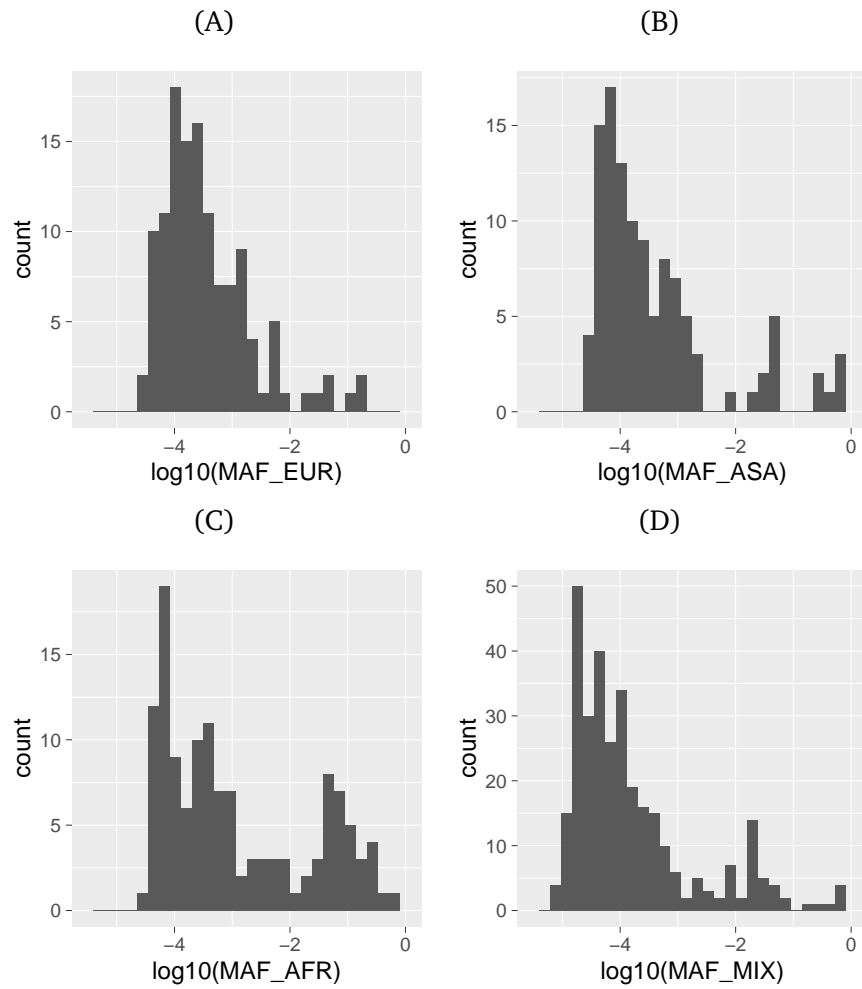


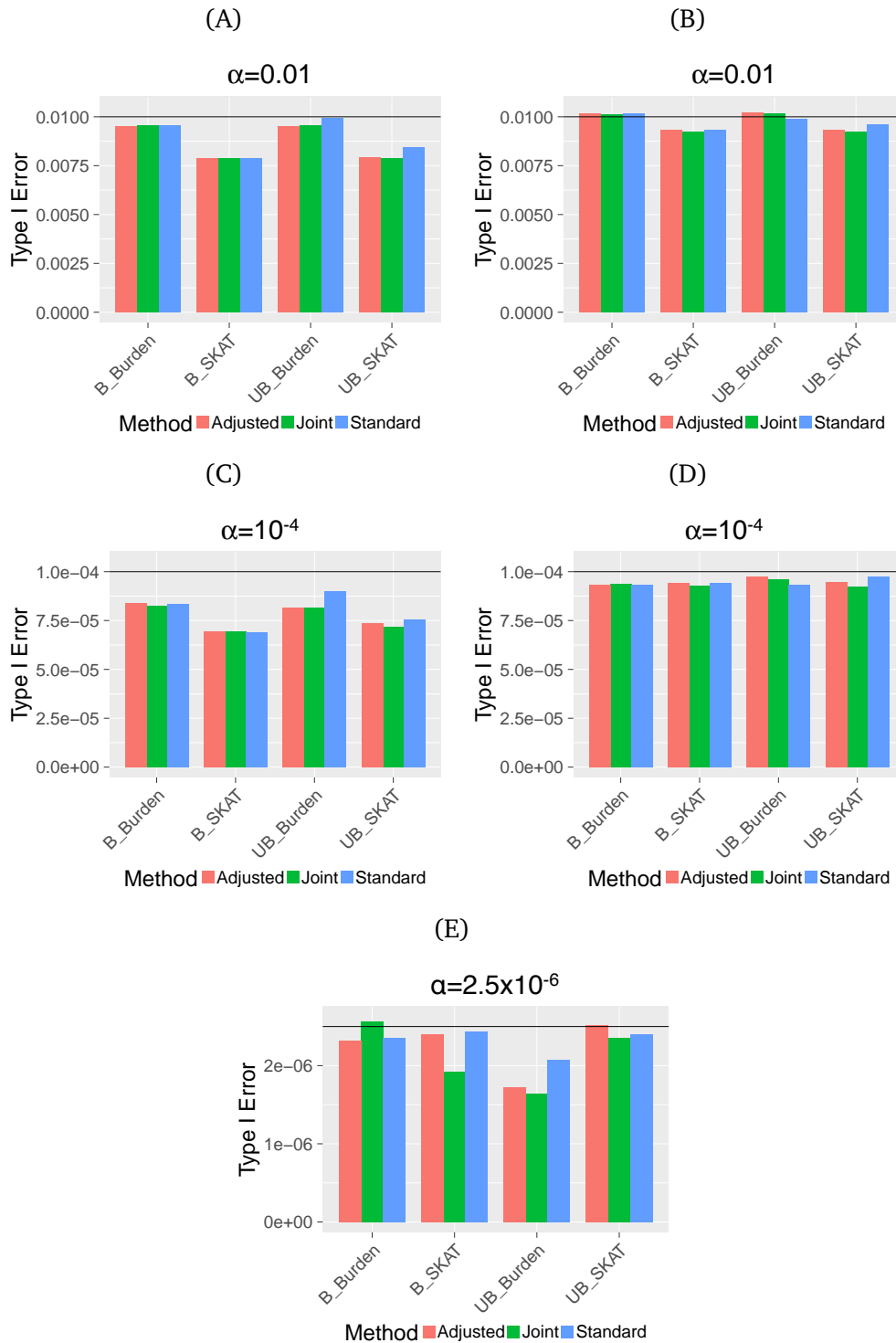
Supplementary Figures

Figure S 1: Spectrum plots of $\log_{10}(\text{MAFs})$ for simulated genotypes.



