyponatremic laboratory test result at admission or emergency department contact. In

line with their results, we found that the median age of patients with a ICD-10 code of hyponatremia recorded in the DNRP, which could be confirmed by laboratory results, was higher than that of hyponatremic patients with no ICD-10 code for hyponatremia recorded in the DNRP. Shea *et al*. also reported higher sensitivity compared to our results (3.5% for a cut-off point of <136 mmol/l and 29.6% for the cut-off point of 125 mmol/l) in their study examining the validity of ICD-9 codes of hyponatremia in an outpatient managed-care population.[14] Outpatient serum sodium laboratory tests were compared with outpatient professional ICD-9 claims registered within 15 days before or after the laboratory claim. The PPV was 62.6% for serum sodium levels <136 mmol/l and 10.4% for levels <125 mmol/l. As noted in the paper, detected hyponatremia may be the cause for follow-up visits in an outpatient setting, without the need for repeat measurements. This could lead to lower PPV compared to our study and the study by Movig *et al*. In addition, managed-care claims databases encompass an employer-based commercially insured population. Shea *et al*.'s study thus may not be representative of elderly populations, in which prevalence of hyponatremia is high.[24, 25] This also may explain why their results differed from ours.

The major strengths of our study are its population-based design and unambiguous individual-level linkage between registries containing complete data on all hospitalizations and laboratory tests in a well-defined population. This eliminates the risk of selection bias. Several potential study limitations must be considered. We relied on only one (the lowest) serum sodium value recorded to define presence of hyponatremia, and also did not consider duration of hyponatremia. Clinicians may be more likely to regard hyponatremia as clinically relevant, and hence to include the condition in discharge diagnoses, if it is detected in more than one measurement. In this context, it is important to note that patient transfers between departments are registered as separate admissions in the DNRP and we examined the validity of ICD-10 coding for each registered admission. The PPV may have been even higher if we had considered contiguous admissions as a single admission. Finally, we

chose to include patients without serum sodium measurements and to consider them as normonatremic in the main analysis. We did so to detect false positive diagnoses and thereby obtain accurate estimates of predictive values. Serum sodium is often measured as a routine procedure, and rarely due to specific suspicion. Though frequently measured, the proportion of patients with unacknowledged hyponatremia is most often unknown. We therefore performed a complete case analysis, including only patients with serum sodium measurements. As the results did not differ markedly from those of the primary analysis, we believe that including patients without serum sodium measurements in the normonatremic group was justified.

We can only speculate on reasons for the low sensitivity of the ICD-10 coding of hyponatremia found in our study. Hyponatremia is mainly considered a part of the clinical picture of underlying diseases. If hyponatremia is mild or transient, and does not require intervention or specific attention, it may not warrant documentation. However, even for very severe hyponatremia (<115 mmol/l), which is potentially fatal and requires immediate intervention, sensitivity was low. Our results suggest that hyponatremia is not coded in the presence of coexisting illness deemed more important, and that the fact that hyponatremia may be an important indicator of a poor prognosis is not yet acknowledged.

The results of this validation study emphasize the need for caution when relying on ICD-10 codes for hyponatremia in research. Based on the estimated PPV and specificity, patients with an ICD-10 code of hyponatremia can safely be assumed to actually have hyponatremia. However, the low sensitivity renders the ICD-10 codes inappropriate for use in studies examining prevalence, incidence, and absolute risk, due to a high degree of misclassification. Sensitivity increased with decreasing serum sodium levels, suggesting that studies using ICD-codes to identify hyponatremia would be based mainly on severe cases. Furthermore, our results indicate that quality of registration differs according

to age, gender, and morbidity status. Hence, studies may be susceptible to differential misclassification, again resulting in biased results.

## CONCLUSION

We found that the ICD-10 coding of hyponatremia in DNRP has high specificity but is highly incomplete, resulting in very low sensitivity. When available, laboratory test results for serum sodium will more correctly identify patients with hyponatremia.

## Contributors

LHB participated in the design of the study, performed the data analysis, provided interpretation of study results and drafted the manuscript. SPU participated in acquisition and analysis of data. CFC and HTS participated in the design of the study, provided interpretation of study results and helped draft the manuscript. TR and JOLJ contributed with interpretation of study results helped draft the manuscript. All authors read and approved the final manuscript.

## Funding

This work was supported by the Clinical Epidemiology Research Foundation and by the Danish Cancer Society (grant no. R73-A4284-13-S17).

## Competing interests

JOLJ has received an unrestricted research grant and lecture fees from Otsuka Pharma Scandinavia AB. TR has received lecture fees from Otsuka Pharma Scandinavia AB.

LHB, CFC, SPU and HTS are salaried employees of Department of Clinical Epidemiology, Aarhus University Hospital. The Department of Clinical Epidemiology receives funding from companies in the form of research grants to (and administered by) Aarhus University.

None of these grants or fees had any had any leverage on the design, implementation or reporting of the present study.

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| | | ICD-10 code of hyponatremia recorded in the DNRP* | |
|---|---|---|---|
| | | Yes | No |
| Hyponatremic serum sodium value recorded in LABKA research database (gold standard) | Yes | A | C |
| | No | B | D |

Validity measures:
Sensitivity= A/(A+C)
Specificity= D/(B+D)
Positive predictive value= A/(A+B)
Negative predictive value=D/(C+D)

*DNRP = Danish National Registry of Patients

Figure 1. Schematic 2x2 table and validity measure estimation formulas
338x190mm (96 x 96 DPI)

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology***

**Checklist for cohort, case-control, and cross-sectional studies (combined)**

| Section/Topic | Item # | Recommendation | Reported on page # |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses | 6 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants | 7 |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-8 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | *6-8* |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9 |
| Study size | 10 | Explain how the study size was arrived at | 6-7 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 8-9 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 8-9 |
| | | (*c*) Explain how missing data were addressed | 9 |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed | |

| | | | |
|---|---|---|---|
| | | *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy | |
| | | (*e*) Describe any sensitivity analyses | 9 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 9 |
| | | (b) Give reasons for non-participation at each stage | 9 |
| | | (c) Consider use of a flow diagram | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 10-11 |
| | | (b) Indicate number of participants with missing data for each variable of interest | 9 |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) | |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time | |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure | |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures | 9 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 11-12 |
| | | (*b*) Report category boundaries when continuous variables were categorized | 11-12 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 13-14 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 14 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15-16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 14-15, 16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 15 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 18 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

# Validity of the International Classification of Diseases, 10th revision (ICD-10) discharge diagnosis codes for hyponatremia in the Danish National Registry of Patients



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|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID: | bmjopen-2014-004956.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 31-Mar-2014 |
| Complete List of Authors: | Holland-Bill, Louise; Aarhus University Hospital, Department of Clinical Epidemiology<br>Christiansen, Christian F; Aarhus University Hospital, Department of Clinical Epidemiology<br>Ulrichsen, Sinna; Aarhus University Hospital, Department of Clinical Epidemiology<br>Ring, Troels; Aalborg University Hospital, Department of Nephrology<br>Jørgensen, Jens Otto; Aarhus University Hospital, Department of Endocrinology and Internal Medicine<br>Toft Sørensen, Henrik; Aarhus University Hospital, Department of Clinical Epidemiology |
| Primary Subject Heading: | Epidemiology |
| Secondary Subject Heading: | Epidemiology, Health services research, Diagnostics, Renal medicine |
| Keywords: | EPIDEMIOLOGY, Nephrology < INTERNAL MEDICINE, STATISTICS & RESEARCH METHODS |
| | |

# Validity of the International Classification of Diseases, 10th revision (ICD-10) discharge diagnosis codes for hyponatremia in the Danish National Registry of Patients

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**Keywords:** validation study; ICD 10; hyponatremia; diagnosis; population register; clinical laboratory information system

**Word count:** 3,005

## ABSTRACT

**OBJECTIVE:** To examine the validity of the *International Classification of Diseases*, 10th revision (ICD-10) codes for hyponatremia in the nationwide population-based Danish National Registry of Patients (DNRP) among inpatients of all ages.

**DESIGN:** Population-based validation study.

**SETTING:** All somatic hospitals in the North and Central Denmark Regions from 2006 through 2011.

**PARTICIPANTS:** Patients of all ages admitted to hospital (n=819,701 individual patients) during the study period. Patient could be included in the study more than once, and we did not restrict to patients with serum sodium measurements (total of n=2,186,642 hospitalizations).

**MAIN OUTCOME MEASURE:** We validated ICD-10 discharge diagnoses of hyponatremia recorded in the DNRP, using serum sodium measurements obtained from the laboratory information systems (LABKA) research database as the gold standard. One sodium value <135 mmol/l measured at any time during hospitalization confirmed the diagnosis. We estimated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for ICD-10 codes for hyponatremia overall and for cut-off points for increasing hyponatremia severity.

**RESULT:** An ICD-10 code for hyponatremia was recorded in the DNRP in 5,850 of the 2,186,642 hospitalizations identified. According to laboratory measurements, however, hyponatremia was present in 306,418 (14%) hospitalizations. Sensitivity of hyponatremia diagnoses was 1.8% (95% confidence interval (CI): 1.7%-1.8%). For sodium values <115mmol/l, sensitivity was 34.3% (95% CI: 32.6%-35.9%). Overall PPV was 92.5% (95% CI: 91.8%-93.1%), and decreased with increasing hyponatremia severity. Specificity and NPV were high for all cut-off points (≥99.8% and ≥86.2% respectively). Hyponatremic patients without a corresponding ICD-10 discharge diagnosis were younger and had higher Charlson Comorbidity Index scores than hyponatremic patients with a hyponatremia code in the DNRP.

**CONCLUSION:** ICD-10 codes for hyponatremia in the DNRP have high specificity, but very low sensitivity. Laboratory test results, not discharge diagnoses, should be used to ascertain hyponatremia.

# Article summery

### Article focus

- Hospital discharge diagnoses for hyponatremia recorded in the Danish National Registry of Patients (DNRP) may constitute valuable data sources for epidemiologic studies, however the validity of data must be established.

### Key Message

- ICD-10 coding of hyponatremia in the Danish National Registry of Patients (DNRP) is highly specific but greatly incomplete.
- Epidemiological studies relying on discharge diagnoses of hyponatremia may be susceptible to differential misclassification.

### Strengths and limitation of this study

- This is the first study to validate the International Classification of Diseases, 10th Revision code for hyponatremia in hospitalized patients of all ages.
- We used a population-based design with unambiguous individual-level linkage between registries containing complete data on all hospitalizations and laboratory, ensuring a large sample size and virtually eliminating the risk of selection bias.
- We did not consider the duration of hyponatremia. Sensitivity may have been higher if presence of hyponatremia required, that it was detected in more than one laboratory measurement during hospitalization.

