

Association between atopic dermatitis and serious cutaneous, multiorgan and systemic infections in US adults

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ABSTRACT

Background: Atopic dermatitis (AD) is associated with barrier disruption, immune dysregulation, and immunosuppressing treatments that can increase the association with an unusual number of infections.

Objective: To determine whether adults with AD have an unusually large number of serious infections and related outcomes.

Methods: Data from the 2002 to 2012 National Inpatient Sample were analyzed, including an approximately 20% sample of all US hospitalizations (n = 72,108,077 adults). Prevalence of serious infections in hospitalized patients with vs without AD, length of stay, cost of care, and inpatient mortality secondary to serious infections were determined.

Results: The prevalence of serious infections expressed as a percentage (95% confidence interval) was higher in adults hospitalized with than in those without AD (42.1% [41.6–42.6] vs 25.4% [25.2–25.6]; $P = .0002$). In logistic regression models with multiple predictors (multivariable logistic regression models), AD was associated with 32 of 38 infections examined. Associated cutaneous infections included eczema herpeticum (odds ratio [95% confidence interval] adjusted for other predictors: 67.93 [47.93–96.28]), erysipelas (11.15 [9.47–13.1]), and cellulitis (4.53 [4.42–4.64]). Associated respiratory infections included aspergillosis (1.51 [1.21–1.88]) and tuberculosis (1.57 [1.41–1.76]). AD was associated with extracutaneous, multiorgan, and systemic infections, including infectious arthropathy (2.01 [1.84–2.20]), endocarditis (1.25 [1.12–1.39]), encephalitis (1.65 [1.40–1.96]), and methicillin-resistant *Staphylococcus aureus* infections (3.29 [3.17–3.42]). Patients with AD hospitalized with vs without any serious infection had an increased geometric mean cost of inpatient care (\$8,273 [8,126–8,423] vs \$7,179 [7,052–7,307]) and length of stay (5.3 days [5.2–5.3] vs 3.9 [3.9–4.0]; $P = .0002$), with \$11 to \$228 million excess annual costs from hospitalization with serious infections in adults with AD.

Conclusion: Adults with AD had increased cutaneous, respiratory, multiorgan, and systemic infections, which were associated with a considerable cost burden.

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Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting 13% of children¹ and 7% to 10% of adults^{2,3} across the United States. It is well established that AD is associated with a higher incidence of certain cutaneous infections, including *Staphylococcus aureus* colonization, molluscum contagiosum, eczema herpeticum (EH),^{4–6} and possibly cutaneous warts.⁷ In fact, predis-

position toward cutaneous infection is one of the minor diagnostic criterion for AD according to Hanifin and Rajka.⁸ The mechanism of such predisposition is believed to be multifactorial, including impaired epidermal barrier function,⁹ decreased expression of antimicrobial peptides,¹⁰ and an abnormal innate immune response in skin.¹¹

Recent US population-based studies have shown that AD also is associated with higher rates of extracutaneous infection in children^{7,12} and adults,¹³ such as infections of the upper and lower respiratory tracts, ears, and urinary tract. Those studies used surveys with questions about self- or caregiver-reported AD and infections. In the present study, we sought to determine whether there is an association between health care-diagnosed AD and serious infections in adults. We hypothesized that adults with AD would have significantly higher prevalences of cutaneous, respiratory, multiorgan, and systemic infections.

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Methods

Data Source

The 2002 to 2012 Nationwide Inpatient Sample (NIS) provided by the Healthcare Cost and Utilization Project (HCUP) from the Agency for Healthcare Research and Quality (AHRQ) was analyzed. Each year of the NIS contains an approximately 20% stratified representative cross-sectional sample of all US hospitalizations. Sample weights were created by the NIS that factored the sampling design of hospitals in the United States. These sample weights allow for representative estimates of hospital discharges across the entire country. All data were de-identified and no attempts were made to identify any of the individuals in the database. All parties with access to the NIS were compliant to the HCUP's formal data use agreement. The study was approved by the institutional review board at Northwestern University (Chicago, Illinois).

Identification of AD and Serious Infections

The databases were searched for a primary and/or secondary diagnosis of AD or eczema using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes 691.8 and 692.9. A previous study validated the use of the discharge diagnosis code 691.8 in the inpatient setting for the study of AD.¹⁴ We also found that the ICD-9-CM codes for AD (691.8) and eczema (692.9) are used interchangeably in the outpatient setting, with a large number of patients with AD being coded as having eczema.¹⁴ Thus, the primary analyses were done for AD and eczema (AD-E) combined. In addition, sensitivity analyses were performed that examined AD alone. This approach provided a range of cost and length of stay (LOS) estimates, recognizing that analysis of AD alone would underestimate the true prevalence and that analysis of AD-E could overestimate the true prevalence.

The control group included all hospitalizations without any diagnosis of AD-E, yielding a representative cohort of US hospitalizations. Previous studies have reported higher rates of serious infections in adults with psoriasis. Therefore, sensitivity analyses also were performed using only hospitalizations with a primary and/or secondary diagnosis of psoriasis (ICD-9-CM code 696.1) as controls. This allowed for comparison of the relative effect size of the association between serious infections in AD-E vs psoriasis. Serious infections were defined as infections that led to hospitalization, were life threatening, or required treatment in an inpatient setting. Serious infections were identified using ICD-9-CM or Clinical Classification Software codes provided in the NIS (eTable 1).

Data Processing and Statistical Analysis

All data analyses and statistical processes were performed using SAS 9.4 (SAS Institute, Cary, North Carolina). Analyses were performed using SURVEY procedures. The unit of analysis was an individual hospitalization. All statistical models included discharge trend weights, sample strata that accounted for a hospital's census region or division, ownership and control, location and teaching status, number of beds that were provided by the NIS, and clustering by individual hospital. Weighted frequency and prevalence (95% confidence intervals [CI]) of a primary or secondary diagnosis of a serious infection were determined among patients with and without a primary or secondary diagnosis of AD-E. The hospital cost for inpatient care was calculated based on the total charge of the hospitalization and the cost-to-charge ratio estimated by the HCUP. All costs were adjusted for inflation to 2014 according to the Consumer Price Index from the US Bureau of Labor Statistics.¹⁵ Summary statistics were generated for each infection, including frequency, prevalence and 95% CI, geometric mean LOS, and inflation-adjusted geometric mean cost of care, including sum

and geometric mean and 95% CI for hospitalizations with a diagnosis of a serious infection.

SURVEY logistic regression models were used to determine the association between AD-E and serious infections. The dependent variable was a diagnosis of serious infection vs no serious infection. The independent variable was a diagnosis of AD-E. Crude odds ratios (ORs) and 95% CIs were estimated. OR represents the odds of having a diagnosis of a serious infection in those with vs without a diagnosis of AD-E, whereas odds is the prevalence of a condition expressed as a percentage divided by 1 minus that prevalence. Two different multivariable models were calculated. Model 1 included age (continuous), sex (male vs female), race (white vs non-white), and insurance status (yes vs no). Model 2 included asthma and hay fever (yes vs no).

Severity of AD-E was not available in the NIS. Previous studies have shown that patients with AD and EH have more severe T-helper cell type 2-polarized disease and a higher prevalence of food allergies and asthma.¹⁶ Therefore, we constructed regression models that included AD-E, EH, and a 2-way interaction term between them as predictors of sufficiently powered infectious outcomes. Interactions were included in the final models only when the *P* value was less than .01 and the modification of estimates was greater than 20%.

To determine the associations of serious infections in inpatients with AD-E, multivariable logistic regression models were constructed by invoking the stepwise selection approach to decide whether to include specific independent variables in the stepwise logistic model ($\alpha = 0.1$). Serious infection was the dependent variable. The covariates analyzed were age (18–39, 40–59, 60–79, ≥ 80 years), sex (female vs male), season of admission (spring, winter, fall, summer), race/ethnicity (white, black, Asian, Hispanic, other or multiracial), median annual income of the hospital ZIP code (quartiles), hospital location (metropolitan ≥ 1 million, fringe or metropolitan < 1 million, micropolitan, not metropolitan or micropolitan), insurance coverage (Medicaid, Medicare, private, self-pay, no charge, other), number of chronic conditions (0–1, 2–5, ≥ 6), hospital region (Northeast, Midwest, South, West), bed size (small, medium, large), teaching status (yes or no), diabetes mellitus (AHRQ pre-coded), obesity (AHRQ pre-coded), asthma, and hay fever.

SURVEY weighted linear regression was performed with logarithmically transformed cost of care or LOS as the dependent variables to determine the impact of serious infections on cost of hospitalization and LOS in patients with AD-E. Cost of care and LOS were logarithmically transformed because they were not normally distributed. The independent variable was a diagnosis of any serious infection vs no serious infection.

Excess LOS and cost of care for an infection indirectly related to AD-E were estimated by: ([prevalence of that infection in patients with AD-E]/[prevalence of that infection in patients without AD-E]) $\times$ (total hospitalization annual days or costs for that infection in patients with AD).

Complete case analysis was performed. Post hoc correction for multiple dependent tests was performed by minimizing the false discovery rate with the approach of Benjamini and Hochberg¹⁷ and corrected *P* values are presented. Two-sided corrected *P* values less than or equal to .05 were considered significant. Uncorrected 95% CI are presented.

Results

Overall, there were 72,108,077 adult discharges captured in the NIS from 2002 to 2012, with 9,290 admissions with AD (weighted frequency 44,605) and 155,909 with eczema (weighted frequency 746,486) as defined by ICD-9-CM codes 691.8 and 692.9, respectively. Adults hospitalized with AD-E were older (58.6 ± 0.2 vs 57.0 ± 0.1 years, respectively), less likely to be women (55.8% vs

Table 1
Patient Demographics

Variable	Atopic dermatitis or eczema	
	No	Yes
Age (y), mean (SEM)	57.0 (0.1)	58.6 (0.2)
Female, frequency (%)	206,858,933 (60.5)	440,151 (55.8)
Race, frequency (%)		
White	189,154,066 (69.3)	454,630 (70.5)
Black	38,343,543 (14.0)	103,415 (16.0)
Asian	6,318,149 (2.3)	18,153 (2.8)
Hispanic	29,487,232 (10.8)	47,774 (7.4)
Multiracial/Other	9,752,857 (3.6)	21,257 (3.3)
Asthma, frequency (%)	21,405,851 (6.3)	108,348 (13.7)
Hay fever, frequency (%)	2,513 (0.001)	13 (0.002)

60.5%), more likely to be white (70.5% vs 69.3%), and more likely to have asthma (13.7% vs 6.3%) and hay fever (0.002% vs 0.001%) than those without AD-E (Table 1). Serious infections were diagnosed in 42.1% (95% CI 41.6–42.6) of all hospitalizations in patients with AD-E but only 25.4% (95% CI 25.2–25.6) of patients without AD-E. Of hospitalizations in patients with AD-E and serious infections, 53.3% of all serious infections and 43.4% of all skin infections were secondary diagnoses in patients admitted primarily for AD-E.

AD and Serious Infections

In logistic regression models with one of the serious infections taken as the dependent variable and AD-E as the only predictor in the model (ie, simple logistic regression), AD-E was significantly associated with 32 of the 38 serious infections examined, including 8 of 8 cutaneous infections, 2 of 3 upper respiratory infections, 4 of 6 lower respiratory tract or lung infections, and cardiac, brain, bone, and gastrointestinal infections (eTable 2). Of note, there was significant statewide variation of methicillin-resistant *S aureus* (MRSA) infections ($P = .0002$; eFig 1).

In multivariable models controlling for age, race/ethnicity, sex, and insurance status, AD-E was significantly associated with any serious infection (adjusted OR [95% CI] 2.18 [2.14–2.23]). Cutaneous infections with the largest effect size included EH (67.93 [47.93–96.28]), erysipelas (11.15 [9.47–13.1]), and cellulitis (4.53 [4.42–4.64]). Respiratory infections with highest odds included aspergillosis, allergic bronchopulmonary aspergillosis, or aspergillosis pneumonia (1.51 [1.21–1.88]), acute pharyngitis (2.19 [1.98–2.41]), acute sinusitis (1.50 [1.34–1.68]), and tuberculosis (1.57 [1.41–1.76]). AD-E also was associated with many other extracutaneous and systemic infections, including encephalitis (1.65 [1.40–1.96]), endocarditis (1.25 [1.12–1.39]), infectious arthropathy (2.01 [1.84–2.20]), enterocolitis (1.27 [1.22–1.33]), methicillin-sensitive *S aureus* (MSSA; 2.50 [2.41–2.59]) and MRSA (3.29 [3.17–3.42]), fungal (3.87 [3.70–4.04]) and viral (2.19 [2.10–2.28]) infections, and septicemia (1.27 [1.23–1.32]; Fig 1, eTable 2). In addition, the associations remained significant for all infections found to be significant in the respective simple logistic regression models except pneumonia and influenza in multivariable models that controlled for asthma and hay fever (eTable 2). In addition, regression models that included interactions of AD-E with asthma and/or hay fever showed that AD-E alone was associated with 32 of 38 infections, whereas AD-E and comorbid asthma and/or hay fever were associated with 24 of 38 infections (eTable 3). Similar results were observed in sensitivity analyses of AD alone (eTables 4 and 5).

Previous studies have shown that psoriasis, another chronic inflammatory skin disease, is associated with higher prevalence of infections. We compared the prevalence of infections in AD-E vs psoriasis in sensitivity analyses. Similar to AD-E, of hospitalizations in patients with psoriasis and serious infections, 52.9% of all serious

infections and 47.4% of all skin infections were secondary diagnoses in patients admitted primarily for their psoriasis.

Atopic dermatitis and eczema was associated with significantly higher odds of 22 of 38 infections examined when compared with psoriasis, including EH, erysipelas, cellulitis, herpes simplex and zoster, acute pharyngitis, bronchitis, endocarditis, MSSA, MRSA, streptococcal infection, pseudomonas, mycobacterium, fungus, virus, and septicemia (eTable 6). The associations remained significant in multivariable models 1 and/or 2 for all infections significant in bivariable models. Only infectious arthropathy, diverticulitis, pyelonephritis, and peritonitis or intestinal abscess were more likely to occur with psoriasis. Similar results were found in sensitivity analyses of AD vs psoriasis (eTable 7).