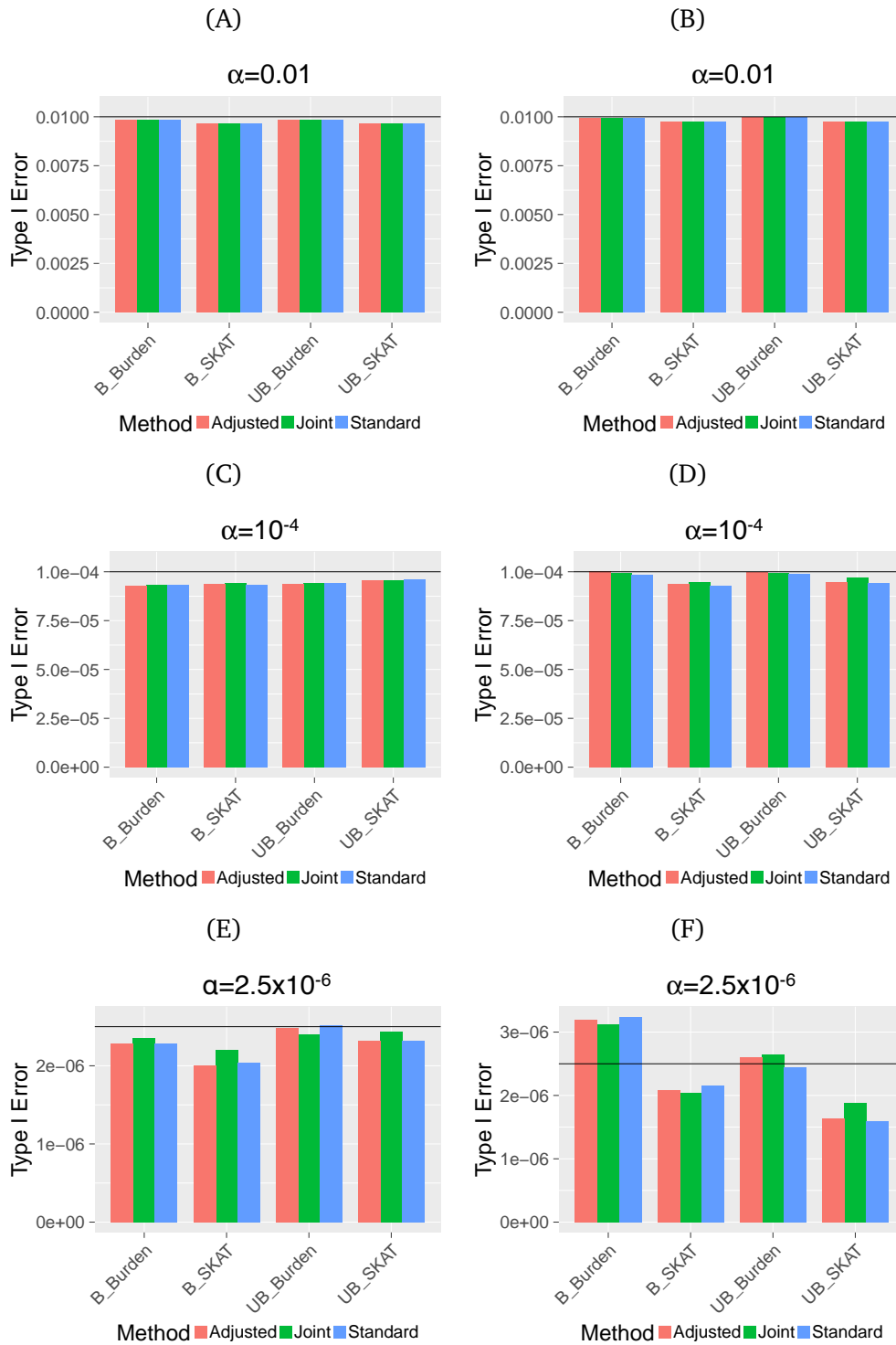
(A) European (EUR); (B) Asian (ASA); (C) African (AFR); (D) Mixed populations (MIX) of EUR, ASA, and AFR.

Figure S 2: Empirical type I errors of meta-Burden test and meta-SKAT with different significance levels ($\alpha = 0.01, 10^{-4}, 2.5 \times 10^{-6}$), for balanced (B) and unbalanced (UB) **dichotomous** studies without population stratifications.



(A, C): Scenarios with common covariates; (B, D, E) Scenarios with different covariates.

Figure S 3: Empirical type I errors of meta-Burden test and meta-SKAT with different significance levels ($\alpha = 0.01, 10^{-4}, 2.5 \times 10^{-6}$), for balanced (B) and unbalanced (UB) **quantitative** studies without population stratifications.



(A, C, E): Common covariates; (B, D, F) Different covariates.

Figure S 4: Empirical type I errors of meta-Burden test and meta-SKAT with different significance levels ($\alpha = 0.01, 10^{-4}$), for balanced (B) and unbalanced (UB) **dichotomous** studies with common covariates and population stratifications.

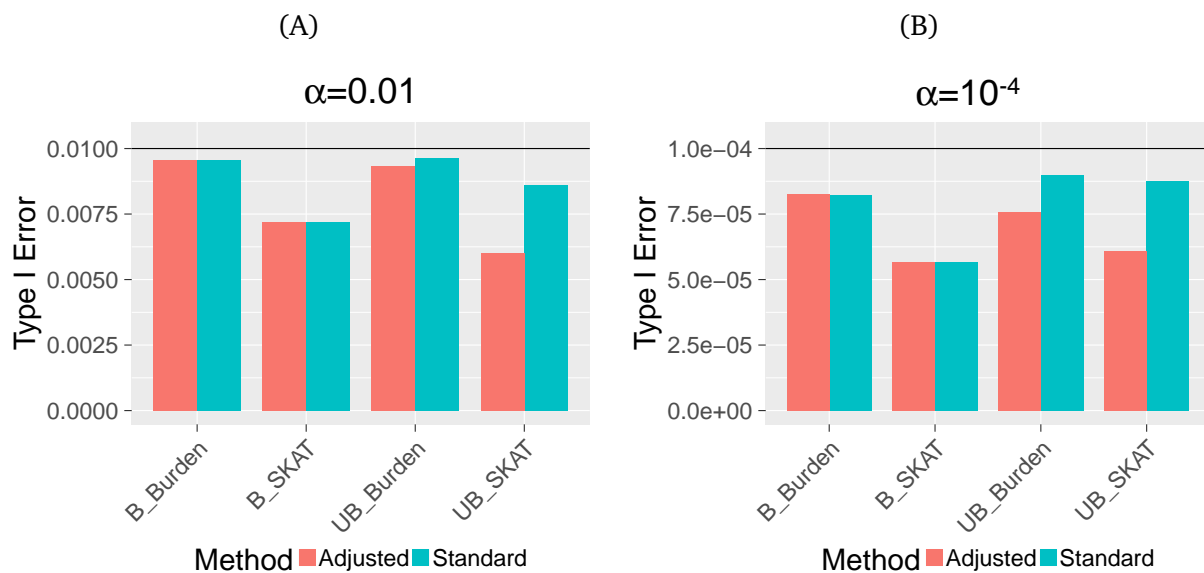
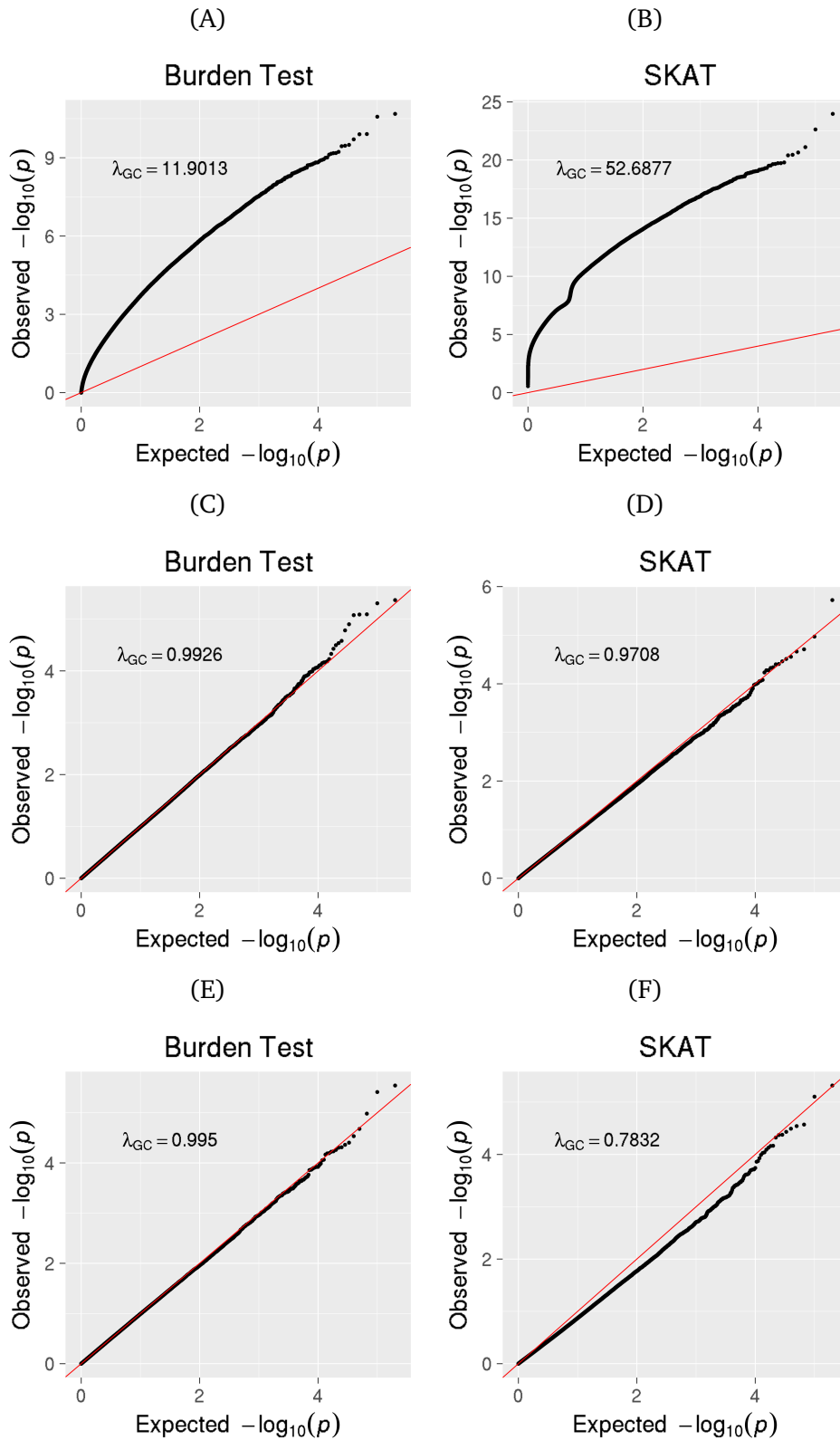


