

## **S1 Fig**

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We post it as supplied by the authors.

Supplement to: Tie-Ning Zhang, Xin-Mei Huang, Xin-Yi Zhao, Wei Wang, Ri Wen, Shan-Yan Gao.  
Risks of specific congenital anomalies in offspring of women with diabetes: A systematic review and meta-analysis of population-based studies including over 80 million births

# **Risks of specific congenital anomalies in offspring of women with diabetes: A systematic review and meta-analysis of population-based studies including over 80 million birth** **Supporting information**

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	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
<b>Congenital anomalies</b>							
Schraw 2021	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Lee 2020	MODERATE RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK	LOW RISK
Wu 2020	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Chen 2019	LOW RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK	LOW RISK
Wei 2019	LOW RISK	NO INFORMATION	MODERATE RISK	LOW RISK	NO INFORMATION	NO INFORMATION	LOW RISK
Yang 2019	LOW RISK	SERIOUS RISK	MODERATE RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Soliman 2018	CRITICAL RISK	SERIOUS RISK	MODERATE RISK	LOW RISK	SERIOUS RISK	NO INFORMATION	LOW RISK
Darke 2016	LOW RISK	MODERATE RISK	NO INFORMATION	LOW RISK	MODERATE RISK	LOW RISK	SERIOUS RISK
Lai 2016	MODERATE RISK	MODERATE RISK	LOW RISK	LOW RISK	MODERATE RISK	LOW RISK	LOW RISK
Øyen 2016	MODERATE RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Liu 2015	MODERATE RISK	SERIOUS RISK	NO INFORMATION	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Feig 2014	SERIOUS RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK	LOW RISK
Vinceti 2014	SERIOUS RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	NO INFORMATION	LOW RISK
Bell 2012	CRITICAL RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK
Bánhidý 2010	MODERATE RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK
Peticca 2009	MODERATE RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	NO INFORMATION	LOW RISK
Sharpe 2005	MODERATE RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Von Kries 1997	CRITICAL RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	NO INFORMATION	LOW RISK
Janssen 1996	MODERATE RISK	MODERATE RISK	SERIOUS RISK	LOW RISK	MODERATE RISK	NO INFORMATION	LOW RISK
KEY		LOW RISK	MODERATE RISK	SERIOUS RISK	CRITICAL RISK	NO INFORMATION	

Fig A. Risk of bias summary: effect on congenital anomalies in offspring with pre-gestational diabetes

	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
<b>Congenital heart defect</b>							
Arendt 2021	MODERATE RISK	SERIOUS RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK
Schraw 2021	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Wu 2020	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Yang 2019	LOW RISK	SERIOUS RISK	MODERATE RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Billionnet 2017	SERIOUS RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK	LOW RISK
Leirgul 2016	MODERATE RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK
Øyen 2016	MODERATE RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Liu 2015	MODERATE RISK	SERIOUS RISK	NO INFORMATION	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Vinceti 2014	SERIOUS RISK	NO INFORMATION	LOW RISK	LOW RISK	NO INFORMATION	NO INFORMATION	LOW RISK
Bell 2012	CRITICAL RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK
Garne 2012	MODERATE RISK	SERIOUS RISK	NO INFORMATION	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Bánhidý 2010	MODERATE RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK
Correa 2008	MODERATE RISK	LOW RISK	LOW RISK	LOW RISK	LOW RISK	NO INFORMATION	LOW RISK
Macintosh 2006	CRITICAL RISK	MODERATE RISK	LOW RISK	LOW RISK	MODERATE RISK	LOW RISK	LOW RISK
Yang 2006	SERIOUS RISK	MODERATE RISK	NO INFORMATION	LOW RISK	MODERATE RISK	NO INFORMATION	LOW RISK
Sharpe 2005	MODERATE RISK	SERIOUS RISK	LOW RISK	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Loffredo 2001	LOW RISK	SERIOUS RISK	NO INFORMATION	LOW RISK	SERIOUS RISK	LOW RISK	LOW RISK
Janssen 1996	MODERATE RISK	MODERATE RISK	SERIOUS RISK	LOW RISK	MODERATE RISK	NO INFORMATION	LOW RISK
<div>KEY</div> <div> <div>LOW RISK</div> <div>MODERATE RISK</div> <div>SERIOUS RISK</div> <div>CRITICAL RISK</div> <div>NO INFORMATION</div> </div>							

**Fig B. Risk of bias summary: effect on congenital heart defects in offspring with pre-gestational diabetes**

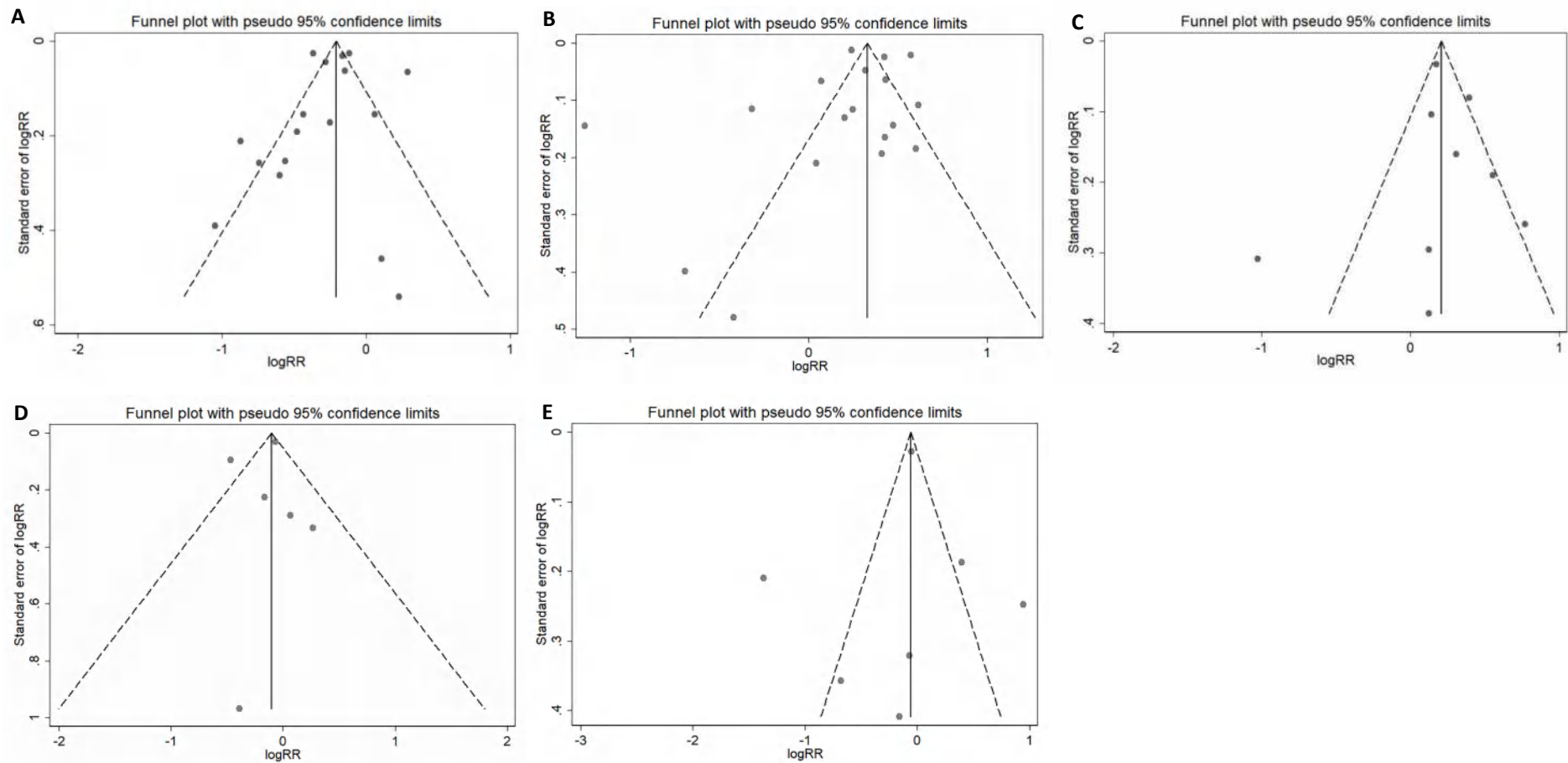
	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result						
Congenital anomalies													
Schraw 2021													
Lee 2020													
Oliveira-Brancati 2020													
Seghieri 2020													
Wu 2020													
Chen 2019													
Hildén 2019													
Yang 2019													
Soliman 2018													
Lai 2016													
Feig 2014													
Wu 2012													
Bánhidý 2010													
Peticca 2009													
Janssen 1996													
<table><tr><td>KEY</td><td> LOW RISK</td><td> MODERATE RISK</td><td> SERIOUS RISK</td><td> CRITICAL RISK</td><td> NO INFORMATION</td></tr></table>								KEY	LOW RISK	MODERATE RISK	SERIOUS RISK	CRITICAL RISK	NO INFORMATION
KEY	LOW RISK	MODERATE RISK	SERIOUS RISK	CRITICAL RISK	NO INFORMATION								

Fig C. Risk of bias summary: effect on congenital anomalies in offspring with gestational diabetes

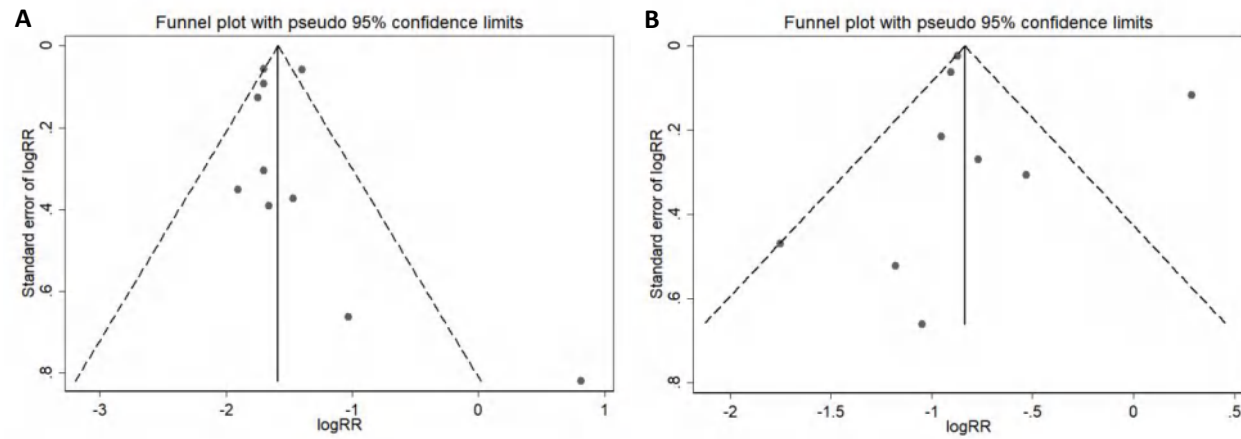


	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
Congenital heart defects							
Schraw 2021	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Wu 2020	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Yang 2019	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Billionnet 2017	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Leirgul 2016	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Øyen 2016	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Liu 2015	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Alverson 2011	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Bánhidý 2010	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Correa 2008	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
Janssen 1996	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>	<div></div>
KEY		<div></div> LOW RISK	<div></div> MODERATE RISK	<div></div> SERIOUS RISK	<div></div> CRITICAL RISK	<div></div> NO INFORMATION	

**Fig D. Risk of bias summary: effect on congenital heart defects in offspring with gestational diabetes**

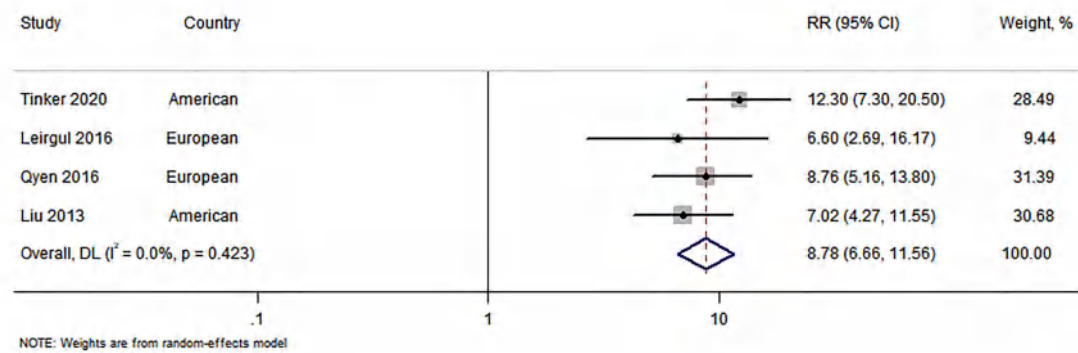


**Fig E. Funnel plots of the relative risks of population-based studies on pre-gestational diabetes and the risk of congenital anomalies.** A. Overall congenital anomalies (Begg's test  $P = 0.880$ , Egger's test  $P = 0.304$ ). B. Congenital heart defects (Begg's test  $P = 0.596$ , Egger's test  $P = 0.845$ ). C. Ventricular septal defects (Begg's test  $P = 1.000$ , Egger's test  $P = 0.935$ ). D. Congenital anomalies of genitourinary system (Begg's test  $P = 0.951$ , Egger's test  $P = 0.094$ ). E. Congenital anomalies of musculoskeletal system (Begg's test  $P = 0.640$ , Egger's test  $P = 0.525$ ). Log RR: natural logarithm of relative risk.

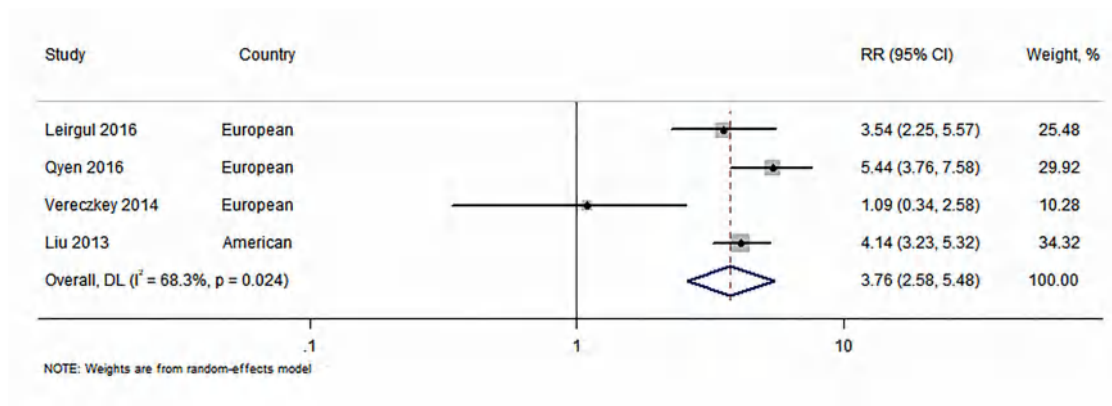


**Fig F. Funnel plots of the relative risks of population-based studies on gestational diabetes mellitus and the risk of congenital anomalies.** A. Overall congenital anomalies (Begg's test  $P = 0.392$ , Egger's test  $P = 0.323$ ). B. Congenital heart defects (Begg's test  $P = 0.837$ , Egger's test  $P = 0.885$ ). Log RR: natural logarithm of relative risk.

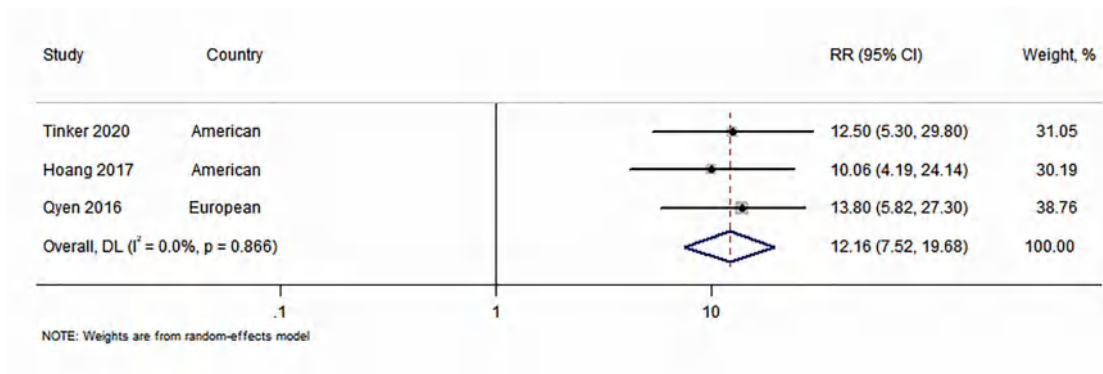




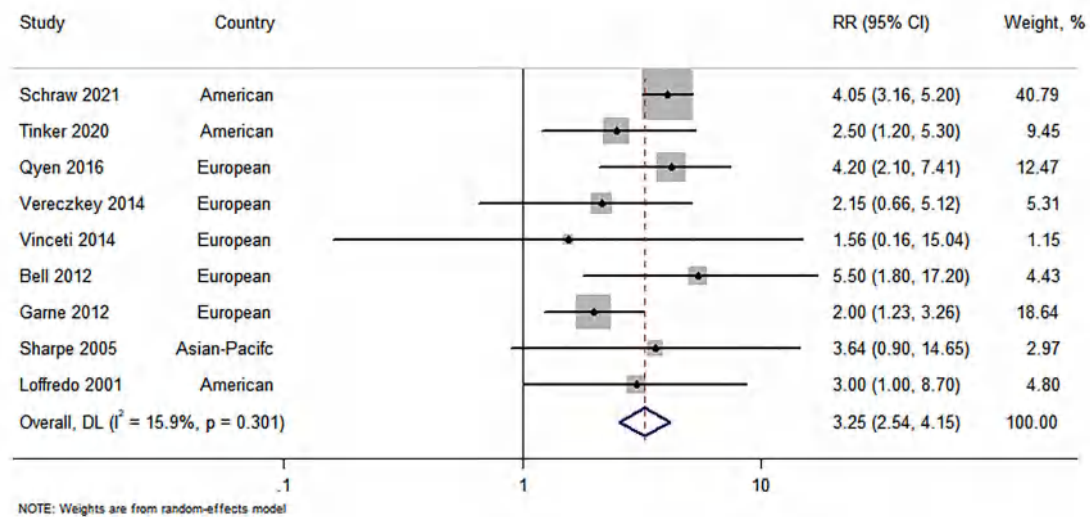
**Fig G1. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of heterotaxia (RR = 8.78, 95% CI, 6.66 to 11.56;  $I^2 = 0.0\%$ ,  $P = 0.423$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



