Supplementary Table 1. Summary of Newcastle-Ottawa Assessment scale of included studies.

Newcastle-Ottawa Assessment scale of eleven case-control studies				
Reference	Selection	Comparability	Exposure	Overall score
Hao et al 2015	***	**	*	6 stars
Sabbagh et al 2015	***	**	**	7 stars
Hoyt et al 2016	***	_	*	4 stars
Kummet et al 2016	***	**	**	7 stars
Mckinney et al 2016	**	**	*	5stars
Dien et al 2017	**	**	*	5 stars
Goveas et al 2017	**	_	*	3 stars
Junaid et al 2017	**	**	*	5 stars
Pi et al 2018	**	**	*	5 stars
Altoe et al 2019	-	*	**	3 stars
Chowchuen et al 2020	**	-	*	3 stars
Newcastle-Ottawa Assessment scale of Cohort studies				
Reference	Selection	Comparability	Outcome	Overall score
Sato et al 2021	***	*	*	5 stars

Supplementary Table 2. Egger's Regression-Based Test.

Parameter	Coefficient	Std. Error	t	p-value		95% CI
(Intercept)	.352	.2345	1.501	.146	-.131	.835
SE	1.103	1.0386	1.062	.298	-1.036	3.243

Random-effects meta-regression

SE Standard error of effect size

Supplementary Table 3. Meta-regression random effects (REML) model.

Covariate	Ref	Coefficient	SE	95% CI		t-value	P-value	VIF
Intercept		0.4888	0.1063	0.2741	0.7034	4.6	0	2.649
Year: >=2013	<2013	-0.6038	0.1754	-0.9581	-0.2495	-3.44	0.0013	1.756
Low quality	High quality	0.727	0.1742	0.3752	1.0788	4.17	0.0002	1.758
Passive smoking	Active smoking	-0.1257	0.1449	-0.4183	0.167	-0.87	0.3909	1.036

Statistics for Model 1

Test of the model: Simultaneous test that all coefficients (excluding intercept) are zero

F = 6.51, df = 3, 41, p = 0.0011

Goodness of fit: Test that unexplained variance is zero

Tau^2 = 0.1177, Tau = 0.3430, I^2 = 79.39%, Q = 198.98, df = 41, p = 0.0000

Comparison of Model 1 with the null model

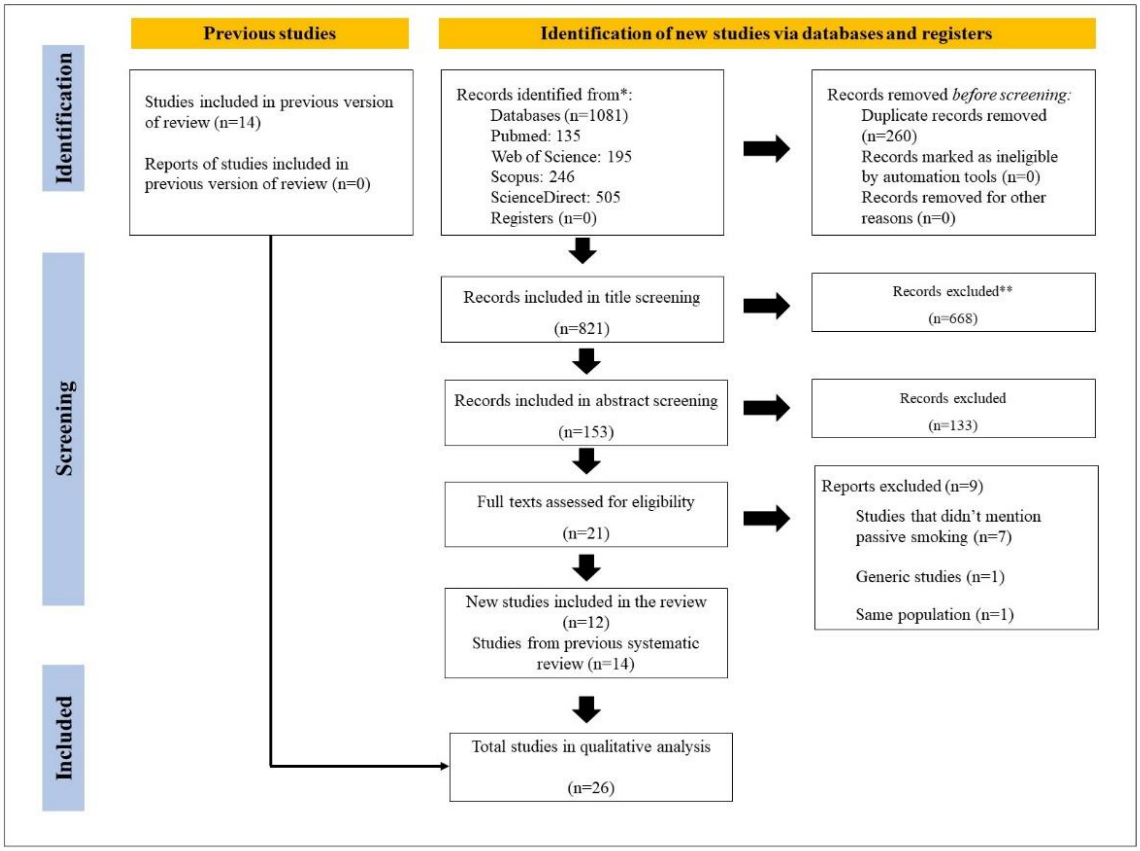
Total between-study variance (intercept only)

