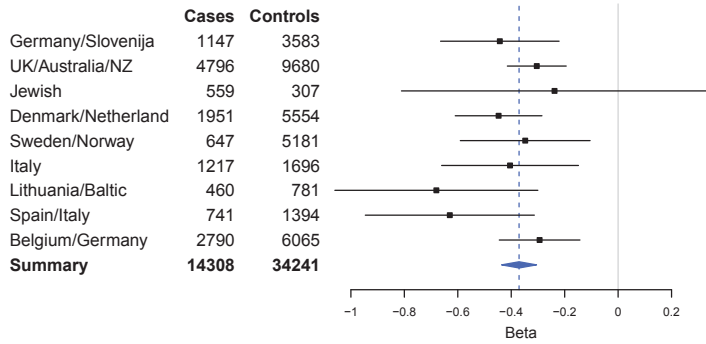


## Supplementary Material on heterogeneity of effects in UC

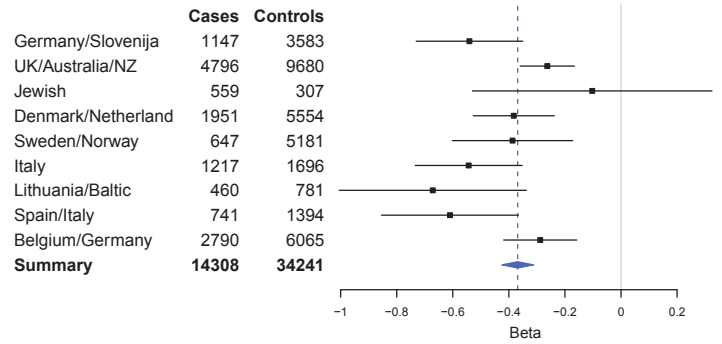
Each plot represents homogeneity/heterogeneity of effect for one reported HLA alleles (from the selected model), index SNP or heterozygote advantage in class II. Effect sizes ( $\log(\text{OR})$ ) with 95% confidence intervals are shown for each of the 9 population clusters (**Online Methods** and **Supplementary Fig. 14**). The blue diamond illustrates the pooled effect and confidence interval, under a fixed-effect model. The p-value for heterogeneity and meta-analysis (pooled effect) is shown below the plot. To be noted, the p-value for the meta-analysis may be slightly different from the main analysis. In UC, 2 variants show heterogeneity of effect under an additive model. Complementary forest plots were added for these, illustrating the additive and dominance effects under the general model.

HLA-DRB1 (4-digit) heterozygote advantage



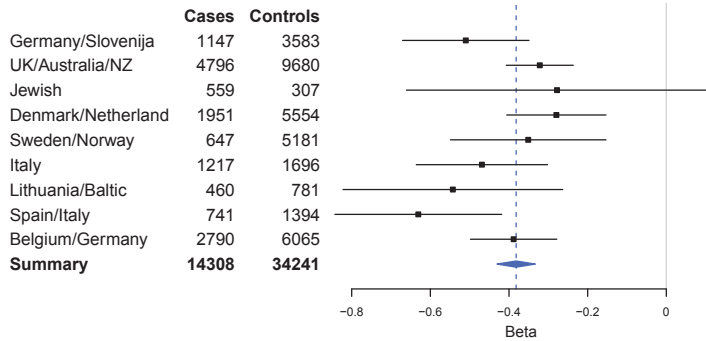
Heterogeneity  $I^2 = 0$  ( $p$ -value =  $4.38 \times 10^{-1}$ ) Association  $p$ -value =  $9.82 \times 10^{-29}$

HLA-DRB1 (2-digit) heterozygote advantage



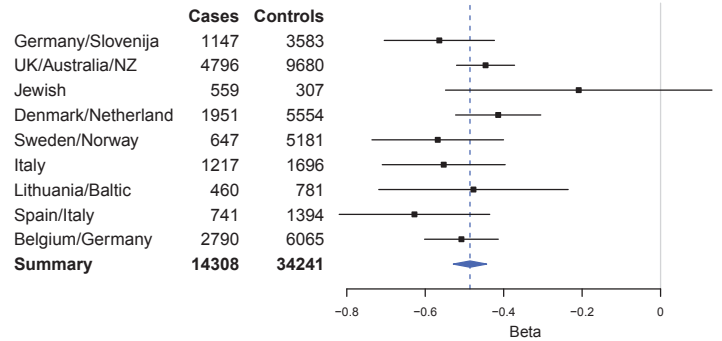
Heterogeneity  $I^2 = 56.44$  ( $p$ -value =  $1.42 \times 10^{-2}$ ) Association  $p$ -value =  $5.54 \times 10^{-38}$

