The Association of GSTM1 Deletion Polymorphism with Lung Cancer Risk in Chinese Population: Evidence from an Updated Meta-analysis

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Previous studies have reported the association of glutathione S-transferase M1 (GSTM1) deletion polymorphism with genetic susceptibility of lung cancer in Chinese population. However, the results remained controversial. The aim of this study was to clarify the association of GSTM1 deletion polymorphism with lung cancer risk in Chinese population. Systematic searches were performed through the search engines of Medline/Pubmed, Web of Science, EMBASE, CNKI and Wanfang Medical Online. The pooled effects were calculated by STATA 10.0 software package and Review Manager 5.0.24. Overall, we observed an association of GSTM1 deletion polymorphism with increased lung cancer risk in Chinese population (odds ratio (OR) = 1.46, 95% confidence interval (95%CI): 1.32–1.66 for null genotype vs. present genotype) based on 53 studies including 7,833 cases and 10,353 controls. We also observed an increased risk of GSTM1 null genotype for lung cancer in stratified analyses by source of control, smoking status and histological type. The findings suggest that GSTM1 deletion polymorphism may contribute to lung cancer risk in Chinese population. Further, well-designed studies with larger sample sizes are required to verify the results.

The global incidence of lung cancer is 1,608,800 per year, with an annual mortality rate of 1,378,400. It was the most commonly diagnosed cancer as well as the leading cause of cancer death in males globally, and among females, it was the fourth most commonly diagnosed cancer and the second leading cause of cancer death. About 85% to 90% of lung cancers are non-small cell lung cancer including squamous cell carcinoma, adenocarcinoma, large cell carcinoma and other subtypes.

Epidemiological data have shown that environmental exposures such as tobacco smoking and asbestos are the main etiological factors in lung carcinogenesis. However, only a small fraction of people, who are exposed to such risk factors, will develop lung cancer. This indicates that an individual's susceptibility might play a certain role in lung carcinogenesis. Recently, increasing evidence has been accumulated to support the hypothesis that common genetic variations of drug-metabolizing enzyme genes may be of importance in determining an individual's sensitivity to develop lung cancer.

Glutathione S-transferases (GSTs) are a group of phase II detoxification enzymes which detoxify a broad range of compounds, including xenobiotics, pesticides, products of oxidative stress, chemotherapeutic drugs and carcinogens such as benzo(a)pyrene and other polycyclic aromatic hydrocarbons. Glutathione S-transferase mu-1 (GSTM1) is a polymorphic member of the mu class gene family of the GSTs. GSTM1 deletion polymorphism has been shown to result in the elimination of the activity of GSTM1 enzymes and modulate lung cancer risk. To date, results from epidemiological studies on the association between GSTM1 deletion polymorphism and lung cancer risk in Chinese population have been mixed. Recently, two meta-analyses have reported the association of GSTM1 deletion polymorphism with increased lung cancer risk in Chinese population. Unfortunately, some overlapping articles were not excluded and several published papers were missing in their papers. In order to obtain a more precise estimation of this relationship, a meta-analysis including a total of 53 studies was conducted, which may provide more comprehensive evidence for the association of GSTM1 deletion polymorphism with lung cancer risk in Chinese population.
Methods

Literature and methods. Systematic searches were performed in Medline/Pubmed, Web of Science, EMBASE, Chinese National Knowledge Infrastructure (CNKI) and Wanfang Medical Online, with the following terms utilized: “lung cancer” or “lung tumor” or “lung carcinoma” or “non-small cell lung cancer” or “small cell lung cancer” and “polymorphism” and “GSTM1” and “Chinese” or “China”. All publications were updated to July 15, 2014. Additional relevant references quoted in the searched articles were also selected.

Criteria of literature inclusion were (a) the subjects of literature must be Chinese; (b) the papers should evaluate the association of GSTM1 deletion polymorphism with lung cancer risk; (c) case-control studies or cohort studies; (d) studies should have sufficient data for estimating odds ratio (OR) with 95% confidence intervals (CI). The exclusion criteria were (a) studies without the number of case and control or other essential information and (b) reviews and repeated or overlapping studies. For repeated studies or overlapping studies, the publication with more information was selected when more than one article was identified for the same study population.

In total, ninety eight published articles were identified with the association of GSTM1 deletion polymorphism with lung cancer risk in Chinese population. We reviewed all papers according to the criteria listed, above; forty one overlapping studies and four reviews were excluded. At last, fifty three original articles that focused on the association between GSTM1 deletion polymorphism and lung cancer risk in Chinese population were determined to be eligible to enter our study (Fig. 1 Flow diagram).

