

# Developmental Disorders and Allergic Disease in the United States

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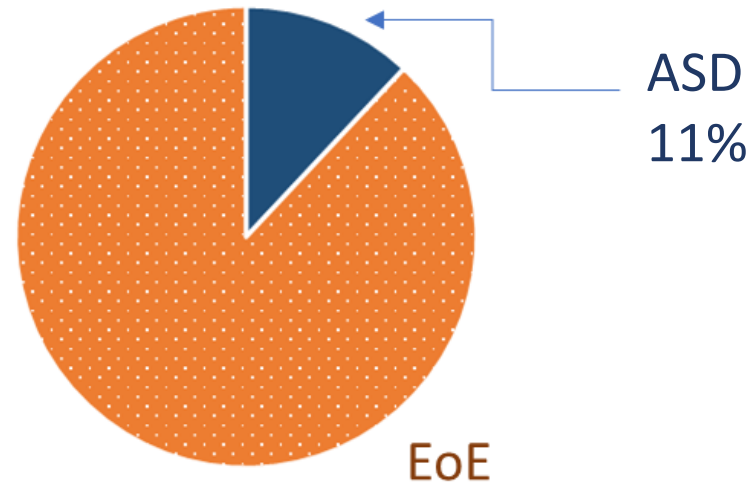
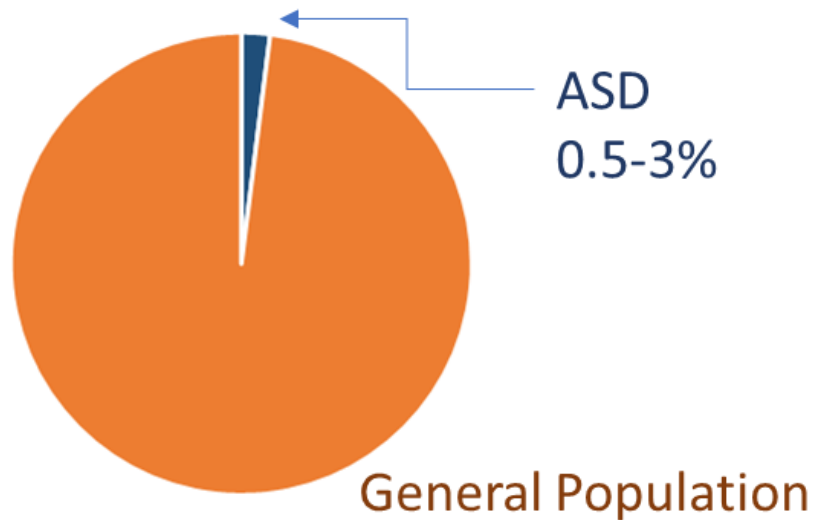
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# DD and EoE at UVA

- Of the 270 patients with EoE  $\leq 18$ yo at UVA:
- 30 have a diagnosis of Autism Spectrum Disorder (ASD) = 11%
- 70 have a Developmental Disorder (DD) = 26%



# Phenotypic Characterization of Eosinophilic Esophagitis in a Large Multicenter Patient Population from the Consortium for Food Allergy Research



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- Reported an association between neurodevelopmental disorders and eosinophilic esophagitis (EoE)

	Number	Percent
<b>Developmental Delay</b>	<b>48</b>	<b>12.4</b>
Prematurity	28	7.3
Depression/anxiety	63	16.3
<b>Autism/behavioral disorder</b>	<b>32</b>	<b>8.3</b>
Mitochondrial disorder	3	0.8

# Association of Food Allergy and Other Allergic Conditions With Autism Spectrum Disorder in Children

Guifeng Xu, MD; Linda G. Snetselaar, PhD; Jin Jing, MD, PhD; Buyun Liu, MD, PhD; Lane Strathearn, MBBS, FRACP, PhD; Wei Bao, MD, PhD

- **Design:** Cross-sectional study of NHIS (National Health Interview Survey)
- **Population:** 199,520 children 3-17 yo with self-reported food allergy
- **Results:** Children with ASD reported higher food, respiratory and skin allergies, adjusted for age, sex, race, SES, geographic region and other allergic conditions

