Secular trends of atopic dermatitis and its comorbidities in United States children between 1997 and 2018

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Background

- Previous studies found increased prevalence of childhood atopic dermatitis (AD) in the United States over the past few decades[1-3]. It is unknown whether the prevalence of AD has plateaued.
- Further, it is unknown whether AD comorbidities have changed over time.

Research Objectives

To assess the prevalence and secular trends of AD and its comorbidities.

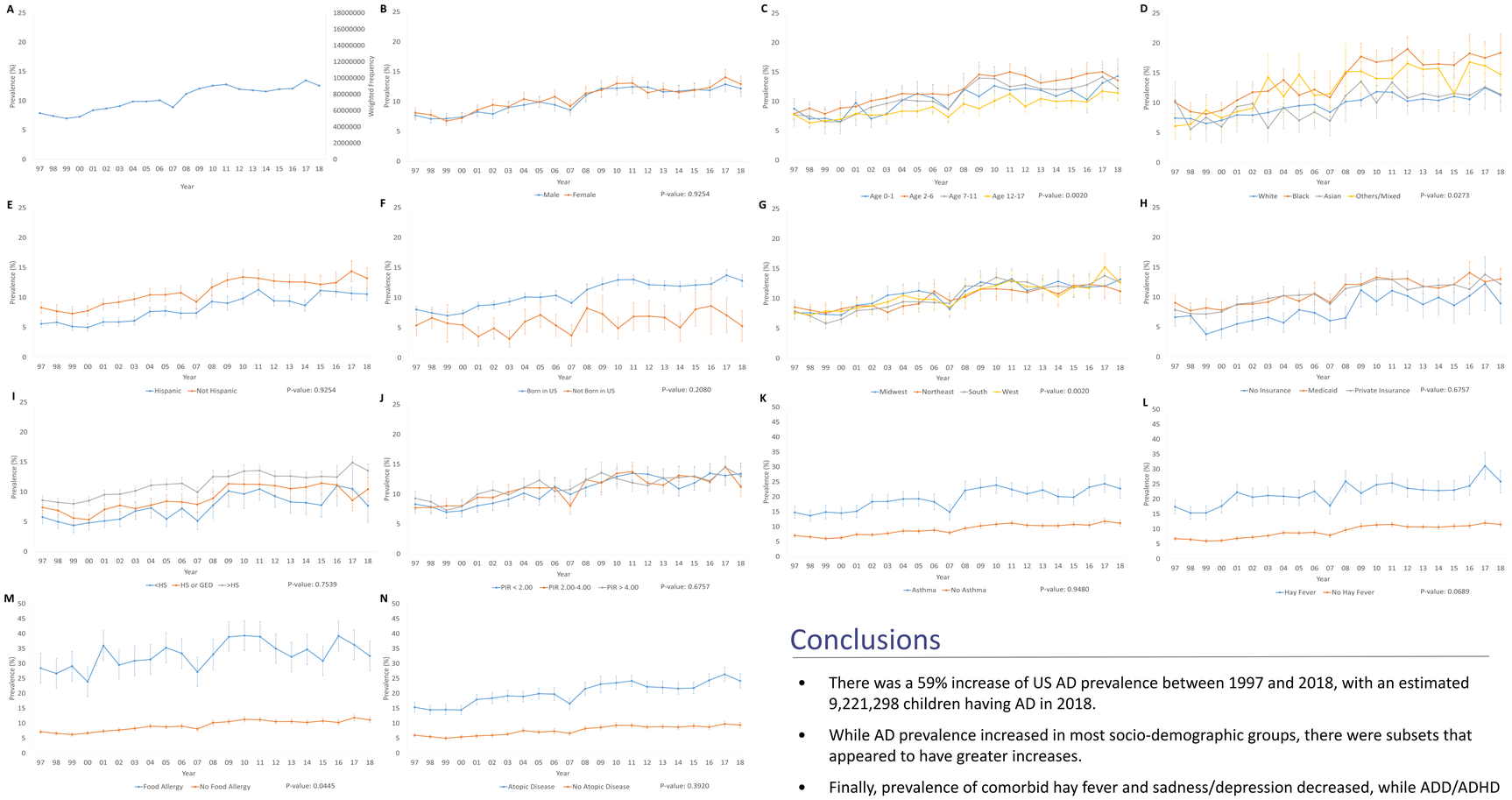
Methods

- Data of 259,818 children ages 0-17 years from the National Health Interview Survey 1997-2018
- Logistic regression models were constructed to determine whether AD (binary outcome) increased over time by comparing odds ratios (OR) and 95% CI of each year using 1997 as a reference.
- The prevalence of AD comorbidities were estimated overall, and in those with and without AD. Multivariable logistic regression models were constructed separately for those with and without AD, with each comorbidity as the dependent variable and year (2018 vs. 1997) as the independent variable. Two-way statistical interactions of AD (yes/no) and year (3 year bins) were examined as predictors of each comorbidity.
- To evaluate change in prevalence of AD comorbidities, the prevalences and 95% CI of asthma, hay fever, and/or food allergy, depression, and ADD/ADHD were estimated, overall and in those with and without AD. Multivariable logistic regression models were constructed separately for those with and without AD, with each comorbidity as the binary dependent variable and year (2018 vs. 1997) as the binary independent variable, adjusting for the abovementioned socio-demographic variables.

Results

- The prevalence [95% confidence interval] of childhood AD steadily increased from 2000 (7.3% [6.8-7.9%]) to 2011 (12.8% [12.1-13.5%]) and remained consistent until 2018 (12.6% [11.6-13.5%]) with a peak in 2017 (13.5% [12.6-14.4%]) (Figure 1).