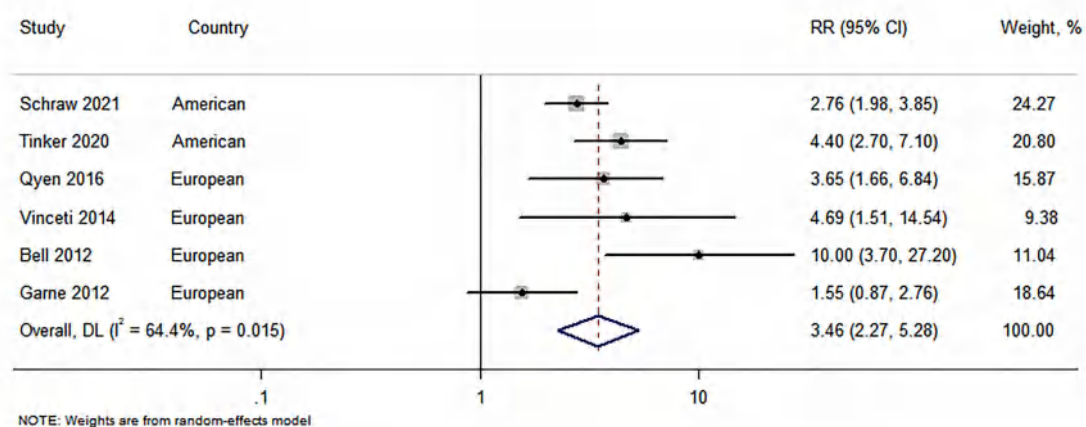
**Fig G2. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of conotruncal defects (RR = 3.76, 95% CI, 2.58 to 5.48;  $I^2 = 68.3\%$ ,  $P = 0.024$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



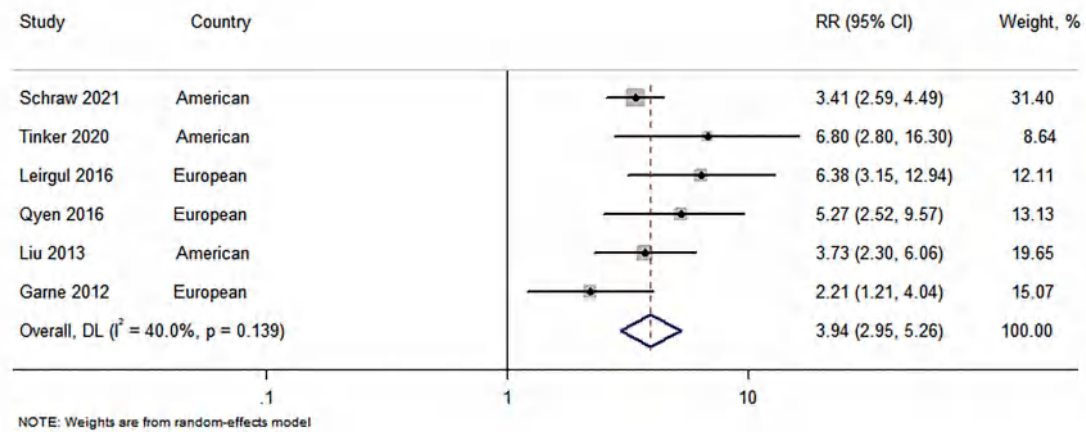
**Fig G3. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of truncus arteriosus (RR = 12.16, 95% CI, 7.52 to 19.68;  $I^2 = 0.0\%$ ,  $P = 0.866$ ).** DL, DerSimonian and Laird random-effects model; RR, relative risk.



**Fig G4. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of transposition of great vessels (RR = 3.25, 95% CI, 2.54 to 4.15;  $I^2 = 15.9\%$ ,  $P = 0.301$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

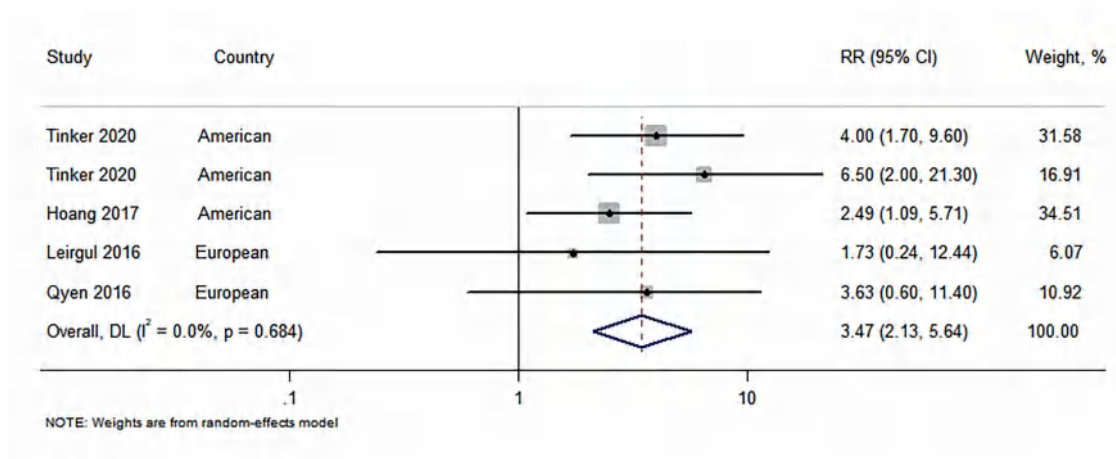


**Fig G5. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of tetralogy of Fallot (RR = 3.46, 95% CI, 2.27 to 5.28;  $I^2 = 64.4\%$ ,  $P = 0.015$ ).** DL, DerSimonian and Laird random-effects model; RR, relative risk.

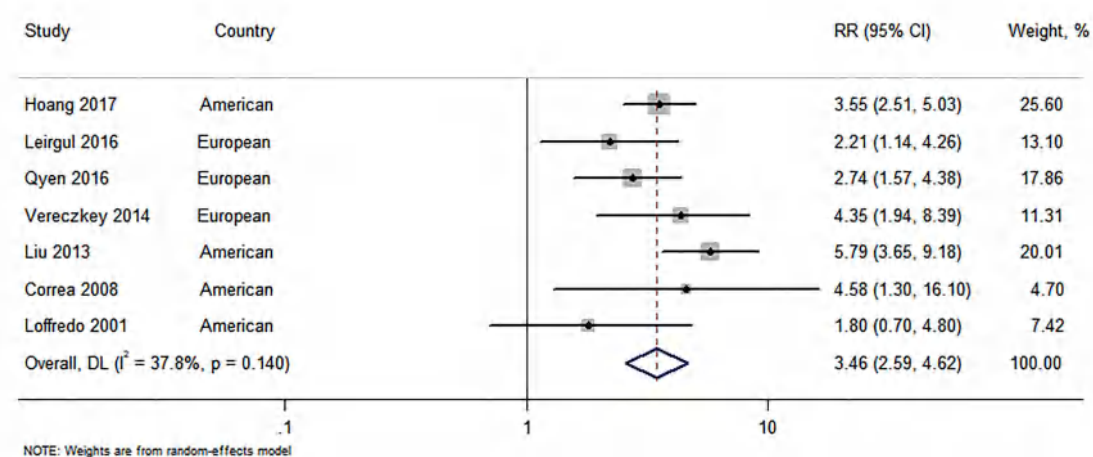


**Fig G6. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of atrioventricular septal defects (RR = 3.94, 95% CI, 2.95 to 5.26;  $I^2 = 40.0\%$ ,  $P = 0.139$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

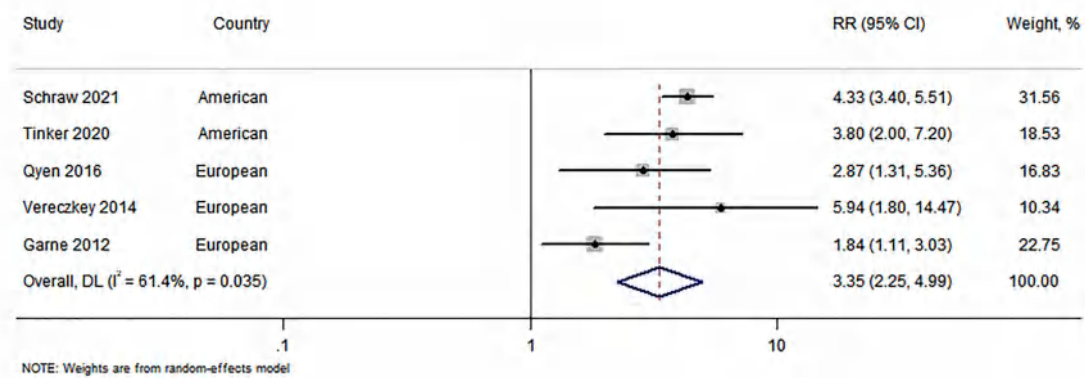




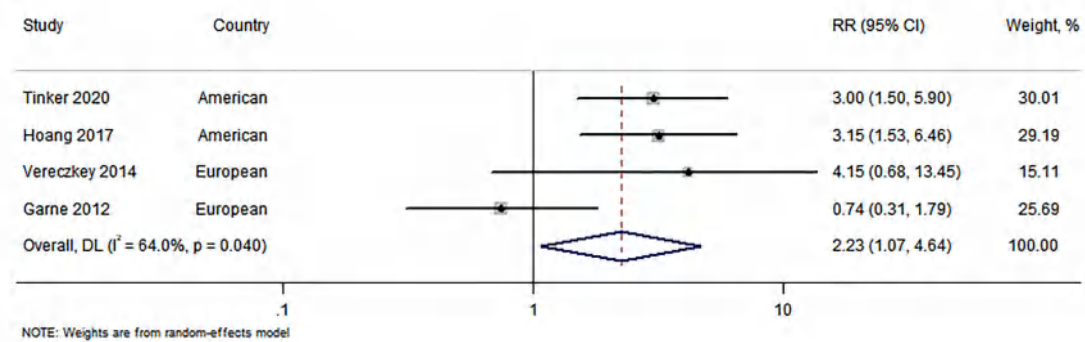
**Fig G7. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of anomalous pulmonary venous return (RR = 3.47, 95% CI, 2.13 to 5.64;  $I^2 = 0.0\%$ ,  $P = 0.684$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



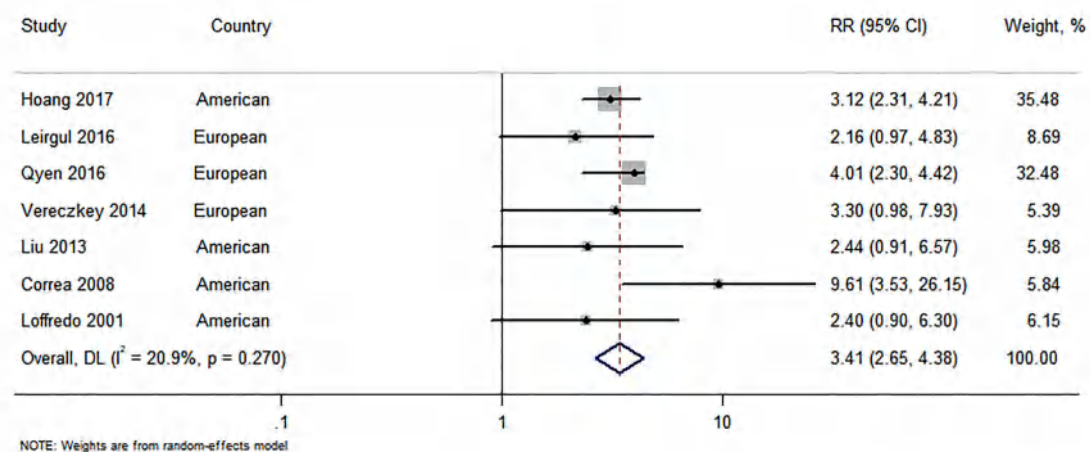
**Fig G8.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of left ventricular outflow tract (RR = 3.46, 95% CI, 2.59 to 4.62;  $I^2 = 37.8\%$ ,  $P = 0.140$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.



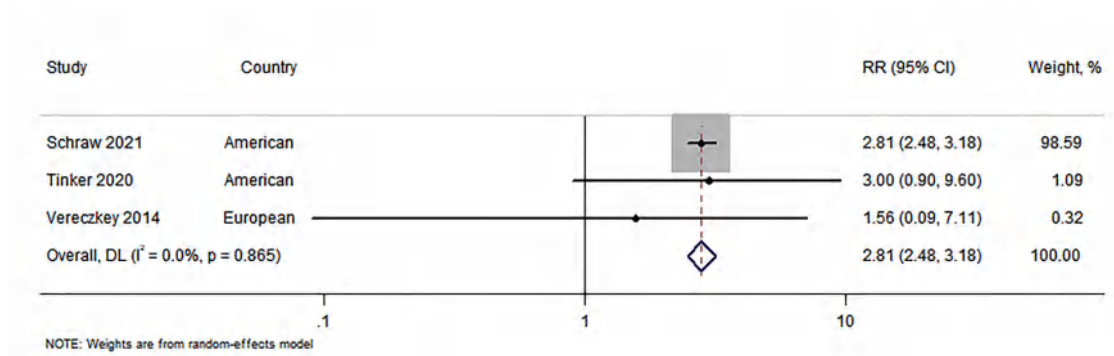
**Fig G9. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of coarctation of aorta (RR = 3.35, 95%CI, 2.25 to 4.99;  $I^2 = 61.4\%$ ,  $P = 0.035$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig G10. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of hypoplastic left heart (RR = 2.23, 95% CI, 1.07 to 4.64;  $I^2 = 64.0\%$ ,  $P = 0.040$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

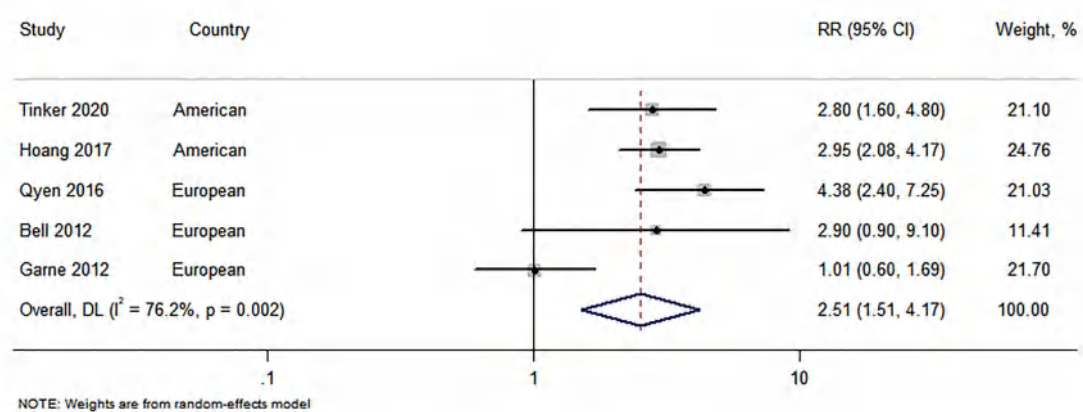


**Fig G11. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of right ventricular outflow tract (RR = 3.41, 95% CI, 2.65 to 4.38;  $I^2 = 20.9\%$ ,  $P = 0.270$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

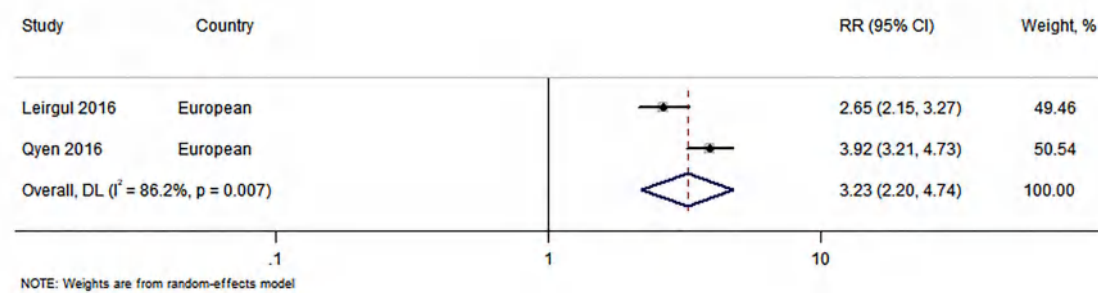


**Fig G12. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of pulmonary artery anomalies (RR = 2.81, 95% CI, 2.48 to 3.18;  $I^2 = 0.0\%$ ,  $P = 0.865$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

