Contemporary trends in necrotizing soft-tissue infections in the United States

Charles M. Psoinos, MD,[a] Julie M. Flahive, MS,[a] Joshua J. Shaw, MD,[a] YouFu Li, MD, MPH,[a,b] Sing Chau Ng, MS,[c] Jennifer F. Tseng, MD, MPH,[c] *and* **Heena P. Santry, MD, MS,[a,b]**
Worcester and Boston, MA

Background. *Necrotizing soft-tissue infections (NSTI) are rare, potentially fatal, operative emergencies. We studied a national cohort of patients to determine recent trends in incidence, treatment, and outcomes for NSTI.*
Methods. *We queried the Nationwide Inpatient Sample (1998–2010) for patients with a primary diagnosis of NSTI. Temporal trends in patient characteristics, treatment (debridement, amputation, hyperbaric oxygen therapy [HBOT]), and outcomes were determined with Cochran-Armitage trend tests and linear regression. To account for trends in case mix (age, sex, race, insurance, Elixhauser index) or receipt of HBOT on outcomes, multivariable analyses were conducted to determine the independent effect of year of treatment on mortality, any major complication, and hospital length of stay (LOS) for NSTI.*
Results. *We identified 56,527 weighted NSTI admissions, with an incidence ranging from approximately 3,800–5,800 cases annually. The number of cases peaked in 2004 and then decreased between 1998 and 2010 (*$P < .0001$*). The percentage of female patients decreased slightly over time (38.6–34.1%,* $P < .0001$*). Patients were increasingly in the 18- to 34–year-old (8.8–14.6%,* $P < .0001$*) and 50- to 64-year-old age groups (33.2–43.5,* $P < .0001$*), Hispanic (6.8–10.5%,* $P < .0001$*), obese (8.9–24.6%,* $P < .0001$*), and admitted with >3 comorbidities (14.5–39.7%,* $P < .0001$*). The percentage of patients requiring only one operative debridement increased somewhat (43.2–46.2%,* $P < .0001$*), whereas the use of HBOT was rare and decreasing (1.6–0.8%,* $P < .0001$*). The percentage of patients requiring operative wound closure decreased somewhat (23.5–20.8%,* $P < .0001$*). Although major complication rates increased (30.9–48.2%,* $P < .0001$*), hospital LOS remained stable (18–19 days) and mortality decreased (9.0–4.9%,* $P < .0001$*) on univariate analyses. On multivariable analyses each 1-year incremental increase in year was associated with a 5% increased odds of complication (odds ratio 1.05), 0.4 times decrease in hospital LOS (coefficient −0.41), and 11% decreased odds of mortality (odds ratio 0.89).*
Conclusion. *There were potentially important national trends in patient characteristics and treatment patterns for NSTI between 1998 and 2010. Importantly, though patient acuity worsened and complication rates increased, but LOS remained relatively stable and mortality decreased. Improvements in early diagnosis, wound care, and critical care delivery may be the cause. (Surgery 2013;153:819-27.)*

From the Department of Surgery, Center for Outcomes Research,[a] and Department of Quantitative Health Sciences,[b] University of Massachusetts Medical School, Worcester; and Division of Surgical Oncology, Beth Israel Deaconess Medical Center,[c] Boston, MA

Necrotizing soft-tissue infections (NSTIs) are a collection of rapidly advancing, often-fatal infections of the subcutaneous tissues and fascia. Mortality for NSTI has been reported to range from 21 to 43% in single-center studies.[1,2] Larger studies have shown a mortality as great as 34%,[3] but more recently there appears to have been a decrease in mortality to 10–12%.[4–6] These epidemiologic studies on NSTIs have provided some data on treatment modalities, such as hyperbaric oxygen therapy (HBOT),[7,8] and the association between a number of comorbidities, such as chronic alcoholism, obesity, diabetes, and immunocompromised status on the development of NSTIs, is evident.[9] In only 2 of these studies did authors examine a national cohort of patients with NSTI.[4,5]

This research was presented as a Quick Shot podium presentation at the Academic Surgical Congress 7th Annual Meeting, February 14–16, 2012, Las Vegas, NV.

Accepted for publication November 30, 2012.

Reprint requests: Heena P. Santry, MD, MS, Department of Surgery, University of Massachusetts Medical School, 55 Lake Ave North, Worcester, MA 01655. E-mail: heena.santry@umassmemorial.org.

0039-6060/$ - see front matter

© 2013 Mosby, Inc. All rights reserved.

http://dx.doi.org/10.1016/j.surg.2012.11.026

It appears that the basic principles of treatment for NSTI have remained unchanged during the past several decades. Early diagnosis and treatment have been the only consistently proven predictors of outcomes for NSTI.[10,11] Aggressive antibiotic therapy with prompt, often serial, operative debridement of all necrotic tissue is paramount to decrease morbidity and mortality.[2,12] We undertook this study to examine recent national trends in incidence, treatment, and outcomes for NSTI from a large representative sample of the US population.

