Supplemental Material

Ambient Air Pollution and Risk of Congenital Anomalies: A Systematic Review and Meta-Analysis

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Supplemental Material, Table 1. Generic and specific congenital anomaly groups analyzed in each study.

Generic group	Specific anomaly groups analyzed	Exclusions / inclusions
Ritz et al. 2002		
Isolated cardiac defects	- Aortic defects * Atrium and atrium septum defects - Endocardial and mitral valve defects - Pulmonary artery and valve anomalies * Conotruncal defects (tetralogy of Fallot, transposition of great vessels, truncus arteriosus communis, double outlet right ventricle, aorticopulmonary window) * Ventricular septal defects (not in conotruncal)	Excluding chromosomal/syndromic cases, cases with other major anomalies
Isolated orofacial clefts	* Cleft lip with or without cleft palate * Cleft palate	Excluding chromosomal/syndromic cases, cases with other major anomalies
Multiple anomalies with cardiac defects or orofacial clefts	- Multiple defects with cardiac and/or cleft defects - Chromosomal defects with cardiac and/or cleft defects - Syndromic defects with cardiac and/or clefts defects	Excluding isolated cases
Gilboa et al. 2005		
Isolated cardiac defects	- Pulmonary artery and valve defects (pulmonary artery/valve stenosis, total anomalous pulmonary venous return, other pulmonary artery lesions, pulmonary artery/valve atresia without VSD) - Aortic artery and valve defect (aortic valve stenosis, coarctation of the aorta, interrupted aortic arch, aortic atresia, other aortic/aortic valve lesions) * Ventricular septal defects (VSD, VSD atrioventricular canal type) * Atrial and atrial septal defects (ostium secundum defect, cor tratriatum, single atrium)	Excluding chromosomal/syndromic cases and cases with other major defects
Multiple cardiac defects	* Conotruncal defects (tetralogy of Fallot, common truncus, transposition of great vessels, double outlet right ventricle) - Endocardial cushion defects and mitral valve defects (endocardial cushion defects, mitral stenosis, hypoplastic left heart)	Excluding chromosomal/syndromic cases; including cases with other major defects.
Isolated orofacial clefts	* Cleft lip with or without cleft palate * Cleft palate	Excluding chromosomal/syndromic cases and cases with other major defects
Individual cardiac defects	- Aortic valve stenosis - Atrial septal defects * Coarctation of the aorta - Endocardial cushion defects - Ostium secundum - Pulmonary artery atresia without VSD - Pulmonary valve stenosis * Tetralogy of Fallot - Ventricular septal defects	Including isolated, multiple and chromosomal/syndromic cases
Kim et al. 2007		
Birth defects	- Birth defects (unspecified)	None described
Hwang and Jaakola 2008		
Oral clefts	* Cleft lip with or without cleft palate	None described
Rankin et al. 2009		
Cardiac defects	- Atrio-ventricular septal defects * Tetralogy of Fallot - Hypoplastic left heart * Coarctation of aorta - Patent ductus arteriosus	Excluding chromosomal cases

