

Association between childhood atopic dermatitis, cutaneous, extracutaneous and systemic infections

Short Title: Infections in childhood AD.

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Abbreviations used: AD=atopic dermatitis; ICD-9-CM=International Classification of Disease 9th edition Clinical Modification; LOS=length of stay; OR=odds ratio; CI=confidence interval

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JI Silverberg had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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What already known:

- Previous studies have shown that atopic dermatitis is associated with higher rates of cutaneous infections and caregiver-reported extra-cutaneous infections.

What this study adds:

- This study found that atopic dermatitis was associated with numerous cutaneous, respiratory, multi-organ and systemic infections in US children.
- Serious infections were associated with \$33 million excess annual costs of care in children with AD.

Dear editor:

Atopic dermatitis (AD) is associated with higher risk of skin infections¹. US population-based studies found that childhood AD is associated with increased risk of caregiver-reported extra-cutaneous infections^{2,3}. We sought to confirm whether AD in childhood is associated with increased rates of healthcare diagnosed cutaneous and extra-cutaneous infections.

The 2002–2012 Nationwide Inpatient Sample was analyzed, containing a 20% sample of US hospitalizations (68,634,999 discharges with age <18 years). Data were de-identified. No attempts were made to identify individuals. All parties were compliant with the data use agreement. The study was approved by the institutional review board at Northwestern University.

Serious infections included infections requiring inpatient treatment. AD and serious infections were identified using primary and/or secondary *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) or Clinical Classification Software codes. A previous study validated the use of a discharge diagnosis code 691.8 in the inpatient setting for studying AD⁴. AD (691.8) and eczema (692.9) codes were both used, as they were found to be used interchangeably in the outpatient setting⁴. The control group included all hospitalizations without any AD diagnosis, yielding a representative cohort of US hospitalizations.

Statistical analyses were performed using SAS SURVEY procedures (version 9.4, SAS Institute, Cary, NC). Weighted prevalence (95% confidence intervals [CI]) of serious infections were determined among patients with and without AD. Unadjusted and multivariable survey logistic regression models were used to determine the association of AD (predictor) and serious infections (outcome). Crude and adjusted odds ratios and 95% confidence interval were estimated. Analysis of variance was performed to determine the impact of serious infections on log-transformed inpatient costs and length of stay (LOS) (outcomes) in AD (predictor). Complete case-analysis was performed. Post-hoc correction for multiple dependent tests were performed by minimizing the false discovery rate⁵; corrected P-values are presented. Two-sided corrected P-values <0.05 were considered statistically significant.

There were 66,112 admissions with AD (weighted frequency: 314,781). Children hospitalized with vs. without AD were older (4.5 ± 0.05 vs. 2.4 ± 0.04 yr), less likely to be female (41.5% vs. 48.9%) or white (36.1% vs. 51.5%). Serious infections were diagnosed in 48.6% vs. 14.6% of hospitalized patients with vs. without AD. Among children with AD, the prevalence of any serious infections remained stable between 2002-2012 ($P > 0.05$).

In bivariable logistic regression models, AD was associated with 47/49 serious infections examined, including 8/8 cutaneous, 9/9 upper respiratory tract, 8/8 lower respiratory or lung, as well as cardiac, brain, gastrointestinal, and bone infections (Table 1). In multivariable models controlling for age, race, gender and insurance status (model-1), AD was associated with cutaneous infections (e.g. eczema herpeticum, erysipelas, herpes simplex, cellulitis), respiratory infections (e.g. acute bronchiolitis, bronchitis, acute nasopharyngitis, aspergillosis), and extra-cutaneous and systemic infections (e.g. encephalitis, endocarditis, infectious arthropathy, infection of bone, methicillin-sensitive and resistant *Staphylococcal aureus*, fungal and viral infections, septicemia). The associations remained significant for most infections in multivariable models that controlled for asthma and hay fever (model-2); though, some associations were no longer significant or had markedly reduced effect sizes. Similar results were found in sensitivity analyses that defined AD using ICD-9-CM code 691.8 alone for sufficiently powered infections (data available upon request).

