Hierarchical Modeling Versus Regression Analysis for Evaluating Results of Orthopaedic Studies That Use the National Inpatient Sample

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Abstract

Background: Owing to its hierarchical sampling structure, the National Inpatient Sample (NIS) often involves clusters of study data. We aimed to (1) understand the statistical methods of currently published orthopaedic studies using NIS and (2) examine the role of hierarchical modeling versus traditional regression analysis in a retrospective cohort of patients from NIS.

Methods: We conducted a systematic review to examine statistical methods of orthopaedic studies (published between 2005 and 2014) using NIS. Ultimately, 132 studies were identified. We noted percentages of studies that used hierarchical modeling versus traditional regression analysis. Using NIS, we identified a retrospective cohort of patients aged 70 years and older who underwent operative fixation of intertrochanteric hip fractures between 2008 and 2012. Patient comorbidities were tested for association with in-hospital mortality and length of stay in hierarchical linear models and traditional regression analysis. Statistical outcomes were compared between the two models.

Results: Seven of 28 (25%) measured comorbidities overestimated the significance of in-hospital mortality in traditional regression compared to hierarchical modeling. Similarly, traditional regression analysis overestimated significance in four of 28 (14%) comorbidities in increasing length of stay. Of the 132 studies, most (74%) used traditional regression analysis, few (7%) used univariate statistics, and even less (2%) used hierarchical modeling. According to these findings, between 11% to 20% of all orthopaedic studies published between 2005 and 2014 using NIS data were at risk of overestimating their clinical results.

Conclusions: Traditional regression analysis may overestimate significance in linear and logistic models owing to the inability to address clustered data. Because healthcare data is often clustered, hierarchical linear modeling should be employed to increase the specificity of outcomes-based research using NIS.

Introduction

The National Inpatient Sample (NIS) is the largest publically available all-payer inpatient healthcare database representative of all United States (US) hospitals.[1] The large sample size helps track epidemiological trends and in-hospital complications for inpatient orthopaedic procedures.[1,2] Interest in the use of NIS for orthopaedic studies has notably increased, with an exponential rise in publications in orthopaedic journals.[4] However, the large dataset comes with unique statistical challenges for researchers.[5] Clinicians should be aware of issues that may affect the conclusions drawn from studies using the database.

One of the main problems in statistical analysis using NIS arises from the large sample size. This causes even small differences to be statistically significant, yet they may not represent a clinical significance.[4] Many authors have suggested reducing the accepted α error (ie, 0.05) to 0.01 or 0.001 to combat the discrepancy.[6-24] However, to date there is no standard method to address this issue.

To improve uniformity of statistical analysis in NIS, the Healthcare Cost and Utilization Project (HCUP; the creators of NIS database) have suggested the use of hierarchical linear modeling (also known as mixed modeling) instead of traditional regression analysis.[5] The use of hierarchical linear modeling accounts for clustering within the data. Clustering refers to grouping in the data, which may affect outcomes. In NIS, patients are inherently clustered owing to treatment by the same physician or hospital. Accounting for clustering with hierarchical linear modeling increases confidence intervals of the outcome variables of interest and, therefore, improves specificity.[26,27] Many orthopedic studies do not account for this clustering and may be overestimating their findings.[28]

This study was designed to determine the effect of hierarchical linear modeling in orthopedic research utilizing NIS. Thus, our aims are: 1) to identify current statistical analysis trends in orthopaedic studies that use NIS; and 2) to determine the effect of hierarchical linear modeling versus traditional regression analysis in an orthopaedic-study population.

Methods

The study was granted exempt status by our institution's investigation review owing to the de-identified quality of the data available in NIS database. To address our two objectives, a two-step study design was created. First, a systematic review of the orthopedic literature was conducted to determine the current use of statistical analysis in orthopaedic studies using NIS. Second, the effect of hierarchical linear modeling versus traditional regression analysis was tested in a retrospective cohort study using NIS.

