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Unplanned readmission after carotid stenting versus endarterectomy: analysis of the United States Nationwide Readmissions Database

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ABSTRACT

Background Hospital readmissions are costly and reflect negatively on care delivered.

Objective To have a better understanding of unplanned readmissions after carotid revascularization, which might help to prevent them.

Methods The Nationwide Readmissions Database was used to determine rates and reasons for unplanned readmission following carotid endarterectomy (CEA) and carotid artery stenting (CAS). Trends were assessed by annual percent change, modified Poisson regression was used to estimate risk ratios (RR) for readmission, and propensity scores were used to match cohorts.

Results Analysis yielded 522 040 asymptomatic and 55 485 symptomatic admissions for carotid revascularization between 2010 and 2015. Higher 30-day readmission rates were noted after CAS versus CEA in both symptomatic (9.1% vs 7.7%, $p<0.001$) and asymptomatic (6.8% vs 5.7%, $p<0.001$) patients. Readmission rates trended lower over time, significantly so for 90-day readmissions in symptomatic patients undergoing CEA. The most common cause for 30-day readmission was stroke in both symptomatic (5.5%) and asymptomatic (3.9%) patients. Factors associated with a higher risk of readmission included age over 80; male gender; Medicaid health insurance; and increases in severity of illness, mortality risk, and comorbidity indices. Analysis of matched cohorts showed that CAS had higher readmission than CEA (RR=1.14 (95% CI 1.06 to 1.22); $p<0.001$) only in asymptomatic patients. Adverse events during initial admission which predicted 30-day readmission included acute renal failure and acute respiratory failure in asymptomatic patients; hematoma and cardiac events were additional predictive adverse events in symptomatic patients.

Conclusions Readmission is not uncommon after carotid revascularization, occurs more often after CAS, and is predicted by baseline factors and by preventable adverse events at initial admission.

INTRODUCTION

Hospital readmissions are increasingly used as a measure of healthcare quality.¹ Unplanned readmissions in surgical patients are viewed as an indicator of poor care and are associated with significant expenses to the healthcare system and to patients.² Consequently, readmission is a target of healthcare reform through the Hospital Readmissions Reduction Program,³ and the Center for Medicare and

Medicaid Services (CMS) may introduce penalties in the form of reduced reimbursement for centers with higher than expected readmission rates.⁴ Of all discharges following a surgical procedure, vascular surgery has the highest readmission rate of 23.9% as compared with 15.6% in the remaining procedures, underlining the importance of studying readmission after carotid revascularization to better understand rates and reasons for readmission.⁵ We therefore used the Nationwide Readmissions Database (NRD) to characterize the rate and causes of 30-day and 90-day unplanned readmissions after carotid endarterectomy (CEA) and stenting (CAS) for symptomatic and asymptomatic carotid stenosis, and analyzed preoperative and postoperative factors associated with readmissions in real-world practice across the United States.

METHODS

Database

The NRD contains all-payer data on hospital inpatient stays from states participating in the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality (AHRQ) and the US Department of Health and Human Services. The 2015 NRD contains all discharges from 27 states and 2367 hospitals, which are geographically dispersed, and account for 58% of the total US resident population and of all US hospitalizations.⁶ Annual NRD datasets from 2010 to 2015 were obtained from the HCUP Central Distributor (Rockville, Maryland, USA). To produce national estimates, discharge weights provided by the AHRQ website were used.⁷ HCUP databases lack unique patient identifiers, and therefore, are exempt from institutional review board review and informed consent under the Health Insurance Portability and Accountability Act.⁸

Patient selection, definitions, and endpoint variables

International Classification of Diseases, ninth Revision, clinical modification (ICD-9-CM) codes were used to define medical diagnoses and inpatient procedures as well as adverse events (online supplemental table 1). Since ICD-9 coding did not specify laterality, stroke complications necessarily included both. All adult patients diagnosed with symptomatic or asymptomatic CAS were included in the study. Treatment procedures were CEA or CAS, and