In logistic regression models, significant interactions were found between AD-E and EH as predictors of several infections. Patients hospitalized with AD-E and no EH had significantly higher odds of cellulitis (1.79 [1.52–2.11]), erysipelas (21.38 [14.90–30.69]), acute sinusitis (6.63 [4.03–10.90]), and pyelonephritis (4.15 [2.52–6.83]). However, patients with AD-E and EH had an even higher odds of cellulitis (3.56 [2.65–4.78]; eTable 8).

Associations of Serious Infections in AD

In multivariable models with stepwise selection, predictors of any serious infection in patients with AD-E included increasing age (40–59: 1.36 [1.34–1.38]; 60–79: 1.52 [1.49–1.55]; ≥80: 2.18 [2.13–2.23]); Hispanic ethnicity (1.07 [1.05–1.09]); lowest median household income (quartile 1: 1.04 [1.03–1.06]); insurance status (Medicare: 1.28 [1.26–1.30]; Medicaid: 1.24 [1.21–1.26]; self-pay: 1.25 [1.21–1.28]; no charge: 1.29 [1.19–1.40]; other: 1.07 [1.03–1.10]); the southern US regions (1.05 [1.03–1.07]); the fall (1.06 [1.04–1.07]), summer (1.04 [1.03–1.06]), and winter (1.02 [1.01–1.04]) seasons; comorbid diabetes mellitus (1.18 [1.17–1.20]); and obesity (1.35 [1.33–1.37]) but inversely associated with female sex (0.95 [0.94–0.96]), non-white race/ethnicity (black: 0.94 [0.92–0.95]; Asian: 0.92 [0.89–0.95], other/multiracial: 0.92 [0.89–0.95]), larger number of chronic conditions (2–5: 0.83 [0.81–0.85]; ≥6: 0.85 [0.83–0.86]), Northeastern (0.89 [0.88–0.90]) and Midwestern (0.95 [0.94–0.97]) US regions, hospital bed size (medium: 0.93 [0.91–0.94]; large: 0.91 [0.89–0.93]), and teaching hospital (0.87 [0.86–0.88]; Table 2). Of patients with AD-E, the prevalence of any serious infections remained stable from 2002 to 2007 ($P > .05$) but increased from 2008 to 2012 compared with 2002 to 2003 ($P = .0002$; Fig 2). Similar results were found in sensitivity analyses of AD alone (eTable 9).

Impact of Serious Infections on LOS

The geometric mean LOS of patients with AD-E and any serious infection (5.3 [5.2–5.3]) was significantly higher than that of patients with AD without any serious infection (3.9 [3.9–4.0]; $P = .0002$ by linear regression) and significantly higher than in those with a serious infection without AD (5.0 [5.0–5.0]; $P = .0002$; Table 3). Many cutaneous, respiratory, systemic, and multiorgan infections were associated with a prolonged LOS compared with patients without any serious infections (eTable 10). There were an estimated 6,975 excess days spent in the hospital for serious infections in patients with AD and 138,942 excess days in those with AD-E. Cellulitis, any skin infection, pneumonia, streptococcal infections, septicemia, urinary tract infections, and fungal infection accounted for the most excess days associated with infections in inpatients with AD-E.

Impact of Serious Infections on Cost of Care

The geometric mean cost of inpatient care for patients with AD and any serious infection (\$8,273 [8,126–8,423]) was significantly higher

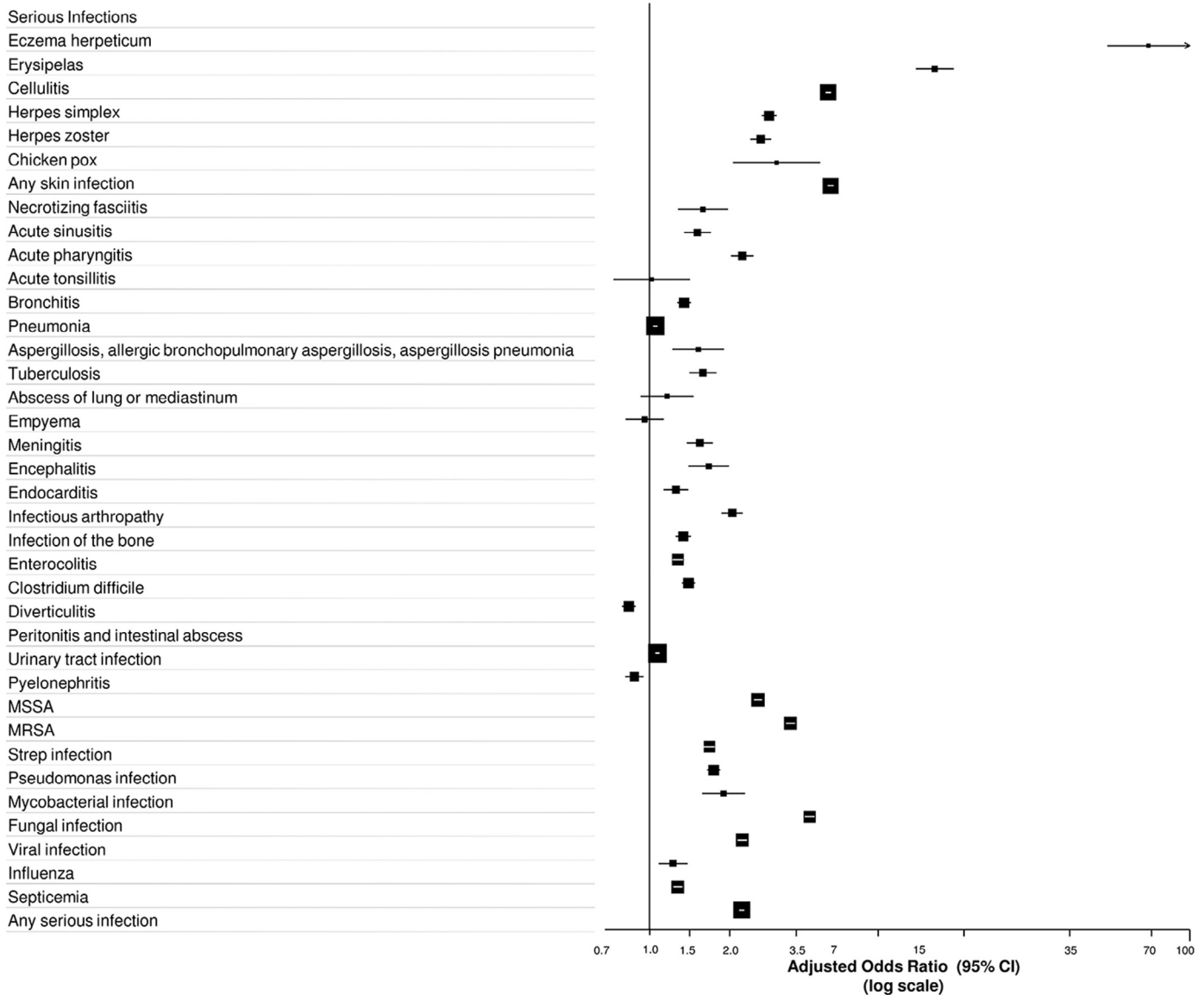


Figure 1. Association between atopic dermatitis or eczema and serious infections. Survey logistic regression models were constructed with atopic dermatitis or eczema as the independent variable and the respective serious infection as the dependent variable. Models included age, sex, race/ethnicity, and insurance status as covariates. Adjusted odds ratios and 95% confidence intervals (CIs) were estimated. Forest plots of adjusted odds ratios and 95% CIs are presented. MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

than for patients with AD without serious infection (\$7,179 [7,052–7,307]); $P = .0002$ by linear regression; Table 3). Many cutaneous, respiratory, systemic, and multiorgan infections were associated with a higher geometric mean cost than in patients without any serious infections (eTable 10). There were estimated \$227,618,460 excess costs of hospital care annually for serious infections in patients with vs without AD-E, with cellulitis, any skin infection, pneumonia, urinary tract infections, septicemia, and fungal infection accounting for the most excess costs associated with infections. There was a strong correlation between total annual LOS and cost of care among serious infections in patients with AD-E (Spearman correlation, $\rho = 0.993$). The excess costs of hospital care for serious infections was \$11,062,120 annually when including patients with AD alone.

Impact of Serious Infections on Inpatient Mortality

Patients with AD-E and any serious infection had higher rates of inpatient mortality (95% CI) than those with AD-E without any

serious infection (1.7% [1.6–1.8] vs 0.6% [0.6–0.7], $P = 0.0002$), including necrotizing fasciitis (2.7% [0.0–5.7]), pneumonia (4.2% [3.8–4.5]), tuberculosis (2.2% [0.8–3.6]), abscess of lung or mediastinum (3.3% [0.0–7.0]), empyema (6.7% [3.1–10.3]), encephalitis (2.8% [0.4–5.3]), endocarditis (4.5% [2.4–6.4]), enterocolitis (2.9% [2.2–3.5]), *Clostridium difficile* (3.8% [3.0–4.7]), peritonitis and intestinal abscess (3.9% [2.3–5.5]), urinary tract infections (1.9% [1.7–2.1]), MRSA (2.1% [1.6–2.5]), pseudomonas infection (2.2% [1.5–2.8]), mycobacterial infection (3.1% [0.4–5.8]), influenza (2.1% [0.4–3.8]), and septicemia (6.9% [6.3–7.4]; Table 3, eTable 10).

Discussion

This study demonstrated that adults with AD and AD-E as judged by ICD-9-CM codes 691.8 and 692.9, respectively, had significantly higher prevalences of serious infections compared with those without AD, including infections of the skin, lower respiratory tract and lungs, heart, brain, gastrointestinal tract, and bones.

Table 2
Associations of Serious Infections in Adults With Atopic Dermatitis or Eczema

Variable	Adjusted OR (95% CI)	P value
Age (y)		
18–39	1.00 (ref)	—
40–59	1.36 (1.34–1.38)	.0002
60–79	1.52 (1.49–1.55)	.0002
≥ 80	2.18 (2.13–2.23)	.0002
Sex		
Female	0.95 (0.94–0.96)	.0002
Male	1.00 (ref)	—
Race		
White	1.00 (ref)	—
Black	0.94 (0.92–0.95)	.0002
Hispanic	1.07 (1.05–1.09)	.0002
Asian	0.92 (0.89–0.95)	.0002
Other	0.92 (0.89–0.95)	.0002
Income quartile		
1	1.04 (1.03–1.06)	.0002
2	1.01 (0.99–1.02)	.5
3	1.00 (0.99–1.02)	.9
4	1.00 (ref)	—
Insurance		
Medicare	1.28 (1.26–1.30)	.0002
Medicaid	1.24 (1.21–1.26)	.0002
Private	1.00 (ref)	—
Self-pay	1.25 (1.21–1.28)	.0002
No charge	1.29 (1.19–1.40)	.0002
Other	1.07 (1.03–1.10)	.002
Chronic conditions (n) ^a		
0–1	1.00 (ref)	—
2–5	0.83 (0.81–0.85)	.0002
≥ 6	0.85 (0.83–0.86)	.0002
Region		
Northeast	0.89 (0.88–0.90)	.0002
Midwest	0.95 (0.94–0.97)	.0002
South	1.05 (1.03–1.07)	.0002
West	1.00 (ref)	—
Season		
Fall	1.06 (1.04–1.07)	.0002
Summer	1.04 (1.03–1.06)	.0002
Winter	1.02 (1.01–1.04)	.01
Spring	1.00 (ref)	—
Hospital location		
Metropolitan (>1 million)	1.00 (ref)	—
Fringe/metropolitan (<1 million)	0.95 (0.93–0.96)	.0002
Micropolitan ^b	0.95 (0.93–0.97)	.0002
Not metro- or micropolitan	0.93 (0.91–0.96)	.0002
Hospital bed size		
Small	1.00 (ref)	—
Medium	0.93 (0.91–0.94)	.0002
Large	0.91 (0.89–0.93)	.0002
Hospital teaching status		
Nonteaching	1.00 (ref)	—
Teaching	0.87 (0.86–0.88)	.0002
Comorbidity		
Diabetes mellitus	1.18 (1.17–1.20)	.0002
Obesity	1.35 (1.33–1.37)	.0002
Asthma	0.95 (0.94–0.97)	.0002

Abbreviations: CI, confidence interval; OR, odds ratio; ref, reference.

^aChronic conditions were defined by Healthcare Cost and Utilization Project (HCUP) as lasting 12 months or longer and meeting one or both of the following: (1) places limitations on self-care, independent living, and social interactions and/or (2) results in the need for ongoing intervention with medical products, services, and special equipment. Chronic condition count was calculated and provided by HCUP.

^bGreater than or equal to 1 urban cluster with a population of 10,000 to 49,999.

Approximately 1 in 2 serious infections overall and skin infections in particular were secondary diagnoses in adults admitted primarily for AD. Higher prevalences of multiple infections occurred in AD vs psoriasis. Further, prevalence of cellulitis was even higher in patients with AD and EH compared with those who had AD alone. Further, higher prevalence of serious infections occurred in patients with AD who were older, men, white, had lower household income, and public or no insurance. These results are consistent with

previous studies that found higher rates of cutaneous and extracutaneous infections in AD.^{7,12,13} A US population-based study of 91,642 children from the National Survey of Children's Health found that children with AD had significantly higher rates of recurrent ear infections.¹² Another US population-based study of 9,417 children from the National Health Interview Survey found that children with AD had significantly higher rates of cutaneous warts, streptococcal throat, other sore throat, head or chest cold, influenza or pneumonia, sinus infections, recurrent ear infections, chickenpox, and urinary tract infections.⁷ A study of 34,613 adults from the National Health Interview Survey found that adults with AD had significantly higher prevalences of influenza or pneumonia, streptococcal throat, head or chest cold, sinus infection, gastroenteritis, chickenpox, infectious diseases or other immune problems, and fever lasting longer than 24 hours.¹³ Together, there appear to be higher rates of extracutaneous and systemic infections in children and adults with AD.

The results of the present study are consistent with prior studies that examined associations between AD and serious infections based on surveys using questions about self- or caregiver-reported AD and serious infections. In contrast, the present study examined the associations between AD and serious infections that were diagnosed and recorded by a health care professional. Furthermore, this study examined serious infections that were not previously examined and illustrated data on usage related to these comorbidities, including hospitalization rates, cost of care, LOS, and mortality, further illustrating the indirect costs and financial burden of AD.