Generic group	Specific anomaly groups analyzed	Exclusions / inclusions
	* Ventricular septal defects	
Oral clefts	* Cleft lip and palate	Excluding chromosomal cases
Other non-chromosomal anomalies	- All anomalies - Nervous system - Respiratory tract - Eye, ear, face and neck - Digestive system - Internal urogenital system - Musculoskeletal - Miscellaneous	Excluding chromosomal cases
Chromosomal anomalies	- All chromosomal anomalies	Including chromosomal cases only
Strickland et al. 2009		
Cardiac defects	* Atrial septal defect, secundum * Coarctation of the aorta (coarctation, aortic arch hypoplasia, interrupted aorctic arch type A) - Hypoplastic left heart syndrome (with or without VSD) - Patent ductus arteriosus (in term infants, persisting for >=6 weeks after delivery) - Pulmonary stenosis, valvar (valvar and unspecified pulmonary stenosis, dysplastic valve) * Tetralogy of Fallot (typical, with absent pulmonary valve, pulmonary atresia with VSD, pulmonary atresia with major aortopulmonary collateral arteries, Fallot-type double-outlet right ventricle) - Transposition of the great arteries (all types with concordant atriventricular connections and discordant ventricular arterial connections, with or without VSD or left ventricular outflow tract obstruction; double-outlet right ventricle with malpositioned great arteries) * Ventricular septal defect, muscular type * Ventricular septal defect, perimembranous type * Conotruncal defects (all under “tetralogy of Fallot” and “transposition of great arteries”; aortopulmonary window defect, other double-outlet right ventricle, interrupted aortic arch type B and unspecified, vascular rings, subarterial VSD) - Left ventricular outflow tract defect (all under “coarctation of aorta” and “hypoplastic left heart”; aortic valve atresia/stenosis, isolated bicuspid aortic valve. - Right ventricular outflow tract defect (all under “pulmonary stenosis, valvar”; pulmonary valve atresia without VSD, tricuspid valve atresia, double-chambered right ventricle, isolated supravalvar pulmonary artery stenosis)	Chromosomal cases excluded; multiple cardiac anomalies classified in separate groups only if embryologically independent
Hansen et al. 2009		
Cardiac defects	- Aortic artery and valve defects (aortic atresia, coarctation of the aorta, insufficency of the aortic valve, aortic valve stenosis, interrupted aortic arch, hypoplasia of the aorta, persistent right aortic arch, overriding aorta, other) - Pulmonary artery and valve defects (pulmonary atresia/stenosis, insufficiency of pulmonary valve, total anomalous pulmonary venous return, other) * Atrial septal defects (ASD, single common atrium, other) * Ventricular septal defects * Conotruncal defects (common truncus, transposition of the great vessels, other transposition, double outlet right ventricle, tetralogy of Fallot) - Endocardial cushion and mitral valve defects (atriventricular defect, hypoplastic left heart, mitral	None described

Generic group	Specific anomaly groups analyzed	Exclusions / inclusions
	stenosis/insufficiency, endocardial suchion defects)	
Oral clefts	- Cleft lip * Cleft lip with or without cleft palate * Cleft palate	None described
Dolk et al. 2010		
Cardiac defects	- Anomalies of cardaic chambers - Transposition of great vessels - Malformations of cardiac septa - Atrioventricular septal defects * Tetralogy of Fallot - Malformations of valves - Hypoplastic left heart syndrome - Malformations of great arteries and veins * Coarctation of aorta	Excluding chromosomal cases, Mendelian syndromes. VSDs excluded.
Oral clefts	* Cleft lip with or without palate * Cleft palate	Excluding chromosomal cases, Mendelian syndromes
Other non-chromosomal anomalies	- All anomalies - Neural tube defects - Hydrocephaly - Digestive system atresia - Bilateral renal agenesis - Cystic kidney disease - Limb reduction defects - Diaphragmetic hernia - Omphalocele - Gastroschisis - Multiple anomalies	Excluding chromosomal cases
Chromosomal anomalies	- All chromosomal anomalies - Down syndrome	Including chromosomal cases only
Marshall et al. 2010		
Oral clefts	* Cleft lip with or without cleft palate * Cleft palate	Excluding chromosomal cases
Dadvand et al. 2011a and Dadvand et al. 2011b		
Cardiac defects	- Congenital malformations of cardiac chambers and connections - Congenital malformations of cardiac septa - Congenital malformations of pulmonary and tricuspid valves - Congenital malformations of aortic and mitral valves - Congenital malformations of great arteries and veins * Ventricular septal defect * Atrial septal defect - Congenital pulmonary valve stenosis * Tetralogy of Fallot * Coarctation of aorta	Excluding chromosomal cases and cases with major anomalies in other organ systems

*Included in the meta-analyses

Supplemental Material, Table 2 – Detailed results of meta-analyses: summary risk estimates and risk estimates from individual studies

