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ABSTRACT

Objectives: While multiple studies have demonstrated variations in the quality of cancer-care in the U.S., payers are increasingly assessing structure-and process-level measures to promote quality improvement. Hospital-acquired-adverse events are one such measure and we examine their national trends after major cancer surgery.

Design: Retrospective, cross-sectional analysis of a weighted-national estimate from the Nationwide Inpatient Sample undergoing major oncological procedures (colectomy, cystectomy, esophagectomy, gastrectomy, hysterectomy, lung resection, pancreatectomy and prostatectomy). The Agency for Healthcare Research and Quality Patient Safety Indicators (PSIs) were utilized to identify trends in hospital-acquired-adverse events.

Setting: Secondary and tertiary care, U.S. hospitals in the Nationwide Inpatient Sample (NIS)

Participants: A weighted-national estimate of 2,508,917 patients (>18 years, 1999-2009) from the NIS.

Primary outcome measures: Hospital-acquired-adverse events.

Results: 324,852 patients experienced ≥1-PSI event (12.9%). Patients with ≥1-PSI experienced higher-rates of in-hospital mortality (OR: 19.38, 95% CI: 18.44-20.37), prolonged length-of-stay (OR: 4.43, 95%CI: 4.31-4.54) and excessive hospital-charges (OR: 5.21, 95%CI: 5.10-5.32). Patients treated at lower-volume hospitals experienced both higher PSI-events *and* failure-to-rescue rates. While a steady increase in the frequency of PSI-events after major cancer surgery has

occurred over the last 10 years (estimated annual % change-EAPC: 3.5%, $p<0.001$), a concomitant decrease in failure-to-rescue rates (EAPC: -3.01%) and overall mortality (EAPC: -2.30%) was noted. (All $p<0.001$)

Conclusions: Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable adverse-events after major cancer surgery, with a detrimental effect on numerous outcome-level measures. However, there was a concomitant reduction in failure-to-rescue rates and overall-mortality rates. Policy changes to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcers and respiratory failure, are required.

Article summary

Article focus

- Variations in the quality of surgical oncology care in the U.S. remain unclear.
- Payers are increasingly assessing structure-and process-level measures to promote quality improvement.
- Hospital-acquired-adverse events are one such measure and we examine their national trends after major cancer surgery.

Key messages

- Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable adverse-events after major cancer surgery but there was also a concomitant reduction in failure-to-rescue rates and overall-mortality rates.
- Patients treated at lower-volume hospitals experienced both higher frequency of potentially avoidable adverse-events *and* failure-to-rescue rates.
- Policy changes to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcers and respiratory failure, are required.

Strength and limitations of this study

- This is the largest study to assess the quality of oncologic surgical care in a nationally representative cohort of U.S. patients.
- Validated Agency for Healthcare Research and Quality Patient Safety Indicators (PSIs) were utilized to identify trends in hospital-acquired-adverse events.
- Inherent to retrospective analyses of large administrative datasets, this study is limited by potential biases due to case-mix and miscoding.
- While PSIs have been shown to perform well as screening tools from an epidemiologic perspective (over-identification and few false-negatives), concerns related to high false-positive rates exist.

INTRODUCTION

There has been much interest in assessing the downstream effects and complexities of the contemporary delivery of health care. However, observational studies examining preventable adverse events are confounded by the loss of information when administrative data are abstracted from patient records. Recently, several initiatives have been directed to improve consistency, relevance and fidelity in the process of transforming clinical data into administrative datasets and subsequent practice-changing results. Following a landmark study by Iezzoni *et al*[1] on computerized algorithms to identify quality of care disparities in administrative datasets, the Agency for Healthcare Research and Quality (AHRQ) developed a standardized system for accrual and reporting of unintended hospital-acquired adverse events, termed patient safety indicators (PSI)[2]. Subsequently, Zhan *et al*[3] examined the relationship between multiple process-, setting- and outcome-level measures and adverse events identified using the AHRQ's PSI system, and reported substantial but variable effects on the health care system.

Nonetheless, there is a paucity of studies evaluating the burden of preventable adverse events and this is particularly true for major surgical oncology care in the United States. Multiple studies have demonstrated that significant variation exists in cancer incidence rates[4] and in access to quality cancer care[5 6], but variations in the actual *quality* of surgical oncology care remain unclear.

Hence, we undertook a national assessment of the quality of major surgical oncology care within a standardized framework of preventable adverse events to

examine trends in patient safety within the United States. We also evaluate the prevailing hypothesis[7-9] explaining the volume-complication-mortality relationship, which states that higher mortality rates for patients undergoing surgery at low-volume hospitals is preferentially explained by higher failure-to-rescue rates (i.e. mortality after a hospital-acquired adverse event), rather than a higher incidence of such adverse events in the first place.

METHODS

Data source

The Nationwide Inpatient Sample (NIS) consists of an array of longitudinal hospital inpatients datasets as part of the Healthcare Cost and Utilization Project (HCUP). It was established by the Agency for Healthcare Research and Quality and functions through a Federal-state affiliation. It is the largest publicly accessible all-payer inpatient database[10]. The database consists of discharge information from 8 million inpatient visits and patients covered by multiple insurance types (including Medicare, Medicaid, private insurance and uninsured patients) are represented.

Study cohort

We relied on hospital discharges for patients undergoing one of eight major cancer surgeries in the United States between 1999-2009. The major oncological surgeries consisted of colectomy, cystectomy, esophagectomy, gastrectomy, hysterectomy, pneumonectomy/lobectomy, pancreatectomy, and prostatectomy. Oncological indications were selected based on ICD-9-CM diagnostic codes. These particular procedures were chosen based on procedure volume and care was taken to include cancer surgeries involving different organ systems across a range of surgical specialties.

Patient and Hospital information

Patient characteristics evaluated included age at inpatient hospitalization, race, gender, insurance characteristics and comorbidities. Regarding race, patients were classified as White, Black, Hispanic and Other (Asian or Pacific Islander, Native American). Regarding insurance characteristics patients were categorized based on the primary payer: Medicare, Medicaid, Private insurance (Blue Cross, commercial carriers, private HMO's and PPO's), and other insurance types (including uninsured patients). Charlson Comorbidity index (CCI) was derived according to Charlson *et al*[11], and adapted according to the previously defined methodology of Deyo and colleagues[12]. Median household income of the patient's ZIP code of residence, as derived from the US Census, was used as to define socioeconomic status and patients were divided into quartiles: <25,000$, 25,000$–34,999$, 35,000$–44,999$, and ≥45,000$. Hospital information examined included hospital location (urban vs. rural) and region (Northeast, Midwest, South and West), as defined by the United States Census Bureau[13] and academic teaching status as derived from the AHA Annual Survey of Hospitals. Hospital volume was categorized into volume quartiles as previously described[14].

Primary Outcomes

The Agency for Healthcare Research and Quality (AHRQ) Patient Safety Indicators (PSIs) were used to identify potentially preventable hospital-acquired adverse events. For the PSI project, AHRQ commissioned experts from the Evidence based Practice Center at the University of California San Francisco and Stanford University and from the University of California Davis to evaluate the

existing literature and help develop an evidence-based approach for improving patient safety[2]. The objective of this project was to facilitate the identification, quantification and reporting of preventable hospital-acquired adverse events from routinely collected administrative information. The process of identification of PSI included initial literature analysis of previously reported patient safety problems, organized peer review of chosen PSIs, structured review of ICD-9 codes for each PSI and finally empirical analysis of each PSI, and feedback from multidisciplinary teams (physicians and specialists, nurses, pharmacists and coding and experts)[2]. The complete set of PSIs utilized is displayed in **Table e1** and is available on the AHRQ website[15]. The list includes various preventable adverse events that have been shown to have reasonable accuracy and validity as indicators for enhancing quality improvement and patient safety.

Statistical Analysis

Proportions, frequencies, means, medians, standard deviation, and interquartile ranges were obtained for each variable. National trends in the frequency of PSI-events, failure-to-rescue (defined as mortality after a PSI-event), and in-hospital mortality were also analyzed as the estimated annual percentage change (EAPC), based on the linear regression methodology described by Anderson *et al*[16]. Logistic regression models were used to examine predictors of PSI events, and to examine the effect of PSI events on multiple outcomes level measures, including in-hospital mortality, excessive charges (≥75th percentile of inflation adjusted charges for each individual procedure) and prolonged length of stay

(≥75th percentile of each individual procedure). Subsequently, we examined the volume-complication-mortality relationship in overall and procedure-specific analyses to study the relationship between mortality at low volume hospitals and failure-to-rescue rates. Generalized estimating equations were used in each multivariable analysis to adjust for clustering among hospitals[17]. All analyses were two-sided, significance was defined as $P<0.05$ and were performed using the R statistical package (R foundation for Statistical Computing, version 2.15.1).

RESULTS

The baseline demographic characteristics of our cohort of patients >18 years old undergoing one of eight major cancer procedures in the United States between 1999-2009 (n=2,508,917) is shown in **Table 1**. A weighted estimate of 324,852 patients experienced ≥ 1-PSI event (12.9%). Patients with ≥ 1-PSI event were more likely to be older, be female, have higher CCI, participate in Medicare, have lower socioeconomic status, and be treated at lower volume non-academic hospitals when compared to patients who did not experience any hospital-acquired preventable adverse events.

The national trends in PSI rates, overall mortality rates and failure-to-rescue rates in patients undergoing major cancer surgery in the United States are depicted in **Figure 1**. While a steady increase in the frequency of PSI-events after major cancer surgery has occurred over the last 10 years (estimated annual % change-EAPC: 3.5%; 95% Confidence Interval-95% CI: 2.8% to 4.1%; P<0.001), a concomitant decrease in failure-to-rescue rates (EAPC: -3.0%; 95% CI: -3.4% to -2.6%; P<0.001) and overall mortality (EAPC: -2.3%; 95% CI: -2.7% to -1.9%; P<0.001) was noted.

While there was a significant increase in overall PSI event rates over the course of the study, substantial heterogeneity was noted in terms of individual PSIs (**Figure 2)**. Substantial increases were noted in the annual incidence of postoperative sepsis (EAPC: 14.1%, 95% CI: 12.0% to 16.2%; P<0.001), pressure ulcer (EAPC: 13.4%, 95% CI: 10.2% to 16.6%; P<0.001) and respiratory failure (EAPC: 5.6%, 95% CI: 4.8% to 6.4%; P<0.001), while

significant advances were made in the prevention of anesthetic complications (EAPC: -17.5%, 95% CI: -27.6% to -7.5%; P=0.008), hip fractures (EAPC: -8.9%, 95% CI: -13.6% to -4.3%; P=0.005) and transfusion reactions (EAPC: -7.9%, 95% CI: -13.1% to -2.8%; P=0.001) in the perioperative period.

Results of a multivariable logistic regression model predicting the odds of ≥ 1-PSI event after major cancer surgery are shown in **Table 2**. These factors included: female gender (vs. male, odds ratio-OR: 0.88, 95% confidence interval-CI: 0.86-0.90; P<0.001), Black race (vs. Caucasians OR: 1.17, 95%CI: 1.13-1.21; P<0.001), higher Charlson comorbidity index (≥3 vs. 0, OR: 1.38, 95%CI: 1.34-1.42; P<0.001), Medicaid (OR: 1.45, 95%CI: 1.39-1.52) and Medicare insurance (OR: 1.16, 95%CI: 1.13-1.19; P<0.001), lower median household income (4^{th} quartile vs. 1^{st} quartile, OR-0.92, 95%CI: 0.89-0.95; P<0.001) and surgeries at lower volume hospitals (4^{th} quartile vs. 1^{st} quartile, OR: 0.76, 95%CI: 0.74-0.78; P<0.001).

The occurrence of ≥ 1-PSI event had significant multivariable effects on specific outcome-level measures after major cancer surgery (**Table 3)**. Patients who suffered from ≥ 1-PSI event experienced higher rates of in-hospital mortality (OR: 19.38, 95% CI: 18.44-20.37), prolonged length of stay (OR: 4.43, 95%CI: 4.31-4.54) and excessive hospital charges (OR: 5.21, 95%CI: 5.10-5.32).

We also assessed the effect of hospital volume on the incidence of PSIs and failure-to-rescue (**Table 4)**. In the overall analysis of patients undergoing any of the eight procedures, very high-volume hospitals (4^{th} quartile) had both lower PSI event rate *and* lower failure-to-rescue rates. However, this relationship was

procedure-specific: for colectomy, esophagectomy, lung resection, pancreatectomy, and prostatectomy, very high-volume hospitals had both lower PSI event rates *and* lower failure-to-rescue rates. For gastrectomy, very high-volume hospitals did not have lower PSI event rates but did have lower failure-to-rescue rates; for hysterectomy very high-volume hospitals had *higher* PSI event rates, but had lower failure-to-rescue rates; for cystectomy very high volume-hospitals had lower PSI event rates and a trend toward lower failure-to-rescue rates.

