Appendix 1. Case and Control Women Reporting Single-Ingredient Acteminophen Use During the First Trimester of Pregnancy for All (Multiple and Isolated) and Isolated-Only Birth Defects

	Controls (n)		All Cases (n)*					Isolated Cases (n)				
	Unexposed	Exposed	Unexposed	Exposed	aOR	95%CI	*P*	Unexposed	Exposed	aOR	95%CI	*P*
NTDs	2,187	1,956	371	339	1.10	0.92–1.30	0.29	326	316	1.15	0.97–1.38	0.11
Anencephaly/craniorachischisis	2,187	1,956	98	98	1.22	0.90–1.66	0.19	87	93	1.31	0.95–1.79	0.10
Spina bifida	2,187	1,956	228	207	1.05	0.85–1.30	0.63	207	194	1.09	0.88–1.36	0.42
Encephalocele	2,187	1,956	45	34	0.98	0.61–1.58	0.94	32	29	1.10	0.65–1.88	0.72
Craniosynostosis	2,187	1,956	239	240	0.97	0.79–1.18	0.74	212	214	0.96	0.78–1.19	0.70
Dandy walker	2,187	1,956	31	33	1.24	0.74–2.10	0.42	20	19	1.05	0.54–2.05	0.88
Holoprosencephaly	2,187	1,956	20	27	1.69	0.91–3.12	0.10	15	19	1.54	0.75–3.16	0.24
Hydrocephalus	2,187	1,956	97	84	0.92	0.67–1.26	0.61	65	61	1.00	0.69–1.45	0.99
Anophthalmia/microphthalmia	2,187	1,956	52	49	1.00	0.66–1.52	0.99	32	26	0.91	0.52–1.58	0.74
Cataract	1,571	1,373	75	56	0.82	0.56–1.19	0.29	57	42	0.86	0.56–1.32	0.49
Glaucoma	1,571	1,373	31	31	1.13	0.66–1.92	0.66	26	22	0.93	0.51–1.71	0.82
Anotia/microtia	2,187	1,956	146	98	1.01	0.76–1.34	0.93	106	72	1.09	0.79–1.52	0.59
Choanal atresia	2,187	1,956	30	23	0.79	0.44–1.40	0.41	12	13	1.01	0.44–2.29	0.99
Oral facial clefts	2,137	1,897	865	815	1.02	0.90–1.15	0.76	742	716	1.03	0.90–1.17	0.68
Cleft lip with and without cleft palate	2,137	1,897	591	519	0.97	0.84–1.11	0.64	521	470	0.98	0.84–1.13	0.75
Cleft palate	2,137	1,897	274	296	1.13	0.94–1.36	0.20	221	246	1.14	0.93–1.40	0.20
Esophageal atresia	2,187	1,956	141	124	0.96	0.73–1.25	0.74	58	53	1.00	0.67–1.49	0.99
Biliary atresia	2,187	1,956	39	21	0.61	0.35–1.07	0.08	34	20	0.63	0.35–1.13	0.12
Intestinal atresia	2,187	1,956	92	82	1.23	0.88–1.70	0.22	75	71	1.32	0.93–1.89	0.12
Anorectal atresia	2,187	1,956	210	155	0.85	0.68–1.07	0.17	91	84	1.08	0.78–1.49	0.64
Diaphragmatic hernia	2,187	1,956	147	153	1.15	0.90–1.48	0.26	113	125	1.23	0.93–1.62	0.15
Omphalocele	2,187	1,956	94	75	0.93	0.67–1.29	0.67	56	45	0.91	0.60–1.38	0.66

