

Supplementary Table 1. Previous studies evaluating the association between early life factors and EoE

Study	Study population	n	Early life factor	Direction of association
Jensen et al. 2013 <sup>1</sup>	Hospital-based cases and controls (non-GI and GI*)	31 cases, 26 controls (age 1-17 yrs.)	Antibiotic use	+
			Cesarean delivery	+
			Breastfeeding (exclusive)	-
			Maternal smoking/postnatal ETS	No association (maternal)
			Acid suppressants	Not reported
			Pets in home	Not reported
Radano et al. 2014 <sup>2</sup>	Hospital-based cases and controls (non-GI)	25 cases, 74 controls (age 1-5 yrs.)	Antibiotic use	+
			Cesarean delivery	+
			Breastfeeding (any)	No association
			Maternal smoking/ postnatal ETS	Not reported
			Acid suppressants	Not reported
			Pets in home	Not reported
Slae et al. 2015 <sup>3</sup>	Hospital-based cases and controls (GI functional disease controls)	102 cases, 167 controls (age 1-18 yrs.)	Antibiotic use	No association
			Cesarean delivery	Not reported
			Breastfeeding (exclusive)	No association
			Maternal smoking/ postnatal ETS	- (postnatal exposure)
			Acid suppressants	Not reported
			Pets in home	No association
Jensen et al. 2016 <sup>4</sup>	Hospital-based cases and population-based controls	127 cases, 121 controls (ages 1-18)	Antibiotic use	+
			Cesarean delivery	+
			Breastfeeding (exclusive)	No association
			Maternal smoking/ postnatal ETS	No association (maternal)
			Acid suppressants	+
			Pets in home	-

\*GI controls were functional disease controls (GERD) and were identified to not adequately represent the underlying source population giving rise to the cases

Supplementary Table 2. Quality control and minor allele frequencies of study SNPs

Chromosome	Gene	SNP	Minor allele	Missing rate*	HWE**			MAF†	
					ALL	EoE	Control	EoE	Control
2	<i>CAPN14</i>	rs6736278	A	0.0007968	0.6509	1	0.7615	0.0778	0.0616
5	<i>TSLP</i>	rs3806932	G	0.0007968	0.5596	0.1808	1	0.3563	0.4391
7	<i>CCL26</i>	rs2302009	C	0.0007968	0.4047	0.3782	0.7761	0.2489	0.2469
15	<i>LOC283710</i> and <i>KLF13</i> region	rs17815905	G	0	0.3504	0.5642	0.5785	0.2056	0.2559
19	<i>TGF-β</i>	rs1800469	A	0	0.4692	0.5171	0.6786	0.32	0.3062