Figure S 5: Quantile-Quantile (QQ) plots of $-\log_{10}(p)$ values of meta-Burden test and meta-SKAT, for null simulations with multi-ethnic samples and unbalanced settings, along with the genomic control factors (λ_{GC}).



(A, B) Joint analysis with first 4 PCs as additional covariates; (C, D) Standard methods; (E, F) Our adjusted methods.

Figure S 6: Score statistic estimates in the **dichotomous** studies under balanced and unbalanced settings, with **different** covariates, without population stratification.

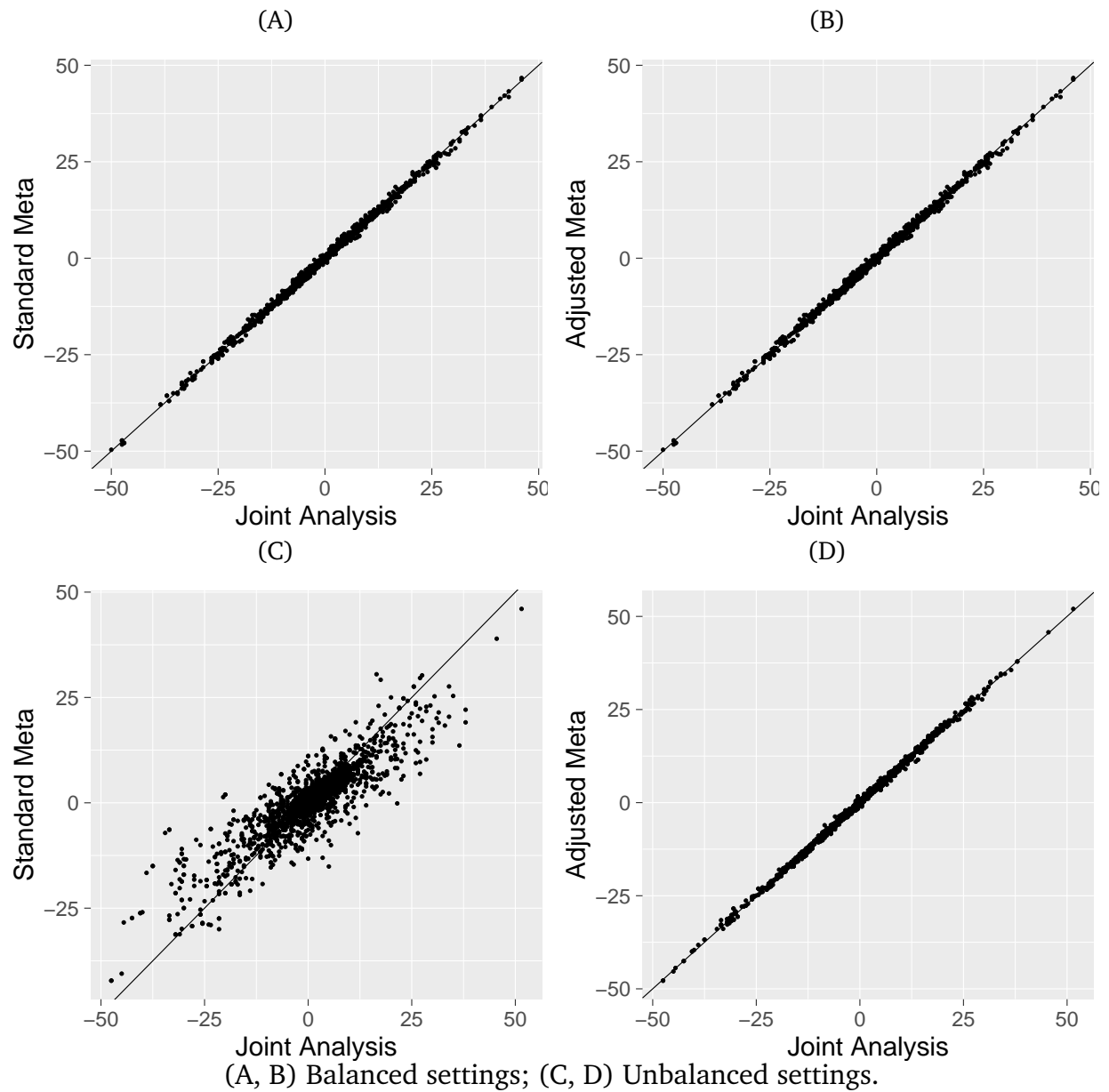


Figure S 7: $-\log_{10}(\text{p values})$ of single-variant score tests in the **dichotomous** studies with **different** covariates, without population stratification.