The financial burden of serious infections in patients with AD was substantial. Thirty-seven of 38 serious infections were associated with increased hospitalization LOS and 31 of 38 were associated with higher costs of care compared with adults with AD and no serious infection. AD was indirectly associated with \$11 to \$228 million of excess health care costs annually for hospitalization from serious infections. Some older studies estimated the direct costs of AD to be \$364 to \$3.8 billion US dollars per year.¹⁸ The present study indicates that there are increased indirect health care costs and mortality related to the comorbid health conditions of AD, such as infections. These results beg for future interventions aimed at lowering the prevalence and improving the management of serious infections in patients with AD.

Infections associated with the highest inpatient mortality in patients with AD were septicemia (6.9%) followed by empyema, endocarditis, pneumonia, peritonitis and intestinal abscess, *C difficile* infection, abscess of lung and mediastinum, mycobacterial infection, enterocolitis, encephalitis, MRSA, and MSSA. The increased prevalence and inpatient mortality of patients with AD secondary to MRSA and other bacterial infections raise concerns about antibiotic treatment in AD and antibiotic resistance. Topical and oral antibiotics are often used for the treatment of AD, despite a lack of evidence supporting their efficacy as a treatment for uninfected AD.¹⁹ Excess use of antibiotics can contribute to higher rates of antibiotic resistance and expose patients with AD to higher risk of mortality from MRSA. The current guidelines recommend antibiotics be used only for the treatment of clinically infected AD.¹⁹

The mechanisms of increased multiorgan and systemic infections are unknown. Epidermal barrier dysfunction⁹ and decreased expression of antimicrobial peptides in skin¹⁰ have been suggested to predispose toward cutaneous infections. Further, previous studies have shown that AD severity is strongly correlated with levels of *S aureus* colonization of skin.^{20,21} In addition, recent studies have demonstrated aberrant toll-like receptor signaling and innate immunity in AD.^{11,22} Barrier disruption, increased bacterial colonization, and immune dysregulation could facilitate transcutaneous penetration of pathogens, thereby becoming a nidus for systemic infection. Recent studies also have found evidence of profound systemic inflammation in patients with AD^{23,24} and multiple comorbid

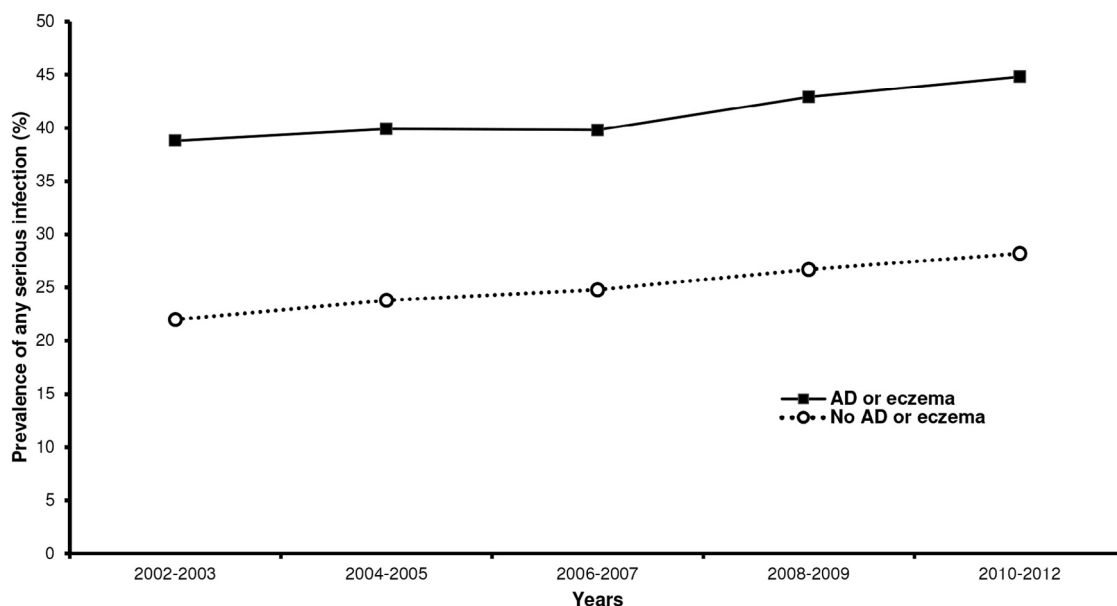


Figure 2. Prevalence of serious infections in hospitalized patients with atopic dermatitis (AD) or eczema (squares) vs without AD (circles). Proportion of hospitalized patients with AD (squares) and without AD (circles) is plotted over time (2002–2003, 2004–2005, 2006–2007, 2008–2009, 2010–2012).

health conditions.²⁵ Some respiratory infections might be due to comorbid asthma and/or atopic disease. However, most associations remained significant even in multivariable models that controlled for asthma and hay fever (model 2). It has been proposed that AD is a systemic disease.²⁵ Thus, topical and/or systemic agents that successfully improve barrier dysfunction and immune regulation in the skin and systemically and decrease *Staphylococcal* colonization might subsequently decrease the association of AD with serious infections. In contrast, the systemic medications most commonly used in North America for the treatment of AD, including corticosteroids, cyclosporine, methotrexate, and mycophenolate mofetil,²⁶ are highly immunosuppressing and could contribute to the higher prevalence of systemic infections. Large quantities of topical corticosteroids and/or calcineurin inhibitors also can affect infectious risk. Use of narrower target-driven systemic or biological agents could have the benefit of not increasing risk of infection. Future research is needed to determine the mechanism(s) of association with systemic infections in patients with AD and optimal approaches toward weakening these associations.

The strengths of this study include a nationally representative sample of more than 87 million hospitalizations spanning 11 years. We previously found code 691.8 to be sufficiently valid for identifying AD in the inpatient setting.¹⁴ We also found that the *ICD-9-CM* codes for AD (691.8) and eczema (692.9) are used interchangeably, with similar proportions of patients meeting diagnostic criteria for AD⁸ whether they were coded as AD or AD-E.¹⁴ Thus, primary analyses of associations with serious infections were performed for AD and AD-E. Estimates of excess costs associated with infection were performed in hospitalizations with AD alone and AD-E. The

use of different *ICD* codes for AD is due largely to the imprecision in nomenclature used for the disease (eg, AD, atopic eczema, eczema, etc).^{14,27} Further, the term *eczema* is associated with the *ICD-9-CM* code for contact dermatitis (692.9), rather than the term for AD or AE (691.8). This issue will likely remain a problem with the *ICD-10*, in which *eczema* is associated with the *ICD-10* code for rash not otherwise specified (L30.9). Standardization of terminology that is in line with the current *ICD* code definitions is essential to address this imprecision of nomenclature and resultant use of *ICD* codes. The International Eczema Council recently reached a consensus in recommending the use of the prefix *atopic* (ie, AD or atopic eczema, but not eczema alone).²⁸ Consistent use of this more precise terminology is likely to improve the validity of using *ICD* codes to identify AD in claims datasets, although this could take many years to reach fruition. We could not determine the department of hospitalization (eg, dermatology vs non-dermatology). The association between AD and serious infections might differ based on department of hospitalization. However, few US hospitals have dedicated dermatology wards. Most patients hospitalized with a dermatologic disorder would be admitted to a non-dermatology ward. The NIS did not record the dates of assigned diagnoses, which precluded assessment of whether the serious infections began before or during hospitalization. Moreover, we could not determine how many hospitalizations were due to readmissions or transfers between hospitals. Some patients might have been admitted repeatedly for infections. Further, because manual chart review was not possible, patient history was not available and the study was limited by our inability to assess the severity or phenotype of AD, history of immunodeficiency, outpatient treatment approaches (eg, oral

Table 3
Costs of Care, LOS, and Inpatient Mortality of Adults With AD or AD-E and Serious Infections

Serious infection	Geometric mean cost (\$) in patients with AD-E (95% CI)	Excess annual cost (\$) secondary to AD-E	Excess annual cost (\$) secondary to AD	Geometric mean LOS (d) in patients with AD-E (95% CI)	Excess annual LOS (d) secondary to AD-E	Excess annual LOS (d) secondary to AD	Inpatient mortality in patients with AD-E (95% CI)
None	7,179 (7,052–7,307)	—	—	3.9 (3.9–4.0)	—	—	0.6 (0.6–0.7)
Any	8,273 (8,126–8,423)	227,618,459.9	11,062,119.96	5.3 (5.2–5.3)	138,941.67	6,974.68	1.7 (1.6–1.8)

Abbreviations: AD, atopic dermatitis; AD-E, atopic dermatitis or eczema CI, confidence interval; LOS, length of stay.

immunosuppressive medications), and how these might have affected the prevalence of serious infections. We did find that patients with AD with vs without EH had even higher odds of cellulitis. This suggests that more severe AD has even higher odds of infection than mild AD. Alternatively, EH might be a sign of a particular subset of patients with AD who are vulnerable to infections. Future studies are needed to determine the impact of EH on serious infections.

In conclusion, adults with AD had significantly higher odds of cutaneous, respiratory, multiorgan, and systemic infections. Serious infections were associated with a substantial financial burden in patients with AD. Further studies are needed to understand the mechanisms of extracutaneous and systemic infections in AD and develop interventions to prevent them.

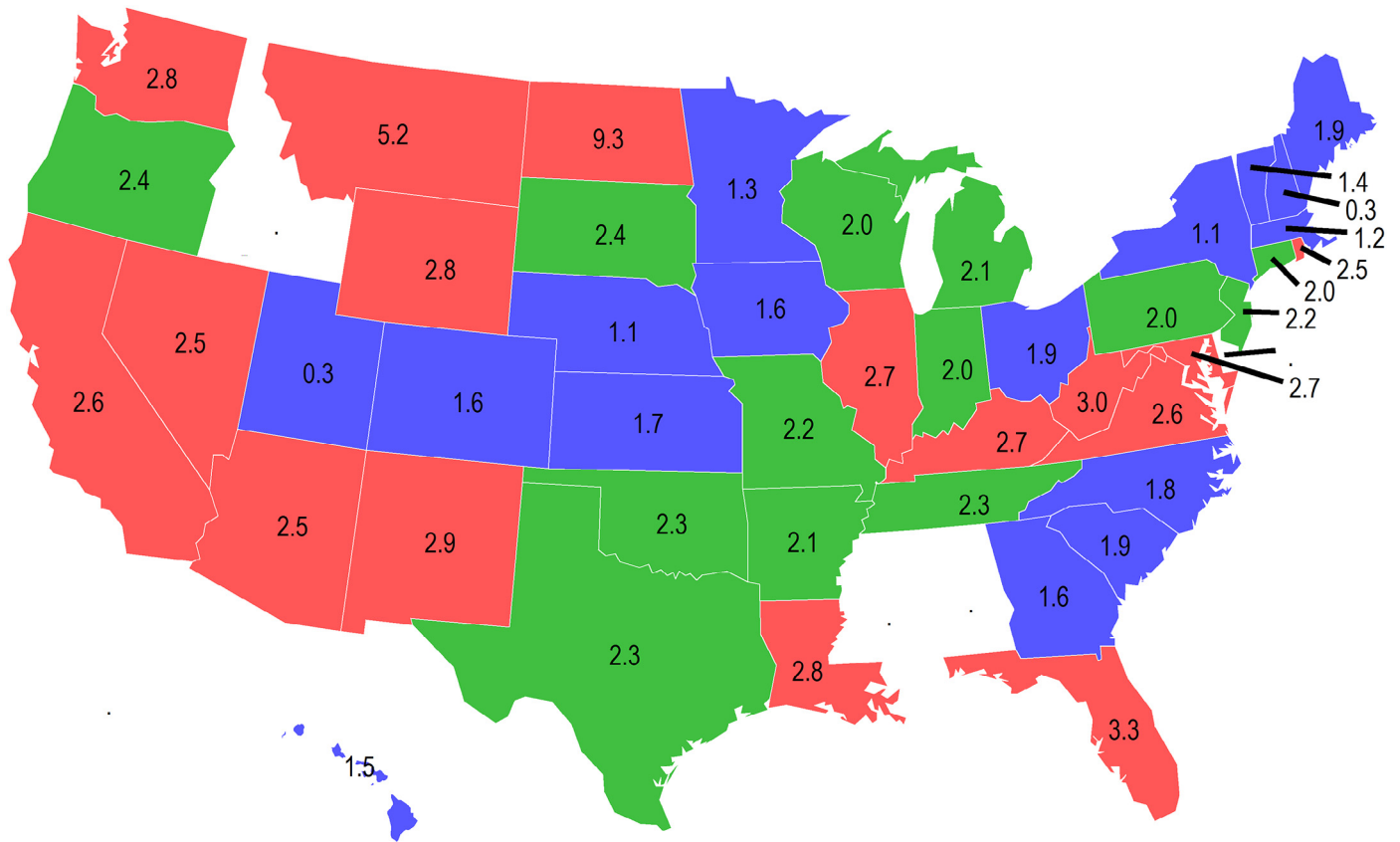
Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.janai.2017.10.019>.