These results confirm previous US population-based studies that found higher rates of caregiver-reported cutaneous and extra-cutaneous infections in AD, including recurrent ear infections, strep throat, influenza or pneumonia, sinus infections, chickenpox and urinary tract infections^{2,3}.

There were also increased indirect healthcare costs and mortality related to the comorbid infections of AD. The geometric-mean LOS and costs of care were higher for 42/49 and 34/49 infections in inpatients with vs. without AD, including cutaneous, respiratory, systemic and other infections (Table 2). There were an estimated 19,049.6 excess days and \$33,079,882.0 excess costs of hospitalization for serious infections in AD patients. Predictors of inpatient mortality in AD patients, included aspergillosis, acute sinusitis, strep pneumonia, meningitis, septicemia, fungal and urinary tract infections.

The mechanisms of increased extra-cutaneous and systemic infections are likely multifactorial, including epidermal barrier disruption, decreased expression of anti-microbial peptides, aberrant toll-like receptor signaling and innate immunity, increased *Staphylococcus aureus* colonization of skin, systemic inflammation and immune dysregulation, including Th2 skewing of the immune system, multiple comorbid health conditions, including atopic disorders⁶, and use of systemic immunosuppressant treatments. Low vaccination rates are unlikely to explain higher rates of influenza and chickenpox, as previous population-based studies found higher rates of healthcare utilization and vaccination in children with AD⁷.

Study strengths include a nationally representative sample of >60 million hospitalizations and multiple sensitivity analyses. Limitations include inability to perform manual chart review, lack of data on prior history, severity, phenotype or treatments of AD, particularly immunosuppressants, and how these have affected hospitalization rates and outcomes.

In conclusion, children with AD had higher odds of cutaneous, respiratory, systemic and other infections. These were associated with a substantial financial-burden in AD patients. Further studies are needed to understand the mechanisms of extra-cutaneous and systemic infections in AD and develop preventive interventions.

Table 1. Associations between childhood atopic dermatitis and serious infections[#].