METHODS

The Nationwide Inpatient Sample (NIS; 1998–2010) was queried for all patients with a primary diagnosis of NSTI (*International Classification of Diseases*, 9th revision codes 728.86 [necrotizing fasciitis], 040.0 [gas gangrene], or 608.83 [Fournier's gangrene]) and at least one operative debridement or at least one amputation (see Appendix I, online version only). The NIS is a dataset from the Healthcare Cost and Utilization Project and represents the largest all-payer inpatient database in the United States. The NIS contains approximately 8 million admission records per year and represents a 20% stratified sample of all acute care hospital admissions nationally.[13]

The NIS contains data on patient characteristics, including demographics (sex, age, insurance status, and race) and comorbidities (measured by the Elixhauser Index),[14] hospital characteristics (geographic region, urban versus rural location, and teaching status), interventions (up to 15 procedures classified), and outcomes (complications recorded in up to 14 secondary diagnoses, length of stay, mortality).

For each year of data, we determined proportions in patient characteristics as well as interventions and outcomes by using descriptive statistics. Interventions were classified as debridements, amputations, wound care, wound closure, and HBOT (see Appendix I). Complications were divided into categories, including cardiac, pulmonary, neurologic, thromboembolic, renal, and infectious (see Appendix II, online version only). Complications also were measured as a dichotomous variable indicating any major complication and a continuous variable counting the total number of complications of these 6 categories. These national point estimates were calculated with the NIS survey weights and sampling frame. Trends over time in these estimates were then determined with the Cochrane-Armitage trend tests for dichotomous variables and linear regression for continuous variables.

To determine whether observed epidemiologic trends in outcomes were caused by simultaneous trends in case mix or receipt of HBOT, we also conducted multivariable analyses of all patients in our cohort to determine predictors of mortality, any major complication, and length of stay (LOS) for NSTI. Covariates in the model included year of treatment, age, sex, race, insurance, Elixhauser index, and treatment with HBOT. The models for mortality and LOS also included total major complications. The model for LOS included only those patients who survived hospitalization.

All analyses were performed using SAS statistical software (version 9.2; SAS Institute, Inc, Cary, NC). This study was deemed exempt by the University of Massachusetts Medical School Institutional Review Board.

RESULTS

Incidence. During the 13-year study period, there were 56,527 weighted NSTI admissions in the United States with an annual incidence ranging from approximately 3,800 to 5,800 admissions per year. The number of cases peaked in 2004 and then decreased between 1998 and 2010 ($P < .0001$).

Demographics. Table I depicts the basic demographics for the entire study population. Although the proportion of patients missing race data improved over time from 21.2 to 15.4% ($P < .0001$), race data were far from complete. Among those with race data recorded, the approximately one-half of patients were white (50.1–52.2%), with the percentage of Hispanics increasing (6.8–10.5%, $P < .0001$), whereas the proportion of black patients remained similar (19.6–18.6%, $P < .01$) during the study period. Although there were fewer women (38.6–34.1%, $P < .0001$), an increasing percentage of NSTI patients were in the 18- to 34–year-old (8.8–14.6%, $P < .0001$) and 50- to 64-year-old age groups (33.2–43.5, $P < .0001$). The proportion of patients on Medicaid also increased during the study period (17.6–20.1, $P < .0001$).

Comorbidities. Patients admitted with NSTIs were more likely to be obese (8.9–24.6%, $P < .0001$), have uncomplicated diabetes (30.4–33.0%, $P < .0001$), and chronic liver disease (1.0–4.0%, $P < .0001$) during the study period. Overall, patients had more pre-existing comorbidities (Elixhauser index >3 increased from 14.5–39.7%, $P < .0001$; Table II and Fig).

Treatment. Trends in treatment of NSTI are detailed in Table III. The percentage of patients requiring only a single operative debridement or multiple debridements (>3) increased slightly

Table I. Trends in patient characteristics 1998–2010 ($N = 56,527$)