HLA-DQA1 (4-digit) heterozygote advantage



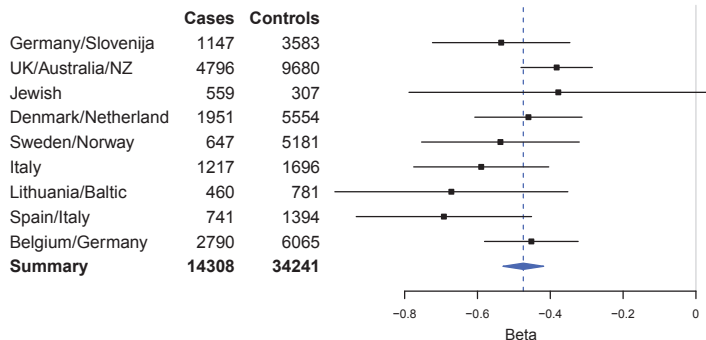
Heterogeneity  $I^2 = 38.85$  ( $p$ -value =  $9.9 \times 10^{-2}$ ) Association  $p$ -value =  $2.92 \times 10^{-53}$

HLA-DQA1 (2-digit) heterozygote advantage



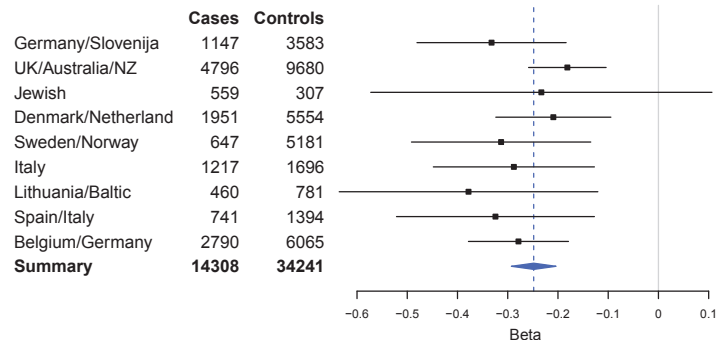
Heterogeneity  $I^2 = 13.16$  ( $p$ -value =  $3.22 \times 10^{-1}$ ) Association  $p$ -value =  $1.44 \times 10^{-111}$

HLA-DQB1 (4-digit) heterozygote advantage

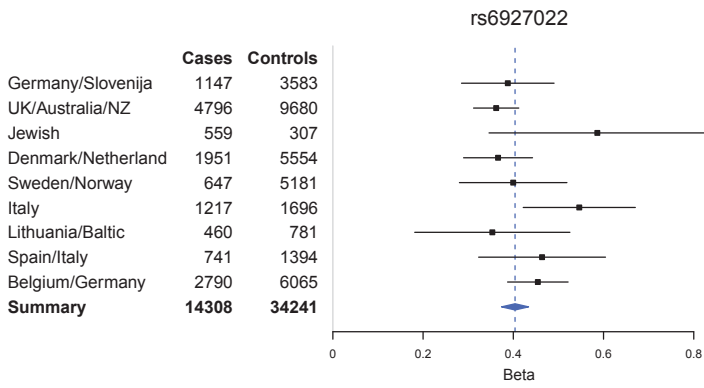


Heterogeneity  $I^2 = 13.86$  ( $p$ -value =  $3.15 \times 10^{-1}$ ) Association  $p$ -value =  $7.54 \times 10^{-62}$