Type of infection	Inpatient diagnosis of atopic dermatitis									
	No					Yes				
	Wtd Freq	% Prev [95% CI]	Wtd Freq	% Prev [95% CI]	Crude OR [95% CI]	P	Model-1*		Model-2**	
							Adj OR [95% CI]	P	Adj OR [95% CI]	P
Eczema Herpeticum	4,881	0.007 [0.006-0.008]	1,415	0.5 [0.4-0.5]	63.65 [53.24-76.08]	.0001	49.57 [40.35-60.91]	.0001	51.78 [40.58-66.08]	.0001
Erysipelas	2,435	0.004 [0.003-0.004]	176	0.06 [0.04-0.07]	15.82 [11.35-22.05]	.0001	13.66 [9.47-19.71]	.0001	17.36 [11.73-25.69]	.0001
Cellulitis	790,029	1.2 [1.1-1.2]	27,082	8.7 [8.2-9.1]	8.11 [7.60-8.66]	.0001	6.60 [6.17-7.07]	.0001	7.60 [7.16-8.06]	.0001
Herpes simplex	80,852	0.1 [0.1-0.1]	3,156	1.0 [0.9-1.1]	8.61 [7.77-9.54]	.0001	7.12 [6.39-7.94]	.0001	7.02 [6.32-7.81]	.0001
Herpes zoster	8,851	0.01 [0.01-0.01]	172	0.06 [0.04-0.07]	4.26 [2.98-6.10]	.0001	3.50 [2.39-5.12]	.0001	3.74 [2.56-5.47]	.0001
Chicken Pox	11,705	0.02 [0.02-0.02]	359	0.1 [0.1-0.1]	6.71 [5.23-8.60]	.0001	5.53 [4.18-7.31]	.0001	5.91 [4.53-7.72]	.0001
Any skin infection	1,002,262	1.5 [1.4-1.5]	33,661	10.8 [10.3-11.3]	8.11 [7.65-8.59]	.0001	6.77 [6.36-7.21]	.0001	8.00 [7.56-8.46]	.0001
Necrotizing fasciitis	2,440	0.004 [0.003-0.004]	38	0.01 [0.00-0.02]	3.41 [1.61-7.23]	.0012	2.67 [1.18-6.06]	.023	3.37 [1.54-7.34]	.002
Acute nasopharyngitis	15,451	0.02 [0.02-0.03]	357	0.1 [0.1-0.1]	5.06 [3.76-6.80]	.0001	4.29 [2.99-6.16]	.0001	2.21 [1.60-3.04]	.0001
Acute sinusitis	72,332	0.1 [0.1-0.1]	1,017	0.3 [0.3-0.4]	3.08 [2.65-3.59]	.0001	2.31 [1.92-2.77]	.0001	1.12 [0.95-1.33]	.21
Acute pharyngitis	169,002	0.2 [0.2-0.3]	1,965	0.6 [0.6-0.7]	2.55 [2.26-2.87]	.0001	2.10 [1.84-2.40]	.0001	1.36 [1.20-1.54]	.0001
Acute tonsillitis	78,786	0.1 [0.1-0.1]	460	0.1 [0.1-0.2]	1.28 [1.02-1.60]	.033	1.03 [0.80-1.32]	.81	0.87 [0.70-1.09]	.21
Strep throat	147,570	0.2 [0.2-0.2]	2,112	0.7 [0.6-0.7]	3.14 [2.82-3.49]	.0001	2.70 [2.42-3.01]	.0001	1.69 [1.53-1.87]	.0001
Acute laryngitis and/or tracheitis, &	70,438	0.1 [0.1-0.1]	819	0.3 [0.2-0.3]	2.55 [2.08-3.12]	.0001	2.15 [1.76-2.62]	.0001	1.45 [1.19-1.77]	.0003

laryngopharyngitis										