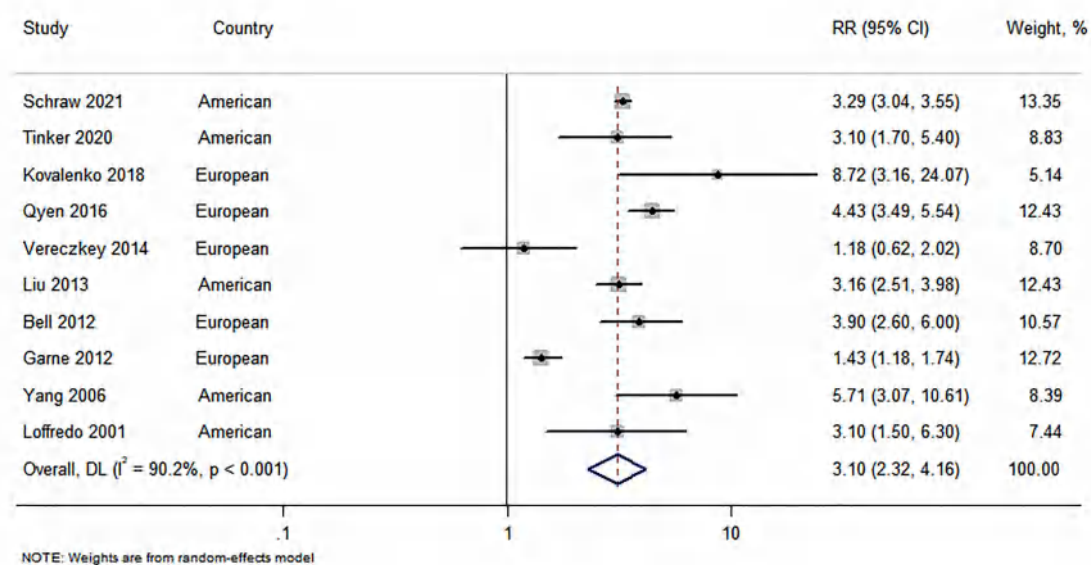




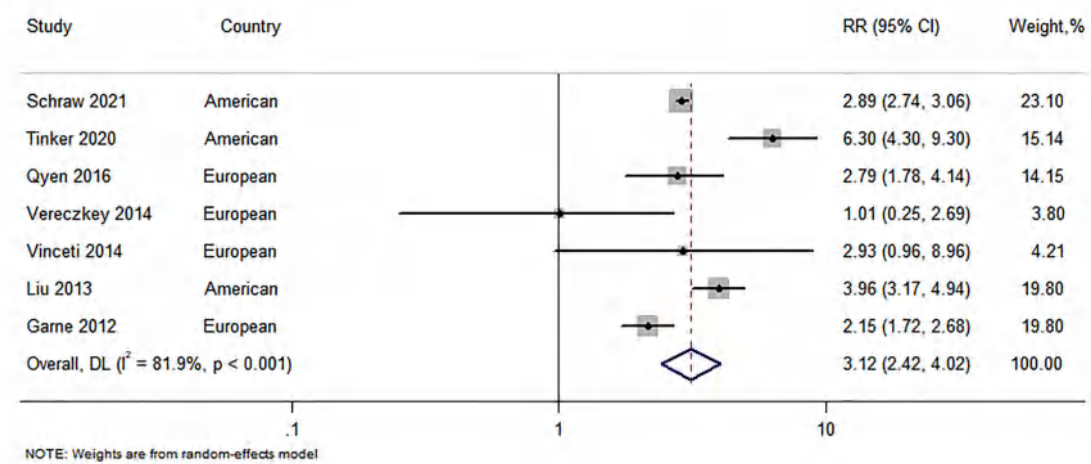
**Fig G13. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of pulmonary valve stenosis (RR = 2.51, 95% CI, 1.51 to 4.17;  $I^2 = 76.2\%$ ,  $P = 0.002$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



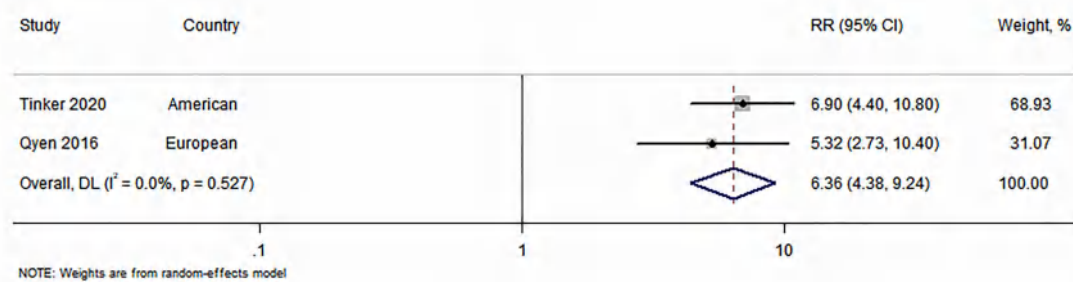
**Fig G14. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of septal defects (RR = 3.23, 95% CI, 2.20 to 4.74;  $I^2 = 86.2\%$ ,  $P = 0.007$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



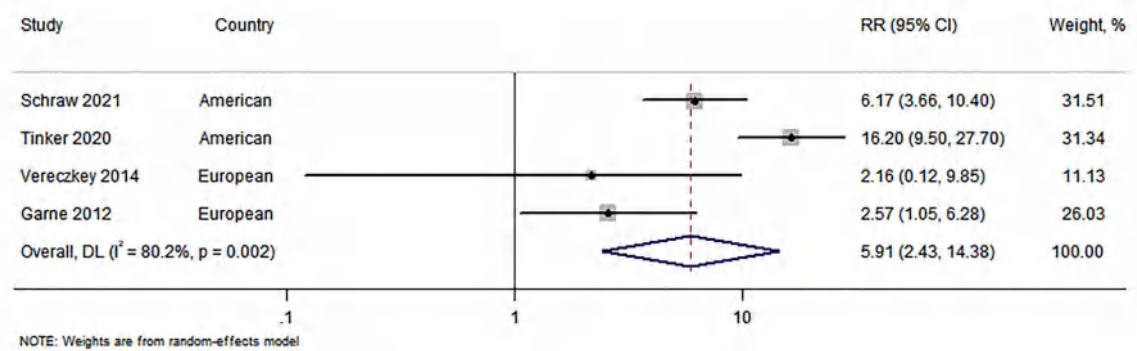
**Fig G15. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of ventricular septal defects (RR = 3.10, 95% CI, 2.32 to 4.16;  $I^2 = 90.2\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig G16. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of atrial septal defects (RR = 3.12, 95% CI, 2.42 to 4.02;  $I^2 = 81.9\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

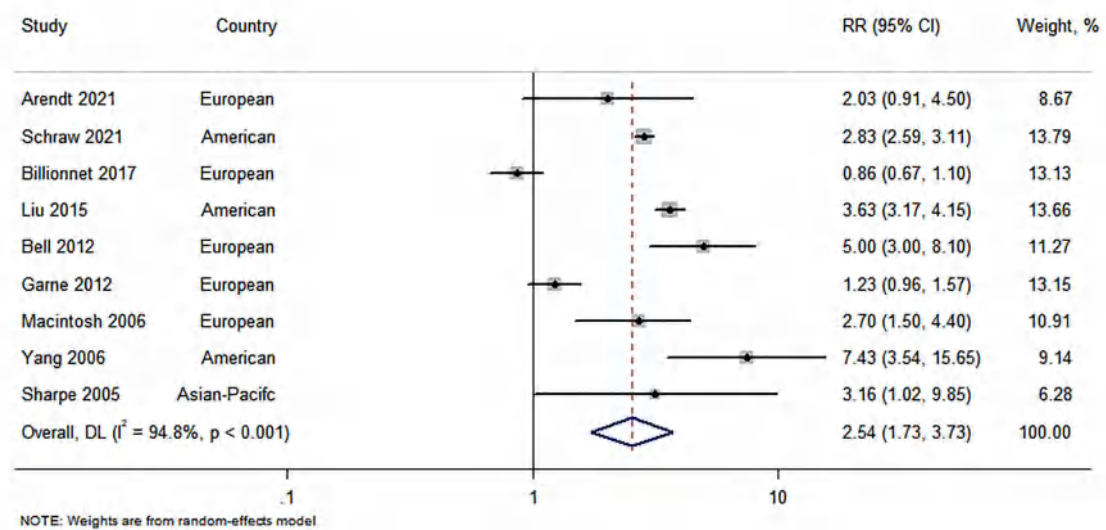


**Fig G17. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of ventricular septal defect and atrial septal defects (RR = 6.36, 95% CI, 4.38 to 9.24;  $I^2 = 0.0\%$ ,  $P = 0.527$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

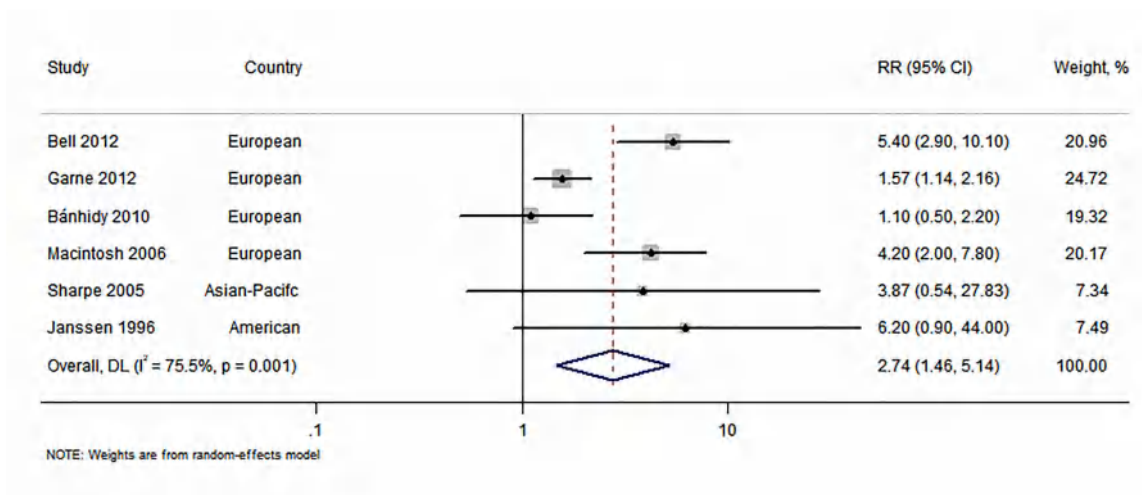


**Fig G18. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of single ventricle (RR = 5.91, 95% CI, 2.43 to 14.38;  $I^2 = 80.2\%$ ,  $P = 0.002$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

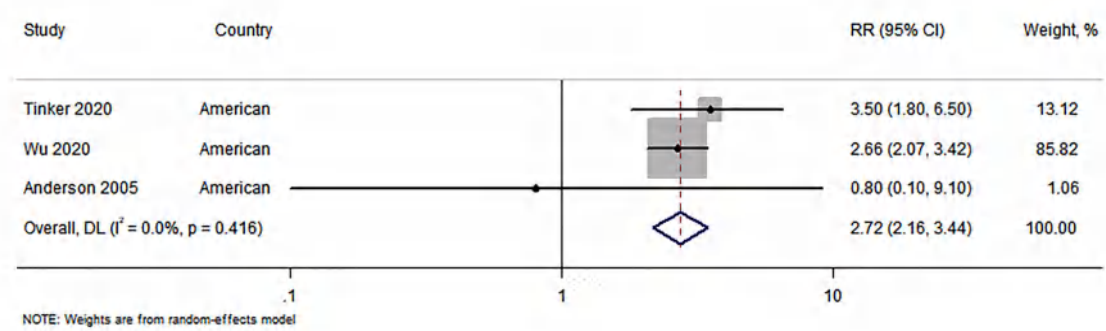




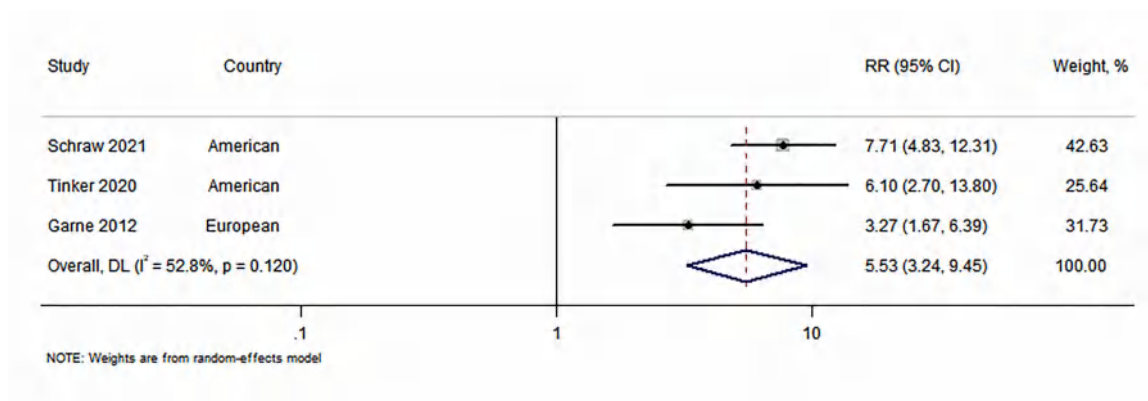
**Fig H1. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of congenital anomalies of nervous system (RR = 2.54, 95% CI, 1.73 to 3.73;  $I^2 = 94.8\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



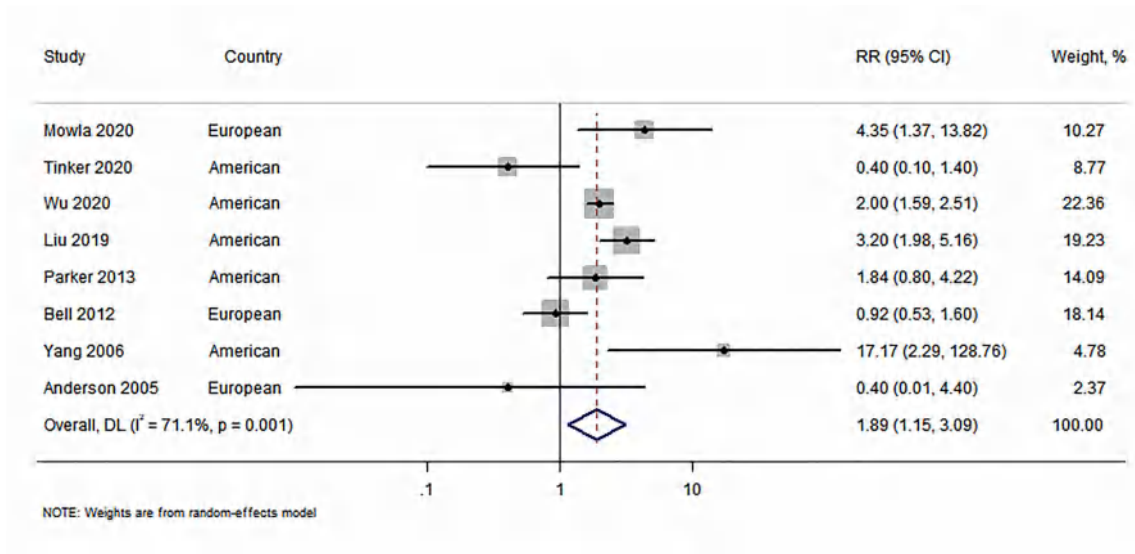
**Fig H2. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of neural tube defects (RR = 2.74, 95% CI, 1.46 to 5.14;  $I^2 = 75.5\%$ ,  $P = 0.001$ ).** DL, DerSimonian and Laird random-effects model; RR, relative risk.



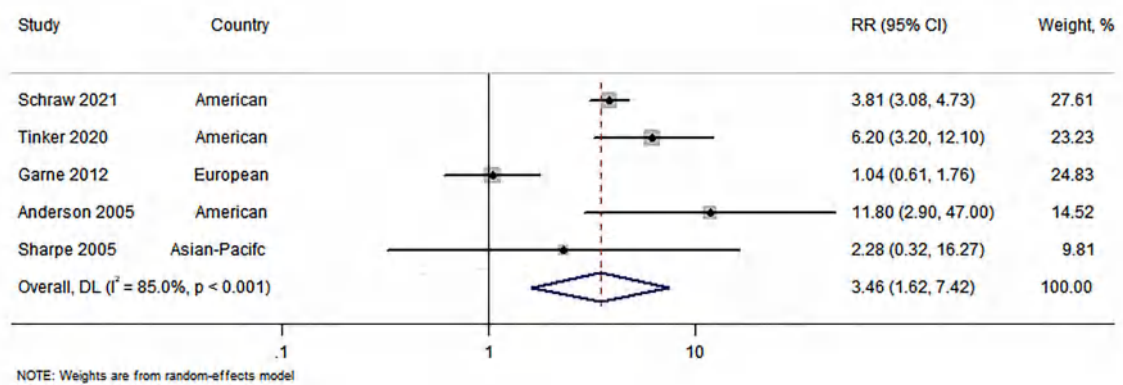
**Fig H3.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of anencephaly (RR = 2.72, 95% CI, 2.16 to 3.44;  $I^2 = 0.0\%$ ,  $P = 0.416$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.



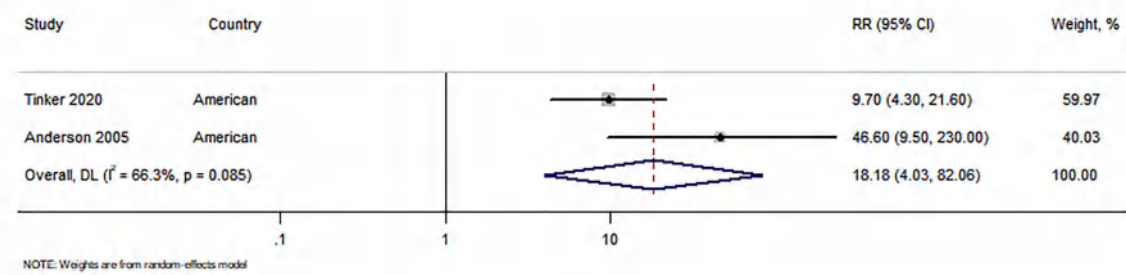
**Fig H4. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of encephalocele (RR = 5.53, 95% CI, 3.24 to 9.45;  $I^2 = 52.8\%$ ,  $P = 0.120$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



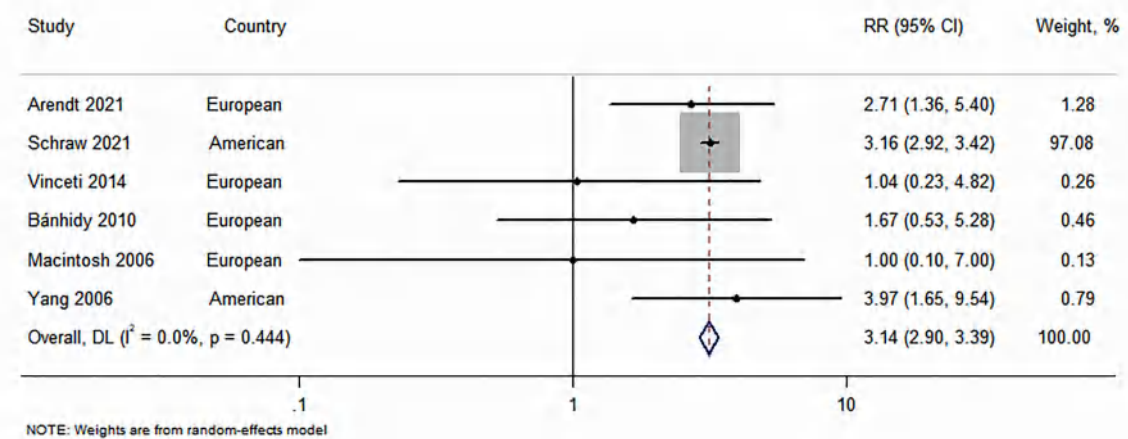
**Fig H5.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of spina bifida (RR = 1.89, 95% CI, 1.15 to 3.09;  $I^2 = 71.1\%$ ,  $P = 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.