- In logistic regression models, the odds of AD were significantly increased in all years from 2003 to 2018 compared to 1997. However, the increased odds of AD over time were attenuated when adjusting for socio-demographic factors. AD prevalence increased in virtually all socio-demographic groups (Figure 1).
- There were significant trends of AD comorbidities over time, with increasing prevalence of attention deficit (hyperactivity) disorder, and decreasing prevalence of hay fever and depression/sadness (Table 1).

Figure 1. Prevalence of eczema in US children from 1997-2018, overall and by socio-demographic subgroup.



Benjamini-Hochberg corrected P-values represent significance of interaction between sociodemographic factors and year as predictors of AD prevalence.

HS, high school; PIR, poverty-income ratio.

Table 2. Prevalence of atopic and mental health comorbidities in 1997 vs 2018 in those with and without AD.

Comorbidity	Total		AD		No AD	
	1997	2018	1997	2018	1997	2018
Asthma	11.4 (10.7-12.0)	11.6 (10.7-12.5)	21.2 (18.5-24.0)	21.1 (18.1-24.1)	10.5 (9.9-11.2)	10.3 (9.4-11.2)
Hay Fever	10.4 (9.8-10.9)	7.1 (6.4-7.8)	22.8 (19.9-25.7)	14.7 (12.3-17.1)	9.3 (8.7-9.9)	6.1 (5.4-6.7)
Food Allergy	3.3 (2.9-3.6)	6.5 (5.8-7.1)	11.8 (9.5-14.1)	16.8 (14.0-19.5)	2.5 (2.2-2.9)	5.0 (4.4-5.6)
Atopic Disease	20.4 (19.6-21.2)	21.2 (20.1-22.2)	39.7 (36.3-43.1)	40.8 (37.0-44.5)	18.8 (18.0-19.6)	18.3 (17.3-19.4)
Depression/sadness	21.9 (20.8-23.1)	10.9 (10.0-11.7)	32.5 (28.3-36.6)	14.6 (11.9-17.4)	21.0 (19.9-22.1)	10.3 (9.5-11.2)
ADD/ADHD	5.2 (4.8-5.7)	9.3 (8.4-10.2)	6.7 (4.9-8.4)	12.6 (10.0-15.2)	5.1 (4.6-5.6)	8.8 (7.9-9.8)

Conclusions

- There was a 59% increase of US AD prevalence between 1997 and 2018, with an estimated 9,221,298 children having AD in 2018.
- While AD prevalence increased in most socio-demographic groups, there were subsets that appeared to have greater increases.
- Finally, prevalence of comorbid hay fever and sadness/depression decreased, while ADD/ADHD increased over time in children with and without AD.
- Given that the US prevalence of childhood AD remains high, more investment is needed into research and cost-effective interventions aimed at AD prevention and treatment.