DISCUSSION

Recently, it has been estimated that the annual cost of medical errors is over 17 billion dollars[18] and there have been a slew of newer initiatives over the last decade to incentivize better quality care. In 2008, Medicare announced that it would restrain the ability of hospitals to get reimbursed for 'reasonably preventable events': avoidable medical errors ranging from pressure ulcers, falls and transfusion of incompatible blood to anesthetic complications, deep vein thrombosis and foreign bodies left in the body of patients during surgery. These and other initiatives are designed to place the burden of responsibility for such hospital-acquired adverse events squarely on hospitals and physicians[19]. While these initiatives have been met with stiff objection from hospital administrations, the Centers for Medicaid and Medicare Services (CMS) has been consistent in its position that accountability for such events should rest with hospitals and not with the taxpayer[19]. The Affordable Care Act of 2010 has added newer dimensions to these quality-improvement initiatives, with reimbursement likely to be dependent on both adherence to standards of care and the perceptions of patients with regard to hospital performance as measured by surveys[20].

A rational approach to improving accountability for substandard care should begin with identifying the true burden of hospital-acquired adverse events. This would be particularly useful in identifying specific adverse events that warrant special attention by payers like CMS and in preferential allocation of resources by hospitals due to the growing temporal burden of such events.

In the current study, we report contemporary trends in the frequency of hospital-acquired adverse events after major surgical oncology care in the United States. Our study has a number of novel findings. First, we report a gradual increase in the national frequency of hospital-acquired adverse events after major cancer surgery over the last decade. This is important as it represents a decline, albeit small and gradual, in the quality of surgical oncology care at the national level, as measured by the primary prevention of PSI events. Second, a simultaneous decrease in failure-to-rescue rates were observed and may indicate that while primary prevention of hospital-acquired adverse events has deteriorated, early recognition and timely management of these complications may have improved in the last decade. These findings may explain the significant annual reduction in mortality for patients undergoing major cancer surgery. Nonetheless, alternate explanations include refinements in coding practices, which may have led to better recognition and recording of non-lethal adverse events, thereby resulting in an apparent decrease in mortality rates. Third, significant heterogeneity in the temporal dynamics of specific hospital-acquired adverse events was noted. While marked and worrisome increases were recorded in the frequency of postoperative sepsis, pressure ulcers and respiratory failure, advances were made in the prevention of anesthetic complications, transfusion-related complications and hip fractures. Thus we identify numerous setting- and process-level measures where resources need to be refocused for further improvement in the quality of surgical oncology care.

We also examined the volume-complication-mortality dynamic in patients undergoing major cancer surgery, as it applies to potentially preventable hospital acquired adverse events (PSI). There is a well-established body of evidence describing the volume-mortality relationship in patients undergoing major cancer procedures and other surgeries. Dudley *et al*[21] examined patients undergoing one of eleven diverse procedures (ranging from coronary angioplasty to esophageal cancer surgery) in California and concluded that 602 deaths could be prevented annually by transferring patients from low-volume to high-volume hospitals. Birkmeyer *et al*[22] reported that Medicare patients treated at very high-volume hospitals experienced up to a 12 percent difference in absolute mortality for certain procedures relative to patients treated at very low-volume hospitals. However, the underlying mechanisms explaining the volume-mortality relationship have not been elucidated clearly. Silber *et al*[23] first introduced the concept of 'failure-to-rescue' in a seminal report that evaluated patients undergoing cholecystectomy or transurethral prostatectomy. They concluded that overall mortality was related to both hospital-level and patient-level factors, while adverse events were related to patient-level factors at admission (severity of illness). However, failure-to-rescue was preferentially associated with hospital-level factors and thus the underlying dynamics for failure-to-rescue were different than that for overall mortality and adverse events. The current hypothesis[7] regarding the volume-complication-mortality relationship is that lower volume hospitals experience higher mortality rates not because of higher complication rates, but due to lower failure-to-rescue rates. Ghaferi *et al*[9] demonstrated that high and low volume hospitals enrolled in the National Surgical Quality Improvement Program (NSQIP) had similar complication rates but different failure-to-rescue rates for multiple procedures. In a subsequent analysis[8] of patients undergoing gastrectomy, pancreatectomy or esophagectomy, similar results were demonstrated. However, in the current study, very high-volume hospitals (4th quartile vs. 1st quartile) had both lower PSI-event rates *and* lower failure-to-rescue rates. Importantly, the volume-complication-mortality relationship, as it applies to PSI events, appears to be procedure-specific and heterogeneous, with the current hypothesis not accounting for multiple individual major cancer surgeries, namely colectomy, esophagectomy, lung resection, pancreatectomy and prostatectomy. This is an important point: CMS currently focuses its quality-improvement initiatives on complication rates, and explicit demonstration that lower failure-to-rescue rates and not higher complication rates underlie the substandard care at low-volume hospitals may require a re-consideration of these initiatives. Our findings indicate that the prevailing hypothesis may need to be re-evaluated, at least for patients undergoing major cancer surgery. In fact, for patients undergoing hysterectomy, this relationship is reversed, with patients at very high-volume hospitals experiencing *higher* PSI event rates and lower failure-to-rescue rates. The underlying reason for this finding is not clear. Previous studies[24] have questioned the impact of hospital volume on hysterectomy outcomes and have reported that surgeon volume trumps hospital volume as the predominant factor underlying the volume-outcomes relationship for hysterectomy. While inclusion of surgeon volume may alter these findings, the higher rates of adverse events in patients undergoing hysterectomy at very high-volume hospitals may need to be re-examined in future reports.

Our study is not without limitations. The drawbacks of using administrative data are well known[25], including limitations regarding risk-adjustment and miscoding. While PSIs have been shown to perform well as screening tools from an epidemiologic perspective (over-identification and few false-negatives), problems related to high false-positive rates exist, with most validation studies reporting positive predictive values of between 43 to >90%[26 27]. While it is clear that these drawbacks limit the use of PSIs to make reimbursement decisions or to compare hospitals, it is unclear how it affects the implications of our study, where it was used as a screening tool to *identify* adverse events[26 27]. Secondly, morbidity and mortality events in the NIS are characterized based on the index admission, and subsequent readmissions, while relevant, are not recorded. This may have resulted in under-recognition of the true burden of adverse events, mortality and charges after the initial cancer surgery. Third: while the heterogeneity identified in the volume-complication-mortality relationship is a key finding in the present report, our study design does not allow for the identification of underlying mechanisms explaining these results. It is also important to emphasize that, in contrast to the previously cited studies where overall complication rates were examined, we evaluated potentially preventable hospital acquired events only. Previous investigators have shown that this restricted definition has limitations since not all deaths are accounted for in a given population sample[28];

alternatively, these drawbacks may not apply to studies focusing on patient safety using PSI as a quality of care measure. Hence, while it may not be illogical to expect lower volume hospitals to provide substandard care secondary to both higher rates of preventable adverse events *and* higher failure-to-rescue rates, it is certainly possible that a majority of hospital-acquired complications are an inevitable result of procedure complexity and patient comorbidities (and not just a failure of setting-level prevention measures). Consequently, while more rigorous patient care pathways might explain the lower incidence of preventable adverse events and subsequent mortality in higher volume hospitals, for the majority of (non-preventable) adverse events, the incidence rates would be the same regardless of hospital volume with lower failure-to-rescue rates preferentially explaining the low mortality rates of higher volume hospitals. Further investigation of these findings is required to test these possibilities and to fully understand the underlying dynamics of the volume-mortality relationship.

CONCLUSION

Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable hospital-acquired adverse events after major cancer surgery, with a detrimental effect on numerous outcome-level measures. However, there was a concomitant reduction in failure-to-rescue rates and, consequently, overall-mortality rates. Policy changes and resource re-allocation to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcer and respiratory failure, are required.

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FIGURE LEGENDS

FIGURE 1. National trends in Patient Safety Indicator (PSI) rates, overall mortality rates and failure-to-rescue rates in patients undergoing major cancer surgery (MCS) in the United States (1999-2009); EAPC-Estimated Annual Percent Change

FIGURE 2. National trends in individual Patient Safety Indicators over the study period (1999-2009) in patients undergoing major cancer surgery (MCS) in the United States

Table 1. Baseline characteristics of patients > 18 years undergoing major cancer surgery, Nationwide Inpatient Sample, 1999-2009.

Variables	Baseline characteristics			
	Overall (%)	Without PSI event (%)	With PSI event (%)	*P*
Weighted number of patients	2508917	2184065 (87.1)	324852 (12.9)	–
Age (years)				
Mean (SD)	65.9 (11.7)	65.4 (11.6)	69.5 (11.7)	<0.001[2]
Median (IQR)	66 (58,74)	65 (57,73)	71 (62,78)	
Gender				
Male	1511361 (60.3)	1331716 (61.1)	179645 (55.3)	<0.001
Female	993704 (39.7)	848527 (38.9)	145177 (44.7)	
Race				
Caucasian	1525021 (60.8)	1324373 (60.6)	200648 (61.8)	<0.001
Black	177986 (7.1)	154028 (7.1)	23958 (7.4)	
Hispanic	98532 (3.9)	86128 (3.9)	12404 (3.8)	
Other	93041 (3.7)	81492 (3.6)	11549 (3.6)	
Unknown	614337 (24.5)	76293 (23.5)	76293 (23.5)	
CCI				
0	1566723 (62.4)	1412545 (64.7)	154178 (47.5)	<0.001
1	623985 (24.9)	516640 (23.7)	107345 (33.0)	
2	127538 (5.1)	102276 (4.7)	25262 (7.8)	
≥3	190670 (7.6)	152603 (7.0)	38067 (11.7)	
Insurance status				
Private	1057919 (42.2)	968015 (44.3)	89904 (27.7)	<0.001
Medicaid	80666 (3.2)	66947 (3.1)	13719 (4.2)	
Medicare	1265920 (50.5)	1056618 (48.4)	209302 (64.4)	
Other	104412 (4.2)	92485 (4.2)	11927 (3.7)	
Median household income by ZIP code				<0.001
1-24,999	369796 (14.7)	313652 (14.4)	56144 (17.3)	
25,000-34,999	596202 (23.8)	513758 (23.5)	82444 (25.4)	
35,000-44,999	646869 (25.8)	563398 (25.8)	83471 (25.7)	
45,000+	842375 (33.6)	746499 (34.2)	95876 (29.5)	
Unknown	53672 (2.1)	46757 (2.1)	6915 (2.1)	
Annual hospital volume				
1st quartile	591675 (23.6)	510024 (23.4)	81651 (25.1)	<0.001
2nd quartile	640229 (25.5)	551980 (25.3)	88249 (27.2)	
3rd quartile	636482 (25.4)	554325 (25.4)	82157 (25.3)	
4th quartile	640531 (25.5)	567737 (26.0)	72794 (22.4)	
Hospital location				
Rural	268349 (10.7)	235606 (10.8)	32743 (10.1)	<0.001
Urban	2239651 (89.3)	1947705 (89.2)	291946 (89.9)	
Hospital region				
Northeast	526593 (21.)	458684 (21.0)	67909 (20.9)	<0.001
Midwest	608988 (24.3)	532951 (24.4)	76037 (23.4)	
South	8822566 (35.2)	762212 (34.9)	120354 (37.0)	
West	490770 (19.6)	430218 (19.7)	60552 (18.6)	
Hospital teaching status				
Non-teaching	1135065 (45.3)	979636 (44.9)	155429 (47.9)	
Teaching	1372935 (54.7)	1203675 (55.1)	169260 (52.1)	<0.001

[1] Multivariable logistic regression analysis adjusted for hospital clustering by generalized estimating equations
[2] Mann-Whitney test was performed.