Data extraction. Data were carefully extracted from all selected articles by two of the authors, independently. The following information was subtracted from selected studies: author’s name, publishing date, area, source of control, number of case and control, and number of null and present genotypes. Data coming from similar stratum were combined to make full use of them if the study provided stratum information. Characteristics of selected studies were summarized in Table 1.

Quantitative data synthesis. The strength of the association between GSTM1 deletion polymorphism and lung cancer risk was measured by OR with 95% CI. The Cochrane Q statistics test was used to assess heterogeneity. The combined OR was estimated using both a fixed-effects model and a random-effects model. The fixed-effects model was used when there was lack of heterogeneity. Otherwise, the random-effects model was used. The potential publication bias was firstly evaluated by visual inspection of the funnel plot. An asymmetric plot indicates that a possible publication bias exists. The funnel plot asymmetry was evaluated by the methods of Egger’s test and Begg’s test.

Statistical analysis was done using Review Manager (Version 5.0.24, the Cochrane Collaboration) and STATA10.0 software package (Stata Corporation, College Station, Texas). All the tests were two-sided, a P value of less than 0.05 for any test or model was considered to be statistically significant.

Results

Meta-analysis databases. A database was built in the light of the extracted information from selected articles. Some essential information was listed in Table 1, which indicated the first author’s name, year of publication, area, source of control, the number of case and control, and stratified factors. There were a total of 53 studies with 7,833 cases and 10,353 controls concerning the GSTM1 deletion polymorphism related to lung cancer risk. The frequency of GSTM1 null genotype was 57.7% and 50.1% in case and control, respectively.

Test of heterogeneity. The heterogeneity of GSTM1 null genotype vs. present genotype was analyzed for 53 selected studies. The results
showed that GSTM1 null genotype vs. present genotype for squamous cell carcinoma, hospitalized patients-based control, smokers and nonsmokers had no heterogeneity with a P value $\geq 0.05$. Therefore, a fixed-effects model was used to calculate the summary ORs for them. A random-effects model was used to calculate the summary ORs for the rest.

Quantitative data synthesis. Table 2 listed the summary ORs of GSTM1 deletion polymorphism related to lung cancer risk in Chinese population on the basis of 7,833 cases and 10,353 controls. We observed an association of GSTM1 deletion polymorphism with increased lung cancer risk in the total population (OR = 1.46, 95%CI: 1.32–1.61 for null vs. present) (Fig. 2). In subgroup analysis for