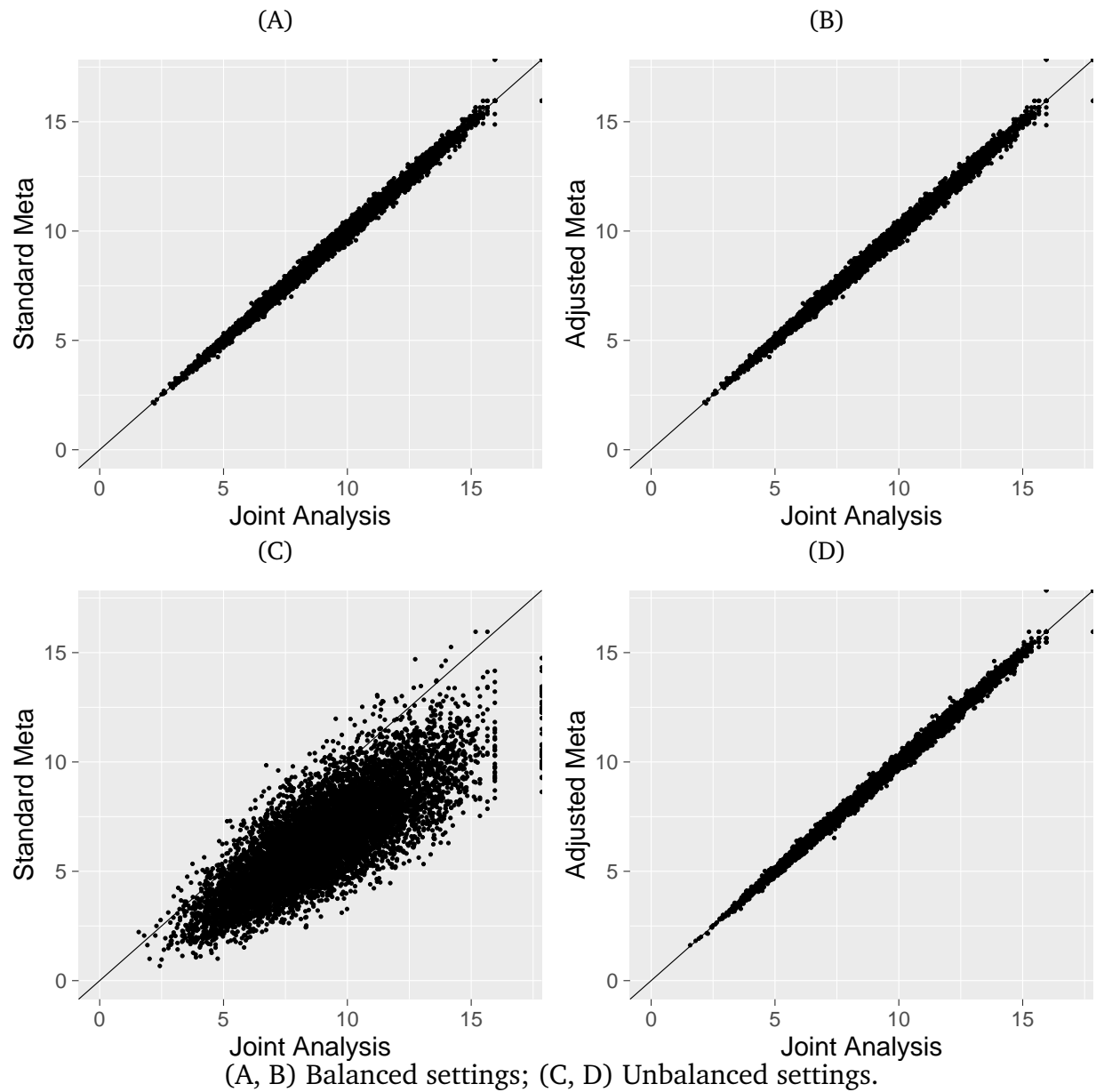


Figure S 8: Power comparison for balanced (B) and unbalanced (UB) **dichotomous** studies with **different** covariates, without population stratification.

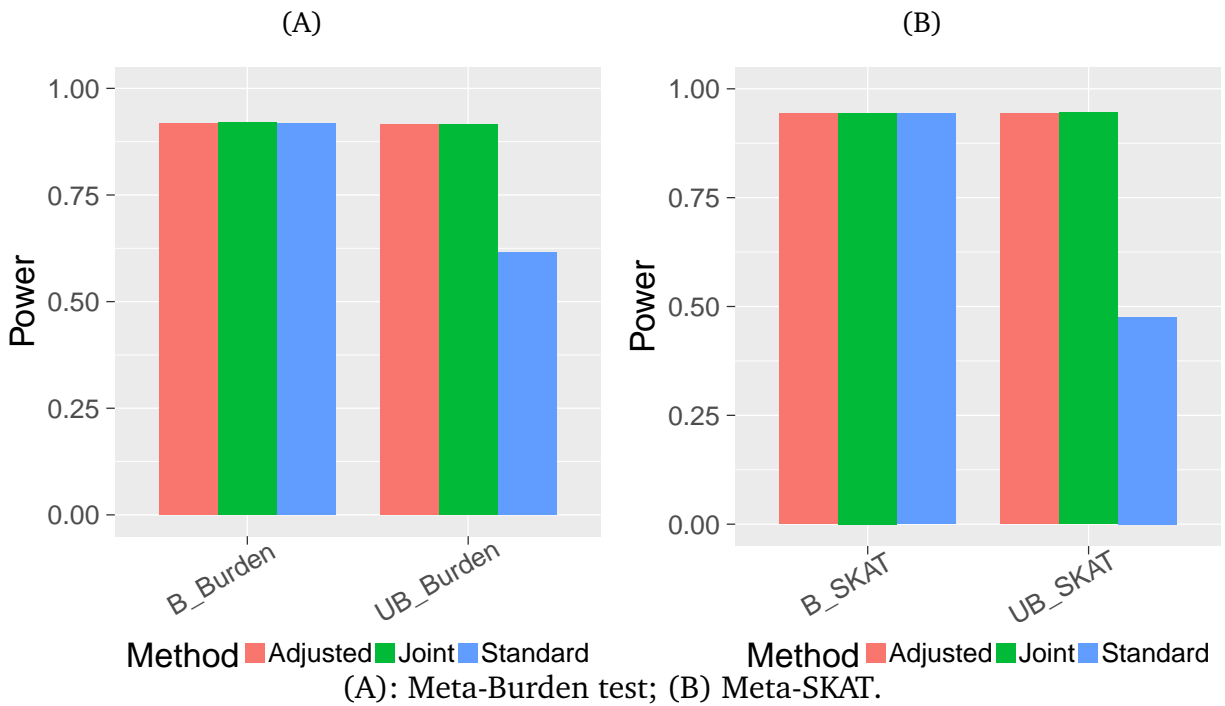


Figure S 9: Score statistic estimates in the **quantitative** studies under balanced and unbalanced settings, with **common** covariates, without population stratification.

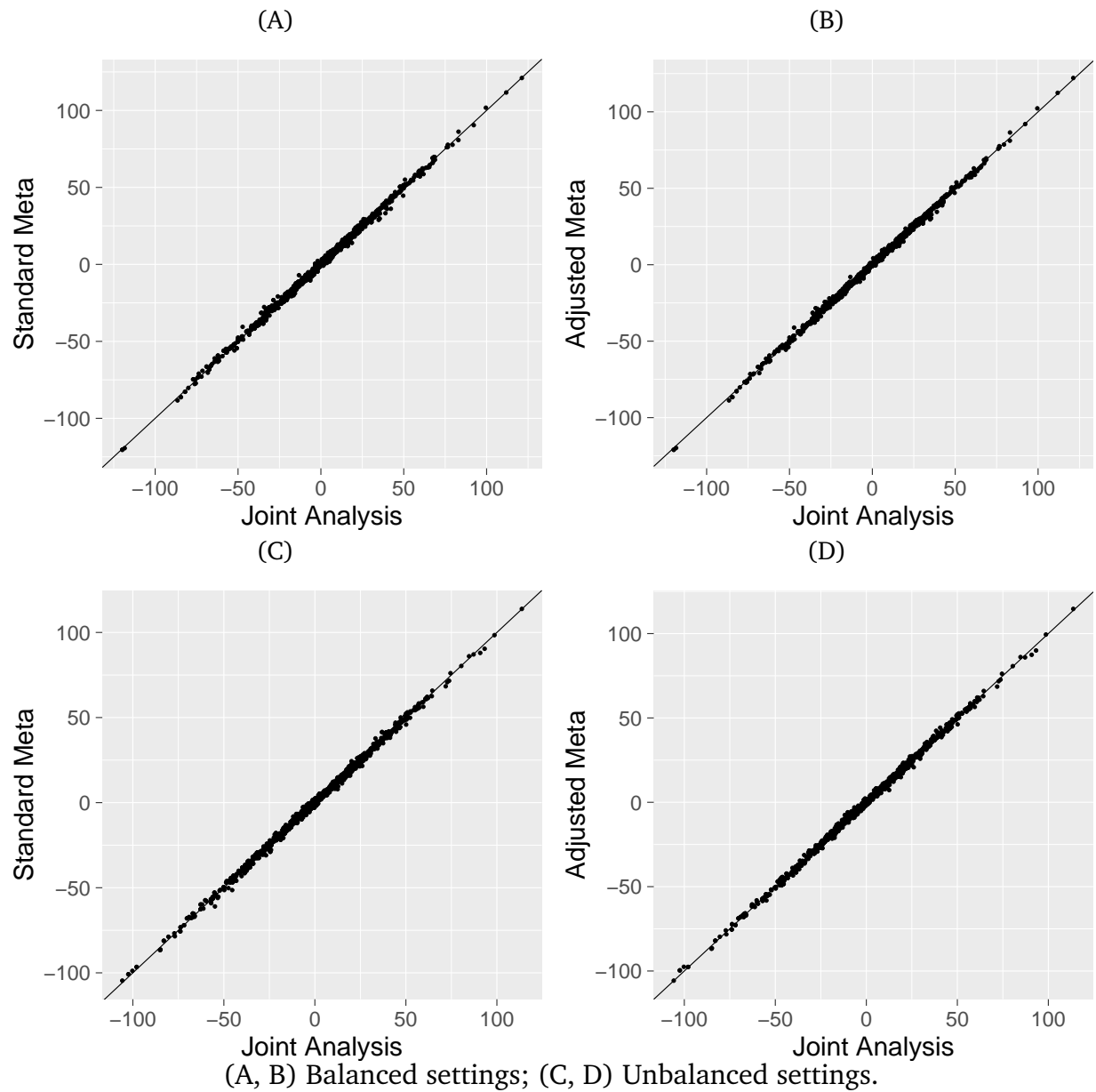


Figure S 10: $-\log_{10}$ (p values) of single-variant score tests in the **quantitative** studies with **common** covariates, without population stratification.