Tau^2 = 0.1768, Tau = 0.4205, I^2 = 83.14%, Q = 261.03, df = 44, p = 0.0000

The proportion of total between-study variance explained by Model 1

R^2 analog = 0.33

Supplementary Figure 1. PRISMA 2020 flow diagram for updated systematic reviews which included searches of databases and registers only.



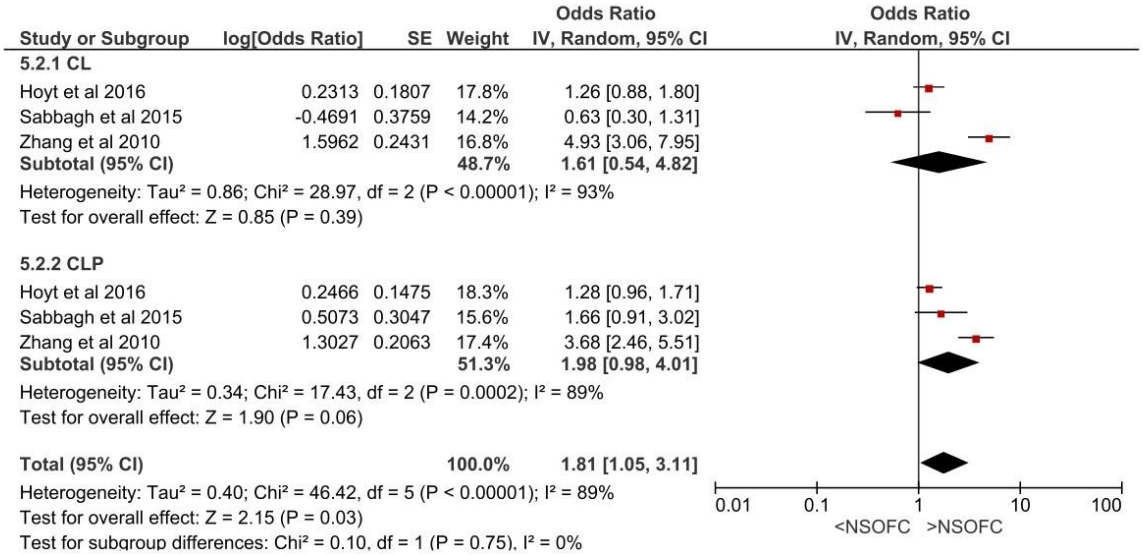
*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

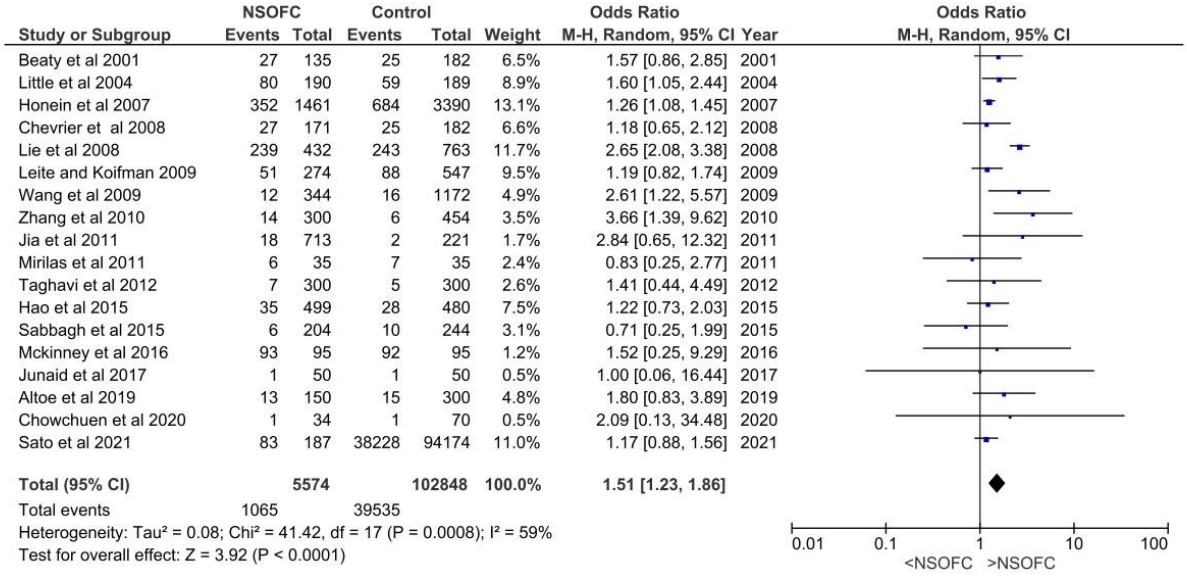
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