Table 2. Multivariable logistic regression predicting occurrence of at least 1 patient safety indicator event

Variables	**Multivariable predictors of ≥ 1 PSI event**[1]	
	OR (95% CI)	***P***
Weighted number of patients		
Age (years)	1.018 (1.017 - 1.019)	<0.001
Gender		
Male	1.0 (ref.)	–
Female	0.878 (0.862 - 0.895)	<0.001
Race		
Caucasian	1.0 (ref.)	–
Black	1.172 (1.132 - 1.213)	<0.001
Hispanic	0.973 (0.930 - 1.019)	0.245
Other	0.938 (0.895 - 0.983)	0.008
Unknown	1.010 (0.988 - 1.033)	0.366
CCI		
0	1.0 (ref.)	–
1	1.227 (1.203 - 1.252)	<0.001
2	1.188 (1.147 - 1.230)	<0.001
≥3	1.377 (1.336 - 1.419)	<0.001
Insurance status		
Private	1.0 (ref.)	–
Medicaid	1.454 (1.388 - 1.523)	<0.001
Medicare	1.155 (1.127 - 1.185)	<0.001
Other	1.127 (1.075 - 1.181)	<0.001
Median household income by ZIP code		
1-24,999	1.0 (ref.)	–
25,000-34,999	0.986 (0.959 - 1.013)	0.305
35,000-44,999	0.960 (0.934 - 0.987)	0.004
45,000+	0.920 (0.894 - 0.946)	<0.001
Unknown	1.003 (0.943 - 1.067)	0.929
Annual hospital volume		
1st quartile	1.0 (ref.)	–
2nd quartile	0.945 (0.922 - 0.969)	<0.001
3rd quartile	0.883 (0.860 - 0.907)	<0.001
4th quartile	0.761 (0.739 - 0.783)	<0.001
Hospital location		
Rural	1.0 (ref.)	–
Urban	1.236 (1.198 - 1.275)	<0.001
Hospital region		
Northeast	1.0 (ref.)	–
Midwest	0.991 (0.964 - 1.019)	0.541
South	1.049 (1.024 - 1.075)	<0.001
West	1.018 (0.989 - 1.047)	0.229
Hospital teaching status		
Non-teaching	1.0 (ref.)	–
Teaching	0.972 (0.952 - 0.992)	0.007

[1]Other predictors included procedure type [colectomy-ref; cystectomy (OR: 1.51, 95%CI: 1.45-1.57), esophagectomy(OR:5.16, 95%CI:4.81-5.54), gastrectomy(OR:2.01, 95%CI:1.93-2.09), hysterectomy(OR:0.56, 95%CI:0.54-0.58), lung resection(OR:2.44, 95%CI:2.39-2.50), pancreatectomy(OR:1.79, 95%CI:1.71-1.88),prostatectomy(OR:0.26, 95%CI:0.25-0.27)] and year of surgery (OR: 1.037, 95%CI: 1.034-1.040). All P<0.001. OR-Odds ratio. CI: confidence interval

Table 3. Multivariable effects of ≥ 1 Patient safety indicator events on in-hospital mortality, prolonged length of stay and excessive hospital charges in patients undergoing major cancer surgery in the United States between 1999-2009.

Variables	**≥ 1 Patient safety indicator vs. no PSI**	
	OR (95% CI)**	***P***
In-hospital mortality (n=51312)*	19.380 (18.439 - 20.368)	<0.001
Prolonged length of stay (n=888220)	4.426 (4.313 - 4.542)	<0.001
Excessive hospital charges (n=609128)	5.207 (5.097 - 5.319)	<0.001

* 1457 patients with missing in-hospital mortality data.

** Each of these effects was derived from individual multivariable logistic regression models adjusted for hospital clustering, procedure type, age, gender, race, CCI, insurance status, socioeconomic status, year of admission, hospital location, hospital region, hospital volume quartiles and institutional academic status.

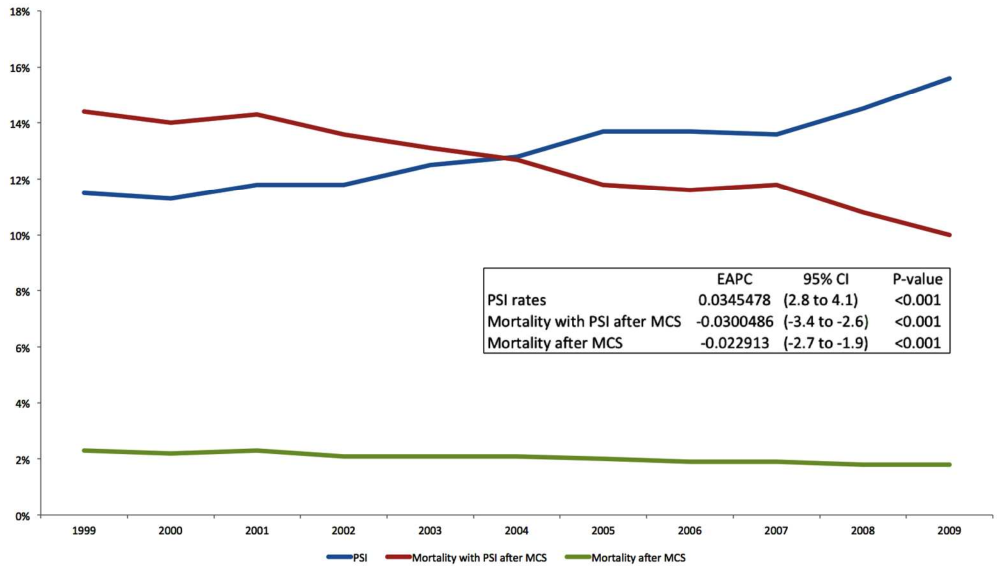
Legend. OR: odds ratio, CI: confidence interval, PSI: patient safety indicator; CCI: Charlson comorbidity index.

Table 4. Impact of hospital volume effect on patient safety indicator event occurrence and on failure to rescue (death after patient safety indicator event) from individual multivariable logistic regression models adjusted for hospital clustering by generalized estimating equation in patients undergoing major cancer surgery, Nationwide Inpatient Sample, 1999-2009.

Procedure	Patient safety indicator occurrence		Failure to rescue	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Overall				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.945 (0.922 - 0.969)	<0.001	0.920 (0.861 - 0.982)	0.013
3rd volume quartile	0.883 (0.860 - 0.907)	<0.001	0.842 (0.784 - 0.904)	<0.001
4th volume quartile	0.761 (0.739 - 0.783)	<0.001	0.716 (0.661 - 0.775)	<0.001
Colectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	1.007 (0.969 - 1.046)	0.728	1.029 (0.936 - 1.132)	0.553
3rd volume quartile	0.940 (0.902 - 0.980)	0.003	0.978 (0.883 - 1.083)	0.670
4th volume quartile	0.842 (0.805 - 0.881)	<0.001	0.831 (0.742 - 0.931)	0.001
Cystectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.816 (0.728 - 0.914)	<0.001	0.872 (0.642 - 1.185)	0.382
3rd volume quartile	0.760 (0.672 - 0.860)	<0.001	0.691 (0.487 - 0.981)	0.039
4th volume quartile	0.585 (0.509 - 0.671)	<0.001	0.706 (0.471 - 1.058)	0.092
Esophagectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.802 (0.653 - 0.986)	0.037	0.633 (0.432 - 0.928)	0.019
3rd volume quartile	0.687 (0.546 - 0.863)	0.001	0.488 (0.309 - 0.770)	0.002
4th volume quartile	0.479 (0.378 - 0.609)	<0.001	0.459 (0.280 - 0.753)	0.002
Gastrectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	1.043 (0.935 - 1.163)	0.455	1.028 (0.820 - 1.289)	0.812
3rd volume quartile	0.973 (0.866 - 1.093)	0.642	0.847 (0.660 - 1.088)	0.193
4th volume quartile	0.905 (0.795 - 1.030)	0.129	0.709 (0.532 - 0.945)	0.019
Hysterectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	1.044 (0.930 - 1.172)	0.468	0.955 (0.895 - 1.020	0.168
3rd volume quartile	1.264 (1.118 - 1.428)	<0.001	0.874 (0.815 - 0.938)	<0.001
4th volume quartile	1.231 (1.083 - 1.399)	0.001	0.758 (0.701 - 0.820)	<0.001
Lung				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.954 (0.911 - 1.000)	0.048	0.820 (0.720 - 0.934)	0.003
3rd volume quartile	0.910 (0.866 - 0.956)	<0.001	0.755 (0.657 - 0.867)	<0.001
4th volume quartile	0.792 (0.750 - 0.836)	<0.001	0.643 (0.548 - 0.753)	<0.001
Pancreatectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.767 (0.676 - 0.870)	<0.001	0.598 (0.460 - 0.775)	<0.001
3rd volume quartile	0.539 (0.468 - 0.621)	<0.001	0.405 (0.291 - 0.564)	<0.001
4th volume quartile	0.416 (0.357 - 0.485)	<0.001	0.362 (0.250 - 0.525)	<0.001
Prostatectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.772 (0.713 - 0.837)	<0.001	1.293 (0.696 - 2.403)	0.415
3rd volume quartile	0.736 (0.673 - 0.805)	<0.001	1.335 (0.687 - 2.591)	0.394
4th volume quartile	0.541 (0.488 - 0.600)	<0.001	0.293 (0.085 - 1.006)	0.051

[1]Multivariable models were generated for the overall model and for each procedure individually. Only the odds ratio (OR) and 95% confidence intervals (CI) for hospital volume are displayed in the table. Other covariates in each model included: age, gender, race, comorbidities, median household income by ZIP code, hospital location, teaching status, region, year of admission and procedure type (for overall model only)

Patient Safety Indicator	ICD-9-CM
Anesthetic Complications	E8763, E9381, E9382, E9383, E9384, E9385, E9386, E9387, E9389, 9681, 9682, 9683, 9684, 9687, E8551
Pressure Ulcers	7072X, 7070, 70700, 70701, 70702, 70703, 70704, 70705, 70706, 70707,70709
Foreign Body	9984, 9987, E871X
Iatrogenic Pneumothorax	5121
Central Venous Catheter-Related Blood Stream Infection	99662, 9993, 99931, 99932
Postoperative Hip Fracture	820XX
Postoperative Hemorrhage or Hematoma	9981X, 388X, 3941, 3998, 4995, 5793, 6094, 1809, 540, 5412, 6094, 5919, 610, 6998, 7014,7109,7591, 7592, 8604
Postoperative Physiologic and Metabolic Derangement (Secondary Diabetes or Acute Kidney Failure)	249XX, 2501X, 2502X, 2503X, 584X, 586, 9975
Postoperative Physiologic and Metabolic Derangement (Dialysis)	3995, 5498
Postoperative Respiratory Failure	5185X, 51881, 51884, 9672, 9670, 9671, 9604
Postoperative Deep Vein Thrombosis or Pulmonary Embolus	4511X, 4512, 45181, 4519, 4534X, 4538, 4539, 4151X
Postoperative Sepsis	038X, 038XX, 9980X, 9959X
Postoperative Wound Dehiscence	5461
Accidental Puncture or Laceration	E870X, 9982
Transfusion Reaction	9996X, 9997X, E8760



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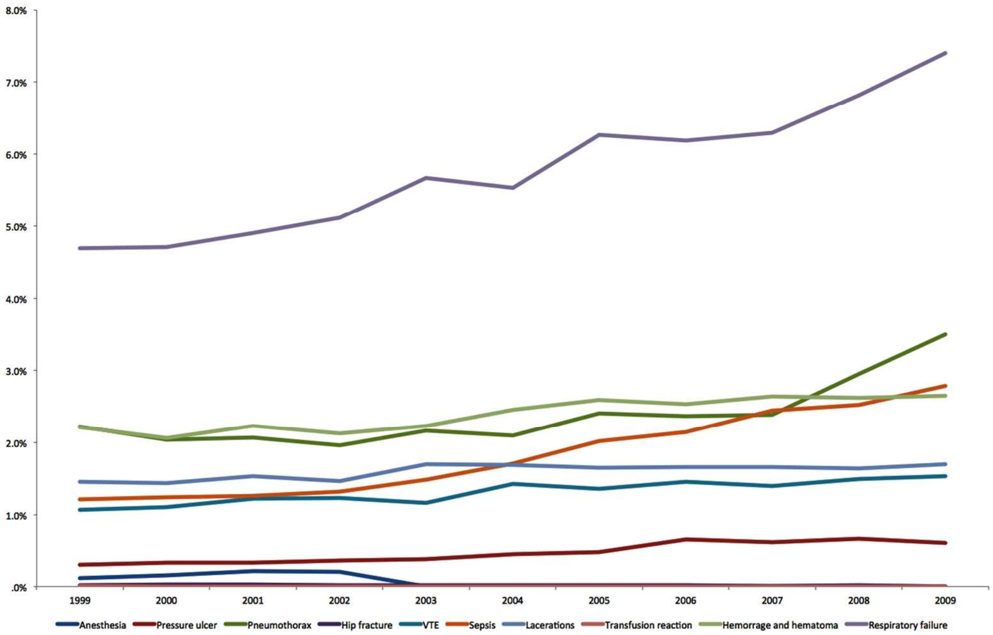

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NATIONAL TRENDS IN HOSPITAL-ACQUIRED PREVENTABLE ADVERSE EVENTS AFTER MAJOR CANCER SURGERY IN THE UNITED STATES

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NATIONAL TRENDS IN HOSPITAL-ACQUIRED PREVENTABLE ADVERSE EVENTS AFTER MAJOR CANCER SURGERY IN THE UNITED STATES

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Running Head: Preventable Adverse Events after Cancer Surgery

ABSTRACT

Objectives: While multiple studies have demonstrated variations in the quality of cancer-care in the U.S., payers are increasingly assessing structure-and process-level measures to promote quality improvement. Hospital-acquired-adverse events are one such measure and we examine their national trends after major cancer surgery.

Design: Retrospective, cross-sectional analysis of a weighted-national estimate from the Nationwide Inpatient Sample undergoing major oncological procedures (colectomy, cystectomy, esophagectomy, gastrectomy, hysterectomy, lung resection, pancreatectomy and prostatectomy). The Agency for Healthcare Research and Quality Patient Safety Indicators (PSIs) were utilized to identify trends in hospital-acquired-adverse events.