**Fig H6. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of hydrocephaly (RR = 3.46, 95% CI, 1.62 to 7.42;  $I^2 = 85.0\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

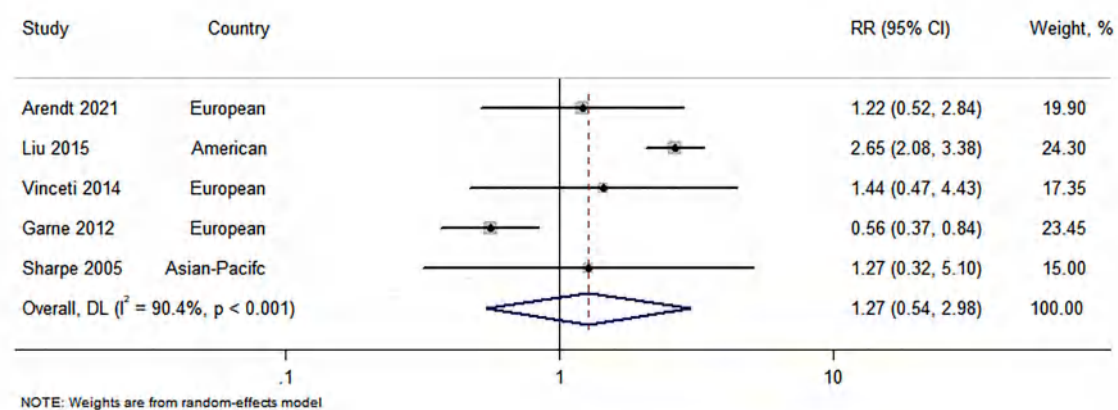


**Fig H7. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of holoprosencephaly (RR = 18.18, 95% CI, 4.03 to 82.06;  $I^2 = 66.3\%$ ,  $P = 0.085$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

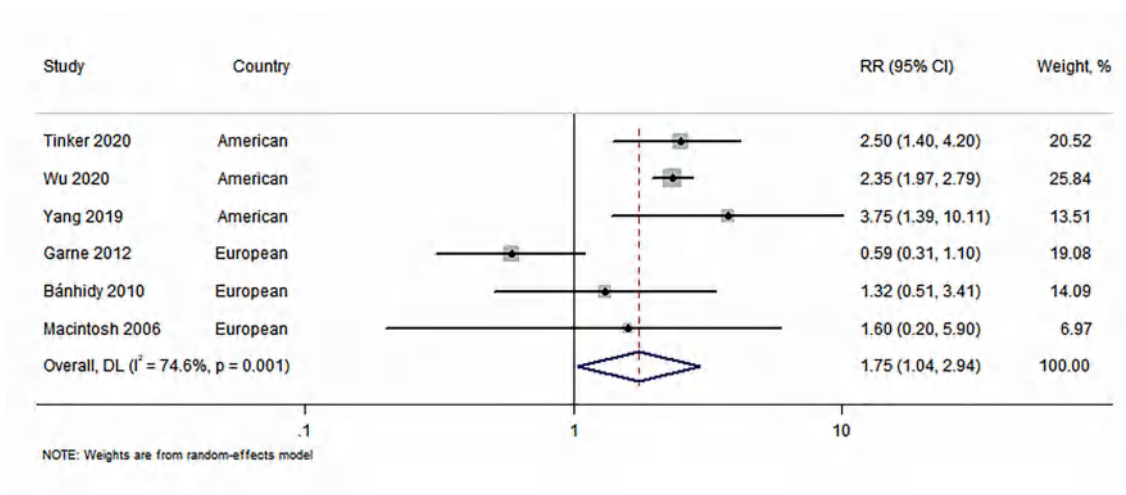


**Fig H8.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of eye, ear, face, and neck (RR = 3.14, 95% CI, 2.90 to 3.39;  $I^2 = 0.0\%$ ,  $P = 0.444$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.

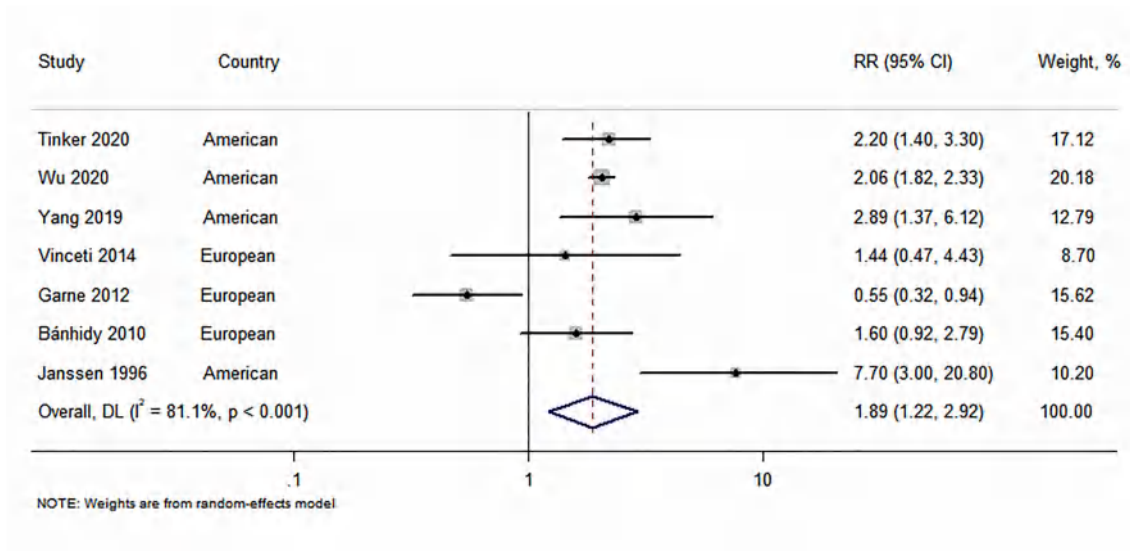




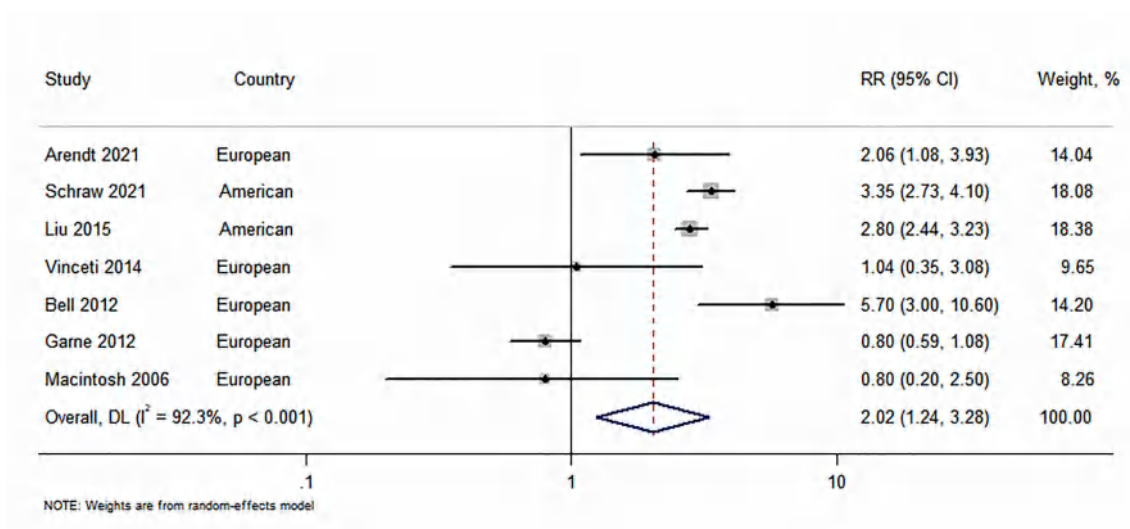
**Fig H9. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of orofacial clefts (RR = 1.27, 95% CI, 0.54 to 2.98;  $I^2 = 90.4\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



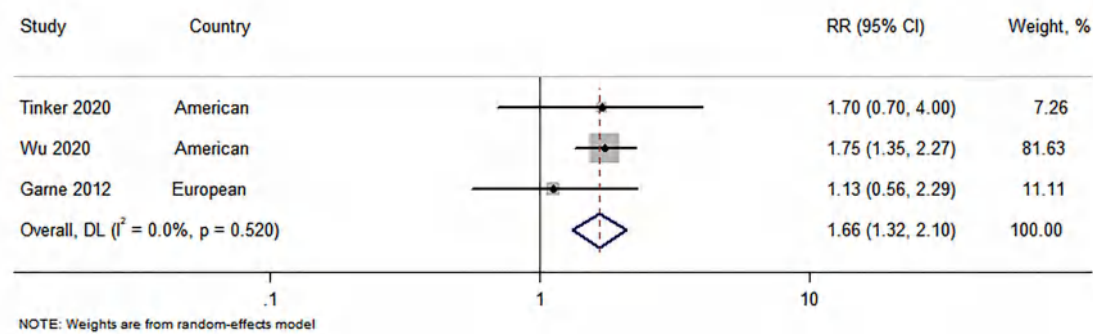
**Fig H10. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of cleft palate (RR = 1.75, 95% CI, 1.04 to 2.94;  $I^2 = 74.6\%$ ,  $P = 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



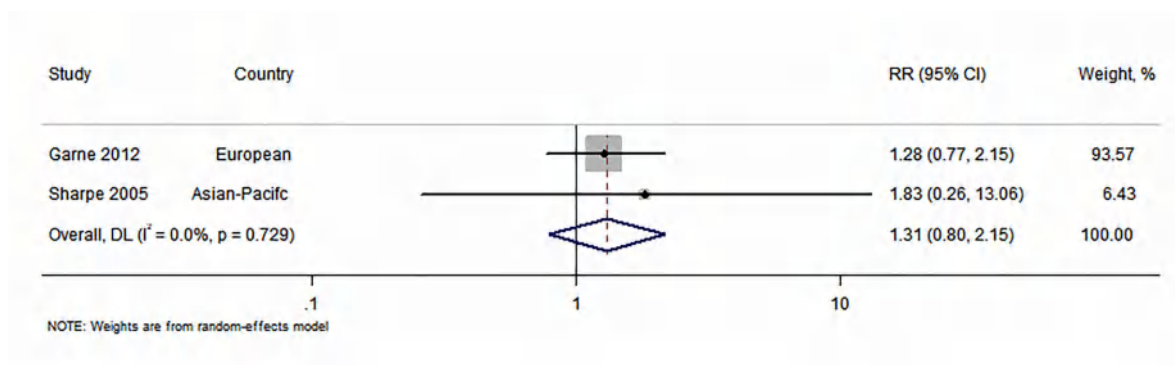
**Fig H11. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of cleft lip with or without palate (RR = 1.89, 95% CI, 1.22 to 2.92;  $I^2 = 81.1\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



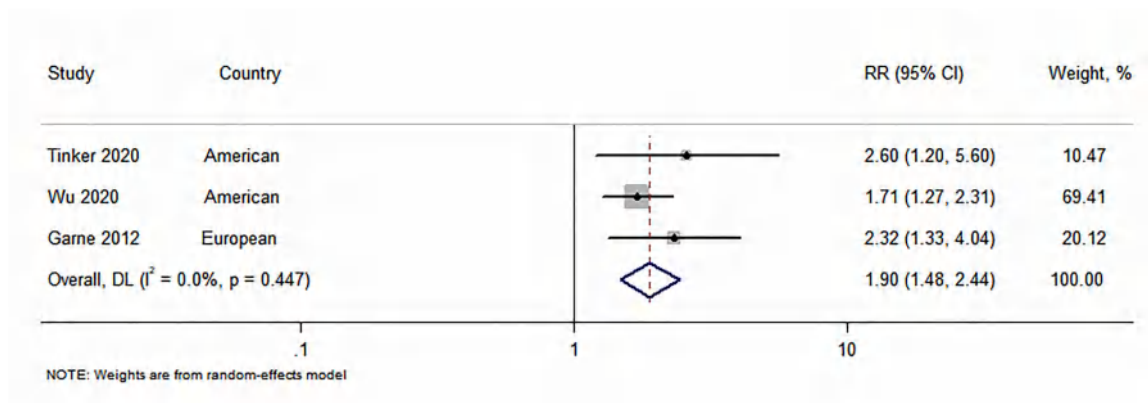
**Fig H12. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of congenital anomalies of digestive system (RR = 2.02, 95% CI, 1.24 to 3.28;  $I^2 = 92.3\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



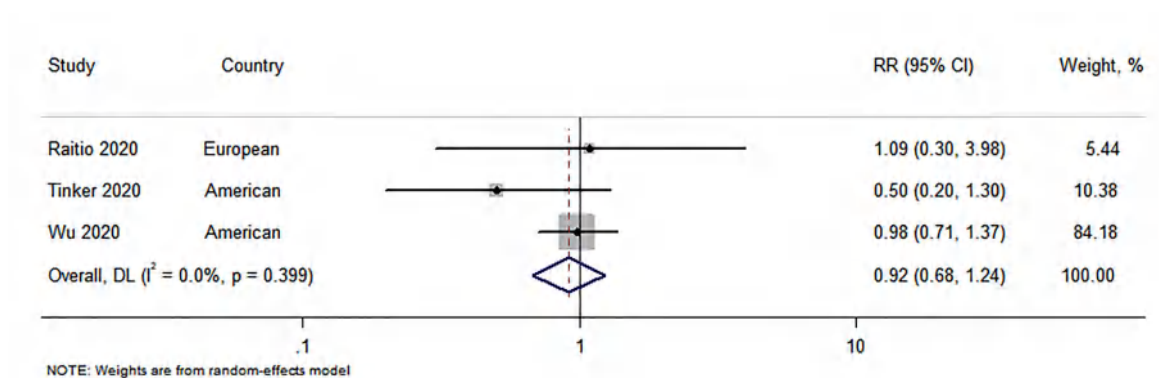
**Fig H13. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of diaphragmatic hernia (RR = 1.66, 95% CI, 1.32 to 2.10;  $I^2 = 0.0\%$ ,  $P = 0.520$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig H14. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of abdominal wall defects (RR = 1.31, 95% CI, 0.80 to 2.15;  $I^2 = 0.0\%$ ,  $P = 0.729$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

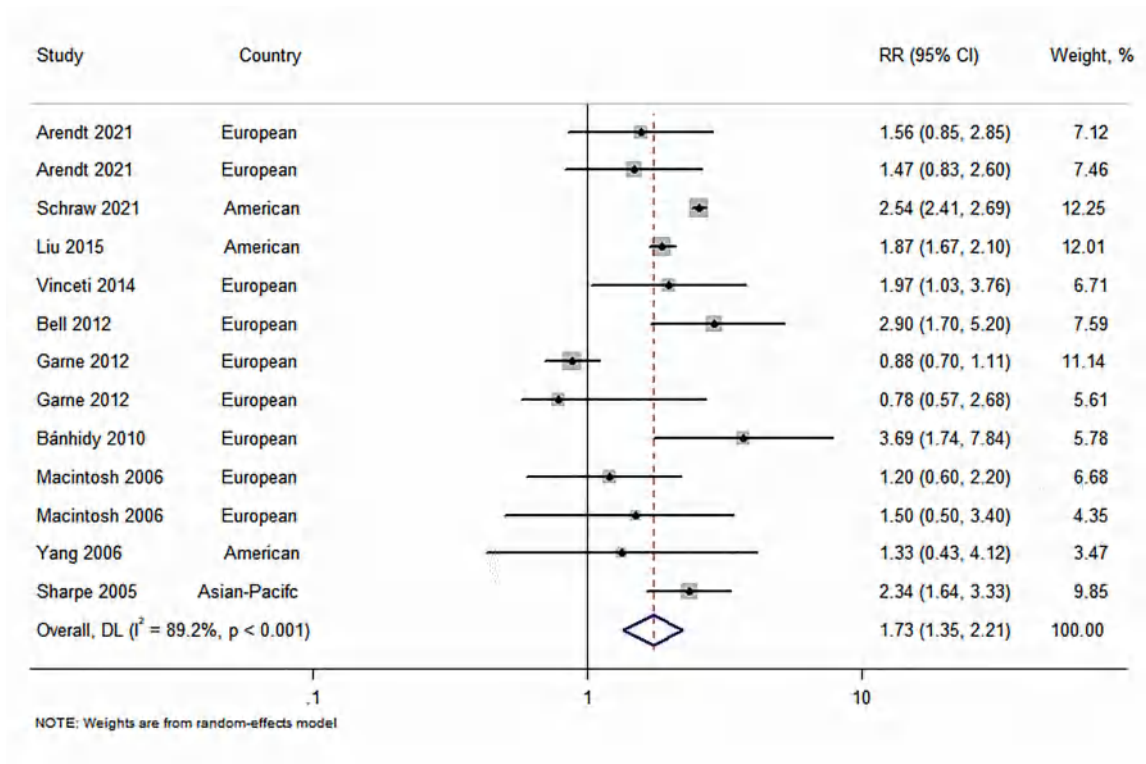


**Fig H15. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of omphalocele (RR = 1.90, 95% CI, 1.48 to 2.44;  $I^2 = 0.0\%$ ,  $P = 0.447$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

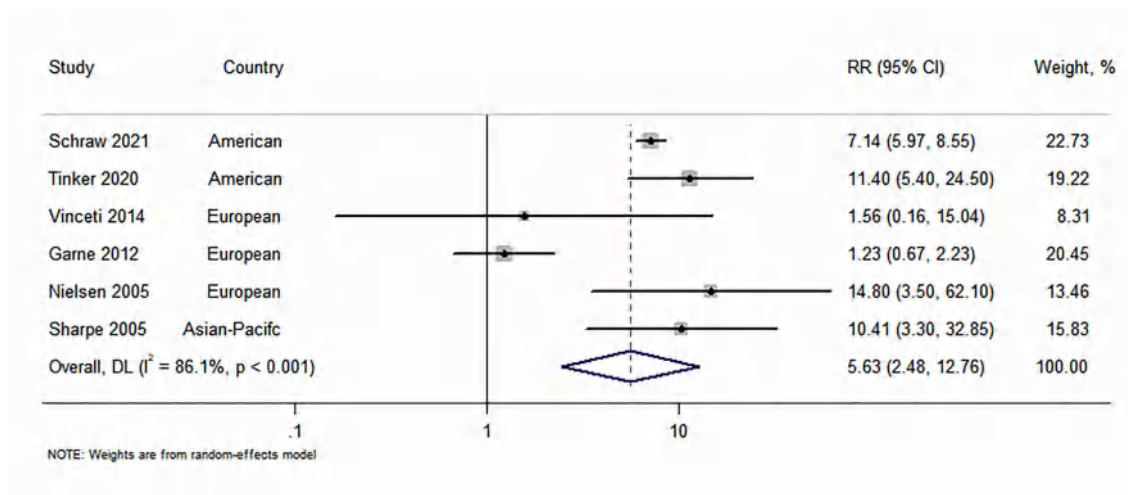


**Fig H16. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of gastroschisis (RR = 0.92, 95% CI, 0.68 to 1.24;  $I^2 = 0.0\%$ ,  $P = 0.399$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