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Gastroschisis	2,187	1,956	255	212	1.03	0.83–1.28	0.79	230	198	1.06	0.84–1.33	0.64
Renal agenesis or hypoplasia†	2,187	1,956	29	29	1.01	0.58–1.75	0.97	24	18	0.77	0.40–1.47	0.43
Cloacal exstrophy	2,187	1,956	20	14	0.76	0.37–1.56	0.45	-	-	NE	-	-
Bladder exstrophy	2,187	1,956	13	22	1.69	0.81–3.57	0.16	12	16	1.20	0.53–2.71	0.65
Hypospadias	1,104	990	425	333	0.89	0.74–1.08	0.23	383	310	0.91	0.74–1.10	0.33
Sacral agenesis	2,187	1,956	8	9	1.21	0.44–3.32	0.71	-	-	NE	-	-
Longitudinal limb deficiency	2,187	1,956	88	82	1.10	0.79–1.52	0.58	44	53	1.27	0.83–1.94	0.28
Transverse limb deficiency	2,187	1,956	122	120	1.19	0.90–1.56	0.23	99	103	1.24	0.92–1.68	0.16
Intercalary limb deficiency	2,187	1,956	8	14	2.08	0.82–5.27	0.12	8	14	2.08	0.82–5.27	0.12
Preaxial limb deficiency	2,187	1,956	54	40	0.94	0.60–1.45	0.77	19	18	1.09	0.55–2.15	0.81
Amniotic bands	2,187	1,956	63	50	0.99	0.66–1.47	0.94	-	-	NE	-	-
Limb-body wall complex	2,187	1,956	6	10	2.96	0.98–8.88	0.05	-	-	NE	-	-
Conotruncal defects	2,187	1,956	420	410	1.11	0.94–1.30	0.21	355	353	1.09	0.92–1.29	0.31
d-Transposition of the great arteries	2,187	1,956	171	171	1.10	0.87–1.39	0.40	158	160	1.10	0.86–1.40	0.44
Tetralogy of fallot	2,187	1,956	204	191	1.05	0.84–1.31	0.65	162	161	1.07	0.84–1.36	0.60
LVOTO defects	2,187	1,956	373	354	0.92	0.78–1.09	0.35	331	318	0.92	0.77–1.10	0.35
Hypoplastic left heart syndrome	2,187	1,956	105	101	0.95	0.71–1.28	0.74	94	95	1.00	0.74–1.36	0.98
Coarctation of the aorta	2,187	1,956	208	188	0.88	0.71–1.10	0.25	180	159	0.84	0.66–1.06	0.13
Aortic stenosis	2,187	1,956	76	73	0.92	0.65–1.29	0.63	71	70	0.94	0.66–1.33	0.71
RVOTO defects	2,187	1,956	312	335	1.09	0.92–1.30	0.33	282	310	1.11	0.93–1.34	0.25
Pulmonary atresia	2,187	1,956	46	49	1.18	0.76–1.82	0.46	42	45	1.19	0.75–1.87	0.47
Tricuspid atresia	2,187	1,956	32	27	0.89	0.51–1.54	0.67	30	24	0.85	0.48–1.51	0.57
Pulmonary valve stenosis	1,957	1,810	241	267	1.11	0.91–1.36	0.28	217	249	1.15	0.94–1.41	0.18
PVS association	2,187	1,956	64	63	1.02	0.70–1.49	0.92	60	59	1.00	0.67–1.47	0.99
Ebstein anomaly	2,187	1,956	26	31	1.22	0.70–2.12	0.49	22	29	1.32	0.73–2.40	0.35
TAPVR	2,187	1,956	51	52	1.15	0.75–1.74	0.52	48	48	1.13	0.73–1.74	0.58

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Heterotaxia with CHD	2,187	1,956	75	52	0.90	0.61–1.31	0.57	6	12	2.54	0.91–7.13	0.08
AVSD	2,187	1,956	55	49	0.90	0.60–1.37	0.63	42	38	0.89	0.56–1.43	0.64
Septal defects	2,187	1,956	1,035	1,010	1.05	0.93–1.17	0.45	859	848	1.05	0.93–1.19	0.42
VSD perimembranous	2,187	1,956	455	408	0.97	0.83–1.14	0.73	390	354	0.97	0.82–1.15	0.75
VSD muscular	272	242	55	80	1.39	0.91–2.12	0.13	49	70	1.37	0.87–2.14	0.17
ASD secundum,NOS	2,187	1,956	595	604	1.06	0.92–1.21	0.45	469	492	1.08	0.92–1.25	0.35

aOR, adjusted odds ratio; CI, conficence interval; NTD, neural tube defect; LVOTO, left ventricular outflow tract obstruction; RVOTO, right ventricular outflow tract obstruction; PVS, pulmonary valve stenosis; TAPVR, total anomalous pulmonary venous return, CHD, congenital heart defect; AVSD, atrial ventricular septal defect; VSD, ventricular septal defect; ASD, atrial septal defect; NOS, not otherwise specified; NE=not estimated due to either a zero cell, less than five total cases, unstable estimates.

Congenital heart defects: subgroups represent the most common within the main grouping.

*Includes both isolated and multiple cases.

† Bilateral cases only.

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