Setting: Secondary and tertiary care, U.S. hospitals in the Nationwide Inpatient Sample (NIS)

Participants: A weighted-national estimate of 2,508,917 patients (>18 years, 1999-2009) from the NIS.

Primary outcome measures: Hospital-acquired-adverse events.

Results: 324,852 patients experienced ≥1-PSI event (12.9%). Patients with ≥1-PSI experienced higher-rates of in-hospital mortality (OR: 19.38, 95% CI: 18.44-20.37), prolonged length-of-stay (OR: 4.43, 95%CI: 4.31-4.54) and excessive hospital-charges (OR: 5.21, 95%CI: 5.10-5.32). Patients treated at lower-volume hospitals experienced both higher PSI-events *and* failure-to-rescue rates. While a steady increase in the frequency of PSI-events after major cancer surgery has

occurred over the last 10 years (estimated annual % change-EAPC: 3.5%, $p<0.001$), a concomitant decrease in failure-to-rescue rates (EAPC: -3.01%) and overall mortality (EAPC: -2.30%) was noted. (All $p<0.001$)

Conclusions: Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable adverse-events after major cancer surgery, with a detrimental effect on numerous outcome-level measures. However, there was a concomitant reduction in failure-to-rescue rates and overall-mortality rates. Policy changes to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcers and respiratory failure, are required.

Article summary

Article focus

- Variations in the quality of surgical oncology care in the U.S. remain unclear.
- Payers are increasingly assessing structure-and process-level measures to promote quality improvement.
- Hospital-acquired-adverse events are one such measure and we examine their national trends after major cancer surgery.

Key messages

- Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable adverse-events after major cancer surgery but there was also a concomitant reduction in failure-to-rescue rates and overall-mortality rates.
- Patients treated at lower-volume hospitals experienced both higher frequency of potentially avoidable adverse-events *and* failure-to-rescue rates.
- Policy changes to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcers and respiratory failure, are required.

Strength and limitations of this study

- This is the largest study to assess the quality of oncologic surgical care in a nationally representative cohort of U.S. patients.
- Validated Agency for Healthcare Research and Quality Patient Safety Indicators (PSIs) were utilized to identify trends in hospital-acquired-adverse events.
- Inherent to retrospective analyses of large administrative datasets, this study is limited by potential biases due to case-mix and miscoding.
- While PSIs have been shown to perform well as screening tools from an epidemiologic perspective (over-identification and few false-negatives), concerns related to high false-positive rates exist.

INTRODUCTION

There has been much interest in assessing the downstream effects and complexities of the contemporary delivery of health care. However, observational studies examining preventable adverse events are confounded by the loss of information when administrative data are abstracted from patient records. Recently, several initiatives have been directed to improve consistency, relevance and fidelity in the process of transforming clinical data into administrative datasets and subsequent practice-changing results. Following a landmark study by Iezzoni *et al*[1] on computerized algorithms to identify quality of care disparities in administrative datasets, the Agency for Healthcare Research and Quality (AHRQ) developed a standardized system for accrual and reporting of unintended hospital-acquired adverse events, termed patient safety indicators (PSI)[2]. Subsequently, Zhan *et al*[3] examined the relationship between multiple process-, setting- and outcome-level measures and adverse events identified using the AHRQ's PSI system, and reported substantial but variable effects on the health care system.

Nonetheless, there is a paucity of studies evaluating the burden of preventable adverse events[4] and this is particularly true for major surgical oncology care in the United States. Multiple studies have demonstrated that significant variation exists in cancer incidence rates[5] and in access to quality cancer care[6 7], but variations in the actual *quality* of surgical oncology care remain unclear.

Hence, we undertook a national assessment of the quality of major surgical oncology care within a standardized framework of preventable adverse events to

examine trends in patient safety within the United States. We also evaluate the prevailing hypothesis[8-10] explaining the volume-complication-mortality relationship, which states that higher mortality rates for patients undergoing surgery at low-volume hospitals is preferentially explained by higher failure-to-rescue rates (i.e. mortality after a hospital-acquired adverse event), rather than a higher incidence of such adverse events in the first place.

METHODS

Data source

The Nationwide Inpatient Sample (NIS) consists of an array of longitudinal hospital inpatients datasets as part of the Healthcare Cost and Utilization Project (HCUP). It was established by the Agency for Healthcare Research and Quality and functions through a Federal-state affiliation. It is the largest publicly accessible all-payer inpatient database[11]. The database consists of discharge information from 8 million inpatient visits and patients covered by multiple insurance types (including Medicare, Medicaid, private insurance and uninsured patients) are represented.

Study cohort

We relied on hospital discharges for patients undergoing one of eight major cancer surgeries in the United States between 1999-2009. The major oncological surgeries consisted of colectomy, cystectomy, esophagectomy, gastrectomy, hysterectomy, pneumonectomy/lobectomy, pancreatectomy, and prostatectomy. Oncological indications were selected based on ICD-9-CM diagnostic codes. These particular procedures were chosen based on procedure volume and care was taken to include cancer surgeries involving different organ systems across a range of surgical specialties.

Patient and Hospital information

Patient characteristics evaluated included age at inpatient hospitalization, race, gender, insurance characteristics and comorbidities. Regarding race, patients were classified as White, Black, Hispanic and Other (Asian or Pacific Islander, Native American). Regarding insurance characteristics patients were categorized based on the primary payer: Medicare, Medicaid, Private insurance (Blue Cross, commercial carriers, private HMO's and PPO's), and other insurance types (including uninsured patients). Charlson Comorbidity index (CCI) was derived according to Charlson *et al*[12], and adapted according to the previously defined methodology of Deyo and colleagues[13]. Median household income of the patient's ZIP code of residence, as derived from the US Census, was used as to define socioeconomic status and patients were divided into quartiles: <25,000$, 25,000$–34,999$, 35,000$–44,999$, and ≥45,000$. Hospital information examined included hospital location (urban vs. rural) and region (Northeast, Midwest, South and West), as defined by the United States Census Bureau[14] and academic teaching status as derived from the AHA Annual Survey of Hospitals. Hospital volume was categorized into volume quartiles as previously described[15].

Primary Outcomes

The Agency for Healthcare Research and Quality (AHRQ) Patient Safety Indicators (PSIs) were used to identify potentially preventable hospital-acquired adverse events. For the PSI project, AHRQ commissioned experts from the Evidence based Practice Center at the University of California San Francisco and Stanford University and from the University of California Davis to evaluate the

existing literature and help develop an evidence-based approach for improving patient safety[2]. The objective of this project was to facilitate the identification, quantification and reporting of preventable hospital-acquired adverse events from routinely collected administrative information. The process of identification of PSI included initial literature analysis of previously reported patient safety problems, organized peer review of chosen PSIs, structured review of ICD-9 codes for each PSI and finally empirical analysis of each PSI, and feedback from multidisciplinary teams (physicians and specialists, nurses, pharmacists and coding and experts)[2]. The complete set of PSIs utilized is displayed in **Table e1** and is available on the AHRQ website[16]. The list includes various preventable adverse events that have been shown to have reasonable accuracy and validity as indicators for enhancing quality improvement and patient safety.

Statistical Analysis

Proportions, frequencies, means, medians, standard deviation, and interquartile ranges were obtained for each variable. National trends in the frequency of PSI-events, failure-to-rescue (defined as mortality after a PSI-event), and in-hospital mortality were also analyzed as the estimated annual percentage change (EAPC), based on the linear regression methodology described by Anderson *et al*[17]. Logistic regression models were used to examine predictors of PSI events, and to examine the effect of PSI events on multiple outcomes level measures, including in-hospital mortality, excessive charges (≥75th percentile of inflation adjusted charges for each individual procedure) and prolonged length of stay

(≥75th percentile of each individual procedure). Subsequently, we examined the volume-complication-mortality relationship in overall and procedure-specific analyses to study the relationship between mortality at low volume hospitals and failure-to-rescue rates. Generalized estimating equations were used in each multivariable analysis to adjust for clustering among hospitals[18]. All analyses were two-sided, significance was defined as $P<0.05$ and were performed using the R statistical package (R foundation for Statistical Computing, version 2.15.1).

RESULTS

The baseline demographic characteristics of our cohort of patients >18 years old undergoing one of eight major cancer procedures in the United States between 1999-2009 (n=2,508,917) is shown in **Table 1**. A weighted estimate of 324,852 patients experienced ≥ 1-PSI event (12.9%). Patients with ≥ 1-PSI event were more likely to be older, be female, have higher CCI, participate in Medicare, have lower socioeconomic status, and be treated at lower volume non-academic hospitals when compared to patients who did not experience any hospital-acquired preventable adverse events.

The national trends in PSI rates, overall mortality rates and failure-to-rescue rates in patients undergoing major cancer surgery in the United States are depicted in **Figure 1**. While a steady increase in the frequency of PSI-events after major cancer surgery has occurred over the last 10 years (estimated annual % change-EAPC: 3.5%; 95% Confidence Interval-95% CI: 2.8% to 4.1%; P<0.001), a concomitant decrease in failure-to-rescue rates (EAPC: -3.0%; 95% CI: -3.4% to -2.6%; P<0.001) and overall mortality (EAPC: -2.3%; 95% CI: -2.7% to -1.9%; P<0.001) was noted.

While there was a significant increase in overall PSI event rates over the course of the study, substantial heterogeneity was noted in terms of individual PSIs (**Figure 2 a-c)**. Substantial increases were noted in the annual incidence of postoperative sepsis (EAPC: 14.1%, 95% CI: 12.0% to 16.2%; P<0.001), pressure ulcer (EAPC: 13.4%, 95% CI: 10.2% to 16.6%; P<0.001) and respiratory failure (EAPC: 5.6%, 95% CI: 4.8% to 6.4%; P<0.001), while

significant advances were made in the prevention of anesthetic complications (EAPC: -17.5%, 95% CI: -27.6% to -7.5%; P=0.008), hip fractures (EAPC: -8.9%, 95% CI: -13.6% to -4.3%; P=0.005) and transfusion reactions (EAPC: -7.9%, 95% CI: -13.1% to -2.8%; P=0.001) in the perioperative period.

Results of a multivariable logistic regression model predicting the odds of ≥ 1-PSI event after major cancer surgery are shown in **Table 2**. These factors included: female gender (vs. male, odds ratio-OR: 0.88, 95% confidence interval-CI: 0.86-0.90; P<0.001), Black race (vs. Caucasians OR: 1.17, 95%CI: 1.13-1.21; P<0.001), higher Charlson comorbidity index (≥3 vs. 0, OR: 1.38, 95%CI: 1.34-1.42; P<0.001), Medicaid (OR: 1.45, 95%CI: 1.39-1.52) and Medicare insurance (OR: 1.16, 95%CI: 1.13-1.19; P<0.001), lower median household income (4th quartile vs. 1st quartile, OR-0.92, 95%CI: 0.89-0.95; P<0.001) and surgeries at lower volume hospitals (4th quartile vs. 1st quartile, OR: 0.76, 95%CI: 0.74-0.78; P<0.001).

The occurrence of ≥ 1-PSI event had significant multivariable effects on specific outcome-level measures after major cancer surgery (**Table 3)**. Patients who suffered from ≥ 1-PSI event experienced higher rates of in-hospital mortality (OR: 19.38, 95% CI: 18.44-20.37), prolonged length of stay (OR: 4.43, 95%CI: 4.31-4.54) and excessive hospital charges (OR: 5.21, 95%CI: 5.10-5.32).

We also assessed the effect of hospital volume on the incidence of PSIs and failure-to-rescue (**Table 4)**. In the overall analysis of patients undergoing any of the eight procedures, very high-volume hospitals (4th quartile) had both lower PSI event rate *and* lower failure-to-rescue rates. However, this relationship was

procedure-specific: for colectomy, esophagectomy, lung resection, pancreatectomy, and prostatectomy, very high-volume hospitals had both lower PSI event rates *and* lower failure-to-rescue rates. For gastrectomy, very high-volume hospitals did not have lower PSI event rates but did have lower failure-to-rescue rates; for hysterectomy very high-volume hospitals had *higher* PSI event rates, but had lower failure-to-rescue rates; for cystectomy very high volume-hospitals had lower PSI event rates and a trend toward lower failure-to-rescue rates.

DISCUSSION

Recently, it has been estimated that the annual cost of medical errors is over 17 billion dollars[19] and there have been a slew of newer initiatives over the last decade to incentivize better quality care. In 2008, Medicare announced that it would restrain the ability of hospitals to get reimbursed for 'reasonably preventable events': avoidable medical errors ranging from pressure ulcers, falls and transfusion of incompatible blood to anesthetic complications, deep vein thrombosis and foreign bodies left in the body of patients during surgery. These and other initiatives are designed to place the burden of responsibility for such hospital-acquired adverse events squarely on hospitals and physicians[20]. While these initiatives have been met with stiff objection from hospital administrations, the Centers for Medicaid and Medicare Services (CMS) has been consistent in its position that accountability for such events should rest with hospitals and not with the taxpayer[20]. The Affordable Care Act of 2010 has added newer dimensions to these quality-improvement initiatives, with reimbursement likely to be dependent on both adherence to standards of care and the perceptions of patients with regard to hospital performance as measured by surveys[21].