	1998	*1999*	*2000*	*2001*	*2002*	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	P *value*
Variable	n = *4,262*	n = *3,850*	n = *4,307*	n = *4,355*	n = *4,557*	n = *5,089*	n = *5,815*	n = *4,653*	n = *4,307*	n = *3,925*	n = *4,033*	n = *3,591*	n = *3,783*	*<.0001*
Age, years														
18–34	8.8	11.0	10.8	12.1	11.3	11.5	10.3	10.3	13.1	8.8	10.3	12.7	14.6	<.0001
35–49	34.2	31.9	31.0	29.9	31.3	29.0	32.1	34.7	29.0	30.6	31.8	28.7	25.6	<.0001
50–64	33.2	33.1	34.8	33.6	35.6	36.0	36.5	37.0	38.7	40.3	39.8	41.7	43.5	<.0001
>64	23.8	24.0	23.4	24.5	21.8	23.5	21.2	18.0	19.2	20.3	18.2	16.8	16.2	<.0001
Female	38.6	41.4	39.2	41.9	39.5	39.3	37.4	41.3	35.3	34.2	40.4	37.5	34.1	<.0001
Race														
White	50.1	50.4	52.5	48.0	43.7	46.0	49.5	44.3	45.7	42.9	52.1	54.1	52.2	.24
Black	19.6	15.2	13.7	12.9	15.2	14.9	13.0	11.2	13.6	15.3	10.7	16.0	18.6	.01
Hispanic	6.8	6.8	11.7	10.2	11.3	10.2	9.2	14.9	11.3	11.9	9.8	9.2	10.5	<.0001
Other	2.3	4.1	3.7	3.6	3.8	2.4	2.7	2.7	4.2	4.5	5.0	5.4	3.3	<.0001
Missing	21.2	23.6	18.4	25.3	26.1	26.6	25.6	26.9	25.2	25.5	22.4	15.3	15.4	<.0001
Insurance														
Medicare	33.1	33.0	32.5	33.3	31.5	33.0	32.6	26.9	31.4	29.0	26.6	26.9	26.1	<.0001
Medicaid	17.6	18.3	13.4	16.2	17.1	17.4	16.6	17.9	17.2	16.3	17.8	22.3	20.1	<.0001
Private	31.1	33.2	34.7	32.7	31.4	33.7	29.6	32.4	29.7	33.6	34.2	26.8	29.7	<.0001
Self-pay	10.1	8.2	10.4	10.8	11.3	9.6	13.5	13.8	11.7	12.6	12.0	15.7	16.6	<.0001
No charge/other*	8.2	7.4	8.9	7.0	8.7	6.3	7.7	9.0	10.0	8.4	9.4	8.3	7.5	.02

*Includes Federal, military, and other.
Values are percentages.

Table II. Trends in specific patient comorbidities 1998–2010 ($N = 56,527$)

Variable	*1998*	*1999*	*2000*	*2001*	*2002*	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	P *value*
Individual comorbidities*														
Obese	8.9	11.6	11.2	12.4	16.4	14.5	12.7	13.7	15.7	16.5	20.4	30.0	24.6	<.0001
Diabetes type 2														
w/chronic complication	17.6	17.3	13.7	14.8	14.0	13.8	13.2	14.5	14.1	15.9	14.4	14.3	14.0	<.0001
w/o chronic complication	30.4	32.4	34.2	32.4	36.8	32.4	31.6	35.3	34.0	32.5	33.8	39.7	33.0	<.0001
Alcohol abuse	5.9	4.8	4.4	4.5	5.1	5.9	5.1	4.8	5.9	6.1	4.3	6.5	5.7	.02
Liver disease	1.4	2.3	3.3	3.3	3.9	4.3	4.1	4.0	5.6	3.7	4.5	4.2	4.0	<.0001
Peripheral vascular disease	6.9	6.3	5.3	5.0	6.0	6.8	5.4	4.8	4.5	5.8	5.9	7.4	5.7	.47
Aggregate comorbidity measure†														
Elixhauser index														
0	12.5	13.0	10.9	11.2	11.1	10.7	12.3	10.6	10.1	7.9	8.9	5.7	8.8	<.0001
1	27.2	22.3	25.9	24.4	20.4	19.8	19.6	19.2	17.4	17.7	15.4	12.9	14.4	<.0001
2	28.2	28.5	28.3	27.1	25.7	26.5	26.6	23.3	23.4	23.1	23.2	20.1	20.1	<.0001
3	17.6	20.6	21.2	20.1	21.7	23.5	21.8	23.4	22.4	23.2	22.3	20.8	17.0	.08
>3	14.5	15.7	13.7	17.1	21.2	19.4	19.7	23.5	26.6	28.2	30.3	40.6	39.7	<.0001

*These individual comorbidities have been shown in the literature to be associated with NSTI. See Appendix III for a list of all comorbidities measured by the Elixhauser Index.
†See Elixhauser et al. Med Care 1998;36:8–27.
Values are percentages.