Allergy Type	Children With ASD, No. (%) (n = 1868) <sup>a</sup>	Children Without ASD, No. (%) (n = 197 652) <sup>a</sup>	OR (95% CI)		
			Model 1 <sup>b</sup>	Model 2 <sup>c</sup>	Model 3 <sup>d</sup>
Food allergy	216 (11.25)	8518 (4.25)	2.87 (2.39-3.45)	2.72 (2.26-3.28)	2.29 (1.87-2.81)
Respiratory allergy	370 (18.73)	24 185 (12.08)	1.59 (1.38-1.84)	1.53 (1.32-1.78)	1.28 (1.10-1.50)
Skin allergy	312 (16.81)	19 087 (9.84)	1.88 (1.62-2.19)	1.80 (1.55-2.09)	1.50 (1.28-1.77)

# Our Study



- **Question:** Is this increased prevalence of self-reported allergy in patients with DD indicative of a true increase in allergic disease?
- **Study design:** Cross-sectional study of children ages 1-17 years enrolled in NHANES
- **Developmental disorders:** Received special education or early intervention services
- **Allergic outcomes:** Self-reported asthma, hay fever, (NHANES 2005-2010), food allergy, (2007-2010) and sensitization (sIgE $\geq$ 0.35 kU/L) to aeroallergen or foods (2005-2006)
- **Statistical analysis:** Multivariable logistic regression, adjusted for race, age, sex, household smokers/income/insurance/education, number of annual healthcare visits, and LBW

# Self-reported Allergic Disease

	n	Adjusted OR* (95% CI)	p value*
<b>Asthma</b>	7335	<b>1.54 (1.13 – 2.09)</b>	<b>0.007</b>
Current asthma	7322	1.45 (1.00 – 2.11)	0.05
<b>Recent attack</b>	<b>6874</b>	<b>1.64 (1.11 – 2.44)</b>	<b>0.02</b>
ED/urgent care	6480	1.39 (0.73 – 2.64)	0.31
<b>Wheezing</b>	<b>10179</b>	<b>1.54 (1.11 – 2.13)</b>	<b>0.01</b>
Allergic rhinitis	10169	1.51 (0.96 – 2.35)	0.07

	n	Adjusted OR* (95% CI)	p value*
Self-reported FA	5915	1.06 (0.67 – 1.70)	0.78
Peanut		2.13 (0.68 – 6.65)	0.19
<b>Milk</b>		<b>2.30 (1.18 – 4.46)</b>	<b>0.02</b>
Wheat		0.71 (0.09 – 5.49)	0.73
<b>Egg</b>		<b>3.58 (1.09 – 11.8)</b>	<b>0.04</b>
Soy		3.63 (0.40 – 33.1)	0.24
Fish		0.53 (0.11 – 2.54)	0.42
Shellfish		0.78 (0.32 – 1.87)	0.56
Corn		2.14 (0.53 – 8.62)	0.27
Tree nuts		2.04 (0.43 – 9.66)	0.35
<b>Other</b>		<b>0.37 (0.21 – 0.66)</b>	<b>0.001</b>



# Sensitization (sIgE)

	n	Adjusted OR* (95% CI)	p value*
Sensitization (IgE) <sup>†</sup>			
Peanut	3706	1.83 (1.04 – 3.22)	0.04
Milk	3661	1.05 (0.58 – 1.93)	0.85
Egg	3696	0.85 (0.45 – 1.62)	0.61
Shrimp	2779	0.45 (0.24 – 0.84)	0.02
Aeroallergens	2948	0.95 (0.66 – 1.36)	0.77



# Results

- Children with DD were more likely to have self-reported asthma, milk, and egg allergy, but not sensitization to either these foods or aeroallergens





# What do these results mean?

- Immune dysregulation is thought to play a role in the development of both atopic disease and DD

However our findings suggest the discrepancy could be from:

- Misdiagnosis by physicians
- Increased perception of allergic disease
- A true increase in non IgE-mediated allergic disease