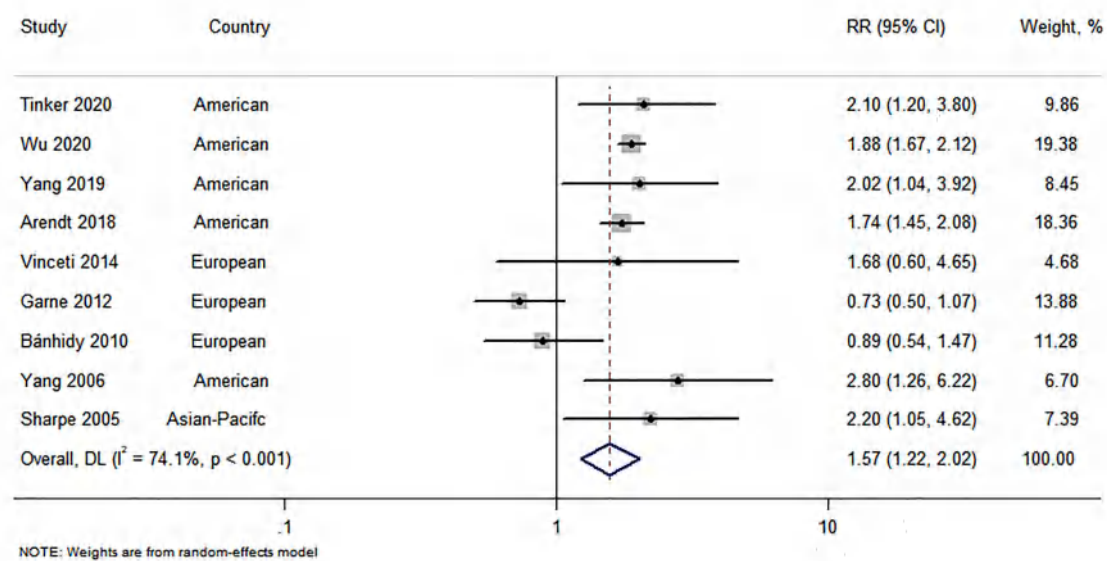




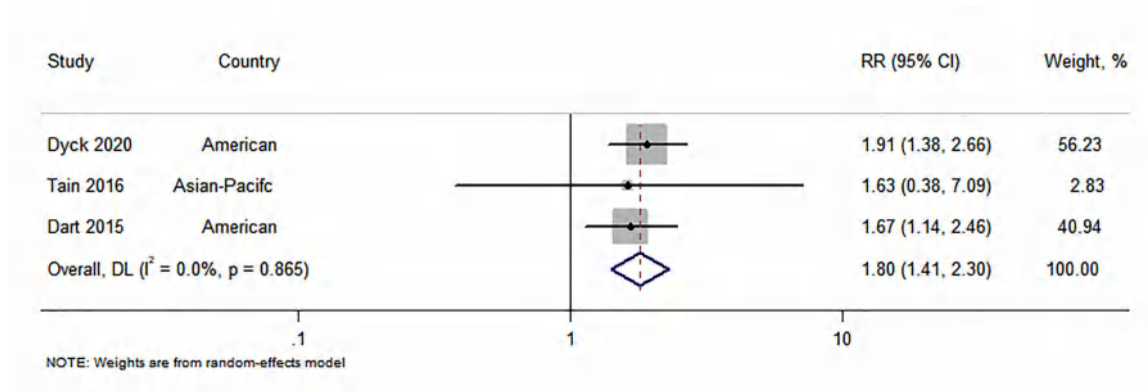
**Fig H17. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of congenital anomalies of genitourinary system (RR = 1.73, 95% CI, 1.35 to 2.21;  $I^2 = 89.2\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



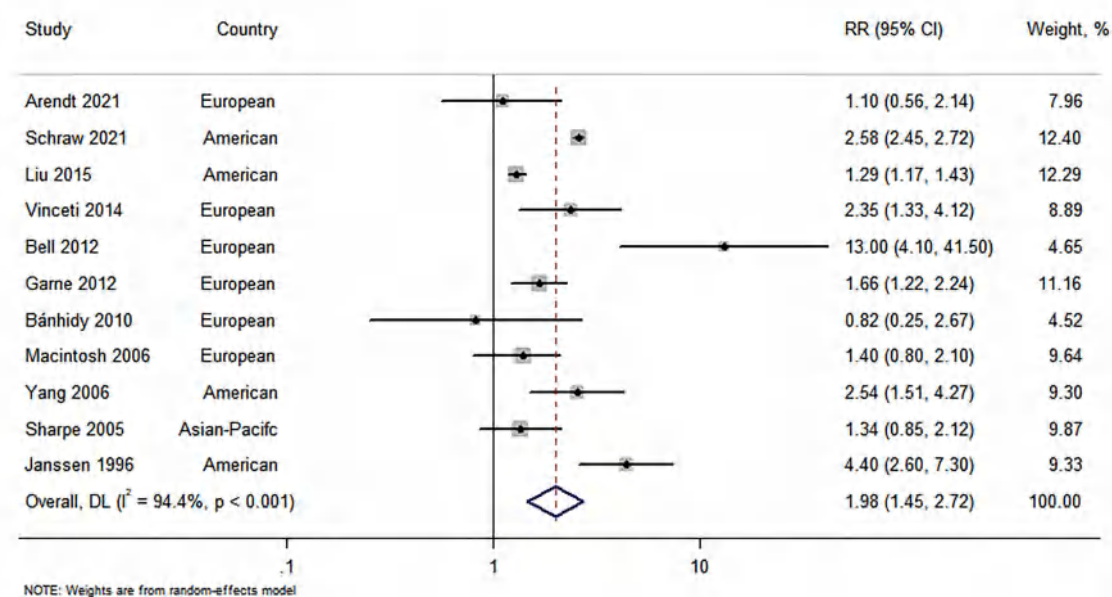
**Fig H18. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of renal agenesis/dysgenesis (RR = 5.63, 95% CI, 2.48 to 12.76;  $I^2 = 86.1\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



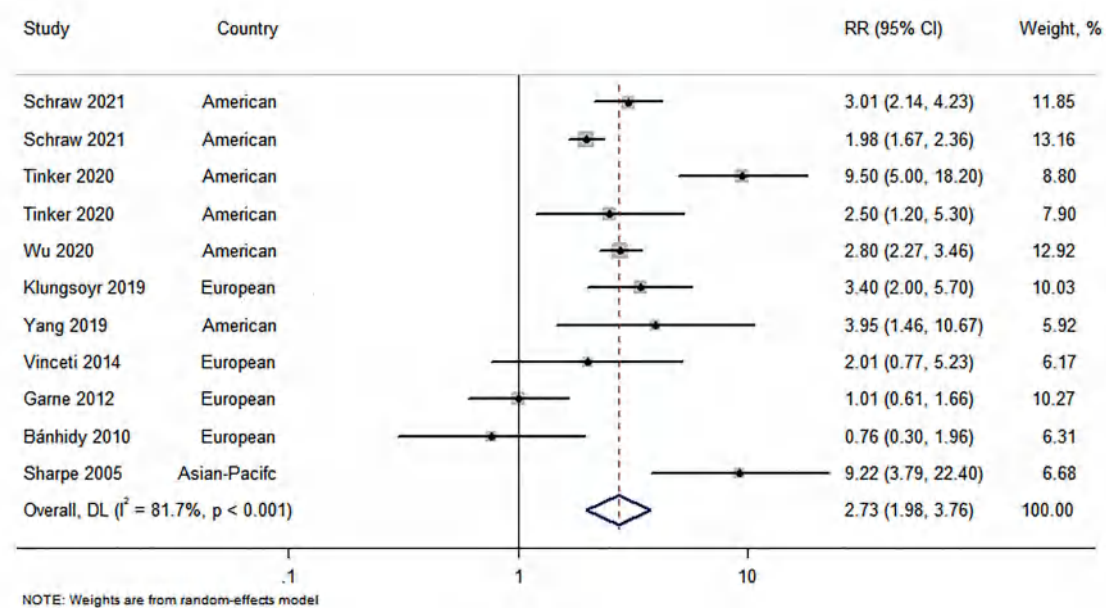
**Fig H19. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of hypospadias (RR = 1.57, 95% CI, 1.22 to 2.02;  $I^2 = 74.1\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



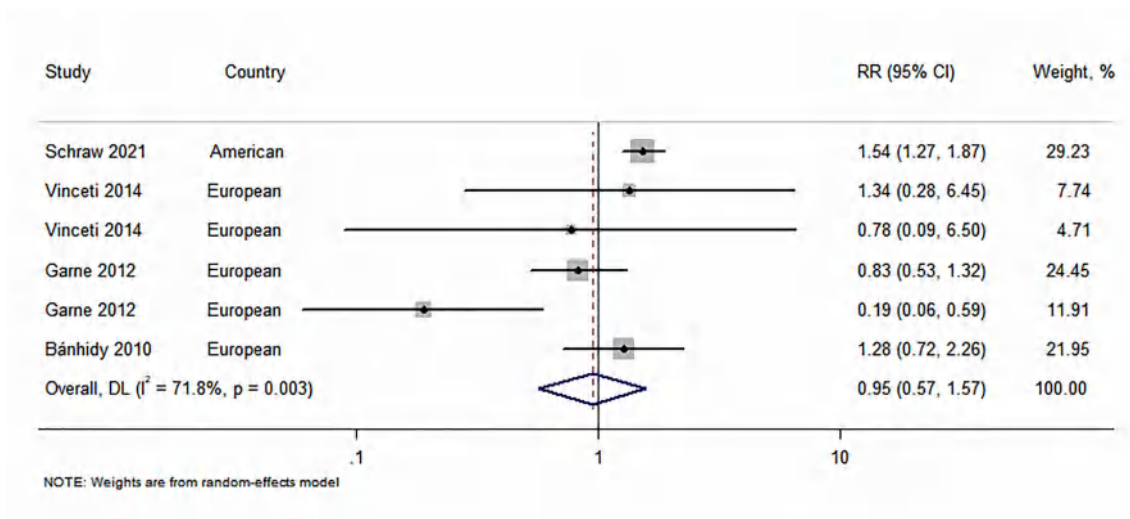
**Fig H20.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of congenital anomalies of the kidney and urinary tract (RR = 1.80, 95% CI, 1.41 to 2.30;  $I^2 = 0.0\%$ ,  $P = 0.865$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.



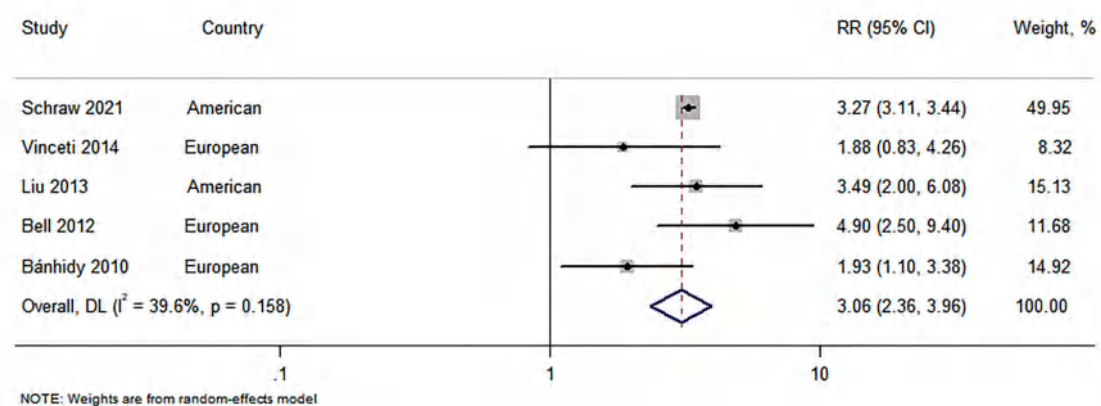
**Fig H21. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of congenital anomalies of musculoskeletal system (RR = 1.98, 95% CI, 1.45 to 2.72;  $I^2 = 94.4\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig H22.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of limb reduction (RR = 2.73, 95% CI, 1.98 to 3.76;  $I^2 = 81.7\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.

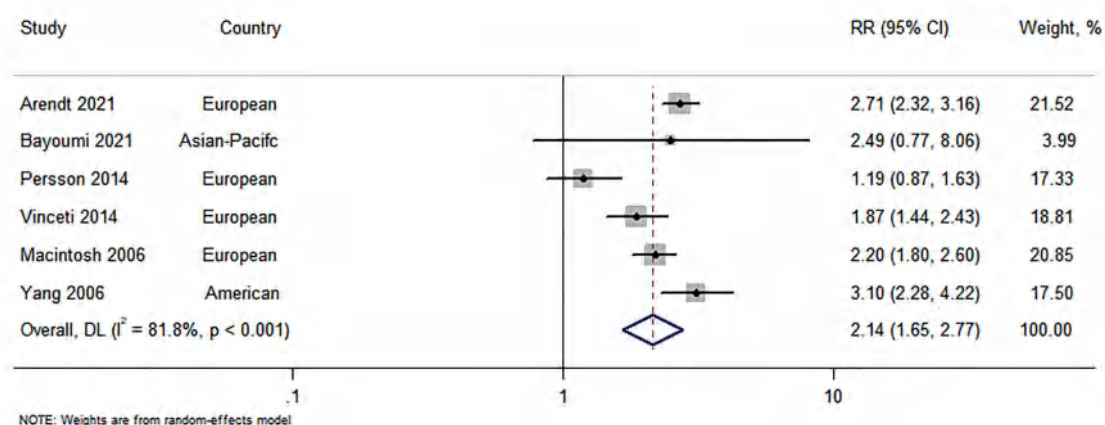


**Fig H23.** Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of poly/syndactyly (RR = 0.95, 95% CI, 0.57 to 1.57;  $I^2 = 71.8\%$ ,  $P = 0.003$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.

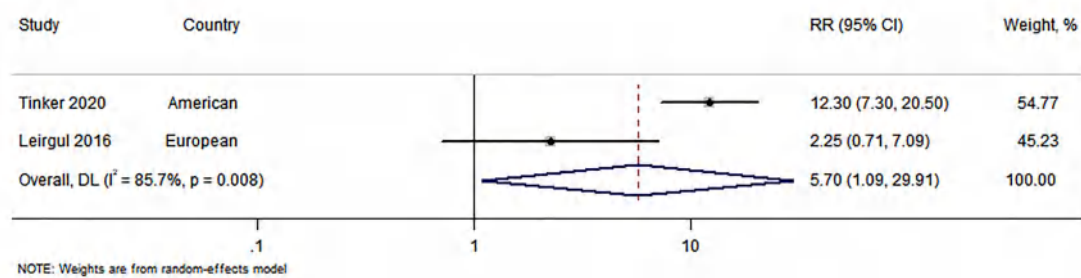


**Fig H24. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of multiple congenital anomalies (RR = 3.06, 95% CI, 2.36 to 3.96;  $I^2 = 39.6\%$ ,  $P = 0.158$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

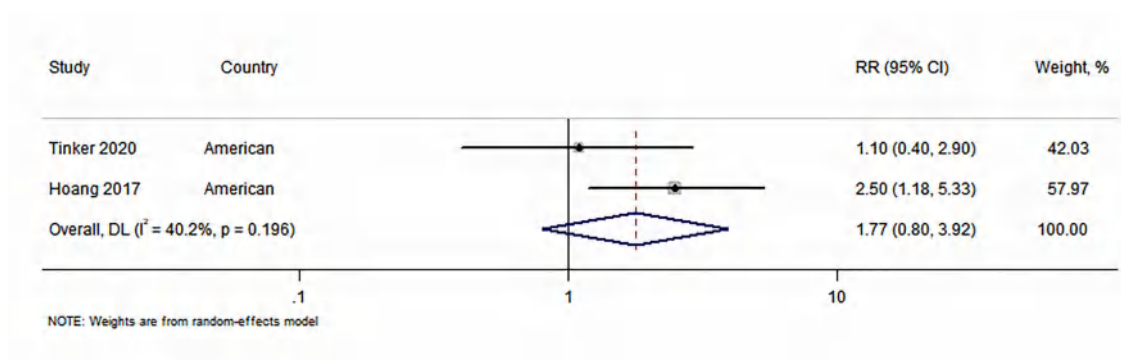




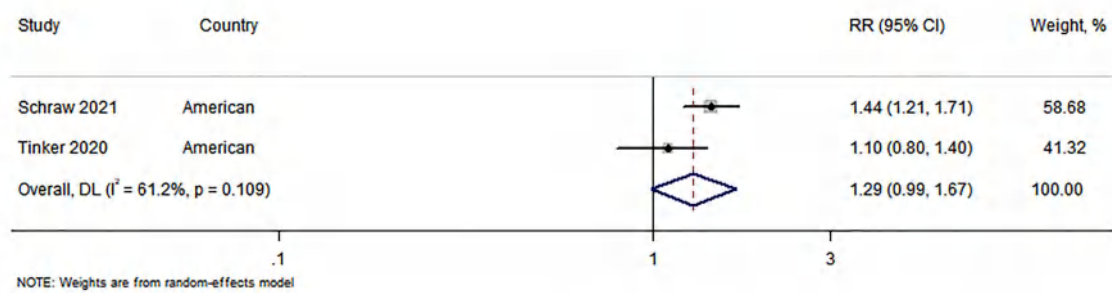
**Fig H25. Forest plot of the relative risks of population-based studies on maternal pre-gestational diabetes and the risk of major congenital anomalies (RR = 2.14, 95% CI, 1.65 to 2.77;  $I^2 = 81.8\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