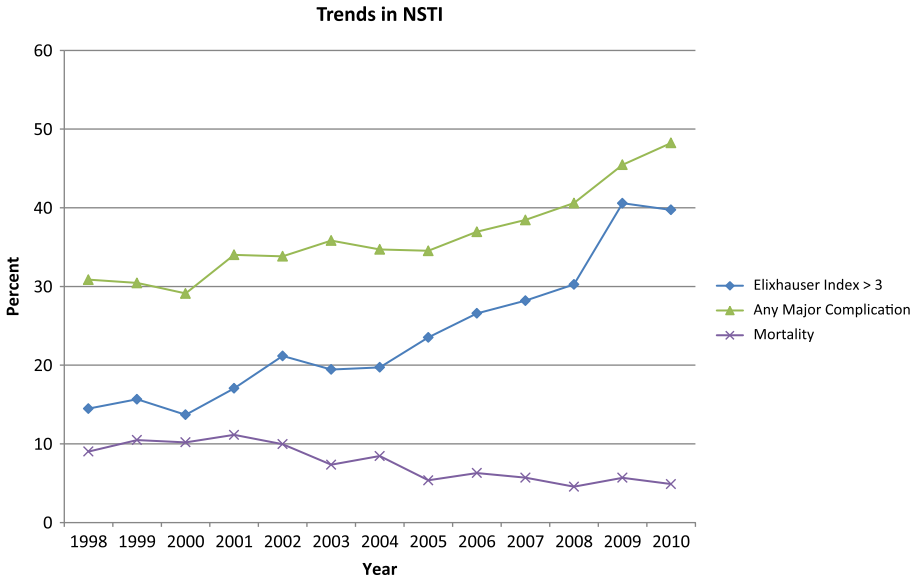


Fig. Trends in Elixhauser >3, incidence of any major complication, and mortality among NSTI patients 1998–2010 ($N = 56,527$). (Color version of figure is available online.)

(43.2–46.2%, $P < .0001$ and 13.5–15.9%, $P < .001$ respectively), whereas those needing 2 and 3 operative interventions decreased (29.5–26.4%, $P < .0001$ and 13.4–11.1%, $P < .0001$ respectively). Amputations were rare and ranged from 1.2 to 1.9% (reported in 3-year intervals per the NIS data use agreement); HBOT (reported in 3-year intervals per the NIS data use agreement) was rarely used and its utilization decreased nationally during our study period (1.6 to 0.8%, $P < .0001$). During the study period, there was increased use of wound therapy (12.7–14.5%, $P < .0001$) and less need for complex wound reconstruction (23.5–20.8, $P < .0001$).

Outcomes. Table IV lists major complications associated with NSTI. The proportion of patients having any major complication increased during the study period (30.9–48.2%, $P < .0001$). Patients, on average, experienced a total of 0.4 to 0.7 major complications during their hospital stay. LOS

Table III. Trends in treatment of NSTI 1998–2010 ($N = 56,527$)

Variable	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	P value
Surgical intervention														
Any debridement	99.6	99.3	99.4	99.2	99.6	99.5	99.3	99.6	99.9	99.9	99.5	99.6	99.6	NS
Amputation*	1.9			1.7			2.0			1.2			—	.004
No. debridements														
1	43.2	41.3	41.4	40.4	43.2	43.3	44.1	44.2	44.1	45.5	47.2	48.7	46.2	<.0001
2	29.5	32.3	31.1	32.2	27.9	29.5	29.0	28.6	29.6	28.8	27.0	25.7	26.4	<.0001
3	13.4	13.9	14.8	14.2	15.0	14.6	15.3	13.0	13.5	12.2	11.8	12.5	11.1	<.0001
More than 3	13.5	11.8	12.1	12.4	13.5	12.2	10.9	13.7	12.6	13.4	13.6	12.6	15.9	.0004
Wound therapy														
HBOT*	1.6			1.6			1.3			0.8			—	<.0001
Wound care	12.7	10.3	9.7	10.6	11.5	12.7	10.4	9.3	11.9	15.1	11.9	11.2	14.5	<.0001
Wound closure	23.5	18.7	17.0	20.2	16.9	15.5	17.1	17.2	17.9	16.3	14.6	14.1	20.8	<.0001

*Per the data use agreement with the Healthcare Utilization Project, we cannot display results with less than 10 patients represented in the aggregate value; thus, these have been collapsed into 3 year intervals from 1998 to 2009 and not shown for 2010.
Values are percentages.
HBOT, Hyperbaric oxygen therapy; *NTSI*, necrotizing soft-tissue infections; *NS*, not significant.

remained stable at 18–19 days, whereas overall mortality notably decreased (9.0–4.9%, $P < .0001$; Fig). On multivariable analyses, we found that age, sex, insurance, and Elixhauser index were predictors of any major complication. Age, race, insurance, Elixhauser index, HBOT treatment, and number of major complications were predictors of LOS. Similarly, age, race, insurance, and number of major complications were predictors of mortality. After accounting for these confounders, each 1-year incremental increase in year was associated with a 5% increased odds of complication (odds ratio 1.05), 0.4 times decrease in hospital LOS (coefficient −0.41), and 11% decreased odds of mortality (odds ratio 0.89; Table V).

DISCUSSION

NSTI, although decreasing in mortality, is a highly morbid disease. Our national, 13-year analysis elucidates recent trends in the incidence, treatment, and outcomes for this high-acuity surgical disease. We have found that there have been several potentially important national trends in patient population, treatment patterns, and outcomes. Patients have been increasingly from Hispanic and publicly insured groups, and overall comorbidities have increased sharply along with complication rates. Despite worsening acuity, LOS has been relatively stable, while mortality has decreased by nearly 50%.