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Supplementary Data



eFigure 1. State-level mean annual prevalence of methicillin-resistant *Staphylococcus aureus* in adults with atopic dermatitis or eczema (blue, lowest tertile; green, middle tertile; red, highest tertile).

eTable 1

International Classification of Diseases, Ninth Revision, Clinical Modification and CCS Codes for Serious Infections and Atopic Disease

Serious infection	Codes
Eczema herpeticum	054.0
Erysipelas	035
Cellulitis	681.00, 681.10, 681.9, 682.0–686.9, 681, 681.0, 681.1, 681.9, 682
Herpes simplex	054.0, 054.10–054.19, 054.2, 054.3, 054.40–054.49, 054.5, 054.6, 054.71–054.79, 054.8, 054.9, 054, 054.1, 054.4, 054.7
Herpes zoster	053, 053.0, 053.1, 053.2, 053.7, 053.8, 053.9
Chicken pox	052, 052.1, 052.2, 052.7, 052.8, 052.9
Any skin infection	CCS 197
Necrotizing fasciitis	728.86
Acute sinusitis	461.3, 461.8, 461.9
Acute pharyngitis	462
Acute tonsillitis	463
Bronchitis	CCS 125
Pneumonia	CCS 122
Aspergillosis + allergic bronchopulmonary aspergillosis + aspergillosis pneumonia	117.3, 518.6, 484.6
Tuberculosis	CCS 1
Abscess of lung or mediastinum	513, 513.0, 513.1
Empyema	510, 510.0, 510.9
Meningitis	CCS 76
Encephalitis	CCS 77
Endocarditis	424.9, 424.90, 424.91, 424.99, 421, 421.0, 421.1, 421.9
Infectious arthropathy	711.0, 711.00–711.09, 711.10–711.19, 711.2, 711.21–711.29, 711.3, 711.31–711.39, 711.4, 711.41–711.49, 711.50–711.59, 711.6, 711.61–711.69, 711.7, 711.71–711.79, 711.90, 711.91–711.99, 711.80, 711.81, 711, 711.82–711.89, 711.4, 711.5, 711.8, 711.9
Infection of bone	730.00–730.09, 730.1, 730.11–730.19, 730.20–730.29, 730.80–730.89, 730.90–730.99, 730.0, 730.1, 730.2, 730.8, 730.9, 730, 015.0
Enterocolitis	CCS 135
<i>Clostridium difficile</i> infection	008.45
Diverticulitis	562.01, 562.03, 562.11, 562.13
Peritonitis and intestinal Abscess	CCS 148
Urinary tract infection	CCS 159
Pyelonephritis	590.0, 590.00, 590.01, 590.1, 590.10, 590.11, 590.2, 590.8, 590.80, 590.81, 590.9
MSSA	041.11, 038.11, 482.41, V02.53
MRSA	041.12, 038.12, 482.42, V025.4, V12.04
Streptococcal infection	041.0, 041.00–041.09, 482.3, 482.30–482.39, 481, 034.0
Pseudomonas infection	041.7, 008.42, 038.43, 482.1
Mycobacterial infections	031, 031.0, 031.1, 031.2, 031.8, 031.9
Fungal infection	CCS 4
Viral infection	CCS 7
Influenza	CCS 123
Septicemia	CCS 2
Asthma	CCS 128
Hay fever	477.0–479.0
Psoriasis	696.1

Abbreviations: CCS, Clinical Classification Software; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*.

eTable 2
Associations Between Atopic Dermatitis or Eczema and Serious Infections

Variable	Inpatient diagnosis of atopic dermatitis or eczema									
	No		Yes		Crude OR (95% CI)	P value	Model 1 ^a		Model 2 ^b	
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)			Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Eczema herpeticum	1,547	0.0005 (0.0004–0.0005)	257	0.03 (0.02–0.04)	72.09 (52.70–98.61)	.0002	67.93 (47.93–96.28)	.0002	62.74 (46.29–85.04)	.0002
Erysipelas	37,983	0.01 (0.01–0.01)	959	0.1 (0.1–0.1)	10.97 (9.47–12.70)	.0002	11.15 (9.47–13.1)	.0002	10.93 (9.43–12.66)	.0002
Cellulitis	12,627,300	3.7 (3.6–3.7)	119,595	15.1 (14.8–15.5)	4.66 (4.56–4.77)	.0002	4.53 (4.42–4.64)	.0002	4.67 (4.57–4.78)	.0002
Herpes simplex	1,145,223	0.3 (0.3–0.3)	6,285	0.8 (0.7–0.8)	2.39 (2.25–2.54)	.0002	2.75 (2.58–2.93)	.0002	2.34 (2.20–2.48)	.0002
Herpes zoster	493,295	0.1 (0.1–0.1)	2,988	0.4 (0.3–0.4)	2.63 (2.43–2.86)	.0002	2.56 (2.34–2.80)	.0002	2.62 (2.41–2.84)	.0002
Chicken pox	23,500	0.007 (0.007–0.007)	174	0.02 (0.01–0.03)	3.21 (2.31–4.46)	.0002	2.93 (2.02–4.24)	.0002	3.22 (2.31–4.48)	.0002
Any skin infection	13,064,444	3.8 (3.8–3.9)	125,460	15.9 (15.6–16.2)	4.76 (4.66–4.87)	.0002	4.62 (4.51–4.74)	.0002	4.77 (4.66–4.88)	.0002
Necrotizing fasciitis	144,621	0.04 (0.04–0.04)	512	0.06 (0.05–0.08)	1.54 (1.26–1.87)	.0002	1.57 (1.27–1.94)	.0002	1.57 (1.29–1.91)	.0002
Acute sinusitis	507,135	0.1 (0.1–0.2)	1,764	0.2 (0.2–0.2)	1.52 (1.37–1.68)	.0002	1.50 (1.34–1.68)	.0002	1.35 (1.22–1.49)	.0002
Acute pharyngitis	508,126	0.1 (0.1–0.2)	2,439	0.3 (0.3–0.3)	2.09 (1.91–2.29)	.0002	2.19 (1.98–2.41)	.0002	1.99 (1.81–2.17)	.0002
Acute tonsillitis	102,112	0.03 (0.03–0.03)	225	0.03 (0.02–0.04)	0.96 (0.72–1.28)	.8	1.02 (0.74–1.41)	.9	0.93 (0.70–1.25)	.7
Bronchitis	2,118,629	0.6 (0.6–0.6)	6,710	0.8 (0.8–0.9)	1.38 (1.31–1.46)	.0002	1.34 (1.26–1.42)	.0002	1.11 (1.05–1.18)	.0003
Pneumonia	24,745,285	7.2 (7.1–7.3)	60,165	7.6 (7.4–7.8)	1.06 (1.04–1.09)	.0002	1.05 (1.02–1.07)	.0007	1.02 (1.00–1.05)	.1
Aspergillosis, allergic bronchopulmonary aspergillosis, aspergillosis pneumonia	143,130	0.04 (0.04–0.04)	519	0.07 (0.05–0.08)	1.57 (1.29–1.92)	.0002	1.51 (1.21–1.88)	.0003	1.41 (1.16–1.72)	.001
Tuberculosis	625,497	0.2 (0.2–0.2)	2,216	0.3 (0.2–0.3)	1.54 (1.38–1.71)	.0002	1.57 (1.41–1.76)	.0002	1.48 (1.33–1.65)	.0002
Abscess of lung or mediastinum	181,850	0.05 (0.05–0.05)	463	0.06 (0.05–0.07)	1.11 (0.90–1.37)	.4	1.16 (0.93–1.45)	.2	1.08 (0.88–1.34)	.5
Empyema	376,096	0.1 (0.1–0.1)	865	0.1 (0.1–0.1)	1.00 (0.86–1.16)	1.0	0.96 (0.81–1.13)	.6	1.00 (0.86–1.17)	1.0
Meningitis	550,790	0.2 (0.2–0.2)	1,840	0.2 (0.2–0.3)	1.46 (1.31–1.62)	.0002	1.53 (1.36–1.71)	.0002	1.46 (1.32–1.63)	.0002
Encephalitis	230,584	0.07 (0.07–0.07)	870	0.11 (0.09–0.13)	1.64 (1.41–1.91)	.0002	1.65 (1.40–1.96)	.0002	1.66 (1.43–1.94)	.0002
Endocarditis	718,292	0.2 (0.2–0.2)	2,063	0.3 (0.2–0.3)	1.25 (1.13–1.38)	.0002	1.25 (1.12–1.39)	.0002	1.27 (1.15–1.40)	.0002
Infectious arthropathy	595,415	0.2 (0.2–0.2)	2,973	0.4 (0.3–0.4)	2.18 (2.00–2.37)	.0002	2.01 (1.84–2.20)	.0002	2.19 (2.01–2.38)	.0002
Infection of bone	2,261,936	0.7 (0.6–0.7)	7,301	0.9 (0.9–1.0)	1.41 (1.33–1.49)	.0002	1.33 (1.25–1.42)	.0002	1.45 (1.37–1.53)	.0002
Enterocolitis	4,778,070	1.4 (1.4–1.4)	13,915	1.8 (1.7–1.8)	1.27 (1.22–1.32)	.0002	1.27 (1.22–1.33)	.0002	1.28 (1.23–1.34)	.0002
<i>Clostridium difficile</i>	3,110,696	0.9 (0.9–0.9)	9,995	1.3 (1.2–1.3)	1.40 (1.33–1.48)	.0002	1.39 (1.32–1.47)	.0002	1.43 (1.36–1.50)	.0002
Diverticulitis	3,316,315	1.0 (1.0–1.0)	6,500	0.8 (0.8–0.9)	0.85 (0.80–0.90)	.0002	0.84 (0.78–0.89)	.0002	0.85 (0.80–0.90)	.0002
Peritonitis and intestinal abscess	1,857,458	0.5 (0.5–0.6)	3,247	0.4 (0.4–0.4)	0.76 (0.70–0.82)	.0002	0.75 (0.69–0.82)	.0002	0.77 (0.71–0.84)	.0002
Urinary tract infection	30,622,692	8.9 (8.8–9.0)	83,487	10.6 (10.3–10.8)	1.20 (1.18–1.23)	.0002	1.07 (1.05–1.09)	.0002	1.23 (1.20–1.26)	.0002
Pyelonephritis	2,444,891	0.7 (0.7–0.7)	4,480	0.6 (0.5–0.6)	0.79 (0.74–0.85)	.0002	0.88 (0.81–0.95)	.001	0.80 (0.75–0.86)	.0002
MSSA	4,462,130	1.3 (1.3–1.3)	25,956	3.3 (3.2–3.4)	2.56 (2.49–2.66)	.0002	2.50 (2.41–2.59)	.0002	2.60 (2.52–2.69)	.0002
MRSA	2,598,316	0.8 (0.7–0.8)	20,169	2.6 (2.4–2.7)	3.43 (3.30–3.56)	.0002	3.29 (3.17–3.42)	.0002	3.35 (3.22–3.47)	.0002
Streptococcal infection	3,645,822	1.1 (1.0–1.1)	14,116	1.8 (1.7–1.9)	1.69 (1.63–1.76)	.0002	1.66 (1.59–1.74)	.0002	1.70 (1.64–1.77)	.0002
Pseudomonas infection	1,975,369	0.6 (0.6–0.6)	8,000	1.0 (1.0–1.1)	1.77 (1.68–1.86)	.0002	1.72 (1.63–1.82)	.0002	1.78 (1.69–1.87)	.0002
Mycobacterial infection	170,408	0.05 (0.05–0.05)	764	0.1 (0.1–0.1)	1.95 (1.65–2.30)	.0002	1.87 (1.56–2.24)	.0002	1.91 (1.62–2.25)	.0002
Fungal infection	5,821,858	1.7 (1.7–1.7)	50,296	6.4 (6.1–6.6)	3.94 (3.78–4.09)	.0002	3.87 (3.70–4.04)	.0002	3.85 (3.70–4.00)	.0002
Viral infection	3,307,853	1.0 (0.9–1.0)	462	2.0 (1.9–2.1)	2.09 (2.01–2.17)	.0002	2.19 (2.10–2.28)	.0002	2.04 (1.97–2.12)	.0002
Influenza	499,358	0.1 (0.1–0.2)	1,380	0.2 (0.2–0.2)	1.20 (1.07–1.35)	.004	1.22 (1.07–1.38)	.004	1.08 (0.96–1.21)	.3
Septicemia	13,798,912	4.0 (4.0–4.1)	39,851	5.0 (4.9–5.2)	1.27 (1.23–1.31)	.0002	1.27 (1.23–1.32)	.0002	1.30 (1.25–1.34)	.0002
Any serious infection	87,010,421	25.4 (25.2–25.6)	332,533	42.1 (41.6–42.6)	2.14 (2.10–2.18)	.0002	2.18 (2.14–2.23)	.0002	2.11 (2.07–2.15)	.0002

Abbreviations: CI, confidence interval; OR, odds ratio; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; Wtd, weighted.

^aIncludes age, sex, race/ethnicity, and insurance status.

^bIncludes asthma and hay fever.

eTable 3

Logistic Regression Models of the Associations Between Asthma and/or Hay Fever, Atopic Dermatitis or Eczema, and Serious Infections in Adults

