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Early treatment with thiamine and mortality among patients with alcohol use disorder who are hospitalized for pneumonia

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Abstract

Background: The paucity of research linking thiamine treatment with improved outcomes may be driving its underutilization among patients at risk for Wernicke encephalopathy.

Objective: To assess relationships of thiamine usage to outcomes of patients hospitalized with alcohol use disorder and pneumonia.

Design, Setting and Participants: This is a retrospective cohort study of adult patients hospitalized with pneumonia who also have alcohol use disorder and were treated with benzodiazepines during the initial two hospital days, between 2010 and 2015 at hospitals participating in the Premier Healthcare Database.

Exposure: Any thiamine treatment, and, among those treated, high-dose thiamine treatment, during the initial two hospital days.

Main Outcome and Measures: Death on days 3–14 of hospitalization (primary); discharge home; transfer to intensive care unit; length of stay (LOS). We used propensity-weighted models to estimate treatment effects.

Results: Among 36,732 patients from 625 hospitals, 26,520 (72.2%) patients received thiamine, with mortality of 6.5% and 8.1% among recipients and nonrecipients, respectively. With propensity score adjustment, thiamine was associated with reduced mortality (odds ratio [OR]: 0.80, 95% confidence interval [CI]: 0.75–0.85) and more frequent discharges to home (OR: 1.10, 95% CI: 1.06–1.14). Other outcomes were similar. Relative to low-dose thiamine, high-dose thiamine was not associated with mortality (adjusted OR: 0.99, 95% CI: 0.89–1.10), but LOS was longer (ratio of means: 1.06, 95% CI: 1.04–1.08), and discharges to home were less frequent (OR: 0.92, 95% CI: 0.87–0.97).

Conclusion: Thiamine is not reliably given to patients with pneumonia and alcohol use disorder receiving benzodiazepines. Improving thiamine administration may represent an opportunity to save lives in this high-risk group of inpatients.

INTRODUCTION

As many as 15 million Americans with alcohol use disorder (AUD)[1] are at risk of developing Wernicke encephalopathy (WE), a devastating neurologic condition caused by thiamine deficiency. Untreated, WE is fatal in up to 20% of patients[2,3] and most survivors have chronic neurologic damage.[4,5] For more than 70 years, thiamine has been the treatment for WE,[4–9] but this recommendation is based only on case reports. Whether administration of thiamine improves outcomes among patients with AUD and the magnitude of any benefit are unknown.

Most research on thiamine treatment was performed in the mid-20th century and consisted of case reports demonstrating improvement of symptoms following thiamine.[4–7,9–11] A Cochrane Review found evidence supporting thiamine for patients with AUD, but could not recommend dose, route, frequency, or duration.[12] There are few guidelines,[13] and the United States lacks quality measures for the prevention of WE.[13,14]

Patients at risk for WE often do not receive thiamine,[15–19] although data on hospitalized patients in the United States is limited. A study of intensive care unit (ICU) patients demonstrated that half of the patients received no thiamine,[20] and, in smaller studies, 15%–36% of hospitalized patients with AU received no thiamine.[15,16,21] Hospitalized patients with AUD are at increased risk for WE; up to 7% of hospitalized patients have AUD,[22] and, of those patients with AUD who die, 12.5% have indications of WE at autopsy.[23] People with AUD are predisposed to WE due to decreased thiamine intake and absorption.[24] Thiamine requirements increase during stress such as hospitalization[24,25] due to its role as a cofactor in carbohydrate metabolism and glycolysis. In the absence of thiamine, acute illness and glucose administration can precipitate WE.[26] Approximately 4% of patients admitted with pneumonia have AUD,[27] making this a useful population in which to estimate the use of thiamine and associated outcomes.

Using data from more than 600 US hospitals, we sought to determine the proportion of hospitalized patients with pneumonia and AUD who receive thiamine treatment, whether thiamine was associated with mortality and other outcomes, and whether higher doses offered benefit.