A rational approach to improving accountability for substandard care should begin with identifying the true burden of hospital-acquired adverse events. This would be particularly useful in identifying specific adverse events that warrant special attention by payers like CMS and in preferential allocation of resources by hospitals due to the growing temporal burden of such events.

In the current study, we report contemporary trends in the frequency of hospital-acquired adverse events after major surgical oncology care in the United States. Our study has a number of novel findings. First, we report a gradual increase in the national frequency of hospital-acquired adverse events after major cancer surgery over the last decade. This is important as it represents a decline, albeit small and gradual, in the quality of surgical oncology care at the national level, as measured by the primary prevention of PSI events. The increase may be attributed to changes in case-mix, including an aging population. Conversely, the emergence of multi-resistant bacteria may contribute to the recorded trends.[22 23] Second, a simultaneous decrease in failure-to-rescue rates were observed and may indicate that while primary prevention of hospital-acquired adverse events has deteriorated, early recognition and timely management of these complications may have improved in the last decade. These findings may explain the significant annual reduction in mortality for patients undergoing major cancer surgery. Nonetheless, alternate explanations include refinements in coding practices, which may have led to better recognition and recording of non-lethal adverse events, thereby resulting in an apparent decrease in mortality rates. Third, significant heterogeneity in the temporal dynamics of specific hospital-acquired adverse events was noted. While marked and worrisome increases were recorded in the frequency of postoperative sepsis, pressure ulcers and respiratory failure, advances were made in the prevention of anesthetic complications, transfusion-related complications and hip fractures. Thus we identify numerous setting- and process-level measures where resources need to be refocused for further improvement in the quality of surgical oncology care.

We also examined the volume-complication-mortality dynamic in patients undergoing major cancer surgery, as it applies to potentially preventable hospital acquired adverse events (PSI). There is a well-established body of evidence describing the volume-mortality relationship in patients undergoing major cancer procedures and other surgeries. Dudley *et al*[24] examined patients undergoing one of eleven diverse procedures (ranging from coronary angioplasty to esophageal cancer surgery) in California and concluded that 602 deaths could be prevented annually by transferring patients from low-volume to high-volume hospitals. Birkmeyer *et al*[25] reported that Medicare patients treated at very high-volume hospitals experienced up to a 12 percent difference in absolute mortality for certain procedures relative to patients treated at very low-volume hospitals. However, the underlying mechanisms explaining the volume-mortality relationship have not been elucidated clearly. Silber *et al*[26] first introduced the concept of 'failure-to-rescue' in a seminal report that evaluated patients undergoing cholecystectomy or transurethral prostatectomy. They concluded that overall mortality was related to both hospital-level and patient-level factors, while adverse events were related to patient-level factors at admission (severity of illness). However, failure-to-rescue was preferentially associated with hospital-level factors and thus the underlying dynamics for failure-to-rescue were different than that for overall mortality and adverse events. The current hypothesis[8] regarding the volume-complication-mortality relationship is that lower volume hospitals experience higher mortality rates not because of higher complication rates, but due to lower failure-to-rescue rates. Ghaferi *et al*[10] demonstrated that high and low volume hospitals enrolled in the National Surgical Quality Improvement Program (NSQIP) had similar complication rates but different failure-to-rescue rates for multiple procedures. In a subsequent analysis[9] of patients undergoing gastrectomy, pancreatectomy or esophagectomy, similar results were demonstrated. However, in the current study, very high-volume hospitals (4th quartile vs. 1st quartile) had both lower PSI-event rates *and* lower failure-to-rescue rates. Importantly, the volume-complication-mortality relationship, as it applies to PSI events, appears to be procedure-specific and heterogeneous, with the current hypothesis not accounting for multiple individual major cancer surgeries, namely colectomy, esophagectomy, lung resection, pancreatectomy and prostatectomy. This is an important point: CMS currently focuses its quality-improvement initiatives on complication rates, and explicit demonstration that lower failure-to-rescue rates and not higher complication rates underlie the substandard care at low-volume hospitals may require a re-consideration of these initiatives. Our findings indicate that the prevailing hypothesis may need to be re-evaluated, at least for patients undergoing major cancer surgery. In fact, for patients undergoing hysterectomy, this relationship is reversed, with patients at very high-volume hospitals experiencing *higher* PSI event rates and lower failure-to-rescue rates. The underlying reason for this finding is not clear. Previous studies[27] have questioned the impact of hospital volume on hysterectomy outcomes and have reported that surgeon volume trumps hospital volume as the predominant factor underlying the volume-outcomes relationship for hysterectomy. While inclusion of surgeon volume may alter these findings, the higher rates of adverse events in patients undergoing hysterectomy at very high-volume hospitals may need to be re-examined in future reports.

Our study is not without limitations. The drawbacks of using administrative data are well known[28], including limitations regarding risk-adjustment and miscoding. While PSIs have been shown to perform well as screening tools from an epidemiologic perspective (over-identification and few false-negatives), problems related to high false-positive rates exist, with most validation studies reporting positive predictive values of between 43 to >90%[29 30]. While it is clear that these drawbacks limit the use of PSIs to make reimbursement decisions or to compare hospitals, it is unclear how it affects the implications of our study, where it was used as a screening tool to *identify* adverse events[29 30]. Secondly, morbidity and mortality events in the NIS are characterized based on the index admission, and subsequent readmissions, while relevant, are not recorded. This may have resulted in under-recognition of the true burden of adverse events, mortality and charges after the initial cancer surgery. Third: while the heterogeneity identified in the volume-complication-mortality relationship is a key finding in the present report, our study design does not allow for the identification of underlying mechanisms explaining these results. It is also important to emphasize that, in contrast to the previously cited studies where overall complication rates were examined, we evaluated potentially preventable hospital acquired events only.

Previous investigators have shown that this restricted definition has limitations since not all deaths are accounted for in a given population sample[31]; alternatively, these drawbacks may not apply to studies focusing on patient safety using PSI as a quality of care measure. Hence, while it may not be illogical to expect lower volume hospitals to provide substandard care secondary to both higher rates of preventable adverse events *and* higher failure-to-rescue rates, it is certainly possible that a majority of hospital-acquired complications are an inevitable result of procedure complexity and patient comorbidities (and not just a failure of setting-level prevention measures). Consequently, while more rigorous patient care pathways might explain the lower incidence of preventable adverse events and subsequent mortality in higher volume hospitals, for the majority of (non-preventable) adverse events, the incidence rates would be the same regardless of hospital volume with lower failure-to-rescue rates preferentially explaining the low mortality rates of higher volume hospitals. Further investigation of these findings is required to test these possibilities and to fully understand the underlying dynamics of the volume-mortality relationship.

CONCLUSION

Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable hospital-acquired adverse events after major cancer surgery, with a detrimental effect on numerous outcome-level measures. However, there was a concomitant reduction in failure-to-rescue rates and, consequently, overall-mortality rates. Policy changes and resource re-allocation to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcer and respiratory failure, are required.

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FIGURE LEGENDS

FIGURE 1. National trends in Patient Safety Indicator (PSI) rates, overall mortality rates and failure-to-rescue rates in patients undergoing major cancer surgery (MCS) in the United States (1999-2009); EAPC-Estimated Annual Percent Change

FIGURE 2 a-c. National trends in individual Patient Safety Indicators over the study period (1999-2009) in patients undergoing major cancer surgery (MCS) in the United States

Table 1. Baseline characteristics of patients > 18 years undergoing major cancer surgery, Nationwide Inpatient Sample, 1999-2009.

Variables	Baseline characteristics			
	Overall (%)	Without PSI event (%)	With PSI event (%)	*P*
Weighted number of patients	2508917	2184065 (87.1)	324852 (12.9)	–
Age (years)				
Mean (SD)	65.9 (11.7)	65.4 (11.6)	69.5 (11.7)	<0.001[2]
Median (IQR)	66 (58,74)	65 (57,73)	71 (62,78)	
Gender				
Male	1511361 (60.3)	1331716 (61.1)	179645 (55.3)	<0.001
Female	993704 (39.7)	848527 (38.9)	145177 (44.7)	
Race				
Caucasian	1525021 (60.8)	1324373 (60.6)	200648 (61.8)	<0.001
Black	177986 (7.1)	154028 (7.1)	23958 (7.4)	
Hispanic	98532 (3.9)	86128 (3.9)	12404 (3.8)	
Other	93041 (3.7)	81492 (3.6)	11549 (3.6)	
Unknown	614337 (24.5)	76293 (23.5)	76293 (23.5)	
CCI				
0	1566723 (62.4)	1412545 (64.7)	154178 (47.5)	<0.001
1	623985 (24.9)	516640 (23.7)	107345 (33.0)	
2	127538 (5.1)	102276 (4.7)	25262 (7.8)	
≥3	190670 (7.6)	152603 (7.0)	38067 (11.7)	
Insurance status				
Private	1057919 (42.2)	968015 (44.3)	89904 (27.7)	<0.001
Medicaid	80666 (3.2)	66947 (3.1)	13719 (4.2)	
Medicare	1265920 (50.5)	1056618 (48.4)	209302 (64.4)	
Other	104412 (4.2)	92485 (4.2)	11927 (3.7)	
Median household income by ZIP code				<0.001
1-24,999	369796 (14.7)	313652 (14.4)	56144 (17.3)	
25,000-34,999	596202 (23.8)	513758 (23.5)	82444 (25.4)	
35,000-44,999	646869 (25.8)	563398 (25.8)	83471 (25.7)	
45,000+	842375 (33.6)	746499 (34.2)	95876 (29.5)	
Unknown	53672 (2.1)	46757 (2.1)	6915 (2.1)	
Annual hospital volume				
1st quartile	591675 (23.6)	510024 (23.4)	81651 (25.1)	<0.001
2nd quartile	640229 (25.5)	551980 (25.3)	88249 (27.2)	
3rd quartile	636482 (25.4)	554325 (25.4)	82157 (25.3)	
4th quartile	640531 (25.5)	567737 (26.0)	72794 (22.4)	
Hospital location				
Rural	268349 (10.7)	235606 (10.8)	32743 (10.1)	<0.001
Urban	2239651 (89.3)	1947705 (89.2)	291946 (89.9)	
Hospital region				
Northeast	526593 (21.)	458684 (21.0)	67909 (20.9)	<0.001
Midwest	608988 (24.3)	532951 (24.4)	76037 (23.4)	
South	8822566 (35.2)	762212 (34.9)	120354 (37.0)	
West	490770 (19.6)	430218 (19.7)	60552 (18.6)	
Hospital teaching status				
Non-teaching	1135065 (45.3)	979636 (44.9)	155429 (47.9)	
Teaching	1372935 (54.7)	1203675 (55.1)	169260 (52.1)	<0.001

[1] Multivariable logistic regression analysis adjusted for hospital clustering by generalized estimating equations
[2] Mann-Whitney test was performed.

Table 2. Multivariable logistic regression predicting occurrence of at least 1 patient safety indicator event

Variables	Multivariable predictors of ≥ 1 PSI event[1]	
	OR (95% CI)	*P*
Weighted number of patients		
Age (years)	1.018 (1.017 - 1.019)	<0.001
Gender		
Male	1.0 (ref.)	–
Female	0.878 (0.862 - 0.895)	<0.001
Race		
Caucasian	1.0 (ref.)	–
Black	1.172 (1.132 - 1.213)	<0.001
Hispanic	0.973 (0.930 - 1.019)	0.245
Other	0.938 (0.895 - 0.983)	0.008
Unknown	1.010 (0.988 - 1.033)	0.366
CCI		
0	1.0 (ref.)	–
1	1.227 (1.203 - 1.252)	<0.001
2	1.188 (1.147 - 1.230)	<0.001
≥3	1.377 (1.336 - 1.419)	<0.001
Insurance status		
Private	1.0 (ref.)	–
Medicaid	1.454 (1.388 - 1.523)	<0.001
Medicare	1.155 (1.127 - 1.185)	<0.001
Other	1.127 (1.075 - 1.181)	<0.001
Median household income by ZIP code		
1-24,999	1.0 (ref.)	–
25,000-34,999	0.986 (0.959 - 1.013)	0.305
35,000-44,999	0.960 (0.934 - 0.987)	0.004
45,000+	0.920 (0.894 - 0.946)	<0.001
Unknown	1.003 (0.943 - 1.067)	0.929
Annual hospital volume		
1st quartile	1.0 (ref.)	–
2nd quartile	0.945 (0.922 - 0.969)	<0.001
3rd quartile	0.883 (0.860 - 0.907)	<0.001
4th quartile	0.761 (0.739 - 0.783)	<0.001
Hospital location		
Rural	1.0 (ref.)	–
Urban	1.236 (1.198 - 1.275)	<0.001
Hospital region		
Northeast	1.0 (ref.)	–
Midwest	0.991 (0.964 - 1.019)	0.541
South	1.049 (1.024 - 1.075)	<0.001
West	1.018 (0.989 - 1.047)	0.229
Hospital teaching status		
Non-teaching	1.0 (ref.)	–
Teaching	0.972 (0.952 - 0.992)	0.007

[1]Other predictors included procedure type [colectomy-ref; cystectomy (OR: 1.51, 95%CI: 1.45-1.57), esophagectomy(OR:5.16, 95%CI:4.81-5.54), gastrectomy(OR:2.01, 95%CI:1.93-2.09), hysterectomy(OR:0.56, 95%CI:0.54-0.58), lung resection(OR:2.44, 95%CI:2.39-2.50), pancreatectomy(OR:1.79, 95%CI:1.71-1.88),prostatectomy(OR:0.26, 95%CI:0.25-0.27)] and year of surgery (OR: 1.037, 95%CI: 1.034-1.040). All P<0.001. OR-Odds ratio. CI: confidence interval

Table 3. Multivariable effects of ≥ 1 Patient safety indicator events on in-hospital mortality, prolonged length of stay and excessive hospital charges in patients undergoing major cancer surgery in the United States between 1999-2009.