| Author | Year | Area | Source of control | Number of case | Number of control | Stratified factors |
|--------|------|------|-------------------|----------------|------------------|-------------------|
| Ai C7 | 2011 | Sichuan | Healthy subjects | 50 | 50 | |
| Chan EC8 | 2005 | Taiwan | Healthy subjects | 75 | 162 | Smoking |
| Chan Y40 | 2002 | Yunnan | Healthy subjects | 56 | 99 | |
| Chan-Yeung M9 | 2004 | Hong Kong | Healthy subjects | 229 | 197 | Histological type |
| Chen CM12 | 2012 | Zhejiang | Healthy subjects | 200 | 189 | Smoking |
| Chen H11 | 2008 | Anhui | Healthy subjects | 158 | 454 | Smoking |
| Chen HC12 | 2006 | Hunan | Healthy subjects | 97 | 197 | |
| Chen U13 | 2003 | Anhui | Healthy subjects | 38 | 99 | Smoking |
| Chen SQ14 | 2001 | Hubei | Healthy subjects | 106 | 106 | Smoking and age |
| Cheng YW15 | 2000 | Taiwan | Hospitalized patients | 73 | 33 | |
| Dong CT16 | 2004 | Sichuan | Hospitalized patients | 82 | 91 | |
| Du GB17 | 2011 | Sichuan | Hospitalized patients | 125 | 125 | Histological type and smoking |
| Fowke JH18 | 2011 | Shanghai | Healthy subjects | 208 | 785 | |
| Gao Y19 | 1999 | Guangdong | Hospitalized patients and healthy subjects | 59 | 132 | Histological type and smoking |
| Ge H20 | 1996 | Hongkong | Hospitalized patients and healthy subjects | 89 | 53 | |
| Gu Y21 | 2007 | Beijing | Hospitalized patients and healthy subjects | 279 | 684 | Histological type and smoking |
| Huang XH22 | 2004 | Guangdong | Hospitalized patients and healthy subjects | 85 | 138 | Histological type and smoking |
| Jiang XY23 | 2014 | Inner Mongolia | Healthy subjects | 180 | 266 | |
| Lan Q24 | 2004 | Yunnan | Healthy subjects | 122 | 122 | |
| Lei FM25 | 2007 | Sichuan | Healthy subjects | 42 | 103 | Smoking and drinking |
| Li DR26 | 2005 | Sichuan | Hospitalized patients | 99 | 66 | Smoking |
| Li YY27 | 2012 | Beijing | Healthy subjects | 217 | 200 | Smoking |
| Li Y28 | 2006 | Henan | Healthy subjects | 98 | 138 | Histological type and smoking |
| Liang GY29 | 2004 | Jiangsu | Hospitalized patients | 152 | 152 | Histological type |
| Liang KC30 | 2012 | Guangxi | Healthy subjects | 68 | 70 | |
| Liu DZ31 | 2012 | Heilongjiang | Healthy subjects | 360 | 360 | Histological type and smoking |
| Liu Q32 | 2008 | Shandong | Healthy subjects | 110 | 125 | |
| London SJ33 | 2000 | Shanghai | Healthy subjects | 232 | 710 | |
| Lu QK34 | 2013 | Guangdong | Healthy subjects | 91 | 138 | Histological type and smoking |
| Luo CL35 | 2004 | Guangdong | Healthy subjects | 63 | 47 | |
| Lv W36 | 2002 | Beijing | Healthy subjects | 314 | 314 | Histological type and smoking |
| Pan CG37 | 2014 | Jiangxi | Healthy subjects | 523 | 523 | Histological type and smoking |
| Persson I38 | 1999 | Beijing | Healthy subjects | 75 | 119 | Histological type and smoking |
| Qian BY39 | 2006 | Tianjin | Healthy subjects | 108 | 108 | Smoking |
| Qiao GB41 | 2005 | Guangdong | Hospitalized patients and healthy subjects | 213 | 199 | Smoking |
| Qu YH42 | 1998 | Shanghai and Heilongjiang | Healthy subjects | 182 | 179 | |
| Shi Y43 | 2002 | Hubei | Healthy subjects | 120 | 120 | Smoking, age and sex |
| Sun GF44 | 1997 | Liaoning | Healthy subjects | 207 | 364 | Smoking |
| Wang JW45 | 2004 | Beijing | Healthy subjects | 164 | 181 | Smoking |
| Wang M46 | 2009 | Inner Mongolia | Healthy subjects | 304 | 316 | |
| Wang N47 | 2012 | Henan | Healthy subjects | 209 | 256 | |
| Wang QM48 | 2006 | Hubei | Healthy subjects | 56 | 42 | Smoking |
| Xia Y49 | 2008 | Gansu | Hospitalized patients | 58 | 116 | Smoking |
| Yang XH50 | 2004 | Liaoning | Healthy subjects | 186 | 139 | |
| Yao W51 | 2006 | Henan | Healthy subjects | 77 | 107 | Histological type |
| Yao Z52 | 2012 | Beijing | Healthy subjects | 150 | 150 | Smoking |
| Zhang HY53 | 2014 | Yunnan | Healthy subjects | 110 | 100 | Histological type and smoking |
| Zhang JK54 | 2002 | Guangdong | Healthy subjects | 161 | 165 | Smoking |
| Zhang JQ55 | 2011 | Yunnan | Healthy subjects | 56 | 50 | |
| Zhang L56 | 2002 | Jiangsu | Healthy subjects | 65 | 60 | Histological type and smoking |
| Zhao B57 | 2001 | Singapore | Hospitalized patients | 233 | 187 | |
| Zheng DJ58 | 2010 | Tianjin | Healthy subjects | 265 | 307 | Histological type |
| Zhu XX59 | 2010 | Hunan | Healthy subjects | 160 | 160 | |
| Table 2 | Summary odds ratios on the relation of the GSTM1 deletion polymorphism to lung cancer risk in Chinese population |
|---|---|
| **Null vs. Present** | Case/Control | Heterogeneity test | Hypothesis test | Begg’s test | Egger’s test |
| **Q** | **P** | Summery OR (95% CI) | **Z** | **P** | **df** | **Z** | **P** | **t** | **P** |
| **All studies** | 7833/10353 | 123.12 | <0.00001 | 1.46 (1.32–1.61) | 7.40 | <0.00001 | 52 | 1.53 | 0.127 | 1.79 | 0.079 |
| Stratification by source of control | Healthy subjects | 6459/8420 | 108.7 | <0.00001 | 1.48 (1.32–1.66) | 6.56 | <0.00001 | 41 | 1.82 | 0.069 | 1.94 | 0.059 |
| | Hospitalized patients | 1735/1933 | 14.88 | 0.31 | 1.40 (1.22–1.60) | 4.77 | <0.00001 | 13 | 0.07 | 0.945 | 0.67 | 0.517 |
| Stratification by smoking status | Yes | 2284/2078 | 22.38 | 0.44 | 1.60 (1.41–1.81) | 7.48 | <0.00001 | 22 | 0.05 | 0.958 | 0.50 | 0.620 |
| | No | 1468/2260 | 26.58 | 0.11 | 1.79 (1.54–2.08) | 7.58 | <0.00001 | 19 | 1.27 | 0.205 | 1.39 | 0.180 |
| Stratification by histological Type | Squamous cell carcinoma | 1218/3375 | 15.96 | 0.25 | 1.50 (1.31–1.72) | 5.89 | <0.00001 | 13 | 0.00 | 1.000 | 0.40 | 0.694 |
| | Adenocarcinoma | 1150/3368 | 28.44 | 0.008 | 1.36 (1.08–1.70) | 2.66 | 0.008 | 13 | 0.99 | 0.324 | 0.79 | 0.443 |