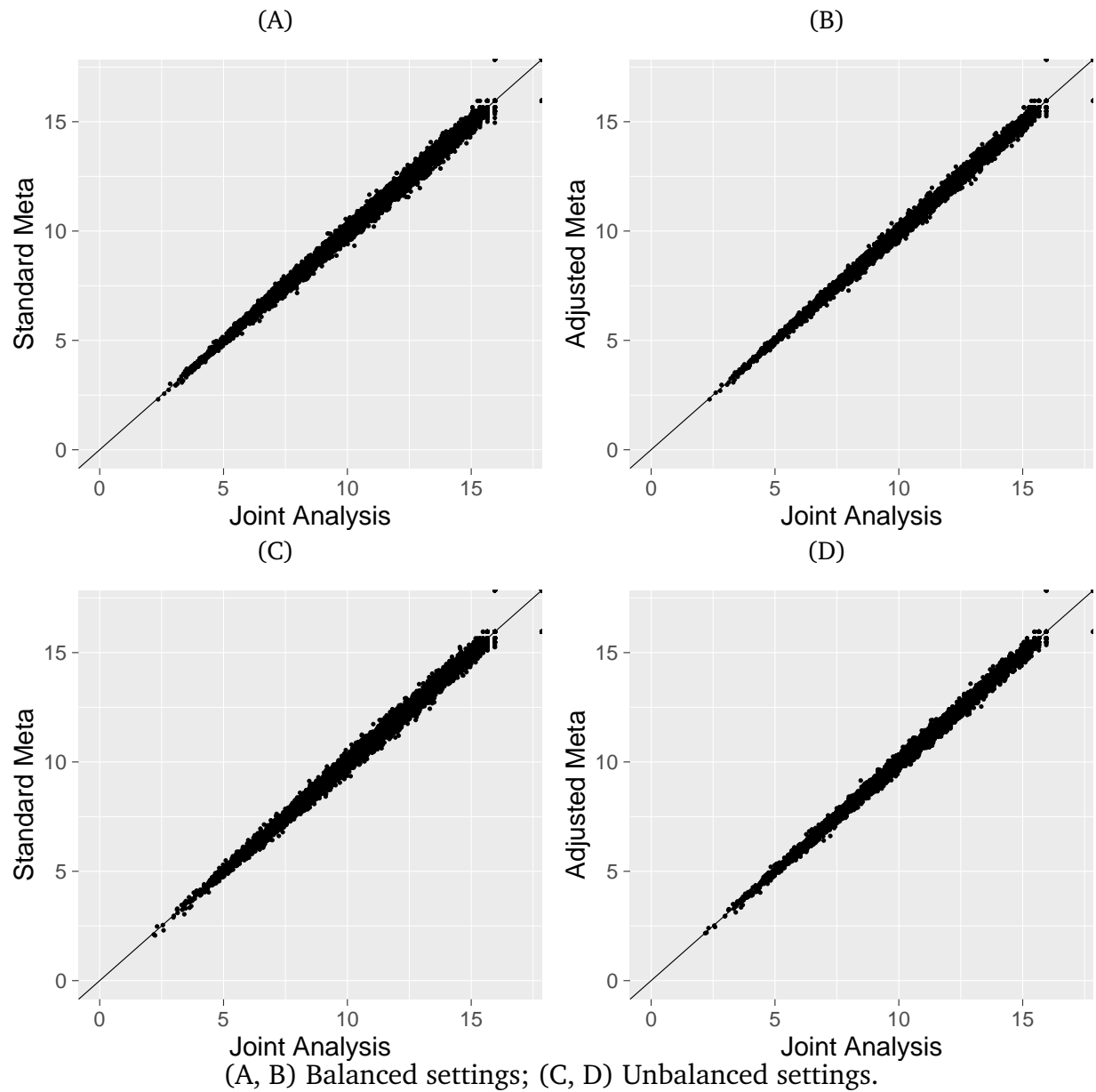


Figure S 11: Score statistic estimates in the **quantitative** studies under balanced and unbalanced settings, with **different** covariates, without population stratification.

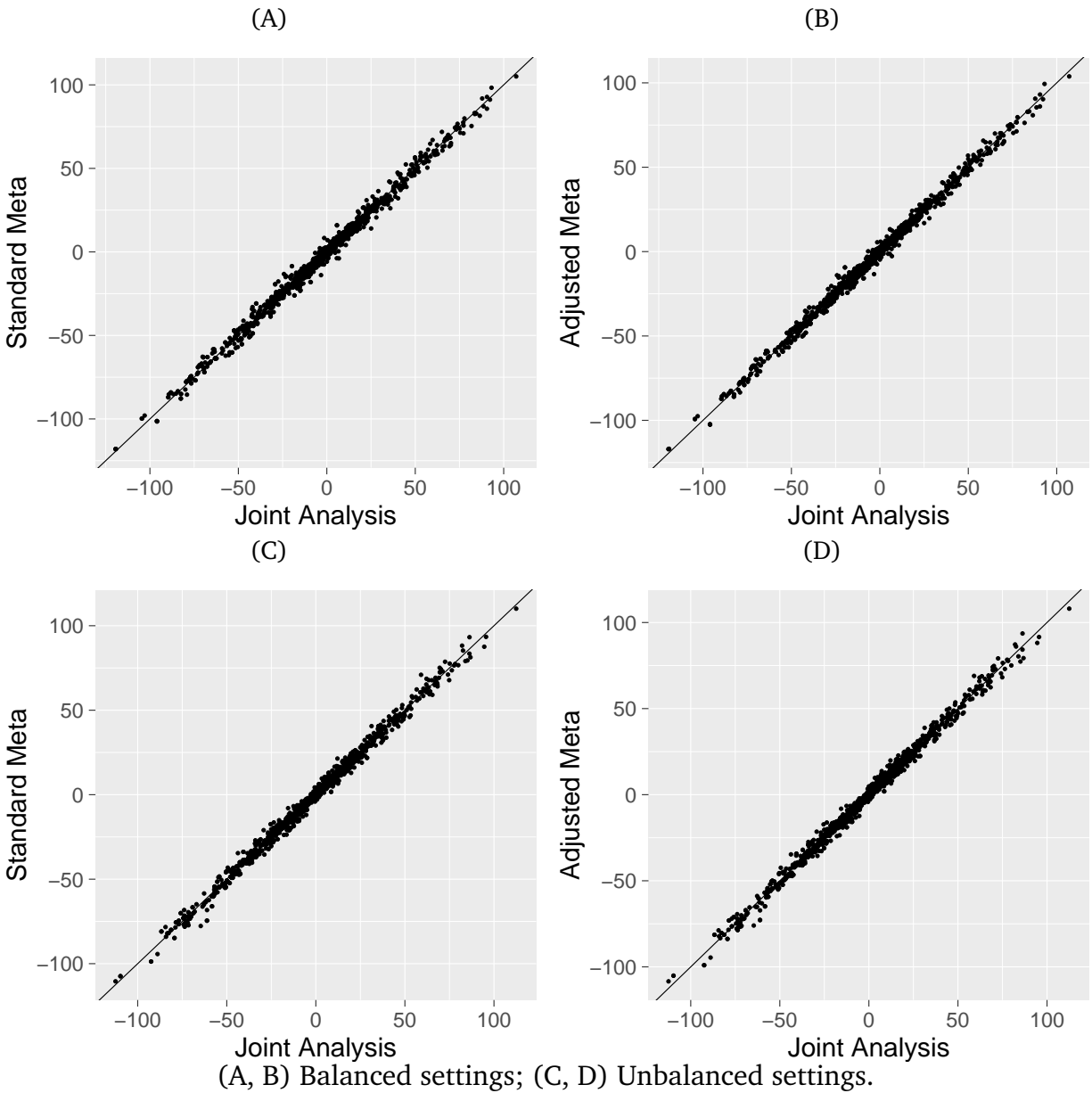


Figure S 12: $-\log_{10}$ (p values) of single-variant score tests in the **quantitative** studies with **different** covariates, without population stratification.

