Burden, risk factors, and infectious complications of cellulitis and erysipelas in US adults and children in the emergency department setting

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Background: Little is known about the use and burden of emergency department (ED) visits for cellulitis/erysipelas in the United States.

Objective: To determine the prevalence, risk factors, complications, and cost of emergency care for cellulitis/erysipelas in the United States.

Methods: Cross-sectional study of the 2006 to 2016 National Emergency Department Sample, including a 20% sample of US ED visits (N = 320,080,467).

Results: The mean annual incidence of ED visits with a primary diagnosis of cellulitis/erysipelas was 2.42 to 3.55 per million adult and 1.14 to 2.09 per million pediatric ED visits. ED visits for cellulitis/erysipelas decreased significantly from 2006 to 2015 (Rao-Scott chi-square, $P < .0001$). ED visits with versus without a primary diagnosis of cellulitis/erysipelas were associated with public or no insurance and lower household income quartiles, and were more likely to occur during weekends and summer months. The mean cost of ED visits for cellulitis/erysipelas more than doubled in adults (from $720 to $1680) and tripled in children (from $939 to $2,823) from 2006 to 2016. ED visits for cellulitis/erysipelas were associated with multiple risk factors and increased infectious complications.

Limitations: No data on cellulitis and erysipelas treatment or recurrence.

Conclusion: There is a substantial and increasing burden of ED visits for cellulitis/erysipelas in the United States. Many ED visits occurred for uncomplicated cellulitis/erysipelas, in part because of health care disparities. (J Am Acad Dermatol 2021;84:1496-503.)

Key words: autoimmune; bacteria; burden; dermatology; epidemiology; health services; infection; inflammatory; skin.

Patient with cellulitis/erysipelas may experience rapid-onset erythema, severe pain, fever, and other symptoms, warranting prompt evaluation and management.[1] Most cases of cellulitis/erysipelas are uncomplicated and can be managed in the outpatient setting. However, some patients with cellulitis/erysipelas might not have adequate access to outpatient care and therefore turn to an emergency department (ED) as a primary place for treatment. We hypothesized that there are socioeconomic and health care disparities that contribute to increased ED visits for cellulitis/erysipelas in the United States.

Additionally, a substantial subset of patients with cellulitis/erysipelas experiences systemic complications, such as extracutaneous infections and

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Funding sources: Supported by the Agency for Healthcare Research and Quality (grant no. K12 HS023011).

IRB approval status: Reviewed and approved by the IRB at Northwestern University.

Accepted for publication November 13, 2020.

Reprints not available from the authors.

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Published online November 22, 2020.

0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2020.11.021

septicemia, warranting emergent evaluation and often hospitalization.[1-4] We hypothesized that cellulitis/erysipelas are associated with a wide array of extracutaneous infectious complications.

ED visits are associated with higher health care costs than outpatient visits,[5] and excessive ED visits can be a strain on limited health care resources. Concerns about appropriate use of ED care are always relevant but are particularly timely during the severe acute respiratory syndrome coronavirus 2 pandemic that is already straining global health care systems. However, little is known about the burden and comorbidity of ED visits for cellulitis/erysipelas in the United States. We sought to determine the frequency, cost burden, risk factors, and infectious complications of ED visits for cellulitis/erysipelas. Finally, we sought to identify risk factors for ED visits for cellulitis/erysipelas, including underlying chronic inflammatory skin disease (CISD) and autoimmune diseases.

CAPSULE SUMMARY

- Although emergency department visits for cellulitis/erysipelas decreased, their mean costs more than doubled in adults and tripled in children over time.
- Many emergency department visits for cellulitis/erysipelas occurred for uncomplicated cellulitis/erysipelas and may have been unnecessary, in part because of health care disparities.

METHODS

Data source

The 2006 to 2016 Nationwide Emergency Department Sample (NEDS) was analyzed. Each year of NEDS contained an approximately 20% stratified representative cross-sectional sample of US hospital-owned EDs. Sample weights were provided by NEDS that factored the sampling design and allowed for representative estimates of ED visits across the United States. All data were deidentified. No attempts were made to identify individuals in the database. All researchers were compliant with the NEDS data use agreement. Identification of cellulitis/erysipelas, comorbidities and infectious complications are presented in Supplemental Methods and Tables (available via Mendeley at https://doi.org/10.17632/sbn6pgb68x.1).