Ischemic stroke

patients with both procedure codes in the same admission were excluded from the analysis. For 30-day and 90-day readmission analyses, encounters discharged each year on or after December 1 and October 1, respectively, were excluded to ensure that all readmissions could be identified. Patients who died during the index admission, or with same-day readmissions to the same hospital, same-day transfers to another hospital, or elective readmissions were excluded from the readmission analyses. Patients with a 30-day readmission were included in the 90-day readmission analysis, and patients with multiple readmissions within a specified time period only had their first readmission analyzed. Relevant comorbidities, such as hypertension and diabetes, were included in the total number of comorbidities and analyzed using the Elixhauser Comorbidity Index score (min=0, max=29).⁹ The All Patient Refined Diagnosis Related Groups (APR-DRG) Classification System was used to classify the severity of illness and risk of mortality. Hospital size, teaching status, and city status were defined by the NRD. Reasons for readmissions were grouped as previously described.¹⁰

Propensity matching

To address potential confounding non-random differences between patients who underwent CEA versus CAS, we used propensity score matching to create two cohorts of patients in each diagnosis (symptomatic and asymptomatic) and readmission (30-day and 90-day) group who were matched on their propensity for undergoing CEA versus CAS. In this process, a logistic regression model was created in each of the four groups to estimate the likelihood of undergoing CEA (rather than CAS) using all patient (age group, sex, household income, health insurance, severity, and comorbidities) and hospital (size, ownership, location, and teaching status) characteristics as potential predictors. The logit coefficients from this model were then used to create a propensity score for each patient in each group, which ranged from 0 to 1 and represented the likelihood of undergoing CEA rather than CAS. We then performed nearest-neighbor matching (with a caliper distance of 0.05) with these propensity scores to create two evenly matched cohorts of CEA and CAS by a caliper-matching algorithm, in each of the four groups. Discharge weights were used in the matching process.

Statistical analysis

Student's t-test and χ^2 test were used in between-group comparisons for continuous and categorical variables, respectively. Trends were assessed over the entire time period by annual percent change (APC) estimates using Joinpoint Regression Program, version 4.6.0.0 (Statistical Methodology and Application Branch, Surveillance Research Program, National Cancer Institute).¹¹ Regression analysis was used to determine factors associated with 30-day and 90-day readmissions in matched cohorts. Modified Poisson regression was used instead of logistic regression to enable adjusted risk ratio (aRR) estimation with high precision for binary data.¹² Poisson regression was performed using generalized estimating equations and clustering at the hospital level on postprocedural adverse events (online supplemental table 1) and outcome (ie, non-routine discharge)¹³ in the index hospitalization. Propensity score matching and statistical analysis were performed using the software R, version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) and MatchIt¹⁴ package for R and using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, New York, USA), respectively. A p value of <0.05 was defined as statistically significant. Data are presented as mean $\pm$ SD and 95% confidence intervals (CIs) are presented in brackets unless otherwise specified.

Figure 1 Readmission rates after CEA or CAS in asymptomatic and symptomatic patients. CAS=carotid artery stenting; CEA=carotid endarterectomy.

RESULTS

We identified a total of 522 040 asymptomatic (mean (SD) age 69.8 (12.5), 58.8% male) and 55 485 symptomatic (mean (SD) age 71.3 (9.6), 62.4% male) patients with carotid artery stenosis who were admitted and treated between 2010 and 2015. Among admissions for asymptomatic stenosis, 460 811 (88.3%) underwent CEA and 61 229 (11.7%) underwent CAS. In the symptomatic group, 44 766 (80.7%) underwent CEA and 10 719 (19.3%) underwent CAS. Baseline demographics and characteristics of the study population are shown in online supplemental table 2.

Readmission rates

In the asymptomatic cohort, 520 610 patients were discharged alive. Of those eligible for readmission analysis, 28 336 (5.8%) were readmitted within 30 days and 41 042 (10.0%) were readmitted within 90 days of their initial hospitalization. Asymptomatic patients who underwent CAS had significantly higher 30-day (6.8% (95% CI 6.5% to 7.0%) vs 5.7% (95% CI 5.6% to 5.8%); $p<0.001$) and 90-day (12.2% (95% CI 11.8% to 12.5%) vs 9.7% (95% CI 9.6% to 9.8%); $p<0.001$) readmission rates than patients who underwent CEA (figure 1). In the symptomatic cohort, 54 704 patients were discharged alive. Of those eligible for readmission analysis, 40 47 (8.0%) patients were readmitted within 30 days and 5833 (13.6%) patients were readmitted within 90 days of their initial hospitalization. Symptomatic patients who underwent CAS had significantly higher 30-day (9.1% (95% CI 8.5% to 9.7%) vs 7.7% (95% CI 7.4% to 8.0%); $p<0.001$) and 90-day (17.0% (95% CI 16.1% to 17.9%) vs 12.8% (95% CI 12.4% to 13.2%); $p<0.001$) readmission rate than patients who underwent CEA (figure 1). There was a trend towards declining 30-day and 90-day readmissions after CEA or CAS in both symptomatic and asymptomatic patients during the study period (figure 2), but this was significant only in 90-day readmissions after CEA for symptomatic stenosis where the readmission rate declined from 13.7% in 2010 to 11.5% in 2015 (APC=−3.12 (95% CI −4.46 to −1.76); $p<0.001$).