METHODS

We conducted a retrospective cohort study of patients admitted from July 2010 to June 2015 to 670 hospitals participating in the Premier Healthcare Database (Premier Inc).[28] Premier is a large, service-level, all-payer hospital discharge database, including geographically diverse nonprofit, nongovernmental, and community and teaching hospitals from both rural and urban areas, and including approximately 25% of all US inpatient admissions. Premier has advantages over other administrative data sets, in that hospitals submit healthcare utilization and financial data with a date-stamped record of each item billed during each hospitalization. This allows for detailed adjustment for billed confounders present at specific times during the hospitalization, for example, antibiotics administered on admission. This study was considered exempt by the institutional review board of The Cleveland Clinic.

Study population

Adult patients with a principal or secondary ICD9 diagnosis code consistent with pneumonia[29] who also had an ICD9 code consistent with an alcohol-related diagnosis were identified (ICD9 codes listed in Supporting Information: eTables 1 and 2).[30] To increase the likelihood that patients had active alcohol use, we included only patients who received a benzodiazepine in the first 2 hospital days, as benzodiazepines are routinely used to prevent and treat alcohol withdrawal (medication list Supporting Information: eTable 3). Those noted to have an alcohol-related diagnosis in remission (ICD9 codes 305.03, 303.93, or 303.03) were excluded. Because the first 2 hospital days were considered the exposure period, we excluded patients who died or were discharged during that time interval to ensure the same opportunity for all patients to have received thiamine and exclude potential reverse causation effects. Patients missing demographic data were excluded. For patients with multiple admissions, we chose one admission at random.

Thiamine therapy

Patients were considered to have received thiamine if any thiamine treatment was given by hospital day 2. We also determined the dose and route. For subgroup analysis, high-dose thiamine was any dose of at least 200 mg parenteral thiamine during the initial two hospital days. Lower parenteral doses or any dose given orally were considered low doses.

Covariates

Baseline demographic and clinical characteristics were examined, including age, gender, race, marital status, admissions in the previous 12 months, and insurance payer. We also examined several factors related to the severity of illness in the first 2 hospital days, including no oral medications given, admission to an ICU, invasive mechanical ventilation, vasopressor use, and organ failure score. The organ failure score was derived from discharge diagnosis codes representing respiratory, cardiovascular, renal, hepatic, metabolic, and neurologic failure.[30] We categorized medical comorbidities into clinical conditions using software from the Agency for Healthcare Research and Quality, based on the work of Elixhauser.[31] Hospital-level characteristics included hospital number of beds, region, urban/rural, and teaching versus nonteaching facility. Antibiotics used for healthcare-associated pneumonia (e.g., vancomycin) were also examined because they tend to be associated with increased mortality.[32]

TABLE 1 Characteristics of hospitalized pneumonia patients with alcohol use disorder by thiamine receipt and dose categories