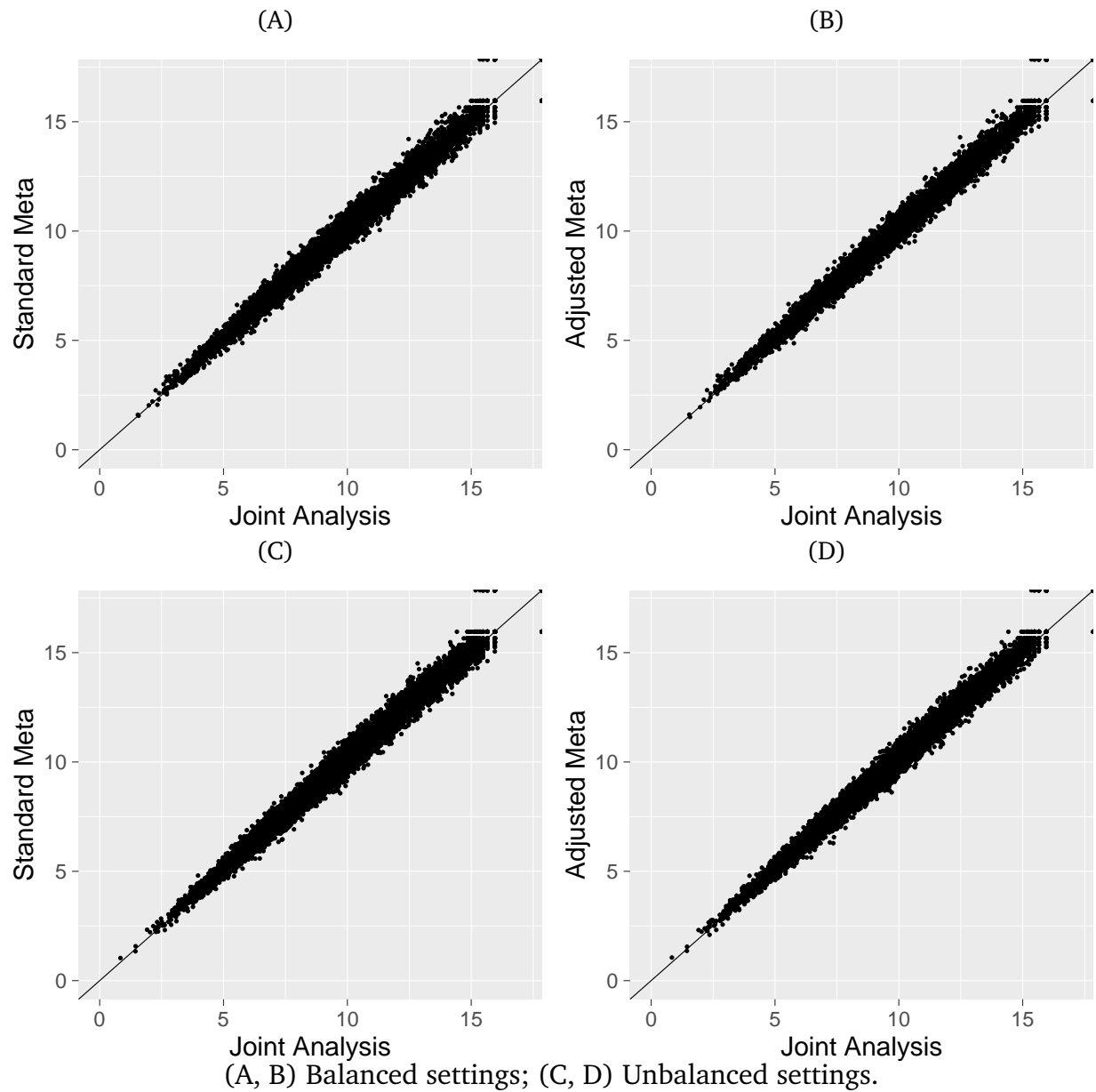


Figure S 13: Power comparison of meta-Burden test and meta-SKAT for balanced (B) and unbalanced (UB) **quantitative** studies without population stratification.

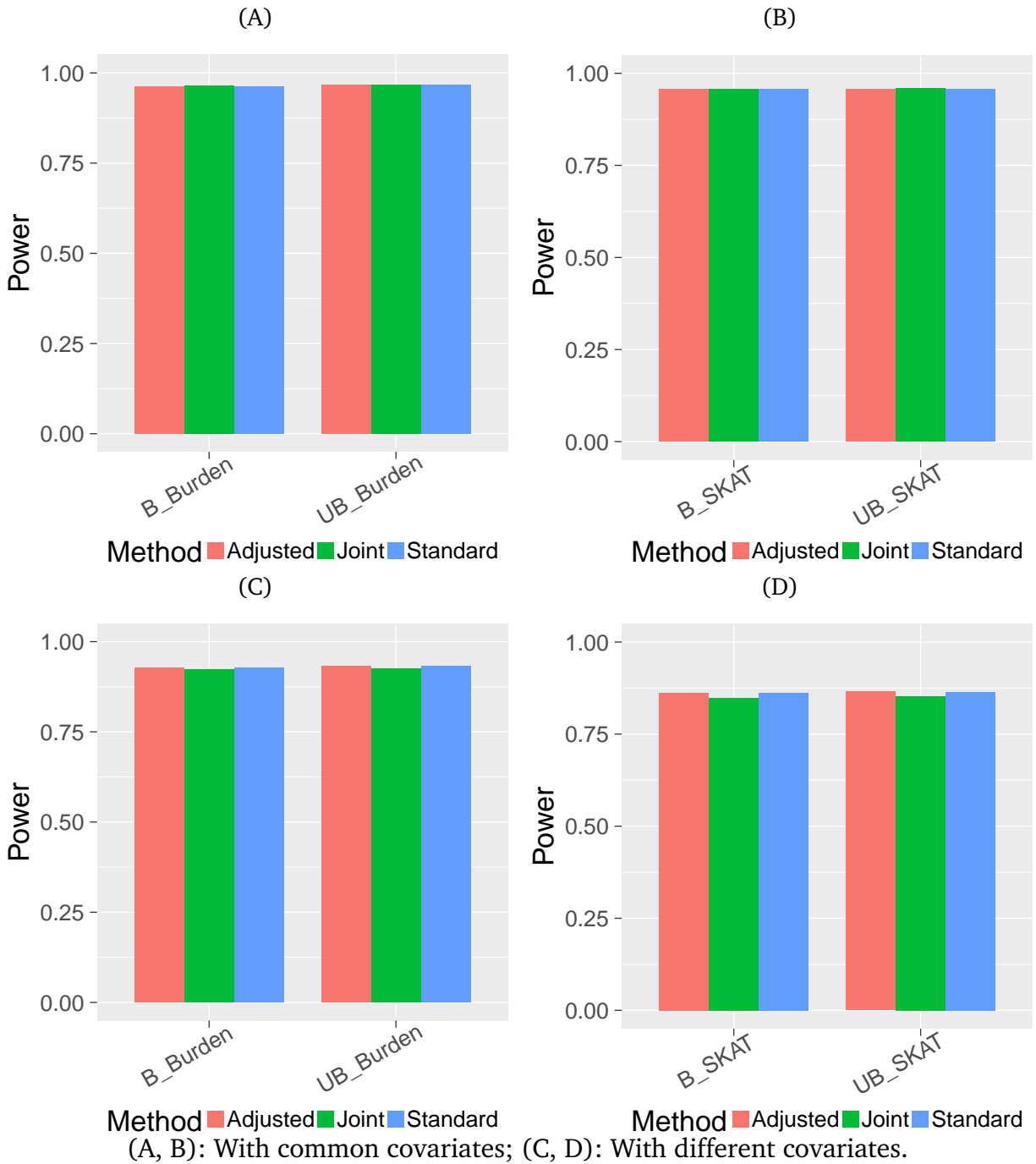


Figure S 14: Empirical type I errors of meta-Burden test and meta-SKAT with different significance levels ($\alpha = 0.01, 10^{-4}, 2.5 \times 10^{-6}$), for permuted multi-ethnic AMD data.