Table 2A – Carbon monoxide (CO)

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure (per 1 ppm)			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value	Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value
Atrial septal defects								
	Summary risk estimate	1337	0.10	0.87 (0.72, 1.05)	0.12	0.17	0.86 (0.75, 0.99)	0.17
	Ritz et al. 2002	385		1.01 (0.81, 1.28)			1.01 (0.76, 1.36)	
	Gilboa et al. 2005	180		0.39 (0.20, 0.76)			0.52 (0.33, 0.82)	
	Hansen et al. 2009	127		0.73 (0.45, 1.21)			0.83 (0.62, 1.12)	
	Strickland et al. 2009	379		0.76 (0.37, 1.59)			0.92 (0.74, 1.15)	
	Dadvand et al. 2011b	266		0.86 (0.38, 1.95)			0.78 (0.49, 1.23)	
Ventricular septal defects								
	Summary risk estimate	3710	<0.001	1.14 (0.66, 1.98)	0.99	<0.001	1.18 (0.82, 1.69)	0.40
	Ritz et al. 2002	260		1.33 (1.00, 1.78)			2.95 (1.44, 6.05)	
	Gilboa et al. 2005	441		1.18 (0.79, 1.75)			1.14 (0.86, 1.51)	
	Hansen et al. 2009	222		0.44 (0.28, 0.66)			0.61 (0.47, 0.78)	
	Strickland et al. 2009	1654		0.93 (0.64, 1.34)			0.98 (0.87, 1.09)	
	Dadvand et al. 2011b	1133		2.98 (2.00, 4.42)			1.66 (1.37, 2.02)	
Conotruncal defects								
	Summary risk estimate	1156	0.02	0.95 (0.57, 1.58)	0.47	0.01	0.95 (0.62, 1.44)	0.85
	Ritz et al. 2002	152		0.98 (0.67, 1.45)			0.95 (0.38, 2.38)	
	Gilboa et al. 2005	280		1.52 (0.96, 2.38)			1.46 (1.03, 2.08)	
	Hansen et al. 2009	63		0.20 (0.06, 0.61)			0.38 (0.18, 0.74)	
	Strickland et al. 2009	661		1.14 (0.68, 1.89)			1.04 (0.89, 1.21)	
Cleft lip with or without cleft palate								
	Summary risk estimate	1498	0.03	0.89 (0.66, 1.20)	0.86	0.002	0.99 (0.79, 1.24)	0.85
	Ritz et al. 2002	450		0.94 (0.76, 1.17)			0.93 (0.72, 1.20)	
	Gilboa et al. 2005	293		1.28 (0.79, 2.06)			1.26 (0.88, 1.81)	
	Hansen et al. 2009	145		0.42 (0.24, 0.69)			0.59 (0.42, 0.80)	
	Marshall et al. 2010	397		0.97 (0.48, 1.94)			1.40 (1.00, 1.90)	
	Hwang et al. 2008	653		1.00 (0.67, 1.34)			1.00 (0.91, 1.10)	

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure (per 1 ppm)			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value	Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value
Celft palate								
	Summary risk estimate	697	0.009	0.68 (0.36, 1.25)	0.30	0.06	0.78 (0.55, 1.12)	0.50
	Ritz et al. 2002	189		1.05 (0.76, 1.45)			1.06 (0.69, 1.64)	
	Gilboa et al. 2005	106		1.09 (0.49, 2.41)			1.06 (0.59, 1.89)	
	Hansen et al. 2009	100		0.61 (0.31, 1.17)			0.74 (0.49, 1.10)	
	Marshall et al. 2010	302		0.24 (0.10, 0.54)			0.50 (0.30, 0.70)	

[a] cases included in the continuous exposure analysis
[b] When heterogeneity p-value is <0.10 the summary OR from the random effects model is shown; otherwise the summary OR from the fixed effect model is shown.