Systematic Review

A systematic review of orthopaedic studies was conducted to identify the current statistical analysis used by studies of NIS in the past 10 years (Figure 1). A PubMed search was undertaken for studies containing "National Inpatient Sample" or "Nationwide Inpatient Sample" (the name of the database was changed from "Nationwide" to "National" Inpatient Sample in 2012) in the top 41 orthopaedic journals as outlined by Moverley et al.[29] Ultimately, a total of 132 studies were identified between 2005 and 2012. The statistical analysis of each study was categorized into one of six statistical groups by two authors (JWH and KM). Statistical categories included: traditional regression analysis, hierarchical linear modeling, univariate statistics, epidemiological population estimations, propensity scoring, and survival analysis.

Retrospective Cohort Study

A retrospective cohort study was conducted using NIS discharge data. All patients aged 70 years and older hospitalized for surgical treatment of intertrochanteric hip fractures between 2008 and 2012 were identified (International Classification of Diseases, 9th revision [ICD-9] code 820.21 for intertrochanteric hip fracture and ICD-9 Clinical Modification procedure code 79.15 or 79.35 for open or closed reduction with internal fixation, femur). A total of 370,307 patients met inclusion criteria. NIS is a stratified survey of all US hospitals, which are randomly selected to achieve a 20% sample.[1] Sampling weights are provided to produce national estimates. All patient numbers in this study were reported as national estimates.

The presence or absence of 28 preoperative comorbidities in patients were identified with the use of HCUP comorbidity software.[30] The primary outcome measures of the cohort study were risk of in-hospital mortality and overall length of stay, which represent a dichotomous and steady outcome variable of interest to orthopaedic surgeons in identifying the effect of statistical modeling on continuous and categorical data.

Statistical Analysis

Descriptive statistics were used to report percentages of studies using different statistical methods from the systematic review. For the retrospective cohort study, each preoperative patient comorbidity was tested for association with either primary outcome measure (ie, in-hospital mortality or overall length of stay). Two separate regression

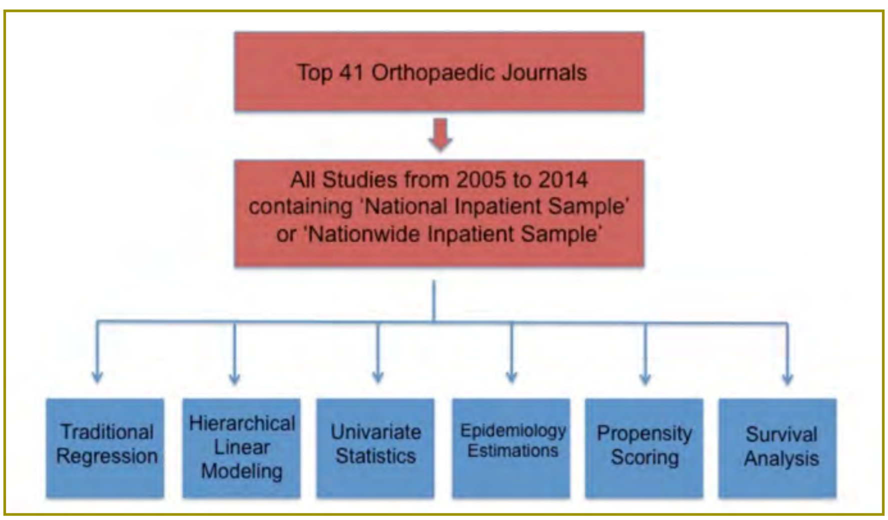

Figure 1. Flow diagram of systematic review study design.

models were run for each outcome variable: one model with traditional regression analysis and another with hierarchical linear modeling. Level of significance for the regression models was placed at $\alpha = 0.05$. The significance from each model was then compared for each preoperative patient comorbidity.

Traditional regression analysis for in-hospital mortality was undertaken with logistic regression. Next, a hierarchical logistic regression model was performed. Patient clustering at the hospital level was accounted for in the hierarchical model. Odds ratios (OR) of each preoperative patient comorbidity were reported from each model.

Next, traditional regression analysis for overall length of stay was undertaken utilizing a gamma regression with a log-link function. A α regression, with a log-link function, was chosen to account for the positive skewness of the length of stay data. Similarly, a hierarchical linear model, with α regression and log-link function, was used to account for patient clustering at the hospital level. The effect of each preoperative patient comorbidity was compared between the two models.