## INTRODUCTION

Hyponatremia, defined as a serum sodium value <135mmol/l, is the most common electrolyte abnormality encountered in clinical practice.[1] It can be caused by a large variety of conditions, such as heart failure, kidney failure, cirrhosis, syndrome of inappropriate antidiuretic hormone, vomiting, and diarrhea, and can also be a side effect of several medications.[2] Results of recent studies have indicated that even a mild to moderate level of hyponatremia may be an important predictor of poor prognosis in patients with cardiovascular disease, kidney and liver disease, and cancer.[3-8] However, key aspects of the etiology and prognosis of hyponatremia remain unknown.

The Danish population-based medical registries may offer a unique opportunity for studies of the epidemiology of hyponatremia, if data are valid. However, as symptoms of mild and moderate hyponatremia may be vague, and concealed by or construed as symptoms of an underlying disease, it is likely that the condition will not be reported.[9,10] Thus, use of only inpatient discharge diagnoses of hyponatremia in epidemiologic studies may cause bias that can affect the validity of study results.[11]

To date, only one study has investigated the validity of *International Classification of Diseases* (ICD), 10$^{th}$ revision (ICD-10) codes for hyponatremia. This Canadian study was restricted to patients 66 years of age or older with serum sodium values at the time of emergency department contact or at hospital admission.[12] The sensitivity of hyponatremia coding was found to be as low as 7%. For inpatients younger than 66 years, knowledge of the validity hyponatremia diagnoses is limited to a study performed in a single hospital in the Netherlands using ICD-9 codes for hyponatremia. In this study, sensitivity was found to be just below 2%, using hospital laboratory data as the reference standard.[13] Similar results were found in a study examining the validity of outpatient professional ICD-9 claims for hyponatremia in the US.[14]

We therefore conducted the first population-based study examining the validity of ICD-10 inpatient discharge diagnoses of hyponatremia in the Danish National Registry of Patients (DNRP), including patients of all ages.

## METHODS

### Setting and data collection

We used the DNRP to identify all admissions to hospitals in the North and Central Denmark Regions (2.1 million inhabitants in the study period) from 1 January 2006 to 31 December 2011. The DNRP contains information, including date of admission and discharge, department code and discharge diagnoses, on all admissions to Danish non-psychiatric hospitals since 1977.[15,16]

By use of the unique 10-digit civil registration number, assigned to all Danish residents since 1968,[17] we linked each patient's DNRP data to the clinical laboratory information system (LABKA) research database. For patients living in the North and Central Denmark Regions, data on virtually all specimens analyzed in clinical laboratories by hospitals and medical practitioners are entered into a computer-based clinical laboratory information system, which functions as a routine diagnostic tool for medical personnel.[18] Data are transferred electronically to the LABKA research database, managed by Aarhus University. Analyses are coded according to the NPU (Nomenclature, Properties and Units) system. The LABKA research database contains the civil registration number, time and date of blood sampling, and identification code of the requesting physician or hospital department.[18] We used the LABKA research database to retrieve information on all serum sodium measurements recorded during each of the identified hospitalizations.

### Hyponatremia diagnosis (ICD-10 code algorithm)

At hospital discharge, the attending physician assigns one primary diagnosis, reflecting the main reason for hospitalization and treatment and up to 19 secondary diagnoses regarding additional

clinically relevant conditions, including underlying diseases, complications and symptoms.[19] Diagnoses recorded in the DNRP have been coded according to the *International Classification of Diseases* (ICD), 10th revision (ICD-10) since 1994.[16]

We developed an algorithm based on ICD-10 codes to identify primary and secondary discharge diagnoses of hyponatremia recorded in the DNRP for each hospitalization. The following ICD-10 codes were included in the algorithm: E87.1 (Hypo-osmolality and hyponatremia), E87.1A (Hyponatremia) and P74.2B (Hyponatremia in newborns [Danish version of ICD-10]).

**Gold Standard (laboratory serum sodium measurements)**

We used serum sodium measurements recorded in the LABKA research database as the gold standard to confirm or disconfirm a diagnosis of hyponatremia identified by the ICD-10 algorithm. Hyponatremia was defined as serum sodium values <135 mmol/l for patients older than 30 days and <133 mmol/l for infants 30 days of age or younger.[20] Patients were considered to have hyponatremia if at least one hyponatremic serum sodium value was recorded during their hospitalization. If no serum sodium measurement was available, the patient was assumed to have a non-hyponatremic serum sodium value (135-145mmol/l). The following cut-off points for increasing severity of hyponatremia were chosen: 135 mmol/l, 130mmol/l, 125mmol/l, 120mmol/l and 115mmol/l.[13] The corresponding levels for infants less than 31 days of age were 133mmol/l, 128mmol/l, 123mmol/l, 118mmol/l and 113mmol/l.

**Other Variables**

For each patient, we assessed comorbidity by information retrieved from the DNRP on the conditions included in the Charlson Comorbidity Index (CCI). The CCI includes 19 medical conditions, each assigned a weighted score between one and six. The sum of these individual scores is used as a measure of a patient's comorbidity burden.[21, 22] We calculated CCI scores for each patient and

defined three comorbidity levels: low (CCI score 0), medium (CCI score 1-2) and high (CCI score of 3 or above). We included morbidities recorded within 10 years prior to the current hospitalization, as conditions requiring hospital treatment within this timeframe would likely influence the attending physician's diagnostic approach and evaluation during the current hospitalization.

Furthermore, we obtained information on department of admission and year of admission from the DNRP. Departments were categorized in the following five groups: internal medicine, surgery, gynecology/obstetrics, pediatrics, and other.

**Statistical analysis**

Patients with a hyponatremic serum sodium value recorded in the LABKA research database were divided into two categories: Those with an ICD-10 code for hyponatremia in the DNRP and those without. We described both groups of patients in terms of gender, age (median and associated interquartile range (IQR)), department of admission, CCI score and specific comorbidities.

We estimated the sensitivity, specificity, PPV, and NPV (see Figure 1) for ICD-10 codes for hyponatremia in the DNRP with corresponding 95% confidence intervals (CI), using the exact method for binomial proportions. We defined sensitivity as the probability an ICD-10 code for hyponatremia being registered in the DNRP, when the laboratory test result identified presence of hyponatremia. Specificity was defined as the probability of an ICD-10 code for hyponatremia not being registered in the DNRP, when hyponatremia was not identified in laboratory test results. We estimated the PPV as the proportion of patients for whom an ICD-10 code for hyponatremia recorded in the DNRP could be confirmed by a serum sodium measurement, and NPV as the proportion of patients with no ICD-10 code for hyponatremia in the DNRP, for whom non-hyponatremic, or no serum sodium values were recorded in the LABKA research database. The analyses were repeated for all hyponatremia cut-off points and after stratification by age group categories, department of admission and admission year.

Finally, we conducted four sensitivity analyses. First, we performed a complete case analysis, a method for dealing with missing data considering only subjects with recorded values for all covariates,[23] meaning that only patients with at least one serum sodium measurement during their hospitalization were included in the analysis. We did so, in order to evaluate the assumption that patients without a serum sodium measurement were normonatremic. In the second sensitivity analysis, we included only patients with more than one serum sodium measurement during their hospitalization. In the third sensitivity analysis, we included only the ICD-10 codes E87.1A (hyponatremia) and P74.2B (hyponatremia in newborns). Because epidemiologic studies often focus on incident cases, we performed a post-hoc sensitivity analysis in which we restricted to the first hospitalization for each patient in the study period

Data analyses were performed using the statistical software package STATA (version 12; Stata Corp, College Station, TX, USA).

The study was approved by the Danish Data Protection Agency (record number 2006-53-1396). All data were obtained from Danish public registries. According to Danish law their use does require informed consent or ethics committee approval.

## RESULTS

### Characteristics

We identified 2,186,642 hospitalizations (819,701 individual patients) within the study period. For 1,308,740 (60%) hospitalizations, at least one serum sodium measurement was recorded in the LABKA research database, and for 1,037,647 (47%) subsequent measurements were recorded. According to the recorded serum sodium value, hyponatremia was present in 306,418 hospitalizations (14%). In the DNRP, we identified 5,850 hospitalizations with an ICD-10 code of hyponatremia (hypo-osmolality and hyponatremia= 3,722, hyponatremia=2,124, hyponatremia in newborns=4) among all

2,186,642 hospitalizations. Of these, 440 did not have a hyponatremic serum sodium value recorded in the LABKA research database.

Table 1 shows the distribution of hospitalizations by presence/absence of an ICD-10 diagnosis of hyponatremia recorded in the DNRP, by gender, age and comorbidity variables, for patients with hyponatremic serum sodium values. Patients who had an ICD-10 code of hyponatremia recorded in the DNRP and a corresponding hyponatremic serum sodium measurement, were on average older, more often female, more likely admitted to an internal medicine department, and characterized by lower comorbidity levels than patients with no hyponatremia diagnosis in the DNRP, but hyponatremic serum sodium values recorded in the LABKA research database. Cerebrovascular disease, dementia, and ulcer disease were the only comorbidities more frequently found in patients with an ICD-10 code for hyponatremia and corresponding hyponatremic serum sodium value, compared to hyponatremic patients without a hyponatremia diagnosis in the DNRP. (Table 1)