**Figure 2** | Forest plot of odds ratio for GSTM1 deletion polymorphism associated with lung cancer risk in Chinese population.
source of control, we observed an increased risk of lung cancer with GSTM1 null genotype in healthy subjects-based control (OR = 1.48, 95%CI: 1.32–1.66) and hospitalized patients-based control (OR = 1.40, 95%CI: 1.22–1.60), respectively. We also observed an increased risk of GSTM1 null genotype for lung cancer stratified by smoking status (OR = 1.60, 95%CI: 1.41–1.81 for smokers and OR = 1.79, 95%CI: 1.54–2.08 for nonsmokers, respectively). We observed an association between GSTM1 null genotype and increased lung cancer risk in stratified analysis by histological type (OR = 1.50, 95%CI: 1.31–1.72 for squamous cell carcinoma and OR = 1.36, 95%CI: 1.08–1.70 for adenocarcinoma, respectively) (Table 2).

Bias diagnosis. Funnel plot was used to assess the publication bias, the shape of funnel plot seemed to be approximately symmetrical (Fig. 3). Results from Egger’s test and Begg’s test indicated that no obvious publication bias existed in this meta-analysis (Table 2).

Sensitivity analysis. The sensitivity analysis was performed to determine the influence of the individual dataset on the summary ORs by consecutively excluding individual studies. The overall effects were not changed significantly when the study was homogenous for GSTM1 null genotype vs. present genotype among total population by removing some eligible studies, indicating that our results were statistically robust (Fig. 4).

Discussion

GSTM1 gene is located on the short arm of chromosome 1 (1p13.3)65. It is 5,950 bp long consisting of seven introns and eight exons, which encodes a cytosolic protein of 218 amino acid residues with a molecular weight of 21/25 kDa. GSTM1 gene has a null variant allele, which results in an absence of enzyme activity. Individuals who carry homozygous deletions in this gene are thought to be increased risks for malignancies because of their reduced capacity to detoxify potential carcinogens56,65. In addition, GSTM1 null/present polymorphisms could predict the treatment response of the platinum-based chemotherapy in NSCLC patients, especially in East-Asian patients66. Some meta-analyses explored the association of GSTM1 deletion polymorphism with lung cancer risk in Chinese population69–72. In this paper, we performed a systematic literature review to comprehensively evaluate the association of GSTM1 deletion polymorphism with lung cancer risk in Chinese population. We also evaluated the possible effect modifications by source of control, smoking status and histological subtype. The frequency of GSTM1 null genotype was 57.7% (range: 34%–76.7%) and 50.1% (range: 14%–66.4%) in case and control, respectively. The highest frequency of GSTM1 null genotype (66.4%) in control was found in Beijing55 and the lowest frequency of GSTM1 null genotype (14%) in control was found in Yunnan55. In summary, we observed an increased lung cancer risk in subjects with GSTM1 null genotype. Two previous meta-analyses have reported the association of GSTM1 deletion polymorphism with increased lung cancer risk in Chinese population60,61. However, there are some key limitations in their studies. For example, three overlapping studies73–75 were not properly excluded from Shi et al’ study and seven papers published before 200613,16,41–43,54,56 were missing. For Liu et al’ paper, eighteen overlapping papers74,76–92 were not properly excluded. Therefore, the findings from these two meta-analyses should be clarified urgently by using the updated data. The present meta-analysis of 53 published studies including 7,833 cases and 10,353 controls might present a precise estimation of the association of GSTM1 deletion polymorphism with lung cancer risk in Chinese population, owing to including the updated data.