Reasons and risk ratios for readmission in asymptomatic patients

Using ICD-9-CM coding, the most frequent reasons for 30-day and 90-day readmissions after asymptomatic carotid revascularization were cerebral artery occlusion with infarct of any laterality (3.9%, 3.5%), myocardial infarction (3.7%, 3.5%), hematoma (3.5%, 2.0%), transient ischemic attack (2.9%,

Figure 2 Trends in readmission rates (A, B) and APC (C, D) from 2010 to 2015 in asymptomatic and symptomatic patients. APC=annual percent change; CAS=carotid artery stenting; CEA=carotid endarterectomy. * $p<0.001$, for all other APCs $p>0.05$.

2.7%), septicemia (2.9%, 3.0%), pneumonia (2.9%, 3.0%), carotid artery stenosis/occlusion without infarction (2.8%, 4.0%) and acute kidney failure (2.1%, 2.4%), respectively. Categorized groups of reasons for readmissions after asymptomatic carotid revascularization are presented in figure 3 and online supplemental figure 1. Asymptomatic patients undergoing CAS had a higher adjusted risk of non-elective 30-day (aRR=1.10 (95% CI 1.06 to 1.14); $p<0.001$) and 90-day (aRR=1.17 (95% CI 1.14 to 1.20); $p<0.001$) readmission than patients having CEA (online supplemental figures 2 and 3), and unplanned carotid revascularization rates were higher after CAS than CEA within 30 days and 90 days (0.20% vs 0.16%, $p=0.04$; 0.50% vs 0.38%, $p<0.001$; respectively) (online supplemental figure 4). Risk of 30-day readmission was higher in patients aged 80 years or older (aRR=1.13 (95% CI 1.08 to 1.18); $p<0.001$), male patients (aRR=1.13 (95% CI 1.11 to 1.16); $p<0.001$), patients with Medicaid health insurance (aRR=1.22 (95% CI 1.14 to 1.3); $p<0.001$), patients with moderate (aRR=1.28 (95% CI 1.24 to 1.32); $p<0.001$), major (aRR=1.36 (95% CI

1.29 to 1.44); $p<0.001$), and extreme (aRR=1.49 (95% CI 1.33 to 1.67); $p<0.001$) APR-DRG mortality risk, patients with moderate (aRR=1.22 (95% CI 1.19 to 1.26); $p<0.001$), major (aRR=1.60 (95% CI 1.52 to 1.69); $p<0.001$), and extreme (aRR=2.27 (95% CI 2.02 to 2.55); $p<0.001$) APR-DRG severity, and patients with higher comorbidity score (aRR=1.11 (95% CI 1.11 to 1.12); $p<0.001$) (online supplemental figure 2). Furthermore, asymptomatic octogenarian and older patients had a significantly higher rate of readmission than younger patients after either CEA (7.2% vs 5.3% at 30 days; 12.2% vs 9.1% at 90 days; $p<0.001$ for both) or CAS (9.2% vs 6.1% at 30 days; 15.2% vs 11.4% at 90 days; $p<0.001$ for both).

Reasons and risk ratios for readmission in symptomatic patients

Using ICD-9-CM coding, the most frequent reasons for 30-day and 90-day readmissions after symptomatic carotid revascularization were cerebral artery occlusion with infarct of any laterality

Figure 3 Grouped categories tabulating proportion of causes of readmission for asymptomatic stenosis (left) and symptomatic stenosis (right). CAS=carotid artery stenting; CEA=carotid endarterectomy; DVT=deep vein thrombosis; ENT=ear, nose, and throat; GI=gastrointestinal; GU=genitourinary; PE=pulmonary embolism.