Our study found demographic changes in the NSTI population, with Hispanics accounting for a greater proportion of patients. A likely explanation for this finding is the rapid expansion of the U.S. Hispanic population. According to the U.S. Census Bureau, greater than one-half of the total population growth within the United States during the 2000 to 2010 decade was attributed to increases in the Hispanic population. This segment grew 43% during this time, with an increase of 15.2 million persons.[13] We also found that the proportion of Medicaid patients also increased during our study period. The fact that Hispanics and Medicaid patients are being affected by this morbid infection at such increasing rates raises further questions concerning etiologies, access to care, and prevalence of risk factors that warrants further investigation. Given our findings, it is important for clinicians caring for patients of diverse backgrounds to consider NSTI in their differential diagnosis for patients who present with signs and symptoms of soft-tissue infection to ensure that all patients benefit equally from early diagnosis, aggressive debridement, and improved wound therapy.

Our results suggest, however, that even after diagnosis, disparities not explained by factors such as age and comorbidities may persist. When controlling for these possible confounders, we found that both Hispanic and Medicaid patients have an odds of mortality 1.6 times greater than white patients and privately insured patients, respectively. Meanwhile, Medicaid patients have greater odds of complications and increased hospital LOS compared with patients with private insurance. Black patients also suffer more complications than their white counterparts with NSTI.

There is a growing body of evidence that patients in the United States get differential treatment on the basis of race/ethnicity and

Table IV. Trends in overall NSTI outcomes 1998–2010 ($N = 56,527$)

Variable	*1998*	*1999*	*2000*	*2001*	*2002*	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	P *value*
Complications, %														
Any major complication	30.9	30.5	29.1	34.0	33.8	35.8	34.7	34.5	36.9	38.5	40.6	45.5	48.2	<.0001
Specific complications														
Cardiac*	1.3			1.4			1.4			1.4			*	.72
Pulmonary	16.2	13.9	14.2	17.7	16.9	17.6	18.0	18.3	18.3	20.1	19.0	22.0	22.8	<.0001
Neurologic*	0.8			0.8			0.6			0.6			—	.02
Thromboembolic	3.1	2.1	3.0	2.5	3.1	4.0	3.8	2.6	4.3	4.7	4.3	4.1	7.2	<.0001
Renal	11.6	13.3	14.6	16.3	16.3	15.3	17.5	18.5	20.3	22.9	23.1	29.7	31.1	<.0001
Infectious	8.2	8.1	5.6	7.5	8.0	8.6	7.4	7.5	8.2	7.9	9.5	7.9	9.1	.0003
Total major complications, mean sum	0.41	0.40	0.40	0.46	0.47	0.48	0.49	0.49	0.53	0.58	0.58	0.65	0.73	<.0001
Outcomes														
LOS, mean days	19.4	19.2	18.1	19.4	18.8	17.9	17.7	17.7	18.5	18.5	18.6	18.2	18.1	.12
LOS, median days	13.3	13.2	11.8	13.1	13.1	12.5	12.0	12.2	12.0	12.4	11.6	12.2	11.9	.10
Mortality (%)	9.0	10.5	10.2	11.1	10.0	7.4	8.5	5.4	6.3	5.7	4.6	5.7	4.9	<.0001

*Per the data use agreement with the Healthcare Utilization Project, we cannot display results with less than 10 patients represented in the aggregate value; thus, these have been collapsed into 3-year intervals from 1998 to 2009 and not shown for 2010.
LOS, Length of stay; *NTSI*, necrotizing soft-tissue infections.

socioeconomic status. The causes of these health care disparities are multiple and the source of much debate.[14–17] One explanation for increased hospital LOS with Medicaid patients may be that their insurance is not favorable for discharge to rehabilitation or skilled nursing facilities.[18] Hospital factors also may be the source of differences in complication rates because in a number of studies authors have shown that hospitals that treat more minority and/or indigent patients have worse outcomes.[19–21] When resources and access are otherwise equitable across groups, differences in outcomes by race, ethnicity, or socioeconomic status may be the result of unconscious bias.[22]

The percentage of patients with NSTI who were obese tripled during the study period. This finding follows the trend of increasing obesity among the general U.S. population during the past several decades. The current lifetime risk of an American becoming overweight or obese exceeds 50% and 25%, respectively.[23] Given the alarming rates of obesity in our population, the overall importance of obesity on the NSTI population may be more clinically important. Although initiatives to prevent obesity traditionally have focused on reducing risk of cardiovascular disease and certain types of cancer, the association between obesity and NSTIs is an important public health concern. Meanwhile, clinicians faced with an obese patient with seemingly subtle cellulitis and pain out of proportion to examination should have a high index of suspicion for a NSTI and possibly use contrast-enhanced computed tomography more frequently to aid in an early diagnosis.[24]

Early and aggressive debridement remains the mainstay of surgical management for NSTIs. During our study period, there were simultaneous increases in the proportion of patients requiring only a single debridement (nearly half in 2010) and the proportion of patients requiring multiple debridements (approximately 16% in 2010). Thus, although a certain percentage of patients appear to be benefiting from early diagnosis and aggressive initial debridement, the number of patients with severe, progressive disease also has increased, although the proportion of patients who need amputation is very small. Notably, the decrease in nonprimary skin closure along with increases in wound care procedures suggests that more recent advances in wound therapy such as negative pressure wound therapy may be benefiting NSTI patients in the modern era. Clinicians should consider using such methods before subjecting patients to an additional donor-site wound as would be needed for complex reconstructions.