Factor	Total, *N* = 36,732	No thiamine, *N* = 10,212 (27.8%)	Thiamine, *N* = 26,520 (72.2%)	*p* Value	Thiamine dose among those treated		
					Low, *N* = 14,465 (54.5%)	High, *N* = 12,055 (45.5%)	*p* Value
Demographics							
Age, median [IQR]	55.0 [48.0, 63.0]	56.0 [48.0, 65.0]	55.0 [48.0, 63.0]	**<0.001**[b]	56.0 [48.0, 63.0]	55.0 [47.0, 62.0]	**<0.001**[b]
Male, *n* (%)	28,737 (78.2)	7544 (73.9)	21,193 (79.9)	**<0.001**[c]	11,428 (79.0)	9765 (81.0)	**<0.001**[c]
Race, *n* (%)				**0.002**[c]			**<0.001**[c]
White	27,450 (74.7)	7651 (74.9)	19,799 (74.7)		10,648 (73.6)	9151 (75.9)	
Black	3812 (10.4)	1133 (11.1)	2679 (10.1)		1474 (10.2)	1205 (10.0)	
Hispanic	172 (0.47)	46 (0.45)	126 (0.48)		61 (0.42)	65 (0.54)	
Other	5298 (14.4)	1382 (13.5)	3916 (14.8)		2282 (15.8)	1634 (13.6)	
Hospital characteristics							
Bed size, *n* (%)				**<0.001**[c]			**<0.001**[c]
≤200 Beds	7322 (19.9)	2263 (22.2)	5059 (19.1)		2873 (19.9)	2186 (18.1)	
201–400 Beds	13,493 (36.7)	3747 (36.7)	9746 (36.7)		5328 (36.8)	4418 (36.6)	
≥401 Beds	15,917 (43.3)	4202 (41.1)	11,715 (44.2)		6264 (43.3)	5451 (45.2)	
Teach, *n* (%)				**0.003**[c]			**<0.001**[c]
No	21,405 (58.3)	6075 (59.5)	15,330 (57.8)		8548 (59.1)	6782 (56.3)	
Yes	15,327 (41.7)	4137 (40.5)	11,190 (42.2)		5917 (40.9)	5273 (43.7)	
Clinical conditions							
Organ failure scores (mean ± SD)	1.02 ± 1.2	1.06 ± 1.2	1.00 ± 1.1	**<0.001**[a]	0.93 ± 1.08	1.10 ± 1.2	**<0.001**[a]
Chronic pulmonary disease, *n* (%)	13,783 (37.5)	4335 (42.5)	9448 (35.6)	**<0.001**[c]	5562 (38.5)	3886 (32.2)	**<0.001**[c]
Other neurological disorders, *n* (%)	6879 (18.7)	1667 (16.3)	5212 (19.7)	**<0.001**[c]	2506 (17.3)	2706 (22.4)	**<0.001**[c]
Depression, *n* (%)	6686 (18.2)	1996 (19.5)	4690 (17.7)	**<0.001**[c]	2580 (17.8)	2110 (17.5)	0.48[c]
Psychoses, *n* (%)	4446 (12.1)	1356 (13.3)	3090 (11.7)	**<0.001**[c]	1700 (11.8)	1390 (11.5)	0.57[c]
Drug use, *n* (%)	7549 (20.6)	2415 (23.6)	5134 (19.4)	**<0.001**[c]	2810 (19.4)	2324 (19.3)	0.76[c]
Liver disease, *n* (%)	9168 (25.0)	2090 (20.5)	7078 (26.7)	**<0.001**[c]	3719 (25.7)	3359 (27.9)	**<0.001**[c]
Confusion (POA), *n* (%)	13,349 (36.3)	2911 (28.5)	10,438 (39.4)	**<0.001**[c]	5064 (35.0)	5374 (44.6)	**<0.001**[c]
Broad-spectrum antibiotics							
Vancomycin,* *n* (%)	6178 (16.8)	2064 (20.2)	4114 (15.5)	**<0.001**[c]	2262 (15.6)	1852 (15.4)	0.54[c]

(Continued)

TABLE 1 (Continued)

Factor	Total, *N* = 36,732	No thiamine, *N* = 10,212 (27.8%)	Thiamine, *N* = 26,520 (72.2%)	*p* Value	Thiamine dose among those treated		
					Low, *N* = 14,465 (54.5%)	High, *N* = 12,055 (45.5%)	*p* Value
Third-generation cephalosporins,* *n* (%)	8736 (23.8)	2540 (24.9)	6196 (23.4)	0.002[c]	3599 (24.9)	2597 (21.5)	**<0.001**[c]
Quinolones,* *n* (%)	7479 (20.4)	2378 (23.3)	5101 (19.2)	**<0.001**[c]	3078 (21.3)	2023 (16.8)	**<0.001**[c]
Piperacillin–tazobactam*, *n* (%)	5046 (13.7)	1498 (14.7)	3548 (13.4)	**0.001**[c]	1855 (12.8)	1693 (14.0)	**0.004**[c]
Other antipseudomonals,* *n* (%)	2534 (6.9)	979 (9.6)	1555 (5.9)	**<0.001**[c]	860 (5.9)	695(5.8)	0.53[c]