(5.5%, 4.7%), septicemia (4.3%, 4.2%), transient ischemic attack (3%, 3.5%), myocardial infarction (2.9%, 2.5%), pneumonia (2.6%, 2.7%), carotid artery stenosis/occlusion without infarction (2.4%, 3.4%), and acute kidney failure (2.4%, 2.6%), respectively. Categorized groups of reasons for readmissions after symptomatic carotid revascularization are presented in figure 3 and online supplemental figure 1. Although the adjusted risk of readmission was not significantly different between symptomatic patients undergoing CEA versus CAS at 30 days (online supplemental figure 2), it was significantly higher at 90 days for patients undergoing CAS (aRR=1.13 (95% CI 1.06 to 1.2); $p<0.001$) (online supplemental figure 3). However, there were no significant differences in unplanned revascularization rates after CEA or CAS within 30 and 90 days (online supplemental figure 4). Risk of 30-day readmission was higher in patients aged 80 years or older (aRR=1.17 (95% CI 1.04 to 1.31); $p=0.009$), male patients (aRR=1.15 (95% CI 1.08 to 1.22); $p<0.001$), patients with Medicaid health insurance (aRR=1.25 (95% CI 1.08 to 1.43); $p=0.002$), patients with moderate (aRR=1.28 (95% CI 1.10 to 1.49); $p=0.001$), major (aRR=1.73 (95% CI 1.46 to 2.05); $p<0.001$), and extreme (aRR=1.54 (95% CI 1.24 to 1.93); $p<0.001$) APR-DRG mortality risk, patients with moderate (aRR=1.19 (95% CI 1.01 to 1.40); $p=0.03$), major (aRR=1.39 (95% CI 1.17 to 1.65); $p<0.001$), and extreme (aRR=2.14 (95% CI 1.71 to 2.69); $p<0.001$) APR-DRG severity, and patients with higher comorbidity score (aRR=1.11 (95% CI 1.09 to 1.12); $p<0.001$) (online supplemental figure 2). Furthermore, symptomatic octogenarian and older patients had a significantly higher rate of readmission than younger patients after either CEA (9.6% vs 7.2% at 30 days; 16.8% vs 11.8% at 90 days; $p<0.001$ for both) or CAS (10.3% vs 8.8% at 30 days; 18.4% vs 16.6% at 90 days; $p<0.001$ for both).

Postoperative adverse events and readmission after CEA versus CAS: propensity-matched asymptomatic patients

Propensity score matching was used to address potential confounding non-random differences between patients undergoing CEA versus CAS for asymptomatic stenosis, yielding 19 900 and 17 116 matched patients for 30-day and 90-day readmission analyses, respectively (online supplemental table 3). Univariable analysis after matching showed higher readmission rates after CAS at both 30 (RR=1.14 (95% CI 1.06 to 1.22); $p<0.001$) and 90 days (RR=1.19 (95% CI 1.13 to 1.26); $p<0.001$) in comparison with CEA. The risk ratio of readmission following adverse events and outcome at the index admission is presented

in figure 4. Specifically, in patients undergoing CEA, the risk of 30-day readmission was higher in those with acute renal failure (RR=2.39 (95% CI 1.84 to 3.10); $p<0.001$), acute respiratory failure (RR=1.77 (95% CI 1.25 to 2.50); $p=0.001$), cardiac events (RR=1.52 (95% CI 1.09 to 2.14); $p=0.02$), or non-routine discharge (RR=1.99 (95% CI 1.76 to 2.26); $p<0.001$) during their initial admission. In patients undergoing CAS, the risk of 30-day readmission was higher in those with acute renal failure (RR=2.10 (95% CI 1.63 to 2.70); $p<0.001$), acute respiratory failure (RR=2.69 (95% CI 1.70 to 4.24); $p<0.001$), and non-routine discharge (RR=2.15 (95% CI 1.90 to 2.44); $p<0.001$). Similar risks were found for readmission at 90 days (online supplemental figure 5).