Results

Systematic Review

There was an exponential rise in the number of studies published after 2011 (Figure 2). Of 132 studies identified, a total of 98 studies (74%) used traditional regression analysis[3,7-15,18-23,25,31-112]; a total of 11 (13%) used epidemiological population estimates[2,4,113-126]; a total of 10 (7%) used univariate statistics[7,16,17,24,127-132]; four (3%) used propensity scoring[133-136]; one (2%) used hierarchical linear modeling[137,138]; and two (1%) utilized survival analysis (Figure 3).[139]

Retrospective Cohort Study

Of the 370,307 patients included, the average age was 84.4 years (range, 70-110 years). A total of 275,132 (74%) were women, and 95,122 (26%) were men. Almost all patients (356,483; 97%) had a least one comorbidity, with many patients having multiple comorbidities (Figure 4). Figure 5 represents the most common comorbidities in patients such as hypertension (72% of patients), deficiency anemias (31%), fluid and electrolyte disorders (30%), chronic obstructive pulmonary disease (21%), hypothyroidism (19%), and diabetes without complications (19%).

The average length of stay among patients was 6.04 days (SD, 4.14 days). Table 1 shows the patient comorbidities that had the largest effect on increasing length of stay in the regression models, including weight loss and malnutrition (6.13 days), congestive heart failure (3.38 days), and paralysis (3.01 days). Of the 28 variables tested in the regression models, four (14%) were significant in the traditional regression analysis but not in the hierarchical linear model.

The overall in-hospital mortality rate among the study population was 2.4%. Table 2 depicts the patient comorbidities that notably increased the odds of in-hospital mortality, which were: liver disease (OR, 2.7), weight loss and malnutrition (OR, 2.7), and congestive heart failure (OR, 2.6). Of the 28 variables tested in the regression models, seven (25%) were significant in the traditional regression analysis but not in the hierarchical linear model.

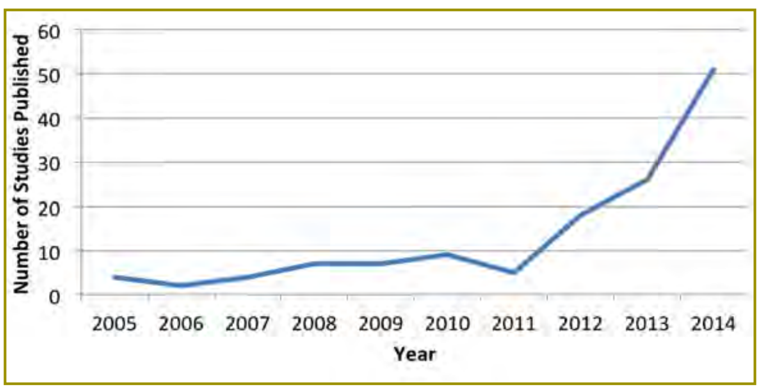

Figure 2. Number of orthopaedic studies using the National Inpatient Sample between 2005 and 2014.

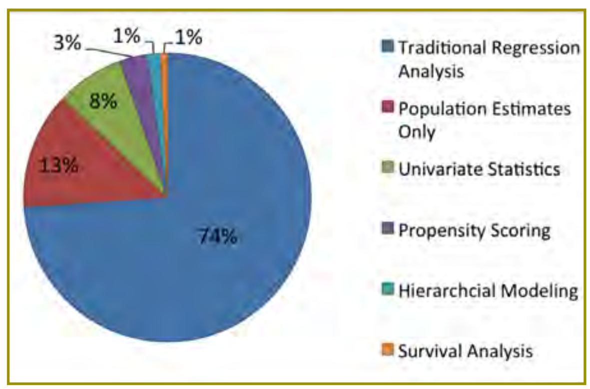

Figure 3. Statistical design of orthopaedic studies using the National Inpatient Sample between 2005 and 2014.