Note: High dose refers to any one dose of ≥200 mg of thiamine administered via intravenous or intramuscular route within the initial 2 days of hospitalization. Low dose refers to any dose administered that does not meet the high-Dose criteria. Broad-spectrum antibiotics refers to any use of vancomycin, third-generation cephalosporins, quinolones, piperacillin–tazobactam, or other antipseudomonals, including systemic cefepime, imipenem, meropenem, amikacin, gentamicin, tobramycin, and aztreonam.

Abbreviation: POA, present on admission. Bold values are statistically significant at $p < 0.05$.

p Values: a = ANOVA, b = Kruskal–Wallis test, c = Pearson's χ^2 test.

*Initial treatments on Day 0 or 1.

Outcomes

The primary outcome was in-hospital death within 3–14 days of admission. Secondary endpoints included length of stay, transfer to ICU after the initial 2 days, and discharge disposition to home versus a facility. Discharge to home included with or without home services and patients who left against medical advice.

Statistical analysis

Statistical analyses were conducted from March 25, 2021 to April 4, 2022. In the primary analysis, outcomes of patients receiving thiamine were compared with outcomes of those not receiving thiamine. In a secondary analysis restricted to patients treated with thiamine, outcomes of those treated with high-dose thiamine were compared to outcomes of those treated with lower doses.

Dichotomous outcomes were initially compared between thiamine groups using χ^2 tests, and length of stay using Wilcoxon's rank-sum test. A bar chart was used to describe the associations of thiamine use with various severity measures, and a histogram to present the distribution of thiamine usage at the hospital level. To address the threat of confounding due to initial differences between groups, we used propensity-weighted models to estimate treatment effects. First, we derived propensity scores for thiamine treatment among all patients and for receiving high dose versus low dose among those treated with thiamine. The propensity scores were calculated using mixed logistic regression models with random hospital effects and fixed covariates: baseline demographics; insurance status; comorbidities; initial disease severity factors (inability to take oral medication, intensive care admission, invasive mechanical ventilation, and vasopressors on the first hospital day); and hospital geographic region, number of beds, teaching status, and urban versus rural location. We then estimated the odds ratios relating thiamine receipt or dose level to dichotomous outcomes using mixed-effects multiple logistic regression models. For continuous outcomes, we estimated the ratios of means between thiamine use (yes/no) or dose level (high/low) subgroups using gamma generalized linear mixed models. We inverse probability-weighted each analysis to estimate the effects of thiamine administration or dose on those so treated (average treatment effect among the treated, or ATT weights), and again including random hospital effects. Covariate balance ("Love") plots were generated to assess the adequacy of the propensity models to equalize distributions of covariates and we included potential confounders with standardized mean differences (SMDs) > 0.1 as covariates in the weighted outcome models. The statistical significance criterion was $p \leq 0.05$. We used the Holm–Bonferroni method to adjust *p* values for the eight simultaneous comparisons of each of the four outcomes between those who did and did not receive thiamine, and between those who received high and low doses, but we report conventional 95% confidence intervals. Forest plots were used to summarize propensity model results. As a "negative control" sensitivity analysis, we replicated the preceding

analyses among patients meeting other inclusion/exclusion criteria, but who were not administered benzodiazepines. Such patients were less likely to have current alcohol abuse and were therefore less likely than our target population to benefit from thiamine.

Analyses were conducted using SAS version 9.4 (SAS Corporation).