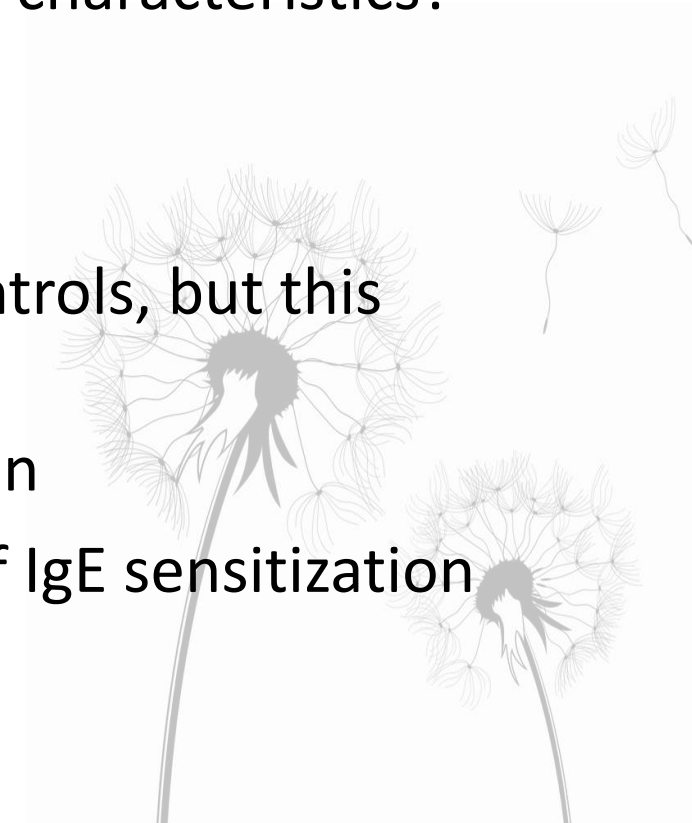
# DD and EoE

## Question:

- What is the prevalence of DD among patients with EoE and do these patients differ in terms of their clinical and immunologic characteristics?

## Hypotheses:

- Higher prevalence of DD in children with EoE than in controls, but this does not hold true for adults (>18yo)
- Age, symptoms, and severity are different at presentation
- Increased odds of self reported atopic disease but not of IgE sensitization



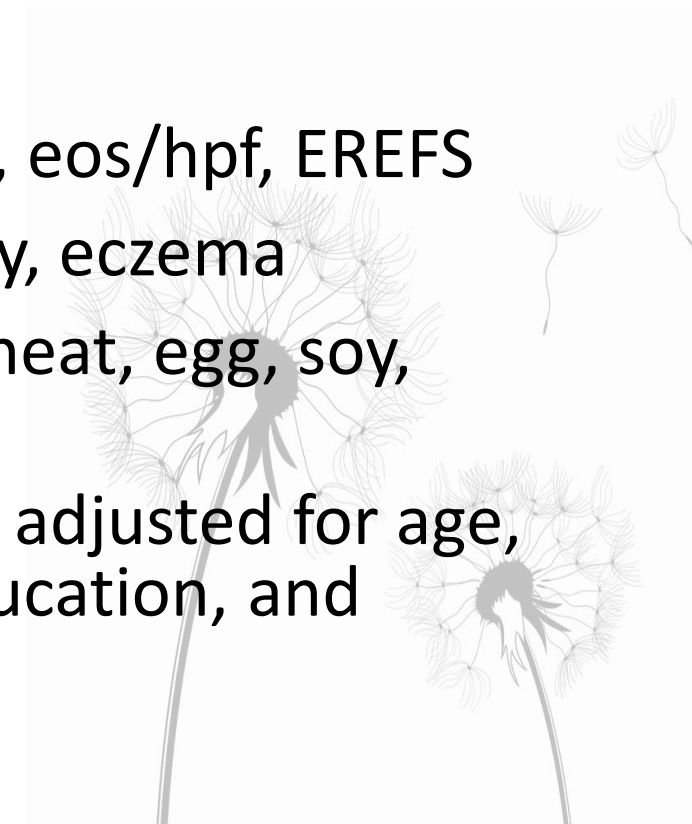
# UVA EoE Cohort

- Established May 2017, enrollment ongoing
- 264 patients (50% pediatric)
- Recruited from multidisciplinary EoE clinic (pediatric or adult)
  - EoE: clinical + histologic evidence (ie symptoms + >15 eos/hpf in absence of other cause)
  - Control: undergoing EGD for esophageal symptoms w/o EoE
- REDCap