Croup	195,980	0.3 [0.3-0.3]	2,338	0.7 [0.7-0.8]	2.62 [2.36-2.90]	.0001	2.83 [2.52-3.17]	.0001	1.56 [1.41-1.73]	.0001
Acute epiglottitis	3,679	0.005 [0.005-0.006]	49	0.02 [0.01-0.03]	2.88 [1.54-5.40]	.0012	2.31 [1.10-4.87]	.033	2.01 [1.05-3.88]	.044
Bronchitis	1,750,687	2.6 [2.4-2.7]	29,171	9.3 [8.9-9.7]	3.91 [3.68-4.17]	.0001	4.75 [4.43-5.10]	.0001	2.08 [1.98-2.19]	.0001
Acute bronchiolitis due to respiratory syncytial virus	902,850	1.3 [1.3-1.4]	13,495	4.3 [4.1-4.6]	3.37 [3.14-3.61]	.0001	4.56 [4.21-4.94]	.0001	2.19 [2.06-2.33]	.0001
Acute bronchiolitis due to other	745,348	1.1 [1.0-1.1]	14,478	4.6 [4.4-4.9]	4.40 [4.11-4.72]	.0001	5.33 [4.93-5.77]	.0001	2.03 [1.91-2.16]	.0001
Strep pneumonia	51,275	0.08 [0.07-0.08]	681	0.2 [0.2-0.3]	2.91 [2.46-3.44]	.0001	2.46 [2.03-2.97]	.0001	1.42 [1.20-1.68]	.0001
Pneumonia	2,304,214	3.4 [3.2-3.5]	38,079	12.2 [11.6-12.7]	3.97 [3.73-4.23]	.0001	3.46 [3.24-3.69]	.0001	1.07 [1.02-1.12]	.008
Abscess of lung or mediastinum	13,602	0.02 [0.02-0.02]	250	0.08 [0.06-0.10]	4.02 [3.01-5.35]	.0001	3.34 [2.44-4.57]	.0001	2.78 [2.05-3.76]	.0001
Empyema	34,910	0.05 [0.05-0.06]	544	0.2 [0.1-0.2]	3.41 [2.82-4.13]	.0001	2.58 [2.09-3.18]	.0001	2.56 [2.12-3.10]	.0001
Meningitis	229,753	0.3 [0.3-0.4]	1,715	0.5 [0.5-0.6]	1.64 [1.46-1.83]	.0001	1.37 [1.21-1.56]	.0001	1.76 [1.57-1.97]	.0001
Encephalitis	38,837	0.06 [0.05-0.06]	387	0.1 [0.1-0.2]	2.18 [1.73-2.75]	.0001	1.77 [1.39-2.25]	.0001	1.98 [1.57-2.50]	.0001
Endocarditis	10,191	0.01 [0.01-0.02]	120	0.04 [0.02-0.05]	2.58 [1.66-4.03]	.0001	2.21 [1.38-3.53]	.0012	2.53 [1.63-3.92]	.0001
Infectious arthropathy	46,395	0.07 [0.06-0.07]	917	0.3 [0.2-0.3]	4.33 [3.72-5.04]	.0001	3.45 [2.94-4.06]	.0001	3.74 [3.19-4.37]	.0001
Infection of the bone	75,313	0.1 [0.1-0.1]	1,686	0.5 [0.5-0.6]	4.91 [4.36-5.54]	.0001	3.63 [3.20-4.11]	.0001	4.30 [3.81-4.85]	.0001
Enterocolitis	720,277	1.1 [1.0-1.1]	8,988	2.9 [2.7-3.1]	2.78 [2.60-2.97]	.0001	2.57 [2.40-2.77]	.0001	2.66 [2.50-2.82]	.0001
<i>Clostridium difficile</i> colitis	83,900	0.1 [0.1-0.1]	1,126	0.4 [0.3-0.4]	2.94 [2.56-3.38]	.0001	2.48 [2.12-2.89]	.0001	2.57 [2.24-2.95]	.0001

