

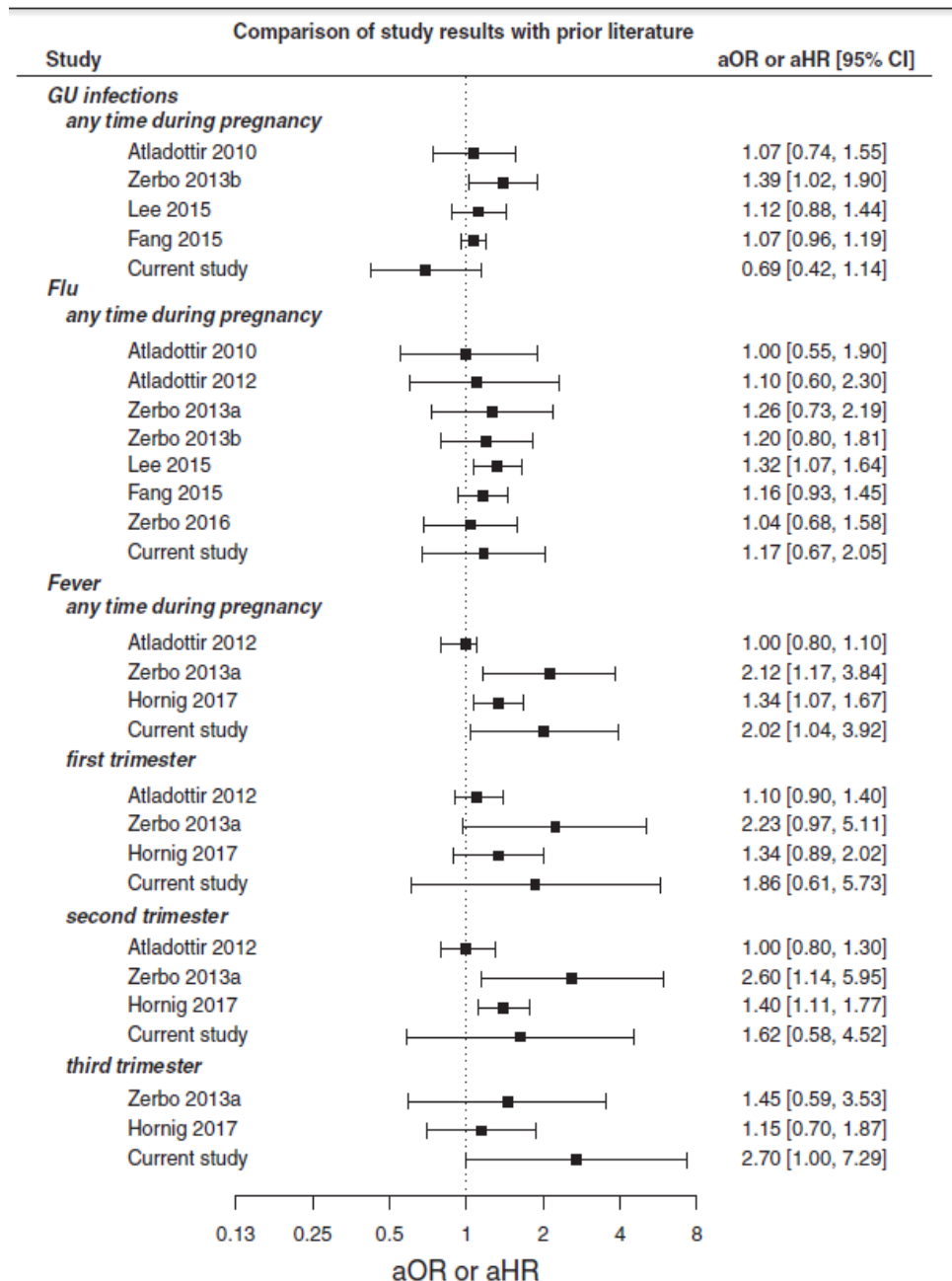
Maternal infection and fever during pregnancy and risk of autism spectrum disorders: findings from the Study to Explore Early Development (SEED)

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Background

- Maternal infection among the earliest suggested non-genetic risk factors (e.g. rubella exposure, measles/mumps, CMV)
- Influenza findings inconsistent
- Fever findings more consistent, but
 - Different timing (which trimester)
 - Difficult to disentangle fever vs infectious agent



Methods

- **Design:** SEED 1 National case-control study
- Ages 2-5, born 2003 – 2006
- 690 ASD, 1016 DD, 972 POP

- **Exposure Source:**
 - Caregiver interview
 - 36 specific infections
 - @ -3mo through birth
 - Medications
 - Fever
 - L&D Medical Record
 - Infections, medications, fever

- **Exposure definitions:**
 - Any infection
 - Organism type
 - Organ affected
 - Timing by trimester

Results 1: Maternal infection during pregnancy, by organ system and organism, SEED, 2003-2006 births

