# Medical Costs of Abnormal Serum Sodium Levels

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## ABSTRACT

An abnormal serum sodium level is the most common electrolyte disorder in the United States and can have a significant impact on morbidity and mortality. The direct medical costs of abnormal serum sodium levels are not well understood. The impact of hyponatremia and hypernatremia on 6-mo and 1-yr direct medical costs was examined by analyzing data from the Integrated HealthCare Information Services National Managed Care Benchmark Database. During the period analyzed, there were 1274 patients (0.8%) with hyponatremia (serum sodium $<$135 mmol/L), 162,829 (97.3%) with normal serum sodium levels, and 3196 (1.9%) with hypernatremia ($>$145 mmol/L). Controlling for age, sex, region, and comorbidities, hyponatremia was a significant independent predictor of costs at 6 mo (41.2% increase in costs; 95% confidence interval, 30.3% to 53.0%) and at 1 yr (45.7% increase; 95% confidence interval, 34.2% to 58.2%). Costs associated with hypernatremia were not significantly different from those incurred by patients with normal serum sodium. In conclusion, hyponatremia is a significant independent predictor of 6-mo and 1-yr direct medical costs.

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Abnormal serum sodium is the most common electrolyte disorder in the United States. Estimates of the prevalence of hyponatremia range from 1% in general acute care populations[1,2] to 18% among elderly nursing home residents[3] and nearly 30% in intensive care settings.[4] Hypernatremia is less common, ranging from 0.3% to 8.9% in hospitalized adults.[5,6] Mild, chronic hyponatremia is often asymptomatic; neurologic and gastrointestinal symptoms generally increase as the condition worsens.[7] Hypernatremia may also be asymptomatic until it exceeds a certain threshold, at which point central nervous system dysfunction develops.[8] However, hyponatremia and hypernatremia of all severity levels have significant effects on morbidity and mortality.

In a cohort of 4123 elderly patients, Terzian *et al.*[9] studied the relationship between hyponatremia at the time of hospital admission and treatment outcomes. After adjustment for age, sex, length of stay, and several clinical factors, hyponatremia was a significant independent predictor of mortality. Similar results have been found for patients with heart failure and myocardial infarction. In a study of patients with suspected congestive heart failure at admission, serum sodium $\leq$135 mmol/L was independently associated with major complications during hospitalization, greater length of stay, higher hospital costs, and greater inpatient mortality.[10] In a more recent trial, patients hospitalized for worsening heart failure with hyponatremia at admission (serum sodium $\leq$135 mmol/L) experienced significantly greater in-hospital and 60-d mortality, compared with patients with normal or high serum sodium.[11] In patients with acute ST-

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elevation myocardial infarction, serum sodium <135 mmol/L at admission or during the first 72 h of hospitalization was an independent predictor of 30-d mortality.[12] Excluding patients with a history of heart failure, serum sodium <136 mmol/L was an independent predictor of readmission for heart failure and postdischarge death.[13]

Several studies have examined the crude rate of mortality among patients with hypernatremia, but there is little information about the independent effect of hypernatremia on outcomes. Palevsky *et al.*[14] observed an overall mortality rate of 41% among adult inpatients; however, hypernatremia was considered a contributing factor in only 16% of the deaths. Using inpatient and outpatient laboratory data to identify 116 patients with hypernatremia, Mandal *et al.*[15] reported a 66% mortality rate. More recently, researchers found that serum sodium >160 mmol/L was an independent predictor of mortality in a neurologic/neurosurgical intensive care unit.[16]

Although the clinical consequences of abnormal serum sodium, particularly in the case of hyponatremia, are well documented, relatively little is known about the relationship between abnormal serum sodium and medical costs. A recent study suggested that the direct costs of treating hyponatremia range from $1.6 billion to $3.6 billion annually and that inpatient costs represent approximately 70% of this value. However, the study relied on 1 yr of inpatient discharge data to determine disease prevalence and on physician panel estimates to assess resource use.[17] To our knowledge, there are no published studies examining the direct costs of hypernatremia. Therefore, we examined the impact of abnormal serum sodium on 6-mo and 1-yr direct medical costs using longitudinal data from a large managed care claims database.