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Presented at the 3rd Annual Revolutionizing Atopic Dermatitis Conference Chicago, IL • December 12, 2020

Association of Atopic Dermatitis with Rheumatoid Arthritis and Systemic Lupus Erythematosus in US Adults

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Background

- Atopic dermatitis (AD) is a chronic inflammatory skin disorder that affects up to 3-5% of adults worldwide[1].
- There have been conflicting studies about the association of AD with the autoimmune disorders rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).
  - A previous study has found a positive association between AD and RA[2]
  - Previous studies have also shown a positive association in bivariate models, but not when adjusting for comorbidity and sociodemographics[3-4]
- Little is known of how the association of AD and RA and SLE differs with and without atopic comorbidities

Research Objectives

Using a population-based survey, we sought to determine whether AD with or without atopic comorbidities, including asthma, hay fever, food allergy, and respiratory allergy is associated with RA and SLE and to determine which subsets of adults have increased likelihood of RA and SLE.

Methods

Data Source

- The National Health Interview Survey (NHIS) is an annual US-population household survey that provides a representative sample of the civilian noninstitutionalized US population.
- Data of 34,242 adults (age ≥18 years) were analyzed from the the 2012 NHIS.

Statistical Analysis

- Statistical analyses were performed in SAS version 9.4 software (SAS Institute, Cary, NC) using survey procedures that accounted for sample weights, clusters, and strata.
- Using survey procedures, weighted frequency and proportions of atopic and autoimmune disease were estimated.
- Bivariate logistic regression models were created to determine associations between AD, with and without comorbidities, and RA and SLE. Crude odds ratio (OR) and 95% confidence intervals (95% CI) were estimated.
- Multivariate logistic regression models adjusted for sex, age, race, highest household education, poverty income ratio (PIR), insurance coverage, and history of depression and anxiety. Adjusted odds ratio (Adj OR) and 95% CI were estimated.

Table 1. Associations of rheumatoid arthritis and lupus and atopic dermatitis, with and without atopic comorbidities