The study was approved by the institutional review board at Northwestern University.

Statistical analysis

Statistical analyses were performed by using SAS, version 9.4.3 (SAS Institute). The unit of analysis was an individual ED visit. Analyses were performed separately in children (age, <18 years) and adults (age, ≥18 years). Analyses were performed by using survey procedures that included discharge trend weights, sample strata that account for the ED's census region or division, ownership/control, location/teaching and number of beds, and clustering by individual hospital-owned ED. Weighted frequency, prevalence, and 95% confidence intervals (CIs) of either a primary or secondary diagnosis of a comorbidity were determined among ED visits with a primary, secondary, or no diagnosis of cellulitis or erysipelas. The cost for ED visit was estimated based on the total charge of the ED visit and the cost-to-charge ratio estimated by Healthcare Cost and Utilization Project. Summary statistics were generated for each comorbidity, including frequency, prevalence, geometric mean, 95% CI, and inflation-adjusted cost of care for ED visits with a diagnosis of cellulitis/erysipelas.

Survey logistic regression models were used to determine the association of cellulitis/erysipelas (independent variable) with comorbidities (binary dependent variable). Multivariable models included age (continuous), sex (male/female), and insurance status (yes/no). Crude and adjusted odds ratios (ORs) and 95% CIs were estimated.

RESULTS

Population characteristics

There were 320,080,467 ED visits captured in NEDS from 2006 to 2016, including 9,783,506 with a diagnosis of cellulitis or erysipelas (7,005,479 primary and 2,778,027 secondary diagnoses). The majority of cases occurred in adults (8,433,833) compared to children (1,349,673).

Prevalence of cellulitis/erysipelas

The mean annual incidence of ED visits with a primary diagnosis of cellulitis or erysipelas fluctuated in the range of 2.42 to 3.55 per million adult ED patients and 1.14 to 2.09 per million pediatric ED patients in 2006 to 2016. The 3 most common primary sites were legs (International Classification of Diseases, Ninth Revision [ICD-9] 682.6), arms (ICD-9 682.3) and trunk (ICD-9 682.2) in adults and the legs (ICD-9 682.6), buttocks (ICD-9 682.5), and arms (ICD-9 682.3) in children.

The proportion of ED visits that had a primary diagnosis of cellulitis or erysipelas significantly decreased from 2006 to 2015 in adults and children (Rao-Scott chi-square test, $P < .0001$) (Fig 1).

Abbreviations used:

AD: atopic dermatitis
CI: confidence interval
CISD: chronic inflammatory skin disease
ED: emergency department
ICD: International Classification of Diseases
NEDS: Nationwide Emergency Department Sample
OR: odds ratio

Associations of cellulitis/erysipelas

Temporal. The prevalence of ED visits with a primary diagnosis of cellulitis or erysipelas was highest during the summer months (July to September) and lowest during the winter months (January to March) for both children and adults (Table I). ED visits occurred more commonly on weekends in both children and adults with versus without a primary diagnosis of cellulitis/erysipelas.

Demographics. Both children and adults with cellulitis/erysipelas had significantly lower household income and were more likely to have public or no insurance.

Associated health factors. The top 3 comorbid diagnoses for patients with a diagnosis of cellulitis/erysipelas were septicemia (weighted prevalence, 5.28%), postoperative infection (4.64%), and diabetes with other specified manifestations (2.07%). In contrast, the top 3 comorbid diagnoses for patients without a diagnosis of cellulitis or erysipelas were acute upper respiratory infections (weighted prevalence, 1.97%), urinary tract infection (1.89%), and chest pain (1.72%). Several health disorders were associated with higher odds of cellulitis/erysipelas. In children and adults, cellulitis/erysipelas were more commonly associated with insect bites and stings, ulcers from other diseases, and wounds from recent surgery but not with animal or human bites, skin trauma, long-term use of corticosteroids, or immunosuppressants. Peripheral vascular disease was associated with cellulitis/erysipelas in adults but not children.

Weekend versus weekday visits. Patients with a primary diagnosis of cellulitis/erysipelas who visited the ED on a weekend versus weekday had slightly higher household income (adult: fourth quartile, 17.48% vs 16.92%; pediatric: fourth quartile, 17.15% vs 15.87%), likelihood of no chronic conditions (adult: 54.09% vs 52.84%; pediatric: 90.12% vs 89.46%), and likelihood of having private insurance (adult: 28.93% vs 25.52%; pediatric 29.56% vs 26.13%) compared with patients who visited the ED on a weekday.