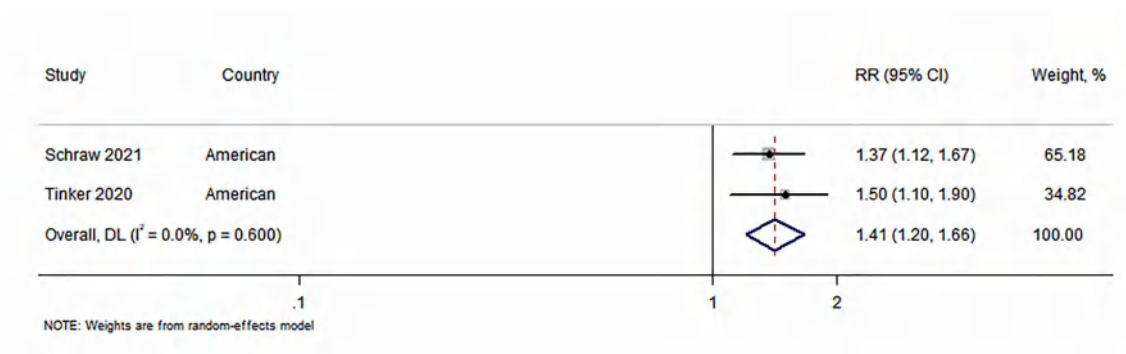
**Fig II. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of heterotaxia (RR = 5.70, 95% CI, 1.09 to 29.91;  $I^2 = 85.7\%$ ,  $P = 0.008$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



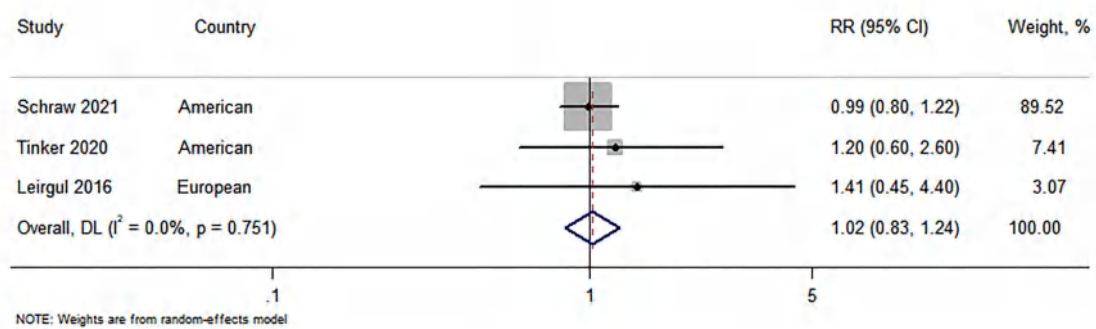
**Fig I2. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of truncus arteriosus (RR = 1.77, 95% CI, 0.80 to 3.92;  $I^2 = 40.2\%$ ,  $P = 0.196$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



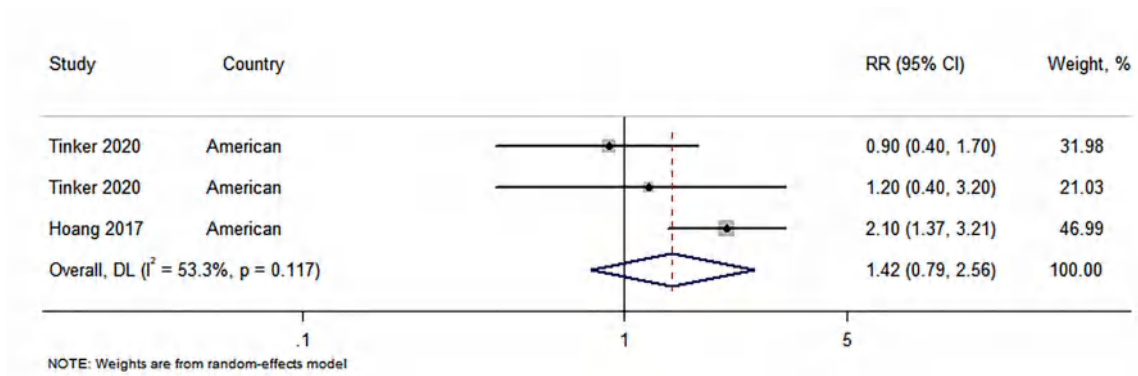
**Fig I3. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of transposition of great vessels (RR = 1.29, 95% CI, 0.99 to 1.67;  $I^2 = 61.2\%$ ,  $P = 0.109$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



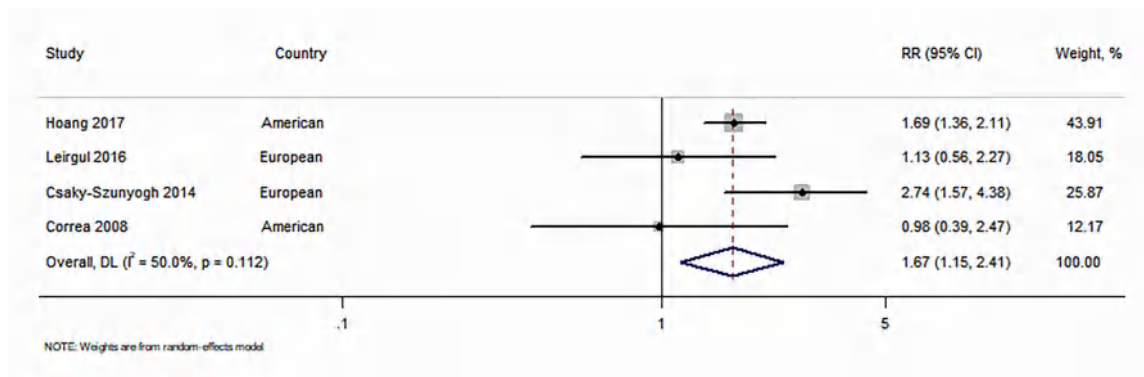
**Fig I4. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of tetralogy of Fallot (RR = 1.41, 95% CI, 1.20 to 1.66;  $I^2 = 0.0\%$ ,  $P = 0.600$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig I5. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of atrioventricular septal defects (RR = 1.02, 95% CI, 0.83 to 1.24;  $I^2 = 0.0\%$ ,  $P = 0.751$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig I6. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of anomalous pulmonary venous return (RR = 1.42, 95% CI, 0.79 to 2.56;  $I^2 = 53.3\%$ ,  $P = 0.117$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

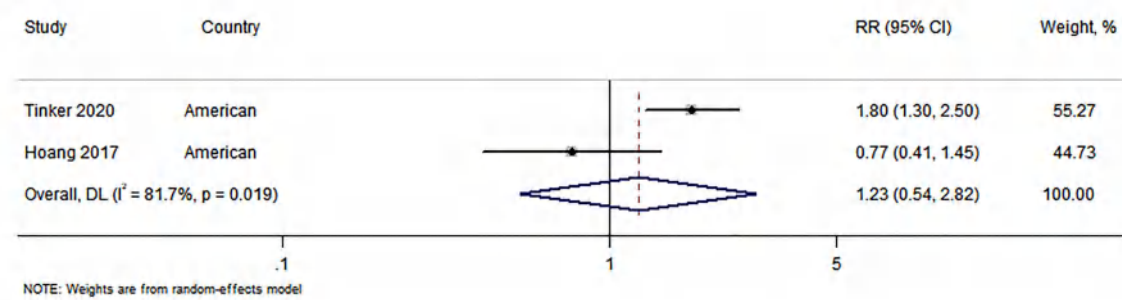


**Fig I7. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of left ventricular outflow tract (RR = 1.67, 95% CI, 1.15 to 2.41;  $I^2 = 50.0\%$ ,  $P = 0.112$ ).** DL, DerSimonian and Laird random-effects model; RR, relative risk.

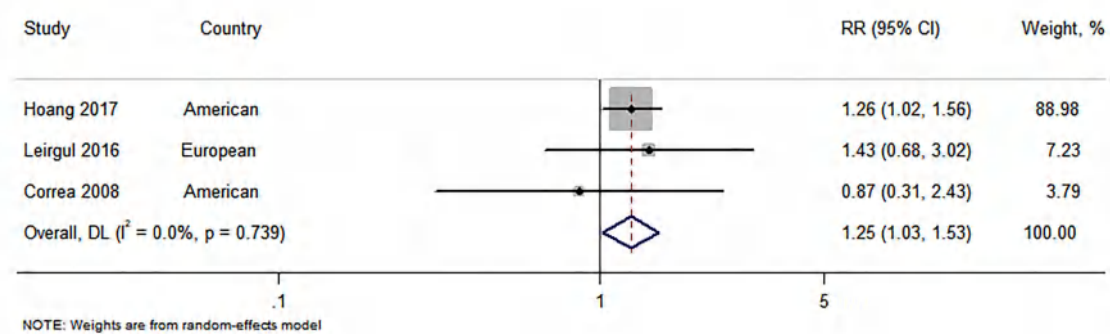




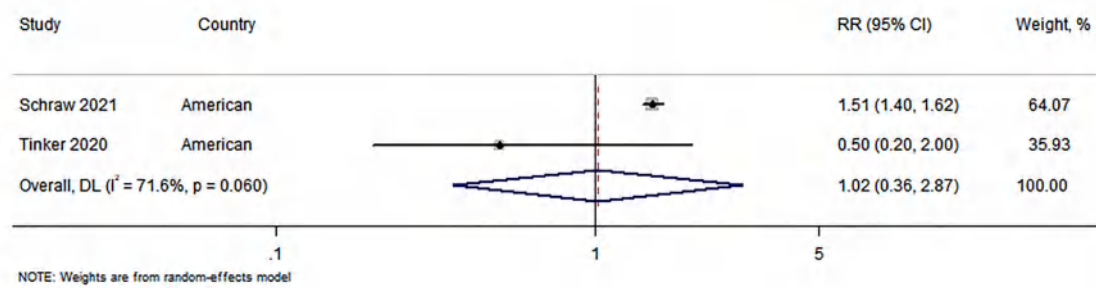
**Fig I8. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of coarctation of aorta (RR = 1.50, 95% CI, 1.23 to 1.83;  $I^2 = 35.4\%$ ,  $P = 0.213$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



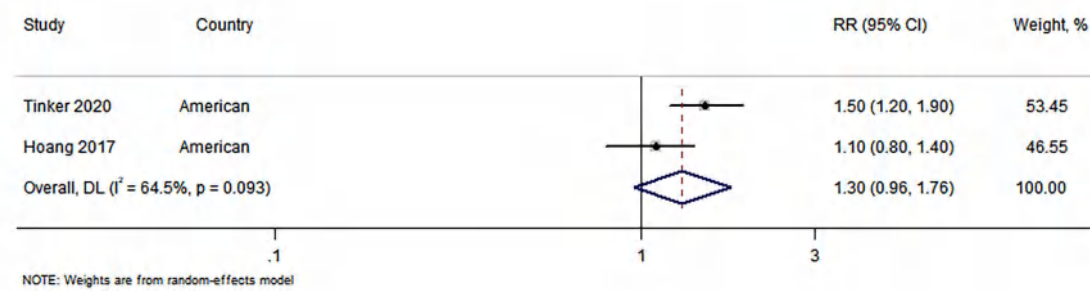
**Fig I9. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of hypoplastic left heart (RR = 1.23, 95% CI, 0.54 to 2.82;  $I^2 = 81.7\%$ ,  $P = 0.019$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig I10. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of right ventricular outflow tract (RR = 1.25, 95% CI, 1.03 to 1.53;  $I^2 = 0.0\%$ ,  $P = 0.739$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



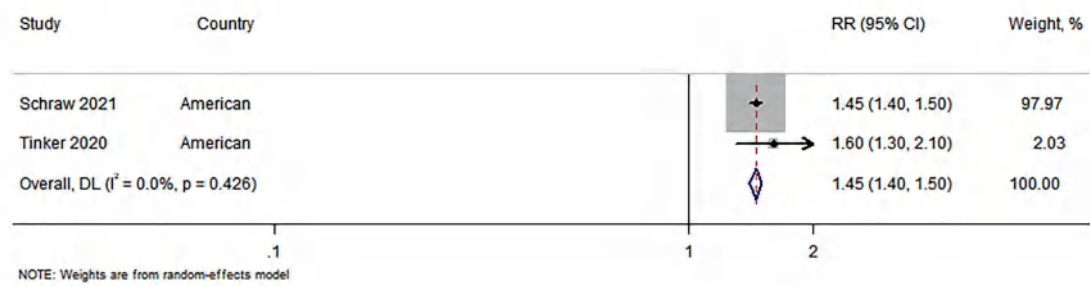
**Fig I11. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of pulmonary artery anomalies (RR = 1.02, 95% CI, 0.36 to 2.87;  $I^2 = 71.6\%$ ,  $P = 0.060$ ).** DL, DerSimonian and Laird random-effects model; RR, relative risk.



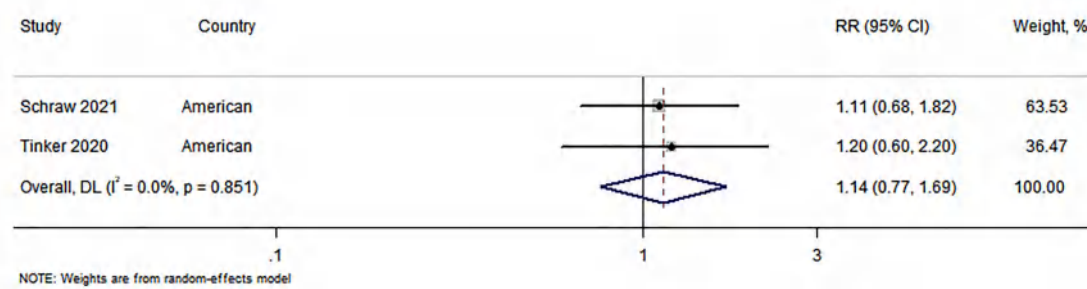
**Fig I12. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of pulmonary valve stenosis (RR = 1.30, 95% CI, 0.96 to 1.76;  $I^2 = 64.5\%$ ,  $P = 0.093$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig I13. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of ventricular septal defects (RR = 1.31, 95% CI, 1.24 to 1.38;  $I^2 = 0.0\%$ ,  $P = 0.960$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

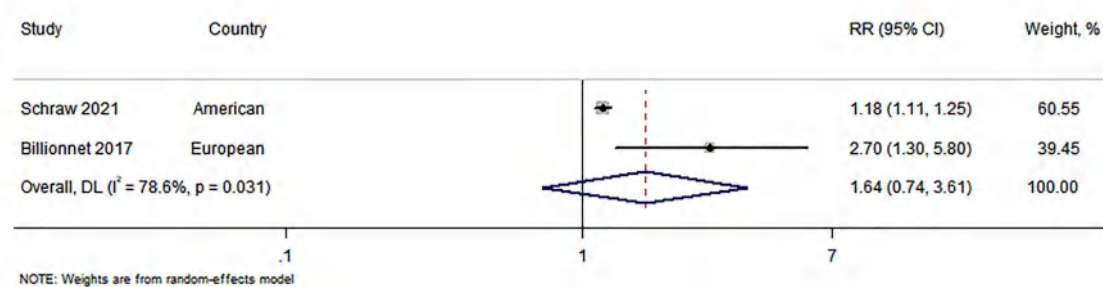


**Fig I14. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of atrial septal defects (RR = 1.45, 95% CI, 1.40 to 1.50;  $I^2 = 0.0\%$ ,  $P = 0.426$ ).** DL, DerSimonian and Laird random-effects model; RR, relative risk.