**Table 1.**

Characteristics of hospitalizations identified in the DNRP from 2006 to 2011

| | Hospitalizations with at least on serum sodium value <135 mmol/l recorded in the LABKA research database | | All hospitalizations (n=2,186,642) n (%) |
|---|---|---|---|
| | ICD-10 code of hyponatremia in the DNRP* (n=5,410) n (%) | No ICD-10 code of hyponatremia in the DNRP* (n=301,008) n (%) | |
| **Sex** | | | |
| Female | 3,643 (67.3) | 148,120 (49.3) | 1,168,803 (53.5) |
| Male | 1,767 (32.7) | 152,588 (50.7) | 1,017,839 (46.5) |
| **Age, years** | | | |
| Median (IQR) | 77.3 (65.7-84.9) | 67.4 (54.2-78.2) | 54.7 (29.3-71.1) |
| **Department of admission** | | | |
| Internal medicine | 5,173 (95.6) | 184,848 (61.6) | 943,121 (43.1) |
| Surgical | 184 (3.4) | 88,378 (29.4) | 630,525 (28.8) |
| Gynaecologic/obstetric | 10 (0.2) | 7,104 (2.4) | 347,365 (15.9) |
| Pediatric | 29 (0.5) | 15,830 (5.3) | 165,289 (7.6) |
| Other | 14 (0.3) | 4,848 (1.6) | 100,342 (4.6) |
| **CCI level (score)** | | | |

| | | | |
|---|---|---|---|
| Low (0) | 2,075 (38.4) | 100,398 (33.4) | 1,232,762 (56.4) |
| Medium (1-2) | 2,182 (40.3) | 106,874 (35.5) | 588,783 (26.9) |
| High (≥3) | 1,153 (21.3) | 93,736 (31.1) | 365,097 (16.7) |
| **Specific comorbidities** | | | |
| Myocardial infarction | 312 (5.8) | 23,269 (7.7) | 108,373 (5.0) |
| Congestive heart failure | 460 (8.5) | 31,236 (10.4) | 121,429 (5.6) |
| Peripheral vascular disease | 464 (8.6) | 29,356 (9.8) | 115,620 (5.3) |
| Cerebrovascular disease | 1,017 (18.8) | 39,466 (13.1) | 182,304 (8.3) |
| Dementia | 107 (3.1) | 4,247 (1.4) | 20,711 (1.0) |
| Chronic pulmonary disease | 870 (16.1) | 48,726 (16.2) | 231,121 (10.6) |
| Connective tissue disease | 291 (5.4) | 13,990 (4.7) | 73,299 (3.4) |
| Ulcer disease | 450 (8.3) | 20,645 (6.9) | 79,050 (3.6) |
| Mild liver disease | 189 (3.5) | 13,413 (4.5) | 37,698 (1.7) |
| Moderate to severe liver disease | 66 (1.2) | 6,279 (2.1) | 14,999 (0.7) |
| Diabetes I and II | 521 (9.6) | 39,995 (13.3) | 150,205 (6.9) |
| Diabetes with complications | 269 (5.0) | 25,083 (8.3) | 85,035 (3.9) |
| Hemiplegia | 35 (0.7) | 2,462 (0.8) | 16,060 (0.7) |
| Moderate to severe renal disease | 143 (2.6) | 20,123 (6.7) | 75,441 (3.5) |
| Malignant tumor | 781 (14.4) | 64,882 (21.6) | 312,845 (14.3) |
| Leukemia | 22 (0.4) | 4,636 (1.5) | 17,190 (0.8) |
| Lymphoma | 51 (0.9) | 7,096 (2.4) | 25,348 (1.2) |
| Metastatic cancer | 183 (3.4) | 23,948 (8.0) | 105,512 (4.8) |
| AIDS | 3 (0.1) | 475 (0.2) | 2,014 (0.1) |

* DNRP = Danish National Registry of Patients

### Sensitivity, specificity, PPV and NPV

For 440 (7.5%) of the 5,850 hospitalizations with an ICD-10 code for hyponatremia recorded in the DNRP, no hyponatremic serum sodium measurement was recorded in the LABKA research database during the hospitalization (for 178, no measurement was recorded at all). This corresponds to a PPV of an ICD-10 code for hyponatremia of 92.5% (95% CI: 91.8%–93.1%) for serum sodium values <135 mmol/l (<133 mmol/l for infants 30 days of age or younger). As expected, PPV decreased with lower serum sodium cut-off points. A total of 5,410 hospitalizations had both an ICD-10 code recorded in the DNRP and a corresponding hyponatremic laboratory measurement, resulting in a sensitivity of the ICD-10 codes of 1.8% (95% CI: 1.7%–1.8%). Sensitivity increased with lower cut-off points for serum

sodium, reaching 34.3% (95% CI: 32.6%–35.9%) for serum sodium <115 mmol/l. Specificity and NPV for serum sodium <135 mmol/l were 100% (97.5% CI: 100%) and 86.2% (95% CI: 86.2%–86.2%), respectively. Specificity and NPV remained high for all serum sodium cut-off points (Table 2).

**Table 2.**

Validity of ICD-10 codes for hyponatremia recorded in the DNRP*, using serum sodium measurements in the LABKA research database as gold standard.

| Hyponatremic serum sodium value recorded in LABKA research database (mmol/l) | | ICD-10 code for hyponatremia recorded in the DNRP* Yes | No | Total | Validity Measures % (95% CI) | |
|---|---|---|---|---|---|---|
| **Overall** | | | | | | |
| Na<135[¤] | Yes | 5,410 | 301,008 | 306,418 | Sensitivity | 1.8 (1.7-1.8) |
| | No | 440 | 1,879,784 | 1,880,224 | Specificity | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 92.5 (91.8-93.1) |
| | | | | | NPV | 86.2 (86.2-86.2) |
| **Cut-off points for increasing severity of hyponatremia** | | | | | | |
| Na<130[§] | Yes | 4,528 | 80,605 | 85,133 | Sensitivity | 5.3 (5.2-5.5) |
| | No | 1,322 | 2,100,187 | 2,101,509 | Specificity | 99.9 (99.9-99.9) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 77.4 (76.3-78.5) |
| | | | | | NPV | 96.3 (96.3-96.3) |
| Na<125[#] | Yes | 3,261 | 21,544 | 24,805 | Sensitivity | 13.1 (12.7-13.6) |
| | No | 2,589 | 2,159,248 | 2,161,837 | Specificity | 99.9 (99.9-99.9) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 55.7 (54.5-57.0) |
| | | | | | NPV | 99.0 (99.0-99.0) |
| Na<120[£] | Yes | 2,061 | 6,219 | 8,280 | Sensitivity | 24.9 (24.0-25.9) |
| | No | 3,789 | 2,174,573 | 2,178,362 | Specificity | 99.8 (99.8-99.8) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 35.2 (34.0-36.5) |
| | | | | | NPV | 99.7 (99.7-99.7) |
| Na<115[$] | Yes | 1,107 | 2,127 | 3,234 | Sensitivity | 34.3 (32.6-35.9) |
| | No | 4,743 | 2,178,665 | 2,183,408 | Specificity | 99.8 (99.8-99.8) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 18.9 (17.9-20.0) |
| | | | | | NPV | 99.9 (99.9-99.9) |

*DNRP = Danish National Registry of Patients
[¤] Corresponding to <133 mmol/l for infants of 30 day or less of age
[§] Corresponding to <128 mmol/l for infants of 30 day or less of age
[#] Corresponding to <123 mmol/l for infants of 30 day or less of age
[£] Corresponding to <118 mmol/l for infants of 30 day or less of age
[$] Corresponding to <113 mmol/l for infants of 30 day or less of age

Sensitivity was higher among admissions to internal medicine departments than among admissions to surgical, gynecologic/obstetric, pediatric, and "other" departments (Table 3). The validity measures were virtually unchanged across strata of admission year.

**Table 3.**

Validity of ICD-10 codes for hyponatremia recorded in the DNRP, stratified by age group categories, year and department of admission, for serum sodium values <135mmol/l[¤] and <125mmol/l[#]

| | Sensitivity % (95% CI) | | Specificity % (95% CI) | | PPV % (95% CI) | | NPV % (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | 135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l |
| **Age, years** | | | | | | | | |
| < 15 | 0.2 (0.1-0.2) | 3.0 (1.5-5.2) | 100 (100-100) | 100 (100-100) | 84.4 (67.2-94.7) | 34.4 (18.6-53.2) | 94.6 (94.6-94.7) | 99.9 (99.9-99.9) |
| 15-34 | 0.2 (0.2-0.3) | 4.7 (3.0-6.9) | 100 (100-100) | 100 (100-100) | 80.0 (65.4-90.4) | 51.1 (35.8-66.3) | 95.5 (95.4-95.5) | 99.9 (99.9-99.9) |
| 35-49 | 0.9 (0.8-1.0) | 7.8 (6.7-9.0) | 100 (100-100) | 100 (100-100) | 91.3 (87.3-94.4) | 67.2 (61.2-72.8) | 90.8 (90.7-90.9) | 99.3 (99.3-99.3) |
| 50-64 | 1.3 (1.3-1.4) | 9.6 (8.9-10.3) | 100 (100-100) | 99.9 (99.9-99.9) | 93.9 (92.2-95.3) | 69.6 (66.7-72.3) | 83.6 (83.5-83.7) | 98.5 (98.4-98.5) |
| 65-79 | 1.8 (1.7-1.9) | 13.6 (12.9-14.4) | 100 (100-100) | 99.8 (99.8-99.8) | 92.9 (91.7-94.0) | 57.2 (55.0-59.3) | 79.1 (78.9-79.2) | 98.5 (98.4-98.5) |
| ≥80 | 3.4 (3.3-3.6) | 21.0 (19.9-22.1) | 99.9 (99.9-99.9) | 99.5 (99.5-99.5) | 92.0 (90.8-93.0) | 47.7 (45.7-49.7) | 75.7 (75.5-75.9) | 98.3 (98.3-98.4) |
| **Admission Year** | | | | | | | | |
| 2006 | 1.5 (1.4-1.7) | 12.5 (11.5-13.5) | 100 (100-100) | 99.9 (99.9-99.9) | 92.8 (90.8-94.5) | 66.6 (63.2-69.9) | 86.8 (86.6-86.9) | 99.0 (98.9-99.0) |
| 2007 | 1.4 (1.3-1.5) | 12.0 (11.0-13.1) | 100 (100-100) | 99.9 (99.9-99.9) | 94.4 (92.4-96.0) | 65.3 (61.6-68.8) | 87.0 (86.9-87.1) | 99.0 (99.0-99.1) |
| 2008 | 1.7 (1.6-1.8) | 12.3 (11.3-13.3) | 100 (100-100) | 99.9 (99.9-99.9) | 91.1 (89.1-92.8) | 53.6 (50.4-56.8) | 85.9 (85.8-86.1) | 99.0 (98.9-99.0) |
| 2009 | 1.8 (1.7-1.9) | 12.6 (11.6-13.6) | 100 (100-100) | 99.9 (99.8-99.9) | 93.4 (91.7-94.8) | 51.4 ( 48.4-54.5) | 85.5 (85.3-85.6) | 99.0 (98.9-99.0) |
| 2010 | 1.9 (1.8-2.0) | 14.2 (13.2-15.4) | 100 (100-100) | 99.9 (99.9-99.9) | 91.6 (89.8-93.2) | 54.4 (51.4-57.4) | 86.3 (86.2-86.4) | 99.1 (99.0-99.1) |
| 2011 | 2.2 (2.0-2.3) | 15.2 (14.1-16.4) | 100 (100-100) | 99.9 (99.9-99.9) | 92.2 (90.6-93.6) | 49.8 (47.0-52.7) | 85.8 (85.7-85.9) | 99.1 (99.0-99.1) |
| **Department** | | | | | | | | |
| Internal medicine | 2.7 (2.7-2.8) | 16.5 (16.0-17.0) | 99.9 (99.9-100) | 99.7 (99.7-99.7) | 92.8 (92.1-93.4) | 56.0 (54.7-57.3) | 80.3 (80.2-80.4) | 98.3 (98.3-98.3) |
| Surgical | 0.2 (0.2-0.2) | 2.3 (1.9-2.8) | 100 (100-100) | 100 (100-100) | 90.6 (85.8-94.3) | 57.6 (50.5-64.5) | 86.0 (85.9-86.1) | 99.2 (99.2-99.2) |
| Gynecologic/ Obstetric | 0.1 (0.1-0.3) | 3.1 (1.2-6.7) | 100 (100-100) | 100 (100-100) | 76.9 (46.2-95.0) | 46.2 (19.2-74.9) | 98.0 (97.9-98.0) | 99.9 (99.9 -100) |
| Pediatric | 0.2 (0.1-0.3) | 3.4 (1.7-5.8) | 100 (100-100) | 100 (100-100) | 85.3 (68.9-95.0) | 35.3 (19.7-53.5) | 90.4 (90.3-90.6) | 99.8 (99.8-99.8) |
| Other | 0.3 (0.2-0.5) | 1.5 (0.4-3.9) | 100 (100-100) | 100 (100-100) | 58.3 (36.6-77.9) | 16.7 (4.74-37.4) | 95.2 (95.0-95.3) | 99.7 (99.7-99.8) |