Association of CISD with cellulitis/erysipelas

Overall, 0.48% of pediatric (95% CI, 0.46-0.50) and 0.94% of adult (95% CI, 0.92-0.95) ED patients with cellulitis/erysipelas were also diagnosed with a CISD. The percentage was significantly higher than adult ED patients without any cellulitis/erysipelas (adult: 0.50%; 95% CI, 0.50-0.51; pediatric: 0.71%; 95% CI, 0.69-0.72). In particular, cellulitis/erysipelas was associated with hidradenitis suppurativa, pyoderma gangrenosum, and dermatomyositis in both adult and pediatric patients and, to a lesser extent, atopic dermatitis (AD), psoriasis, pemphigus, pemphigoid, lichen planus, mycosis fungoides, Sézary syndrome, morphea, cutaneous lupus, erythema nodosum, and/or vitiligo (Supplemental Table II; available via Mendeley at https://doi.org/10.17632/sbn6pgb68x.1). In both adult (adjusted OR, 2.37; 95% CI, 2.26-2.50) and pediatric (adjusted OR, 2.48; 95% CI, 2.09-2.95) ED patients with cellulitis/

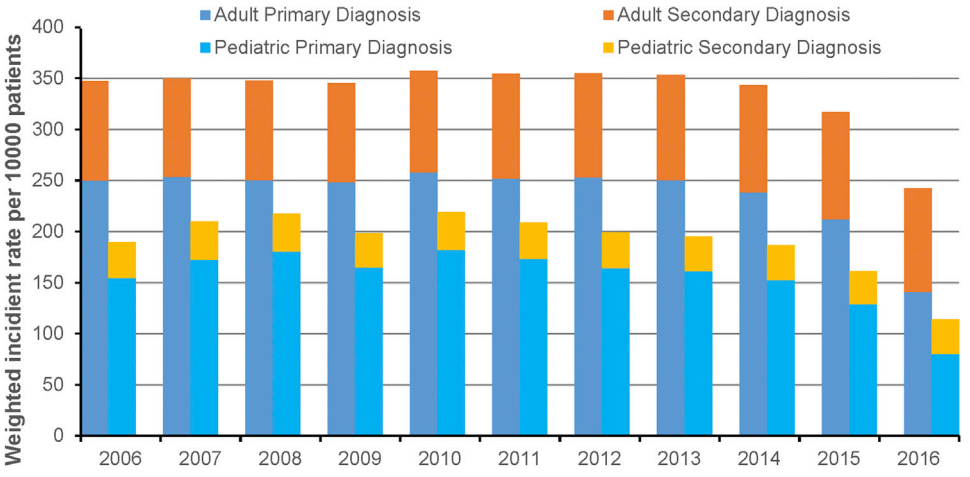

Fig 1. Annual weighted incident rate for primary and/or secondary diagnosis of cellulitis and erysipelas in adults and children.

Table I. Associations with a primary diagnosis of cellulitis or erysipelas among pediatric and adult ED patients in 2006 to 2016