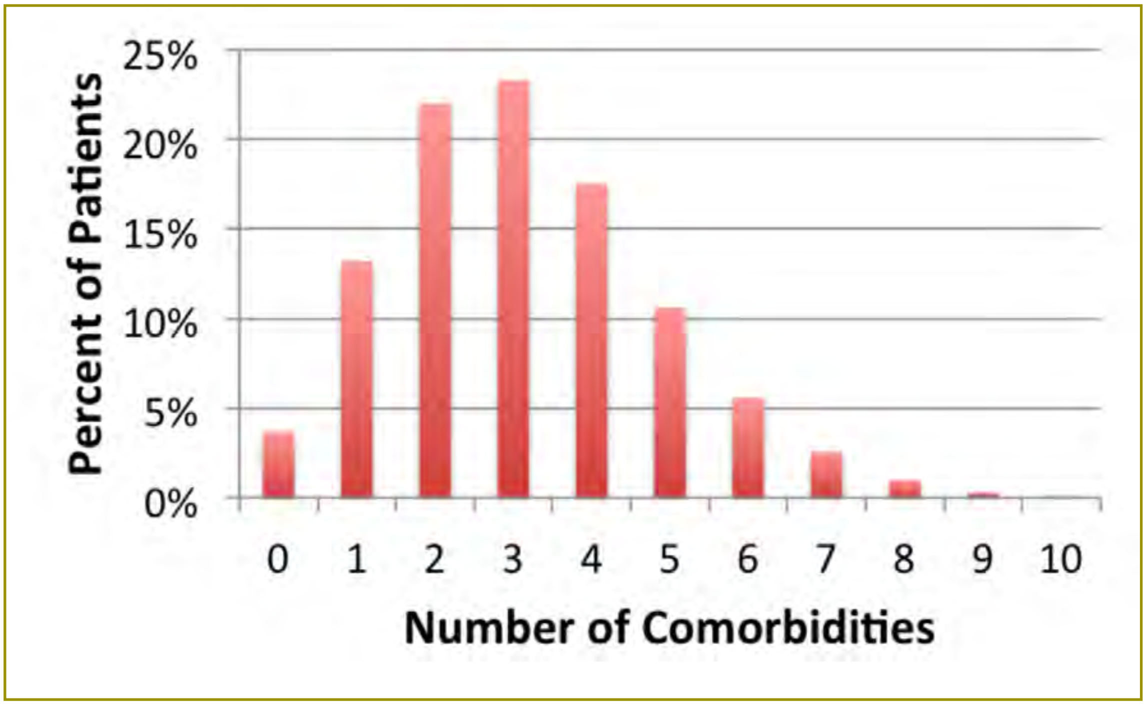

Figure 4. Percent of patients with multiple comorbidities.