Variable	No AD-E		AD-E without asthma and/or hay fever				AD-E with asthma and/or hay fever			
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value
Eczema herpeticum	1,547	0.0005 (0.0004–0.0005)	115	0.02 (0.01–0.02)	37.52 (24.79–56.80)	.0002	142	0.1 (0.1–0.2)	289.58 (188.53–444.80)	.0002
Erysipelas	37,983	0.01 (0.01–0.01)	795	0.1 (0.1–0.1)	10.54 (8.99–12.35)	.0002	164	0.2 (0.1–0.2)	13.66 (9.66–19.30)	.0002
Cellulitis	12,627,300	3.7 (3.6–3.7)	106,466	15.6 (15.3–16.0)	4.84 (4.73–4.95)	.0002	13,129	12.1 (11.6–12.6)	3.60 (3.44–3.77)	.0002
Herpes simplex	1,145,223	0.3 (0.3–0.3)	5,079	0.7 (0.7–0.8)	2.24 (2.10–2.39)	.0002	1,206	1.1 (1.0–1.3)	3.37 (2.96–3.83)	.0002
Herpes zoster	493,295	0.1 (0.1–0.1)	2,625	0.4 (0.4–0.4)	2.68 (2.46–2.92)	.0002	363	0.3 (0.3–0.4)	2.33 (1.86–2.93)	.0002
Chicken pox	23,500	0.007 (0.007–0.007)	160	0.02 (0.02–0.03)	3.42 (2.42–4.83)	.0002	14	0.01 (0.00–0.03)	1.87 (0.60–5.82)	.3
Any skin infection	13,064,444	3.8 (3.8–3.9)	111,445	16.4 (16.0–16.7)	4.93 (4.82–5.05)	.0002	14,015	12.9 (12.4–13.4)	3.75 (3.58–3.92)	.0002
Necrotizing fasciitis	144,621	0.04 (0.04–0.04)	476	0.07 (0.06–0.08)	1.66 (1.35–2.03)	.0002	36	0.03 (0.01–0.06)	0.79 (0.39–1.59)	.6
Acute sinusitis	507,135	0.1 (0.1–0.2)	1,306	0.2 (0.2–0.2)	1.30 (1.15–1.46)	.0002	458	0.4 (0.3–0.5)	2.86 (2.33–3.52)	.0002
Acute pharyngitis	508,126	0.1 (0.1–0.2)	1,975	0.3 (0.3–0.3)	1.96 (1.77–2.16)	.0002	464	0.4 (0.3–0.5)	2.90 (2.37–3.54)	.0002
Acute tonsillitis	102,112	0.03 (0.03–0.03)	192	0.03 (0.02–0.04)	0.95 (0.69–1.29)	.8	33	0.03 (0.01–0.05)	1.03 (0.49–2.14)	1.0
Bronchitis	2,118,629	0.6 (0.6–0.6)	4,480	0.7 (0.6–0.7)	1.06 (1.00–1.14)	.1	2,229	2.1 (1.9–2.3)	3.39 (3.07–3.73)	.0002
Pneumonia	24,745,285	7.2 (7.1–7.3)	50,837	7.5 (7.3–7.7)	1.04 (1.01–1.06)	.01	9,328	8.6 (8.2–9.0)	1.21 (1.15–1.27)	.0002
Aspergillosis, allergic bronchopulmonary aspergillosis, aspergillosis pneumonia	143,130	0.04 (0.04–0.04)	329	0.05 (0.04–0.06)	1.16 (0.91–1.47)	.3	190	0.2 (0.1–0.2)	4.19 (2.98–5.89)	.0002
Tuberculosis	625,497	0.2 (0.2–0.2)	1,888	0.3 (0.2–0.3)	1.52 (1.36–1.70)	.0002	328	0.3 (0.2–0.4)	1.66 (1.24–2.24)	.001
Abscess of lung or mediastinum	181,850	0.05 (0.05–0.05)	380	0.06 (0.04–0.07)	1.05 (0.83–1.33)	.7	83	0.08 (0.04–0.11)	1.45 (0.90–2.33)	.2
Empyema	376,096	0.1 (0.1–0.1)	723	0.1 (0.1–0.1)	0.97 (0.82–1.14)	.7	142	0.1 (0.1–0.2)	1.19 (0.79–1.80)	.5
Meningitis	550,790	0.2 (0.2–0.2)	1,642	0.2 (0.2–0.3)	1.51 (1.35–1.68)	.0002	199	0.2 (0.1–0.2)	1.14 (0.84–1.55)	.5
Encephalitis	230,584	0.07 (0.07–0.07)	793	0.1 (0.1–0.1)	1.73 (1.47–2.03)	.0002	77	0.07 (0.04–0.11)	1.06 (0.65–1.73)	.8
Endocarditis	718,292	0.2 (0.2–0.2)	1,890	0.3 (0.2–0.3)	1.33 (1.20–1.47)	.0002	173	0.2 (0.1–0.2)	0.76 (0.55–1.07)	.1
Infectious arthropathy	595,415	0.2 (0.2–0.2)	2,505	0.4 (0.3–0.4)	2.12 (1.94–2.33)	.0002	468	0.4 (0.3–0.5)	2.51 (2.04–3.09)	.0002
Infection of bone	2,261,936	0.7 (0.6–0.7)	6,566	1.0 (0.9–1.0)	1.47 (1.39–1.56)	.0002	735	0.7 (0.6–0.8)	1.03 (0.87–1.21)	.8
Enterocolitis	4,778,070	1.4 (1.4–1.4)	12,566	1.8 (1.8–1.9)	1.33 (1.27–1.39)	.0002	1,350	1.2 (1.1–1.4)	0.89 (0.79–1.00)	.08
<i>Clostridium difficile</i>	3,110,696	0.9 (0.9–0.9)	9,220	1.4 (1.3–1.4)	1.50 (1.43–1.58)	.0002	775	0.7 (0.6–0.8)	0.79 (0.67–0.92)	.005
Diverticulitis	3,316,315	1.0 (1.0–1.0)	5,683	0.8 (0.8–0.9)	0.86 (0.81–0.92)	.0002	817	0.8 (0.6–0.9)	0.78 (0.67–0.91)	.002
Peritonitis and intestinal abscess	1,857,458	0.5 (0.5–0.6)	2,896	0.4 (0.4–0.5)	0.78 (0.72–0.85)	.0002	351	0.3 (0.3–0.4)	0.60 (0.48–0.75)	.0002
Urinary tract infection	30,622,692	8.9 (8.8–9.0)	76,189	11.2 (10.9–11.4)	1.28 (1.25–1.31)	.0002	7,298	6.7 (6.4–7.1)	0.74 (0.70–0.78)	.0002
Pyelonephritis	2,444,891	0.7 (0.7–0.7)	3,780	0.6 (0.5–0.6)	0.78 (0.72–0.84)	.0002	699	0.6 (0.5–0.8)	0.90 (0.77–1.07)	.3
MSSA	4,462,130	1.3 (1.3–1.3)	22,481	3.3 (3.2–3.4)	2.59 (2.50–2.68)	.0002	3,474	3.2 (3.0–3.5)	2.51 (2.31–2.72)	.0002
MRSA	2,598,316	0.8 (0.7–0.8)	16,946	2.5 (2.4–2.6)	3.34 (3.21–3.48)	.0002	3,223	3.0 (2.7–3.2)	4.01 (3.68–4.37)	.0002
Streptococcal infection	3,645,822	1.1 (1.0–1.1)	12,595	1.8 (1.8–1.9)	1.75 (1.68–1.83)	.0002	1,521	1.4 (1.2–1.6)	1.32 (1.18–1.48)	.0002
Pseudomonas infection	1,975,369	0.6 (0.6–0.6)	7,381	1.1 (1.0–1.1)	1.89 (1.79–1.99)	.0002	619	0.6 (0.5–0.7)	0.99 (0.83–1.18)	.9
Mycobacterial infection	170,408	0.05 (0.05–0.05)	691	0.1 (0.1–0.1)	2.04 (1.72–2.43)	.0002	73	0.07 (0.03–0.10)	1.36 (0.82–2.24)	.3
Fungal infection	5,821,858	1.7 (1.7–1.7)	44,583	6.5 (6.3–6.8)	4.05 (3.89–4.22)	.0002	5,713	5.3 (4.9–5.6)	3.22 (3.01–3.44)	.0002
Viral infection	3,307,853	1.0 (0.9–1.0)	13,161	1.9 (1.8–2.1)	2.02 (1.94–2.11)	.0002	2,576	2.4 (2.2–2.6)	2.51 (2.30–2.75)	.0002
Influenza	499,358	0.1 (0.1–0.2)	1,034	0.2 (0.1–0.2)	1.04 (0.91–1.20)	.6	346	0.3 (0.2–0.4)	2.20 (1.73–2.80)	.0002
Septicemia	13,798,912	4.0 (4.0–4.1)	35,574	5.2 (5.0–5.4)	1.31 (1.27–1.36)	.0002	4,277	3.9 (3.7–4.2)	0.98 (0.91–1.05)	.6
Any serious infection	87,010,421	25.4 (25.2–25.6)	291,357	42.8 (42.3–43.3)	2.20 (2.15–2.24)	.0002	41,175	38.0 (37.2–38.8)	1.80 (1.44–1.86)	.0002

Abbreviations: AD-E, atopic dermatitis or eczema; CI, confidence interval; OR, odds ratio; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; Wtd, weighted.

eTable 4

Associations Between Atopic Dermatitis and Serious Infections

Variable	Inpatient diagnosis of atopic dermatitis									
	No		Yes		Crude OR (95% CI)	P value	Model 1 ^a		Model 2 ^b	
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)			Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Eczema herpeticum	1,615	0.0005 (0.0004–0.0005)	189	0.4 (0.3–0.6)	906.50 (630.33– > 1000.00)	.0002	>765.74 (513.58– > 1000.00)	.0002	688.67 (481.32–985.33)	.0002
Erysipelas	38,868	0.01 (0.01–0.01)	74	0.2 (0.1–0.2)	14.83 (9.02–24.36)	.0002	16.08 (9.19–28.14)	.0002	14.55 (8.83–23.98)	.0002
Cellulitis	12,739,908	3.7 (3.7–3.8)	6,987	15.7 (14.8–16.6)	4.85 (4.54–5.18)	.0002	4.78 (4.44–5.15)	.0002	4.86 (4.55–5.19)	.0002
Herpes simplex	1,150,862	0.3 (0.3–0.3)	646	1.4 (1.2–1.7)	4.37 (3.68–5.19)	.0002	4.48 (3.71–5.41)	.0002	4.15 (3.49–4.92)	.0002
Herpes zoster	496,105	0.1 (0.1–0.1)	178	0.4 (0.3–0.5)	2.77 (2.00–3.83)	.0002	3.42 (2.46–4.76)	.0002	2.72 (1.97–3.77)	.0002
Chicken pox	23,660	0.1 (0.01–0.01)	14	0.03 (0.00–0.07)	4.51 (1.45–13.99)	.01	3.35 (0.84–13.43)	.1	4.53 (1.46–14.07)	.01
Any skin infection	13,182,119	3.8 (3.8–3.9)	7,785	17.5 (16.5–18.4)	5.34 (5.01–5.69)	.0002	5.25 (4.88–5.65)	.0002	5.34 (5.01–5.70)	.0002
Necrotizing fasciitis	145,105	0.04 (0.04–0.04)	29	0.07 (0.01–0.1)	1.56 (0.71–3.44)	.3	1.42 (0.59–3.41)	.5	1.63 (0.73–3.61)	.3
Acute sinusitis	508,760	0.1 (0.1–0.2)	139	0.3 (0.2–0.4)	2.11 (1.48–3.02)	.0002	1.97 (1.30–3.00)	.003	1.77 (1.29–2.41)	.0007
Acute pharyngitis	510,424	0.1 (0.1–0.2)	141	0.3 (0.2–0.4)	2.13 (1.45–3.12)	.0002	2.22 (1.47–3.36)	.0003	1.90 (1.30–2.79)	.002
Acute tonsillitis	102,319	0.03 (0.03–0.03)	19	0.04 (0.00–0.08)	1.40 (0.53–3.69)	.6	0.72 (0.19–2.83)	.7	1.32 (0.50–3.51)	.6
Bronchitis	2,124,851	0.6 (0.6–0.6)	488	1.1 (0.9–1.3)	1.78 (1.45–2.18)	.0002	1.71 (1.35–2.16)	.0002	1.14 (0.93–1.41)	.2
Pneumonia	24,802,315	7.2 (7.1–7.3)	3,135	7.0 (6.5–7.6)	0.97 (0.89–1.06)	.5	1.05 (0.96–1.15)	.4	0.90 (0.82–0.97)	.002
Aspergillosis, allergic bronchopulmonary aspergillosis, aspergillosis pneumonia	143,598	0.04 (0.04–0.04)	50	0.1 (0.0–0.2)	2.67 (1.43–5.01)	.003	2.82 (1.45–5.48)	.004	2.12 (1.13–3.96)	.03
Tuberculosis	627,541	0.2 (0.2–0.2)	173	0.4 (0.3–0.5)	2.13 (1.52–2.99)	.0002	1.88 (1.30–2.72)	.001	1.96 (1.39–2.75)	.0002
Abscess of lung or mediastinum	182,289	0.05 (0.05–0.05)	24	0.05 (0.01–0.10)	1.00 (0.41–2.42)	1.0	1.16 (0.48–2.78)	.8	0.96 (0.40–2.31)	.9
Empyema	376,942	0.1 (0.1–0.1)	19	0.04 (0.00–0.08)	0.39 (0.14–1.03)	.08	0.35 (0.11–1.07)	.09	0.39 (0.15–1.05)	.08
Meningitis	552,525	0.2 (0.2–0.2)	106	0.2 (0.1–0.3)	1.48 (0.97–2.26)	.09	1.26 (0.77–2.07)	.4	1.51 (0.99–2.30)	.08
Encephalitis	231,375	0.1 (0.1–0.1)	79	0.2 (0.1–0.3)	2.67 (1.64–4.32)	.0002	2.27 (1.29–3.98)	.006	2.73 (1.67–4.46)	.0002
Endocarditis	720,169	0.2 (0.2–0.2)	186	0.4 (0.3–0.6)	1.99 (1.43–2.78)	.0002	2.08 (1.44–3.01)	.0002	2.08 (1.49–2.90)	.0002
Infectious arthropathy	598,170	0.2 (0.2–0.2)	219	0.5 (0.3–0.6)	2.82 (2.06–3.86)	.0002	2.43 (1.72–3.44)	.0002	2.87 (2.10–3.92)	.0002
Infection of bone	2,268,798	0.7 (0.6–0.7)	439	1.0 (0.8–1.2)	1.50 (1.21–1.86)	.0003	1.49 (1.19–1.86)	.001	1.60 (1.30–1.98)	.0002
Enterocolitis	4,791,358	1.4 (1.4–1.4)	627	1.4 (1.2–1.7)	1.00 (0.83–1.20)	1.0	1.14 (0.94–1.38)	.2	1.03 (0.86–1.24)	.8
Clostridium difficile	3,120,319	0.9 (0.9–0.9)	373	0.8 (0.6–1.0)	0.92 (0.72–1.17)	.6	1.05 (0.81–1.35)	.8	0.96 (0.75–1.23)	.8
Diverticulitis	3,322,498	1.0 (1.0–1.0)	316	0.7 (0.5–0.9)	0.73 (0.57–0.94)	.01	0.73 (0.56–0.97)	.04	0.73 (0.57–0.93)	.01
Peritonitis and intestinal abscess	1,860,580	0.5 (0.5–0.6)	125	0.3 (0.2–0.4)	0.52 (0.35–0.77)	.002	0.56 (0.37–0.85)	.009	0.54 (0.37–0.81)	.003
Urinary tract infection	30,702,434	8.9 (8.9–9.0)	3,745	8.4 (7.7–9.1)	0.94 (0.86–1.02)	.2	1.01 (0.92–1.12)	.8	0.98 (0.89–1.07)	.7
Pyelonephritis	2,449,121	0.7 (0.7–0.7)	249	0.6 (0.4–0.7)	0.78 (0.60–1.02)	.09	0.81 (0.61–1.09)	.2	0.80 (0.61–1.04)	.1
MSSA	4,485,542	1.3 (1.3–1.3)	2,543	5.7 (5.1–6.3)	4.57 (4.12–5.07)	.0002	4.37 (3.89–4.91)	.0002	4.68 (4.22–5.18)	.0002
MRSA	2,616,901	0.8 (0.7–0.8)	1,584	3.6 (3.1–4.0)	4.80 (4.23–5.44)	.0002	4.68 (4.10–5.33)	.0002	4.53 (3.99–5.14)	.0002
Streptococcal infection	3,659,167	1.1 (1.0–1.1)	771	1.7 (1.5–2.0)	1.65 (1.40–1.94)	.0002	1.58 (1.32–1.89)	.0002	1.66 (1.41–1.95)	.0002
Pseudomonas infection	1,982,954	0.6 (0.6–0.6)	415	0.9 (0.7–1.1)	1.63 (1.31–2.03)	.0002	1.79 (1.41–2.27)	.0002	1.65 (1.32–2.06)	.0002
Mycobacterial infection	171,120	0.05 (0.05–0.05)	52	0.1 (0.0–0.2)	2.37 (1.29–4.36)	.008	2.10 (1.07–4.11)	.04	2.26 (1.22–4.16)	.01
Fungal infection	5,869,433	1.7 (1.7–1.7)	2,721	6.1 (4.9–7.3)	3.75 (3.07–4.59)	.0002	3.67 (3.04–4.43)	.0002	3.54 (2.89–4.34)	.0002
Viral infection	3,322,371	1.0 (1.0–1.0)	1,220	2.7 (2.4–3.1)	2.88 (2.53–3.28)	.0002	2.90 (2.51–3.34)	.0002	2.74 (2.40–3.11)	.0002
Influenza	500,616	0.1 (0.1–0.2)	122	0.3 (0.2–0.4)	1.88 (1.28–2.75)	.002	2.31 (1.57–3.41)	.0002	1.49 (1.01–2.18)	.05
Septicemia	13,836,256	4.0 (4.0–4.1)	2,507	5.6 (5.1–6.2)	1.42 (1.29–1.57)	.0002	1.50 (1.35–1.68)	.0002	1.50 (1.36–1.66)	.0002
Any serious infection	87,323,612	25.4 (25.2–25.6)	19,342	43.4 (42.0–44.7)	2.25 (2.12–2.38)	.0002	2.43 (2.28–2.58)	.0002	2.18 (2.06–2.31)	.0002

