

Supplementary Table1. Four kinds of primers of present 13 studies

Author	Year	Forward (bp)	Reverse (bp)	Island(bp)
Dong et al (2007, Korea)	2007	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Feng et al (2008, USA)	2008	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Hanabata et al (2004, Japan)	2004	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Hsu et al (2007, Taiwan)	2007	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Jin et al (2009, Japan)	2009	chr16:82,627,104-82,627,124	chr16:82,627,187-82,627,206	chr16:82660651-82661813
Nikolaidis et al (2012, UK)	2012	chr16:82,660,654-82,660,671	chr16:82,660,705-82,660,726	chr16:82660651-82661813
Toyooka et al (2001, USA)	2001	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Toyooka et al (2003, USA)	2003	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Tsou et al (2007, USA)	2007	chr16:82,660,709-82,660,729	chr16:82,660,792-82,660,811	chr16:82660651-82661813
Ulivi et al (2006, Italy)	2006	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Wang et al (2008, China)	2008	NA	NA	chr16:82660651-82661813
Zhai et al (2014, China)	2014	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813
Zhang et al (2011, China)	2011	chr16:82,660,749-82,660,767	chr16:82,660,652-82,660,673	chr16:82660651-82661813

NA: not found in the article.

Supplementary Table 2. Differential CDH13 methylation, odds ratio between adenocarcinoma, squamous cell carcinoma and their counterparts from

GSE39279 & GSE52401 dataset

Type	Position	CpG site	McaM	McoM	$\Delta\beta$	p-value ^a	p-value ^b
LUAD	chr16:82660670	cg08747377	0.32658	0.1609	0.16568	1.11E-51	4.43E-28
	chr16:82660727	cg05374412	0.23438	0.04392	0.19046	9.02E-77	1.29E-22
	chr16:82661421	cg08856946	0.2117	0.07414	0.13756	2.63E-68	1.21E-24
	chr16:82661521	cg13759328	0.28992	0.17442	0.11549	9.78E-61	1.29E-28
	chr16:82661638	cg09189772	0.28967	0.1819	0.10778	2.63E-49	9.12E-26
	chr16:82661725	cg19369556	0.27121	0.22947	0.04173	6.98E-09	6.44E-09
LUSC	chr16:82660670	cg08747377	0.23598	0.1609	0.07507	8.92E-12	1.61E-10
	chr16:82660727	cg05374412	0.12757	0.04392	0.08365	3.65E-33	6.34E-14
	chr16:82661421	cg08856946	0.14118	0.07414	0.06704	3.55E-30	6.01E-17
	chr16:82661521	cg13759328	0.24259	0.17442	0.06817	2.59E-26	1.71E-17
	chr16:82661638	cg09189772	0.23064	0.1819	0.04875	9.62E-10	1.51E-10
	chr16:82661725	cg19369556	0.22208	0.22947	0.00739	0.005638311	0.145187084

McaM and McoM represent the mean of case methylation (Beta) and mean of control methylation (Beta). Methylation levels are calculated with formula: Beta = (M/M + U).

Position represents the chromosome position of each CpG site according to GRCh37/hg19.

P-value^a was calculated from Wilcoxon rank sum test after false discovery rate(FDR adjustment).

P-value^b was calculated from logistic regression analysis after false discovery rate(FDR adjustment).

Supplementary Table 3. Differential methylation, odds ratio between adenocarcinoma, squamous cell carcinoma and their counterparts from

GSE56044 dataset

Type	CpG site	Position	McaM	McoM	$\Delta\beta$	p-value^a	p-value^b
LUAD	cg08747377	chr16:82660670	0.31	0.07	0.24	3.73E-5	0.009
	cg05374412	chr16:82660727	0.26	0.02	0.24	1.98E-5	0.03
	cg00806490	chr16:82660873	0.25	0.07	0.18	1.20E-5	0.009
	cg08856946	chr16:82661421	0.18	0.05	0.13	3.80E-5	0.02
	cg13759328	chr16:82661521	0.22	0.10	0.12	3.80E-5	0.01
	cg09189772	chr16:82661638	0.24	0.12	0.12	0.001	0.01
	cg19369556	chr16:82661725	0.20	0.17	0.03	0.85	0.52
LUSC	cg08747377	chr16:82660670	0.17	0.07	0.10	0.02	0.08
	cg05374412	chr16:82660727	0.10	0.02	0.08	0.16	0.21
	cg00806490	chr16:82660873	0.15	0.07	0.08	0.003	0.08
	cg08856946	chr16:82661421	0.11	0.05	0.06	0.14	0.17
	cg13759328	chr16:82661521	0.19	0.10	0.09	0.008	0.08
	cg09189772	chr16:82661638	0.18	0.12	0.06	0.24	0.27
	cg19369556	chr16:82661725	0.15	0.17	0.02	0.15	0.50

McaM and McoM represent the mean of case methylation (Beta) and mean of control methylation (Beta). Methylation levels are calculated with formula: $\text{Beta} = (M/M + U)$.