Despite the many reports regarding the utility of HBOT in the treatment of NSTI,[7,8,25,26] including several in which the authors report a survival advantage,[8,26] the use of HBOT in the United States is rare. This is likely because HBOT is a specialized treatment not readily available at all hospitals. Our data suggest, however, that patients who did undergo HBOT had no obvious improvements in complication rates or mortality, but their hospital

Table V. Predictors of outcomes for NSTI in multivariable analyses*

	Outcome of interest					
	Any complication		*Hospital LOS*		*Mortality*	
Variable	*OR*	*95% CI*	*Coefficient*	*95%CI*	*OR*	*95% CI*
Year	1.05	(1.04, 1.07)	−0.41	(−0.49, −0.32)	0.89	(0.87, 0.91)
Age, years						
18–34	ref		ref		ref	
35–49	1.30	(1.12, 1.52)	1.29	(0.39, 2.19)	1.35	(0.95, 1.92)
50–64	1.69	(1.45, 1.97)	2.07	(1.15, 3.00)	2.05	(1.46, 2.88)
>64	1.85	(1.54, 2.22)	1.65	(0.41, 2.89)	3.03	(2.07, 4.44)
Sex						
Male	ref		ref		ref	
Female	1.19	(1.09, 1.29)	0.46	(−0.16, 1.08)	1.01	(0.86, 1.18)
Race						
White	ref		ref		ref	
Black	1.13	(1.00, 1.27)	0.38	(−0.56, 1.33)	0.97	(0.77, 1.23)
Hispanic	0.99	(0.86, 1.14)	0.92	(−0.09, 1.93)	1.57	(1.23, 2.00)
Asian/Pacific Islander/Native American/other	1.04	(0.84, 1.30)	0.92	(−0.59, 2.43)	1.77	(1.25, 2.51)
Missing/unknown	1.04	(0.94, 1.15)	−1.29	(−1.99, −0.60)	1.14	(0.94, 1.38)
Insurance						
Private	ref		ref		ref	
Medicare	1.42	(1.26, 1.60)	0.35	(−0.56, 1.26)	1.64	(1.30, 2.06)
Medicaid	1.24	(1.10, 1.40)	3.76	(2.82, 4.70)	1.55	(1.21, 1.97)
Self-pay	0.72	(0.62, 0.83)	1.58	(0.68, 2.49)	1.50	(1.12, 2.00)
No charge/other*	0.85	(0.72, 1.00)	1.94	(0.88, 3.00)	1.19	(0.85, 1.69)
Elixhauser index						
0	ref		ref		ref	
1	1.54	(1.30, 1.83)	0.92	(−0.06, 1.90)	1.10	(0.80, 1.52)
2	1.76	(1.49, 2.08)	2.37	(1.39, 3.35)	1.07	(0.78, 1.46)
3	2.03	(1.71, 2.41)	2.49	(1.46, 3.51)	0.99	(0.72, 1.37)
>3	2.89	(2.44, 3.43)	3.70	(2.61, 4.80)	1.01	(0.73, 1.40)
HBOT treatment	0.82	(0.57, 1.18)	3.47	(1.11, 5.84)	0.57	(0.26, 1.26)
Total major complications	—	—	9.46	(8.9, 10.01)	2.67	(2.47, 2.88)

*Covariates in the model included year of treatment, age group, sex, race, insurance, Elixhauser index, and HBOT treatment. The models for mortality and LOS also included total major complications. The model for LOS included only those patients who survived hospitalization.
CI, Confidence interval; *HBOT*, hyperbaric oxygen therapy; *LOS*, length of stay; *NTSI*, necrotizing soft-tissue infections.

LOS was nearly 3.5 days greater than patients who did not undergo HBOT. Thus, our study provides no convincing advantages for HBOT as an adjunct treatment for NSTI even when readily available.

Overall, the mortality rate of NSTI has decreased to 4.9% nationally during the past decade. This mortality is considerably less than similar national studies in which the authors used both NIS and NSQIP data (10.9% and 12% respectively).[4,5] We found that increasing age was associated with more complications and greater rates of mortality. In addition, although greater comorbidity burden increased complications and LOS, this burden had no effect on mortality. Importantly, however, each added complication increased LOS by almost 9.5 days and resulted in a 2.7 increased odds of mortality when we controlled for confounders. This finding suggests that patients who may have previously died from NSTI are now surviving with some measure of morbidity. Possible explanations for the stable LOS and reduced mortality despite the trend toward increased baseline comorbidities and greater complications during treatment course include increased awareness and early diagnosis by local physicians, improvements in intensive care and resuscitative efforts, better would care options, and improved antibiotic coverage.