Variables	≥ 1 Patient safety indicator vs. no PSI	
	OR (95% CI)**	***P***
In-hospital mortality (n=51312)*	19.380 (18.439 - 20.368)	<0.001
Prolonged length of stay (n=888220)	4.426 (4.313 - 4.542)	<0.001
Excessive hospital charges (n=609128)	5.207 (5.097 - 5.319)	<0.001

* 1457 patients with missing in-hospital mortality data.
** Each of these effects was derived from individual multivariable logistic regression models adjusted for hospital clustering, procedure type, age, gender, race, CCI, insurance status, socioeconomic status, year of admission, hospital location, hospital region, hospital volume quartiles and institutional academic status.
Legend. OR: odds ratio, CI: confidence interval, PSI: patient safety indicator; CCI: Charlson comorbidity index.

Table 4. Impact of hospital volume effect on patient safety indicator event occurrence and on failure to rescue (death after patient safety indicator event) from individual multivariable logistic regression models adjusted for hospital clustering by generalized estimating equation in patients undergoing major cancer surgery, Nationwide Inpatient Sample, 1999-2009.

Procedure	Patient safety indicator occurrence		Failure to rescue	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Overall				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.945 (0.922 - 0.969)	<0.001	0.920 (0.861 - 0.982)	0.013
3rd volume quartile	0.883 (0.860 - 0.907)	<0.001	0.842 (0.784 - 0.904)	<0.001
4th volume quartile	0.761 (0.739 - 0.783)	<0.001	0.716 (0.661 - 0.775)	<0.001
Colectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	1.007 (0.969 - 1.046)	0.728	1.029 (0.936 - 1.132)	0.553
3rd volume quartile	0.940 (0.902 - 0.980)	0.003	0.978 (0.883 - 1.083)	0.670
4th volume quartile	0.842 (0.805 - 0.881)	<0.001	0.831 (0.742 - 0.931)	0.001
Cystectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.816 (0.728 - 0.914)	<0.001	0.872 (0.642 - 1.185)	0.382
3rd volume quartile	0.760 (0.672 - 0.860)	<0.001	0.691 (0.487 - 0.981)	0.039
4th volume quartile	0.585 (0.509 - 0.671)	<0.001	0.706 (0.471 - 1.058)	0.092
Esophagectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.802 (0.653 - 0.986)	0.037	0.633 (0.432 - 0.928)	0.019
3rd volume quartile	0.687 (0.546 - 0.863)	0.001	0.488 (0.309 - 0.770)	0.002
4th volume quartile	0.479 (0.378 - 0.609)	<0.001	0.459 (0.280 - 0.753)	0.002
Gastrectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	1.043 (0.935 - 1.163)	0.455	1.028 (0.820 - 1.289)	0.812
3rd volume quartile	0.973 (0.866 - 1.093)	0.642	0.847 (0.660 - 1.088)	0.193
4th volume quartile	0.905 (0.795 - 1.030)	0.129	0.709 (0.532 - 0.945)	0.019
Hysterectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	1.044 (0.930 - 1.172)	0.468	0.955 (0.895 - 1.020	0.168
3rd volume quartile	1.264 (1.118 - 1.428)	<0.001	0.874 (0.815 - 0.938)	<0.001
4th volume quartile	1.231 (1.083 - 1.399)	0.001	0.758 (0.701 - 0.820)	<0.001
Lung				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.954 (0.911 - 1.000)	0.048	0.820 (0.720 - 0.934)	0.003
3rd volume quartile	0.910 (0.866 - 0.956)	<0.001	0.755 (0.657 - 0.867)	<0.001
4th volume quartile	0.792 (0.750 - 0.836)	<0.001	0.643 (0.548 - 0.753)	<0.001
Pancreatectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.767 (0.676 - 0.870)	<0.001	0.598 (0.460 - 0.775)	<0.001
3rd volume quartile	0.539 (0.468 - 0.621)	<0.001	0.405 (0.291 - 0.564)	<0.001
4th volume quartile	0.416 (0.357 - 0.485)	<0.001	0.362 (0.250 - 0.525)	<0.001
Prostatectomy				
1st volume quartile	1.0 (ref.)	-	1.0 (ref.)	-
2nd volume quartile	0.772 (0.713 - 0.837)	<0.001	1.293 (0.696 - 2.403)	0.415
3rd volume quartile	0.736 (0.673 - 0.805)	<0.001	1.335 (0.687 - 2.591)	0.394
4th volume quartile	0.541 (0.488 - 0.600)	<0.001	0.293 (0.085 - 1.006)	0.051

[1]Multivariable models were generated for the overall model and for each procedure individually. Only the odds ratio (OR) and 95% confidence intervals (CI) for hospital volume are displayed in the table. Other covariates in each model included: age, gender, race, comorbidities, median household income by ZIP code, hospital location, teaching status, region, year of admission and procedure type (for overall model only)

Patient Safety Indicator	ICD-9-CM
Anesthetic Complications	E8763, E9381, E9382, E9383, E9384, E9385, E9386, E9387, E9389, 9681, 9682, 9683, 9684, 9687, E8551
Pressure Ulcers	7072X, 7070, 70700, 70701, 70702, 70703, 70704, 70705, 70706, 70707,70709
Foreign Body	9984, 9987, E871X
Iatrogenic Pneumothorax	5121
Central Venous Catheter-Related Blood Stream Infection	99662, 9993, 99931, 99932
Postoperative Hip Fracture	820XX
Postoperative Hemorrhage or Hematoma	9981X, 388X, 3941, 3998, 4995, 5793, 6094, 1809, 540, 5412, 6094, 5919, 610, 6998, 7014,7109,7591, 7592, 8604
Postoperative Physiologic and Metabolic Derangement (Secondary Diabetes or Acute Kidney Failure)	249XX, 2501X, 2502X, 2503X, 584X, 586, 9975
Postoperative Physiologic and Metabolic Derangement (Dialysis)	3995, 5498
Postoperative Respiratory Failure	5185X, 51881, 51884, 9672, 9670, 9671, 9604
Postoperative Deep Vein Thrombosis or Pulmonary Embolus	4511X, 4512, 45181, 4519, 4534X, 4538, 4539, 4151X
Postoperative Sepsis	038X, 038XX, 9980X, 9959X
Postoperative Wound Dehiscence	5461
Accidental Puncture or Laceration	E870X, 9982
Transfusion Reaction	9996X, 9997X, E8760

NATIONAL TRENDS IN HOSPITAL-ACQUIRED PREVENTABLE ADVERSE EVENTS AFTER MAJOR CANCER SURGERY IN THE UNITED STATES

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ABSTRACT

Objectives: While multiple studies have demonstrated variations in the quality of cancer-care in the U.S., payers are increasingly assessing structure-and process-level measures to promote quality improvement. Hospital-acquired-adverse events are one such measure and we examine their national trends after major cancer surgery.

Design: Retrospective, cross-sectional analysis of a weighted-national estimate from the Nationwide Inpatient Sample undergoing major oncological procedures (colectomy, cystectomy, esophagectomy, gastrectomy, hysterectomy, lung resection, pancreatectomy and prostatectomy). The Agency for Healthcare Research and Quality Patient Safety Indicators (PSIs) were utilized to identify trends in hospital-acquired-adverse events.

Setting: Secondary and tertiary care, U.S. hospitals in the Nationwide Inpatient Sample (NIS)

Participants: A weighted-national estimate of 2,508,917 patients (>18 years, 1999-2009) from the NIS.

Primary outcome measures: Hospital-acquired-adverse events.

Results: 324,852 patients experienced ≥1-PSI event (12.9%). Patients with ≥1-PSI experienced higher-rates of in-hospital mortality (OR: 19.38, 95% CI: 18.44-20.37), prolonged length-of-stay (OR: 4.43, 95%CI: 4.31-4.54) and excessive hospital-charges (OR: 5.21, 95%CI: 5.10-5.32). Patients treated at lower-volume hospitals experienced both higher PSI-events *and* failure-to-rescue rates. While a steady increase in the frequency of PSI-events after major cancer surgery has

occurred over the last 10 years (estimated annual % change-EAPC: 3.5%, $p<0.001$), a concomitant decrease in failure-to-rescue rates (EAPC: -3.01%) and overall mortality (EAPC: -2.30%) was noted. (All $p<0.001$)

Conclusions: Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable adverse-events after major cancer surgery, with a detrimental effect on numerous outcome-level measures. However, there was a concomitant reduction in failure-to-rescue rates and overall-mortality rates. Policy changes to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcers and respiratory failure, are required.

Article summary

Article focus

- Variations in the quality of surgical oncology care in the U.S. remain unclear.
- Payers are increasingly assessing structure-and process-level measures to promote quality improvement.
- Hospital-acquired-adverse events are one such measure and we examine their national trends after major cancer surgery.

Key messages

- Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable adverse-events after major cancer surgery but there was also a concomitant reduction in failure-to-rescue rates and overall-mortality rates.
- Patients treated at lower-volume hospitals experienced both higher frequency of potentially avoidable adverse-events *and* failure-to-rescue rates.
- Policy changes to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcers and respiratory failure, are required.

Strength and limitations of this study

- This is the largest study to assess the quality of oncologic surgical care in a nationally representative cohort of U.S. patients.
- Validated Agency for Healthcare Research and Quality Patient Safety Indicators (PSIs) were utilized to identify trends in hospital-acquired-adverse events.
- Inherent to retrospective analyses of large administrative datasets, this study is limited by potential biases due to case-mix and miscoding.
- While PSIs have been shown to perform well as screening tools from an epidemiologic perspective (over-identification and few false-negatives), concerns related to high false-positive rates exist.

INTRODUCTION

There has been much interest in assessing the downstream effects and complexities of the contemporary delivery of health care. However, observational studies examining preventable adverse events are confounded by the loss of information when administrative data are abstracted from patient records. Recently, several initiatives have been directed to improve consistency, relevance and fidelity in the process of transforming clinical data into administrative datasets and subsequent practice-changing results. Following a landmark study by Iezzoni *et al*[1] on computerized algorithms to identify quality of care disparities in administrative datasets, the Agency for Healthcare Research and Quality (AHRQ) developed a standardized system for accrual and reporting of unintended hospital-acquired adverse events, termed patient safety indicators (PSI)[2]. Subsequently, Zhan *et al*[3] examined the relationship between multiple process-, setting- and outcome-level measures and adverse events identified using the AHRQ's PSI system, and reported substantial but variable effects on the health care system.

Nonetheless, there is a paucity of studies evaluating the burden of preventable adverse events[4] and this is particularly true for major surgical oncology care in the United States. Multiple studies have demonstrated that significant variation exists in cancer incidence rates[5] and in access to quality cancer care[6 7], but variations in the actual *quality* of surgical oncology care remain unclear.

Hence, we undertook a national assessment of the quality of major surgical oncology care within a standardized framework of preventable adverse events to

examine trends in patient safety within the United States. We also evaluate the prevailing hypothesis[8-10] explaining the volume-complication-mortality relationship, which states that higher mortality rates for patients undergoing surgery at low-volume hospitals is preferentially explained by higher failure-to-rescue rates (i.e. mortality after a hospital-acquired adverse event), rather than a higher incidence of such adverse events in the first place.

METHODS

Data source

The Nationwide Inpatient Sample (NIS) consists of an array of longitudinal hospital inpatients datasets as part of the Healthcare Cost and Utilization Project (HCUP). It was established by the Agency for Healthcare Research and Quality and functions through a Federal-state affiliation. It is the largest publicly accessible all-payer inpatient database[11]. The database consists of discharge information from 8 million inpatient visits and patients covered by multiple insurance types (including Medicare, Medicaid, private insurance and uninsured patients) are represented.