Abbreviations: CI, confidence interval; OR, odds ratio; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; Wtd, weighted.

^aIncludes age, sex, race/ethnicity, and insurance status.

^bIncludes asthma and hay fever.

eTable 5

Logistic Regression Models of Associations Between Asthma and/or Hay Fever, AD, and Serious Infections in Adults

Variable	No AD		AD without asthma and hay fever				AD with asthma and hay fever			
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value
Eczema herpeticum	1,615	0.0005 (0.0004–0.0005)	67	0.2 (0.1–0.3)	418.35 (246.01–711.40)	.0002	122	1.2 (0.6–1.7)	>1000.00 (>1000.00– > 1000.00)	.0002
Erysipelas	38,868	0.01 (0.01–0.01)	46	0.1 (0.0–0.2)	11.92 (6.24–22.76)	.0002	29	0.3 (0.1–0.5)	23.90 (10.71–53.37)	.0002
Cellulitis	12,739,908	3.7 (3.7–3.8)	5,552	16.3 (15.3–17.3)	5.10 (4.74–5.48)	.0002	1,435	13.6 (12.0–15.2)	4.09 (3.57–4.68)	.0002
Herpes simplex	1,150,862	0.3 (0.3–0.3)	390	1.1 (0.9–1.4)	3.45 (2.78–4.28)	.0002	255	2.4 (1.8–3.1)	7.38 (5.61–9.70)	.0002
Herpes zoster	496,105	0.1 (0.1–0.1)	145	0.4 (0.3–0.6)	2.97 (2.09–4.21)	.0002	33	0.3 (0.1–0.5)	2.13 (1.02–4.48)	.06
Chicken pox	23,660	0.007 (0.007–0.007)	<10	0.03 (0.00–0.06)	3.77 (0.94–15.05)	.08	<10	0.05 (0.00–0.14)	6.88 (0.97–48.85)	.07
Any skin infection	13,182,119	3.8 (3.8–3.9)	6,086	17.9 (16.8–18.9)	5.50 (5.13–5.90)	.0002	1,699	16.1 (14.3–17.9)	4.83 (4.24–5.50)	.0002
Necrotizing fasciitis	145,105	0.04 (0.04–0.04)	20	0.06 (0.00–0.12)	1.38 (0.52–3.68)	.6	<10	0.1 (0.0–0.2)	2.10 (0.53–8.39)	.4
Acute sinusitis	508,760	0.1 (0.1–0.2)	84	0.2 (0.1–0.4)	1.67 (1.05–2.66)	.04	55	0.5 (0.2–0.8)	3.55 (2.02–6.26)	.0002
Acute pharyngitis	510,424	0.1 (0.1–0.2)	88	0.3 (0.1–0.4)	1.73 (1.09–2.76)	.03	53	0.5 (0.2–0.8)	3.40 (1.87–6.18)	.0002
Acute tonsillitis	102,319	0.03 (0.03–0.03)	19	0.05 (0.00–0.11)	1.83 (0.69–4.84)	.3	0	—	0.002 (0.002–0.003)	.0002
Bronchitis	2,124,851	0.6 (0.6–0.6)	205	0.6 (0.4–0.8)	0.97 (0.71–1.33)	.9	283	2.7 (2.0–3.4)	4.42 (3.35–5.83)	.0002
Pneumonia	24,802,315	7.2 (7.1–7.3)	2,260	6.6 (6.0–7.3)	0.92 (0.83–1.01)	.1	876	8.3 (7.2–9.4)	1.17 (1.01–1.36)	.05
Aspergillosis, allergic bronchopulmonary aspergillosis, aspergillosis pneumonia	143,598	0.04 (0.04–0.04)	10	0.03 (0.00–0.07)	0.71 (0.18–2.86)	.7	40	0.4 (0.1–0.6)	9.02 (4.47–18.20)	.0002
Tuberculosis	627,541	0.2 (0.2–0.2)	140	0.4 (0.3–0.6)	2.26 (1.56–3.27)	.0002	33	0.3 (0.1–0.6)	1.72 (0.75–3.95)	.2
Abscess of lung or mediastinum	182,289	0.05 (0.05–0.05)	14	0.04 (0.00–0.09)	0.79 (0.26–2.47)	.7	<10	0.1 (0.0–0.2)	1.70 (0.43–6.73)	.5
Empyema	376,942	0.1 (0.1–0.1)	<10	0.03 (0.0–0.7)	0.25 (0.06–0.99)	.07	10	0.1 (0.0–0.2)	0.83 (0.20–3.35)	.8
Meningitis	552,525	0.2 (0.2–0.2)	86	0.3 (0.1–0.4)	1.59 (1.02–2.49)	.06	19	0.2 (0.0–0.4)	1.14 (0.44–3.00)	.8
Encephalitis	231,375	0.07 (0.07–0.07)	69	0.2 (0.1–0.3)	3.03 (1.79–5.11)	.0002	10	0.1 (0.0–0.2)	1.35 (0.34–5.41)	.7
Endocarditis	720,169	0.2 (0.2–0.2)	128	0.4 (0.2–0.5)	1.80 (1.21–2.67)	.006	58	0.5 (0.2–0.9)	2.65 (1.51–4.64)	.001
Infectious arthropathy	598,170	0.2 (0.2–0.2)	166	0.5 (0.3–0.7)	2.81 (1.99–3.96)	.0002	53	0.5 (0.2–0.8)	2.87 (1.51–5.44)	.002
Infection of bone	2,268,798	0.7 (0.6–0.7)	352	1.0 (0.8–1.3)	1.58 (1.25–1.99)	.0002	87	0.8 (0.4–1.2)	1.25 (0.79–1.99)	.4
Enterocolitis	4,791,358	1.4 (1.4–1.4)	512	1.5 (1.2–1.8)	1.08 (0.88–1.33)	.5	115	1.1 (0.6–1.5)	0.80 (0.53–1.20)	.3
<i>Clostridium difficile</i>	3,120,319	0.9 (0.9–0.9)	316	0.9 (0.7–1.2)	1.02 (0.78–1.33)	.9	57	0.5 (0.2–0.9)	0.59 (0.33–1.09)	.1
Diverticulitis	3,322,498	1.0 (1.0–1.0)	273	0.8 (0.6–1.0)	0.83 (0.63–1.09)	.2	42	0.4 (0.1–0.7)	0.43 (0.23–0.81)	.01
Peritonitis and intestinal abscess	1,860,580	0.5 (0.5–0.6)	125	0.4 (0.2–0.5)	0.68 (0.46–1.00)	.07	0	—	<0.001 (<0.001– < 0.001)	.0002
Urinary tract infection	30,702,434	8.9 (8.9–9.0)	3,253	9.6 (8.7–10.4)	1.08 (0.98–1.18)	.2	492	4.7 (3.7–5.6)	0.50 (0.41–0.62)	.0002
Pyelonephritis	2,449,121	0.7 (0.7–0.7)	191	0.6 (0.4–0.7)	0.79 (0.58–1.07)	.2	58	0.6 (0.2–0.9)	0.78 (0.44–1.36)	.4
MSSA	4,485,542	1.3 (1.3–1.3)	1,856	5.5 (4.9–6.0)	4.36 (3.89–4.88)	.0002	687	6.5 (5.3–7.7)	5.27 (4.35–6.37)	.0002
MRSA	2,616,901	0.8 (0.7–0.8)	1,136	3.3 (2.9–3.8)	4.50 (3.91–5.18)	.0002	448	4.2 (3.3–5.1)	5.77 (4.63–7.19)	.0002
Streptococcal infection	3,659,167	1.1 (1.0–1.1)	601	1.8 (1.4–2.1)	1.69 (1.41–2.02)	.0002	170	1.6 (1.1–2.1)	1.53 (1.10–2.13)	.02
Pseudomonas infection	1,982,954	0.6 (0.6–0.6)	331	1.0 (0.7–1.2)	1.71 (1.34–2.18)	.0002	84	0.8 (0.4–1.2)	1.39 (0.85–2.26)	.2
Mycobacterial infection	171,120	0.05 (0.05–0.05)	52	0.2 (0.1–0.3)	3.09 (1.68–5.69)	.0005	0	—	0.003 (0.002–0.003)	.0002
Fungal infection	5,869,433	1.7 (1.7–1.7)	2,147	6.3 (4.9–7.7)	3.89 (3.06–4.96)	.0002	574	5.4 (4.4–6.4)	3.31 (2.72–4.03)	.0002
Viral infection	3,322,371	1.0 (1.0–1.0)	850	2.5 (2.1–2.9)	2.62 (2.23–3.08)	.0002	370	3.5 (2.7–4.3)	3.72 (2.98–4.65)	.0002
Influenza	500,616	0.1 (0.1–0.2)	83	0.2 (0.1–0.4)	1.67 (1.05–2.65)	.04	39	0.4 (0.1–0.6)	2.57 (1.30–5.10)	.01
Septicemia	13,836,256	4.0 (4.0–4.1)	1,941	5.7 (5.1–6.3)	1.44 (1.28–1.62)	.0002	565	5.4 (4.4–6.3)	1.35 (1.11–1.64)	.004
Any serious infection	87,323,612	25.4 (25.2–25.6)	14,934	43.9 (42.3–45.4)	2.29 (2.15–2.44)	.0002	4,408	41.7 (39.4–44.07)	2.10 (1.91–2.31)	.0002

Abbreviations: AD, atopic dermatitis; CI, confidence interval; OR, odds ratio; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; Wtd, weighted.

eTable 6

Comparison of Associations of Serious Infections Between Atopic Dermatitis or Eczema and Psoriasis