RESULTS

Patient and hospital characteristics

The study cohort included 36,732 patients from 625 hospitals (Supporting Information: eFigure 1). Of these, 26,520 (72.2%) received thiamine in the first 2 days of hospitalization. Patient and hospital characteristics are summarized in Table 1 and Figure 1 (additional detail in Supporting Information: eTable 4). The median age was 55 years (interquartile range: 48, 63), 78.2% were male and 74.7% were White. Compared to patients not receiving thiamine, patients receiving thiamine were more likely to be male (79.9% vs. 73.9%) and less likely to have Medicare insurance (32.3% vs. 40.0%). They were more likely to have coagulopathy (23.1% vs. 15.1%), fluid and electrolyte disorders (47.6% vs. 40.8%), liver disease (26.7% vs. 20.5%), and confusion present prior to admission (39.4% vs. 28.5%); and less likely to have chronic pulmonary disease (35.6% vs. 42.5%), renal failure (6.6% vs. 10.9%), or congestive heart failure (13.5% vs. 19.3%). The proportion who went to ICU on hospital day 1 was similar (41.0% of thiamine patients vs. 39.2%), although receipt of thiamine was associated with less invasive mechanical ventilation (20.9% vs. 25.5%) or vasopressors (8.8% vs. 12.8%). Across hospitals, the percentage of patients receiving thiamine ranged from 24% to 90% (Figure 2). Hospital characteristics varied only slightly with thiamine utilization.

Inverse propensity-weighted SMDs were well below the 10% threshold for each individual potential predictor of thiamine utilization, but the composite propensity model linear predictor derived from them modestly exceeded this threshold and was included in the outcome models (Supporting Information: eFigure 2A). The primary outcome, in-hospital mortality within 3–14 days of admission, occurred less in patients who had received thiamine than in those who had not (6.5% vs. 8.1%) and this association was confirmed by the propensity-adjusted analysis (odds ratio [OR]: 0.80, 95% confidence interval [CI]: 0.75–0.85, $p < 0.001$) (Figure 3). In the propensity-adjusted models, thiamine administration was also associated with discharge home (OR: 1.10, 95% CI: 1.06–1.14, $p < 0.001$), but not statistically significantly associated with length of stay (adjusted ratio of means: 1.003, 95% CI: 0.99–1.02, $p = 1$) or ICU transfers (adjusted OR: 0.96, 95% CI: 0.91–1.03, $p = 1$). (Note that Holm-Bonferroni adjustment can frequently yield the maximum possible p-value of 1).

Subgroup dosage analysis

Of the 26,520 patients who were included in the dosage analysis, 12,055 (45.5%) received high-dose thiamine. Compared to those who received lower doses, those receiving high-dose thiamine were sicker—they were statistically significantly more likely to have confusion prior to admission (44.6% vs. 35.5%), to not receive oral medications (41.5% vs. 35.9%), to be in ICU on hospital day 1 (45.8% vs. 37.1%), mechanically ventilated (24.5% vs. 17.8%), or on vasopressors (10.1% vs. 7.8%). They also had higher mean organ failure scores (1.10 vs. 0.93). Patients at larger (>200 beds, 46.0%) urban (46.1%), and teaching hospitals (47.1%) were only slightly more likely to receive high-dose thiamine than patients at smaller (≤200 beds, 43.2%), rural (40.0%), and nonteaching (44.2%) facilities. As