## RESULTS

There were 167,299 patients in the sample. On the basis of the highest qualifying serum sodium level, 1274 patients (0.8%) had hyponatremia, 162,829 patients (97.3%) had normal serum sodium, and 3196 patients (1.9%) had hypernatremia (Table 1). Median serum sodium was 133 mmol/L (interquartile range, 131 to 134 mmol/L) for patients with hyponatremia and 146 mmol/L (interquartile range, 146 to 147 mmol/L) for patients with hypernatremia, indicating a fairly mild level of severity for each state (Table 2). For 0.75% of claims, we adjusted the serum sodium values because blood glucose was >300 mg/dl.

Patients with hyponatremia were older (64 *versus* 53 yr; $P < 0.001$) and more likely to be female (66% *versus* 57%; $P < 0.001$) than patients with normal serum sodium (Table 2). Patients with hypernatremia were also older, although to a lesser degree (59 *versus* 53 yr; $P < 0.001$), and were slightly less likely to be female (55% *versus* 57%; $P < 0.001$). Patients with abnormal serum sodium were significantly more likely than patients with normal serum sodium to have been diagnosed with cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, hypertension, or peripheral vascular disease ($P < 0.05$), although crude rates of comorbid conditions were higher among patients with hyponatremia than among patients with hypernatremia. Patients with hyponatremia were also significantly more likely to have been diagnosed with coronary heart disease ($P < 0.001$). A greater proportion of claims for medications known to cause hyponatremia was observed for this group as well ($P < 0.001$).

Unadjusted 6-mo medical costs were significantly higher among patients with hyponatremia or hypernatremia, compared with patients with normal serum sodium (Table 3). One-year medical costs among patients with hypernatremia were approximately 16% higher than among patients with normal serum sodium, and 1-yr medical costs for patients with hyponatremia were more than double the costs among patients with normal serum sodium. At both 6 mo and 1 yr, patients with hypernatremia incurred approximately one third more inpatient discharges and costs than patients with normal serum sodium. Patients with hyponatremia had approximately 2.5 times as many inpatient stays as patients with normal serum sodium. Correspondingly, mean 6-mo and 1-yr inpatient costs for patients with hyponatremia were more than twice those for patients with normal serum sodium.

Inpatient costs were also a higher proportion of total medical costs for patients with hyponatremia than for other patients. Six-month inpatient facility and professional services costs represented 53%, 38%, and 46% of total medical costs for patients with hyponatremia, normal serum sodium, and hypernatremia, respectively. One-year inpatient costs represented 55%, 37%, and 43% of total medical costs, respectively (Table 3).

Table 4 shows the effects of hyponatremia and hypernatremia on total medical costs and inpatient costs. In univariate analyses, hyponatremia was associated with 99% higher 6-mo costs, and hypernatremia was associated with 17% higher 6-mo costs. Hyponatremia was also associated with 108% higher 1-yr medical costs, whereas costs for patients with hypernatremia were 19% higher. Controlling for age, sex, geographic region, and comorbid diagnoses, hyponatremia was a

**Table 1.** Distribution of serum sodium level by serum sodium category

| Distribution | Serum Sodium Category | | |
|---|---|---|---|
| | <135 mmol/L | 135–145 mmol/L | >145 mmol/L |
| *N* | 1274 | 162,829 | 3196 |
| Serum sodium (mean ± SD) | 132 ± 2.2 | 141 ± 1.9 | 147 ± 2.1 |
| Serum sodium [median (interquartile range)] | 133 (131–134) | 141 (140–142) | 146 (146–147) |