	Primary diagnosis of cellulitis or erysipelas					
	Yes				No	
	Pediatric		Adult		Pediatric	Adult
Variable	Weighted mean (95% CI)	*P*	Weighted mean (95% CI)	*P*	Weighted mean (95% CI)	Weighted mean (95% CI)
Age, y	8.68 (8.59-8.78)	<.0001	47.00 (46.80-47.20)	<.0001	7.64 (7.57-7.72)	47.78 (47.62-47.94)
Charge, US$	$1113 (1077-1149)	<.0001	$1681 (1643-1719)	<.0001	$1356 (1321-1390)	$2678 (2615-2741)
	Weighted % (95% CI)	***P***	**Weighted % (95% CI)**	***P***	**Weighted % (95% CI)**	**Weighted % (95% CI)**
Median household income						
Q1 (lowest)	39.25 (37.93-40.57)	<.0001	35.63 (34.49-36.77)	<.0001	34.23 (33.01-35.45)	33.35 (32.31-34.38)
Q2	28.53 (27.65-29.41)		27.74 (26.96-28.53)		27.62 (26.77-28.46)	27.34 (26.61-28.07)
Q3	20.12 (19.25-21.00)		21.49 (20.72-22.26)		21.90 (21.12-22.68)	22.24 (21.55-22.93)
Q4 (highest)	12.09 (11.32-12.86)		15.13 (14.29-15.98)		16.28 (15.31-17.22)	17.07 (16.20-17.95)
Season						
Winter (January-March)	18.85 (18.71-18.99)	<.0001	20.76 (20.68-20.84)	<.0001	26.24 (26.15-26.32)	24.39 (24.35-24.44)
Spring (April-June)	26.33 (26.18-26.47)		25.74 (25.67-25.81)		24.70 (24.64-24.76)	25.18 (25.15-25.21)
Summer (July-September)	33.32 (33.15-33.50)		30.30 (30.20-30.39)		23.77 (23.70-23.85)	25.87 (25.83-25.91)
Fall (October-December)	21.50 (21.34-21.66)		23.20 (23.10-23.30)		25.29 (25.21-25.37)	24.56 (24.51-24.60)
Weekend admission	31.52 (31.33-31.71)	<.0001	29.38 (29.28-29.47)	<.0001	30.57 (30.46-30.67)	27.96 (27.90-28.02)
Sex						
Female	49.99 (49.83-50.15)	<.0001	52.90 (52.73-53.07)	<.0001	48.34 (48.25-48.43)	42.62 (42.45-42.79)
Male	50.01 (49.85-50.17)		47.10 (46.93-47.28)		51.66 (51.57-51.75)	57.38 (57.21-57.55)
	Weighted incident rate per 10,000	***P***	**Weighted incident rate per 10,000**	***P***	**Weighted incident rate per 10,000**	**Weighted incident rate per 10,000**
Mortality						
Died in ED	0.08381656	<.0001	0.290030096	<.0001	3.002918017	18.53804072
Died in hospital	0.010276675		5.743472775		1.40837717	52.36028855
	Weighted % (95% CI)	***P***	**Weighted % (95% CI)**	***P***	**Weighted % (95% CI)**	**Weighted % (95% CI)**
Insurance						
Public	58.55 (57.78-59.33)	<.0001	41.75 (41.16-42.33)	<.0001	53.66 (52.85-54.47)	47.55 (47.09-48.01)
Private	27.21 (26.49-27.92)		26.52 (26.05-26.99)		34.29 (33.50-35.08)	29.61 (29.18-30.04)
None	14.24 (13.70-14.77)		31.73 (31.05-32.41)		12.05 (11.61-12.49)	22.84 (22.35-23.33)
Disposition of the patient at discharge from ED						
Routine discharge	90.25 (89.57-90.93)	<.0001	81.09 (80.61-81.56)	<.0001	93.30 (92.75-93.86)	79.02 (78.65-79.41)
Admitted as inpatient	7.80 (7.25-8.35)		16.73 (16.37-17.09)		3.83 (3.61-4.06)	17.68 (17.42-17.95)
Other	1.95 (1.49-2.41)		2.18 (1.90-2.46)		2.86 (2.34-3.38)	3.30 (3.02-3.58)
Number of chronic conditions						
0	89.66 (89.30-90.03)	<.0001	53.21 (52.45-53.97)	<.0001	82.64 (82.29-82.99)	40.87 (40.34-41.39)
1-2	9.68 (9.34-10.01)		28.60 (28.05-29.16)		15.92 (15.63-16.20)	32.27 (32.00-32.54)
3-5	0.59 (0.55-0.64)		11.51 (11.28-11.74)		1.27 (1.20-1.34)	15.95 (15.72-16.19)
≥6	0.07 (0.06-0.08)		6.68 (6.49-6.86)		0.17 (0.15-0.19)	10.91 (10.69-11.14)

CI, Confidence interval; *ED*, emergency department; *Q*, quartile.

erysipelas, antibiotic resistant infections were associated with significantly increased odds of CISD.