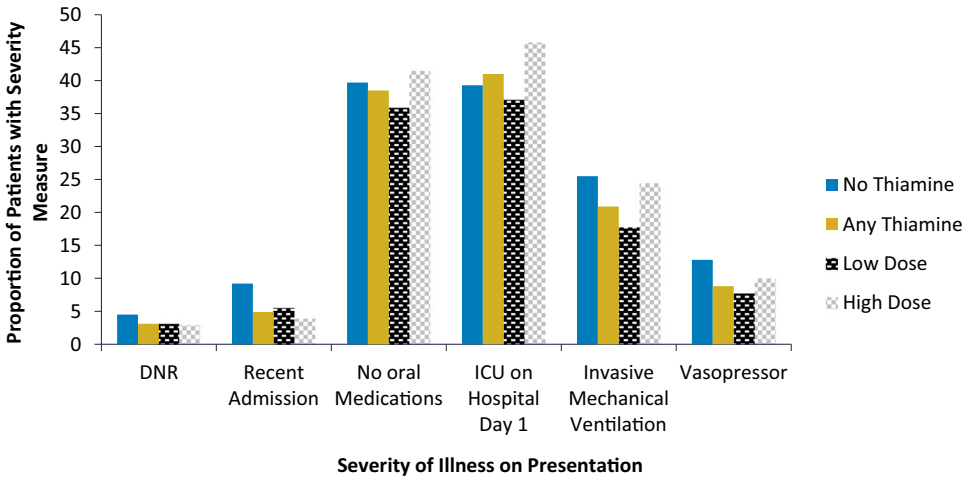

FIGURE 1 Proportion of patients with various severity of illness measures on presentation among those receiving no thiamine, any thiamine, low-dose thiamine, and high-dose thiamine. Recent admission refers to any admission within the previous 12 months. Comparisons were performed for those receiving no thiamine versus those receiving any thiamine and for those receiving low-dose thiamine versus those receiving high-dose thiamine. All comparisons were statistically significant (Supporting Information: eTable 4), except for DNR status between those receiving low- and high-dose thiamine. DNR, do not resuscitate order; ICU, intensive care unit.

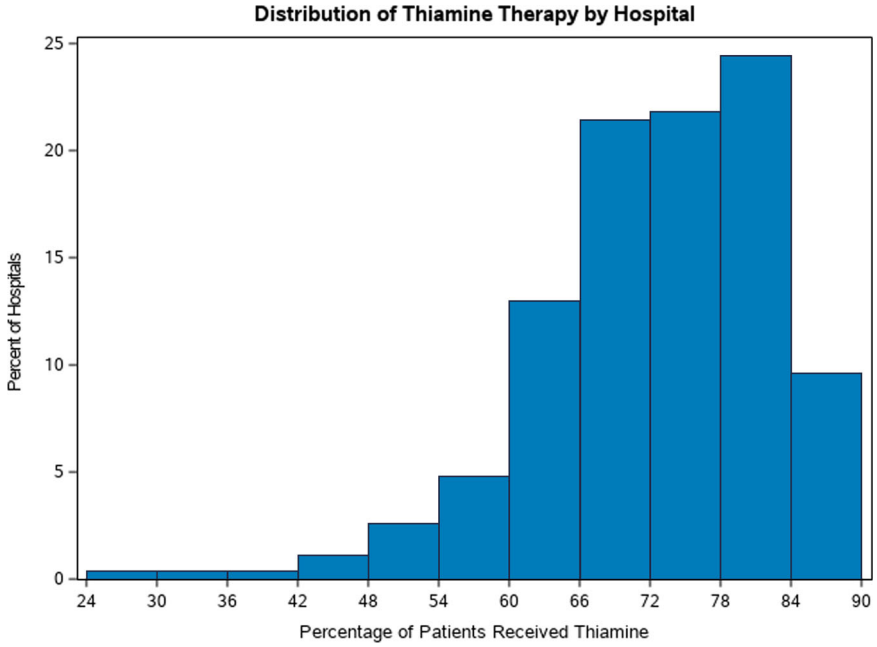

FIGURE 2 Distribution of hospitals delivering any thiamine therapy. Any thiamine therapy given within the initial 2 days of hospitalization, regardless of dose, was included. Hospitals with less than 100 patients in the analysis were excluded.

above, the linear predictor but no individual covariate was included in outcome models (Supporting Information: eFigure 2B).

In-hospital mortality on Days 3–14 was similar for those who received high-dose and low-dose thiamine (adjusted OR: 0.99, 95% CI: 0.89–1.10). In other propensity-adjusted models, high-dose thiamine was associated with worse outcomes: longer lengths of stay (adjusted ratio of means: 1.06, 95% CI: 1.04–1.08), and less frequent discharge to home (adjusted OR: 0.92, 95% CI: 0.87–0.97).