Atopic disorder	Rheumatoid arthritis				Systemic lupus erythematosus			
	Raw Freq	% Prev (95% CI)	Crude OR (95% CI)	Adj OR (95% CI)	Raw Freq	% Prev (95% CI)	Crude OR (95% CI)	Adj OR (95% CI)
Atopic Dermatitis								
No	822	2.3 (2.1-2.5)	1.00 (ref)	1.00 (ref)	100	0.3 (0.2-0.4)	1.00 (ref)	1.00 (ref)
Yes	128	4.9 (3.9-5.9)	2.21 (1.73-2.82)	1.65 (1.27-2.16)	32	1.2 (0.6-1.8)	3.86 (2.14-6.94)	2.62 (1.40-4.90)
Atopic Dermatitis Alone								
No	900	2.4 (2.2-2.6)	1.00 (ref)	1.00 (ref)	121	0.4 (0.3-0.5)	1.00 (ref)	1.00 (ref)
Yes	50	4.0 (2.5-5.4)	1.67 (1.12-2.47)	1.44 (0.95-2.19)	11	0.6 (0.1-1.0)	1.63 (0.72-3.69)	1.44 (0.59-3.50)
AD and Asthma								
No	905	2.4 (2.2-2.6)	1.00 (ref)	1.00 (ref)	121	0.4 (0.3-0.4)	1.00 (ref)	1.00 (ref)
Yes	44	6.6 (4.1-9.0)	2.01 (1.64-2.46)	2.27 (1.46-3.52)	11	1.7 (0.4-2.9)	2.07 (1.26-3.39)	2.75 (1.13-6.70)
AD and Hay Fever								
No	926	2.4 (2.2-2.7)	1.00 (ref)	1.00 (ref)	127	0.4 (0.3-0.5)	1.00 (ref)	1.00 (ref)
Yes	24	6.0 (3.2-8.8)	1.52 (1.17-1.96)	1.76 (1.03-3.02)	5	1.2 (0.0-2.6)	1.48 (0.72-3.05)	1.37 (0.33-5.75)
AD and Food Allergy								
No	918	2.4 (2.2-2.6)	1.00 (ref)	1.00 (ref)	123	0.3 (0.3-0.4)	1.00 (ref)	1.00 (ref)
Yes	31	7.3 (4.2-10.3)	2.80 (2.11-3.72)	2.05 (1.23-3.42)	9	3.3 (0.7-5.8)	4.91 (2.51-9.62)	6.58 (2.71-16.0)
AD and Respiratory Allergy								
No	904	2.4 (2.2-2.6)	1.00 (ref)	1.00 (ref)	115	0.3 (0.2-0.4)	1.00 (ref)	1.00 (ref)
Yes	45	5.8 (3.8-7.8)	1.69 (1.36-2.09)	1.75 (1.14-2.68)	17	2.6 (0.8-4.3)	2.40 (1.42-4.07)	5.34 (2.21-12.9)
Any atopic disease								
None	512	1.9 (1.7-2.1)	1.00 (ref)	1.00 (ref)	58	0.3 (0.2-0.3)	1.00 (ref)	1.00 (ref)
1	244	3.3 (2.8-3.8)	1.73 (1.42-2.11)	1.56 (1.27-1.90)	40	0.6 (0.3-0.8)	2.31 (1.31-4.06)	1.96 (1.12-3.45)
≥2	191	5.0 (4.1-5.9)	2.67 (2.15-3.31)	2.01 (1.60-2.52)	34	0.9 (0.5-1.4)	3.72 (2.01-6.89)	2.51 (1.32-4.76)

Bivariable logistic regression models were constructed to determine whether RA or SLE (outcomes) were associated with eczema, eczema alone, and eczema with comorbid asthma, hay fever, food allergy, respiratory allergy, or number of atopic disease (0/1/≥2). Crude OR (OR) and 95% CI were estimated. Multivariable models included sex (male, female), age (continuous), race (white, black, other), education (less than high school (HS), HS or greater), poverty income ratio (PIR) (<1.00, ≥1.00), insurance coverage (Y/N), history of depression (Y/N), and anxiety (Y/N). Adjusted OR and 95% CI were estimated.

Results

- In bivariate and multivariate weighted logistic regression models, RA was associated with AD overall (adjusted odds ratio [95% CI]: 1.65 [1.27-2.16]), and AD with comorbid asthma (2.27 [1.46-3.52]), hay fever (1.76 [1.03-3.02]), food allergy (2.05 [1.23-3.42]), and respiratory allergy (1.75 [1.14-2.68]).
- RA was associated with AD without atopic comorbidities in bivariate models, but not in multivariate models adjusting for sociodemographic characteristics (1.44 [0.95-2.19]).
- Similarly, SLE was associated with AD overall (2.62 [1.40-4.90]), and AD with comorbid asthma (2.75 [1.13-6.70]), food allergy (6.58 [2.71-16.0]), or respiratory allergy (5.34 [2.21-12.9]), but not AD alone (1.44 [0.59-3.50]) or AD with comorbid hay fever (1.37 [0.33-5.75]).

Limitations

- Atopic and autoimmune disease assessment by self-report without physical exam, which may lead to potential misclassification
- NHIS did not collect data on severity or phenotype of atopic diseases precluding analysis of autoimmune disease prevalence by AD severity.

Conclusions

- A subset of adult AD patients, particularly those with comorbid atopic disease, have higher prevalences of RA and SLE.
- AD is characterized by type 2 inflammation, while autoimmune diseases, e.g. RA and SLE, are characterized by type 1 and/or 3 inflammation[5].
- The overlap of atopic and autoimmune comorbidities may represent a distinct immune-profile and patient-subset.
- Further investigation is needed to understand the mechanisms and management of these overlapping disorders.