For more information, visit: http://www.prisma-statement.org/

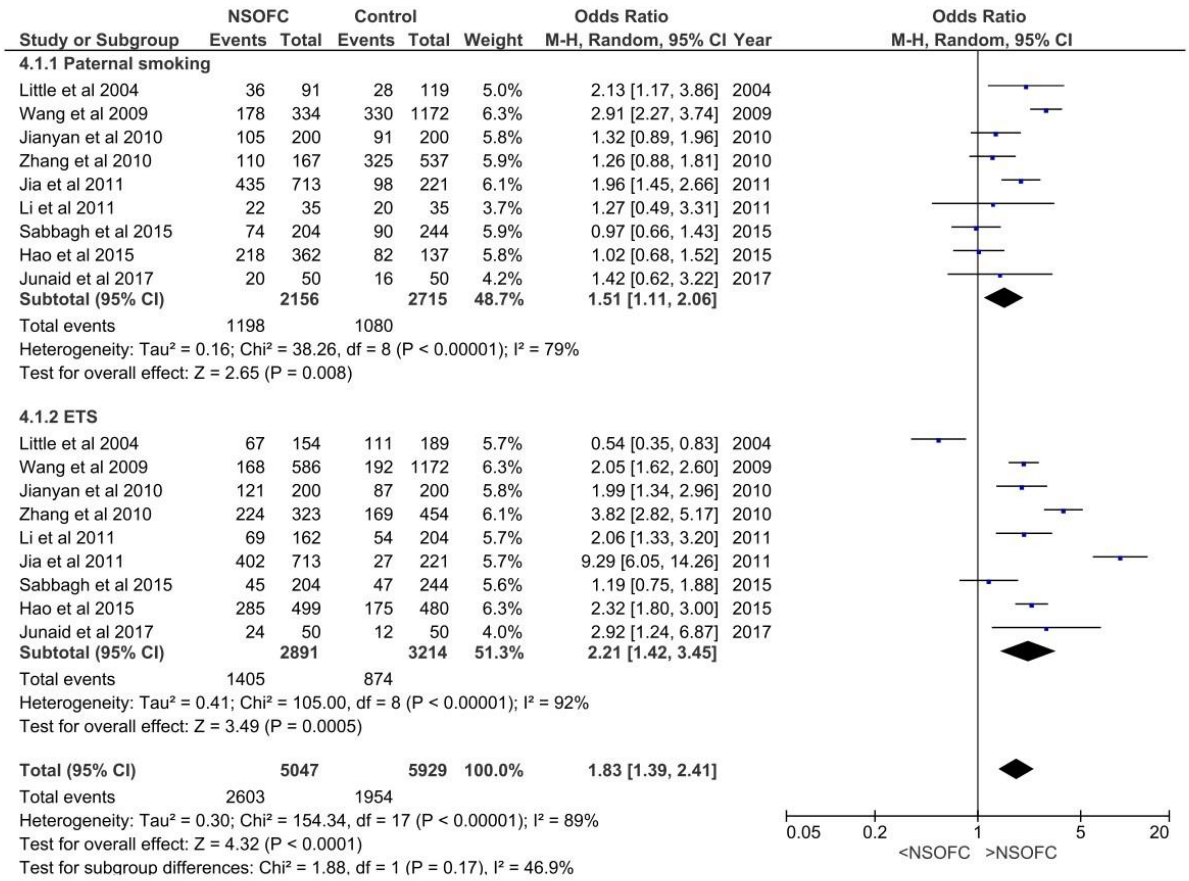
Supplementary Figure 2. Forest plot for meta-analysis of the association between maternal environmental tobacco exposure and the risk of having an infant NSOFC sub-grouped according to CL/P phenotypes (CLP and CP).