Position represents the chromosome position of each CpG site according to GRCh37/hg19.

P-values^a are calculated from Wilcoxon rank sum test after false discovery rate (FDR adjustment).

P-value^b and OR^b and 95%CI^b are from logistic regression analysis with P-value^b were also after false discovery rate (FDR adjustment).

Supplementary Table 4. Diagnosis sensitivity, specificity, accuracy and AUC based on logistic regression with fivefold cross-validation

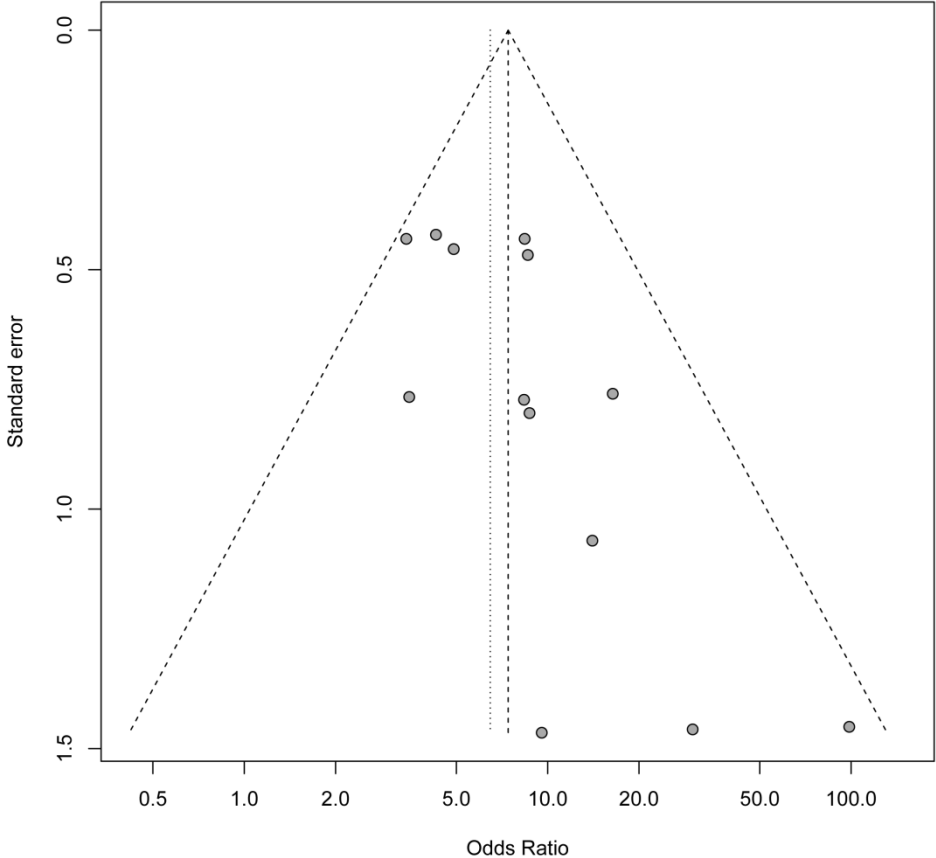
	CpGsite	Sensitivity	Specificity	Accuracy	AUC
LUAD vs.	cg08747377	0.884	0.774	0.82	0.866
	cg05374412	0.924	0.886	0.898	0.936
Control	cg08856946	0.894	0.818	0.85	0.896
	cg09189772	0.87	0.752	0.8	0.828
LUSC vs.	cg08747377	0.756	0.572	0.686	0.658
	cg05374412	0.806	0.698	0.764	0.744
Control	cg08856946	0.758	0.7	0.734	0.722
	cg09189772	0.762	0.524	0.672	0.596
LUAD vs. LUSC	cg08747377	0.784	0.768	0.776	0.816
	cg05374412	0.824	0.832	0.828	0.87
	cg08856946	0.802	0.756	0.78	0.83
	cg09189772	0.776	0.742	0.762	0.78

Logistic regression was conducted to perform the diagnosis analysis. Sensitivity, specificity, accuracy and AUC were derived from the test result of the model