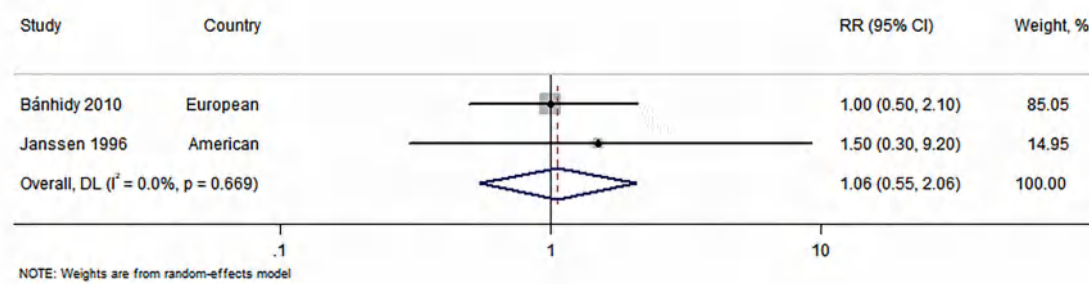


**Fig I15. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of single ventricle (RR = 1.14, 95% CI, 0.77 to 1.69;  $I^2 = 0.0\%$ ,  $P = 0.851$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

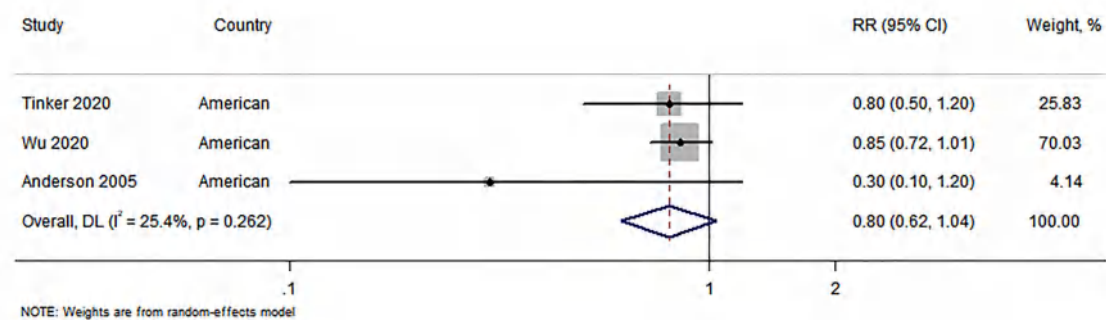




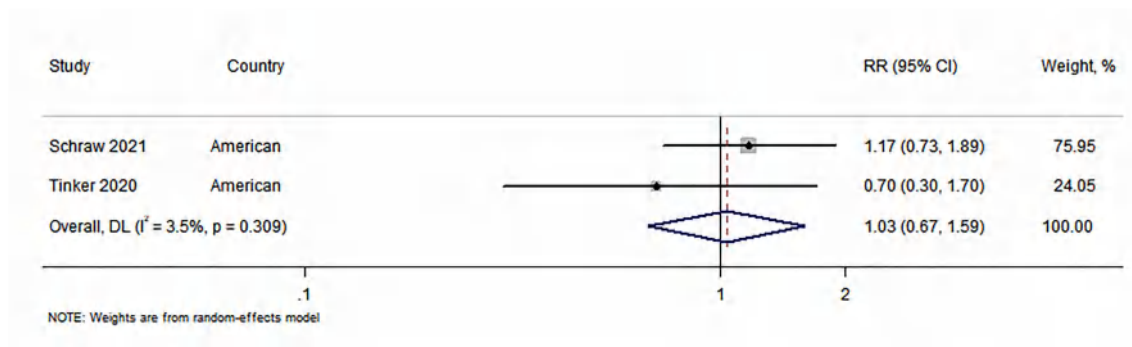
**Fig J1. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of congenital anomalies of nervous system (RR = 1.64, 95% CI, 0.74 to 3.61;  $I^2 = 78.6\%$ ,  $P = 0.031$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



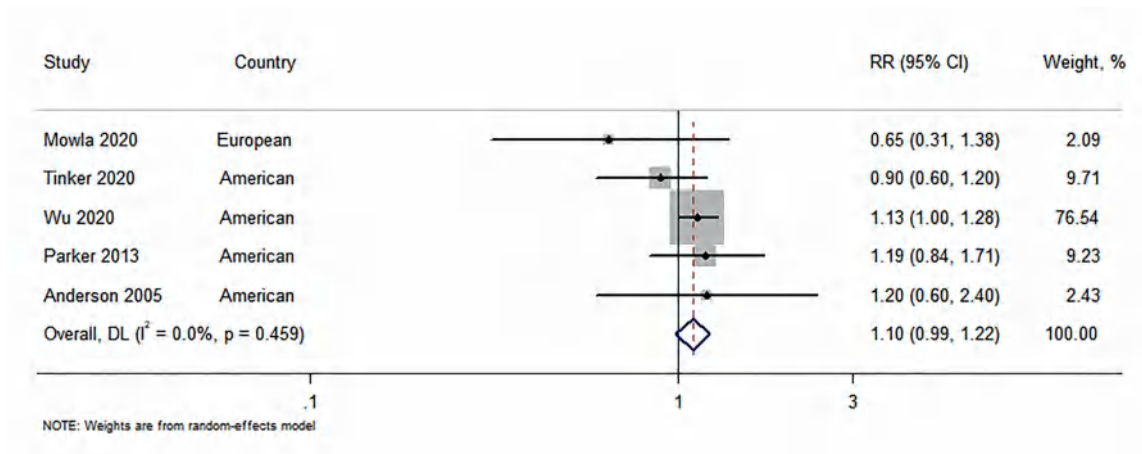
**Fig J2. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of neural tube defects (RR = 1.06, 95% CI, 0.55 to 2.06;  $I^2 = 0.0\%$ ,  $P = 0.669$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



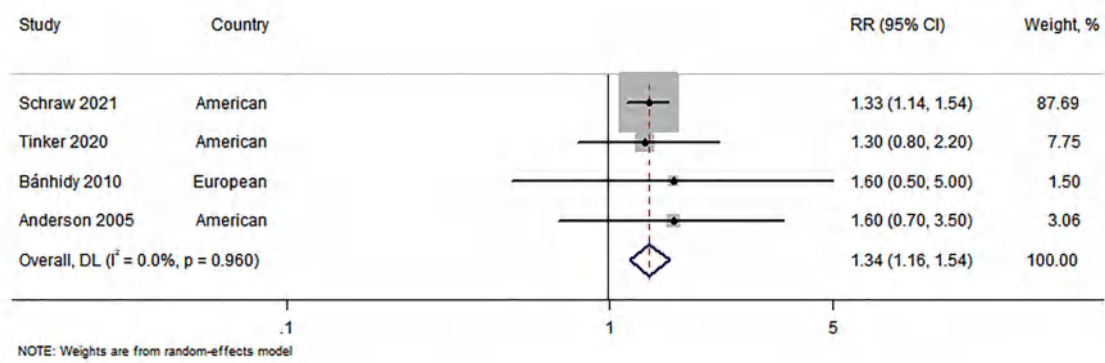
**Fig J3. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of anencephaly (RR = 0.80, 95% CI, 0.62 to 1.04;  $I^2 = 25.4\%$ ,  $P = 0.262$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



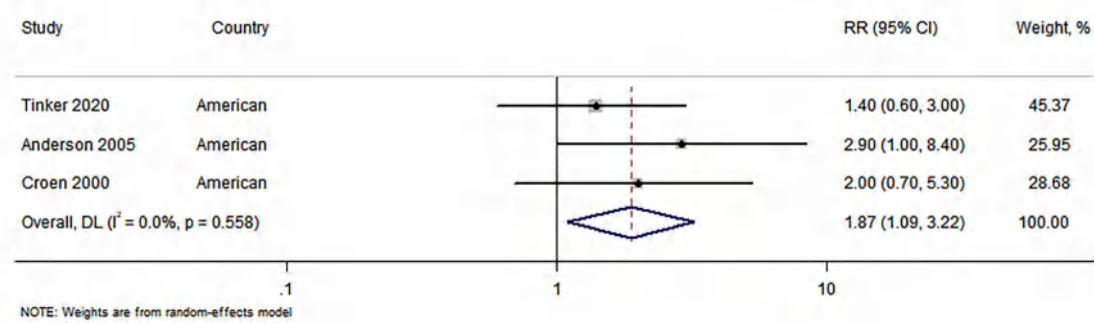
**Fig J4. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of encephalocele (RR = 1.03, 95% CI, 0.67 to 1.59;  $I^2 = 3.5\%$ ,  $P = 0.309$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



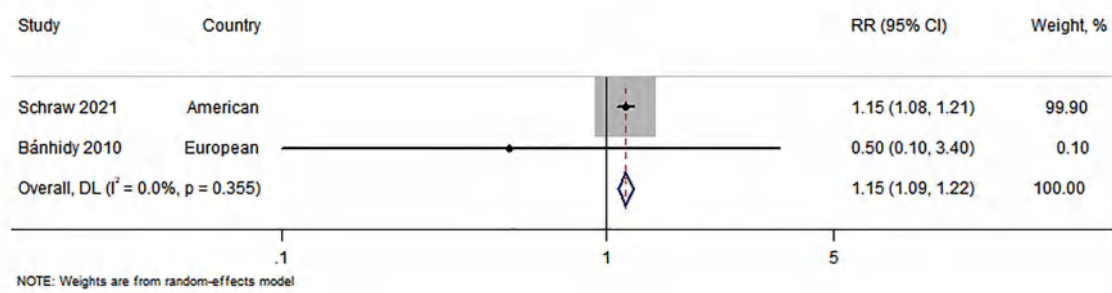
**Fig J5.** Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of spina bifida (RR = 1.10, 95% CI, 0.99 to 1.22;  $I^2 = 0.0\%$ ,  $P = 0.459$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.



**Fig J6. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of hydrocephaly (RR = 1.34, 95% CI, 1.16 to 1.54;  $I^2 = 0.0\%$ ,  $P = 0.960$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

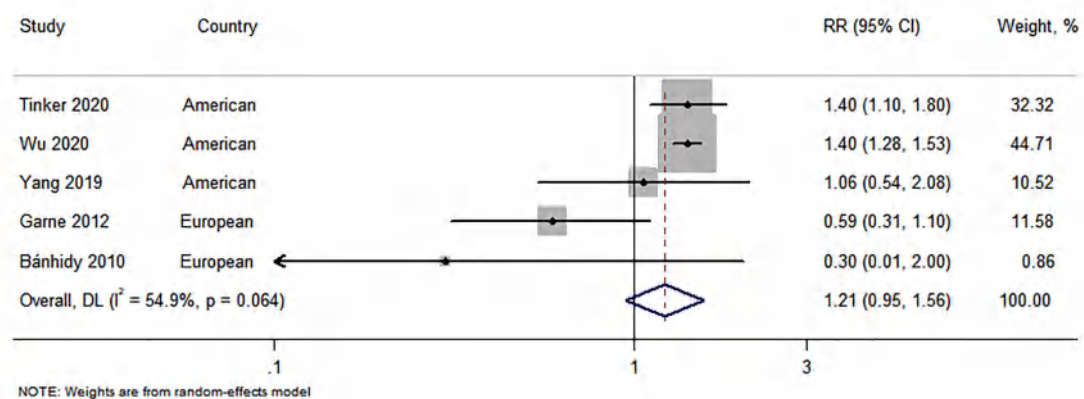


**Fig J7. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of holoprosencephaly (RR = 1.87, 95% CI, 1.09 to 3.22;  $I^2 = 0.0\%$ ,  $P = 0.558$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

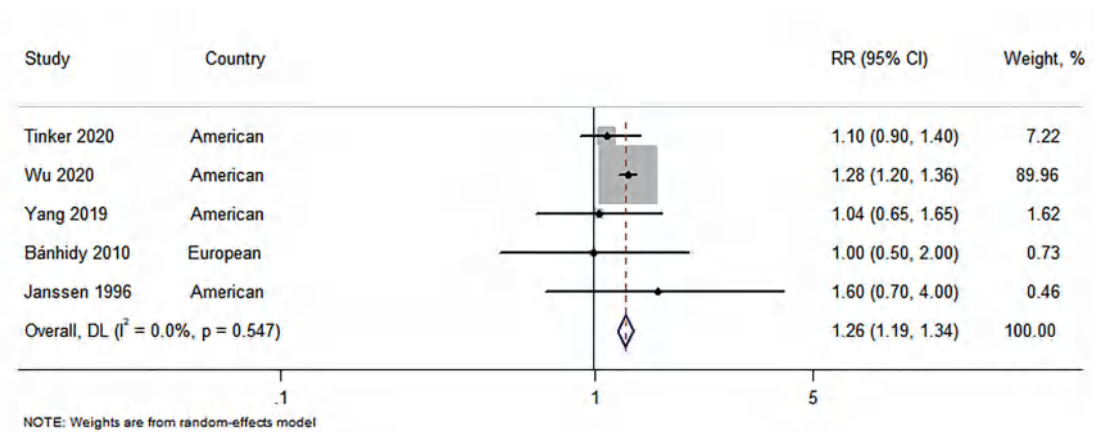


**Fig J8. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of eye, ear, face, and neck (RR = 1.15, 95% CI, 1.09 to 1.22;  $I^2 = 0.0\%$ ,  $P = 0.355$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

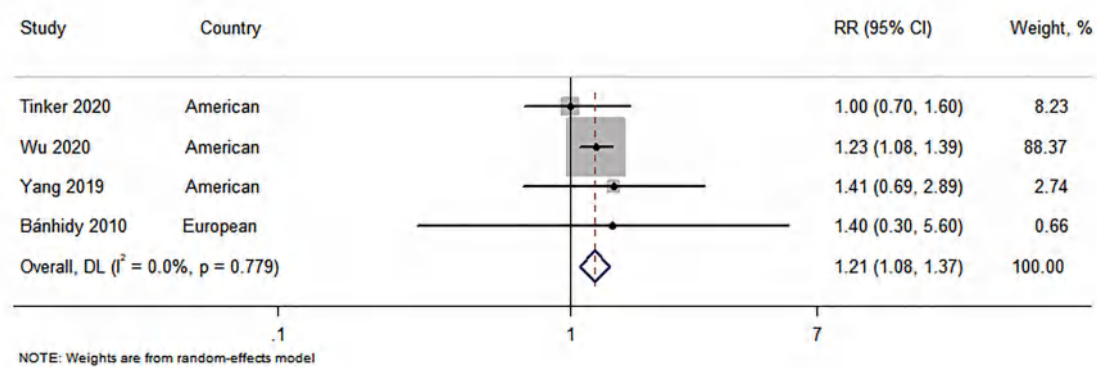




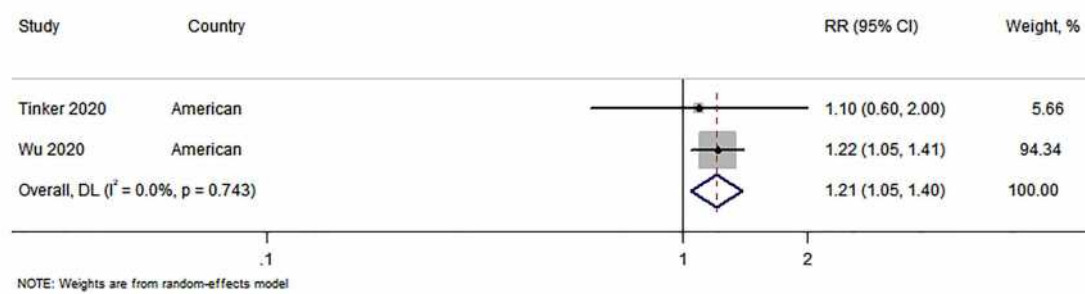
**Fig J9. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of cleft palate (RR = 1.21, 95% CI, 0.95 to 1.56;  $I^2 = 54.9\%$ ,  $P=0.064$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



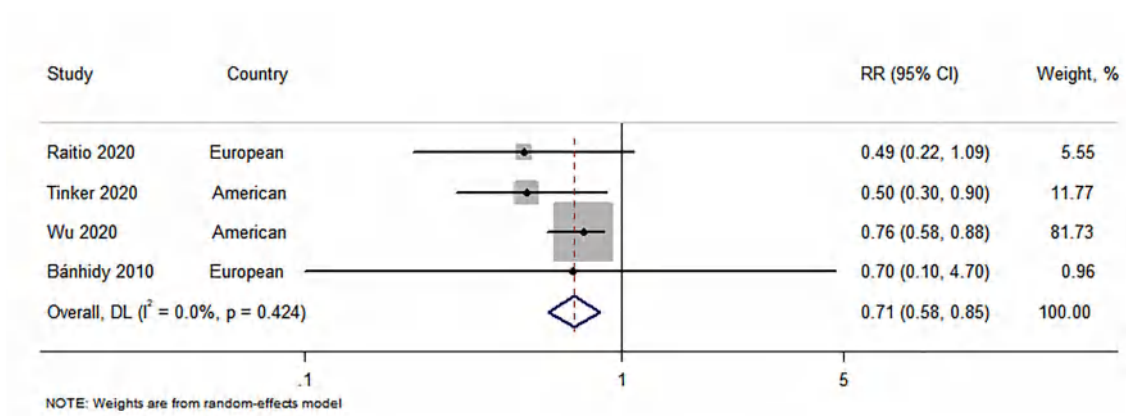
**Fig J10. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of cleft lip with or without palate (RR = 1.26, 95% CI, 1.19 to 1.34;  $I^2 = 0.0\%$ ,  $P = 0.547$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



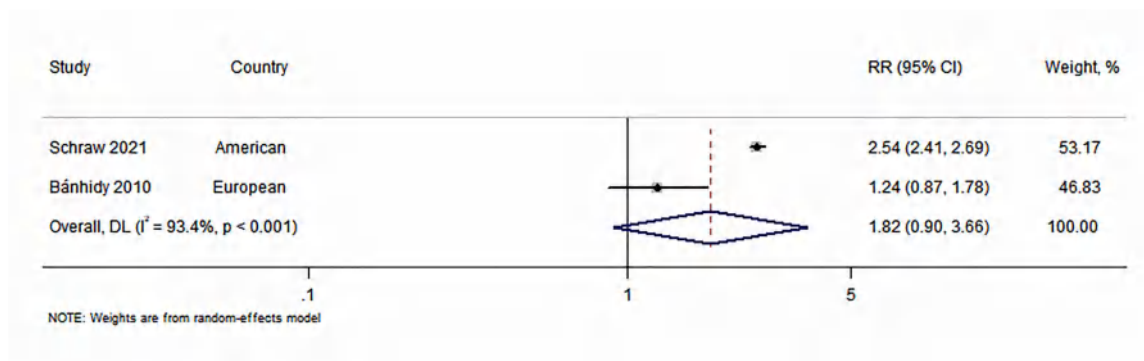
**Fig J11. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of diaphragmatic hernia (RR = 1.21, 95% CI, 1.08 to 1.37;  $I^2 = 0.0\%$ ,  $P = 0.779$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



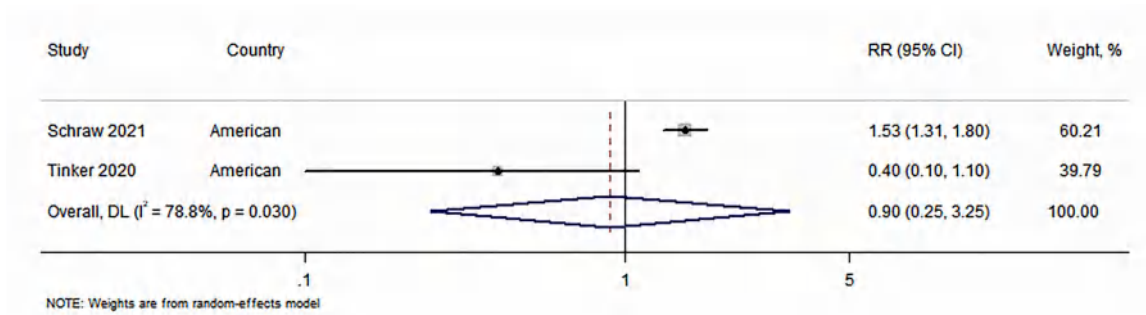
**Fig J12. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of omphalocele (RR = 1.21, 95% CI, 1.05 to 1.40;  $I^2 = 0.0\%$ ,  $P = 0.743$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