Postoperative adverse events and readmission after CEA versus CAS: propensity-matched symptomatic patients

Propensity score matching yielded 3617 and 3054 matched symptomatic patients for 30-day and 90-day readmission analysis, respectively (online supplemental table 4). Univariable analysis after matching did not show any significant difference in readmission rate following CAS versus CEA, at both 30 and 90 days ($p=0.88$ and $p=0.09$, respectively). In patients, undergoing CEA, the risk of 30-day readmission was higher if patients had hematoma/hemorrhage (RR=1.67 (95% CI 1.18 to 2.37); $p=0.004$), acute renal failure (RR=1.80 (95% CI 1.40 to 2.31); $p<0.001$), acute respiratory failure (RR=1.86 (95% CI 1.39 to 2.48); $p<0.001$), cardiac events (RR=2.03 (95% CI 1.44 to 2.85); $p<0.001$), or non-routine discharge (RR=2.15 (95% CI 1.76 to 2.61); $p<0.001$) during their initial admission. In CAS patients, risk of 30-day readmission was higher if patients had hematoma/hemorrhage (RR=1.73 (95% CI 1.10 to 2.74); $p=0.02$), acute renal failure (RR=1.89 (95% CI 1.45 to 2.48); $p<0.001$), acute respiratory failure (RR=1.79 (95% CI 1.30 to 2.45); $p<0.001$), cardiac events (RR=2.09 (95% CI 1.49 to 2.92); $p<0.001$), or non-routine discharge (RR=2.08 (95% CI 1.70 to 2.54); $p<0.001$) (figure 4). Similar risks were found for readmission at 90 days (online supplemental figure 5).

DISCUSSION

Since CMS began publishing 30-day readmission data for selected disorders, hospital readmissions have become an important metric of quality of care, and higher than expected readmission rates can be associated with financial penalties.^{3 4} Readmissions following vascular intervention outnumber those following any

Figure 4 Postoperative adverse events or outcome at initial carotid revascularization and risk ratio of 30-day readmission. CAS=carotid artery stenting; CEA=carotid endarterectomy; CI=CI interval; DVT=deep vein thrombosis; PE=pulmonary embolism; RR=risk ratio.

other procedure type,⁵ and therefore a clear understanding of rates and reasons for readmission after carotid revascularization in real-world practice is important for all neurovascular practitioners. Using a nationally representative database spanning modern-era carotid revascularization, we show higher readmission rates after CAS than CEA in both symptomatic and asymptomatic patients, without significant improvement over time except in 90-day readmissions after CEA for symptomatic stenosis. This is concordant with smaller studies examining readmissions in Medicare beneficiaries,^{15 16} although other authors have found CAS to have similar¹⁷ or lower¹⁸ readmissions when examining single-state or smaller commercial databases. Our data are unique in comparison with the handful of prior analyses^{19–22} in that we used the largest available nationally representative database, analyzed all patients irrespective of age, excluded planned readmissions, distinguished contributors to readmission across multiple steps in the care pathway, and examined symptomatic and asymptomatic patients separately. This last point is important since symptomatic and asymptomatic patients are very different populations, with differing natural history of disease and treatment recommendations based on distinct randomized trial data.²³ It is interesting that CAS, a less invasive procedure, is associated with a higher unadjusted readmission rate in both symptomatic and asymptomatic patients. However, this higher readmission rate may reflect inherent selection bias as patients undergoing CAS often have higher comorbidities.²⁴ Accordingly, both multivariate analysis and propensity matching largely nullified differences in readmission rates between CAS and CEA in symptomatic patients in our data, although higher rates and risk ratios of readmission after CAS persisted in asymptomatic patients.

While noting differences in readmission rates between CEA and CAS is important, this distinction is less likely to influence daily practice than the ability to predict and potentially prevent such readmissions. We therefore analyzed the reasons and risks for readmission after each of these two procedures at three distinguishable clinical stages: preoperative characteristics at baseline, postoperative adverse events and outcomes, and diagnoses underlying the subsequent readmission. When examining baseline characteristics, we found a significantly higher risk ratio for readmission in octogenarian and older patients, male patients, patients on Medicaid, and patients with higher APR-DRG mortality, APR-DRG severity of illness, and Elixhauser Comorbidity Index scores, largely in agreement with previous smaller studies^{17 18 24 25} as well as studies restricted to Medicare beneficiaries.^{15 16} Our data would therefore suggest that for prevention of readmission, targeting octogenarian and older patients, those with higher comorbidities, and patients on Medicaid might be a worthwhile strategy, although evidence for preadmission intervention in surgical patients remains sparse.²⁶

