PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Validity of the International Classification of Diseases, 10th revision (ICD-10) discharge diagnosis codes for hyponatremia in the Danish National Registry of Patients
AUTHORS	Holland-Bill, Louise; Christiansen, Christian F; Ulrichsen, Sinna; Ring, Troels; Jørgensen, Jens Otto; Toft Sørensen, Henrik

VERSION 1 - REVIEW

REVIEWER	Yeonghau H Lien University of Arizona, Tucson, AZ, USA
REVIEW RETURNED	02-Feb-2014

GENERAL COMMENTS	General: The authors confirmed that physicians tend to ignore hyponatremia, but such a low sensitivity, 1.8% for Na<135 and 34.2% for <115, is still surprising. I totally agree that discharge ICD10 codes for hyponatremia are unreliable for studying inpatient hyponatremia. Comments; 1. It is hard to image that physicians will ignore Na <115. I suspect that physicians actually "forgot" the diagnosis of hyponatremia at the time of discharge. It is particularly understandable if hyponatremia is mild and reversed at the time of discharge. Maybe if authors study physician's billing codes, the sensitivity would not be so low. 2. The finding that patients with reported hyponatremia have lower comorbidity levels is also interesting. It is possible that sicker patients have a longer list of diagnoses, so the significance of hyponatremia is diluted and ignored. 3. Non-internal medicine physicians failed to report 95% or more of hyponatremia even if Na<125. Is it possible that those physicians do not deal with hyponatremia, thus fail to report it at the time of discharge? 4. The authors stated that the gold standard of hyponatremia is lab value. However, the possibility of "pseudohyponatremia" may have been missed if one only looks at Na value only. It should be mentioned if attempts were made to correct Na with severe hyperglycemia. 5. The authors shall discuss how to improve the coding of hyponatremia. In the era of electronic medical records, the discharge diagnoses should not be dependent only on the discharging physicians.

REVIEWER	Sonja Gandhi Western Univeristy, Canada
REVIEW RETURNED	21-Feb-2014

GENERAL COMMENTS	General Comments: The authors conducted a population-based validation study describing the validity of the International Classification of Diseases, 10th revision (ICD-10) codes for hyponatremia in inpatients of all ages using the Danish National Registry of Patients (DNRP). Serum sodium values from the LABKA database served as the gold standard. Overall, the manuscript is well written and clearly presented. Some comments are presented.

Major Comments

1. The authors included patients with multiple hospitalizations in the study. Patients who have been diagnosed with hyponatremia once might be more likely to be diagnosed with it again in a subsequent admission. Maybe consider doing a sensitivity analysis, restricting to the first hospitalization per patient.
2. The point of this study was to assess the validity of the ICD-10 code for hyponatremia in patients of all ages. However, age is an important risk factor for developing hyponatremia. Because such a wide age range was considered, it would be useful to see a subgroup analysis by age category.

Minor Comments

Abstract

Participants section

3. Page 2, Line 17: add the word "to" to the following - "Patients of all ages admitted TO hospital…"
4. Page 2, Line 22: add an "s" to the word hospitalization

Main Outcome Measure

5. Line 28: add the word "the" to the following - "…(LABKA) research database as THE gold standard."

Introduction

6. Page 5, Line 41: Patients did not present with a hyponatremic serum sodium value. Instead, patients with any serum sodium value at emergency department contact or at hospital admission were included in the study. Please change the sentence to the following – "…years of age or older with serum sodium values at the time of emergency department contact or at hospital admission."
7. Page 5, Lines 4-11: This sentence sounds a little awkward. Consider removing the following line - "in terms of sensitivity, specific, positive predictive value (PPV), and negative predictive value (NPV)"

Methods

Hyponatremia Diagnosis (ICD-10 algorithm)

	8. Please indicate which diagnosis types were used to define hyponatremia (main, secondary or both).
	Discussion
	9. Page 14, Line 52 – sensitivities indicated are for emergency department setting. It would be better to indicate the hospital admission values as this is what was looked at in the current study. <135 mmol/l = 6.4%; <125 mmol/l = 41.7%
	10. See comment #6.

VERSION 1 – AUTHOR RESPONSE

Reviewer:
Yeonghau H Lien
Institution and Country University of Arizona, Tucson, AZ, USA

General: The authors confirmed that physicians tend to ignore hyponatremia, but such a low sensitivity, 1.8% for Na<135 and 34.2% for <115, is still surprising. I totally agree that discharge ICD10 codes for hyponatremia are unreliable for studying inpatient hyponatremia.

Response: We thank the reviewers for the feedback on our work. We greatly appreciate the suggestions for improvements and discussion.