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Presented at the 3rd Annual Revolutionizing Atopic Dermatitis Conference Chicago, IL • December 12, 2020

The Effect of Secular Trends of Birthweights on Atopic Dermatitis Prevalence in United States Children between 1997 and 2018

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Background

- Atopic dermatitis (AD) is a common chronic inflammatory skin disease with increasing prevalence in US children[1-3].
- Previous studies have found positive associations between higher birthweight and AD[4-6].
- However, It is unknown how trends of birthweights affect childhood AD prevalence in the US.

Research Objectives

This study sought to confirm the association of birthweight and childhood AD, and determine whether trends of birthweight were associated with trends of childhood AD prevalence over time in the US.

Methods

Data Source

- The National Health Interview Survey (NHIS) is an annual US-population household survey that provides a representative sample of the civilian noninstitutionalized US population.
- Data of 238,767 children (age ≤17 years) were analyzed from the 1997-2018 NHIS.

Statistical Analysis

- The weighted mean, frequency, proportion and 95% confidence interval (CI95) of birthweight categories and AD prevalence were estimated annually and in 3-year bins.
- Multivariable logistic regression models were constructed with AD (yes/no) as the dependent variable, birthweight (continuous) as the independent variable, and sex, age, race, highest household education, poverty-to-income ratio, and insurance coverage as covariates.
- The effects of secular trends of birthweight on trends of AD prevalence were examined using logistic regression models with 1-year history of AD as the dependent variables, and survey year (3-year bins), low birthweight (<5th/≥5th percentile) and a two-way interaction term between them as the independent variables, as well as the aforementioned socio-demographics as covariables.
- Models were also stratified by age (0-5/6-10/11-17 years) and repeated with high birthweight (≤95th/>95th percentile) as the independent variable. Models were tested using linear and spline interactions.
- Interactions between covariates were included in the final models if P-value <0.01, cell frequencies >5 for each level of interaction and modification of estimates by >20%.

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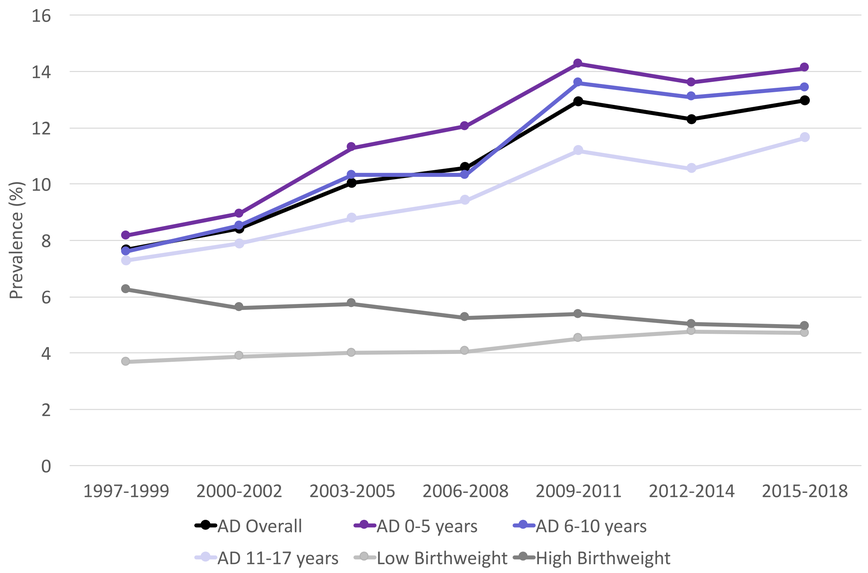
Results