Study cohort

We relied on hospital discharges for patients undergoing one of eight major cancer surgeries in the United States between 1999-2009. The major oncological surgeries consisted of colectomy, cystectomy, esophagectomy, gastrectomy, hysterectomy, pneumonectomy/lobectomy, pancreatectomy, and prostatectomy. Oncological indications were selected based on ICD-9-CM diagnostic codes. These particular procedures were chosen based on procedure volume and care was taken to include cancer surgeries involving different organ systems across a range of surgical specialties.

Patient and Hospital information

Patient characteristics evaluated included age at inpatient hospitalization, race, gender, insurance characteristics and comorbidities. Regarding race, patients were classified as White, Black, Hispanic and Other (Asian or Pacific Islander, Native American). Regarding insurance characteristics patients were categorized based on the primary payer: Medicare, Medicaid, Private insurance (Blue Cross, commercial carriers, private HMO's and PPO's), and other insurance types (including uninsured patients). Charlson Comorbidity index (CCI) was derived according to Charlson *et al*[12], and adapted according to the previously defined methodology of Deyo and colleagues[13]. Median household income of the patient's ZIP code of residence, as derived from the US Census, was used as to define socioeconomic status and patients were divided into quartiles: <25,000$, 25,000$–34,999$, 35,000$–44,999$, and ≥45,000$. Hospital information examined included hospital location (urban vs. rural) and region (Northeast, Midwest, South and West), as defined by the United States Census Bureau[14] and academic teaching status as derived from the AHA Annual Survey of Hospitals. Hospital volume was categorized into volume quartiles as previously described[15].

Primary Outcomes

The Agency for Healthcare Research and Quality (AHRQ) Patient Safety Indicators (PSIs) were used to identify potentially preventable hospital-acquired adverse events. For the PSI project, AHRQ commissioned experts from the Evidence based Practice Center at the University of California San Francisco and Stanford University and from the University of California Davis to evaluate the

existing literature and help develop an evidence-based approach for improving patient safety[2]. The objective of this project was to facilitate the identification, quantification and reporting of preventable hospital-acquired adverse events from routinely collected administrative information. The process of identification of PSI included initial literature analysis of previously reported patient safety problems, organized peer review of chosen PSIs, structured review of ICD-9 codes for each PSI and finally empirical analysis of each PSI, and feedback from multidisciplinary teams (physicians and specialists, nurses, pharmacists and coding and experts)[2]. The complete set of PSIs utilized is displayed in **Table e1** and is available on the AHRQ website[16]. The list includes various preventable adverse events that have been shown to have reasonable accuracy and validity as indicators for enhancing quality improvement and patient safety.

Statistical Analysis

Proportions, frequencies, means, medians, standard deviation, and interquartile ranges were obtained for each variable. National trends in the frequency of PSI-events, failure-to-rescue (defined as mortality after a PSI-event), and in-hospital mortality were also analyzed as the estimated annual percentage change (EAPC), based on the linear regression methodology described by Anderson *et al*[17]. Logistic regression models were used to examine predictors of PSI events, and to examine the effect of PSI events on multiple outcomes level measures, including in-hospital mortality, excessive charges (≥75th percentile of inflation adjusted charges for each individual procedure) and prolonged length of stay

(≥75th percentile of each individual procedure). Subsequently, we examined the volume-complication-mortality relationship in overall and procedure-specific analyses to study the relationship between mortality at low volume hospitals and failure-to-rescue rates. Generalized estimating equations were used in each multivariable analysis to adjust for clustering among hospitals[18]. All analyses were two-sided, significance was defined as $P<0.05$ and were performed using the R statistical package (R foundation for Statistical Computing, version 2.15.1).

RESULTS

The baseline demographic characteristics of our cohort of patients >18 years old undergoing one of eight major cancer procedures in the United States between 1999-2009 (n=2,508,917) is shown in **Table 1**. A weighted estimate of 324,852 patients experienced ≥ 1-PSI event (12.9%). Patients with ≥ 1-PSI event were more likely to be older, be female, have higher CCI, participate in Medicare, have lower socioeconomic status, and be treated at lower volume non-academic hospitals when compared to patients who did not experience any hospital-acquired preventable adverse events.

The national trends in PSI rates, overall mortality rates and failure-to-rescue rates in patients undergoing major cancer surgery in the United States are depicted in **Figure 1**. While a steady increase in the frequency of PSI-events after major cancer surgery has occurred over the last 10 years (estimated annual % change-EAPC: 3.5%; 95% Confidence Interval-95% CI: 2.8% to 4.1%; P<0.001), a concomitant decrease in failure-to-rescue rates (EAPC: -3.0%; 95% CI: -3.4% to -2.6%; P<0.001) and overall mortality (EAPC: -2.3%; 95% CI: -2.7% to -1.9%; P<0.001) was noted.

While there was a significant increase in overall PSI event rates over the course of the study, substantial heterogeneity was noted in terms of individual PSIs (**Figure 2 a-c**). Substantial increases were noted in the annual incidence of postoperative sepsis (EAPC: 14.1%, 95% CI: 12.0% to 16.2%; P<0.001), pressure ulcer (EAPC: 13.4%, 95% CI: 10.2% to 16.6%; P<0.001) and respiratory failure (EAPC: 5.6%, 95% CI: 4.8% to 6.4%; P<0.001), while

significant advances were made in the prevention of anesthetic complications (EAPC: -17.5%, 95% CI: -27.6% to -7.5%; P=0.008), hip fractures (EAPC: -8.9%, 95% CI: -13.6% to -4.3%; P=0.005) and transfusion reactions (EAPC: -7.9%, 95% CI: -13.1% to -2.8%; P=0.001) in the perioperative period.

Results of a multivariable logistic regression model predicting the odds of ≥ 1-PSI event after major cancer surgery are shown in **Table 2**. These factors included: female gender (vs. male, odds ratio-OR: 0.88, 95% confidence interval-CI: 0.86-0.90; P<0.001), Black race (vs. Caucasians OR: 1.17, 95%CI: 1.13-1.21; P<0.001), higher Charlson comorbidity index (≥3 vs. 0, OR: 1.38, 95%CI: 1.34-1.42; P<0.001), Medicaid (OR: 1.45, 95%CI: 1.39-1.52) and Medicare insurance (OR: 1.16, 95%CI: 1.13-1.19; P<0.001), lower median household income (4^{th} quartile vs. 1^{st} quartile, OR-0.92, 95%CI: 0.89-0.95; P<0.001) and surgeries at lower volume hospitals (4^{th} quartile vs. 1^{st} quartile, OR: 0.76, 95%CI: 0.74-0.78; P<0.001).

The occurrence of ≥ 1-PSI event had significant multivariable effects on specific outcome-level measures after major cancer surgery (**Table 3)**. Patients who suffered from ≥ 1-PSI event experienced higher rates of in-hospital mortality (OR: 19.38, 95% CI: 18.44-20.37), prolonged length of stay (OR: 4.43, 95%CI: 4.31-4.54) and excessive hospital charges (OR: 5.21, 95%CI: 5.10-5.32).

We also assessed the effect of hospital volume on the incidence of PSIs and failure-to-rescue (**Table 4)**. In the overall analysis of patients undergoing any of the eight procedures, very high-volume hospitals (4^{th} quartile) had both lower PSI event rate *and* lower failure-to-rescue rates. However, this relationship was

procedure-specific: for colectomy, esophagectomy, lung resection, pancreatectomy, and prostatectomy, very high-volume hospitals had both lower PSI event rates *and* lower failure-to-rescue rates. For gastrectomy, very high-volume hospitals did not have lower PSI event rates but did have lower failure-to-rescue rates; for hysterectomy very high-volume hospitals had *higher* PSI event rates, but had lower failure-to-rescue rates; for cystectomy very high volume-hospitals had lower PSI event rates and a trend toward lower failure-to-rescue rates.

DISCUSSION

Recently, it has been estimated that the annual cost of medical errors is over 17 billion dollars[19] and there have been a slew of newer initiatives over the last decade to incentivize better quality care. In 2008, Medicare announced that it would restrain the ability of hospitals to get reimbursed for 'reasonably preventable events': avoidable medical errors ranging from pressure ulcers, falls and transfusion of incompatible blood to anesthetic complications, deep vein thrombosis and foreign bodies left in the body of patients during surgery. These and other initiatives are designed to place the burden of responsibility for such hospital-acquired adverse events squarely on hospitals and physicians[20]. While these initiatives have been met with stiff objection from hospital administrations, the Centers for Medicaid and Medicare Services (CMS) has been consistent in its position that accountability for such events should rest with hospitals and not with the taxpayer[20]. The Affordable Care Act of 2010 has added newer dimensions to these quality-improvement initiatives, with reimbursement likely to be dependent on both adherence to standards of care and the perceptions of patients with regard to hospital performance as measured by surveys[21].

A rational approach to improving accountability for substandard care should begin with identifying the true burden of hospital-acquired adverse events. This would be particularly useful in identifying specific adverse events that warrant special attention by payers like CMS and in preferential allocation of resources by hospitals due to the growing temporal burden of such events.

In the current study, we report contemporary trends in the frequency of hospital-acquired adverse events after major surgical oncology care in the United States. Our study has a number of novel findings. First, we report a gradual increase in the national frequency of hospital-acquired adverse events after major cancer surgery over the last decade. This is important as it represents a decline, albeit small and gradual, in the quality of surgical oncology care at the national level, as measured by the primary prevention of PSI events. The increase may be attributed to changes in case-mix, including an aging population. Conversely, the emergence of multi-resistant bacteria may contribute to the recorded trends.[22 23] Second, a simultaneous decrease in failure-to-rescue rates were observed and may indicate that while primary prevention of hospital-acquired adverse events has deteriorated, early recognition and timely management of these complications may have improved in the last decade. These findings may explain the significant annual reduction in mortality for patients undergoing major cancer surgery. Nonetheless, alternate explanations include refinements in coding practices, which may have led to better recognition and recording of non-lethal adverse events, thereby resulting in an apparent decrease in mortality rates. Third, significant heterogeneity in the temporal dynamics of specific hospital-acquired adverse events was noted. While marked and worrisome increases were recorded in the frequency of postoperative sepsis, pressure ulcers and respiratory failure, advances were made in the prevention of anesthetic complications, transfusion-related complications and hip fractures. Thus we identify numerous setting- and process-level measures where resources need to be refocused for further improvement in the quality of surgical oncology care.

We also examined the volume-complication-mortality dynamic in patients undergoing major cancer surgery, as it applies to potentially preventable hospital acquired adverse events (PSI). There is a well-established body of evidence describing the volume-mortality relationship in patients undergoing major cancer procedures and other surgeries. Dudley *et al*[24] examined patients undergoing one of eleven diverse procedures (ranging from coronary angioplasty to esophageal cancer surgery) in California and concluded that 602 deaths could be prevented annually by transferring patients from low-volume to high-volume hospitals. Birkmeyer *et al*[25] reported that Medicare patients treated at very high-volume hospitals experienced up to a 12 percent difference in absolute mortality for certain procedures relative to patients treated at very low-volume hospitals. However, the underlying mechanisms explaining the volume-mortality relationship have not been elucidated clearly. Silber *et al*[26] first introduced the concept of 'failure-to-rescue' in a seminal report that evaluated patients undergoing cholecystectomy or transurethral prostatectomy. They concluded that overall mortality was related to both hospital-level and patient-level factors, while adverse events were related to patient-level factors at admission (severity of illness). However, failure-to-rescue was preferentially associated with hospital-level factors and thus the underlying dynamics for failure-to-rescue were different than that for overall mortality and adverse events. The current hypothesis[8] regarding the volume-complication-mortality relationship is that lower volume hospitals experience higher mortality rates not because of higher complication rates, but due to lower failure-to-rescue rates. Ghaferi *et al*[10] demonstrated that high and low volume hospitals enrolled in the National Surgical Quality Improvement Program (NSQIP) had similar complication rates but different failure-to-rescue rates for multiple procedures. In a subsequent analysis[9] of patients undergoing gastrectomy, pancreatectomy or esophagectomy, similar results were demonstrated. However, in the current study, very high-volume hospitals (4th quartile vs. 1st quartile) had both lower PSI-event rates *and* lower failure-to-rescue rates. Importantly, the volume-complication-mortality relationship, as it applies to PSI events, appears to be procedure-specific and heterogeneous, with the current hypothesis not accounting for multiple individual major cancer surgeries, namely colectomy, esophagectomy, lung resection, pancreatectomy and prostatectomy. This is an important point: CMS currently focuses its quality-improvement initiatives on complication rates, and explicit demonstration that lower failure-to-rescue rates and not higher complication rates underlie the substandard care at low-volume hospitals may require a re-consideration of these initiatives. Our findings indicate that the prevailing hypothesis may need to be re-evaluated, at least for patients undergoing major cancer surgery. In fact, for patients undergoing hysterectomy, this relationship is reversed, with patients at very high-volume hospitals experiencing *higher* PSI event rates and lower failure-to-rescue rates. The underlying reason for this finding is not clear. Previous studies[27] have questioned the impact of hospital volume on hysterectomy outcomes and have reported that surgeon volume trumps hospital volume as the predominant factor underlying the volume-outcomes relationship for hysterectomy. While inclusion of surgeon volume may alter these findings, the higher rates of adverse events in patients undergoing hysterectomy at very high-volume hospitals may need to be re-examined in future reports.