Variable	Psoriasis		Atopic dermatitis or eczema							
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value	Model 1 ^a		Model 2 ^b	
							Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Eczema herpeticum	40	0.004 (0.001–0.006)	252	0.03 (0.03–0.04)	8.76 (4.11–18.70)	.0002	4.29 (1.93–9.54)	.0007	7.46 (3.53–15.77)	.0002
Erysipelas	645	0.06 (0.05–0.07)	940	0.1 (0.1–0.1)	2.01 (1.60–2.52)	.0002	2.36 (1.81–3.08)	.0002	2.00 (1.60–2.51)	.0002
Cellulitis	99,994	9.4 (9.2–9.6)	115,869	15.0 (14.7–15.3)	1.70 (1.66–1.75)	.0002	1.73 (1.69–1.78)	.0002	1.72 (1.67–1.76)	.0002
Herpes simplex	4,353	0.4 (0.4–0.4)	6,190	0.8 (0.7–0.9)	1.97 (1.80–2.15)	.0002	1.58 (1.42–1.75)	.0002	1.93 (1.77–2.12)	.0002
Herpes zoster	2,687	0.3 (0.2–0.3)	2,950	0.4 (0.3–0.4)	1.52 (1.35–1.71)	.0002	1.43 (1.25–1.63)	.0002	1.52 (1.35–1.71)	.0002
Chicken pox	139	0.01 (0.01–0.02)	169	0.02 (0.01–0.03)	1.68 (1.02–2.76)	.05	1.31 (0.73–2.36)	.5	1.71 (1.04–2.81)	.05
Any skin infection	103,658	9.7 (9.5–9.9)	121,563	15.7 (15.4–16.0)	1.73 (1.69–1.77)	.0002	1.76 (1.71–1.81)	.0002	1.75 (1.70–1.79)	.0002
Necrotizing fasciitis	731	0.07 (0.06–0.08)	494	0.06 (0.05–0.08)	0.93 (0.72–1.21)	.7	0.96 (0.71–1.29)	.8	0.95 (0.73–1.23)	.7
Acute sinusitis	2,105	0.2 (0.2–0.2)	1,750	0.2 (0.2–0.2)	1.15 (0.99–1.32)	.08	1.14 (0.97–1.34)	.1	1.10 (0.95–1.27)	.2
Acute pharyngitis	2,098	0.2 (0.2–0.2)	2,419	0.3 (0.3–0.3)	1.59 (1.39–1.82)	.0002	1.41 (1.22–1.64)	.0002	1.58 (1.38–1.80)	.0002
Acute tonsillitis	258	0.02 (0.02–0.03)	225	0.03 (0.03–0.04)	1.20 (0.80–1.80)	.5	0.89 (0.53–1.50)	.7	1.19 (0.79–1.79)	.5
Bronchitis	7,173	0.7 (0.6–0.7)	6,594	0.9 (0.8–0.9)	1.27 (1.17–1.37)	.0002	1.22 (1.12–1.33)	.0002	1.17 (1.08–1.26)	.0002
Pneumonia	79,601	7.5 (7.3–7.6)	59,179	7.6 (7.5–7.8)	1.03 (1.00–1.06)	.1	1.05 (1.02–1.09)	.003	1.02 (0.99–1.04)	.4
Aspergillosis, allergic bronchopulmonary aspergillosis, aspergillosis pneumonia	547	0.05 (0.04–0.0)	514	0.07 (0.05–0.08)	1.29 (0.97–1.72)	.1	1.20 (0.88–1.65)	.3	1.20 (0.90–1.59)	.2
Tuberculosis	2,623	0.2 (0.2–0.3)	2,168	0.3 (0.2–0.3)	1.14 (0.99–1.30)	.08	1.02 (0.89–1.18)	.8	1.13 (0.99–1.30)	.09
Abscess of lung or mediastinum	691	0.06 (0.05–0.08)	453	0.06 (0.05–0.07)	0.90 (0.68–1.19)	.6	1.02 (0.75–1.38)	.9	0.88 (0.67–1.17)	.5
Empyema	1,223	0.1 (0.1–0.1)	865	0.1 (0.1–0.1)	0.97 (0.80–1.19)	.8	1.11 (0.90–1.38)	.4	0.97 (0.79–1.18)	.7
Meningitis	2,240	0.2 (0.2–0.2)	1,792	0.2 (0.2–0.3)	1.10 (0.95–1.28)	.2	0.95 (0.80–1.12)	.6	1.10 (0.95–1.28)	.2
Encephalitis	963	0.1 (0.1–0.1)	860	0.1 (0.1–0.1)	1.23 (1.00–1.52)	.07	1.12 (0.89–1.41)	.4	1.25 (1.01–1.54)	.05
Endocarditis	2,413	0.2 (0.2–0.2)	2,025	0.3 (0.2–0.3)	1.16 (1.01–1.32)	.04	1.14 (0.99–1.32)	.1	1.18 (1.03–1.35)	.03
Infectious arthropathy	4,980	0.5 (0.4–0.5)	2,901	0.4 (0.3–0.4)	0.80 (0.72–0.89)	.0002	0.79 (0.70–0.89)	.0003	0.80 (0.72–0.90)	.0002
Infection of bone	9,878	0.9 (0.9–1.0)	7,083	0.9 (0.9–1.0)	0.99 (0.92–1.06)	.7	1.02 (0.94–1.11)	.7	1.00 (0.93–1.08)	.9
Enterocolitis	17,246	1.6 (1.6–1.7)	13,723	1.8 (1.7–1.9)	1.10 (1.04–1.16)	.001	1.14 (1.08–1.21)	.0002	1.11 (1.05–1.17)	.0003
<i>Clostridium difficile</i>	10,520	1.0 (0.9–1.0)	9,861	1.3 (1.2–1.3)	1.30 (1.21–1.39)	.0002	1.32 (1.23–1.42)	.0002	1.32 (1.23–1.41)	.0002
Diverticulitis	13,282	1.2 (1.2–1.3)	6,400	0.8 (0.8–0.9)	0.66 (0.62–0.71)	.0002	0.69 (0.64–0.75)	.0002	0.66 (0.62–0.71)	.0002
Peritonitis and intestinal abscess	6,570	0.6 (0.6–0.7)	3,189	0.4 (0.4–0.4)	0.67 (0.61–0.74)	.0002	0.68 (0.61–0.76)	.0002	0.67 (0.61–0.75)	.0002
Urinary tract infection	88,137	8.3 (8.1–8.4)	82,246	10.6 (10.4–10.9)	1.32 (1.29–1.35)	.0002	1.27 (1.23–1.30)	.0002	1.34 (1.31–1.38)	.0002
Pyelonephritis	6,664	0.6 (0.6–0.7)	4,389	0.6 (0.5–0.6)	0.91 (0.83–0.99)	.04	0.82 (0.74–0.90)	.0002	0.91 (0.83–0.99)	.04
MSSA	25,075	2.4 (2.3–2.4)	25,226	3.3 (3.1–3.4)	1.40 (1.34–1.46)	.0002	1.37 (1.30–1.44)	.0002	1.40 (1.34–1.47)	.0002
MRSA	19,712	1.8 (1.8–1.9)	19,482	2.5 (2.4–2.6)	1.37 (1.30–1.44)	.0002	1.40 (1.33–1.48)	.0002	1.36 (1.29–1.43)	.0002
Streptococcal infection	15,518	1.5 (1.4–1.5)	13,873	1.8 (1.7–1.9)	1.24 (1.17–1.31)	.0002	1.27 (1.19–1.34)	.0002	1.25 (1.18–1.32)	.0002
Pseudomonas infection	6,518	0.6 (0.6–0.6)	7,813	1.0 (1.0–1.1)	1.66 (1.54–1.79)	.0002	1.69 (1.56–1.83)	.0002	1.68 (1.56–1.81)	.0002
Mycobacterial infection	628	0.06 (0.05–0.07)	751	0.1 (0.1–0.1)	1.65 (1.29–2.11)	.0002	1.37 (1.04–1.81)	.03	1.67 (1.30–2.14)	.0002
Fungal infection	36,299	3.4 (3.3–3.5)	49,095	6.3 (6.1–6.6)	1.92 (1.84–2.01)	.0002	1.90 (1.81–1.99)	.0002	1.93 (1.85–2.02)	.0002
Viral infection	13,794	1.3 (1.2–1.3)	15,514	2.0 (1.9–2.1)	1.56 (1.48–1.65)	.0002	1.42 (1.34–1.50)	.0002	1.55 (1.47–1.63)	.0002
Influenza	1,866	0.2 (0.2–0.2)	1,362	0.2 (0.2–0.2)	1.01 (0.86–1.18)	1.0	1.01 (0.84–1.20)	.9	0.95 (0.81–1.12)	.7
Septicemia	48,031	4.5 (4.4–4.6)	39,026	5.0 (4.9–5.2)	1.13 (1.08–1.17)	.0002	1.12 (1.08–1.17)	.0002	1.14 (1.10–1.18)	.0002
Any serious infection	353,092	33.1 (32.8–33.5)	325,164	42.0 (41.5–42.5)	1.46 (1.44–1.49)	.0002	1.48 (1.45–1.51)	.0002	1.47 (1.44–1.50)	.0002

Abbreviations: CI, confidence interval; OR, odds ratio; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; Wtd, weighted.^aIncludes age, sex, race/ethnicity, and insurance status.^bIncludes asthma and hay fever.

eTable 7
Comparison of Associations of Serious Infections Between Atopic Dermatitis and Psoriasis

Variable	Psoriasis		Atopic dermatitis		Crude OR (95% CI)	P value	Model 1 ^a		Model 2 ^b	
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)			Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Eczema herpeticum	44	0.004 (0.001–0.007)	189	0.4 (0.3–0.6)	106.46 (50.63–223.87)	.0002	47.64 (21.08–107.66)	.0002	74.25 (35.73–154.27)	.0002
Erysipelas	660	0.06 (0.05–0.07)	69	0.2 (0.1–0.2)	2.61 (1.51–4.51)	.001	2.85 (1.54–5.29)	.002	2.64 (1.53–4.55)	.0008
Cellulitis	103,439	9.6 (9.4–9.8)	6,706	15.4 (14.5–16.3)	1.72 (1.61–1.84)	.0002	1.66 (1.54–1.79)	.0002	1.73 (1.62–1.86)	.0002
Herpes simplex	4,439	0.4 (0.4–0.4)	636	1.5 (1.2–1.7)	3.59 (3.00–4.30)	.0002	2.50 (2.02–3.09)	.0002	3.41 (2.85–4.09)	.0002
Herpes zoster	2,725	0.3 (0.2–0.3)	178	0.4 (0.3–0.5)	1.62 (1.16–2.27)	.008	1.85 (1.31–2.61)	.0008	1.64 (1.17–2.30)	.006
Chicken pox	143	0.01 (0.01–0.02)	14	0.03 (0.00–0.07)	2.39 (0.75–7.60)	.2	1.29 (0.34–4.89)	.7	2.43 (0.78–7.61)	.2
Any skin infection	107,256	9.9 (9.7–10.1)	7,486	17.2 (16.2–18.1)	1.88 (1.76–2.01)	.0002	1.80 (1.67–1.93)	.0002	1.90 (1.78–2.03)	.0002
Necrotizing fasciitis	749	0.1 (0.1–0.1)	29	0.1 (0.0–0.1)	0.97 (0.43–2.19)	.9	0.76 (0.31–1.89)	.7	0.99 (0.44–2.23)	1.0
Acute sinusitis	2,119	0.2 (0.2–0.2)	139	0.3 (0.2–0.4)	1.63 (1.13–2.36)	.002	1.49 (0.96–2.32)	.1	1.46 (1.01–2.12)	.06
Acute pharyngitis	2,117	0.2 (0.2–0.2)	141	0.3 (0.2–0.4)	1.65 (1.12–2.43)	.01	1.42 (0.92–2.20)	.1	1.65 (1.12–2.43)	.01
Acute tonsillitis	258	0.02 (0.02–0.03)	19	0.04 (0.00–0.08)	1.78 (0.64–4.91)	.4	0.54 (0.14–2.15)	.5	1.77 (0.62–5.06)	.4
Bronchitis	7,284	0.7 (0.6–0.7)	483	1.1 (0.9–1.3)	1.65 (1.34–2.04)	.0002	1.54 (1.21–1.98)	.001	1.25 (1.01–1.55)	.05
Pneumonia	80,521	7.5 (7.3–7.6)	3,069	7.0 (6.5–7.6)	0.94 (0.86–1.02)	.2	1.03 (0.94–1.13)	.7	0.90 (0.82–0.98)	.01
Aspergillosis, allergic bronchopulmonary aspergillosis, aspergillosis pneumonia	552	0.05 (0.04–0.06)	50	0.1 (0.0–0.2)	2.24 (1.15–4.35)	.03	2.26 (1.07–4.77)	.04	1.80 (0.94–3.46)	.1
Tuberculosis	2,666	0.2 (0.2–0.3)	168	0.4 (0.2–0.5)	1.56 (1.09–2.23)	.01	1.19 (0.80–1.77)	.5	1.53 (1.07–2.21)	.03
Abscess of lung or mediastinum	701	0.06 (0.05–0.08)	24	0.05 (0.01–0.10)	0.84 (0.34–2.01)	.7	0.99 (0.40–2.43)	1.0	0.75 (0.31–1.85)	.6
Empyema	1,223	0.1 (0.1–0.1)	19	0.04 (0.00–0.09)	0.38 (0.14–1.04)	.08	0.41 (0.13–1.31)	.2	0.37 (0.14–1.01)	.07
Meningitis	2,288	0.2 (0.2–0.2)	106	0.2 (0.1–0.3)	1.15 (0.74–1.77)	.6	0.72 (0.66–1.21)	.2	1.11 (0.72–1.72)	.7
Encephalitis	968	0.1 (0.1–0.1)	74	0.2 (0.1–0.3)	1.89 (1.11–3.23)	.03	1.43 (0.77–2.65)	.4	1.98 (1.15–3.38)	.01
Endocarditis	2,446	0.2 (0.2–0.2)	181	0.4 (0.3–0.6)	1.84 (1.30–2.59)	.001	1.75 (1.20–2.56)	.006	1.91 (1.35–2.68)	.0003
Infectious arthropathy	5,047	0.5 (0.4–0.5)	214	0.5 (0.3–0.6)	1.05 (0.77–1.44)	.8	0.93 (0.64–1.34)	.7		
Infection of bone	10,076	0.9 (0.9–1.0)	419	1.0 (0.8–1.2)	1.03 (0.83–1.29)	.8	1.10 (0.86–1.39)	.5	1.10 (0.88–1.37)	.5
Enterocolitis	17,423	1.6 (1.5–1.7)	613	1.4 (1.1–1.7)	0.87 (0.72–1.05)	.1	0.98 (0.80–1.19)	.8	0.89 (0.74–1.08)	.2
<i>Clostridium difficile</i>	10,644	1.0 (0.9–1.0)	363	0.8 (0.6–1.0)	0.84 (0.66–1.08)	.2	0.96 (0.74–1.25)	.8	0.88 (0.69–1.14)	.4
Diverticulitis	13,372	1.2 (1.2–1.3)	306	0.7 (0.5–0.9)	0.57 (0.44–0.73)	.0002	0.57 (0.43–0.76)	.0002	0.56 (0.44–0.72)	.0002
Peritonitis and intestinal abscess	6,628	0.6 (0.6–0.7)	125	0.3 (0.2–0.4)	0.47 (0.31–0.69)	.0003	0.49 (0.32–0.74)	.002	0.48 (0.32–0.72)	.0007
Urinary tract infection	89,309	8.3 (8.1–8.4)	3,677	8.4 (7.7–9.1)	1.02 (0.93–1.12)	.7	1.03 (0.94–1.13)	.6	1.06 (0.97–1.16)	.2
Pyelonephritis	6,750	0.6 (0.6–0.7)	245	0.6 (0.4–0.7)	0.90 (0.68–1.19)	.5	0.77 (0.56–1.04)	.1	0.92 (0.69–1.21)	.6
MSSA	25,736	2.4 (2.3–2.5)	2,475	5.7 (5.1–6.2)	2.47 (2.22–2.74)	.0002	2.16 (1.92–2.44)	.0002	2.49 (2.24–2.77)	.0002
MRSA	20,339	1.9 (1.8–2.0)	1,525	3.5 (3.0–3.9)	1.89 (1.66–2.15)	.0002	1.86 (1.63–2.13)	.0002	1.85 (1.62–2.12)	.0002
Streptococcal infection	15,744	1.5 (1.4–1.5)	754	1.7 (1.5–2.0)	1.19 (1.01–1.41)	.05	1.13 (0.94–1.37)	.2	1.20 (1.02–1.42)	.04
Pseudomonas infection	6,692	0.6 (0.6–0.7)	403	0.9 (0.7–1.1)	1.50 (1.19–1.89)	.001	1.66 (1.30–2.12)	.0002	1.51 (1.20–1.90)	.0008
Mycobacterial infection	641	0.06 (0.05–0.07)	52	0.1 (0.0–0.2)	2.03 (1.07–3.87)	.04	1.40 (0.67–2.90)	.5	2.08 (1.07–4.03)	.04
Fungal infection	37,416	3.5 (3.4–3.6)	2,637	6.0 (4.9–7.2)	1.80 (1.46–2.20)	.0002	1.65 (1.36–2.01)	.0002	1.78 (1.44–2.19)	.0002
Viral infection	14,002	1.3 (1.2–1.4)	1,205	2.8 (2.4–3.1)	2.17 (1.89–2.48)	.0002	1.87 (1.61–2.18)	.0002	2.11 (1.84–2.43)	.0002
Influenza	1,884	0.2 (0.2–0.2)	122	0.3 (0.2–0.4)	1.60 (1.08–2.38)	.03	1.90 (1.27–2.86)	.003	1.35 (0.90–2.03)	.1
Septicemia	48,790	4.5 (4.4–4.6)	2,441	5.6 (5.1–6.1)	1.25 (1.14–1.39)	.0002	1.24 (1.11–1.38)	.0002	1.30 (1.17–1.43)	.0002
Any serious infection	359,905	33.3 (32.9–33.7)	18,787	43.1 (41.7–44.5)	1.52 (1.43–1.61)	.0002	1.51 (1.42–1.60)	.0002	1.51 (1.42–1.60)	.0002

Abbreviations: CI, confidence interval; OR, odds ratio; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*; Wtd, weighted.