Peritonitis and Intestinal Abscess	56,159	0.08 [0.08-0.09]	314	0.10 [0.07-0.13]	1.22 [0.91-1.64]	.21	1.00 [0.73-1.37]	.99	1.24 [0.92-1.67]	.21
Appendicitis	873,224	1.3 [1.2-1.3]	1,684	0.5 [0.5-0.6]	0.42 [0.37-0.47]	.0001	0.33 [0.29-0.38]	.0001	0.36 [0.33-0.41]	.0001
Urinary tract infection	933,825	1.4 [1.3-1.4]	7,701	2.5 [2.3-2.6]	1.82 [1.69-1.97]	.0001	1.59 [1.47-1.72]	.0001	1.83 [1.71-1.96]	.0001
Pyelonephritis	334,466	0.5 [0.5-0.5]	2,385	0.8 [0.7-0.8]	1.56 [1.40-1.75]	.0001	1.45 [1.29-1.63]	.0001	1.72 [1.54-1.91]	.0001
Influenza	232,495	0.3 [0.3-0.4]	3,581	1.1 [1.0-1.3]	3.39 [3.07-3.75]	.0001	2.94 [2.64-3.27]	.0001	1.49 [1.37-1.63]	.0001
Roseola	1,129	0.002 [0.001-0.002]	34	0.01 [0.00-0.02]	6.55 [2.85-15.02]	.0001	9.25 [3.97-21.59]	.0001	7.37 [2.90-18.75]	.0001
Septicemia	855,892	1.3 [1.2-1.3]	7,614	2.4 [2.3-2.6]	1.97 [1.82-2.13]	.0001	1.82 [1.68-1.99]	.0001	2.40 [2.23-2.57]	.0001
Organism										
Methicillin-Resistant Staphylococcus Aureus	156,611	0.2 [0.2-0.3]	6,609	2.1 [1.9-2.4]	9.40 [8.60-10.28]	.0001	7.95 [7.24-8.72]	.0001	6.76 [6.14-7.45]	.0001
Methicillin-Sensitive Staphylococcus Aureus	366,598	0.5 [0.5-0.6]	13,659	4.4 [4.0-4.8]	8.47 [7.77-9.23]	.0001	6.89 [6.24-7.60]	.0001	7.58 [6.93-8.29]	.0001
Any strep infection	401,841	0.6 [0.6-0.6]	6,818	2.2 [2.0-2.3]	3.77 [3.52-4.03]	.0001	3.18 [2.96-3.41]	.0001	2.64 [2.47-2.81]	.0001
Pseudomonas	136,429	0.2 [0.2-0.2]	1,422	0.5 [0.4-0.5]	2.28 [1.98-2.63]	.0001	1.84 [1.58-2.15]	.0001	1.50 [1.30-1.73]	.0001
Mycobacterial infection	5,250	0.008 [0.006-0.009]	57	0.02 [0.01-0.03]	2.36 [1.26-4.42]	.009	2.19 [1.19-4.04]	.011	1.57 [0.82-3.04]	.21
Tuberculosis	10,035	0.01 [0.01-0.02]	93	0.03 [0.02-0.04]	2.03 [1.28-3.22]	.003	1.26 [0.74-2.14]	.41	1.43 [0.88-2.32]	.1
Aspergillus	12,330	0.02 [0.01-0.02]	242	0.08 [0.05-0.10]	4.30 [3.24-5.71]	.0001	3.41 [2.56-4.54]	.0001	1.93 [1.42-2.63]	.0001
Coccidiomycosis	2,408	0.004 [0.002-0.005]	34	0.01 [0.00-0.02]	3.07 [1.52-6.20]	.0023	2.20 [1.08-4.48]	.033	2.13 [1.02-4.45]	.044
Histoplasmosis	1,353	0.002	20	0.006	3.16	.023	1.80	.41	1.58	.41