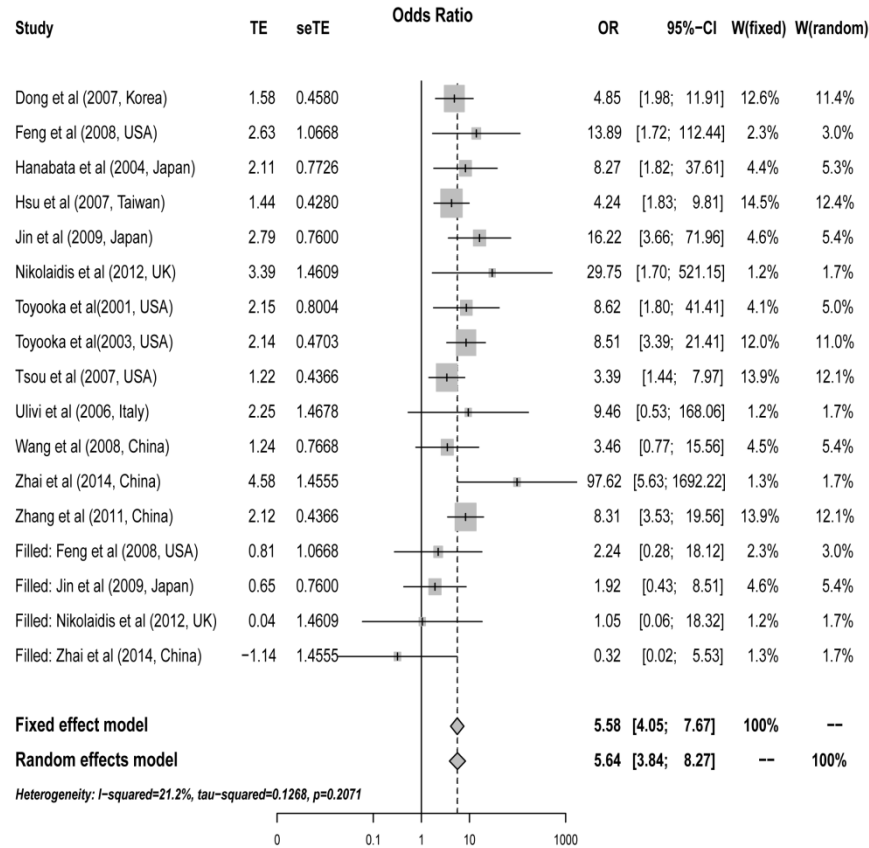
Supplementary Table 5. The QUADAS results for the 13 publications in the meta-analysis

Study	QUADAS Question														Total Score
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Dong et al (2007, Korea)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Feng et al (2008, USA)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Hanabata et al (2004, Japan)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Hsu et al (2007, Taiwan)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Jin et al (2009, Japan)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Nikolaidis et al (2012, UK)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Toyooka et al (2001, USA)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Toyooka et al (2003, USA)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11
Tsou et al (2007, USA)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Ulivi et al (2006, Italy)	1	1	1	1	0	1	1	1	1	0	1	1	0	0	10
Wang et al (2008, China)	1	1	1	1	1	1	1	1	1	0	1	1	1	0	12
Zhai et al (2014, China)	1	1	1	1	0	1	1	1	1	0	1	1	0	0	10
Zhang et al (2011, China)	1	1	1	1	1	1	1	1	1	0	1	1	0	0	11

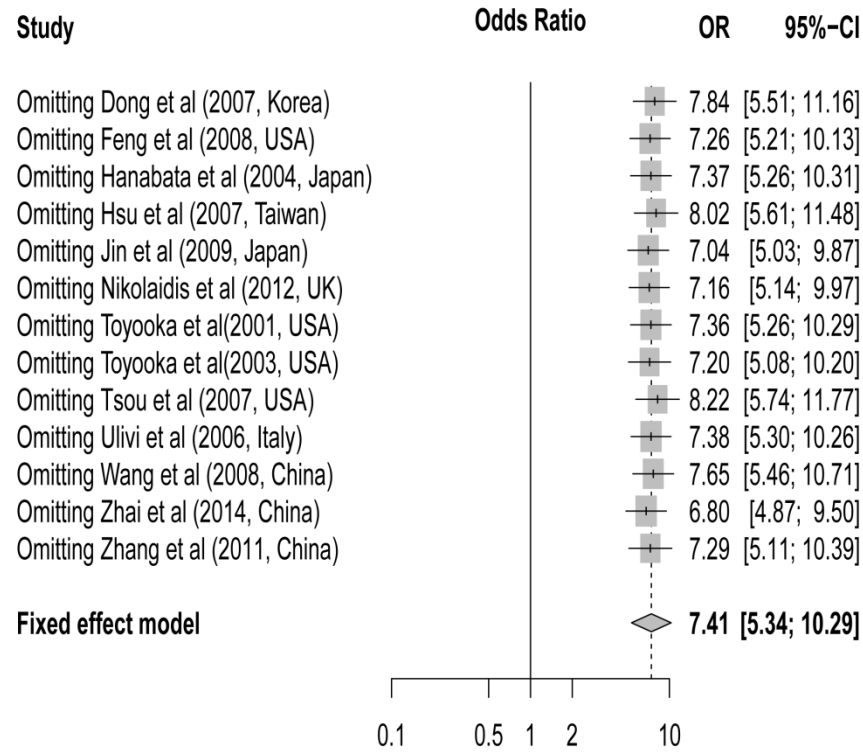
Supplementary Figure 1. Funnel plot to diagnosis of the publication bias