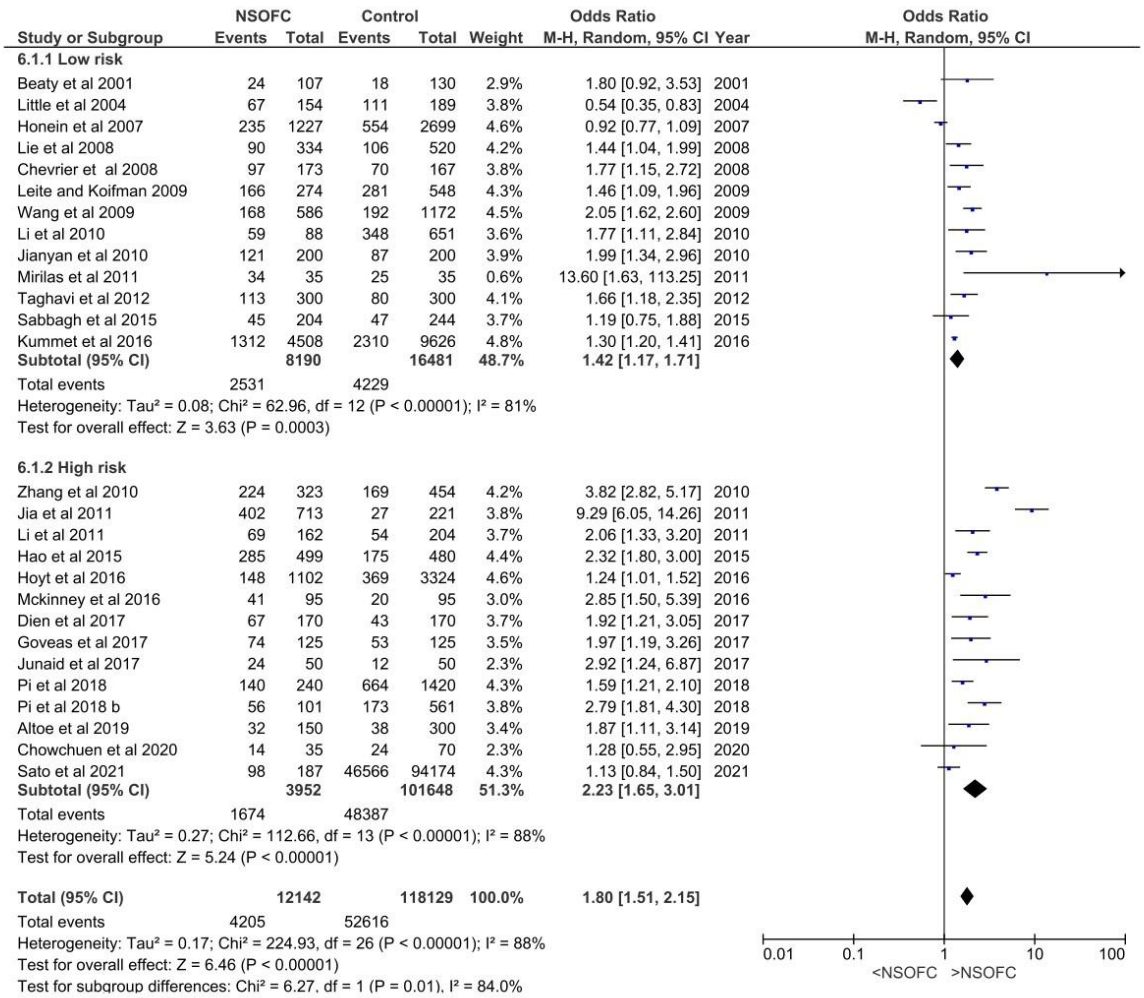
Supplementary Figure 3. Forest plot for meta-analysis of the association between the risk of having an infant with NSOFC and its association with maternal active smoking.