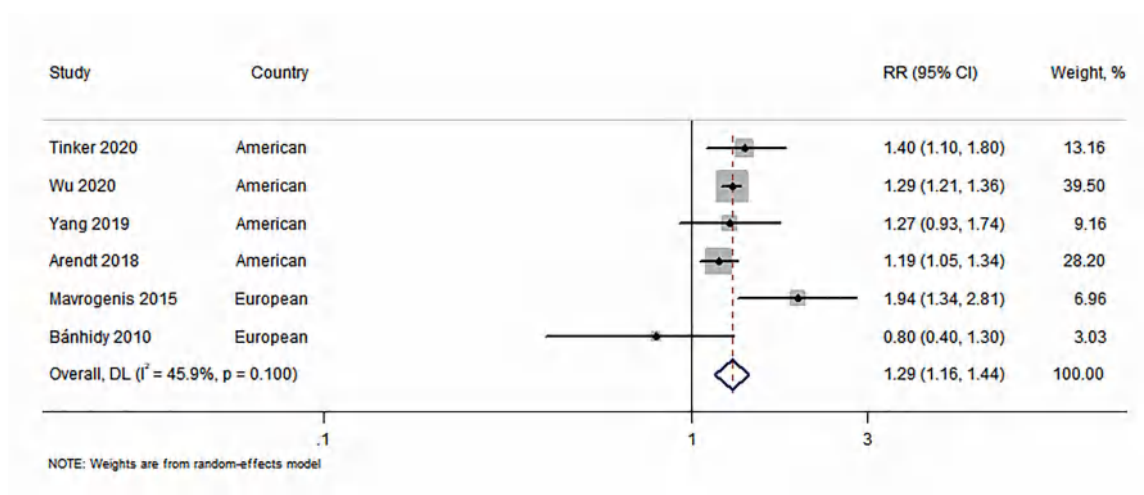
**Fig J13. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of gastroschisis (RR = 0.71, 95% CI, 0.58 to 0.85;  $I^2 = 0.0\%$ ,  $P = 0.424$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig J14. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of congenital anomalies of genitourinary system (RR = 1.82, 95% CI, 0.90 to 3.66;  $I^2 = 93.4\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

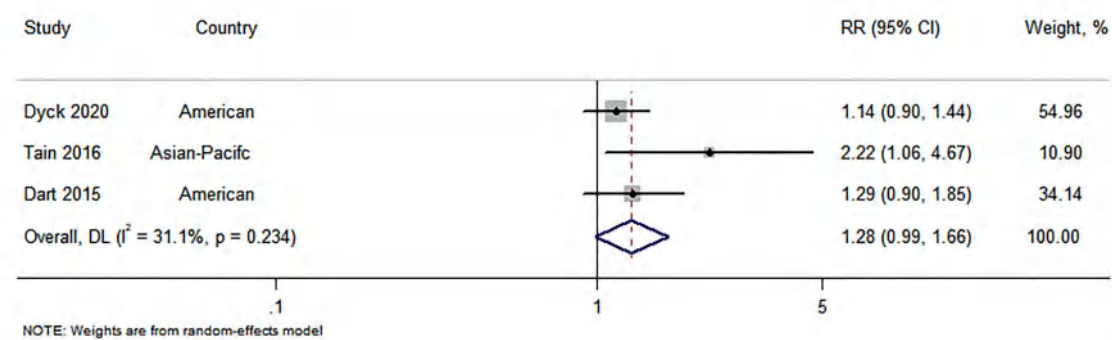


**Fig J15. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of renal agenesis/dysgenesis (RR = 0.90, 95% CI, 0.25 to 3.25;  $I^2 = 78.8\%$ ,  $P = 0.030$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

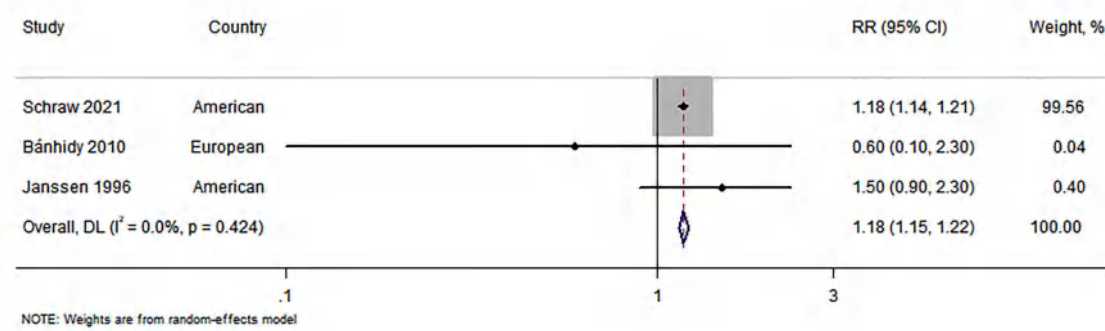


**Fig J16. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of hypospadias (RR = 1.29, 95% CI, 1.16 to 1.44;  $I^2 = 45.9\%$ ,  $P=0.100$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

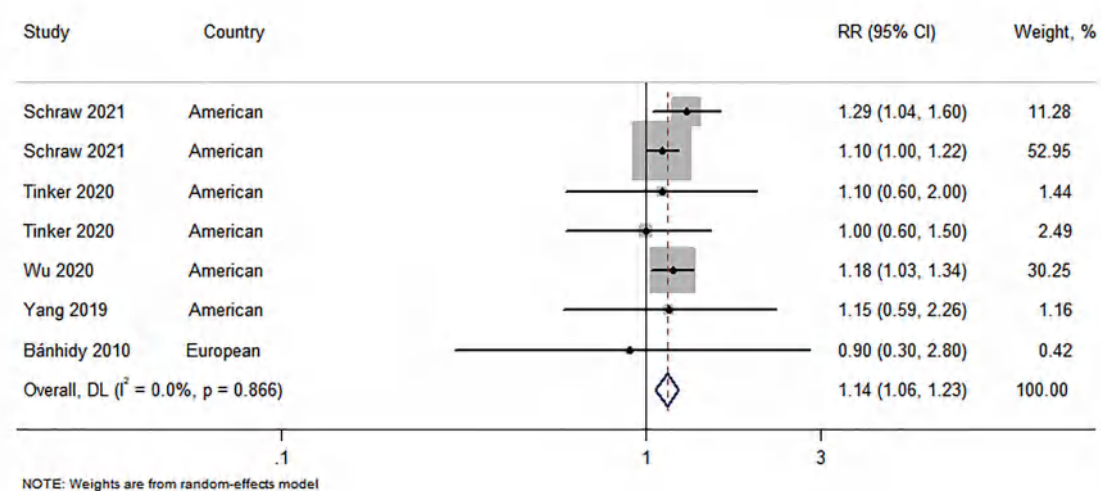




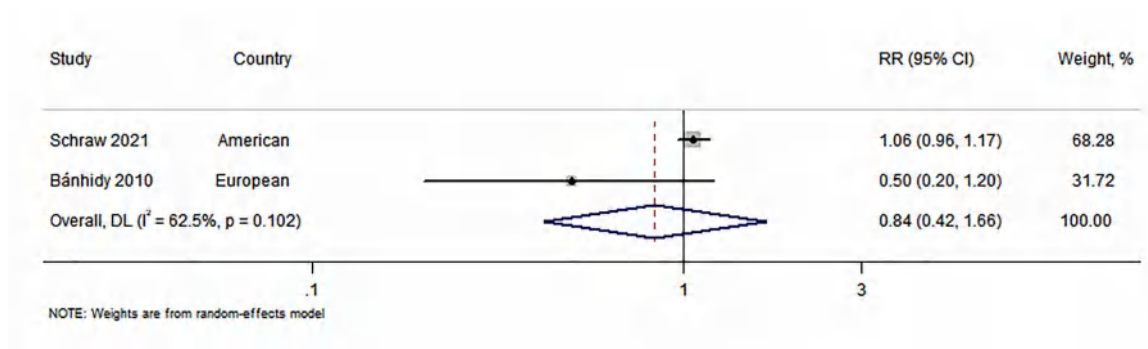
**Fig J17. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of congenital anomalies of the kidney and urinary tract (RR = 1.28, 95% CI, 0.99 to 1.66;  $I^2 = 31.1\%$ ,  $P = 0.234$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



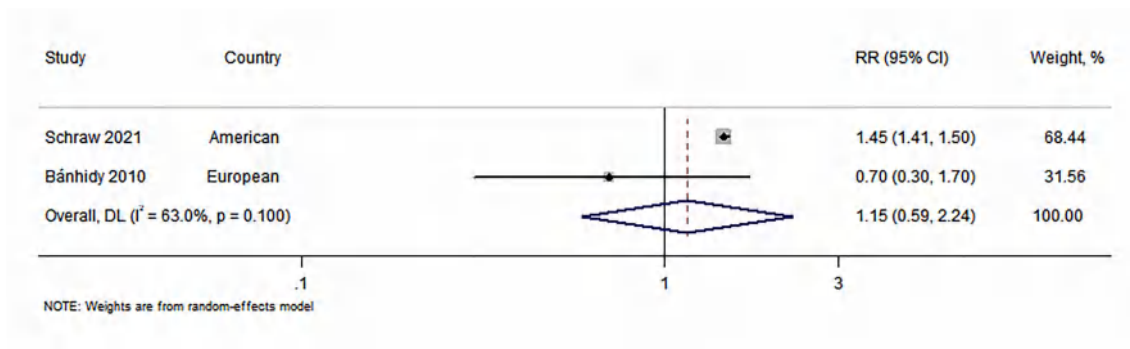
**Fig J18. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of congenital anomalies of musculoskeletal system (RR = 1.18, 95% CI, 1.15 to 1.22;  $I^2 = 0.0\%$ ,  $P = 0.424$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



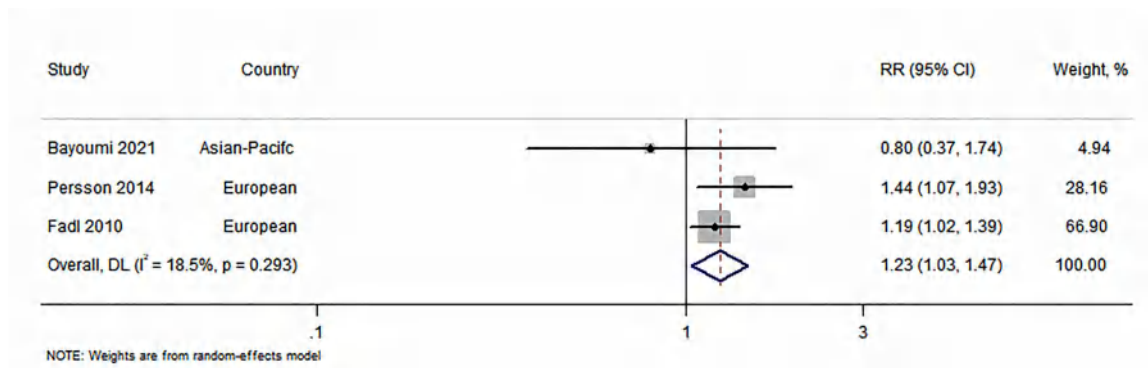
**Fig J19. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of limb reduction (RR = 1.14, 95% CI, 1.06 to 1.23;  $I^2 = 0.0\%$ ,  $P = 0.866$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



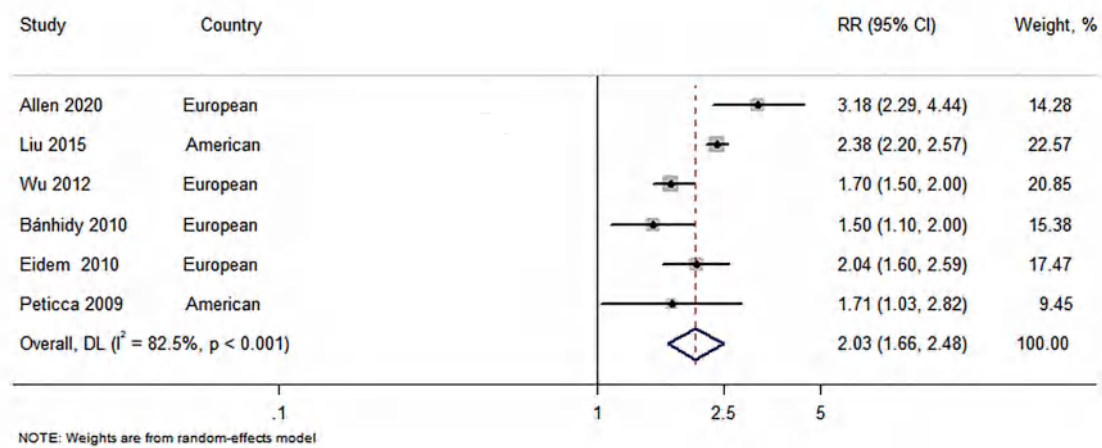
**Fig J20. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of poly/syndactyly (RR = 0.84, 95% CI, 0.42 to 1.66;  $I^2 = 62.5\%$ ,  $P = 0.102$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



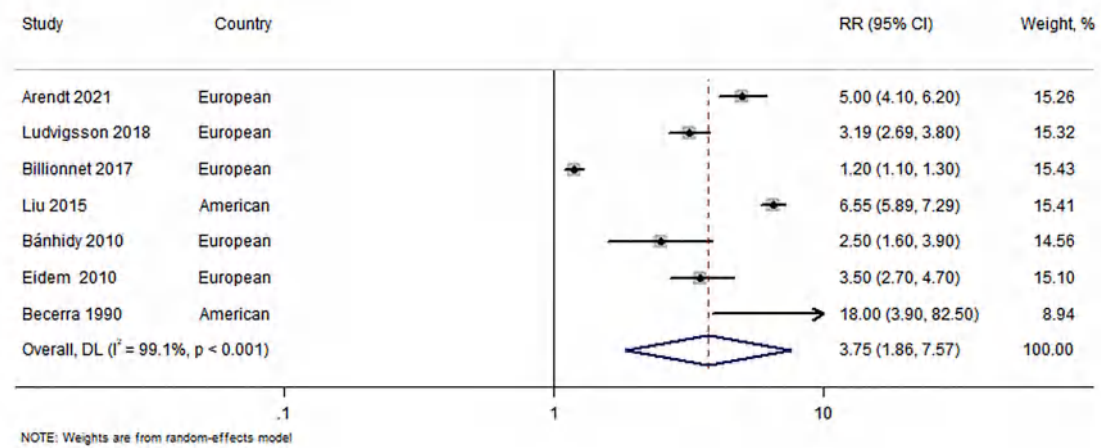
**Fig J21. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of multiple congenital anomalies (RR = 1.15, 95% CI, 0.59 to 2.24;  $I^2 = 63.0\%$ ,  $P = 0.100$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**



**Fig J22. Forest plot of the relative risks of population-based studies on maternal gestational diabetes and the risk of major congenital anomalies (RR = 1.23, 95% CI, 1.03 to 1.47;  $I^2 = 18.5\%$ ,  $P = 0.293$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

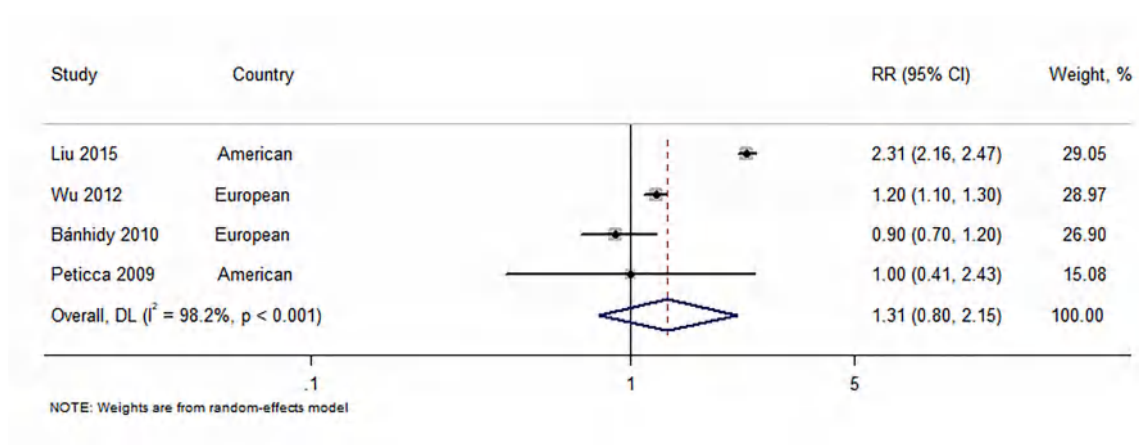


**Fig K1. Forest plot of the relative risks of population-based studies on maternal Type 1 diabetes and the risk of overall congenital anomalies (RR = 2.03, 95% CI, 1.66 to 2.48;  $I^2 = 82.5\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

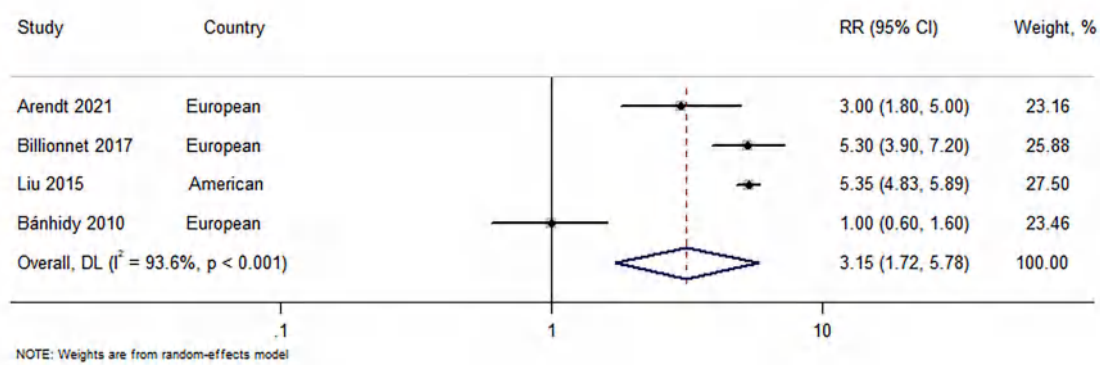


**Fig K2. Forest plot of the relative risks of population-based studies on maternal Type 1 diabetes and the risk of congenital heart defects (RR = 3.75, 95% CI, 1.86 to 7.57;  $I^2 = 99.1\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**





**Fig L1.** Forest plot of the relative risks of population-based studies on maternal Type 2 diabetes and the risk of overall congenital anomalies (RR = 1.31, 95% CI, 0.80 to 2.15;  $I^2 = 98.2\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.



**Fig L2. Forest plot of the relative risks of population-based studies on maternal Type 2 diabetes and the risk of congenital heart defects (RR = 3.15, 95% CI, 1.72 to 5.78;  $I^2 = 93.6\%$ ,  $P < 0.001$ ). DL, DerSimonian and Laird random-effects model; RR, relative risk.**

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