Sensitivity analysis

Among 55,450 patients who did not receive benzodiazepines, 39.5% received thiamine, of whom 36.2% received high-dose thiamine, as compared, respectively, to 72.2% and 45.5% among benzodiazepine recipients. No mortality benefit of thiamine or mortality effect of dose was evident in those not receiving benzodiazepines. However, among these patients, thiamine administration was associated with small reductions in length of stay (ratio of means: 0.97, 95% CI: 0.96–0.98) and ICU transfers (OR: 0.90, 95% CI: 0.84–0.97). Results for other comparisons were similar to those for patients who received benzodiazepines (Supporting Information: eTable 5).

DISCUSSION

In this cohort study of over 35,000 patients with pneumonia and AUD who received benzodiazepines, thiamine treatment was associated with a significantly lower risk of 14-day mortality, but high-dose versus low-dose thiamine was not associated with improved mortality. We also noted substantial variability in thiamine administration, and 28% of patients received no thiamine at all.

This study, the largest to date on the benefit of thiamine and the first large study of the effectiveness of thiamine use in the United States, supports what we have believed for over 100 years—treatment with thiamine reduces mortality among those with AUD. Only one ICU-based cohort study has previously examined outcomes related to thiamine treatment; no mortality difference was seen, although a subgroup analysis of thiamine-deficient patients demonstrated a difference in survival curves.[33] Other data regarding thiamine's benefit is limited to highly convincing case reports in which all thiamine-deficient patients experienced resolution of symptoms following thiamine administration.[5,9] Despite the lack of trials proving efficacy, thiamine deficiency has long been assumed to cause WE given its role as a cofactor in carbohydrate metabolism and in glycolysis. Animal models demonstrate that thiamine depletion causes changes similar to WE, which are reversible with thiamine treatment.[34] Ours study appears to be the first large-scale effectiveness study in humans.

There is even more limited evidence to support specific dosing recommendations. One small, randomized trial comparing five doses of intramuscular thiamine among patients found improved cognitive outcomes with higher doses.[35] It is recommended to consume at least 1.1 mg of thiamine daily to maintain body stores; however, once these stores are depleted, higher doses are needed.[36] Also, in patients actively drinking alcohol, gut changes, decreased liver storage capacity, increased renal losses, and poor overall nutrition hampers absorption.[25] Consequently, patients with AUD account for 90% of those with thiamine deficiency.[24] To avoid absorption issues, many medical societies recommend parenteral administration.[37,38] Although we found no mortality benefit associated with specific dosing, high doses seem reasonable given that parenteral