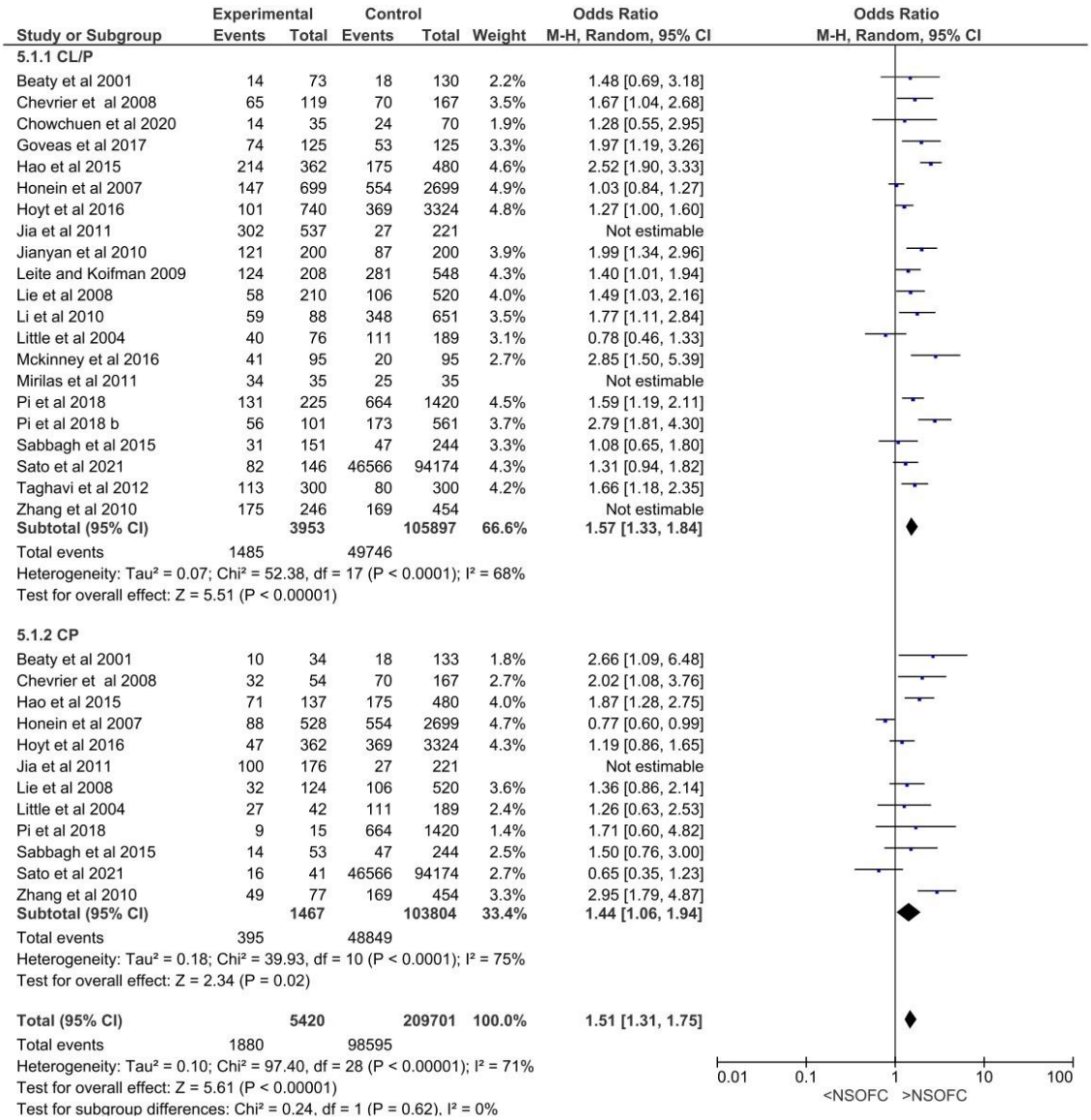
Supplementary Figure 4. Forest plot for meta-analysis of the association between the risk of having an infant with NSOFC and its association with paternal active smoking compared to maternal environmental tobacco smoking.