- The prevalence [CI95] of childhood AD increased from 1997 (7.9% [7.4-8.5%]) to 2018 (12.6 [11.6-13.5%]) overall, and particularly in ages 0-5 years (8.2% [7.6-8.8%] to 14.1% [13.3-14.9%]), 6-10 years (7.6% [7.0%-8.3%] to 13.4% [12.5-14.3%]), and 11-17 years (7.3% [6.8-7.8%] to 11.6% [11.0-12.3%]) (Figure 1).
- In contrast, mean [CI95] birthweight decreased from 1997 (3.35 kg [3.34-3.37 kg]) to 2018 (3.30 kg [3.28-3.31 kg]).
- Moreover, the prevalence [CI95] of low birthweight (<5th percentile) increased from 1997-1999 (3.7% [3.4-3.9%]) to 2015-2018 (4.7% [4.4-5.0%]).
- Prevalence of high birthweight (>95th percentile) decreased (6.3% [5.9-6.6%] to 4.9% [4.6-5.2%]) (Figure 1).

Figure 1. Secular trends of prevalence of low and high birthweight and AD, overall and by age group (0-5 years, 6-10 years, 11-17 years), among US children from 1997-1999 to 2015-2018.



Results (cont.)

- Across all age groups, a 1-kilogram increase in birthweight was associated with a slightly increased odds of AD (adjusted OR [CI95]: 1.039 [1.009-1.070]) overall, particularly in ages 0-5 years (1.065 [1.017-1.116]), but not ages 6-10 years (1.036 [0.98-1.096]) or 11-17 years (1.017 [0.97-1.067]).
- There were no significant interactions between low or high birthweight and year as predictors of childhood AD prevalence overall (low: P=0.9178, high: P=0.6040), or in ages 0-5 (low: P=0.4833, high: P=0.2082), 6-10 (low: P=0.6494, high: P=0.2952) or 11-17 years (low: P=0.6008, high: P=0.4252).

Limitations

- Data regarding AD and birthweight were collected via caregiver report rather than a clinician's exam, which may lead to response bias.
- There was a lack of data on potential confounders such as gestational age, AD severity and age of onset.

Conclusions

- These results show only a slight relationship between birthweight and childhood AD, particularly in children ages 0-5 years.
- Proposed mechanisms include the "hygiene hypothesis," such that lower-weight infants are exposed to more frequent infections and allergens that may have a protective effect against future AD development[5, 7-8].
- Despite this, we found that decreasing birthweight did not have an effect on trends of AD prevalence in any age group.
- Other risk factors should be pursued for the prevention of childhood AD.

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Presented at the 3rd Annual Revolutionizing Atopic Dermatitis Conference Chicago, IL • December 12, 2020

Association of Influenza Vaccination on the Prevalence and Secular Trends of Atopic Dermatitis in United States Children

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Background

- Atopic dermatitis (AD) is a chronic, pruritic inflammatory skin disease with increasing prevalence among children in the United States[1-3].
- A previous study found that children with AD had higher rates of vaccination for influenza and other pathogens[4].
- However, little is known of how the secular trend of influenza vaccination affects AD prevalence in the United States.

Research Objectives

This study sought to confirm the association between childhood AD and influenza vaccination, and determine whether the secular trend of influenza vaccinations accounts for the trend of increasing AD over time among US children.