Table 2B – Nitrogen dioxide (NO_2)

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure per 10 ppb			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value	Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value
Atrial septal defects								
	Summary risk estimate	952	0.81	1.10 (0.91, 1.33)	0.59	0.28	1.07 (0.90, 1.26)	0.12
	Gilboa et al. 2005	180		1.06 (0.80, 1.42)			0.61 (0.33, 1.10)	
	Strickland et al. 2009	379		1.28 (0.86, 1.87)			1.15 (0.92, 1.43)	
	Hansen et al. 2009	127		1.24 (0.54, 2.99)			1.09 (0.78, 1.55)	
	Dadvand et al. 2011b	266		1.00 (0.68, 1.45)			1.02 (0.63, 1.65)	
Ventricular septal defects								
	Summary risk estimate	3460	0.002	1.12 (0.87, 1.44)	0.84	0.03	0.92 (0.77, 1.12)	0.08
	Gilboa et al. 2005	451		0.91 (0.77, 1.08)			0.86 (0.64, 1.15)	
	Strickland et al. 2009	1654		1.18 (0.99, 1.42)			1.10 (0.99, 1.22)	
	Hansen et al. 2009	222		0.77 (0.37, 1.55)			0.90 (0.67, 1.19)	
	Dadvand et al. 2011b	1133		1.45 (1.21, 1.74)			0.78 (0.62, 1.00)	
Coarctation of the aorta								
	Summary risk estimate	756	0.31	1.20 (1.00, 1.44)	0.22	0.13	1.04 (0.86, 1.26)	0.64
	Gilboa et al. 2005	183		1.05 (0.81, 1.36)			0.96 (0.62, 1.47)	
	Strickland et al. 2009	275		1.20 (0.78, 1.83)			1.11 (0.87, 1.41)	
	Dolk et al. 2010	176		1.28 (0.82, 1.99)			1.41 (0.76, 2.62)	
	Dadvand et al. 2011b	122		1.74 (1.00, 2.50)			0.48 (0.23, 1.00)	
Tetralogy of Fallot								
	Summary risk estimate	704	0.2**3**	1.25 (1.02, 1.51)	0.80	0.06	1.04 (0.70, 1.55)	0.68
	Gilboa et al. 2005	134		1.25 (0.94, 1.67)			1.56 (0.93, 2.61)	
	Strickland et al. 2009	299		0.90 (0.59, 1.38)			0.94 (0.74, 1.20)	
	Dolk et al. 2010	146		1.30 (0.78, 2.16)			1.44 (0.71, 2.93)	
	Dadvand et al. 2011b	125		1.74 (1.00, 2.50)			0.51 (0.24, 1.07)	
Cleft lip with or without cleft palate								
	Summary risk estimate	1423	0.**43**	1.00 (0.87, 1.16)	0.27	0.25	1.06 (0.88, 1.28)	0.32
	Gilboa et al. 2005	285		0.93 (0.75, 1.14)			0.82 (0.56, 1.19)	
	Hansen et al. 2009	145		1.61 (0.65, 4.05)			1.21 (0.84, 1.75)	
	Dolk et al. 2010	586		0.93 (0.68, 1.27)			0.91 (0.59, 1.40)	

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure per 10 ppb			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value	Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value
Cleft palate	Marshall et al. 2010	407		1.15 (0.88, 1.50)			1.30 (0.90, 1.80)	
	Summary risk estimate	809	0.12	0.91 (0.76, 1.08)	0.81	0.23	0.79 (0.62, 1.01)	0.02
	Gilboa et al. 2005	104		1.24 (0.88, 1.74)			1.30 (0.72, 2.34)	
	Hansen et al. 2009	100		0.46 (0.14, 1.42)			0.73 (0.46, 1.15)	
	Dolk et al. 2010	302		0.88 (0.62, 1.26)			0.84 (0.51, 1.38)	
	Marshall et al. 2010	303		0.78 (0.59, 1.02)			0.60 (0.40, 1.00)	

[a] cases included in the continuous exposure analysis
[b] When heterogeneity p-value is <0.10 the summary OR from the random effects model is shown; otherwise the summary OR from the fixed effect model is shown.