\*Missing rate=proportion of alleles that were not genotyped

\*\*HWE=Hardy Weinberg Equilibrium

†MAF=Minor Allele Frequency

Supplementary Table 3. Case-only assessment of gene-environment interaction

	<i>CAPN14</i> rs6736278 n=80		<i>TSLP</i> rs3806932 n=126		<i>CCL26</i> rs2302009 n=126		<i>LOC283710 and KLF13 region</i> rs17815905 n=126		<i>TGF-β</i> rs1800469 n=126	
	Crude OR (95% CI); p	aOR (95% CI); p	Crude OR (95% CI); p	aOR (95% CI); p	Crude OR (95% CI); p	aOR (95% CI); p	Crude OR (95% CI); p	aOR (95% CI); p	Crude OR (95% CI); p	aOR (95% CI); p
Cesarean delivery										
No	referent	referent	referent	referent	referent	referent	referent	referent	referent	referent
Yes	0.53 (0.10, 2.72) p=0.44	0.43 (0.08, 2.36) p=0.33	0.92 (0.42, 2.00) p=0.83	0.86 (0.38, 1.97) p=0.73	1.95 (0.38, 10.10) p=0.43	2.08 (0.36, 11.95) p=0.41	1.01 (0.48, 2.11) p=0.98	1.06 (0.49, 2.26) p=0.89	0.94 (0.27, 3.31) p=0.92	0.97 (0.26, 3.61) p=0.96
Preterm delivery										
No	referent	referent	referent	referent	referent	referent	referent	referent	referent	referent
Yes	1.07 (0.20, 5.68) p=0.94	0.80 (0.14, 4.68) p=0.81	0.86 (0.33, 2.29) p=0.77	1.03 (0.37, 2.88) p=0.95	not estimable	not estimable	0.52 (0.21, 1.30) p=0.16	0.53 (0.21, 1.35) p=0.18	0.90 (0.18, 4.39) p=0.89	1.05 (0.21, 5.29) p=0.95
NICU admission										
No	referent	referent	referent	referent	referent	referent	referent	referent	referent	referent
Yes	1.07 (.20, 5.68) p=0.94	0.78 (0.13, 4.84) p=0.79	2.73 (1.11, 6.67) p=0.03	2.46 (0.97, 6.23) p=0.06**	0.81 (0.09, 7.25) p=0.85	0.66 (0.07, 6.26) p=0.72	0.35 (0.14, 0.86) p=0.02	0.34 (0.13, 0.85) p=0.02**	0.80 (0.16, 3.91) p=0.78	0.78 (0.16, 3.90) p=0.76
Breastfed										
No	referent	referent	referent	referent	referent	referent	referent	referent	referent	referent
Yes	0.15 (0.03, 0.63) p=0.01	0.16 (0.04, 0.71) p=0.02**	0.85 (0.34, 2.13) p=0.73	0.71 (0.27, 1.85) p=0.48	0.99 (0.11, 9.16) p=0.99	0.99 (0.11, 9.16) p=0.99	1.55 (0.64, 3.72) p=0.33	1.52 (0.63, 3.70) p=0.36	1.25 (0.26, 6.10) p=0.78	1.11 (0.22, 5.52) p=0.78
Antibiotics in infancy*										
No	referent	referent	referent	referent	referent	referent	referent	referent	referent	referent
Yes	not estimable	not estimable	0.47 (0.17, 1.28) p=0.14	0.43 (0.15, 1.26) p=0.12	1.08 (0.12, 9.85) p=0.94	1.07 (0.12, 9.93) p=0.95	1.18 (0.44, 3.20) p=0.74	1.17 (0.43, 3.17) p=0.76	2.57 (0.31, 21.21) p=0.38	2.55 (0.31, 21.14) p=0.38
Cats or dogs in infancy										
Yes	referent	referent	referent	referent	referent	referent	referent	referent	referent	referent
No	1.22 (0.30, 4.90) p=0.78	1.20 (0.29, 4.93) p=0.80	1.93 (0.90, 4.14) p=0.09	2.22 (1.00, 4.91) p=0.05**	0.42 (0.07, 2.36) p=0.32	0.44 (0.08, 2.53) p=0.36	1.21 (0.60, 2.44) p=0.60	1.20 (0.59, 2.43) p=0.64	1.83 (0.52, 6.43) p=0.34	1.88 (0.53, 6.63) p=0.33

\*21 missing antibiotic use in infancy

\*\*assumption of independence tested – Supplementary Table 4

Supplementary Table 4. Test of independence assumption for case only design\*

	<i>CAPN14</i> and breastfeeding aOR (95% CI); p	<i>TSLP</i> and NICU admission aOR (95% CI); p	<i>TSLP</i> and no furry pets aOR (95% CI); p	<i>LOC283710</i> and <i>KLF13</i> region and NICU admission aOR (95% CI); p
Association in cases	0.16 (0.04, 0.71); p=0.02	2.46 (0.97, 6.23); p=0.06	2.22 (1.00, 4.91); p=0.05	0.34 (0.13, 0.85); p=0.02
Association in controls	2.22 (0.46, 10.67); p=0.32	0.74 (0.41, 1.34); p=0.89	0.80 (0.37, 1.77); p=0.59	1.98 (0.56, 7.00); p=0.29

\*for those with  $p \leq 0.10$  in case-only test of interaction - models include adjustment for maternal education and population stratification

## References

1. Jensen ET, Kappelman MD, Kim HP, et al. Early life exposures as risk factors for pediatric eosinophilic esophagitis. *J Pediatr Gastroenterol Nutr* 2013;57:67-71.
2. Radano MC, Yuan Q, Katz A, et al. Cesarean section and antibiotic use found to be associated with eosinophilic esophagitis. *J Allergy Clin Immunol Pract* 2014;2:475-477 e1.
3. Slae M, Persad R, Leung A-T, et al. Role of Environmental Factors in the Development of Pediatric Eosinophilic Esophagitis. *Digestive Diseases and Sciences* 2015:1-9.
4. Jensen ET, Kuhl JT, Martin L, et al. 664 Prenatal, Antenatal, and Early Life Factors Are Associated With Risk of Eosinophilic Esophagitis. *Gastroenterology*;150:S135-S136.