		[0.001-0.003]		[0.000-0.012]	[1.16-8.62]		[0.44-7.38]		[0.55-4.51]	
Any fungal infection	386,086	0.6 [0.5-0.6]	10,202	3.3 [3.1-3.5]	5.93 [5.51-6.40]	.0001	5.11 [4.72-5.53]	.0001	4.57 [4.26-4.90]	.0001
Any viral infection	1,096,184	1.6 [1.5-1.7]	23,649	7.6 [7.1-8.1]	5.02 [4.69-5.38]	.0001	4.40 [4.10-4.73]	.0001	2.81 [2.67-2.96]	.0001
Any serious infection	9,952,691	14.6 [14.0-15.1]	151,941	48.6 [47.7-49.5]	5.55 [5.25-5.87]	.0001	4.87 [4.58-5.17]	.0001	3.07 [2.91-3.23]	.0001

Table 2. Excess inpatient length of stay and cost of care secondary to serious infections in children with atopic dermatitis.

Type of infection	Geometric-mean cost in patients with AD [95% CI]	Excess annual cost secondary to AD	Geometric-mean LOS in patients with AD (days) [95% CI]	Excess annual LOS secondary to AD	Inpatient mortality in patients with AD [95% CI]
None	\$3,982 [\$3,826-\$4,144]	-	2.5 [2.5-2.6]	-	0.1 [0.1-0.1]
Any	\$4,112 [\$3,938-\$4,293]	33,079,882.0	2.8 [2.8-2.9]	19,049.6	0.1 [0.1-0.1]
Eczema Herpeticum	\$4,693 [\$4,276-\$5,150]	1,050.9	3.6 [3.3-3.8]	0.8	0
Erysipelas	\$2,801 [\$2,417-\$3,246]	3,421.4	2.5 [2.2-2.8]	3.0	0
Cellulitis	\$3,515 [\$3,348-\$3,690]	1,812,277.0	2.7 [2.6-2.8]	1,249.2	0.02 [0.00-0.06]
Herpes simplex	\$4,658 [\$4,283-\$5,067]	218,353.4	3.6 [3.3-3.8]	153.1	0.2 [0.0-0.5]
Herpes zoster	\$4,770 [\$3,544-\$6,419]	25,738.0	3.4 [2.6-4.4]	15.7	0
Chicken Pox	\$3,823 [\$3,302-\$4,425]	34,098.6	3.0 [2.6-3.4]	22.9	0
Any skin infection	\$3,501 [\$3,332-\$3,678]	2,324,951.6	2.7 [2.6-2.8]	1,585.9	0.02 [0.00-0.05]
Necrotizing fasciitis	\$30,863 [NE]	62,158.5	9.6 [NE]	14.4	0
Acute nasopharyngitis	\$3,510 [\$2,955-\$4,169]	51,599.8	2.8 [2.3-3.3]	29.7	1.3 [0.0-3.7]
Acute sinusitis	\$5,067 [\$4,040-\$6,354]	301,548.8	3.3 [2.9-3.6]	149.1	0.5 [0.0-1.4]
Acute pharyngitis	\$3,559 [\$3,237-\$3,913]	336,397.4	2.7 [2.5-2.9]	266.3	0
Acute tonsillitis	\$3,539 [\$3,125-\$4,008]	-	2.5 [2.2-2.8]	-	0
Strep throat	\$3,445 [\$3,166-\$3,749]	273,378.4	2.5 [2.3-2.7]	209.0	0
Acute laryngitis and/or tracheitis & laryngopharyngitis	\$24,372 [\$19,655-30,221]	1,490,170.3	10.3 [8.4-12.6]	605.2	1.2 [0.0-2.8]

Croup	\$2,356 [\$2,174-\$2,553]	289,097.6	1.7 [1.6-1.8]	183.9	0
Acute epiglottitis	\$7,073 [\$1,324-\$37,770]	33,356.1	4.4 [1.1-17.4]	14.6	0
Bronchitis	\$3,336 [\$3,204-\$3,474]	3,715,146.9	2.4 [2.4-2.5]	2,397.9	0.05 [0.00-0.10]
Acute bronchiolitis due to respiratory syncytial virus	\$3,669 [\$3,489-\$3,858]	2,113,030.6	2.7 [2.7-2.8]	1375.7	0.1 [0.0-0.2]
Acute bronchiolitis due to other	\$3,077 [\$2,948-\$3,212]	1,394,891.9	2.2 [2.1-2.2]	885.3	0
Strep pneumonia	\$9,484 [\$7,894-\$11,394]	476,791.9	5.2 [4.5-6.0]	203.6	0.8 [0.0-2.3]
Pneumonia	\$4,450 [\$4,252-\$4,657]	7,926,519.5	2.8 [2.7-2.9]	4,176.3	0.1 [0.1-0.2]
Abscess of lung or mediastinum	\$20,151 [\$14,943-\$27,175]	198,904.8	10.3 [8.1-13.1]	89.7	1.9 [0.0-5.5]
Empyema	\$25,632 [\$22,023-\$29,832]	427,812.0	11.0 [9.9-12.2]	167.0	0.9 [0.0-2.7]
Meningitis	\$7,286 [\$6,578-\$8,069]	1,381,801.4	4.5 [4.1-5.0]	839.2	0.3 [0.0-0.8]
Encephalitis	\$16,868 [\$12,832-\$22,174]	565,479.9	7.5 [5.8-9.6]	266.1	0
Endocarditis	\$26,788 [\$16,580-\$43,281]	105,357.9	12.5 [8.5-18.2]	50.5	4.2 [0.0-12.1]
Infectious arthropathy	\$10,868 [\$9,760-\$12,101]	310,117.1	5.8 [5.2-6.4]	171.1	0
Infection of the bone	\$12,586 [\$11,283-\$14,032]	516,373.9	6.9 [6.2-7.6]	298.1	0.3 [0.0-0.9]
Enterocolitis	\$3,706 [\$3,446-\$3,985]	2,681,792.9	2.9 [2.8-3.1]	1,645.7	0.1 [0.0-0.3]
<i>Clostridium difficile</i> colitis	\$12,631 [\$10,698-\$14,914]	725,932.4	7.3 [6.4-8.4]	349.8	0.4 [0.0-1.3]
Peritonitis and Intestinal Abscess	\$27,974 [\$20,549-\$38,082]	1,175,805.6	10.5 [8.5-13.0]	430.3	1.6 [0.0-4.7]
Appendicitis	\$9,805 [\$9,088-\$10,578]	-	3.1 [2.8-3.4]	-	0
Urinary tract infection	\$5,962 [\$5,481-\$6,484]	5,754,998.4	4.1 [3.8-4.3]	3,117.7	0.3 [0.0-0.5]