Our study is not without limitations. The drawbacks of using administrative data are well known[28], including limitations regarding risk-adjustment and miscoding. While PSIs have been shown to perform well as screening tools from an epidemiologic perspective (over-identification and few false-negatives), problems related to high false-positive rates exist, with most validation studies reporting positive predictive values of between 43 to >90%[29 30]. While it is clear that these drawbacks limit the use of PSIs to make reimbursement decisions or to compare hospitals, it is unclear how it affects the implications of our study, where it was used as a screening tool to *identify* adverse events[29 30]. Secondly, morbidity and mortality events in the NIS are characterized based on the index admission, and subsequent readmissions, while relevant, are not recorded. This may have resulted in under-recognition of the true burden of adverse events, mortality and charges after the initial cancer surgery. Third: while the heterogeneity identified in the volume-complication-mortality relationship is a key finding in the present report, our study design does not allow for the identification of underlying mechanisms explaining these results. It is also important to emphasize that, in contrast to the previously cited studies where overall complication rates were examined, we evaluated potentially preventable hospital acquired events only.

Previous investigators have shown that this restricted definition has limitations since not all deaths are accounted for in a given population sample[31]; alternatively, these drawbacks may not apply to studies focusing on patient safety using PSI as a quality of care measure. Hence, while it may not be illogical to expect lower volume hospitals to provide substandard care secondary to both higher rates of preventable adverse events *and* higher failure-to-rescue rates, it is certainly possible that a majority of hospital-acquired complications are an inevitable result of procedure complexity and patient comorbidities (and not just a failure of setting-level prevention measures). Consequently, while more rigorous patient care pathways might explain the lower incidence of preventable adverse events and subsequent mortality in higher volume hospitals, for the majority of (non-preventable) adverse events, the incidence rates would be the same regardless of hospital volume with lower failure-to-rescue rates preferentially explaining the low mortality rates of higher volume hospitals. Further investigation of these findings is required to test these possibilities and to fully understand the underlying dynamics of the volume-mortality relationship.

CONCLUSION

Over the past decade, there has been a substantial increase in the national frequency of potentially avoidable hospital-acquired adverse events after major cancer surgery, with a detrimental effect on numerous outcome-level measures. However, there was a concomitant reduction in failure-to-rescue rates and, consequently, overall-mortality rates. Policy changes and resource re-allocation to improve the increasing burden of specific adverse events, such as postoperative sepsis, pressure ulcer and respiratory failure, are required.

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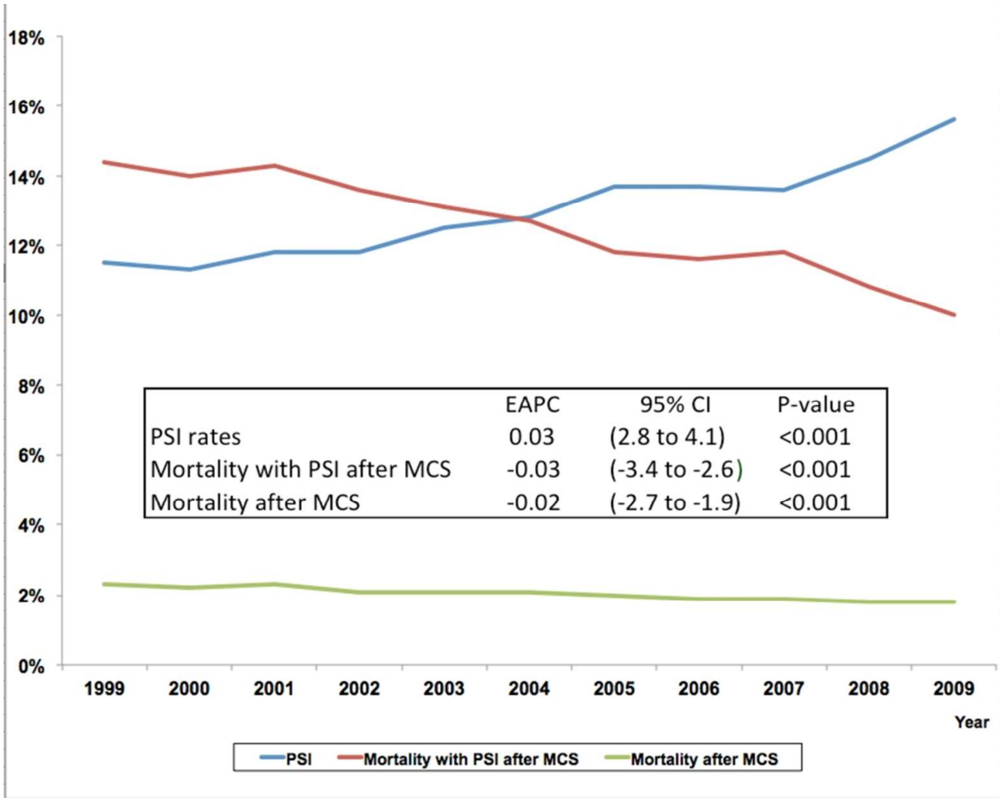
FIGURE LEGENDS

FIGURE 1. National trends in Patient Safety Indicator (PSI) rates, overall mortality rates and failure-to-rescue rates in patients undergoing major cancer surgery (MCS) in the United States (1999-2009); EAPC-Estimated Annual Percent Change

FIGURE 2 a-c. National trends in individual Patient Safety Indicators over the study period (1999-2009) in patients undergoing major cancer surgery (MCS) in the United States



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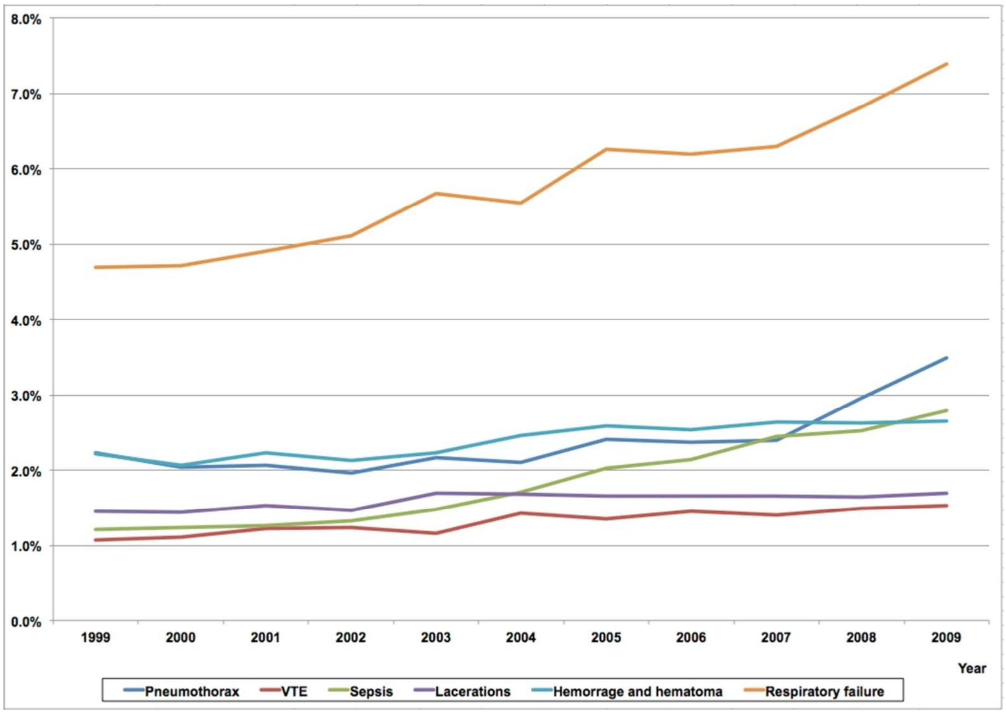

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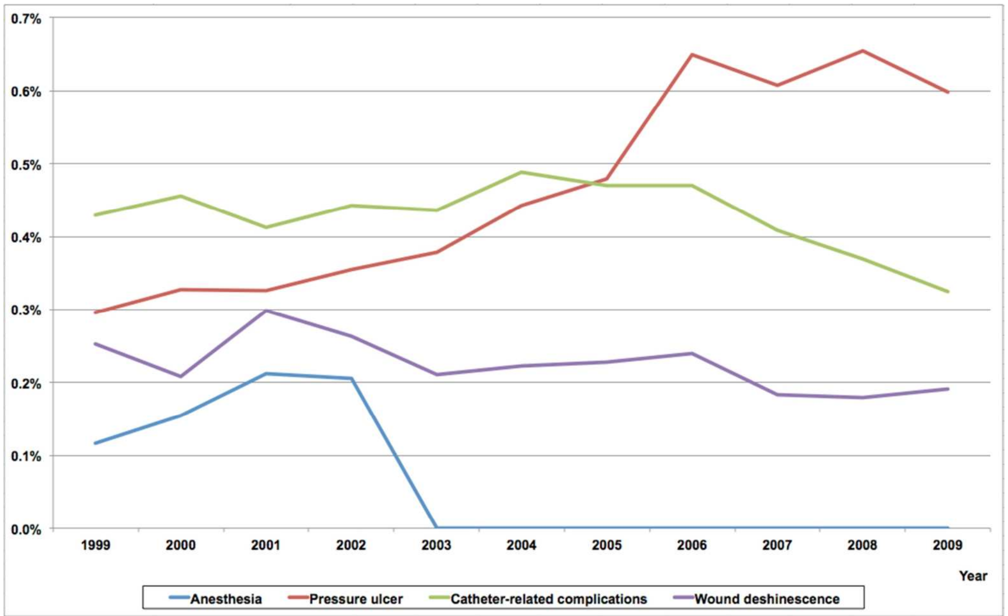

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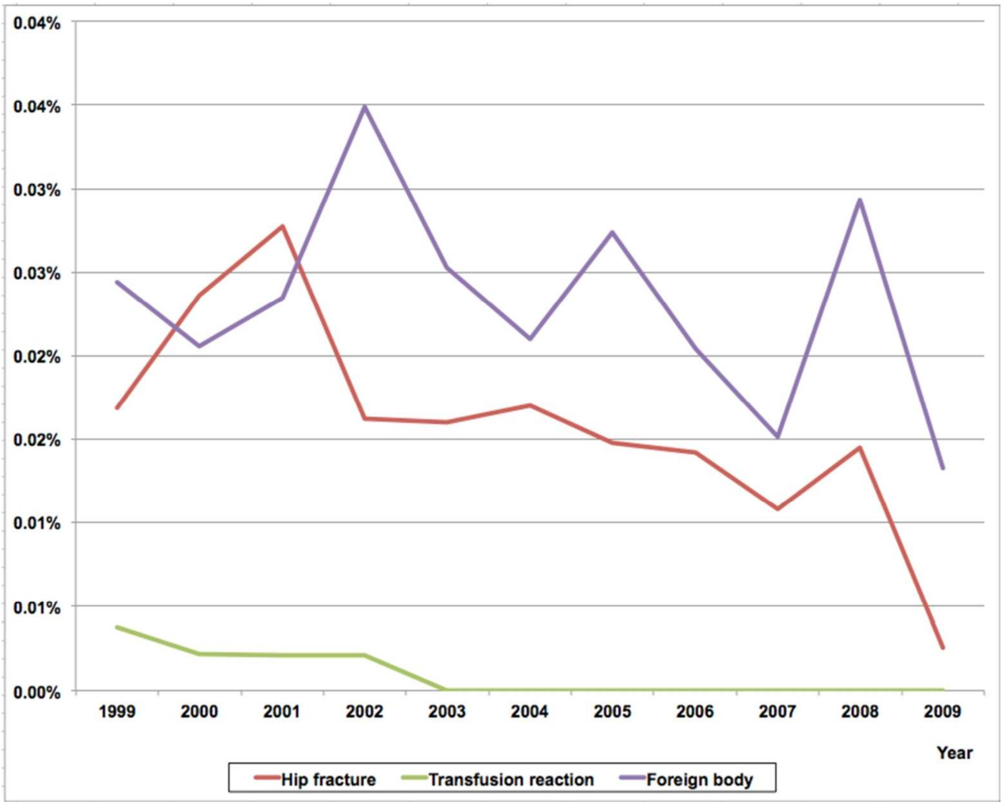

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