Our findings have implications for surgeon–patient discussions at the time of diagnosis of NSTI. What in the past may have been a discussion about the very high likelihood of death despite aggressive interventions is today more appropriately a detailed discussion of a long hospital course involving multiple trips to the operating room for removal of affected tissue and wound care and many potential complications.

This study has a number of important limitations. The NIS is an administrative dataset reliant on UB-40 billing sheets generated by sampled hospitals. Relying on administrative data may result in underestimation of true NSTIs. Nevertheless, we believe our selection strategy, combining at least one operative debridement with a diagnosis code for NSTI, would minimize this effect. Previous research on NSTI has detailed changes in microbiology with single-organism infections more prevalent in the past and polymicrobial infection more prevalent in the modern era.[10] Unfortunately, the NIS does not provide any clinical data on wound microbiology or choice of antimicrobial therapy. Without access to clinical data, administrative databases are also subject misclassification/underestimation errors for both measures of comorbidity and complication severity. The Elixhauser Index, although validated and commonly used in studies using administrative data,[27–34] measures the presence or absence of comorbid conditions without gauging the individual severity of each comorbidity with the possible of exception of diabetes (see Appendix III, online version only). Furthermore, there has been recent criticism of Elixhauser's method but this newer application has yet to be applied widely to the literature due to a delay in implementation of *International Classification of Diseases*, 10th revision, codes in U.S. administrative data.[27]

Similarly, we are also unable to measure complication severity using common, validated metrics such as the Accordion Severity Grading System of Surgical Complications, Acute Physiology and Chronic Health Evaluation (APACHE) score or the Sequential Organ Failure Assessment (SOFA) score that rely on actual clinical data points that are not available in the NIS. In addition, factors not captured by the administrative database may lead to an underestimation complications rates because of both limitations on the total number of fields available for coding complications and lack of readmission data (NIS treats each admission as a stand-alone event). Our finding of an increase in comorbidity burden during the study period may have resulted from up-coding by billing specialists or improved documentation by providers rather than a true increase in pre-existing conditions among NSTI patients. However, on the basis of other studies on the overall health of the U.S. population, we believe that our findings represent a true change in patient characteristics.[35,36] It is also possible that increases in complications were attributable similar "improvements" in coding. It is well known that race is coded poorly in administrative data; thus, our demographic findings may also be at risk for misclassifications; however, we know of no other large national dataset that would provide more precise race data for NSTI patients. Finally, the overall use of HBOT and amputations was very low and our ability to judge trends in these treatments was thus limited.

Despite these limitations, this nationwide analysis of NSTI is, to our knowledge, the largest population-based sample of NSTI in the US population and has shown that demographics and comorbidity shifts have occurred and complications have increased. Meanwhile, however, LOS has been relatively stable and mortality has decreased. This suggests improvements of our modern health care system during this study period may be at play.

We are grateful to Gordon Fitzgerald, PhD from the Center for Outcomes Research at the University of Massachusetts Medical School for his assistance in statistical review for this manuscript. The research was supported by Dr. Santry's University of Massachusetts Clinical Research Scholar Award (K13, UL1RR031982 1KL2RR031981-01).

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version at 10.1016/j.surg.2012.11.026.

REFERENCES

1. Ward RG, Walsh MS. Necrotizing fasciitis: 10 years' experience in a district general hospital. Br J Surg 1991;78:488-9.
2. Wong CH, Chang HC, Pasupathy S, et al. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. J Bone Joint Surg Am 2003;85-A:1454-60.
3. Kaul R, McGreer A, Low DE, et al. Population-based surveillance for group A streptococcal necrotizing fasciitis: clinical features, prognostic indicators, and microbiologic analysis of seventy-seven cases. Ontario Group A Streptococcal Study. Am J Med 1997;103:18-24.
4. Mills MK, Faraklas I, Davis C, et al. Outcomes from treatment of necrotizing soft-tissue infections: results from the National Surgical Quality Improvement Program database. Am J Surg 2010;200:790-6.
5. Endorf FW, Klein MB, Mack CD, et al. Necrotizing soft-tissue infections: differences in patients treated at burn centers and non-burn centers. J Burn Care Res 2008;29:933-8.
6. Mulla ZD, Gibbs SG, Aronoff DM. Correlates of length of stay, cost of care, and mortality among patients hospitalized for necrotizing fasciitis. Epidemiol Infect 2007;135:868-76.
7. Jallali N, Withey S, Butler PE. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. Am J Surg 2005;189:462-6.
8. Wilkinson D, Doolette D. Hyperbaric oxygen treatment and survival from necrotizing soft tissue infection. Arch Surg 2004;139:1339-45.