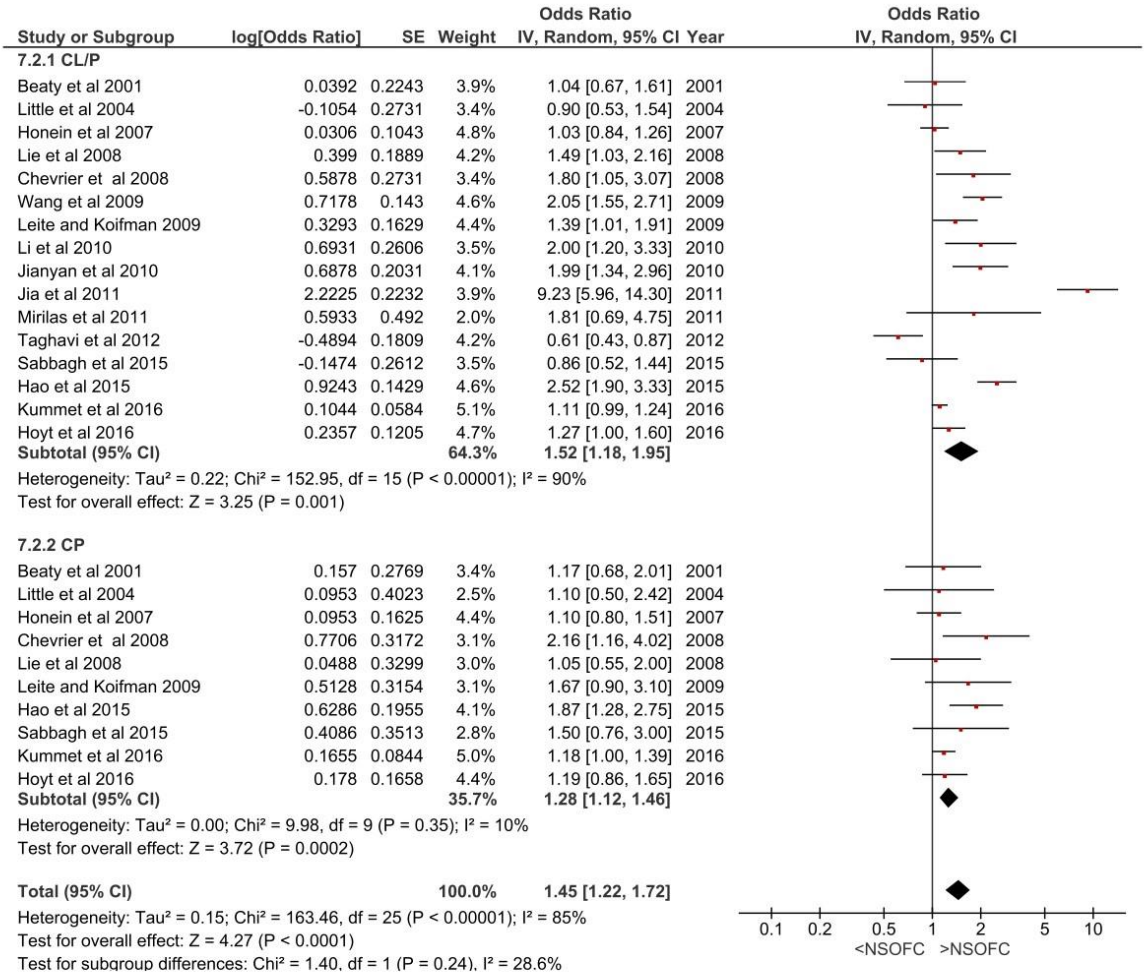
Supplementary Figure 5. Forest plot for meta-analysis of the association between the risk of having an infant NSOFC and its association with environmental tobacco smoking sub-grouped according to risk of bias.