Table 2C – Ozone (O_3)

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure per 10 ppb			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value	Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value
Atrial septal defects								
	Summary risk estimate	1307	0.08	1.10 (0.92, 1.32)	0.58	0.31	0.99 (0.83, 1.19)	0.43
	Ritz et al. 2002	385		0.85 (0.67, 1.07)			0.75 (0.52, 1.07)	
	Gilboa et al. 2005	192		1.27 (1.01, 1.61)			1.48 (0.85, 2.57)	
	Strickland et al. 2009	379		1.05 (0.88, 1.26)			1.16 (0.67, 2.00)	
	Hansen et al. 2009	127		1.06 (0.59, 1.88)			1.03 (0.77, 1.37)	
	Dadvand et al. 2011b	224		1.48 (1.00, 2.16)			0.97 (0.54, 1.74)	
Ventricular septal defects								
	Summary risk estimate	3577	0.04	0.94 (0.82, 1.08)	0.56	0.02	0.93 (0.73, 1.18)	0.68
	Ritz et al. 2002	261		1.13 (0.84, 1.52)			1.13 (0.50, 2.54)	
	Gilboa et al. 2005	490		0.82 (0.70, 0.95)			0.64 (0.48, 0.90)	
	Strickland et al. 2009	1654		1.02 (0.94, 1.12)			1.07 (0.82, 1.41)	
	Hansen et al. 2009	222		0.67 (0.44, 1.02)			0.82 (0.66, 1.01)	
	Dadvand et al. 2011b	930		1.00 (0.82, 1.22)			1.25 (0.92, 1.70)	
Conotruncal defects								
	Summary risk estimate	1164	0.64	1.07 (0.96, 1.19)	0.65	0.45	1.13 (0.89, 1.42)	0.04
	Ritz et al. 2002	151		1.36 (0.91, 2.03)			2.50 (0.82, 7.66)	
	Gilboa et al. 2005	289		1.02 (0.84, 1.24)			1.09 (0.70, 1.70)	
	Strickland et al. 2009	661		1.07 (0.93, 1.23)			1.22 (0.81, 1.85)	
	Hansen et al. 2009	63		0.96 (0.45, 2.05)			0.98 (0.67, 1.43)	
Cleft lip with or without cleft palate								
	Summary risk estimate	1950	0.20	1.10 (0.99, 1.21)	0.05	0.22	1.06 (0.96, 1.17)	0.58
	Ritz et al. 2002	450		1.13 (0.90, 1.40)			1.25 (0.80, 1.95)	
	Gilboa et al. 2005	305		1.09 (0.90, 1.31)			1.09 (0.70, 1.69)	
	Hwang et al. 2008	653		1.22 (1.03, 1.46)			1.12 (0.99, 1.27)	
	Hansen et al. 2009	145		0.67 (0.40, 1.12)			0.82 (0.63, 1.06)	
	Marshall et al. 2010	397		0.96 (0.75, 1.24)			0.90 (0.60, 1.30)	
Cleft palate								
	Summary risk estimate	702	0.79	0.99 (0.83, 1.18)	0.12	0.42	1.00 (0.79, 1.26)	0.70
	Ritz et al. 2002	189		0.95 (0.68, 1.32)			0.91 (0.51, 1.62)	

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure per 10 ppb			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value	Heterogeneity p-value	OR (95%CI)[b]	Egger test p-value
	Gilboa et al. 2005	114		1.08 (0.81, 1.45)			1.02 (0.50, 2.08)	
	Hansen et al. 2009	100		0.76 (0.38, 1.44)			0.87 (0.62, 1.20)	
	Marshall et al. 2010	299		0.98 (0.71, 1.35)			1.40 (0.90, 2.30)	

[a] of cases included in the continuous exposure analysis
[b] When heterogeneity p-value is <0.10 the summary OR from the random effects model is shown; otherwise the summary OR from the fixed effect model is shown.