Comments:

1. It is hard to image that physicians will ignore Na <115. I suspect that physicians actually "forgot" the diagnosis of hyponatremia at the time of discharge. It is particularly understandable if hyponatremia is mild and reversed at the time of discharge. Maybe if authors study physician's billing codes, the sensitivity would not be so low.

Response: We agree with the reviewer and find it unlikely that physicians would ignore serum sodium values <115mmol/l. To ensure that this statement is evident, we have included the following paragraph in the discussion section (page 17, lines 19-20): "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."
Denmark has a tax-supported universal health care system. This implies that hospitalized patients are not billed directly. Since 2000, information recorded in the Danish National Registry of Patients (DNRP) has constituted the basis for financial reimbursement from the government to hospitals via the Diagnostic Related Group (DRG) system. Primary and secondary discharge diagnosis codes constitute an important element for allocation of DRG points, and thereby financial reimbursement [1].

2. The finding that patients with reported hyponatremia have lower comorbidity levels is also

interesting. It is possible that sicker patients have a longer list of diagnoses, so the significance of hyponatremia is diluted and ignored.

Response: We agree that hyponatremia may be less likely recorded in patients with high comorbidity levels. It is likely to be explained by these patients having a longer list of diagnoses per se, causing hyponatremia to be ignored during the assignment of discharge diagnoses. The same phenomenon has been encountered in for example hospital coding of diabetes mellitus [2]. This study suggested that receiving a discharge diagnosis of diabetes mellitus was less complete in patients with other and more severe illnesses.
We acknowledge the significance of this phenomenon and the following paragraph in the discussion section page 17, lines 14-16 now reads: "A diagnosis of hyponatremia was less likely recorded in patients with high comorbidity levels, which may indicate that hyponatremia is mainly considered a bystander of the underlying disease."

3. Non-internal medicine physicians failed to report 95% or more of hyponatremia even if Na<125. Is it possible that those physicians do not deal with hyponatremia, thus fail to report it at the time of discharge?

Response: Our data did not include information on whether hyponatremia was corrected during hospitalization or on interventions indicating that correction of hyponatremia was attempted. We are therefore unable to discuss whether coding practice reflects the clinical management of hyponatremia.

4. The authors stated that the gold standard of hyponatremia is lab value. However, the possibility of "pseudohyponatremia" may have been missed if one only looks at Na value only. It should be mentioned if attempts were made to correct Na with severe hyperglycemia.

Response: This is an important point. We acknowledge the reviewer's concern regarding the possible impact of "pseudohyponatremia". The clinical laboratory information system (LABKA) research database contains information on glucose measurements. However, we chose not to correct the serum sodium concentration in the presence of severe hyperglycemia, as it was not an aim of our study to distinguish between causes of hyponatremia. Correcting for hyperglycemia has been shown to have little effect on both the absolute prevalence of hyponatremia and the association between hyponatremia and mortality [3].

5. The authors shall discuss how to improve the coding of hyponatremia. In the era of electronic medical records, the discharge diagnoses should not be dependent only on the discharging physicians.

Response: Integration of diagnostic tools, such as laboratory measurements, into the electronic medical record systems potentially enables automatic generation of diagnosis codes when test results deviate from the reference standard. This would be feasible as it would certainly increase the completeness of the diagnosis. It will still rest upon the discharging physician to describe the main reasons for treatment and care in the discharge summery and by extension to assess which discharge diagnoses are most adequate. We therefore believe that it is equally important to increase awareness of the prognostic implications of hyponatremia.

In the revised discussion, we have added the following sentence (page 17, lines 20-24): "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."

References:
1. Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. Scand J Public Health 2011;39(Suppl 7):30-33.

2. Glynn RJ, Monane M, Gurwitz JH, et al. Agreement between drug treatment data and a discharge diagnosis of diabetes mellitus in the elderly. Am J Epidemiol. 1999;149:541-549.

3. Waikar SS, Mount DB, Curhan GC. Mortality after hospitalization with mild, moderate, and severe hyponatremia. Am J Med. 2009;122:857-865.

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Reviewer: Sonja Gandhi
Institution and Country Western University, Canada

I did not see a comment on ethics. Please address this.

Response: Danish law does not require informed consent or Ethics Committee approval for studies relying solely on registry data. We have included a statement explaining this at the end of the statistical analysis section (page 9, lines 16-18).

General Comments: The authors conducted a population-based validation study describing the validity of the International Classification of Diseases, 10th revision (ICD-10) codes for hyponatremia in inpatients of all ages using the Danish National Registry of Patients (DNRP). Serum sodium values from the LABKA database served as the gold standard. Overall, the manuscript is well written and clearly presented. Some comments are presented.