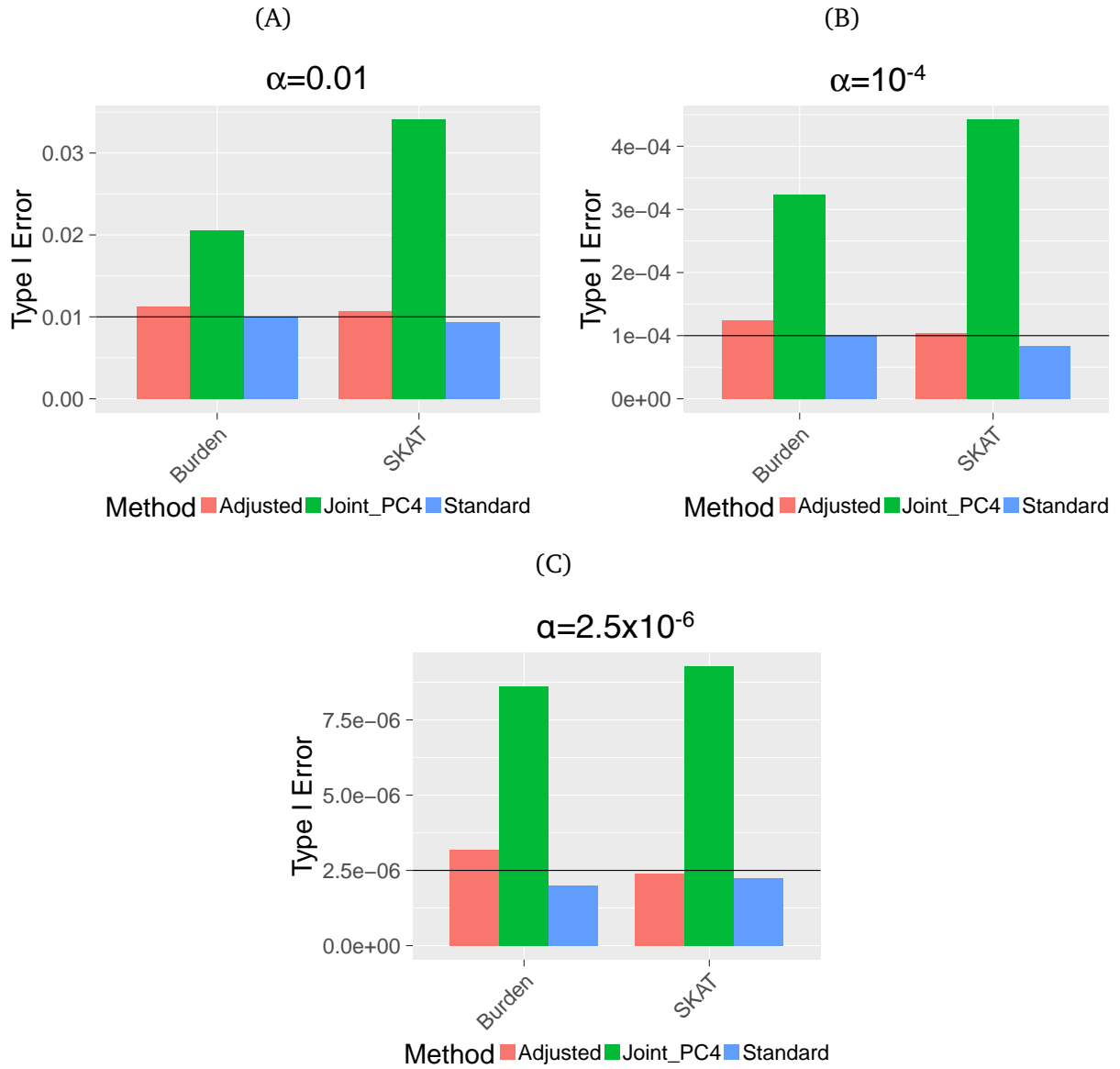


Figure S 15: Histograms of the type 2 diabetes phenotypes that were jointly corrected for age, gender, BMI, and first four joint PCs.

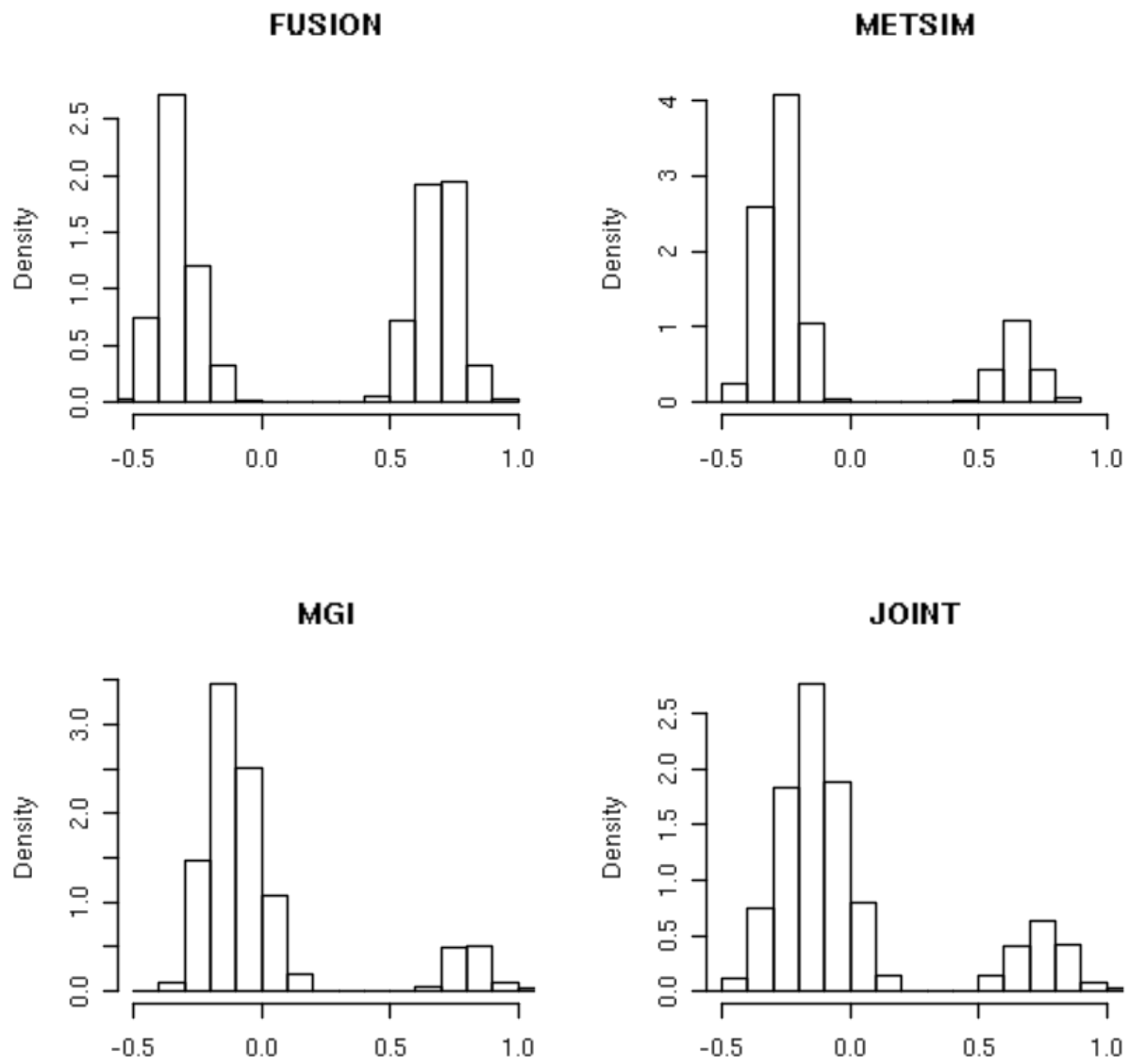


Figure S 16: First two joint PCs of type 2 diabetes GWASs.