Table 2D – Particulate Matter (PM_{10})

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure per 10µg/m^3			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger Test	Heterogeneity p-value	OR (95%CI)[b]	Egger Test
Atrial septal defects								
	Summary risk estimate	951	0.10	1.14 (1.01, 1.28)	0.64	0.02	1.23 (0.91, 1.67)	0.44
	Gilboa et al. 2005	189		1.33 (1.11, 1.60)			2.27 (1.43, 3.60)	
	Strickland et al. 2009	379		1.08 (0.87, 1.35)			1.12 (0.82, 1.53)	
	Hansen et al. 2009	127		1.16 (0.69, 1.93)			1.06 (0.86, 1.30)	
	Dadvand et al. 2011b	256		0.90 (0.74, 1.22)			0.97 (0.61, 1.53)	
Ventricular septal defects								
	Summary risk estimate	3410	0.12	1.03 (0.96, 1.10)	0.22	0.70	0.93 (0.84, 1.02)	0.85
	Gilboa et al. 2005	464		0.98 (0.86, 1.13)			0.98 (0.73, 1.32)	
	Strickland et al. 2009	1654		0.99 (0.88, 1.10)			0.98 (0.84, 1.15)	
	Hansen et al. 2009	222		0.71 (0.46, 1.10)			0.87 (0.73, 1.04)	
	Dadvand et al. 2011b	1070		1.11 (1.00, 1.22)			0.87 (0.68, 1.10)	
Coarctation of the aorta								
	Summary risk estimate	761	0.02	1.10 (0.88, 1.39)	0.63	0.48	1.00 (0.79, 1.26)	0.76
	Gilboa et al. 2005	198		0.88 (0.70, 1.09)			0.75 (0.48, 1.15)	
	Strickland et al. 2009	275		1.10 (0.88, 1.38)			1.15 (0.84, 1.58)	
	Dolk et al. 2010	176		1.12 (0.38, 3.30)			1.09 (0.48, 2.46)	
	Dadvand et al. 2011b	112		1.34 (1.10, 1.48)			1.00 (0.48, 2.11)	
Tetralogy of Fallot								
	Summary risk estimate	546	0.37	1.00 (0.87, 1.15)	0.62	0.02	0.91 (0.53, 1.56)	0.81
	Gilboa et al. 2005	132		1.14 (0.91, 1.41)			1.45 (0.85, 2.48)	
	Strickland et al. 2009	299		0.91 (0.74, 1.14)			0.88 (0.65, 1.20)	
	Dolk et al. 2010	146		1.68 (0.48, 5.93)			1.48 (0.57, 3.84)	
	Dadvand et al. 2011b	115		0.90 (0.67, 1.34)			0.33 (0.14, 0.75)	
Cleft lip with or without cleft palate								
	Summary risk estimate	2072	0.70	1.01 (0.96, 1.06)	0.64	0.45	1.02 (0.94, 1.11)	0.51
	Gilboa et al. 2005	290		1.09 (0.92, 1.27)			1.37 (0.94, 2.00)	
	Hwang et al. 2008	653		1.00 (0.95, 1.05)			1.00 (0.91, 1.10)	
	Hansen et al. 2009	145		1.13 (0.65, 1.93)			1.05 (0.84, 1.30)	

Anomaly group	Studies included	Total number of cases[a]	Continuous exposure per 10μg/m^3			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[b]	Egger Test	Heterogeneity p-value	OR (95%CI)[b]	Egger Test
	Dolk et al. 2010	586		0.72 (0.35, 1.49)			0.78 (0.45, 1.35)	
	Marshall et al. 2010	398		1.06 (0.83, 1.35)			1.10 (0.80, 1.50)	
Cleft palate								
	Summary risk estimate	803	0.01	0.91 (0.58, 1.41)	0.26	0.15	0.86 (0.70, 1.07)	0.58
	Gilboa et al. 2005	102		1.01 (0.76, 1.35)			1.11 (0.60, 2.06)	
	Hansen et al. 2009	100		0.40 (0.18, 0.83)			0.69 (0.50, 0.93)	
	Dolk et al. 2010	302		0.71 (0.32, 1.57)			0.77 (0.42, 1.40)	
	Marshall et al. 2010	299		1.44 (1.09, 1.89)			1.20 (0.80, 1.80)	