* DNRP = Danish National Registry of Patients

[¤]Corresponding to <133mmol/l for infants of 30 day or less of age

[#]Corresponding to <123mmol/l for infants of 30 day or less of age

## Sensitivity analyses

Compared to the primary analyses, we observed no changes in neither sensitivity nor specificity estimates, when including only patients with at least one serum sodium measurement during their hospitalization in the analysis. PPV increased slightly for all serum sodium cut-off points, while NPV decreased for the three highest cut-off points. Including only patients with more than one serum sodium measurement also yielded almost identical results (Table 4).

After restriction to the most specific ICD-10 codes for hyponatremia, PPV increased slightly and sensitivity decreased (94.6% (95% CI: 93.6%–95.6%) and 0.7% (95% CI: 0.6%–0.7%), respectively). Estimates of specificity and NPV were virtually unchanged (Table 4).

We observed a slight increase in sensitivity for serum sodium cut-off points <130 mmol/l but not for the overall estimate when restricting to the first hospitalization in the study period. PPV and NPV generally increased, although only very slightly for the overall estimate (Table 4).

**Table 4.**

Sensitivity Analyses.

| Hyponatremic serum sodium value recorded in LABKA research database (mmol/l) | | Primary Analysis (including all admissions for all patients in the study period) % (95% CI) | Sensitivity Analyses | | | |
|---|---|---|---|---|---|---|
| | | | Requiring at least one serum sodium measurement during hospitalization % (95% CI) | Requiring >1 serum sodium measurement during hospitalization % (95% CI) | ICD-10 algorithm restricted to code E87.1A and P74.2B % (95% CI) | Restricting to first admission per patient in the study period % (95% CI) |
| **Overall** | | | | | | |
| Na<135 | Sensitivity | 1.8 (1.7-1.8) | 1.8 (1.7-1.8) | 1.9 (1.8-2.0) | 0.7 (0.6-0.7) | 1.7(1.7-1.9) |
| | Specificity | 100 (100-100) | 100 (100-100) | 100 (100-100) | 100 (100-100) | 100 (100-100) |
| | PPV | 92.5 (91.8-93.1) | 95.4 (94.8-95.9) | 95.8 (95.2-96.3) | 94.6 (93.6-95.6) | 93.5 (92.0-94.7) |
| | NPV | 86.2 (86.2-86.2) | 76.9 (76.8-77.0) | 74.7 (74.6-74.8) | 86.1 (86.0-86.1) | 91.6 (91.6-91.7) |
| **Cut-off points for increasing severity of hyponatremia** | | | | | | |
| Na<130 | Sensitivity | 5.3 (5.2-5.5) | 5.3 (5.2-5.5) | 5.6 (5.4-5.7) | 2.1 (2.0-2.2) | 6.3 (5.9-6.7) |
| | Specificity | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) | 100 (100-100) | 100 (100-100) |
| | PPV | 77.4 (76.3-78.5) | 79.8 (78.7-80.9) | 80.5 (79.4-81.6) | 83.0 (81.4-84.6) | 82.2 (80.7-84.8) |
| | NPV | 96.3 (96.3-96.3) | 93.8 (93.8-93.9) | 93.0 (93.0-93.1) | 96.2 (96.2-96.2) | 97.9 (97.9-98.0) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Na<125 | Sensitivity | 13.1 (12.7-13.6) | 13.1 (12.7-13.6) | 13.6 (13.1-14.0) | 5.4 (5.1-5.7) | 15.6 (14.6-16.6) |
| | Specificity | 99.9 (99.9-99.9) | 99.8 (99.8-99.8) | 99.8 (99.8-99.8) | 100 (100-100) | 99.9 (99.9-99.9) |
| | PPV | 55.7 (54.5-57.0) | 57.5 (56.2-58.8) | 57.9 (56.5-59.2) | 62.5 (60.4-64.5) | 62.3 (59.6-64.8) |
| | NPV | 99.0 (99.0-99.0) | 98.3 (98.3-98.4) | 98.1 (98.1-98.1) | 98.9 (98.9-98.9) | 99.4 (99.4-99.4) |
| Na<120 | Sensitivity | 24.9 (24.0-25.9) | 24.9 (24.0-25.8) | 25.4 (24.5-26.4) | 6.3 (5.8-6.9) | 29.3 (27.3-31.3) |
| | Specificity | 99.8 (99.8-99.8) | 99.7 (99.7-99.7) | 99.7 (99.7-99.7) | 100 (100-100) | 99.9 (99.9-99.9) |
| | PPV | 35.2 (34.0-36.5) | 36.3 (35.1-37.6) | 36.3 (35.0-37.6) | 50.6 (47.5-53.7) | 43.7 (41.0-46.4) |
| | NPV | 99.7 (99.7-99.7) | 99.5 (99.5-99.5) | 99.5 (99.4-99.5) | 99.6 (99.6-99.7) | 99.8 (99.8-99.8) |
| Na<115 | Sensitivity | 34.3 (32.6-35.9) | 34.2 (32.6-35.9) | 34.9 (33.1-36.6) | 9.3 (8.3-10.3) | 38.8 (35.5-42.1) |
| | Specificity | 99.8 (99.8-99.8) | 99.7 (99.6-99.7) | 99.6 (99.6-99.6) | 100 (100-100) | 99.9 (99.9-99.9) |
| | PPV | 18.9 (17.9-20.0) | 19.5 (18.5-20.6) | 19.5 (18.4-20.6) | 28.8 (26.1-31.7) | 24.2 (22.0-26.6) |
| | NPV | 99.9 (99.9-99.9) | 99.8 (99.8-99.8) | 99.8 (99.8-99.8) | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) |

## DISCUSSION

This is the first study to report on the validity of ICD-10 coding of hyponatremia using comprehensive population-based medical registries, and including patients of all ages. A record of a hyponatremia diagnosis in the DNRP was found to be specific to and highly predictive of hyponatremia confirmed by laboratory values. However, the disorder was greatly underreported, though to a lesser extent in patients admitted to an internal medicine department compared to other departments. We found sensitivity to be low even for severe degrees of hyponatremia. These results were robust when we used a stricter definition of hyponatremia and complete case analysis.

Our findings correspond with those of Movig *et al.*'s single-center study conducted in The Netherlands, in which ICD-9-CM coding of hyponatremia in inpatient discharge records was compared with hospital laboratory data.[13] As in our study, sensitivity at the cut-off point of 135 mmol/l was 1.7%, and increased with decreasing serum sodium levels. Sensitivity thus reached 30.6% for values below 115 mmol/l. In addition, their estimates for PPV, NPV, and specificity were similar to our results (91.7%, 79.5% and <99.9%, respectively). A Canadian study by Gandhi *et al.* examined ICD-10 coding for hyponatremia and reported a sensitivity of 6.4% for the cut-off point of <135 mmol/l and 41.7% for the cut-off point of 125 mmol/l.[12] The study was, however, restricted to patients ≥66 years of age presenting with serum sodium values at time of admission or emergency department contact. In line

with their results, we found that the median age of patients with an ICD-10 code of hyponatremia recorded in the DNRP, which could be confirmed by laboratory results, was higher than that of hyponatremic patients with no ICD-10 code for hyponatremia recorded in the DNRP. However, the sensitivity estimates did not reach those found by Gandhi et al. even for patients 65-79 and ≥80 years of age. Shea *et al*. also reported higher sensitivity compared to our results (3.5% for a cut-off point of <136 mmol/l and 29.6% for the cut-off point of 125 mmol/l) in their study examining the validity of ICD-9 codes of hyponatremia in an outpatient managed-care population.[14] Outpatient serum sodium laboratory tests were compared with outpatient professional ICD-9 claims registered within 15 days before or after the laboratory claim. The PPV was 62.6% for serum sodium levels <136 mmol/l and 10.4% for levels <125 mmol/l. As noted in the paper, detected hyponatremia may be the cause for follow-up visits in an outpatient setting, without the need for repeat measurements. This could lead to lower PPV compared to our study and the study by Movig *et al*. In addition, managed-care claims databases encompass an employer-based commercially insured population. Shea *et al*.'s study thus may not be representative of elderly populations, in which prevalence of hyponatremia is high.[24, 25] This also may explain why their results differed from ours.

The major strengths of our study are its population-based design and unambiguous individual-level linkage between registries containing complete data on all hospitalizations and laboratory tests in a well-defined population. This eliminates the risk of selection bias. Several potential study limitations must be considered. We relied on only one (the lowest) serum sodium value recorded to define presence of hyponatremia, and also did not consider duration of hyponatremia. Clinicians may be more likely to regard hyponatremia as clinically relevant, and hence to include the condition in discharge diagnoses, if it is detected in more than one measurement. In this context, it is important to note that patient transfers between departments are registered as separate admissions in the DNRP and we examined the validity of ICD-10 coding for each registered admission. The PPV may have

been even higher if we had considered contiguous admissions as a single admission. Finally, we chose to include patients without serum sodium measurements and to consider them as normonatremic in the main analysis. We did so to detect false positive diagnoses and thereby obtain accurate estimates of predictive values. Serum sodium is often measured as a routine procedure, and rarely due to specific suspicion. Though frequently measured, the proportion of patients with unacknowledged hyponatremia is most often unknown. We therefore performed a complete case analysis, including only patients with serum sodium measurements. As the results did not differ markedly from those of the primary analysis, we believe that including patients without serum sodium measurements in the normonatremic group was justified.