Pyelonephritis	\$4,559 [\$4,211-\$4,935]	926,568.5	3.4 [3.1-3.6]	632.1	0
Influenza	\$4,427 [\$4,031-\$4,863]	855,313.7	2.7 [2.6-2.9]	417.8	0.1 [0.0-0.4]
Roseola	\$3,306 [\$1,650-\$6,623]	9,993.5	3.5 [1.8-6.5]	5.1	0
Septicemia	\$12,460 [\$11,332-\$13,700]	11,200,721.9	7.7 [7.1-8.2]	5,317.2	0.7 [0.3-1.2]
Organism					
Methicillin resistant Staphylococcus aureus	\$5,491 [\$5,086-\$5,927]	652,939.7	3.5 [3.3-3.7]	328.5	0.1 [0.0-0.2]
Methicillin sensitive Staphylococcus aureus	\$5,389 [\$5,040-\$5,763]	1,397,003.5	3.9 [3.8-4.1]	850.6	0.2 [0.0-0.4]
Any strep infection	\$5,709 [\$5,238-\$6,224]	2,254,841.3	3.9 [3.6-4.1]	1,153.9	0.2 [0.0-0.4]
Pseudomonas	\$17,745 [\$15,412-\$20,431]	1,872,958.1	8.9 [8.0-9.9]	775.9	0.7 [0.0-1.6]
Mycobacterial infection	\$9,481 [\$4,605-\$19,523]	24,693.2	6.2 [4.2-9.2]	20.5	0
Coccidiomycosis	\$20,887 [\$7,771-\$56,139]	87,056.7	7.0 [3.1-15.6]	16.9	14.7 [0.0-41.4]
Histoplasmosis	\$28,024 [NE]	16,845.5	8.8 [NE]	5.3	0
Tuberculosis	\$8,515 [\$5,996-\$12,091]	41,966.8	5.5 [3.8-8.0]	32.0	0
Aspergillus	\$13,973 [\$9,046-\$21,583]	145,995.6	6.0 [4.5-8.0]	58.1	2.2 [0.0-6.4]
Any fungal infection	\$6,205 [\$5,657-\$6,806]	2,830,955.8	4.3 [4.0-4.6]	1,515.5	0.3 [0.1-0.6]
Any viral infection	\$4,048 [\$3,813-\$4,297]	3,569,864.1	2.6 [2.5-2.7]	1,877.9	0.1 [0.0-0.2]

Excess length of stay (LOS) and cost of care per infection indirectly related to AD were estimated by: $((\text{prevalence of infection in AD patients})/(\text{prevalence of infection in non-AD patients})) \times (\text{total hospitalization annual days or costs for that infection in AD patients})$.

AD, atopic dermatitis; LOS, length of stay; CI, confidence interval

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All statistical models included discharge trend weights allowing for representative estimates of hospital discharges across the US, strata that account for hospital's census region/division, ownership/control, location/teaching and number of beds, and clustering by individual hospital.

* Model 1 included age (continuous), gender (female/male), race/ethnicity (white/black/Asian/other), and insurance coverage (Medicaid, private, self-pay, no charge/other) as covariates.

* Model 2 included history of asthma and hay fever as covariates.

OR, odds ratio; CI, confidence interval; Adj, adjusted