Considering that cigarette smoking is an evident risk factor for lung cancer, and that GSTM1 is involved in the metabolism of various carcinogens present in cigarette smoking, a subgroup analysis regarding smoking status was conducted. After being stratified by smoking status, the GSTM1 null genotype was associated with an increased risk of lung cancer in both smokers and nonsmokers.

Lung cancer consists of at least three major histological subtypes: squamous cell carcinoma, adenocarcinoma and small cell carcinoma. It is well-known that the development of squamous cell carcinoma and small cell carcinoma is strongly correlated with cigarette smoking, whereas that of adenocarcinoma is less correlated compared with those two subtypes, which indicates that carcinogenic processes are
different among the different subtypes of lung cancer. Therefore, a stratified analysis was conducted by histological subtype. We observed significant associations of GSTM1 deletion polymorphism with the increased risk of both squamous cell carcinoma and adenocarcinoma. Further stratified analyses were not done in additional histological subtypes, since the sample size for them was relatively small.

This meta-analysis should be interpreted within the context of its potential limitations. First, the combined ORs were based on individual unadjusted estimates, while a more precise analysis depending on adjusted factors should be performed if detailed individual data were available. Secondly, only published papers were enrolled in this study, which may cause publication bias. To address this issue, Egger’s test and Begg’s test were conducted at the same time. Our findings demonstrated that the likelihood of key publication bias might not be present in this meta-analysis. Thirdly, each study had different eligibility criteria for subjects and different source of controls, which should be taken into account while expounding the