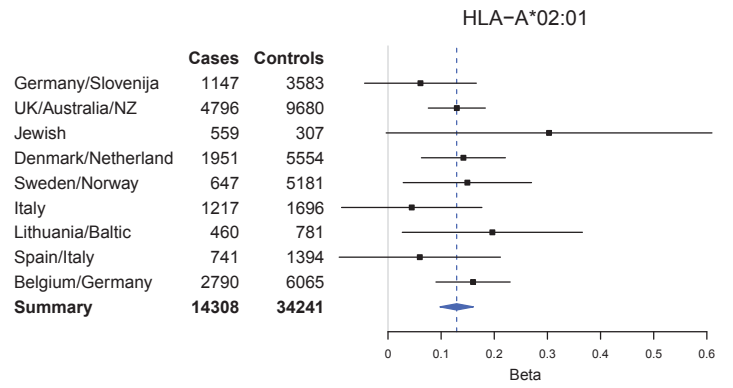
HLA-DQB1 (2-digit) heterozygote advantage



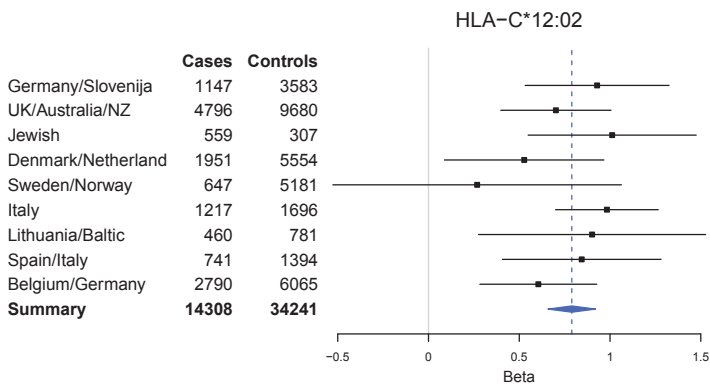
Heterogeneity  $I^2 = 0$  ( $p$ -value =  $6.21 \times 10^{-1}$ ) Association  $p$ -value =  $7.64 \times 10^{-28}$



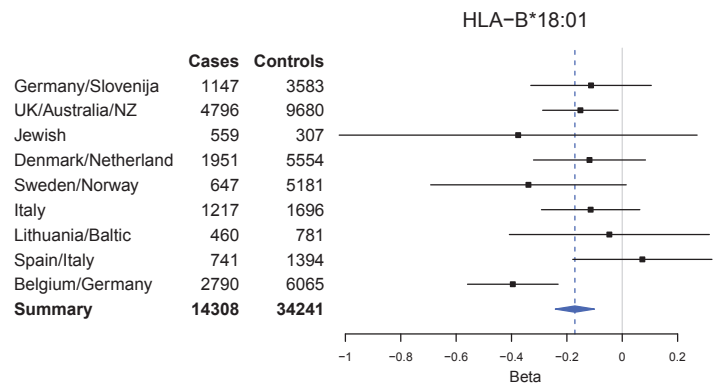
Heterogeneity  $I^2 = 35.88$  ( $p\text{-value} = 1.21 \times 10^{-1}$ ) Association  $p\text{-value} = 1.43 \times 10^{-153}$



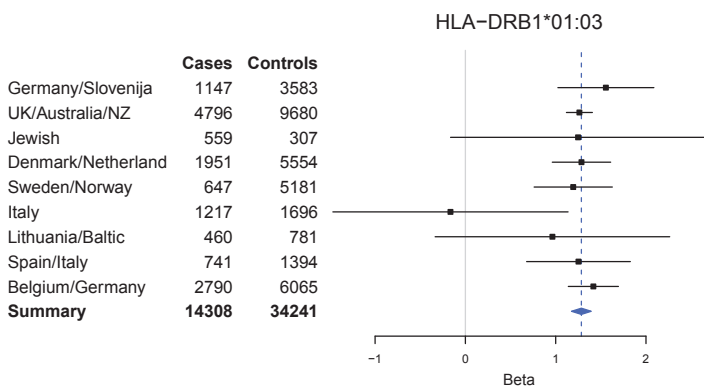
Heterogeneity  $I^2 = 0$  ( $p\text{-value} = 6.66 \times 10^{-1}$ ) Association  $p\text{-value} = 8.71 \times 10^{-16}$