Association of extracutaneous autoimmune disease with cellulitis/erysipelas

Overall, 0.48% (95% CI, 0.46-0.51) of pediatric and 2.67% (95% CI, 2.63-2.72) of adult ED patients with cellulitis or erysipelas were also diagnosed with an extracutaneous autoimmune disease, which was higher than those without cellulitis/erysipelas (0.35% [95% CI, 0.33-0.37] and 1.97% [95% CI, 1.93-2.00] respectively). In particular, cellulitis/erysipelas was associated with polymyositis and systemic sclerosis, as

Table II. Association of infectious complications with cellulitis and erysipelas in ED patients

	Primary or secondary diagnosis of cellulitis or erysipelas					
	No		Yes			
Comorbidities	Weighted frequency	Weighted % prevalence (95% CI)	Weighted frequency	Weighted % prevalence (95% CI)	Adjusted OR* (95% CI)	*P*
Adult						
MSSA	1,662,621	0.15 (0.15-0.16)	1,136,167	3.00 (2.91-3.09)	20.30 (19.84-20.77)	<.0001
MRSA	1,465,166	0.13 (0.13-0.14)	1,080,712	2.86 (2.79-2.92)	22.10 (21.66-22.55)	<.001
Group A *Streptococcus*	58,016	0.0053 (0.0050-0.0057)	71,389	0.19 (0.18-0.20)	34.89 (32.91-37.00)	<.0001
Antibiotic resistant infection	1,114,846	0.10 (0.10-0.11)	939,407	2.48 (2.42-2.55)	25.37 (24.77-25.99)	<.0001
Lymphangitis	65,994	0.0061 (0.0059-0.0063)	63,965	0.17 (0.16-0.18)	26.75 (25.75-27.79)	<.0001
Gangrene	410,171	0.038 (0.037-0.039)	217,895	0.58 (0.56-0.59)	15.72 (15.36-16.08)	<.0001
Septic arthritis	310,411	0.029 (0.028-0.029)	116,223	0.31 (0.30-0.32)	10.59 (10.34-10.85)	<.0001
Osteomyelitis	1,293,441	0.12 (0.12-0.12)	728,837	1.93 (1.88-1.97)	16.47 (16.08-16.86)	<.0001
Toxic shock syndrome	8983	0.0008 (0.0008-0.0009)	4497	0.012 (0.011-0.013)	15.30 (14.06-16.65)	<.0001
Endocarditis	405,550	0.037 (0.036-0.039)	18,674	0.049 (0.047-0.052)	1.43 (1.37-1.49)	<.0001
Meningitis	86,352	0.0079 (0.0076-0.0083)	2278	0.006 (0.0054-0.0066)	0.76 (0.69-0.83)	<.0001
Shock	328,068	0.030 (0.029-0.031)	10,333	0.027 (0.026-0.029)	0.95 (0.90-0.99)	.022
Diabetes mellitus	10,0645,893	9.26 (9.14-9.37)	4,119,659	10.89 (10.76-11.01)	1.27 (1.27-1.28)	<.0001
Venous insufficiency	1,784,154	0.16 (0.16-0.17)	830,169	2.19 (2.14-2.24)	15.02 (14.74-15.30)	<.0001
Lymphedema	628,959	0.058 (0.056-0.060)	350,001	0.92 (0.90-0.95)	17.68 (17.37-18.00)	<.0001
Cancer	35,306,074	3.25 (3.17-3.32)	1,077,920	2.85 (2.77-2.92)	0.94 (0.93-0.95)	<.0001
Septicemia	12,308,198	1.13 (1.11-1.16)	1,332,291	3.52 (3.43-3.61)	3.47 (3.43-3.52)	<.0001
Pediatric						
MSSA	104,909	0.034 (0.030-0.037)	154,578	2.55 (2.29-2.81)	80.55 (74.90-86.62)	<.0001
MRSA	69,671	0.022 (0.020-0.024)	144,780	2.39 (2.21-2.57)	115.06 (107.98-122.61)	<.0001
Group A *Streptococcus*	34,240	0.011 (0.009-0.013)	11,875	0.20 (0.18-0.22)	18.42 (15.96-21.26)	<.0001
Antibiotic resistant infection	66,287	0.021 (0.020-0.023)	139,225	2.30 (2.13-2.47)	116.22 (109.95-122.85)	<.0001
Lymphangitis	19,072	0.0061 (0.0058-0.0064)	13,601	0.22 (0.21-0.24)	35.16 (33.01-37.45)	<.0001
Gangrene	2755	0.0009 (0.0008-0.0010)	533	0.0088 (0.0070-0.0106)	9.63 (7.71-12.03)	<.0001
Septic arthritis	29,212	0.0094 (0.0085-0.010)	4440	0.073 (0.066-0.081)	7.92 (7.26-8.65)	<.0001
Osteomyelitis	46,239	0.015 (0.013-0.017)	12,812	0.21 (0.19-0.24)	13.88 (12.98-14.84)	<.0001
Toxic shock syndrome	4379	0.0014 (0.0012-0.0016)	1022	0.017 (0.014-0.020)	11.07 (9.38-13.05)	<.0001
Endocarditis	8024	0.0026 (0.0023-0.0028)	139	0.0023 (0.0013-0.0032)	0.87 (0.58-1.31)	.5
Meningitis	35,212	0.011 (0.011-0.012)	315	0.0052 (0.0040-0.0064)	0.48 (0.38-0.61)	<.0001
Shock	11,217	0.0036 (0.0028-0.0044)	227	0.0038 (0.0022-0.0053)	1.09 (0.77-1.55)	.64
Diabetes mellitus	549,381	0.18 (0.17-0.18)	19,102	0.32 (0.30-0.33)	1.54 (1.49-1.60)	<.0001
Venous insufficiency	2082	0.0007 (0.0006-0.0008)	248	0.0041 (0.0029-0.0053)	5.42 (3.98-7.39)	<.0001
Lymphedema	6803	0.0022 (0.0020-0.0024)	1488	0.025 (0.021-0.028)	10.58 (9.16-12.21)	<.0001
Cancer	207,496	0.067 (0.058-0.075)	4006	0.066 (0.054-0.078)	0.97 (0.87-1.07)	.54
Septicemia	346,857	0.11 (0.10-0.12)	17,976	0.30 (0.27-0.32)	2.88 (2.71-3.06)	<.0001