| Study or Subgroup | Experimental Events | Control Events | Odds Ratio M-H, Fixed, 95% CI |
|-------------------|---------------------|----------------|--------------------------------|
| Ai C 2011        | 36                  | 50             | 3.02 [1.32, 6.93]              |
| Chan EC 2005     | 31                  | 75             | 0.55 [0.32, 0.96]              |
| Chan Y 2002      | 43                  | 58             | 1.73 [0.82, 3.65]              |
| Chan-Yeung M 2004| 130                 | 223            | 0.90 [0.61, 1.32]              |
| Chen CM 2012     | 123                 | 200            | 1.15 [0.78, 1.72]              |
| Chen H 2008      | 99                  | 158            | 1.42 [0.98, 2.08]              |
| Chen HC 2006     | 60                  | 97             | 1.97 [1.20, 3.33]              |
| Chen LJ 2003     | 24                  | 38             | 1.26 [0.58, 2.73]              |
| Chen SQ 2001     | 56                  | 106            | 1.92 [1.11, 3.33]              |
| Cheng YW 2000    | 34                  | 73             | 0.82 [0.36, 1.87]              |
| Dong CT 2004     | 48                  | 82             | 2.16 [1.17, 3.96]              |
| Du GB 2011       | 73                  | 125            | 1.07 [0.65, 1.76]              |
| Fowke JH 2011    | 110                 | 208            | 0.81 [0.40, 1.10]              |
| Gao Y 1999       | 34                  | 59             | 1.40 [0.75, 2.60]              |
| Ge H 1986       | 59                  | 89             | 1.01 [0.48, 2.07]              |
| Gu YF 2007       | 164                 | 279            | 1.58 [1.19, 2.09]              |
| Huang XH 2004    | 53                  | 85             | 1.47 [0.85, 2.56]              |
| Jiang XY 2014    | 102                 | 180            | 1.88 [1.28, 2.76]              |
| Lan Q 2004       | 82                  | 122            | 2.12 [1.28, 3.56]              |
| Lei FM 2007      | 24                  | 42             | 1.08 [0.52, 2.22]              |
| Li DR 2005       | 57                  | 99             | 1.98 [1.04, 3.69]              |
| Li WY 2012       | 127                 | 217            | 1.56 [1.05, 2.30]              |
| Li Y 2011        | 59                  | 98             | 1.91 [1.13, 3.23]              |
| Liang GY 2004    | 82                  | 152            | 1.08 [0.69, 1.70]              |
| Liang KC 2012    | 47                  | 66             | 1.78 [0.89, 3.57]              |
| Liu DZ 2012      | 145                 | 360            | 1.59 [1.17, 2.17]              |
| Liu Q 2008       | 66                  | 110            | 1.79 [1.06, 3.01]              |
| London SJ 2000   | 122                 | 232            | 0.74 [0.55, 0.99]              |
| Lu QK 2013       | 61                  | 91             | 1.98 [1.14, 3.42]              |
| Luo CL 2004      | 45                  | 63             | 2.40 [1.09, 5.28]              |
| Lv WF 2002       | 158                 | 314            | 1.04 [0.76, 1.42]              |
| Pan CG 2014      | 305                 | 523            | 1.87 [1.48, 2.39]              |
| Persson J 1989   | 48                  | 75             | 0.90 [0.48, 1.66]              |
| Qian BY 2003     | 69                  | 108            | 1.84 [1.07, 3.16]              |
| Qiao GB 2005     | 130                 | 213            | 1.71 [1.16, 2.54]              |
| Qu YH 1998       | 102                 | 182            | 1.15 [0.76, 1.74]              |
| Shi Y 2002       | 74                  | 120            | 2.03 [1.22, 3.40]              |
| Sun GF 1997      | 147                 | 207            | 2.34 [1.63, 3.37]              |
| Wang JW 2003     | 97                  | 164            | 1.46 [0.96, 2.24]              |
| Wang MJ 2009     | 143                 | 304            | 1.47 [1.07, 2.03]              |
| Wang N 2012      | 122                 | 209            | 1.77 [1.23, 2.57]              |
| Wang GM 2006     | 40                  | 56             | 3.03 [1.31, 7.01]              |
| Xia Y 2008       | 34                  | 58             | 1.28 [0.68, 2.42]              |
| Yang XH 2004     | 108                 | 188            | 1.16 [0.78, 1.74]              |
| Yao W 2006       | 45                  | 77             | 1.94 [1.07, 3.51]              |
| Yao ZQ 2012      | 96                  | 150            | 2.14 [1.35, 3.41]              |
| Zhang HY 2014    | 66                  | 110            | 2.07 [1.19, 3.59]              |
| Zhang JK 2002    | 94                  | 161            | 1.11 [0.72, 1.73]              |
| Zhang JQ 2011    | 17                  | 50             | 3.16 [1.18, 8.52]              |
| Zhang LZ 2002    | 41                  | 65             | 2.09 [1.02, 4.27]              |
| Zhao B 2001      | 146                 | 233            | 0.98 [0.64, 1.43]              |
| Zheng DJ 2010    | 150                 | 285            | 0.98 [0.71, 1.37]              |
| Zhu X 2010       | 93                  | 160            | 1.70 [1.08, 2.64]              |

Total (95% CI) 6532 7711 100.0% 1.55 [1.44, 1.65]
Total events 3803 3700
Heterogeneity: Chi² = 56.63, df = 46 (P = 0.10); I² = 22%
Test for overall effect: Z = 12.50 (P < 0.00001)

Figure 4 | Sensitivity analysis for GSTM1 null genotype vs. present genotype in Chinese population.
combined effects. When subgroup analysis was performed by source of control, we observed an association between GSTM1 deletion polymorphism and increased lung cancer risk in both healthy subjects–based control and hospitalized patients–based control.

In conclusion, this comprehensive review demonstrates that GSTM1 null genotype might be a risk factor for lung cancer in the Chinese population. Large scale studies with the pooling of individual study data should be taken into consideration in the future studies to verify the results from this present meta-analysis.
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Author contributions
Conceived and designed the experiments: W.Y. and Y.H.; Performed the experiments: Y.S., S.F. and W.H.; Analyzed the data: Y.H. and L.J.; Contributed reagents/materials/analysis tools: Y.S., S.F. and W.H.; Wrote the main manuscript text: W.Y. and Y.H.; Reference collection and data management: L.J. and Y.S.; Statistical analyses and paper writing: Y.H. and W.Y.; Study design: W.Y. and Y.H.; Prepared figures 1–4: W.H.; All authors reviewed the manuscript.

Additional information
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