Figure S 17: Manhattan plots of the individual GWASs of type 2 diabetes.

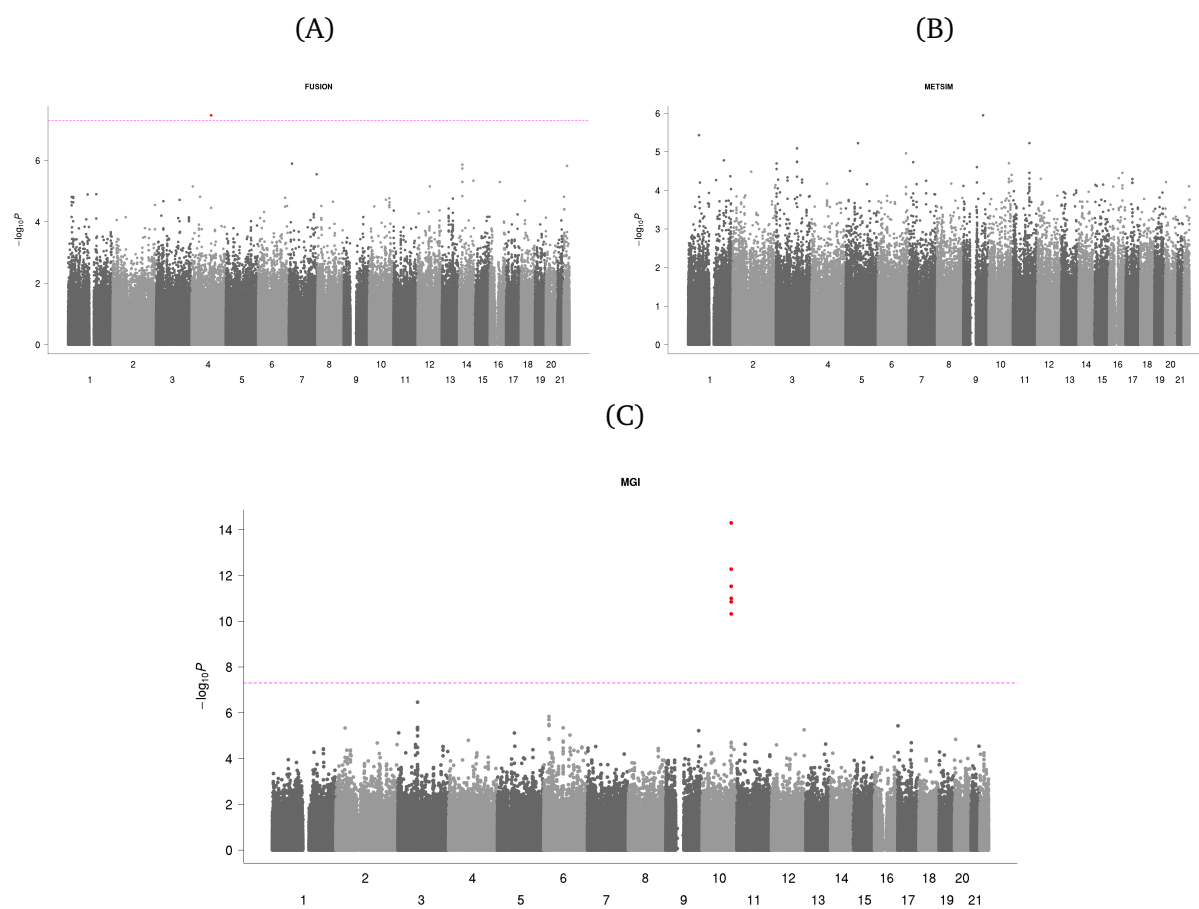


Figure S 18: QQ plots of $-\log_{10}(p \text{ values})$ by single-variant score tests of type 2 diabetes GWASs.

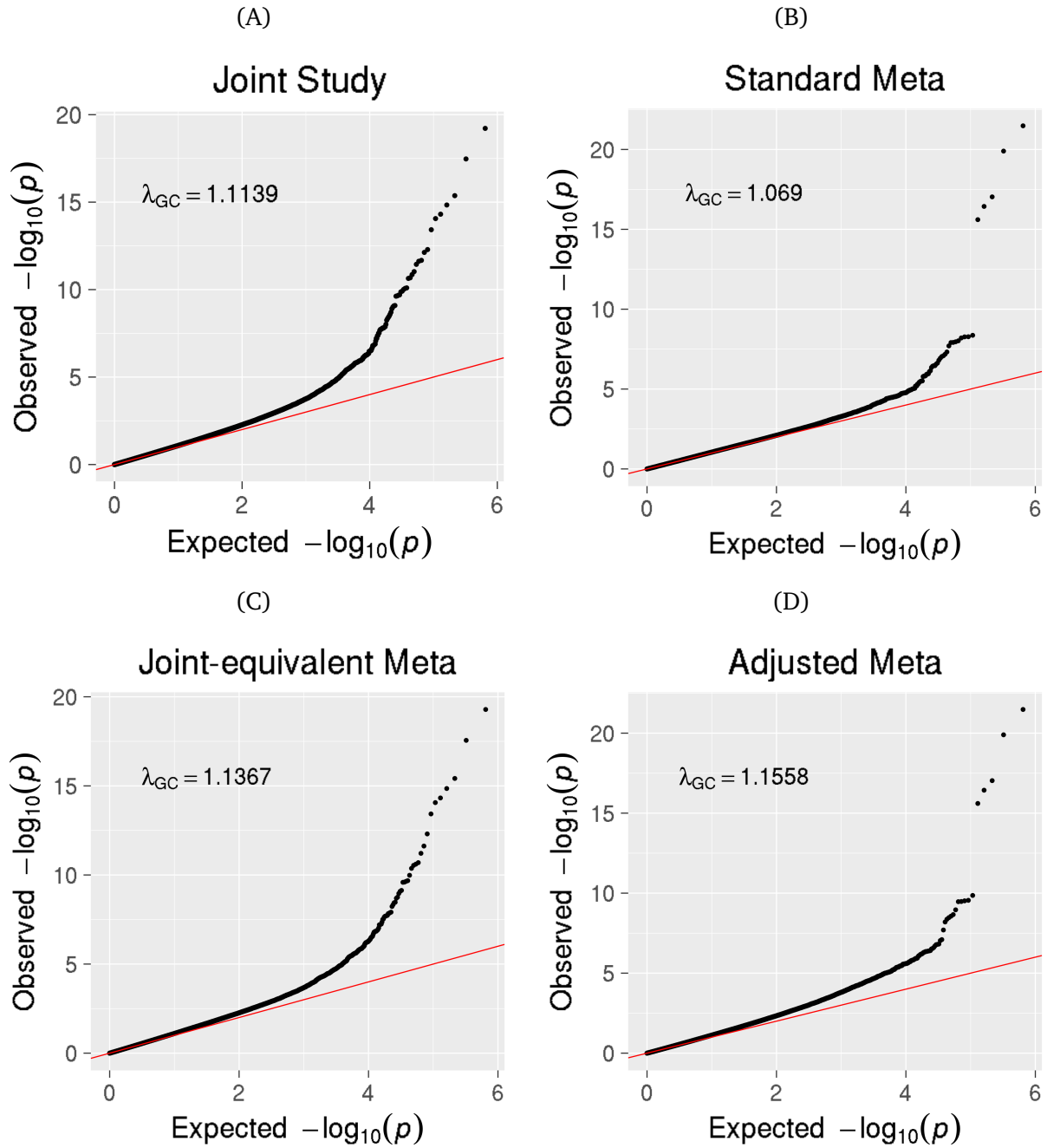


Figure S 19: Compare the MAFs in three individual GWASs for the genome-wide significant variants by joint analysis.