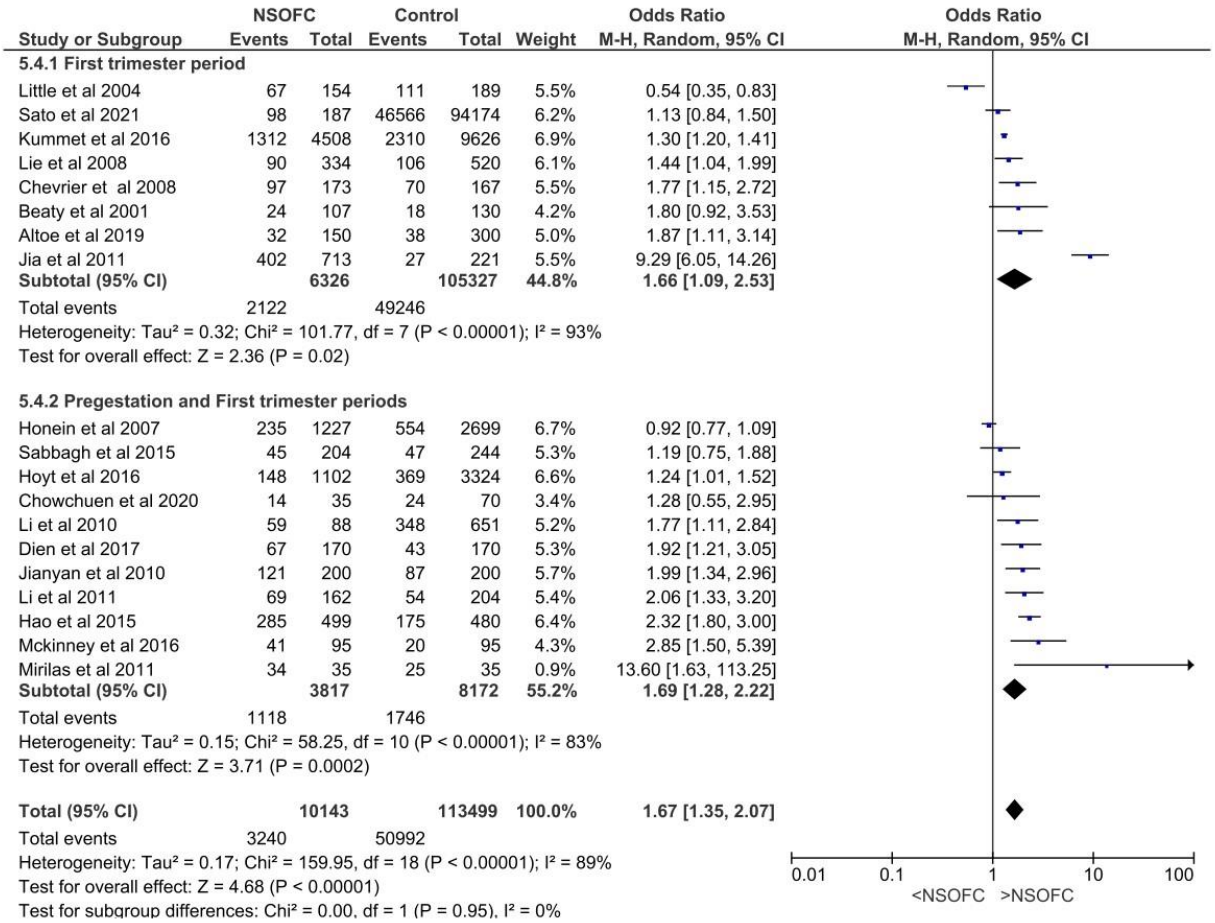
Supplementary Figure 6. Forest plot for meta-analysis of the association between maternal environmental tobacco smoking and the risk of having an infant with cleft lip and palate or cleft lip and its association with environmental tobacco smoking after excluding Jia et al, 2011 and Mirilas et al. 2011



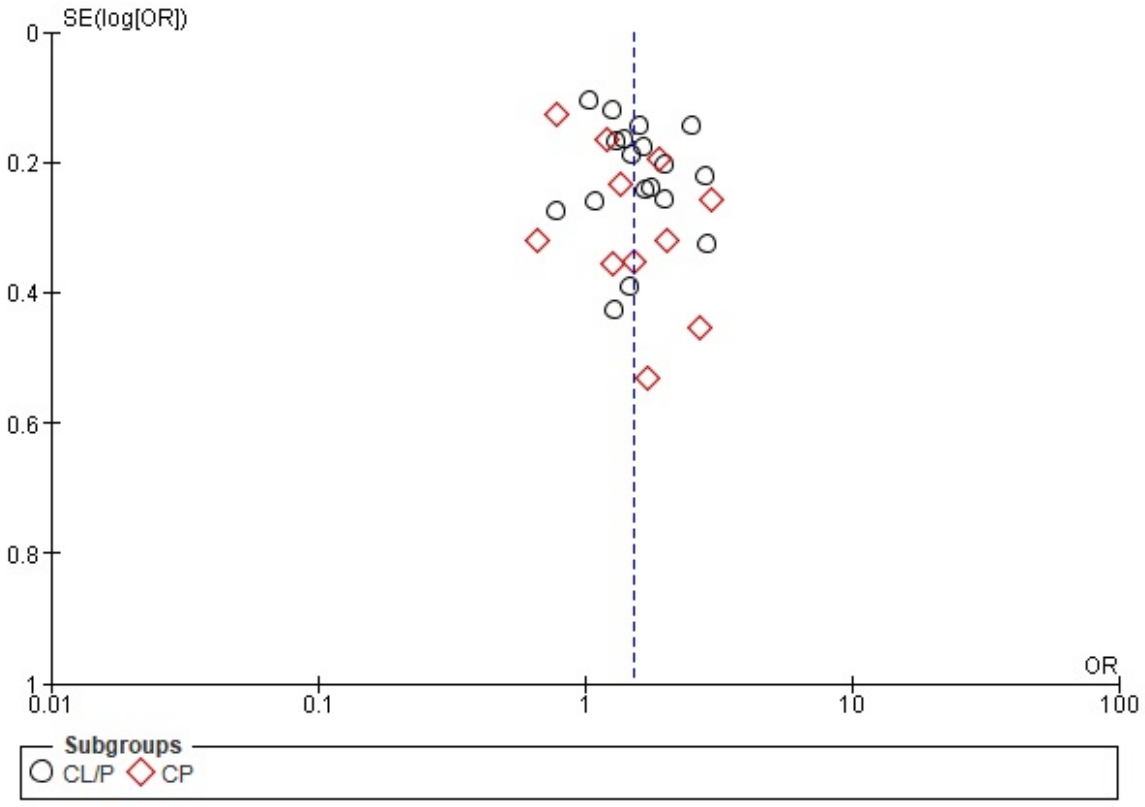
Supplementary Figure 7. Forest plot for meta-analysis of the association between maternal environmental tobacco smoking and the risk of having an infant with cleft lip and palate or cleft lip and its association with environmental tobacco smoking using the reported adjusted odds ratio.