Methods

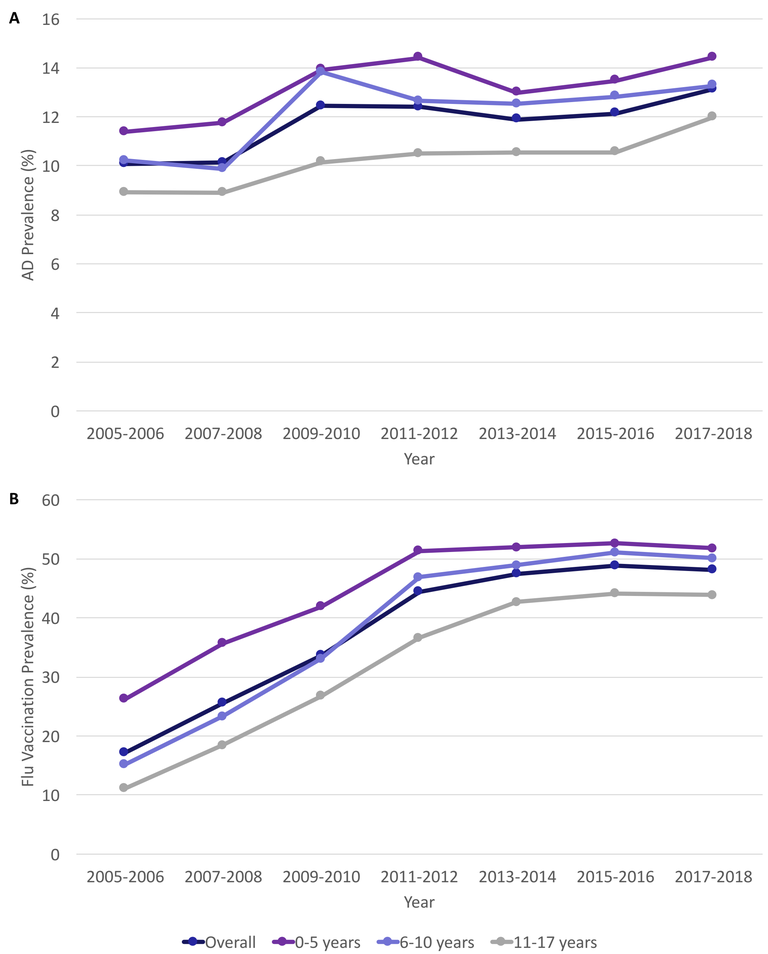
Data Source

- The National Health Interview Survey (NHIS) is an annual US-population household survey that provides a representative sample of the civilian noninstitutionalized US population.
- Data of 151,189 children (age ≤17 years) were analyzed from the the 2005-2018 NHIS.

Statistical Analysis

- Using survey procedures, weighted frequency and proportions of AD and influenza vaccination were estimated in 2-year bins.
- To determine associations between AD and influenza vaccination, multivariate logistic regression models were constructed adjusting for sex, age, race, highest household education, poverty income ratio (PIR), insurance coverage, asthma, hay fever, and food allergy. Adjusted odds ratio (OR) and 95% confidence intervals (95% CI) were estimated.
- To determine the relationship between secular trends of influenza vaccination and AD prevalence, logistic regression models were constructed with 1-year history of AD as the dependent variables, and survey year (2 year bins), influenza vaccination, and a two-way interaction term between them as the independent variables, and the aforementioned socio-demographics as covariables.
- Models were also stratified by age (0-5/6-10/11-17 years).
- Interactions between covariates were included in the final models if P-value <0.01, cell frequencies >5 for each level of interaction and modification of estimates by >20%.

Figure 1. Secular trends of (A) AD and (B) influenza vaccination, overall and by age group among US children from 1997-1999 to 2015-2018.



Results

- Children with AD had significantly higher odds of influenza vaccination (adjusted OR [CI95]: 1.144 [1.092-1.200]) overall, and particularly in ages 0-5 years (1.251 [1.163-1.346]) and 6-10 years (1.152 [1.056-1.257]), but not in ages 11-17 years (1.003 [0.924-1.089]).
- There was no significant interaction between influenza vaccination and year as predictors of AD in children overall (P=0.6725), or in ages 0-5 years (P=0.5191), 6-10 years (P=0.7455), or 11-17 years (P=0.9151).
- Interactions were also non-significant in higher order linear (overall: P=0.7144, 0-5 years: P=0.4497, 6-10 years: P=0.9604, 11-17 years: P=0.5585) and spline models (overall: P=0.6106, 0-5 years: P=0.5344, 6-10 years: P=0.9248, 11-17 years: P=0.4650)

Limitations

- Data on AD and influenza vaccination were collected through caregiver report rather than a clinician's exam, which may lead to potential misclassification.
- Lack of data regarding AD severity, route of vaccination, and other vaccination types.

Conclusions

- These findings confirm that children with AD have higher odds of influenza vaccination in US children, but not adolescents, which is likely attributable to increased healthcare utilization among those with AD[4-5].
- However, the increasing trend of influenza vaccinations do not appear to be a driving factor for the increasing prevalence of childhood AD over time.
- Further research should examine potential alternate risk factors of AD.

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