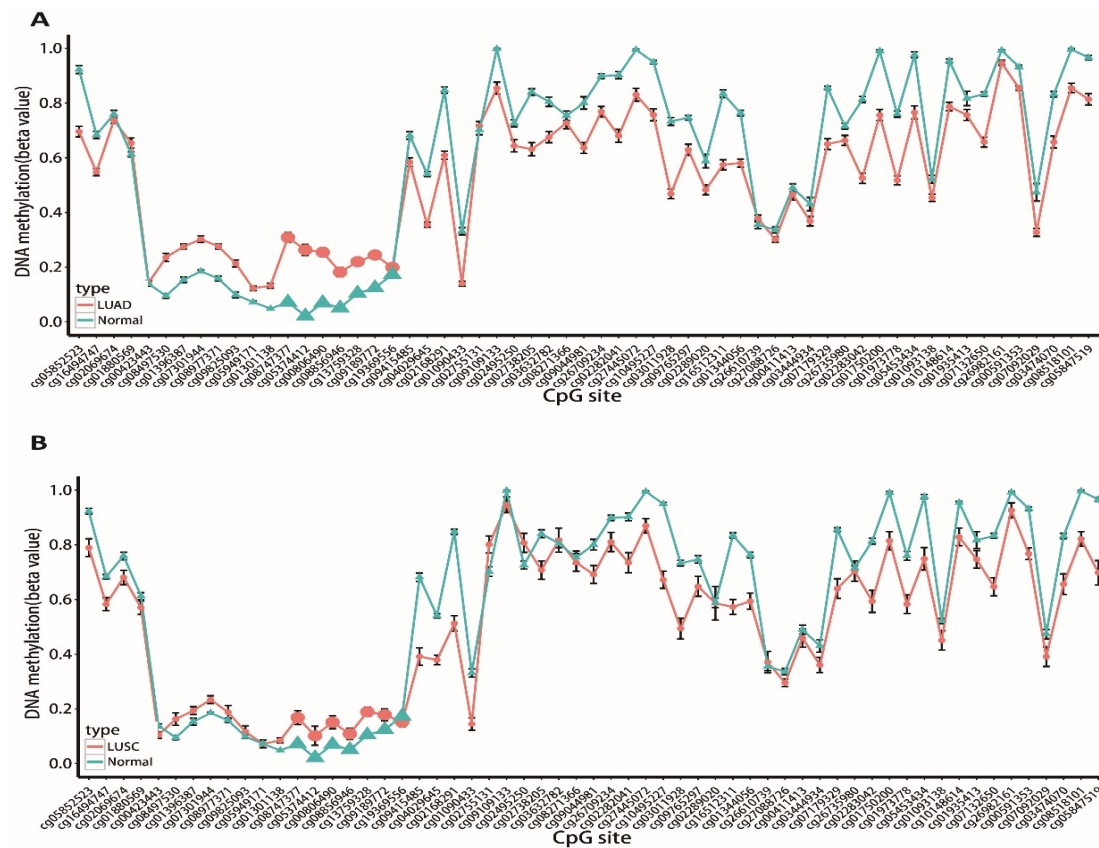
Supplementary Figure 2. Combined estimates for the association between CDH13 methylation and NSCLC after trim-fill treatment.



Supplementary Figure 3. Sensitivity analyses of the overall effect by omitting a single study.



Supplementary Figure 5. CpG sites on the Illumina Infinium HumanMethylation450 Beadchip array across CDH13 gene region from GSE56044 dataset.



The x-axis showed the different CpG sites in CDH13 gene and the y-axis shows the beta value of each CpG site to represent the methylation level of each CpG site.