Maternal infection	ASD (N=606)	DD (N=856)	POP (N=796)	ASD vs POP	DD vs POP
	N (%)	N (%)	N (%)	p-Value	p-Value
Any Infection	367 (60.56)	504 (58.88)	470 (59.05)	0.58	0.96
Organ System					
Cardiovascular	1 (0.17)	0 (0.00)	1 (0.13)	1.00	
Skin	11 (1.82)	15 (1.57)	6 (0.75)	0.09	0.08
Eye	5 (0.83)	4 (0.47)	6 (0.75)	1.00	0.54
GI	17 (2.81)	32 (3.74)	24 (3.02)	0.87	0.50
Lower Respiratory	6 (0.99)	11 (1.29)	6 (0.75)	0.77	0.34
Other Respiratory	144 (23.76)	217 (25.35)	201 (25.25)	0.53	1.00
Genitourinary	191 (31.52)	244 (28.50)	210 (26.38)	0.04	0.35
Other Organ	25 (4.13)	35 (4.09)	29 (3.64)	0.68	0.70
Unknown Organ	189 (31.19)	206 (20.07)	198 (24.87)	0.01	0.73
Organism					
Bacteria	220 (36.30)	264 (30.84)	249 (31.28)	0.05	0.87
Virus	82 (13.53)	114 (13.32)	104 (13.07)	0.81	0.88
Fungus	82 (13.53)	101 (11.80)	90 (11.31)	0.22	0.76
Parasite	9 (1.49)	20 (2.34)	11 (1.38)	1.00	0.20
Unknown	188 (31.22)	269 (31.43)	244 (30.65)	0.91	0.75

Results 2: Maternal infection by timing during pregnancy and risk of ASD and DD, SEED, 2003-2006 births

Trimester	ASD	DD (N=856)	POP	ASD vs POP			DD vs POP		
	(N=606)		(N=796)	Crude OR	ORadj1	ORadj2	Crude OR	ORadj1	ORadj2
	N (%)	N (%)	N (%)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Any Infection									
T0	76 (12.5)	73 (8.5)	62 (7.8)	1.70 (1.2-2.4)	1.58 (1.05-2.37)	1.73 (1.03-2.93)	1.10 (.08-1.57)	0.98 (0.65-1.46)	0.91 (0.53-1.57)
T1	174 (28.71)	227 (26.52)	203 (25.50)	1.18 (0.93-1.49)	1.19 (0.90-1.56)	1.09 (0.79-1.50)	1.05 (0.85-1.31)	0.99 (0.77-1.28)	0.93 (0.69-1.25)
T2	187 (30.86)	260 (30.37)	221 (27.76)	1.16 (0.92-1.46)	1.02 (0.78-1.33)	0.87 (0.65-1.17)	1.14 (0.92-1.40)	0.88 (0.69-1.13)	0.81 (0.62-1.06)
T3	252 (41.58)	308 (35.98)	311 (39.07)	1.11 (0.90-1.38)	1.04 (0.81-1.33)	1.11 (0.84-1.45)	0.88 (0.72-1.07)	0.74 (0.59-0.93)	0.83 (0.65-1.06)
Pregnancy	367 (60.6)	504 (58.9)	470 (59.0)	1.07 (0.86-1.3)	1.02 (0.79-1.31)	0.94 (0.68-1.31)	0.99 (0.81-1.2)	0.84 (0.67-1.05)	0.80 (0.59-1.08)

ORadj1 = adjusted by child sex, maternal age, maternal race, maternal education, income during pregnancy, maternal psych disease hx, hypertension, site

ORadj2 = adjusted by child sex, maternal age, maternal race, maternal education, income during pregnancy, maternal psych disease hx, hypertension, site, any medication for infection

Results 3: Maternal infection with and without fever by timing during pregnancy and risk of ASD, SEED, 2003-2006 births

	ASD	DD	POP	ASD vs POP		
	N (%)	N (%)	N (%)	Crude OR (95% CI)	ORadj1 (95% CI)	ORadj2 (95% CI)
Any Infection <u>with</u> Fever						
T0	11 (2.03)	4 (0.51)	7 (0.94)	2.18 (0.84-5.65)	2.11 (0.68-6.58)	-
T1	20 (4.42)	16 (2.48)	25 (4.05)	1.10 (0.60-2.00)	0.91 (0.46-1.79)	0.87 (0.32-2.40)
T2	31 (6.89)	38 (5.99)	21 (3.52)	2.03 (1.15-3.58)	2.19 (1.14-4.23)	2.05 (0.95-4.45)
T3	30 (7.81)	48 (8.05)	44 (8.32)	0.93 (0.58-1.52)	0.80 (0.45-1.40)	1.04 (0.56-1.93)
Pregnancy	73 (23.40)	92 (20.72)	86 (20.87)	1.16 (0.81-1.65)	1.08 (0.71-1.62)	0.95 (0.45-1.98)
Any Infection <u>without</u> Fever						
T0	65 (10.92)	69 (8.10)	55 (6.97)	1.64 (1.12-2.33)	1.51 (0.98-2.31)	1.72 (1.01-2.94)
T1	154 (26.28)	211 (25.12)	178 (23.09)	1.19 (0.93-1.52)	1.23 (0.92-1.64)	1.16 (0.84-1.62)
T2	156 (27.13)	222 (27.14)	200 (25.81)	1.07 (0.84-1.37)	0.92 (0.69-1.22)	0.83 (0.61-1.12)
T3	222 (38.45)	260 (32.18)	267 (35.51)	1.14 (0.91-1.43)	1.07 (0.83-1.38)	1.13 (0.85-1.49)
Pregnancy	294 (55.16)	412 (53.93)	384 (54.08)	1.04 (0.83-1.31)	1.01 (0.78-1.31)	0.96 (0.68-1.36)

Summary

- Maternal infection during pregnancy was relatively common, occurring in approximately 60% of all women.
- Risk of ASD was increased only among:
 - Women with infection accompanied by fever during the second trimester
 - Women with infection without fever during the three months prior to conception
 - After controlling for several covariates including treatment with medication
- By contrast, neither maternal infection with or without fever was associated with DD
- Growing evidence of fever-based associations