We can only speculate on reasons for the low sensitivity of the ICD-10 coding of hyponatremia found in our study. A diagnosis of hyponatremia was less likely recorded in patients with high levels of comorbidity, which may indicate that hyponatremia is mainly considered a bystander of the underlying diseases. If hyponatremia is mild or transient, and does not require intervention or specific attention, it may not warrant documentation. However, even for very severe hyponatremia (<115 mmol/l), which is potentially fatal and requires immediate intervention, sensitivity was low. We believe that this most likely reflects negligence of proper coding practice rather than lack of attention to the clinical importance of low serum sodium levels. With the increasing use of electronic medical records it would be feasible and worthwhile to automatically assign discharge diagnoses to patients with gross abnormal laboratory values. However, the ultimate responsibility for summarizing the most important reasons for treatment and care still rests upon the discharging physician. Our results suggest that hyponatremia is not coded in the presence of coexisting illness deemed more important, and that the fact that hyponatremia may be an important indicator of a poor prognosis is not yet acknowledged.

The results of this validation study emphasize the need for caution when relying on ICD-10 codes for hyponatremia in research. Based on the estimated PPV and specificity, patients with an ICD-10 code of hyponatremia can safely be assumed to actually have hyponatremia. However, the low sensitivity renders the ICD-10 codes inappropriate for use in studies examining prevalence, incidence, and absolute risk, due to a high degree of misclassification. Sensitivity increased with decreasing serum sodium levels, suggesting that studies using ICD-codes to identify hyponatremia would be based mainly on severe cases. Furthermore, our results indicate that quality of registration differs according to age, gender, and morbidity status. Hence, studies may be susceptible to differential misclassification, again resulting in biased results.

## CONCLUSION

We found that the ICD-10 coding of hyponatremia in DNRP has high specificity but is highly incomplete, resulting in very low sensitivity. When available, laboratory test results for serum sodium will more correctly identify patients with hyponatremia.

## Contributors

LHB participated in the design of the study, performed the data analysis, provided interpretation of study results and drafted the manuscript. SPU participated in acquisition and analysis of data. CFC and HTS participated in the design of the study, provided interpretation of study results and helped draft the manuscript. TR and JOLJ contributed with interpretation of study results helped draft the manuscript. All authors read and approved the final manuscript.

## Funding

This work was supported by the Clinical Epidemiology Research Foundation and by the Danish Cancer Society (grant no. R73-A4284-13-S17).

## Competing interests

JOLJ has received an unrestricted research grant and lecture fees from Otsuka Pharma Scandinavia AB. TR has received lecture fees from Otsuka Pharma Scandinavia AB.

LHB, CFC, SPU and HTS are salaried employees of Department of Clinical Epidemiology, Aarhus University Hospital. The Department of Clinical Epidemiology receives funding from companies in the form of research grants to (and administered by) Aarhus University.

None of these grants or fees had any had any leverage on the design, implementation or reporting of the present study.

**Data Sharing Statement:** No additional data

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# Validity of the International Classification of Diseases, 10th revision (ICD-10) discharge diagnosis codes for hyponatremia in the Danish National Registry of Patients

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**Keywords:** validation study; ICD 10; hyponatremia; diagnosis; population register; clinical laboratory information system

**Word count:** ~~2,829~~3,005

## ABSTRACT

**OBJECTIVE:** To examine the validity of the *International Classification of Diseases*, 10th revision (ICD-10) codes for hyponatremia in the nationwide population-based Danish National Registry of Patients (DNRP) among inpatients of all ages.

**DESIGN:** Population-based validation study.

**SETTING:** All somatic hospitals in the North and Central Denmark Regions from 2006 through 2011.

**PARTICIPANTS:** Patients of all ages admitted to hospital (n=819,701 individual patients) during the study period. Patient could be included in the study more than once, and we did not restrict to patients with serum sodium measurements (total of n=2,186,642 hospitalizations).

**MAIN OUTCOME MEASURE:** We validated ICD-10 discharge diagnoses of hyponatremia recorded in the DNRP, using serum sodium measurements obtained from the laboratory information systems (LABKA) research database as the gold standard. One sodium value <135 mmol/l measured at any time during hospitalization confirmed the diagnosis. We estimated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for ICD-10 codes for hyponatremia overall and for cut-off points for increasing hyponatremia severity.

**RESULT:** An ICD-10 code for hyponatremia was recorded in the DNRP in 5,850 of the 2,186,642 hospitalizations identified. According to laboratory measurements, however, hyponatremia was present in 306,418 (14%) hospitalizations. Sensitivity of hyponatremia diagnoses was 1.8% (95% confidence interval (CI): 1.7%-1.8%). For sodium values <115mmol/l, sensitivity was 34.3% (95% CI: 32.6%-35.9%). Overall PPV was 92.5% (95% CI: 91.8%-93.1%), and decreased with increasing hyponatremia severity. Specificity and NPV were high for all cut-off points (≥99.8% and ≥86.2% respectively). Hyponatremic patients without a corresponding ICD-10 discharge diagnosis were younger and had higher Charlson Comorbidity Index scores than hyponatremic patients with a hyponatremia code in the DNRP.

**CONCLUSION:** ICD-10 codes for hyponatremia in the DNRP have high specificity, but very low sensitivity. Laboratory test results, not discharge diagnoses, should be used to ascertain hyponatremia.

## Article summery

### Article focus

- Hospital discharge diagnoses for hyponatremia recorded in the Danish National Registry of Patients (DNRP) may constitute valuable data sources for epidemiologic studies, however the validity of data must be established.

### Key Message

- ICD-10 coding of hyponatremia in the Danish National Registry of Patients (DNRP) is highly specific but greatly incomplete.
- Epidemiological studies relying on discharge diagnoses of hyponatremia may be susceptible to differential misclassification.

### Strengths and limitation of this study

- This is the first study to validate the International Classification of Diseases, 10th Revision code for hyponatremia in hospitalized patients of all ages.
- We used a population-based design with unambiguous individual-level linkage between registries containing complete data on all hospitalizations and laboratory, ensuring a large sample size and virtually eliminating the risk of selection bias.
- We did not consider the duration of hyponatremia. Sensitivity may have been higher if presence of hyponatremia required, that it was detected in more than one laboratory measurement during hospitalization.

## INTRODUCTION

Hyponatremia, defined as a serum sodium value <135mmol/l, is the most common electrolyte abnormality encountered in clinical practice.[1] It can be caused by a large variety of conditions, such as heart failure, kidney failure, cirrhosis, syndrome of inappropriate antidiuretic hormone, vomiting, and diarrhea, and can also be a side effect of several medications.[2] Results of recent studies have indicated that even a mild to moderate level of hyponatremia may be an important predictor of poor prognosis in patients with cardiovascular disease, kidney and liver disease, and cancer.[3-8] However, key aspects of the etiology and prognosis of hyponatremia remain unknown.

The Danish population-based medical registries may offer a unique opportunity for studies of the epidemiology of hyponatremia, if data are valid. However, as symptoms of mild and moderate hyponatremia may be vague, and concealed by or construed as symptoms of an underlying disease, it is likely that the condition will not be reported.[9,10] Thus, use of only inpatient discharge diagnoses of hyponatremia in epidemiologic studies may cause bias that can affect the validity of study results.[11]

To date, only one study has investigated the validity of *International Classification of Diseases* (ICD), 10th revision (ICD-10) codes for hyponatremia. This Canadian study was restricted to patients 66 years of age or older ~~presenting~~ with ~~a hyponatremic~~ serum sodium values at the time of emergency department contact or at hospital admission.[12] The sensitivity of hyponatremia coding was found to be as low as 7%. For inpatients younger than 66 years, knowledge of the validity hyponatremia diagnoses is limited to a study performed in a single hospital in the Netherlands using ICD-9 codes for hyponatremia. In this study, sensitivity was found to be just below 2%, using hospital laboratory data as the reference standard.[3] Similar results were found in a study examining the validity of outpatient professional ICD-9 claims for hyponatremia in the US.[14]

We therefore conducted the first population-based study examining the validity of ICD-10 inpatient discharge diagnoses of hyponatremia in the Danish National Registry of Patients (DNRP), ~~in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV),~~ including patients of all ages.

## METHODS

### Setting and data collection

We used the DNRP to identify all admissions to hospitals in the North and Central Denmark Regions (2.1 million inhabitants in the study period) from 1 January 2006 to 31 December 2011. The DNRP contains information, including date of admission and discharge, department code and discharge diagnoses, on all admissions to Danish non-psychiatric hospitals since 1977.[15,16]

By use of the unique 10-digit civil registration number, assigned to all Danish residents since 1968,[17] we linked each patient's DNRP data to the clinical laboratory information system (LABKA) research database. For patients living in the North and Central Denmark Regions, data on virtually all specimens analyzed in clinical laboratories by hospitals and medical practitioners are entered into a computer-based clinical laboratory information system, which functions as a routine diagnostic tool for medical personnel.[18] Data are transferred electronically to the LABKA research database, managed by Aarhus University. Analyses are coded according to the NPU (Nomenclature, Properties and Units) system. The LABKA research database contains the civil registration number, time and date of blood sampling, and identification code of the requesting physician or hospital department.[18] We used the LABKA research database to retrieve information on all serum sodium measurements recorded during each of the identified hospitalizations.

### Hyponatremia diagnosis (ICD-10 code algorithm)

At hospital discharge, the attending physician assigns one primary diagnosis, reflecting the main reason for hospitalization and treatment and up to 19 secondary diagnoses regarding additional clinically relevant conditions, including underlying diseases, complications and symptoms.[19] Diagnoses recorded in the DNRP have been coded according to the *International Classification of Diseases* (ICD), 10th revision (ICD-10) since 1994.[16]

We developed an algorithm based on ICD-10 codes to identify primary and secondary discharge diagnoses of hyponatremia recorded in the DNRP for each hospitalization. The following ICD-10 codes were included in the algorithm: E87.1 (Hypo-osmolality and hyponatremia), E87.1A (Hyponatremia) and P74.2B (Hyponatremia in newborns [Danish version of ICD-10]).

**Gold Standard (laboratory serum sodium measurements)**

We used serum sodium measurements recorded in the LABKA research database as the gold standard to confirm or disconfirm a diagnosis of hyponatremia identified by the ICD-10 algorithm. Hyponatremia was defined as serum sodium values <135 mmol/l for patients older than 30 days and <133 mmol/l for infants 30 days of age or younger.[20] Patients were considered to have hyponatremia if at least one hyponatremic serum sodium value was recorded during their hospitalization. If no serum sodium measurement was available, the patient was assumed to have a non-hyponatremic serum sodium value (135-145mmol/l). The following cut-off points for increasing severity of hyponatremia were chosen: 135 mmol/l, 130mmol/l, 125mmol/l, 120mmol/l and 115mmol/l.[13] The corresponding levels for infants less than 31 days of age were 133mmol/l, 128mmol/l, 123mmol/l, 118mmol/l and 113mmol/l.