**Table 2.** Distribution of study variables by serum sodium category[a]

| Variable | Serum Sodium Category | | | $P^b$ | $P^c$ |
|---|---|---|---|---|---|
| | Hyponatremia ($n$ = 1274) | Normal ($n$ = 162,829) | Hypernatremia ($n$ = 3196) | | |
| Age, yr (mean ± SD) | 64 ± 13.7 | 53 ± 14.9 | 59 ± 13.4 | <0.001 | <0.001 |
| Female | 845 (66.3) | 92,137 (56.6) | 1759 (55.0) | <0.001 | <0.001 |
| Geographic region | | | | | |
| Middle Atlantic | 1079 (84.7) | 145,040 (89.1) | 2830 (88.5) | <0.001 | <0.001 |
| other | 195 (15.3) | 17,789 (10.9) | 366 (11.5) | <0.001 | <0.001 |
| Underlying conditions and comorbidities | | | | | |
| cerebrovascular disease | 57 (4.5) | 3630 (2.2) | 87 (2.7) | <0.001 | 0.003 |
| chronic obstructive pulmonary disease | 134 (10.5) | 10,988 (6.7) | 270 (8.4) | <0.001 | 0.03 |
| congestive heart failure | 62 (4.9) | 3227 (2.0) | 102 (3.2) | <0.001 | 0.007 |
| coronary heart disease | 175 (13.7) | 15,798 (9.7) | 404 (12.6) | <0.001 | 0.32 |
| dementia | 4 (0.3) | 226 (0.1) | 8 (0.3) | 0.07 | 0.71 |
| diabetes mellitus | 176 (13.8) | 21,740 (13.4) | 473 (14.8) | 0.63 | 0.40 |
| hypertension | 551 (43.2) | 44,050 (27.1) | 1016 (31.8) | <0.001 | <0.001 |
| kidney disease | 14 (1.1) | 1091 (0.7) | 33 (1.0) | 0.06 | 0.84 |
| liver cirrhosis | 0 (0.0) | 1 (0.0) | 0 (0.0) | 0.93 | — |
| metastatic carcinoma | 32 (2.5) | 2175 (1.3) | 41 (1.3) | <0.001 | 0.003 |
| nephritis, nephrotic syndrome, and nephrosis | 18 (1.4) | 1531 (0.9) | 44 (1.4) | 0.08 | 0.93 |
| peripheral vascular disease | 45 (3.5) | 2716 (1.7) | 55 (1.7) | <0.001 | <0.001 |
| rheumatic disease | 40 (3.1) | 4314 (2.6) | 80 (2.5) | 0.28 | 0.23 |
| syndrome of inappropriate secretion of antidiuretic hormone | 7 (0.5) | 34 (0.0) | 1 (0.0) | <0.001 | <0.001 |
| Medications known to cause hyponatremia | 121 (9.5) | 10,924 (6.7) | 200 (6.3) | <0.001 | <0.001 |

[a]Values are expressed as no. (%) unless otherwise indicated.
[b]*P* value for the comparison between patients with hyponatremia (serum sodium <135 mmol/L) and patients with normal serum sodium (135–145 mmol/L).
[c]*P* value for the comparison between patients with hypernatremia (serum sodium >145 mmol/L) and patients with normal serum sodium (135–145 mmol/L).

significant independent predictor of total medical costs at 6 mo and 1 yr; however, 6-mo and 1-yr adjusted costs for patients with hypernatremia were not significantly higher. In multivariable analyses, hyponatremia was an independent predictor of inpatient costs at both 6 mo (estimated change, 76.4%; 95% confidence interval [CI], 55.0 to 100.7) and 1 yr (95.6%; 95% CI, 73.3 to 120.8). Higher inpatient costs for patients with hypernatremia were also significant at 6 mo (18.5%; 95% CI, 5.7 to 32.9) and 1 yr (14.7%; 95% CI, 2.4 to 28.5), although to a much lesser degree.

The results were qualitatively unchanged following a sensitivity analysis that included the truncation of costs. Excluding patients who were censored at 365 d after the reference date, unweighted multivariable analyses of 1-yr total medical costs also yielded results that were qualitatively similar to those obtained using weighted regression (data not shown). Finally, after adding an indicator variable for the presence of claims for drugs known to cause hyponatremia to the model, multivariable results for 6-mo (41.0%; 95% CI, 30.1 to 52.8) and 1-yr costs (45.8%; 95% CI, 34.3 to 58.2) associated with hyponatremia were essentially unchanged.

## DISCUSSION

We examined the impact of abnormal serum sodium on 6-mo and 1-yr direct medical costs using longitudinal data from the Integrated HealthCare Information Services (IHCIS) National

**Table 3.** Mean resource use by serum sodium category

| Resource Use | Serum Sodium Category[a] | | |
|---|---|---|---|
| | Hyponatremia | Normal | Hypernatremia |
| 6 mo | | | |
| medical costs, $ [mean (SD)] | 11,078 (390) | 5571 (34) | 6491 (246) |
| inpatient costs only, $ [mean (SD)] | 5853 (276) | 2125 (24) | 2969 (174) |
| inpatient discharges per 1000 patients (95% CI) | 39.8 (36.7–42.9) | 16.6 (16.4–16.9) | 21.4 (19.4–23.4) |
| 1 yr | | | |
| medical costs, $ [mean (SD)] | 19,215 (702) | 9257 (62) | 10,972 (443) |
| inpatient costs only, $ [mean (SD)] | 10,636 (474) | 3468 (42) | 4734 (299) |
| inpatient discharges per 1000 patients (95% CI) | 71.5 (66.4–76.7) | 27.3 (26.8–27.7) | 34.8 (31.5–38.0) |

CI, confidence interval.
[a]*P* <0.001 for all comparisons.