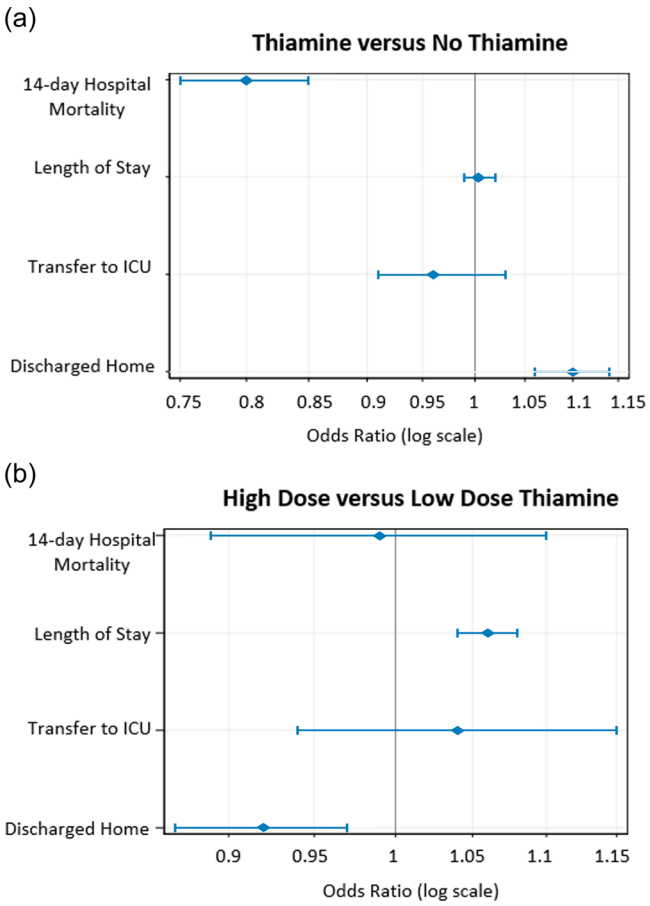

FIGURE 3 Propensity-weighted* comparisons of outcomes between patients receiving and not receiving thiamine (q) and high-dose versus low-dose thiamine (b). *All variables from Supporting Information: eTable 4 were included in the propensity model. High dose refers to any one dose of ≥200 mg of thiamine administered via intravenous or intramuscular route within the initial 2 days of hospitalization. Low dose refers to any dose administered that does not meet the high-dose criteria. Analysis for the length of stay is the mean multiplier, not the odds ratio. Discharged home was limited to patients who survived and were discharged home within 14 days. ICU, intensive care unit.

thiamine is inexpensive, easy to deliver, has no contraindications, and allergic reactions are extremely rare.[39,40]

The inconsistent use of thiamine across hospitals presents a potential opportunity to save lives. That 28% of patients received no thiamine is notable given that inclusion in our cohort required benzodiazepine use indicative of possible alcohol withdrawal. In 2018, in the United States, there were over 300,000 admissions with AUD,[41] of whom 1.97% of patients died in the hospital (6521 deaths); a 20% reduction in mortality, as seen here, could prevent up to 1300 deaths annually. Given current evidence, randomized trials are unlikely, so this retrospective data may represent the strongest evidence available. Some institutions have demonstrated that improvement in thiamine dosing is achievable[19] and national guidelines, bolstered by quality measures, could propagate such improvements. Despite thiamine being the standard of care in WE for a century, there are no quality measures for thiamine administration in the US people with AUD suffering from disparities in treatment,[42] and this may be an opportunity to rectify that disparity and save lives.

There are several limitations to this work. First, the use of anonymized, administrative data sets, such as the Premier Healthcare Database, does not allow for the review of charts or clinical data, including laboratory results, vital signs, or cause of death. Secondly, ICD9 diagnosis codes may have undercounted patients with AUD. Conversely, they likely also apprehended patients who would not meet the criteria for AUD; hence, the benzodiazepine requirement. Nevertheless, our findings should be applicable to those patients who were included and, if anything, we may have overestimated thiamine use at the hospital level. In fact, among patients who did not receive benzodiazepines, no mortality benefit of thiamine was observed, strengthening the case that the benzodiazepine requirement likely identified patients at risk. Third, there may have been confounding indications. We tried to adjust for this by using markers of illness severity on admission, but there may have been unmeasured confounding. For example, it is possible that hospitals that deliver evidence-based care are more likely to prescribe thiamine and treat pneumonia effectively. Similarly, we assumed that appropriate treatment was chosen for pneumonia, though we have adjusted for antibiotic choice in the analysis. Fourth, we could not determine mechanisms by which thiamine reduced mortality. Thiamine treatment may be important, for example, in sepsis more generally,[17] and therefore may have a meaningful role in treating pneumonia beyond those with AUD.

CONCLUSIONS

In this study of patients with pneumonia and AUD who received benzodiazepines, more than a quarter of patients received no thiamine. However, those who received thiamine therapy had a 20% lower odds of dying. Given these findings, it seems reasonable to administer thiamine to all inpatients with current AUD and pneumonia. Clinical guidelines and quality metrics could support this effort as improving thiamine administration may represent an opportunity to save lives.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest. We thank Ning Guo, MS, for assistance with statistical computing during the final stages of publication.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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