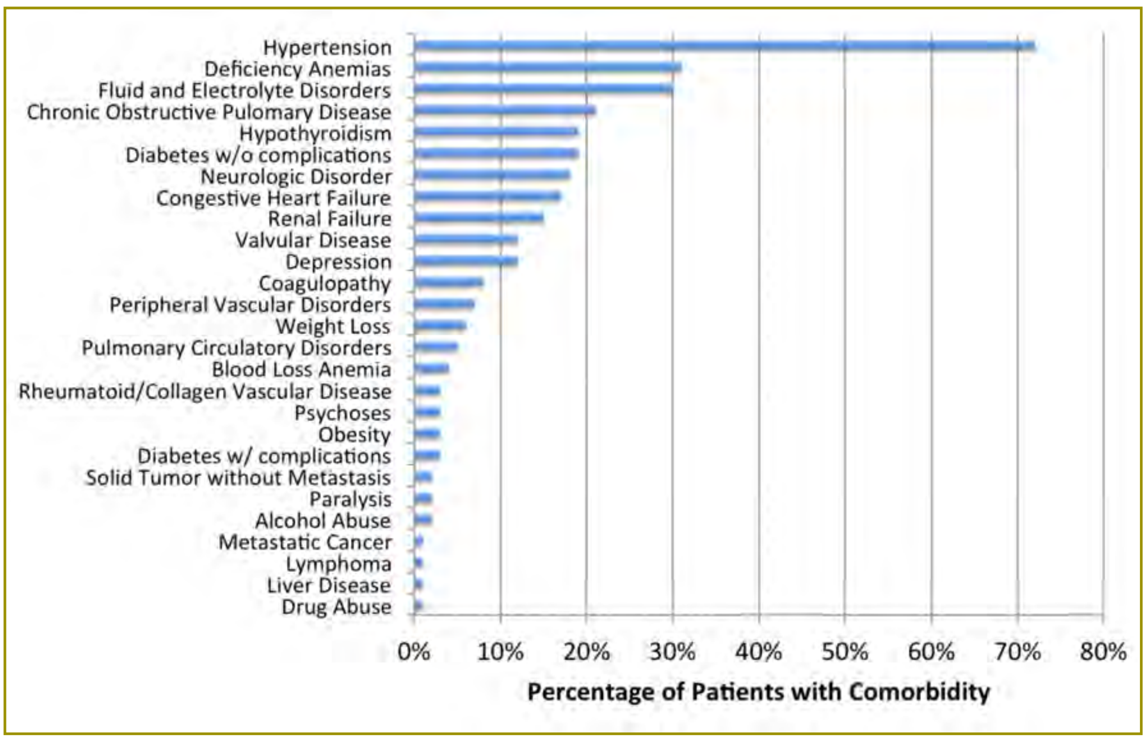

Figure 5. Percent of patients with each of the 29 measured comorbidities.

Table 1. Comparison of significance between traditional regression and hierarchical models measuring association between preoperative patient comorbidities and overall length of stay[a]

Study variable	Statistical model	Odds ratio	95% confidence interval Lower	Upper	P value
Alcohol abuse	OLS	-.25	.00	.51	0.05
	HLM	0.46	-0.03	0.95	0.064
Blood loss anemia	OLS	0.88	0.72	1.04	< 0.001
	HLM	1.14	0.77	1.51	< 0.001
Chronic obstructive pulmonary disease	OLS	0.55	0.47	0.63	< 0.001
	HLM	0.73	0.56	0.91	< 0.001
Coagulopathy	OLS	1.18	1.03	1.33	< 0.001
	HLM	1.33	1.03	1.63	< 0.001
Congestive heart failure	OLS	3.33	3.17	3.49	< 0.001
	HLM	3.38	3.03	3.73	< 0.001
Deficiency anemias	OLS	0.76	0.68	0.83	< 0.001
	HLM	0.58	0.42	0.74	< 0.001
Depression	OLS	-0.27	-0.36	-0.18	< 0.001
	HLM	-0.08	-0.38	0.24	0.618
Diabetes with complications	OLS	1.22	1.02	1.43	< 0.001
	HLM	1.45	1.01	1.89	< 0.001
Diabetes without complications	OLS	0.29	0.21	0.37	< 0.001
	HLM	0.13	-0.03	0.28	0.112
Drug abuse	OLS	2.89	1.89	3.90	< 0.001
	HLM	2.58	0.67	4.49	0.008
Fluid and electrolyte disorders	OLS	2.87	2.74	3.01	< 0.001
	HLM	2.88	2.56	3.19	< 0.001
Sex (female)	OLS	-1.24	-1.33	-1.15	< 0.001
	HLM	-1.30	-.149	-1.12	< 0.001
Hypertension	OLS	-0.73	-0.82	-0.65	< 0.001
	HLM	-0.65	-0.84	-0.46	< 0.001
Hypothyroidism	OLS	-0.60	-0.67	-0.53	< 0.001
	HLM	-0.31	-0.47	-0.16	< 0.001
Liver disease	OLS	1.35	0.97	1.73	< 0.001
	HLM	1.15	0.39	1.91	0.003
Lymphoma	OLS	1.50	1.10	1.90	< 0.001
	HLM	1.49	0.64	2.35	0.001
Metastatic cancer	OLS	2.20	1.77	2.64	< 0.001
	HLM	2.07	1.27	2.88	< 0.001
Neurologic disorder	OLS	0.28	0.19	0.36	< 0.001
	HLM	0.40	0.22	0.58	< 0.001
Obesity	OLS	0.92	0.72	1.12	< 0.001
	HLM	1.41	0.97	1.85	< 0.001
Paralysis	OLS	3.06	2.76	3.37	< 0.001
	HLM	3.01	2.36	3.64	< 0.001
Peripheral vascular disorders	OLS	0.55	0.42	0.68	< 0.001
	HLM	0.71	0.43	0.98	< 0.001
Psychoses	OLS	1.04	0.83	1.24	< 0.001
	HLM	1.22	0.78	1.66	< 0.001
Pulmonary circulatory disorders	OLS	2.71	2.51	2.92	< 0.001
	HLM	2.66	2.24	3.08	< 0.001
Renal failure	OLS	1.16	1.05	1.27	< 0.001
	HLM	1.39	1.15	1.64	< 0.001
Rheumatoid arthritis and collagen vascular disease	OLS	-0.45	-0.60	-0.29	< 0.001
	HLM	-0.08	-0.39	0.23	0.162
Solid tumor without metastasis	OLS	1.36	1.06	1.66	< 0.001
	HLM	1.25	0.64	1.86	< 0.001
Valvular disease	OLS	0.43	0.34	0.52	< 0.001
	HLM	0.48	0.27	0.69	< 0.001
Weight loss and nutritional deficiency	OLS	5.87	5.55	6.18	< 0.001
	HLM	6.13	5.41	6.85	< 0.001