9. Czymek R, Hildebrand P, Kleemann M, et al. New insights into the epidemiology and etiology of Fournier's gangrene: a review of 33 patients. Infection 2009;37:306-12.
10. Sarani B, Strong M, Pascual J, Schwab CW. Necrotizing fasciitis: current concepts and review of the literature. J Am Coll Surg 2009;208:279-88.
11. Anaya DA, Dellinger EP. Necrotizing soft-tissue infection: diagnosis and management. Clin Infect Dis 2007;44:705-10.
12. Awsakulsutthi S. A retrospective review of necrotizing fasciitis in Thammasat University Hospital. J Med Assoc Thai 2010;93(Suppl 7):S246-53.
13. Humes KR, Jones NA, Ramirez R. Overview of race and Hspanic origin: 2010 (2010 Census Briefs). Washington, DC: United States Census Bureau; 2011. Available fromhttp://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf.
14. Smedley BD. Unequal treatment: confronting racial and ethnic disparities in health care. Washington, DC: National Academy Press; 2003.
15. Bach PB, Schrag D, Brawley OW, et al. Survival of blacks and whites after a cancer diagnosis. JAMA 2002;287:2106-13.
16. Slatore CG, Au DH, Gould MK. An official American Thoracic Society systematic review: insurance status and disparities in lung cancer practices and outcomes. Am J Respir Crit Care Med 2010;182:1195-205.
17. Vogel TR. Update and review of racial disparities in sepsis. Surg Infect (Larchmt) 2012;13:203-8.
18. Lane-Fall MB, Iwashyan TJ, Cooke CR, et al. Insurance and racial differences in long-term acute care utilization after critical illness. Crit Care Med 2012;40:1143-9.
19. Ly DP, Lopez L, Isaac T, Jha AK. How do black-serving hospitals perform on patient safety indicators? Implications for national public reporting and pay-for-performance. Med Care 2010;48:1133-7.
20. Hasnain-Wynia R, Baker DW, Nerenz D, et al. Disparities in health care are driven by where minority patients seek care: examination of the hospital quality alliance measures. Arch Intern Med 2007;167:1233-9.
21. Bach PB. Racial disparities and site of care. Ethn Dis 2005; 15(2 Suppl 2):S31-3.
22. Santry HP, Wren SM. The role of unconscious bias in surgical safety and outcomes. Surg Clin North Am 2012;92:137-51.
23. Vasan RS, Pencina MJ, Cobain M, et al. Estimated risks for developing obesity in the Framingham Heart Study. Ann Intern Med 2005;143:473-80.
24. Zacharias N, Velmahos GC, Salama A, et al. Diagnosis of necrotizing soft tissue infections by computed tomography. Arch Surg 2010;145:452-5.
25. Massey PR, Sakran JV, Mills AM, et al. Hyperbaric oxygen therapy in necrotizing soft tissue infections. J Surg Res 2012;177:146-51.
26. Escobar SJ, Slade JB Jr, Hunt TK, Cianci P. Adjuvant hyperbaric oxygen therapy (HBO2)for treatment of necrotizing fasciitis reduces mortality and amputation rate. Undersea Hyperb Med 2005;32:437-43.
27. Van Walraven C, Austin PC, Jennings A, et al. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care 2009;47:626-33.
28. Drolet S, Maclean AR, Stewart DA, et al. Primary colorectal lymphoma-clinical outcomes in a population-based series. J Gastrointest Surg 2011;15:1851-7.
29. Kaplan GG, Hubbard J, Panaccione R, et al. Risk of comorbidities on postoperative outcomes in patients with inflammatory bowel disease. Arch Surg 2011;146: 959-64.
30. Csikesz NG, Nguyen LN, Tseng JF, Shah SA. Nationwide volume and mortality after elective surgery in cirrhotic patients. J Am Coll Surg 2009;208:96-103.
31. Myers RP, Quan H, Hubbard JN, et al. Predicting in-hospital mortality in patients with cirrhosis: results differ across risk adjustment methods. Hepatology 2009;49:568-77.
32. Singla A, Csikesz NG, Simons JP, et al. National hospital volume in acute pancreatitis: analysis of the Nationwide Inpatient Sample 1998-2006. HPB (Oxford) 2009;11:391-7.
33. Singla A, Li Y, Ng SC, et al. Is the growth in laparoscopic surgery reproducible with more complex procedures? Surgery 2009;146:367-74.
34. Santry HP, Gillen DL, Lauderdale DS. Trends in bariatric surgical procedures. JAMA 2005;294:1909-17.
35. Nguyen NT, Mango CP, Lane KT, et al. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the National Health and Nutrition Examination Survey, 1999 to 2004. J Am Coll Surg 2008; 207:928-34.
36. U.S. Department of Health and Human Resources, Center for Disease Control and Prevention, National Center for Health Statistics. Health, United States, 2010. Available from: http://www.cdc.gov/nchs/data/hus/hus10.pdf.