**Other Variables**

For each patient, we assessed comorbidity by information retrieved from the DNRP on the conditions included in the Charlson Comorbidity Index (CCI). The CCI includes 19 medical conditions, each

assigned a weighted score between one and six. The sum of these individual scores is used as a measure of a patient's comorbidity burden.[21, 22] We calculated CCI scores for each patient and defined three comorbidity levels: low (CCI score 0), medium (CCI score 1-2) and high (CCI score of 3 or above). We included morbidities recorded within 10 years prior to the current hospitalization, as conditions requiring hospital treatment within this timeframe would likely influence the attending physician's diagnostic approach and evaluation during the current hospitalization.

Furthermore, we obtained information on department of admission and year of admission from the DNRP. Departments were categorized in the following five groups: internal medicine, surgery, gynecology/obstetrics, pediatrics, and other.

**Statistical analysis**

Patients with a hyponatremic serum sodium value recorded in the LABKA research database were divided into two categories: Those with an ICD-10 code for hyponatremia in the DNRP and those without. We described both groups of patients in terms of gender, age (median and associated interquartile range (IQR)), department of admission, CCI score and specific comorbidities.

We estimated the sensitivity, specificity, PPV, and NPV (see Figure 1) for ICD-10 codes for hyponatremia in the DNRP with corresponding 95% confidence intervals (CI), using the exact method for binomial proportions. We defined sensitivity as the probability an ICD-10 code for hyponatremia being registered in the DNRP, when the laboratory test result identified presence of hyponatremia. Specificity was defined as the probability of an ICD-10 code for hyponatremia not being registered in the DNRP, when hyponatremia was not identified in laboratory test results. We estimated the PPV as the proportion of patients for whom an ICD-10 code for hyponatremia recorded in the DNRP could be confirmed by a serum sodium measurement, and NPV as the proportion of patients with no ICD-10 code for hyponatremia in the DNRP, for whom non-hyponatremic, or no serum sodium values were

recorded in the LABKA research database. The analyses were repeated for all hyponatremia cut-off points and after stratification by age group categories, department of admission and admission year. Finally, we conducted ~~three~~ four sensitivity analyses. First, we performed a complete case analysis, a method for dealing with missing data considering only subjects with recorded values for all covariates,[23] meaning that only patients with at least one serum sodium measurement during their hospitalization were included in the analysis. We did so, in order to evaluate the assumption that patients without a serum sodium measurement were normonatremic. In the second sensitivity analysis, we included only patients with more than one serum sodium measurement during their hospitalization. In the third sensitivity analysis, we included only the ICD-10 codes E87.1A (hyponatremia) and P74.2B (hyponatremia in newborns). Because epidemiologic studies often focus on incident cases, we performed a post-hoc sensitivity analysis in which we restricted to the first hospitalization for each patient in the study period

Data analyses were performed using the statistical software package STATA (version 12; Stata Corp, College Station, TX, USA).

The study was approved by the Danish Data Protection Agency (record number 2006-53-1396). All data were obtained from Danish public registries. According to Danish law their use does require informed consent or ethics committee approval.

## RESULTS

### Characteristics

We identified 2,186,642 hospitalizations (819,701 individual patients) within the study period. For 1,308,740 (60%) hospitalizations, at least one serum sodium measurement was recorded in the LABKA research database, and for 1,037,647 (47%) subsequent measurements were recorded. According to the recorded serum sodium value, hyponatremia was present in 306,418 hospitalizations

(14%). In the DNRP, we identified 5,850 hospitalizations with an ICD-10 code of hyponatremia (hypo-osmolality and hyponatremia= 3,722, hyponatremia=2,124, hyponatremia in newborns=4) among all 2,186,642 hospitalizations. Of these, 440 did not have a hyponatremic serum sodium value recorded in the LABKA research database.

Table 1 shows the distribution of hospitalizations by presence/absence of an ICD-10 diagnosis of hyponatremia recorded in the DNRP, by gender, age and comorbidity variables, for patients with hyponatremic serum sodium values. Patients who had an ICD-10 code of hyponatremia recorded in the DNRP and a corresponding hyponatremic serum sodium measurement, were on average older, more often female, more likely admitted to an internal medicine department, and characterized by lower comorbidity levels than patients with no hyponatremia diagnosis in the DNRP, but hyponatremic serum sodium values recorded in the LABKA research database. Cerebrovascular disease, dementia, and ulcer disease were the only comorbidities more frequently found in patients with an ICD-10 code for hyponatremia and corresponding hyponatremic serum sodium value, compared to hyponatremic patients without a hyponatremia diagnosis in the DNRP. (Table 1)

**Table 1.**

Characteristics of hospitalizations identified in the DNRP from 2006 to 2011

| | Hospitalizations with at least on serum sodium value <135 mmol/l recorded in the LABKA research database | | All hospitalizations (n=2,186,642) n (%) |
|---|---|---|---|
| | ICD-10 code of hyponatremia in the DNRP* (n=5,410) n (%) | No ICD-10 code of hyponatremia in the DNRP* (n=301,008) n (%) | |
| **Sex** | | | |
| Female | 3,643 (67.3) | 148,120 (49.3) | 1,168,803 (53.5) |
| Male | 1,767 (32.7) | 152,588 (50.7) | 1,017,839 (46.5) |
| **Age, years** | | | |
| Median (IQR) | 77.3 (65.7-84.9) | 67.4 (54.2-78.2) | 54.7 (29.3-71.1) |
| **Department of admission** | | | |
| Internal medicine | 5,173 (95.6) | 184,848 (61.6) | 943,121 (43.1) |
| Surgical | 184 (3.4) | 88,378 (29.4) | 630,525 (28.8) |

| | | | |
|---|---|---|---|
| Gynaecologic/obstetric | 10 (0.2) | 7,104 (2.4) | 347,365 (15.9) |
| Pediatric | 29 (0.5) | 15,830 (5.3) | 165,289 (7.6) |
| Other | 14 (0.3) | 4,848 (1.6) | 100,342 (4.6) |
| **CCI level (score)** | | | |
| Low (0) | 2,075 (38.4) | 100,398 (33.4) | 1,232,762 (56.4) |
| Medium (1-2) | 2,182 (40.3) | 106,874 (35.5) | 588,783 (26.9) |
| High (≥3) | 1,153 (21.3) | 93,736 (31.1) | 365,097 (16.7) |
| **Specific comorbidities** | | | |
| Myocardial infarction | 312 (5.8) | 23,269 (7.7) | 108,373 (5.0) |
| Congestive heart failure | 460 (8.5) | 31,236 (10.4) | 121,429 (5.6) |
| Peripheral vascular disease | 464 (8.6) | 29,356 (9.8) | 115,620 (5.3) |
| Cerebrovascular disease | 1,017 (18.8) | 39,466 (13.1) | 182,304 (8.3) |
| Dementia | 107 (3.1) | 4,247 (1.4) | 20,711 (1.0) |
| Chronic pulmonary disease | 870 (16.1) | 48,726 (16.2) | 231,121 (10.6) |
| Connective tissue disease | 291 (5.4) | 13,990 (4.7) | 73,299 (3.4) |
| Ulcer disease | 450 (8.3) | 20,645 (6.9) | 79,050 (3.6) |
| Mild liver disease | 189 (3.5) | 13,413 (4.5) | 37,698 (1.7) |
| Moderate to severe liver disease | 66 (1.2) | 6,279 (2.1) | 14,999 (0.7) |
| Diabetes I and II | 521 (9.6) | 39,995 (13.3) | 150,205 (6.9) |
| Diabetes with complications | 269 (5.0) | 25,083 (8.3) | 85,035 (3.9) |
| Hemiplegia | 35 (0.7) | 2,462 (0.8) | 16,060 (0.7) |
| Moderate to severe renal disease | 143 (2.6) | 20,123 (6.7) | 75,441 (3.5) |
| Malignant tumor | 781 (14.4) | 64,882 (21.6) | 312,845 (14.3) |
| Leukemia | 22 (0.4) | 4,636 (1.5) | 17,190 (0.8) |
| Lymphoma | 51 (0.9) | 7,096 (2.4) | 25,348 (1.2) |
| Metastatic cancer | 183 (3.4) | 23,948 (8.0) | 105,512 (4.8) |
| AIDS | 3 (0.1) | 475 (0.2) | 2,014 (0.1) |

* DNRP = Danish National Registry of Patients

**Sensitivity, specificity, PPV and NPV**

For 440 (7.5%) of the 5,850 hospitalizations with an ICD-10 code for hyponatremia recorded in the DNRP, no hyponatremic serum sodium measurement was recorded in the LABKA research database during the hospitalization (for 178, no measurement was recorded at all). This corresponds to a PPV of an ICD-10 code for hyponatremia of 92.5% (95% CI: 91.8%–93.1%) for serum sodium values <135 mmol/l (<133 mmol/l for infants 30 days of age or younger). As expected, PPV decreased with lower serum sodium cut-off points. A total of 5,410 hospitalizations had both an ICD-10 code recorded in the

DNRP and a corresponding hyponatremic laboratory measurement, resulting in a sensitivity of the ICD-10 codes of 1.8% (95% CI: 1.7%–1.8%). Sensitivity increased with lower cut-off points for serum sodium, reaching 34.3% (95% CI: 32.6%–35.9%) for serum sodium <115 mmol/l. Specificity and NPV for serum sodium <135 mmol/l were 100% (97.5% CI: 100%) and 86.2% (95% CI: 86.2%–86.2%), respectively. Specificity and NPV remained high for all serum sodium cut-off points (Table 2).