**Table 4.** Effects of hyponatremia and hypernatremia on total direct medical costs[a]

| Costs | Effect of Hyponatremia | | Effect of Hypernatremia | |
|---|---|---|---|---|
| | Univariate Model | Multivariable Model[b] | Univariate Model | Multivariable Model[b] |
| 6 mo | | | | |
| medical costs | 98.8 (80.4 to 119.2) | 41.2 (30.3 to 53.0) | 16.5 (7.5 to 26.3) | 5.4 (−1.4 to 12.6) |
| inpatient costs only | 175.4 (136.3 to 221.0) | 76.4 (55.0 to 100.7) | 39.7 (21.9 to 60.1) | 18.5 (5.7 to 32.9) |
| 1 yr | | | | |
| medical costs | 107.6 (87.2 to 130.1) | 45.7 (34.2 to 58.2) | 18.5 (8.7 to 29.2) | 6.3 (−0.8 to 13.8) |
| inpatient costs only | 206.7 (163.3 to 257.3) | 95.6 (73.3 to 120.8) | 37.4 (19.0 to 58.7) | 14.7 (2.4 to 28.5) |

[a]Values are expressed as the estimated percent change in costs (95% confidence interval).
[b]The multivariable model controlled for age, sex, geographic region, underlying and comorbid conditions, and medications known to cause hyponatremia.

Managed Care Benchmark Database (IHCIS, Waltham, MA). After controlling for demographic variables and other clinical predictors of poor outcomes, we found that hyponatremia was a significant independent predictor of total medical costs. Although total costs for patients with hypernatremia were higher than those for patients with normal serum sodium, the differences were not significant in multivariable analysis. Cost increases associated with hyponatremia were more than 7 times greater than those associated with hypernatremia. The proportion of total medical costs attributable to inpatient care was also significantly greater among patients with hyponatremia than among patients with normal serum sodium or hypernatremia. Medical costs for patients with hyponatremia at 6 mo and 1 yr were more than double those incurred by patients with normal serum sodium. These findings are consistent with previous studies suggesting that hyponatremia is an independent predictor of clinical complications, length of stay, and readmission,[12,13,18–22] all of which are drivers of costs.

To our knowledge, there are no studies of the cost of hypernatremia, and only one other study has examined the direct medical costs of hyponatremia. Relying on inpatient hospital discharge data and expert panel estimates, Boscoe *et al.*[17] suggested that hospitalizations account for 70% of the total costs attributable to hyponatremia (serum sodium <130 mmol/L) and that annual per patient inpatient costs directly attributable to hyponatremia range from $1528 to $3441. The authors estimated annual prevalence at between 3.16 million and 6.07 million people in the United States. However, these values were based largely on the number of hospital discharges coded with an ICD-9-CM diagnosis of hyponatremia.

It has been shown that only a small percentage of patients with hyponatremia receive an ICD-9-CM diagnosis code for hyponatremia[23]; therefore, we used outpatient laboratory test results to identify serum sodium values. Furthermore, because hypernatremia is also associated with higher mortality and can be an indicator of infection,[14,15,24] we expected patients with hypernatremia to incur higher costs than patients with normal serum sodium. Thus, we classified patients as having normal serum sodium, hyponatremia, or hypernatremia in all analyses.

We found that inpatient costs accounted for just over half of all direct medical costs. However, 1-yr mean inpatient costs for patients with hyponatremia were approximately $10,636, more than 3 times higher than the previous estimate.[17] Consistent with our expectations, we observed higher costs for patients with hyponatremia and patients with hypernatremia, although costs were much higher for patients with hyponatremia. Given that higher costs persisted after adjustment for demographic and clinical confounders, our findings suggest that hyponatremia is an important predictor of cost.

This study has several limitations. First, health plan members without laboratory data or who did not meet eligibility requirements were not included in the analysis. IHCIS estimates that laboratory data are available for approximately 10% of its members. Compared with members who met our eligibility requirements and had at least two serum sodium values, members excluded from the analysis were significantly younger (mean age, 45 *versus* 53 yr) and had significantly lower rates of comorbid illness. However, given that abnormal serum sodium has been associated with both aging and a number of chronic conditions,[3] these differences between groups were not unexpected.