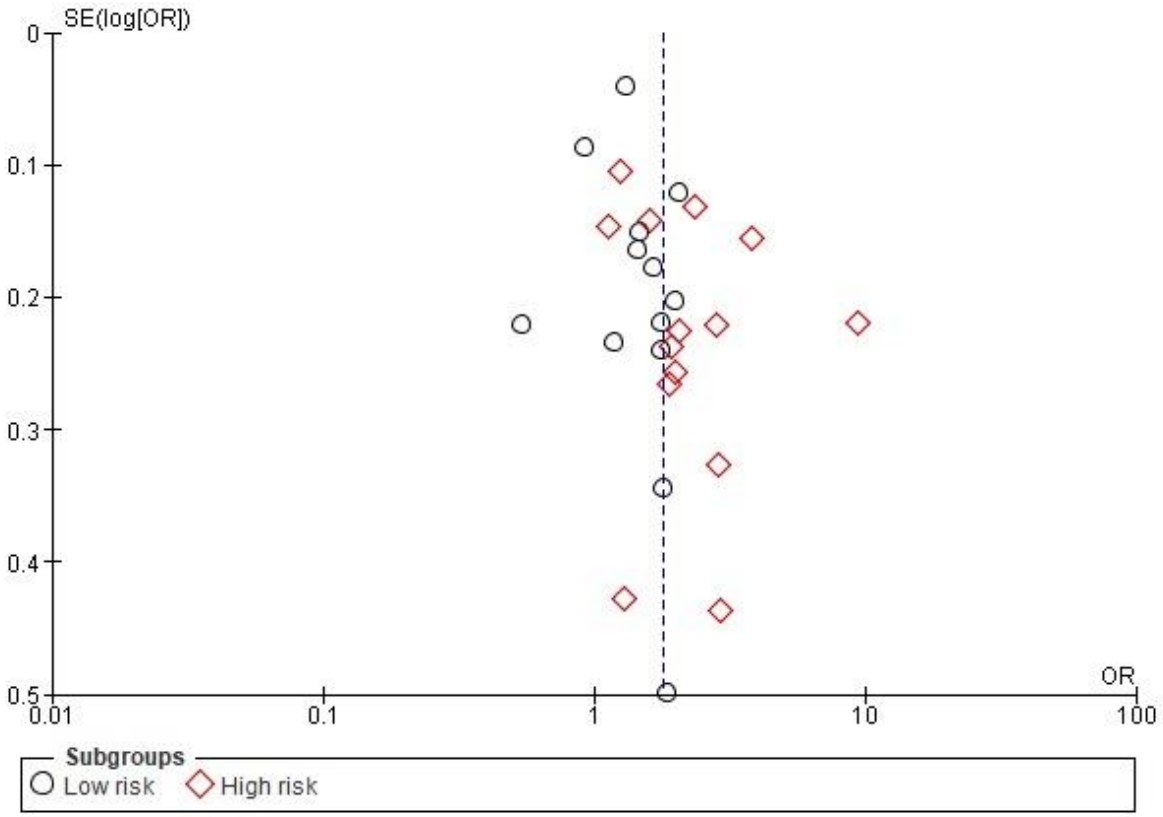
Supplementary Figure 8. Forest plot for meta-analysis of the association between maternal environmental tobacco smoking and the risk of having an infant with NSOFC according to period of exposure



Supplementary Figure 9. Funnel plot for studies showing the relationship between maternal environmental tobacco exposure and both CL/P and CP.



Supplementary Figure 10. Funnel plot for studies showing the relationship between maternal environmental tobacco exposure and NSOFC for both low risk and high risk studies.



Supplementary Figure 11. Cumulative meta-analysis for the stability of evidence from 2011 through 2021.