We then examined adverse events and outcomes during the initial admission for revascularization that might predict a higher risk for readmission. We identified acute renal failure, acute respiratory failure, and non-routine discharge as predictors for readmission after both CAS and CEA in asymptomatic patients; in symptomatic patients, hematoma and cardiac events were additional adverse events that predicted readmission. Other authors have similarly noted that renal and cardiac complications, postoperative hematoma, and non-routine discharge are associated with a higher readmission rate after carotid revascularization.^{16–18} These imply practical targets exist for prevention of readmission after both CAS and CEA. For example, perioperative β blocker use is associated with improved outcomes after CAS,²⁷ and use of protamine has been shown to improve bleeding

complications after both CEA²⁸ and CAS²⁹ without increasing myocardial infarction, stroke, death, or thromboembolic events.

Lastly, we tabulated readmission diagnoses, finding that stroke was the most frequent cause of readmission after carotid revascularization. This is concordant with other authors' findings when examining patients of all ages in a large commercial US hospital-based, all-payer database¹⁸ and in a state-wide database of hospital and surgical facility discharges in Pennsylvania¹⁷; in the Medicare population, cardiac complications appear to outweigh stroke as a reason for readmission after carotid revascularization.^{15 16} A potential strategy to target readmissions after carotid revascularization may therefore be to improve compliance with post-discharge medical management. For example, investigators for the Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2) have found poor compliance with hypertension management guidelines,³⁰ and others have similarly found suboptimal compliance with statin³¹ and antiplatelet³² use in patients with carotid stenosis.

An important implication of our data relates to CMS policies, which continue to restrict reimbursement of CAS to patients at high risk for CEA who have either (a) $\geq 70\%$ symptomatic stenosis, (b) 50–70% symptomatic stenosis, or (c) $\geq 80\%$ asymptomatic stenosis; with the last two categories reimbursed only if performed within designated clinical trials or post-approval studies.³³ This has led to continued controversy over calls for expansion of routine CMS coverage to include standard and low-risk patients and/or those treated outside of trials.^{34–36} Given CMS' focus on reducing costs associated with readmissions,^{3 4} proponents of such an expansion would probably need to show at least equivalence between CEA and CAS readmission rates. However, our data demonstrate higher unadjusted readmission rates after CAS in both symptomatic and asymptomatic NRD cohorts; and while propensity-matched analysis found higher readmission rates after CAS only in asymptomatic patients, this group of patients was nearly an order of magnitude larger than those treated for symptomatic stenosis during the study period.

Our data and analysis have several limitations. The NRD is a retrospective administrative database without the granularity required to comprehensively assess underlying reasons behind the choice of revascularization procedures and their associated inpatient complications. For example, ICD-9 coding did not permit distinction between ipsilateral and contralateral strokes, hence stroke complications were analyzed in aggregate. However, the NRD is likely to be a better representation of real-world practice than randomized trials (which typically enroll highly selected centers and patients) or registries and selected case series that are subject to publication bias. Our analysis does not include data from 2016 onward owing to changes in NRD methodology, which limits our ability to assess the impact of newer iterations of endovascular devices.

CONCLUSION

Readmission is not uncommon after carotid revascularization in the United States, occurs most commonly due to stroke, and is more frequent after CAS in both symptomatic and asymptomatic patients. These differences are less apparent in symptomatic patients across matched cohorts or after adjusting for patient and hospital characteristics, but persist in asymptomatic patients. Importantly, readmission is predicted in both asymptomatic and symptomatic patients, after either CEA or CAS, by a small subset of patient and hospital characteristics and by several potentially preventable adverse events during the initial revascularization admission.

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Contributors All authors contributed to the presented work by substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work and drafting the manuscript or revising it critically for important intellectual content and final approval of the version to be published. BSJ serves as the guarantor and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Patient consent for publication Not applicable.

Ethics approval Healthcare Cost and Utilization Project databases lack unique patient identifiers, and therefore, are exempt from institutional review board review and informed consent under the Health Insurance Portability and Accountability Act (see Methods section).

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