CI, Confidence interval; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-sensitive *Staphylococcus aureus*.
*Adjusted for age (continuous), gender (male vs. female), insurance status (insured vs. uninsured).

well as multiple other autoimmune disorders, particularly in adults (Supplemental Table II). In both adult (adjusted OR, 2.40; 95% CI, 2.32-2.48) and pediatric (adjusted OR, 2.51; 95% CI, 2.15-2.93) ED patients with cellulitis/erysipelas, antibiotic-resistant infections were associated

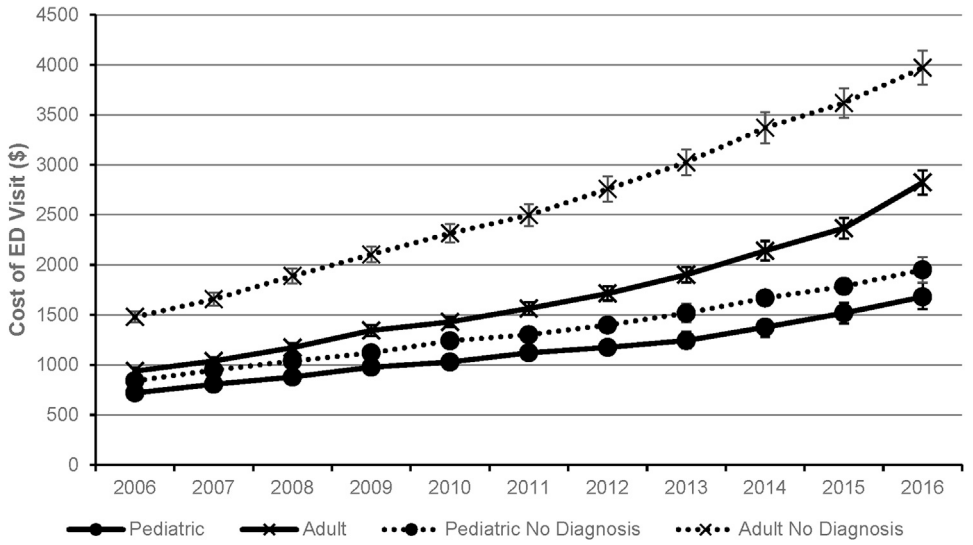

Fig 2. Mean (95% confident interval) annual cost of ED visits for primary and/or secondary diagnosis for cellulitis or erysipelas in adults and children. *ED*, Emergency department.

with significantly increased odds for extracutaneous autoimmune diseases.