Second, the data are from a managed care claims database and represent the experiences of an employer-based, commercially insured population. People with different types of health insurance and people without health insurance are not represented. We also expect that the elderly are significantly underrepresented. Similarly, rates of comorbidities known to be associated with disturbances in serum sodium, such as liver cirrhosis, kidney disease, and syndrome of inappropriate secretion of antidiuretic hormone, were extremely low in our sample. Because individuals with these conditions and elderly persons are at the highest risk for serum sodium disturbances, our findings may underestimate total medical costs. Inconsistent and inaccurate coding and the absence of clinical data regarding disease severity may have also affected our estimates. Because of the high degree of movement into and out of commercial managed care plans, we required only 60 d of continuous coverage before the reference serum sodium date. However, this approach limited the time frame in which we could observe comorbidity claims, which may have led us to overestimate the independent effect of hyponatremia on medical costs.

In summary, our findings suggest that hyponatremia is a significant independent predictor of costs at 6 mo and 1 yr.

Future research should examine whether effective treatment of hyponatremia would also reduce total medical spending.

## CONCISE METHODS

### Data Source

We obtained data for 1999 through 2005 from the National Managed Care Benchmark Database, which includes medical history and eligibility data for more than 25 million people enrolled in more than 30 health insurance plans in the United States. Outpatient laboratory data are available for approximately 10% of health plan members, and complete pharmacy history is available for 90% of members. IHCIS removed all direct identifiers from the data to protect members' confidentiality. Information about beneficiaries' race/ethnicity and mortality was not available.

In addition to medical, pharmacy, and laboratory claims, the database includes basic demographic information and a standardized cost variable. IHCIS applies standard pricing algorithms to the 5 major service categories in the database (facility inpatient, facility outpatient, professional services, ancillary services, and pharmacy) to develop a single, standardized cost variable that represents the allowed payment for each service provided. In this way, service costs can be compared across health plans despite variations in contractual arrangements.

### Study Population

We limited the analysis to adults aged 18 yr and older with health plan eligibility on or after January 1, 2002. We considered multiple, successive periods of eligibility, defined as an observed coverage end date followed immediately by a new coverage start date, to be switches in product and not discontinuations of coverage. Therefore, we did not consider such changes to represent interruptions in coverage, but rather to constitute single, continuous periods of eligibility. If a health plan member had several noncontinuous periods of eligibility, we retained only the first period for analysis.

For each qualifying member, we obtained all outpatient serum sodium laboratory tests performed between January 1, 2002 and December 31, 2005. We retained tests performed at least 60 d after the start of insurance coverage and 180 d before the end of coverage. We excluded serum sodium values of zero because these were considered data errors. We then identified the first two consecutive serum sodium tests with dates of service $\leq$60 d apart. We used the higher of the two values to assign serum sodium status (*i.e.*, hyponatremia, hypernatremia, and normal), and we used the date of service for that test as the reference point for further analysis. If the results of both tests were identical, we used the second test date as the reference date.

To reduce heterogeneity in etiology, we excluded members with professional claims for dialysis from 2002 through 2005 and members with serum or plasma creatinine $>$2.0 mg/dl because of the likelihood that deviations in serum sodium in these patients were related to kidney-related functional disorders rather than disorders of water metabolism. We also excluded members with blood hemoglobin $>$18 g/dl, blood hematocrit $>$54%, or serum or plasma triglycerides $>$400 mg/dl, as measured 15 d before or after the reference serum sodium date, because of the possibility that observed changes in serum sodium were related to pseudohyponatremia or acute volume depletion. If blood glucose was $>$300 mg/dl, as measured 15 d before or after the reference serum sodium date, we adjusted serum sodium by a factor of 1.6 (original value + [(glucose − 100)/100] × 1.6).[25]

We reviewed inpatient, outpatient, and professional claims for evidence of underlying comorbid conditions within the 60-d period preceding the reference serum sodium date. Specifically, we searched for evidence of congestive heart failure, liver cirrhosis, nephritis, nephrotic syndrome, nephrosis, and syndrome of inappropriate secretion of antidiuretic hormone. We also identified comorbid conditions using the coding algorithms described by Birman-Deych *et al.*[26] and Quan *et al.*[27] We searched all inpatient, outpatient, and professional claims for 60 d preceding the reference serum sodium date for evidence of cerebrovascular disease, chronic obstructive pulmonary disease, coronary heart disease, dementia, diabetes mellitus, hypertension, kidney disease, metastatic carcinoma, peripheral vascular disease, and rheumatic disease (Table 5).