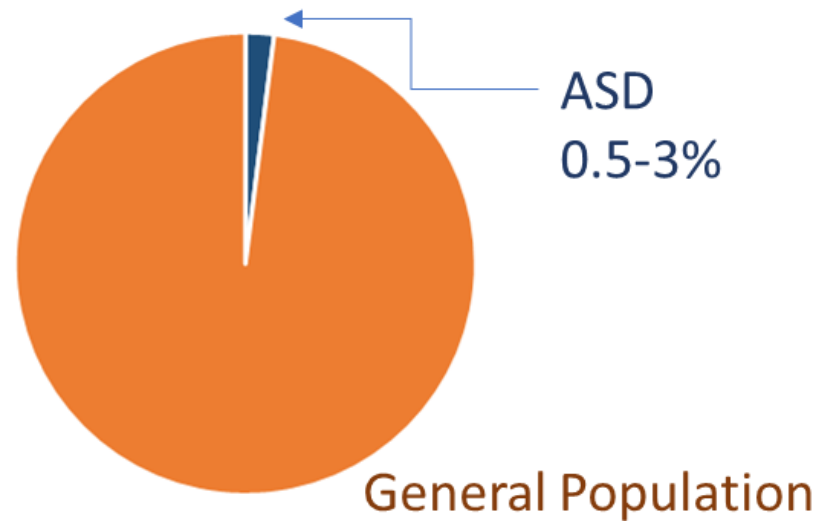
# Methods

- **Study Designs:**
  - Cross-sectional study of subjects at UVA using TriNetX
  - Case-control study of subjects in the UVA EoE cohort
- **DD:** physician diagnosis or positive survey
- **Presentation:** age and self-reported symptoms, AEC, eos/hpf, EREFS
- **Clinical allergic disease:** rhinitis, asthma, food allergy, eczema
- **Immunologic characteristics:** total IgE, sIgE: milk, wheat, egg, soy, tree nuts, peanuts, shrimp, aeroallergens
- **Statistical analysis:** multivariable logistic regression, adjusted for age, race, sex, household smokers/income/insurance/education, and prematurity



# DD and EoE in Adults

- Prevalence of DD/ASD in adults is  $10/510 = 2\%$
- Phenomenon only in kids



# Presentation in Children with DD

	Developmental Disorder (%) n=35	Without DD (%) n=52	P value
<b>Male</b>	32 (91.4)	35 (67.3)	<b>0.01</b>
Race			0.50
<i>White</i>	31 (88.6)	44 (84.6)	
<i>Black</i>	4 (11.4)	6 (11.5)	
<i>Other</i>	0 (0)	2 (3.85)	
Age at presentation			
Presenting symptom			
<i>Dysphagia</i>	8 (26.7)	20 (38.5)	0.28
<i>Abdominal pain</i>	10 (33.3)	27 (51.9)	0.10
<i>Vomiting</i>	16 (53.3)	22 (42.3)	0.34
<i>FTT</i>	7 (38.9)	8 (21.1)	0.16
<i>Disordered eating</i>	6 (29.6)	7 (23.3)	0.19
<b>EREFS <math>\geq 3</math></b>	8 (57.1)	7 (25.9)	<b>0.05</b>
Peak eos/hpf			

\* FTT = failure to thrive; EREFS = Eosinophilic Esophagitis Reference Score

# Future Directions

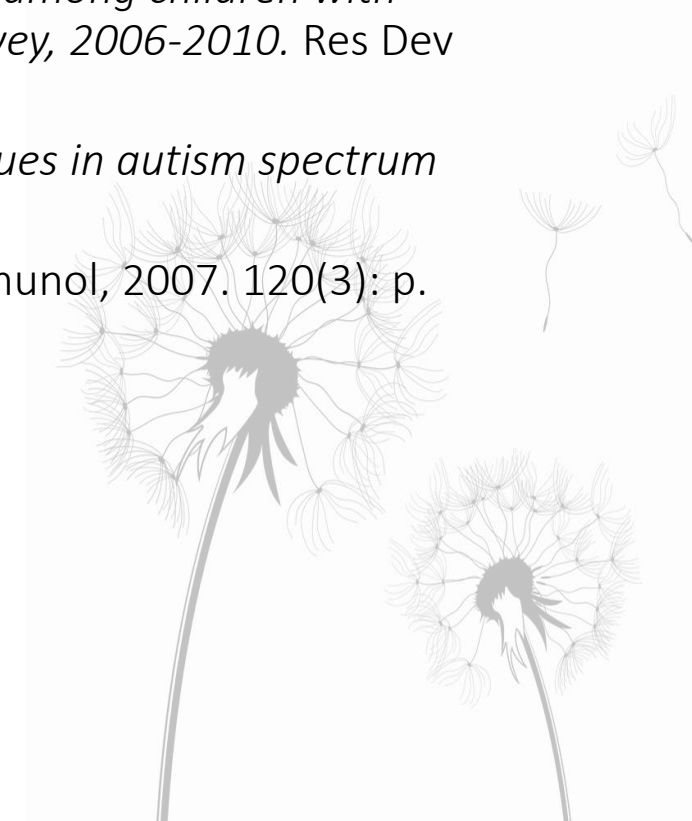
- Are there genetic differences between the DD subjects and matched controls?
- Potential expansion: is there undiagnosed EoE in an ASD cohort?
  - Cytosponge?





# References

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