[a] N of cases included in the continuous exposure analysis
[b] When heterogeneity p-value is <0.10 the summary OR from the random effects model is shown; otherwise the summary OR from the fixed effect model is shown.

Table 2E – Sulfur dioxide (SO_2)

Anomaly group	Studies included[a]	Total cases[b]	Continuous exposure per 1 ppb			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[c]	Egger test	Heterogeneity p-value	OR (95%CI)[c]	Egger test
Atrial septal defects								
	Summary risk estimate [2, 5, 6, 9]	909	0.01	0.96 (0.86, 1.07)	0.68	0.01	0.85 (0.57, 1.28)	0.07
	Summary risk estimate [2, 5, 6, 10]	914	0.01	0.97 (0.87, 1.07)	0.90	0.02	0.92 (0.63, 1.33)	0.05
	Gilboa et al. 2005	137		0.81 (0.71, 0.94)			0.42 (0.22, 0.78)	
	Strickland et al. 2009	379		1.00 (0.92, 1.08)			1.00 (0.72, 1.38)	
	Hansen et al. 2009	127		1.55 (0.98, 2.52)			1.30 (0.99, 1.74)	
	Dadvand et al. 2011b	266		0.97 (0.92, 1.05)			0.73 (0.45, 1.19)	
	Dadvand et al. 2011a	271		1.00 (0.95, 1.03)			0.95 (0.61, 1.48)	
Ventricular septal defects								
	Summary risk estimate [2, 5, 6, 9]	3217	<0.001	1.03 (0.97, 1.11)	0.95	<0.001	0.96 (0.63, 1.46)	0.45
	Summary risk estimate [2, 5, 6, 10]	3056	<0.001	1.01 (0.94, 1.07)	0.60	<0.001	1.08 (0.81, 1.44)	0.12
	Summary risk estimate [2, 4, 5 , 6]					<0.001	1.05 (0.76, 1.46)	0.37
	Gilboa et al. 2005	278		1.14 (1.08, 1.21)			2.16 (1.51, 3.09)	
	Strickland et al. 2009	546		0.99 (0.95, 1.03)			0.97 (0.82, 1.14)	
	Hansen et al. 2009	222		0.75 (0.54, 1.03)			0.84 (0.69, 1.02)	
	Dadvand et al. 2011b	1133		1.03 (1.00, 1.05)			0.53 (0.41, 0.68)	
	Dadvand et al. 2011a	902		0.97 (0.97, 1.00)			0.90 (0.73, 1.11)	
	Rankin et al. 2009	415					0.78 (0.58, 1.04)	
Coarctation of the aorta								
	Summary risk estimate [2, 5, 7, 9]	682	0.71	1.04 (1.00, 1.08)	0.51	0.29	1.06 (0.89, 1.27)	0.20
	Summary risk estimate [2, 5, 7, 10]	687	0.02	1.01 (0.94, 1.07)	0.72	0.01	0.89 (0.61, 1.32)	0.29
	Summary risk estimate [2, 4, 5, 7]					0.95	1.10 (0.92, 1.31)	0.36
	Gilboa et al. 2005	109		1.08 (0.99, 1.18)			1.10 (0.63, 1.91)	
	Rankin et al. 2009	69					0.99 (0.55, 1.80)	
	Strickland et al. 2009	275		1.01 (0.93, 1.09)			1.04 (0.75, 1.43)	
	Dolk et al. 2010	176		1.03 (0.98, 1.10)			1.15 (0.90, 1.47)	
	Dadvand et al. 2011b	122		1.05 (0.97, 1.14)			0.52 (0.24, 1.11)	
	Dadvand et al. 2011a	127		0.92 (0.87, 1.00)			0.39 (0.22, 0.70)	
Tetralogy of Fallot								
	Summary risk estimate [2, 5, 7, 9]	655	0.10	1.04 (1.00, 1.08)	0.67	<0.001	0.80 (0.45, 1.41)	0.30