We also examined outpatient pharmacy claims for medications known to cause hyponatremia. We used national drug codes to identify claims for carbamazepine, chlorpropamide, clofibrate, cyclophosphamide, desmopressin, opiate derivatives, oxytocin, phenothiazine, prostaglandin synthesis inhibitors, selective serotonin reuptake inhibitors, thiazide diuretics, tricyclic antidepressants, and vincristine incurred within 5 d before or after the reference serum sodium date.

### Statistical Analysis

We defined hyponatremia as serum sodium $<$135 mmol/L, normal as serum sodium between 135 and 145 mmol/L, and hypernatremia as serum sodium $>$145 mmol/L.[4,8,12,15,28,29–31] We used descriptive statistics to summarize demographic characteristics, comorbidities, prescription drug use, laboratory values, and 6-mo and 1-yr costs by serum sodium status. We assessed differences between groups using $\chi^2$ tests for categorical variables and Wilcoxon rank sum tests for continuous variables. Mortality information was not available.

We calculated total medical costs by summing the IHCIS standardized cost values for all inpatient facility, outpatient facility, professional services, and ambulatory services incurred from 1 d after the reference serum sodium date through December 31, 2005, or through the end of insurance coverage, whichever came first. We adjusted all costs to 2000 U.S. dollars. Because not all members in the IHCIS database had a pharmacy benefit, pharmacy costs were not considered in our analyses.

We calculated 6-mo mean medical costs, 6-mo inpatient costs, and 6-mo inpatient resource use by group and used analysis of variance (ANOVA) to test for group differences. We used generalized linear models to calculate unadjusted and adjusted effects of hyponatremia and hypernatremia, relative to normal serum sodium levels, on 6-mo costs and resource use, controlling for demographic and clinical confounders. These Poisson-like models specified a log link for the mean and a variance proportional to the mean.[32] Analyses of 6-mo costs and utilization included data for all patients.

Analyses of 1-yr medical costs, 1-yr inpatient costs, and 1-yr inpatient resource use included data only for patients who had not been censored at 365 d after the reference date. Managed care beneficiaries

**Table 5.** ICD-9-CM codes used to identify underlying and comorbid conditions

| Condition | ICD-9-CM Codes |
|---|---|
| Cerebrovascular disease | 362.34, 430.x-438.x |
| Chronic obstructive pulmonary disease | 416.8, 416.9, 490.x-505.x, 506.4, 508.1, 508.8 |
| Congestive heart failure | 428.0 |
| Coronary heart disease | 410.x-414.x, 429.2, V45.81 |
| Dementia | 290.x, 294.1, 331.2 |
| Diabetes mellitus | 250.x |
| Hypertension | 401.x-405.x, 437.2 |
| Kidney disease | 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0–583.7, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x |
| Liver cirrhosis | 572.4 |
| Metastatic carcinoma | 196.x-199.x |
| Nephritis, nephrotic syndrome, and nephrosis | 580–589 |
| Peripheral vascular disease | 093.0, 437.3, 440.x, 441.x, 443.1–443.9, 47.1, 557.1, 557.9, V43.4 |
| Rheumatic disease | 446.5, 710.0 through 710.4, 714.0–714.2, 714.8, 725.x |
| Syndrome of inappropriate secretion of antidiuretic hormone | 253.6 |

Abbreviations: ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification.*

are a transient population; beneficiaries switch plans and move into and out of coverage with great frequency. In this analysis, censoring occurred when a beneficiary's period of eligibility ended before the end of the observation period. We weighted these uncensored patients to account for patients lost to censoring.[33] We determined the weights by using proportional hazards regression analysis to model the probability of being censored on demographic and clinical characteristics. We calculated weighted 1-yr costs and resource use by group and used weighted ANOVA to test for group differences. We used weighted generalized linear models to calculate unadjusted and adjusted effects of hyponatremia and hypernatremia, relative to normal serum sodium levels, on 1-yr costs and resource use, controlling for demographic and clinical confounders. Again, these models specified a log link for the mean and a variance proportional to the mean.

In sensitivity analyses, we evaluated the robustness of the findings. We truncated medical costs to $60 000 for 6-mo costs and $120 000 for 1-yr costs to eliminate cost outliers. Next, we repeated all multivariable analyses of costs for patients with hyponatremia, including a variable for patients who received drugs known to cause hyponatremia in the model. We also observed 1-yr costs for the unweighted sample of patients for whom 365 d of follow-up data were available.

We used SAS, version 9.1.5, for all analyses (SAS Institute, Cary, NC). The institutional review board of the Duke University Health System approved this study.

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## DISCLOSURES

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