Response: We thank the reviewer for the positive assessment of our work, for relevant comments and suggestions, which we hope to have addressed satisfactorily.

Major Comments

1. The authors included patients with multiple hospitalizations in the study. Patients who have been diagnosed with hyponatremia once might be more likely to be diagnosed with it again in a subsequent admission. Maybe consider doing a sensitivity analysis, restricting to the first hospitalization per patient.

Response: This is an interesting point. We chose to include all hospitalizations in the study period in order achieve as complete a picture of coding practice as possible. We acknowledge that patients with a prior diagnosis of hyponatremia may be more likely to receive a hyponatremia diagnosis on

subsequent admissions. However, we expect that a subsequent hyponatremia diagnosis most likely is given on the basis of a new hyponatremic sodium value measured during the subsequent hospitalization (a true positive diagnosis) and not merely based on a previous diagnosis without supporting laboratory findings (a false positive diagnosis). The high specificity and positive predictive value of the diagnosis overall supports this.

That being said, the reviewer points to the important fact that epidemiologic studies often focus on incident cases, wherefore we have followed the reviewer's suggestion and performed a sensitivity analysis, in which we restricted to the first hospitalization for each patient in the study period.

We have mentioned the post-hoc analysis in the statistical analysis section (page 9, lines 10-12: "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."). The results are displayed in a new table (Table 4, page 14-15), in which we have gathered all four sensitivity analyses and results of the primary analysis to improve readability. The results are summarized in the result section (page 14, lines 14-16: "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).")

2. The point of this study was to assess the validity of the ICD-10 code for hyponatremia in patients of all ages. However, age is an important risk factor for developing hyponatremia. Because such a wide age range was considered, it would be useful to see a subgroup analysis by age category.

Response: We acknowledge the relevance of presenting estimates for different age categories. We performed a subgroup analysis, which has been described in the statistical analysis section (page 9, line 1-2 now reads: "The analyses were repeated for all hyponatremia cut-off points and after stratification by age group, department of admission and admission year."). The results are presented in Table 3 (page 13), and discussed in the discussion section (page 16, lines 6-7:" However, the sensitivity estimates did not reach those found by Gandhi et al. even for patients 65-79 and ≥80 years of age.").

Minor Comments

Abstract
Participants section

3. Page 2, Line 17: add the word "to" to the following - "Patients of all ages admitted TO hospital…"

Response: Thank you for noticing. "to" has been added (page 2, line 7).

4. Page 2, Line 22: add an "s" to the word hospitalization

Response: "s" has been added (page 2, line 9).

Main Outcome Measure

5. Line 28: add the word "the" to the following - "…(LABKA) research database as THE gold standard."

Response: "the" has been added to the sentence as suggested (page 2, line 12).

Introduction

6. Page 5, Line 41: Patients did not present with a hyponatremic serum sodium value. Instead, patients with any serum sodium value at emergency department contact or at hospital admission were included in the study. Please change the sentence to the following – "…years of age or older with serum sodium values at the time of emergency department contact or at hospital admission."

Response: We apologize for this error and appreciate that it was brought to our attention. The sentence has been reworded as suggested (page 5, lines 18-19).

7. Page 5, Lines 4-11: This sentence sounds a little awkward. Consider removing the following line - "in terms of sensitivity, specific, positive predictive value (PPV), and negative predictive value (NPV)"

Response: We have deleted the line as suggested (page 6, lines 2-3).

Methods
Hyponatremia Diagnosis (ICD-10 algorithm)

8. Please indicate which diagnosis types were used to define hyponatremia (main, secondary or both).

Response: We used both primary and secondary discharge diagnoses to identify hospitalizations in which an ICD-10 code of hyponatremia was recorded. We have now included this in the sentence: "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." (page 7, line 6).

Discussion

9. Page 14, Line 52 – sensitivities indicated are for emergency department setting. It would be better to indicate the hospital admission values as this is what was looked at in the current study. <135 mmol/l = 6.4%; <125 mmol/l = 41.7%

Response: Duly noted and corrected (page 15, line 18).

10. See comment #6.

Response: Please see our response to Reviewer 2's comment #6. Paragraph corrected (page 16, line 2).

VERSION 2 – REVIEW

REVIEWER	Yeong-hau H Lien Univ of AZ, USA
REVIEW RETURNED	02-Apr-2014

GENERAL COMMENTS	Authors have addressed adequately on all comments and have revised the manuscript accordingly.