**Online Supplementary Material 5**

**Results**

1. Outliers detection from eligible studies

****The *meta* and *metafor* packages for R were used to detect the outliers from all eligible studies. Four samples (Abellán ([2010](#_ENREF_1)) data 1, Sun ([2011](#_ENREF_5)) data 2, Ya ([2017](#_ENREF_6)) data 1 and data 2) were detected out and will be removed for R219K and HDLC level analysis (Figure S5-1 and Figure S5-2)

Figure S5-1. Plot of the various diagnostic measures of influence analyses. The influence measures of each study: ***retudent***, the externally standardized residuals; ***diffits***, DFFITS values; ***cook.d***, Cook’s distances; ***cov.r***, covariance ratios; ***tau2.del***, estimates of T2; ***QE.del***, the test statistics for (residual) heterogeneity when each study is removed in turn; ***hat***, the diagonal elements of the hat matrix; ***weight***, the weights (in%) given to the observed outcomes during the model fitting. Study considered to be influential, was colored in red in the plot.



Figure S5-2. Plot of DFBETAS values of influence analyses. Study considered to be influential, was colored in red in the plot.

1. Publication bias analysis

The publication bias of current study was assessed with *Begg*’s rank correlation ([Begg and Mazumdar 1994](#_ENREF_2)) and *Egger*’s weighted regression ([Egger, Smith et al. 1997](#_ENREF_4)) methods, and visualized by funnel plots (Figure S5-3). The missing studies were estimated by *trim-and-fill* method ([Duval 2005](#_ENREF_3)), and analyzed the difference between the effect values and their adjusted values considering missing studies.

The results of publication bias showed that both the *Begg’s* correlation (*Tau* = -0.24, *Z* = 3.83, two-tailed *P*<0.001) and the *Egger’s* regression (*t* (110) = 3.82, two-tailed *P*< 0.001) showed significant bias. The initial effect of R219K on HDLC level was significantly changed (the estimated missing studies n = 23, *SMD*adj = -0.26, 95% CI = -0.31 ~ -0.20; *t* = 2.34, *P* = 0.020) after adjustment with missing studies.

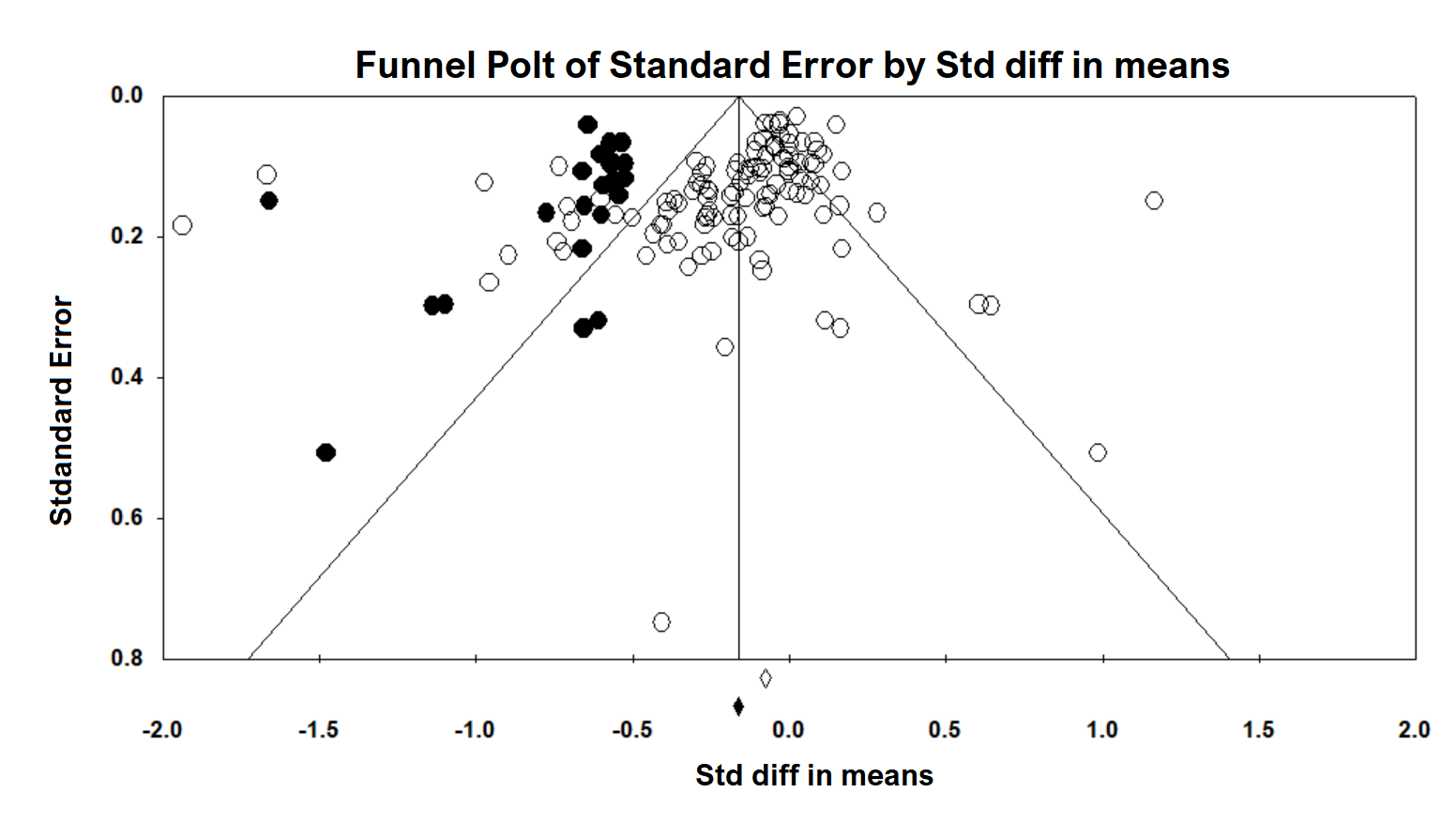


Figure S5-3: Shows the visually assessing on the asymmetry of funnel plot with imputed number of studies in all data (the black dots in the figure indicate the data that may be predicted).

References:

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