OLS, traditional regression model; HLM, traditional hierarchal model.

[a] Comorbidities that were overestimated in traditional regression models are outlined in red.

Table 2. Comparison of significance between traditional regression and hierarchical models measuring association between preoperative patient comorbidities and in-hospital mortality[a]

Study variable	Statistical model	Odds ratio	95% confidence interval Lower	95% confidence interval Upper	P value
Alcohol abuse	OLS	0.586	0.480	0.714	< 0.001
	HLM	0.629	0.406	0.972	0.037
Blood loss anemia	OLS	0.610	0.535	0.695	< 0.001
	HLM	0.588	0.430	0.803	0.001
Chronic obstructive pulmonary disease	OLS	1.390	1.324	1.459	< 0.001
	HLM	1.423	1.272	1.593	< 0.001
Coagulopathy	OLS	1.159	1.081	1.244	< 0.001
	HLM	1.231	1.042	1.454	< 0.001
Congestive heart failure	OLS	2.542	2.420	2.669	0.003
	HLM	2.610	2.320	2.938	<0.001
Deficiency anemias	OLS	0.859	0.820	0.901	< 0.001
	HLM	0.610	0.535	0.695	0.040
Depression	OLS	0.785	0.730	0.845	< 0.001
	HLM	0.789	0.670	0.928	0.004
Diabetes with complications	OLS	0.764	0.668	0.873	< 0.001
	HLM	0.757	0.552	1.038	0.084
Diabetes without complications	OLS	0.913	0.861	0.968	< 0.001
	HLM	0.757	0.552	1.038	0.906
Drug abuse	OLS	0.271	0.668	0.873	< 0.001
	HLM	0.282	0.038	2.084	0.215
Fluid and electrolyte disorders	OLS	1.721	1.645	1.800	< 0.001
	HLM	1.786	1.602	1.991	< 0.001
Sex (female)	OLS	0.566	0.540	0.593	< 0.001
	HLM	0.557	0.503	0.616	< 0.001
Hypertension	OLS	0.718	0.685	0.752	< 0.001
	HLM	0.726	0.649	0.812	< 0.001
Hypothyroidism	OLS	0.976	0.923	1.033	0.412
	HLM	1.019	0.894	1.161	0.780
Liver disease	OLS	2.643	2.256	3.098	< 0.001
	HLM	2.794	1.935	4.032	< 0.001
Lymphoma	OLS	0.818	0.621	1.078	0.156
	HLM	0.847	0.452	1.587	0.603
Metastatic cancer	OLS	1.511	1.253	1.822	< 0.001
	HLM	1.579	1.045	2.385	< 0.001
Neurologic disorder	OLS	1.091	1.032	1.154	0.002
	HLM	1.112	0.974	1.270	< 0.001
Obesity	OLS	0.674	0.570	0.797	0.115
	HLM	0.730	0.499	1.068	0.105
Paralysis	OLS	1.494	1.309	1.704	< 0.001
	HLM	1.503	1.086	2.079	0.014
Peripheral vascular disorders	OLS	1.273	1.187	1.367	< 0.001
	HLM	1.371	1.156	1.627	< 0.001
Psychoses	OLS	0.931	0.819	1.057	0.272
	HLM	0.922	0.691	1.230	0.581
Pulmonary circulatory disorders	OLS	2.119	1.964	2.286	< 0.001
	HLM	2.306	1.933	2.751	< 0.001
Renal failure	OLS	1.638	1.551	1.729	< 0.001
	HLM	1.733	1.524	1.970	< 0.001
Rheumatoid arthritis and collagen vascular disease	OLS	0.769	0.662	0.892	0.001
	HLM	0.748	0.532	1.052	0.095
Solid tumor without metastasis	OLS	1.348	1.184	1.537	< 0.001
	HLM	1.328	1.000	1.763	0.06
Valvular disease	OLS	0.937	0.878	1.001	0.05
	HLM	0.986	0.843	1.154	0.861
Weight loss and nutritional deficiency	OLS	2.590	2.435	2.756	< 0.001
	HLM	2.744	2.352	3.200	<0.001

OLS, traditional regression model; HLM, traditional hierarchal model.
[a] Comorbidities that were overestimated in traditional regression models are outlined in red.