^aIncludes age, sex, race/ethnicity, and insurance status.

^bIncludes asthma and hay fever.

eTable 8

Logistic Regression Models of Associations Among Eczema Herpeticum, Atopic Dermatitis or Eczema, and Serious Infections in Adults

Serious infection	No AD-E or eczema herpeticum		AD-E without eczema herpeticum				AD-E with eczema herpeticum			
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value
Cellulitis	12,627,022	3.7 (3.6–3.7)	119,512	15.1 (14.8–15.5)	1.79 (1.52–2.11)	.0002	257	32.3 (19.3–45.2)	3.56 (2.65–4.78)	.0002
Erysipelas	37,983	0.01 (0.01–0.01)	950	0.1 (0.1–0.1)	21.38 (14.90–30.69)	.0002	<10	3.5 (0.0–8.3)	18.1 (8.85–36.9)	.0002
Acute sinusitis	507,135	0.1 (0.1–0.2)	1,758	0.2 (0.2–0.2)	6.63 (4.03–10.90)	.0002	<10	2.0 (0.0–5.9)	3.71 (1.38–9.98)	.01
Pyelonephritis	2,444,891	0.7 (0.7–0.7)	4,475	0.6 (0.5–0.6)	4.15 (2.52–6.83)	.0002	<10	1.8 (0.0–5.2)	1.58 (0.59–4.26)	.5
Fungal infection	5,821,740	1.7 (1.7–1.7)	50,287	6.4 (6.1–6.6)	1.16 (0.80–1.69)	.5	10	3.7 (0.0–8.8)	1.49 (0.73–3.04)	.4
Serious infection	No AD or eczema herpeticum		AD without eczema herpeticum				AD with eczema herpeticum			
	Wtd frequency	% Prevalence (95% CI)	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value	Wtd frequency	% Prevalence (95% CI)	Crude OR (95% CI)	P value
Any skin infection	13,181,715	3.8 (3.8–3.9)	7,699	17.3 (16.4–18.3)	1.92 (1.62–2.26)	.0002	87	45.8 (30.6–61.1)	4.64 (3.41–6.31)	.0002
Cellulitis	12,739,601	3.7 (3.7–3.8)	6,933	15.6 (14.7–16.5)	1.70 (1.41–2.06)	.0002	54	28.3 (13.7–43.0)	3.26 (2.29–4.65)	.0002

Abbreviations: AD, atopic dermatitis; AD-E, atopic dermatitis or eczema; CI, confidence interval; OR, odds ratio; Wtd, weighted.

eTable 9

Associations of Serious Infections in Adults With Atopic Dermatitis

Variable	Adjusted OR (95% CI)	P value
Age (y)		
18–39	1.00 (ref)	—
40–59	1.12 (1.05–1.19)	.008
60–79	1.10 (1.02–1.20)	.05
≥ 80	1.56 (1.42–1.72)	.0002
Sex		
Female	0.93 (0.89–0.97)	.01
Male	1.00 (ref)	—
Race		
White	1.00 (ref)	—
Black	0.86 (0.81–0.92)	.0002
Hispanic	0.86 (0.78–0.94)	.008
Asian	0.78 (0.70–0.87)	.0002
Other	1.02 (0.91–1.15)	.8
Income quartile		
1	1.03 (0.96–1.11)	.5
2	1.16 (1.09–1.25)	.0005
3	1.19 (1.12–1.27)	.0002
4	1.00 (ref)	—
Insurance		
Medicare	1.31 (1.23–1.40)	.0002
Medicaid	1.37 (1.27–1.48)	.0002
Private	1.00 (ref)	—
Self-pay	1.40 (1.26–1.54)	.0002
No charge	1.14 (0.86–1.51)	.5
Other	1.39 (1.22–1.57)	.0002
Chronic conditions (n) ^a		
0–1	1.00 (ref)	—
2–5	0.95 (0.85–1.07)	.5
≥ 6	0.83 (0.73–0.94)	.01
Region		
Northeast	1.14 (1.07–1.21)	.002
Midwest	0.98 (0.91–1.05)	.7
South	1.31 (1.22–1.40)	.0002
West	1.00 (ref)	—
Hospital location		
Metropolitan (>1 million)	1.00 (ref)	—
Fringe/metropolitan (<1 million)	0.93 (0.88–0.98)	.03
Micropolitan ^b	1.05 (0.96–1.15)	.5
Not metro- or micropolitan	1.09 (0.97–1.22)	.3
Hospital bed size		
Small	1.00 (ref)	—
Medium	1.09 (1.01–1.17)	.1
Large	1.23 (1.14–1.32)	.0002
Hospital teaching status		
Nonteaching	1.00 (ref)	—
Teaching	0.92 (0.88–0.97)	.009
Comorbidity		
Diabetes mellitus	1.11 (1.03–1.19)	.03
Obesity	1.12 (1.05–1.21)	.01
Asthma	1.07 (1.02–1.13)	.05

Abbreviations: CI, confidence interval; OR, odds ratio; ref, reference.

^aChronic conditions were defined by Healthcare Cost and Utilization Project (HCUP) as lasting 12 months or longer and meeting one or both of the following: (1) places limitations on self-care, independent living, and social interactions and/or (2) results in the need for ongoing intervention with medical products, services, and special equipment. Chronic condition count was calculated and provided by HCUP.^bGreater than or equal to 1 urban cluster with a population of 10,000 to 49,999.

eTable 10

Costs of Care, Length of Stay, and Inpatient Mortality of Individual Infections in Adults With Atopic Dermatitis or Eczema

Serious infection	Geometric mean cost (\$) in patients with AD-E (95% CI)	Excess annual cost (\$) secondary to AD-E	Excess annual cost (\$) secondary to AD	Geometric mean LOS (d) in patients with AD-E (95% CI)	Excess annual LOS (d) secondary to AD-E	Excess annual LOS (d) secondary to AD	Inpatient mortality in patients with AD-E (95% CI)
Eczema herpeticum	6,349 (5,093–7,915)	3,158.9	193.12	4.7 (3.8–5.7)	2.36	0.13	0 (–)
Erysipelas	4,977 (4,560–5,431)	41,763.2	3,247.33	3.8 (3.6–4.1)	32.15	1.95	0 (–)
Cellulitis	6,366 (6,253–6,481)	23,787,311.9	1,181,725.17	4.5 (4.5–4.6)	16,322.40	832.00	0.6 (0.5–0.7)
Herpes simplex	8,935 (8,419–9,484)	3,221,247.5	119,553.08	5.2 (5.0–5.5)	1,870.99	72.58	0.7 (0.2–1.1)
Herpes zoster	8,433 (7,827–9,085)	1,211,751.1	5,773.25	5.1 (4.8–5.5)	760.25	3.57	1.6 (0.6–2.5)
Chicken pox	10,365 (7,176–14,973)	161,727.3	—	6.0 (4.3–8.5)	79.45	—	0 (–)
Any skin infection	6,380 (6,268–6,494)	24,914,278.7	1,203,653.59	4.5 (4.5–4.6)	17,059.79	846.05	0.6 (0.5–0.7)
Necrotizing fasciitis	21,925 (18,695–25,712)	968,947.6	62,157.82	10.3 (9.0–11.7)	444.18	19.32	2.7 (0.0–5.7)
Acute sinusitis	8,173 (7,395–9,033)	1,490,410.9	43,527.42	4.8 (4.4–5.2)	825.93	29.00	0.3 (0.0–0.8)
Acute pharyngitis	8,363 (7,645–9,150)	1,540,900.8	42,436.39	6.0 (5.5–6.5)	1,110.22	39.39	0.6 (0.0–1.3)
Acute tonsillitis	6,312 (4,323–9,215)	—	10,101.07	4.2 (3.0–5.7)	—	4.50	0 (–)
Bronchitis	6,855 (6,563–7,161)	4,388,766.5	214,380.5	4.4 (4.2–4.6)	2,840.53	164.05	0.5 (0.1–0.9)
Pneumonia	11,231 (10,960–11,508)	89,101,443.5	—	6.1 (6.0–6.3)	46,155.73	—	4.2 (3.8–4.5)
Aspergillosis, allergic bronchopulmonary aspergillosis, pneumonia	19,426 (15,435–24,450)	1,063,487.5	95,514.9	8.4 (7.0–10.0)	389.35	41.66	1.0 (0.0–2.9)
Tuberculosis	10,110 (9,196–11,115)	2,018,867.5	126,606.1	5.7 (5.3–6.3)	1,222.60	78.29	2.2 (0.8–3.6)
Abscess of lung or mediastinum	18,899 (16,499–21,647)	872,733.3	—	10.1 (8.9–11.5)	438.03	—	3.3 (0.0–7.0)
Empyema	27,599 (24,368–31,258)	—	—	12.2 (11.0–13.6)	—	—	6.7 (3.1–10.3)
Meningitis	11,973 (10,736–13,352)	2,580,121.8	—	6.0 (5.5–6.6)	1,130.00	—	1.5 (0.3–2.7)
Encephalitis	16,268 (14,192–18,649)	1,181,946.4	113,613.9	8.1 (7.2–9.2)	599.22	56.39	2.8 (0.4–5.3)
Endocarditis	15,658 (14,407–17,017)	3,474,859.1	245,285.86	8.1 (7.5–8.8)	1,693.22	90.14	4.5 (2.4–6.4)
Infectious arthropathy	13,239 (12,447–14,082)	2,098,488.6	160,824.80	6.8 (6.4–7.2)	1,148.23	83.05	1.6 (0.6–2.6)
Infection of bone	13,603 (12,901–14,343)	9,371,655.1	673,466.18	7.9 (7.5–8.2)	5,587.57	383.35	1.2 (0.6–1.8)
Enterocolitis	11,097 (10,593–11,625)	17,543,062.9	—	6.7 (6.4–6.9)	10,222.19	—	2.9 (2.2–3.5)
<i>Clostridium difficile</i>	14,177 (13,466–14,926)	14,110,711.1	—	8.6 (8.3–8.9)	8,191.63	—	3.8 (3.0–4.7)
Diverticulitis	9,107 (8,703–9,530)	—	—	5.0 (4.8–5.2)	—	—	0.9 (0.4–1.5)
Peritonitis and intestinal abscess	19,465 (18,057–20,983)	—	—	9.0 (8.4–9.6)	—	—	3.9 (2.3–5.5)
Urinary tract infection	9,436 (9,232–9,644)	89,143,351.8	—	6.0 (5.9–6.1)	56,045.43	—	1.9 (1.7–2.1)
Pyelonephritis	7,329 (6,938–7,742)	—	—	4.3 (4.1–4.5)	—	—	0.7 (0.2–1.3)
MSSA	9,723 (9,432–10,023)	13,419,636.4	726,915.63	6.3 (6.2–6.5)	8,249.85	408.10	1.7 (1.4–2.1)
MRSA	9,681 (9,360–10,013)	8,057,009.9	418,137.54	5.6 (5.4–5.8)	4,353.07	244.97	2.1 (1.6–2.5)
Streptococcal infections	10,595 (10,198–11,008)	—	736,915.47	6.6 (6.4–6.8)	—	429.29	1.2 (0.8–1.6)
Pseudomonas	12,827 (12,191–13,496)	8,668,015.3	496,304.73	8.0 (7.7–8.3)	4,854.09	259.64	2.2 (1.5–2.8)
Mycobacterial infection	13,369 (11,628–15,371)	736,813.1	58,534.68	7.3 (6.4–8.2)	372.27	25.14	3.1 (0.4–5.8)
Fungal infection	9,659 (9,382–9,945)	18,750,800.0	893,041.4	6.4 (6.2–6.5)	11,678.06	592.87	1.8 (1.5–2.0)
Viral infection	8,134 (7,821–8,460)	9,127,606.6	376,984.7	4.8 (4.7–5.0)	5,229.62	247.60	1.1 (0.8–1.5)
Influenza	7,992 (7,188–8,886)	1,406,377.6	27,253.1	4.8 (4.3–5.3)	759.35	17.72	2.1 (0.4–3.8)
Septicemia	14,943 (14,463–15,440)	66,432,339.6	3,155,293.9	7.8 (7.6–8.0)	32,416.00	1,626.75	6.9 (6.3–7.4)

Abbreviations: AD, atopic dermatitis; AD-E, atopic dermatitis or eczema; CI, confidence interval; LOS, length of stay; MRSA, methicillin-resistant *Staphylococcal aureus*; MSSA, methicillin-sensitive *Staphylococcal aureus*.