**Table 2.**

Validity of ICD-10 codes for hyponatremia recorded in the DNRP*, using serum sodium measurements in the LABKA research database as gold standard.

| Hyponatremic serum sodium value recorded in LABKA research database (mmol/l) | | ICD-10 code for hyponatremia recorded in the DNRP* Yes | No | Total | Validity Measures % (95% CI) | |
|---|---|---|---|---|---|---|
| **Overall** | | | | | | |
| Na<135¤ | Yes | 5,410 | 301,008 | 306,418 | Sensitivity | 1.8 (1.7-1.8) |
| | No | 440 | 1,879,784 | 1,880,224 | Specificity | 100 (100-100) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 92.5 (91.8-93.1) |
| | | | | | NPV | 86.2 (86.2-86.2) |
| **Cut-off points for increasing severity of hyponatremia** | | | | | | |
| Na<130§ | Yes | 4,528 | 80,605 | 85,133 | Sensitivity | 5.3 (5.2-5.5) |
| | No | 1,322 | 2,100,187 | 2,101,509 | Specificity | 99.9 (99.9-99.9) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 77.4 (76.3-78.5) |
| | | | | | NPV | 96.3 (96.3-96.3) |
| Na<125# | Yes | 3,261 | 21,544 | 24,805 | Sensitivity | 13.1 (12.7-13.6) |
| | No | 2,589 | 2,159,248 | 2,161,837 | Specificity | 99.9 (99.9-99.9) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 55.7 (54.5-57.0) |
| | | | | | NPV | 99.0 (99.0-99.0) |
| Na<120£ | Yes | 2,061 | 6,219 | 8,280 | Sensitivity | 24.9 (24.0-25.9) |
| | No | 3,789 | 2,174,573 | 2,178,362 | Specificity | 99.8 (99.8-99.8) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 35.2 (34.0-36.5) |
| | | | | | NPV | 99.7 (99.7-99.7) |
| Na<115$ | Yes | 1,107 | 2,127 | 3,234 | Sensitivity | 34.3 (32.6-35.9) |
| | No | 4,743 | 2,178,665 | 2,183,408 | Specificity | 99.8 (99.8-99.8) |
| | Total | 5,850 | 2,180,792 | 2,186,642 | PPV | 18.9 (17.9-20.0) |
| | | | | | NPV | 99.9 (99.9-99.9) |

*DNRP = Danish National Registry of Patients
¤ Corresponding to <133 mmol/l for infants of 30 day or less of age
§ Corresponding to <128 mmol/l for infants of 30 day or less of age
# Corresponding to <123 mmol/l for infants of 30 day or less of age
£ Corresponding to <118 mmol/l for infants of 30 day or less of age

[$] Corresponding to <113 mmol/l for infants of 30 day or less of age

Sensitivity was higher among admissions to internal medicine departments than among admissions to surgical, gynecologic/obstetric, pediatric, and "other" departments (Table 3). The validity measures were virtually unchanged across strata of admission year.

**Table 3.**

Validity of ICD-10 codes for hyponatremia recorded in the DNRP, stratified by age group categories, year and department of admission, for serum sodium values <135mmol/l[¤] and <125mmol/l[#]

| | Sensitivity % (95% CI) | | Specificity % (95% CI) | | PPV % (95% CI) | | NPV % (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | 135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l | <135 mmol/l | <125 mmol/l |
| **Age, years** | | | | | | | | |
| < 15 | 0.2 (0.1-0.2) | 3.0 (1.5-5.2) | 100 (100-100) | 100 (100-100) | 84.4 (67.2-94.7) | 34.4 (18.6-53.2) | 94.6 (94.6-94.7) | 99.9 (99.9-99.9) |
| 15-34 | 0.2 (0.2-0.3) | 4.7 (3.0-6.9) | 100 (100-100) | 100 (100-100) | 80.0 (65.4-90.4) | 51.1 (35.8-66.3) | 95.5 (95.4-95.5) | 99.9 (99.9-99.9) |
| 35-49 | 0.9 (0.8-1.0) | 7.8 (6.7-9.0) | 100 (100-100) | 100 (100-100) | 91.3 (87.3-94.4) | 67.2 (61.2-72.8) | 90.8 (90.7-90.9) | 99.3 (99.3-99.3) |
| 50-64 | 1.3 (1.3-1.4) | 9.6 (8.9-10.3) | 100 (100-100) | 99.9 (99.9-99.9) | 93.9 (92.2-95.3) | 69.6 (66.7-72.3) | 83.6 (83.5-83.7) | 98.5 (98.4-98.5) |
| 65-79 | 1.8 (1.7-1.9) | 13.6 (12.9-14.4) | 100 (100-100) | 99.8 (99.8-99.8) | 92.9 (91.7-94.0) | 57.2 (55.0-59.3) | 79.1 (78.9-79.2) | 98.5 (98.4-98.5) |
| ≥80 | 3.4 (3.3-3.6) | 21.0 (19.9-22.1) | 99.9 (99.9-99.9) | 99.5 (99.5-99.5) | 92.0 (90.8-93.0) | 47.7 (45.7-49.7) | 75.7 (75.5-75.9) | 98.3 (98.3-98.4) |
| **Admission Year** | | | | | | | | |
| 2006 | 1.5 (1.4-1.7) | 12.5 (11.5-13.5) | 100 (100-100) | 99.9 (99.9-99.9) | 92.8 (90.8-94.5) | 66.6 (63.2-69.9) | 86.8 (86.6-86.9) | 99.0 (98.9-99.0) |
| 2007 | 1.4 (1.3-1.5) | 12.0 (11.0-13.1) | 100 (100-100) | 99.9 (99.9-99.9) | 94.4 ( (92.4-96.0) | 65.3 (61.6-68.8) | 87.0 (86.9-87.1) | 99.0 (99.0-99.1) |
| 2008 | 1.7 (1.6-1.8) | 12.3 (11.3-13.3) | 100 (100-100) | 99.9 (99.9-99.9) | 91.1 (89.1-92.8) | 53.6 (50.4-56.8) | 85.9 (85.8-86.1) | 99.0 (98.9-99.0) |
| 2009 | 1.8 (1.7-1.9) | 12.6 (11.6-13.6) | 100 (100-100) | 99.9 (99.8-99.9) | 93.4 (91.7-94.8) | 51.4 ( 48.4-54.5) | 85.5 (85.3-85.6) | 99.0 (98.9-99.0) |
| 2010 | 1.9 (1.8-2.0) | 14.2 (13.2-15.4) | 100 (100-100) | 99.9 (99.9-99.9) | 91.6 (89.8-93.2) | 54.4 (51.4-57.4) | 86.3 (86.2-86.4) | 99.1 (99.0-99.1) |
| 2011 | 2.2 (2.0-2.3) | 15.2 (14.1-16.4) | 100 (100-100) | 99.9 (99.9-99.9) | 92.2 (90.6-93.6) | 49.8 (47.0-52.7) | 85.8 (85.7-85.9) | 99.1 (99.0-99.1) |
| **Department** | | | | | | | | |
| Internal medicine | 2.7 (2.7-2.8) | 16.5 (16.0-17.0) | 99.9 (99.9-100) | 99.7 (99.7-99.7) | 92.8 (92.1-93.4) | 56.0 (54.7-57.3) | 80.3 (80.2-80.4) | 98.3 (98.3-98.3) |
| Surgical | 0.2 (0.2-0.2) | 2.3 (1.9-2.8) | 100 (100-100) | 100 (100-100) | 90.6 (85.8-94.3) | 57.6 (50.5-64.5) | 86.0 (85.9-86.1) | 99.2 (99.2-99.2) |
| Gynecologic/ Obstetric | 0.1 (0.1-0.3) | 3.1 (1.2-6.7) | 100 (100-100) | 100 (100-100) | 76.9 (46.2-95.0) | 46.2 (19.2-74.9) | 98.0 (97.9-98.0) | 99.9 (99.9 -100) |
| Pediatric | 0.2 (0.1-0.3) | 3.4 (1.7-5.8) | 100 (100-100) | 100 (100-100) | 85.3 (68.9-95.0) | 35.3 (19.7-53.5) | 90.4 (90.3-90.6) | 99.8 (99.8-99.8) |
| Other | 0.3 | 1.5 | 100 | 100 | 58.3 | 16.7 | 95.2 | 99.7 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | (0.2-0.5) | (0.4-3.9) | (100-100) | (100-100) | (36.6-77.9) | (4.74-37.4) | (95.0-95.3) | (99.7-99.8) |

* DNRP = Danish National Registry of Patients
[¤]Corresponding to <133mmol/l for infants of 30 day or less of age
[#]Corresponding to <123mmol/l for infants of 30 day or less of age

**Sensitivity analyses**

Compared to the primary analyses, we observed no changes in neither sensitivity nor specificity estimates, when including only patients with at least one serum sodium measurement during their hospitalization in the analysis. PPV increased slightly for all serum sodium cut-off points, while NPV decreased for the three highest cut-off points. Including only patients with more than one serum sodium measurement also yielded almost identical results (Table ~~2~~4).

After restriction to the most specific ICD-10 codes for hyponatremia, PPV increased slightly and sensitivity decreased (94.6% (95% CI: 93.6%–95.6%) and 0.7% (95% CI: 0.6%–0.7%), respectively). Estimates of specificity and NPV were virtually unchanged (Table ~~2~~4).

We observed a slight increase in sensitivity for serum sodium cut-off points <130 mmol/l but not for the overall estimate when restricting to the first hospitalization in the study period. PPV and NPV generally increased, although only very slightly for the overall estimate (Table 4).

**Table 4.**

Sensitivity Analyses.