Anomaly group	Studies included[a]	Total cases[b]	Continuous exposure per 1 ppb			High compared to low exposure		
			Heterogeneity p-value	OR (95%CI)[c]	Egger test	Heterogeneity p-value	OR (95%CI)[c]	Egger test
	Summary risk estimate [2, 5, 7, 10]	670	0.05	1.03 (0.97, 1.09)	0.82	0.06	1.02 (0.75, 1.39)	0.42
	Summary risk estimate [2, 4, 5, 7]					0.13	1.13 (0.93, 1.36)	0.54
	Gilboa et al. 2005	85		1.09 (0.98, 1.20)			1.10 (0.61, 1.99)	
	Rankin et al. 2009	46					0.87 (0.38, 1.99)	
	Strickland et al. 2009	299		0.96 (0.88, 1.04)			0.85 (0.61, 1.17)	
	Dolk et al. 2010	146		1.08 (1.02, 1.15)			1.38 (1.07, 1.79)	
	Dadvand et al. 2011b	125		1.00 (0.92, 1.08)			0.23 (0.11, 0.49)	
	Dadvand et al. 2011a	140		1.00 (0.95, 1.05)			0.75 (0.45, 1.26)	
Cleft lip with or without cleft palate								
	Summary risk estimate [2, 3, 6, 7, 8]	1976	0.06	0.99 (0.94, 1.05)	0.22	0.01	1.06 (0.87, 1.29)	0.47
	Summary risk estimate [2, 3, 4, 6, 7, 8]					0.02	1.06 (0.89, 1.27)	0.42
	Gilboa et al. 2005	185		0.92 (0.84, 1.01)			0.75 (0.49, 1.15)	
	Hwang et al. 2008	653		0.98 (0.95, 1.02)			0.96 (0.86, 1.06)	
	Rankin et al. 2009	195					1.09 (0.71, 1.67)	
	Hansen et al. 2009	145		1.49 (1.02, 2.24)			1.27 (1.01, 1.62)	
	Dolk et al. 2010	586		0.98 (0.93, 1.03)			0.92 (0.73, 1.15)	
	Marshall et al. 2010	407		1.09 (0.97, 1.23)			1.60 (1.10, 2.20)	
Cleft palate								
	Summary risk estimate [2, 6, 7, 8]	764	0.35	1.03 (0.98, 1.07)	0.83	0.17	0.94 (0.81, 1.10)	0.83
	Gilboa et al. 2005	59		1.03 (0.90, 1.18)			1.22 (0.56, 2.66)	
	Hansen et al. 2009	100		0.75 (0.48, 1.15)			0.84 (0.64, 1.09)	
	Dolk et al. 2010	302		1.02 (0.97, 1.07)			1.09 (0.88, 1.35)	
	Marshall et al. 2010	303		1.11 (0.97, 1.27)			0.70 (0.50, 1.10)	

[a] 1: Ritz et al. 2002, 2: Gilboa et al. 2005, 3: Hwang et al. 2008, 4: Rankin et al. 2009, 5: Strickland et al. 2009, 6: Hansen et al. 2009, 7: Dolk et al. 2010, 8: Marshall et al. 2010; 9: Dadvand et al. 2011b, 10: Dadvand et al. 2011a.
[b] N of cases included in the continuous exposure analysis
[c] When heterogeneity p-value is <0.10 the summary OR from the random effects model is shown; otherwise the summary OR from the fixed effect model is shown.

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