Infectious complications of cellulitis/erysipelas

Cellulitis/erysipelas was associated with approximately 30-fold and 100-fold higher odds of methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *S aureus*, and other antibiotic-resistant infections in adults and children, respectively (Table II). In children, ED visits for cellulitis/erysipelas were associated with higher odds of extracutaneous and infectious complications, including lymphangitis, gangrene, septic arthritis, osteomyelitis, septicemia and/or toxic shock syndrome but not with endocarditis, meningitis, or shock. In adults, ED visits for cellulitis/erysipelas were associated with higher odds of lymphangitis, gangrene, endocarditis, septic arthritis, osteomyelitis, septicemia, and/or toxic shock syndrome but not with meningitis or shock.

Disposition

Most ED patients with cellulitis or erysipelas were discharged to home. However, ED patients with versus without cellulitis or erysipelas were more likely to be admitted as inpatients for adults and children ($P < .0001$ for both).

ED visit cost

The mean (95% CI) inflation-adjusted cost of pediatric and adult ED visits with a primary or secondary diagnosis of cellulitis/erysipelas was \$1113 (\$1077-\$1149) and \$1681 (\$1643-\$1719), respectively. The mean costs significantly increased over time among ED patients with a primary or secondary diagnosis of cellulitis/erysipelas (Rao-Scott chi-square, $P < .0001$) (Fig 2). The mean (95% CI) costs more than doubled from \$720 (\$683-\$758) in 2006 to \$1680 (\$1538-\$1823) in 2016 among children and more than tripled from \$939 (\$903-\$975) in 2006 to \$2823 (\$2701-\$2945) in 2016 among adults. In 2016, the total annual cost of pediatric and adult ED visits with a primary or secondary diagnosis of cellulitis/erysipelas was \$493,811,752 (\$418,779,512-\$568,843,991) and \$6,271,714,356 (\$5,753,479,732-\$6,789,948,979), respectively.

DISCUSSION

This nationwide observational study found that cellulitis/erysipelas was associated with a high frequency, cost, and morbidity of ED visits in the United States. The total annual cost of ED visits for cellulitis/erysipelas was approximately \$500 million in 2016, with the cost per visit doubling to tripling between 2006 to 2016. ED patients with cellulitis or erysipelas were also more likely to be admitted to the hospital. ED visits for cellulitis/erysipelas pose a major burden to the US health care system.

We identified multiple potential risk factors for cellulitis/erysipelas. First, ED visits for cellulitis/erysipelas had the highest incidence during the summer months. These results are consistent with previous findings[6,7] and suggest that environmental triggers, such as increased temperature, humidity, and outdoor exposure to insects, may be risk factors for cellulitis/erysipelas. Moreover, we found that cellulitis/erysipelas were increased with insect bites

and stings, ulcers from other diseases, wounds from recent surgery, and/or peripheral vascular disease. These associations are consistent with previous studies and case reports of increased cellulitis/erysipelas in ED patients with animal bites or stings in Taiwan.[8] Furthermore, ulcers and peripheral vascular disease were reported as common comorbidities in patients hospitalized with erysipelas.[6] These risk factors likely contribute to the most common sites of cellulitis/erysipelas being the legs (exposed to insect bites and vulnerable to venous stasis and chronic ulcers) and arms (exposed to insect bites).

We found that cellulitis and erysipelas were associated with multiple chronic conditions in general and particularly CISD and autoimmune diseases, including AD, psoriasis, polymyositis, dermatomyositis, and systemic sclerosis. In fact, 3.5% of ED patients with cellulitis or erysipelas had a comorbid CISD or autoimmune disease. Previous studies of hospitalized patients in the United States found that AD, psoriasis, pemphigus, and pemphigoid were all associated with higher odds of cellulitis and other cutaneous and extracutaneous infections.[9,10,11,12] These disorders are associated with multiple potential risk factors for cellulitis/erysipelas, including skin barrier disruption, immune dysregulation, and/or use of immunosuppressive therapy. Taken together, patients with insect bites, ulcers, CISD, and autoimmune diseases have increased risk for cellulitis/erysipelas.

These results are clinically relevant. First, patients at higher risk for cellulitis/erysipelas should be counseled about appropriate skin care and how to clean skin lesions, ulcers, and wounds. Second, topical antiseptics, such as povidone-iodine, can help prevent skin infections in patients with chronic ulcers and wounds.[13,14] Topical antiseptics can be applied to pre-existing ulcers and wounds that are at risk of becoming infected. Alternatively, patients could apply antiseptics to areas prone to recurrent cellulitis. Third, adequate treatment of some CISDs, particularly AD, led to lower rates of bacterial skin infections.[15] It is possible that tighter control of other CISDs similarly leads to lower rates of bacterial skin infections. However, many systemic treatments used in CISD and autoimmune diseases are immunosuppressing and might confer additional risk of cellulitis/erysipelas. Future studies are warranted to determine the optimal strategies to minimize the risk of cellulitis/erysipelas in higher-risk patients.