Discussion

The National Inpatient Sample (NIS) is commonly used in orthopaedic surgery outcomes-based research. The use of NIS data is particularly helpful in identifying national trends and evaluating rare outcomes.[2,66,88,114,122,128,139]

However, the large sample size obtained from NIS provides researchers with unique difficulties in interpreting study data.[5,27,34] Although many orthopaedic clinicians may not be overly interested in statistics, certain limitations in database research are important to consider when conducting associated studies.

One main difficulty in interpreting large databases is determining the significance of research outcomes. For many casual readers, a *P* value of 0.05 is used to determine the "significance" of findings. However, in large database projects, this simplified interpretation may lead readers to overestimate specific study findings. The large numbers of patients in database projects cause even small differences to be statistically significant, which may not actually represent a clinical significance. In the current study, a variety in α levels of significance was found among different authors who used NIS,[7-25] providing a "rule of thumb" to help guide clinicians in determining the significance of a study outcome for their own clinical practice.

In our own research using NIS, the HCUP (creators of NIS) recommended to use hierarchical linear modeling instead of traditional regression analysis.[5] However, we have rarely seen this type of analysis conducted in orthopaedic studies. This study was designed to better understand the recommendation from HCUP and the effect it would have on current studies conducted using NIS.

The result of the current study suggest that, in orthopaedic studies published between 2005 and 2014 that used NIS, only 2% used hierarchical modeling analysis. About 74% and 7% used traditional regression analysis and univariate statistics, respectively, which do not account for clustering in the dataset. Furthermore, these data suggest that traditional regression analysis overestimated study findings in 14% of comorbidities in the continuous variable of interest (length of stay) and in 25% of comorbidities in the dichotomous variable of interest (in-hospital mortality). Because most orthopaedic studies examine continual or dichotomous outcomes, between 14% to 25% of study variables may be overestimated in orthopaedic research when using traditional regression analysis. Furthermore, we found that 81% of studies used traditional regression analysis or univariate statistics (both of which do not account for clustering), suggesting that between 11% to 20% of orthopaedic studies published between 2005 and 2014 were at risk for overestimating the significance of results.

The current study has limitations that may affect the generalizability of our findings. First, we tested a specific population of orthopaedic patients. We identified this group to examine the effect of comorbidities on in-hospital mortality and length of stay in patients who underwent operative treatment of intertrochanteric hip fractures, which represents a commonly studied orthopaedic population experiencing osteoporotic fractures. However, this is a specific population, and the findings are specific to these patients. It may be that a study on different populations of patients would produce different results. Other authors have found similar results as in the current study, showing increased specificity with hierarchical linear modeling in other non-orthopaedic populations.[26,27] We believe, therefore, that our findings may have general application to all orthopaedic populations included in NIS.

Second, we categorized studies in the systematic review into six statistical groups. This was done to simplify the interpretation of 10 years of study results in 132 studies. In certain situations, this categorization may oversimplify the intended statistical analysis. We recognize that many ways exist to apply statistical principles in interpreting data. However, we believe this interpretation is an honest representation of traditional regression versus hierarchical linear modeling currently used by orthopaedic studies.

The findings of the current study echo the call from HCUP for additional hierarchical linear modeling analysis in orthopaedic research using NIS. Orthopaedic clinicians should be aware that study results from NIS should be interpreted with care. An interpretation of effect sizes and clinical relevance is essential in addition to simply looking at *P* values. One way to improve specificity would be for additional studies to use hierarchical linear modeling instead of traditional regression analysis. If we do so as an orthopaedic community, we may greatly increase the specificity of results and, therefore, the clinical applicability of findings.

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Conflict of Interest

The authors report no conflicts of interest.

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