| Hyponatremic serum sodium value recorded in LABKA research database (mmol/l) | | Primary Analysis (including all admissions for all patients in the study period) % (95% CI) | Sensitivity Analyses | | | |
|---|---|---|---|---|---|---|
| | | | Requiring at least one serum sodium measurement during hospitalization % (95% CI) | Requiring >1 serum sodium measurement during hospitalization % (95% CI) | ICD-10 algorithm restricted to code E87.1A and P74.2B % (95% CI) | Restricting to first admission per patient in the study period % (95% CI) |
| **Overall** | | | | | | |
| Na<135 | Sensitivity | 1.8 (1.7-1.8) | 1.8 (1.7-1.8) | 1.9 (1.8-2.0) | 0.7 (0.6-0.7) | 1.7(1.7-1.9) |
| | Specificity | 100 (100-100) | 100 (100-100) | 100 (100-100) | 100 (100-100) | 100 (100-100) |
| | PPV | 92.5 (91.8-93.1) | 95.4 (94.8-95.9) | 95.8 (95.2-96.3) | 94.6 (93.6-95.6) | 93.5 (92.0-94.7) |
| | NPV | 86.2 (86.2-86.2) | 76.9 (76.8-77.0) | 74.7 (74.6-74.8) | 86.1 (86.0-86.1) | 91.6 (91.6-91.7) |
| **Cut-off points for increasing severity of hyponatremia** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Na<130 | Sensitivity | 5.3 (5.2-5.5) | 5.3 (5.2-5.5) | 5.6 (5.4-5.7) | 2.1 (2.0-2.2) | 6.3 (5.9-6.7) |
| | Specificity | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) | 100 (100-100) | 100 (100-100) |
| | PPV | 77.4 (76.3-78.5) | 79.8 (78.7-80.9) | 80.5 (79.4-81.6) | 83.0 (81.4-84.6) | 82.2 (80.7-84.8) |
| | NPV | 96.3 (96.3-96.3) | 93.8 (93.8-93.9) | 93.0 (93.0-93.1) | 96.2 (96.2-96.2) | 97.9 (97.9-98.0) |
| Na<125 | Sensitivity | 13.1 (12.7-13.6) | 13.1 (12.7-13.6) | 13.6 (13.1-14.0) | 5.4 (5.1-5.7) | 15.6 (14.6-16.6) |
| | Specificity | 99.9 (99.9-99.9) | 99.8 (99.8-99.8) | 99.8 (99.8-99.8) | 100 (100-100) | 99.9 (99.9-99.9) |
| | PPV | 55.7 (54.5-57.0) | 57.5 (56.2-58.8) | 57.9 (56.5-59.2) | 62.5 (60.4-64.5) | 62.3 (59.6-64.8) |
| | NPV | 99.0 (99.0-99.0) | 98.3 (98.3-98.4) | 98.1 (98.1-98.1) | 98.9 (98.9-98.9) | 99.4 (99.4-99.4) |
| Na<120 | Sensitivity | 24.9 (24.0-25.9) | 24.9 (24.0-25.8) | 25.4 (24.5-26.4) | 6.3 (5.8-6.9) | 29.3 (27.3-31.3) |
| | Specificity | 99.8 (99.8-99.8) | 99.7 (99.7-99.7) | 99.7 (99.7-99.7) | 100 (100-100) | 99.9 (99.9-99.9) |
| | PPV | 35.2 (34.0-36.5) | 36.3 (35.1-37.6) | 36.3 (35.0-37.6) | 50.6 (47.5-53.7) | 43.7 (41.0-46.4) |
| | NPV | 99.7 (99.7-99.7) | 99.5 (99.5-99.5) | 99.5 (99.4-99.5) | 99.6 (99.6-99.7) | 99.8 (99.8-99.8) |
| Na<115 | Sensitivity | 34.3 (32.6-35.9) | 34.2 (32.6-35.9) | 34.9 (33.1-36.6) | 9.3 (8.3-10.3) | 38.8 (35.5-42.1) |
| | Specificity | 99.8 (99.8-99.8) | 99.7 (99.6-99.7) | 99.6 (99.6-99.6) | 100 (100-100) | 99.9 (99.9-99.9) |
| | PPV | 18.9 (17.9-20.0) | 19.5 (18.5-20.6) | 19.5 (18.4-20.6) | 28.8 (26.1-31.7) | 24.2 (22.0-26.6) |
| | NPV | 99.9 (99.9-99.9) | 99.8 (99.8-99.8) | 99.8 (99.8-99.8) | 99.9 (99.9-99.9) | 99.9 (99.9-99.9) |

## DISCUSSION

This is the first study to report on the validity of ICD-10 coding of hyponatremia using comprehensive population-based medical registries, and including patients of all ages. A record of a hyponatremia diagnosis in the DNRP was found to be specific to and highly predictive of hyponatremia confirmed by laboratory values. However, the disorder was greatly underreported, though to a lesser extent in patients admitted to an internal medicine department compared to other departments. We found sensitivity to be low even for severe degrees of hyponatremia. These results were robust when we used a stricter definition of hyponatremia and complete case analysis.

Our findings correspond with those of Movig *et al*.'s single-center study conducted in The Netherlands, in which ICD-9-CM coding of hyponatremia in inpatient discharge records was compared with hospital laboratory data.[13] As in our study, sensitivity at the cut-off point of 135 mmol/l was 1.7%, and increased with decreasing serum sodium levels. Sensitivity thus reached 30.6% for values below 115 mmol/l. In addition, their estimates for PPV, NPV, and specificity were similar to our results (91.7%, 79.5% and <99.9%, respectively). A Canadian study by Gandhi *et al.* examined ICD-10 coding for hyponatremia and reported a sensitivity of ~~4.5~~6.4% for the cut-off point of <135 mmol/l and ~~34.4~~41.7%

for the cut-off point of 125 mmol/l.[12] The study was, however, restricted to patients ≥66 years of age presenting with ~~hyponatremic laboratory test result~~serum sodium values at time of admission or emergency department contact. In line with their results, we found that the median age of patients with an ICD-10 code of hyponatremia recorded in the DNRP, which could be confirmed by laboratory results, was higher than that of hyponatremic patients with no ICD-10 code for hyponatremia recorded in the DNRP. However, the sensitivity estimates did not reach those found by Gandhi et al. even for patients 65-79 and ≥80 years of age. Shea *et al.* also reported higher sensitivity compared to our results (3.5% for a cut-off point of <136 mmol/l and 29.6% for the cut-off point of 125 mmol/l) in their study examining the validity of ICD-9 codes of hyponatremia in an outpatient managed-care population.[14] Outpatient serum sodium laboratory tests were compared with outpatient professional ICD-9 claims registered within 15 days before or after the laboratory claim. The PPV was 62.6% for serum sodium levels <136 mmol/l and 10.4% for levels <125 mmol/l. As noted in the paper, detected hyponatremia may be the cause for follow-up visits in an outpatient setting, without the need for repeat measurements. This could lead to lower PPV compared to our study and the study by Movig *et al*. In addition, managed-care claims databases encompass an employer-based commercially insured population. Shea *et al*.'s study thus may not be representative of elderly populations, in which prevalence of hyponatremia is high.[24, 25] This also may explain why their results differed from ours.

The major strengths of our study are its population-based design and unambiguous individual-level linkage between registries containing complete data on all hospitalizations and laboratory tests in a well-defined population. This eliminates the risk of selection bias. Several potential study limitations must be considered. We relied on only one (the lowest) serum sodium value recorded to define presence of hyponatremia, and also did not consider duration of hyponatremia. Clinicians may be more likely to regard hyponatremia as clinically relevant, and hence to include the condition in discharge diagnoses, if it is detected in more than one measurement. In this context, it is important to

note that patient transfers between departments are registered as separate admissions in the DNRP and we examined the validity of ICD-10 coding for each registered admission. The PPV may have been even higher if we had considered contiguous admissions as a single admission. Finally, we chose to include patients without serum sodium measurements and to consider them as normonatremic in the main analysis. We did so to detect false positive diagnoses and thereby obtain accurate estimates of predictive values. Serum sodium is often measured as a routine procedure, and rarely due to specific suspicion. Though frequently measured, the proportion of patients with unacknowledged hyponatremia is most often unknown. We therefore performed a complete case analysis, including only patients with serum sodium measurements. As the results did not differ markedly from those of the primary analysis, we believe that including patients without serum sodium measurements in the normonatremic group was justified.

We can only speculate on reasons for the low sensitivity of the ICD-10 coding of hyponatremia found in our study. A diagnosis of hyponatremia was less likely recorded in patients with high levels of comorbidity, which may indicate that ~~H~~hyponatremia is mainly considered a ~~part of the clinical picture of underlying~~ bystander of the underlying diseases. If hyponatremia is mild or transient, and does not require intervention or specific attention, it may not warrant documentation. However, even for very severe hyponatremia (<115 mmol/l), which is potentially fatal and requires immediate intervention, sensitivity was low. We believe that this most likely reflects negligence of proper coding practice rather than lack of attention to the clinical importance of low serum sodium levels. With the increasing use of electronic medical records it would be feasible and worthwhile to automatically assign discharge diagnoses to patients with gross abnormal laboratory values. However, the ultimate responsibility for summarizing the most important reasons for treatment and care still rests upon the discharging physician. Our results suggest that hyponatremia is not coded in the presence of coexisting illness

deemed more important, and that the fact that hyponatremia may be an important indicator of a poor prognosis is not yet acknowledged.

The results of this validation study emphasize the need for caution when relying on ICD-10 codes for hyponatremia in research. Based on the estimated PPV and specificity, patients with an ICD-10 code of hyponatremia can safely be assumed to actually have hyponatremia. However, the low sensitivity renders the ICD-10 codes inappropriate for use in studies examining prevalence, incidence, and absolute risk, due to a high degree of misclassification. Sensitivity increased with decreasing serum sodium levels, suggesting that studies using ICD-codes to identify hyponatremia would be based mainly on severe cases. Furthermore, our results indicate that quality of registration differs according to age, gender, and morbidity status. Hence, studies may be susceptible to differential misclassification, again resulting in biased results.

**CONCLUSION**

We found that the ICD-10 coding of hyponatremia in DNRP has high specificity but is highly incomplete, resulting in very low sensitivity. When available, laboratory test results for serum sodium will more correctly identify patients with hyponatremia.

**Contributors**

LHB participated in the design of the study, performed the data analysis, provided interpretation of study results and drafted the manuscript. SPU participated in acquisition and analysis of data. CFC and HTS participated in the design of the study, provided interpretation of study results and helped draft the manuscript. TR and JOLJ contributed with interpretation of study results helped draft the manuscript. All authors read and approved the final manuscript.

**Funding**

This work was supported by the Clinical Epidemiology Research Foundation and by the Danish Cancer Society (grant no. R73-A4284-13-S17).

**Competing interests**

JOLJ has received an unrestricted research grant and lecture fees from Otsuka Pharma Scandinavia AB. TR has received lecture fees from Otsuka Pharma Scandinavia AB.

LHB, CFC, SPU and HTS are salaried employees of Department of Clinical Epidemiology, Aarhus University Hospital. The Department of Clinical Epidemiology receives funding from companies in the form of research grants to (and administered by) Aarhus University.
None of these grants or fees had any had any leverage on the design, implementation or reporting of the present study.

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| | | ICD-10 code of hyponatremia recorded in the DNRP* | |
|---|---|---|---|
| | | Yes | No |
| Hyponatremic serum sodium value recorded in LABKA research database (gold standard) | Yes | A | C |
| | No | B | D |

Validity measures:
Sensitivity= A/(A+C)
Specificity= D/(B+D)
Positive predictive value= A/(A+B)
Negative predictive value=D/(C+D)

*DNRP = Danish National Registry of Patients

Figure 1. Schematic 2x2 table and validity measure estimation formulas
160x90mm (300 x 300 DPI)

**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology***

**Checklist for cohort, case-control, and cross-sectional studies (combined)**

| Section/Topic | Item # | Recommendation | Reported on page # |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 2-3 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses | 6 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6 |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants | 7 |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-8 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | *6-8* |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9 |
| Study size | 10 | Explain how the study size was arrived at | 6-7 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 8-9 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 8-9 |
| | | (*c*) Explain how missing data were addressed | 7 and 9 |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed | |

| | | | |
|---|---|---|---|
| | | *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy | |
| | | (*e*) Describe any sensitivity analyses | 9 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 9-10 |
| | | (b) Give reasons for non-participation at each stage | 9-10 |
| | | (c) Consider use of a flow diagram | |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 10-11 |
| | | (b) Indicate number of participants with missing data for each variable of interest | 9-10 |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) | |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time | |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure | |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures | 9-10 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 11-13 |
| | | (*b*) Report category boundaries when continuous variables were categorized | 11-13 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 14-15 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 15 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 16-17 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 15-18 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 16-17 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 19 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.