Previously published guidelines recommend considering inpatient admission if any of the following are present: hypotension; elevated creatinine, creatine phosphokinase, or C-reactive protein level; low serum bicarbonate level; or marked left shift on the complete blood count with differential.[16] Other complicating factors for cellulitis include diabetic ulcer; chronic venous stasis; peripheral arterial disease; severe sepsis; bacteremia; deep-tissue infections; surgical wound; indwelling medical device; recurrent cellulitis; human or animal bites; or perirectal, periorbital or orbital cellulitis.[17] Indeed, we found that cellulitis and erysipelas were associated with multiple infectious complications, including antibiotic-resistant infections, lymphangitis, gangrene, septic arthritis, osteomyelitis, septicemia, toxic shock syndrome, and/or endocarditis. However, less than 30% of adult and less than 10% of pediatric ED patients with cellulitis/erysipelas had 1 of these complicating factors. Thus, many patients with uncomplicated cellulitis/erysipelas could have been treated in the outpatient setting if there was sufficient access to care.

However, we found that ED visits for cellulitis/erysipelas were associated with lower household income and public or no insurance in both children and adults. These results indicate there are socioeconomic and health care disparities with respect to ED visits for cellulitis/erysipelas. Moreover, there were significant increases of weekend ED visits for cellulitis/erysipelas among privately insured persons with higher household income. Thus, even patients with good health care access in general may have gone to an ED because they could not get timely outpatient care on a weekend. These issues could be mitigated by primary care and specialty practices offering walk-in appointments or flexible scheduling for urgent complaints on weekdays, evenings, and weekends. Telehealth may also be helpful for patients with limited access to care owing to living geographically far away from a health care provider, limited transportation, limited childcare, or not being able to take off from work.

These results have important public health ramifications. First, ED visits often cost more than 5 times more than outpatient care and 2 to 3 times more than ambulatory visits.[5,18] It is more cost effective to manage uncomplicated cases of cellulitis or erysipelas in the outpatient compared to ED setting. The high frequency of ED visits for cellulitis/erysipelas may pose a strain on the already limited resources and staffing in most EDs. This is particularly true in the current severe acute respiratory syndrome coronavirus 2 pandemic, which has placed an enormous strain on EDs and health care systems around the world. It is more important than ever to reduce superfluous strain on EDs by decreasing unnecessary ED visits for cellulitis or erysipelas. Fortunately, there appeared to be a decline in the prevalence of ED visits for cellulitis/erysipelas in

2015 and 2016, possibly related to increased insurance coverage and/or changes in health care use patterns from the Affordable Care Act.

Strengths of our study include analysis of a nationally representative cohort of ED visits in the United States, with more than 320 million ED visits overall and 9 million visits for cellulitis/erysipelas in 2006 to 2016, and multiple sensitivity analyses for children and adults. However, there are potential limitations. All disorders were determined by using ICD codes. Although previous studies validated the use of ICD codes to classify patients with cellulitis/erysipelas,[7,19] we were unable to confirm the diagnoses by medical record review. Given the overlapping use of ICD codes for cellulitis/erysipelas, we were unable to fully distinguish between them. Because of the cross-sectional design of our analyses, we are unable to determine the causal relationship of cellulitis/erysipelas with comorbidities or which patients had multiple ED visits for cellulitis/erysipelas. Some important variables, including race/ethnicity and past medical history, were not recorded in NEDS. Finally, NEDS allowed for examination of associations of cellulitis/erysipelas at the national level. Some associations may be present only in certain geographic regions of the country. We were unable to assess associations at the state or local level.

In conclusion, our study shows a very high cost burden of ED visits for cellulitis/erysipelas. Cellulitis/erysipelas was associated with a wide array of infectious complications in a large subset of ED patients. Multiple risk factors were identified for cellulitis/erysipelas, including summer months, insect bites and stings, ulcers and wounds, and CISD and autoimmune diseases. Future studies are needed to determine the optimal solution for prevention of ED visits for cellulitis/erysipelas.

Conflicts of interest

None reported.

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