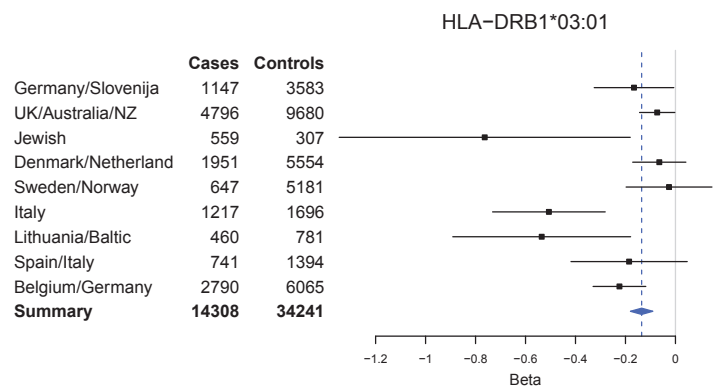
Heterogeneity  $I^2 = 0$  ( $p\text{-value} = 5.48 \times 10^{-1}$ ) Association  $p\text{-value} = 4.83 \times 10^{-32}$



Heterogeneity  $I^2 = 32.88$  ( $p\text{-value} = 1.45 \times 10^{-1}$ ) Association  $p\text{-value} = 2.08 \times 10^{-6}$

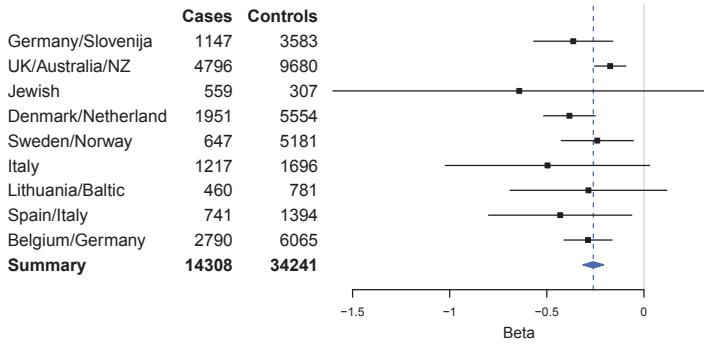


Heterogeneity  $I^2 = 0$  ( $p\text{-value} = 6.3 \times 10^{-1}$ ) Association  $p\text{-value} = 2.29 \times 10^{-117}$



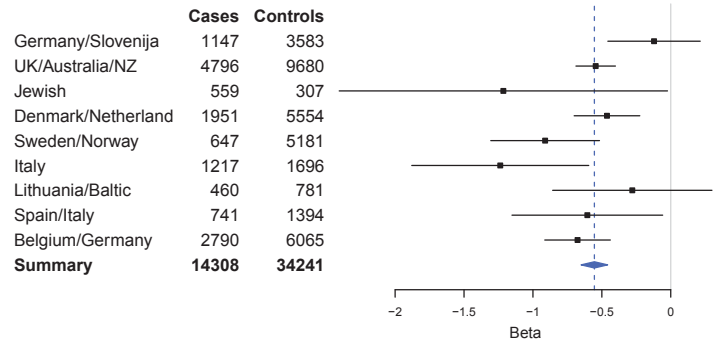
Heterogeneity  $I^2 = 68.67$  ( $p\text{-value} = 7.22 \times 10^{-4}$ ) Association  $p\text{-value} = 3.5 \times 10^{-9}$

HLA-DRB1\*04:01



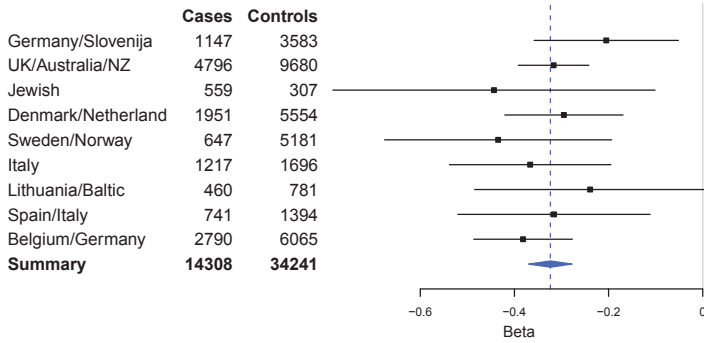
Heterogeneity  $I^2 = 18.54$  ( $p$ -value =  $2.72 \times 10^{-1}$ ) Association  $p$ -value =  $2.89 \times 10^{-21}$

HLA-DRB1\*04:04



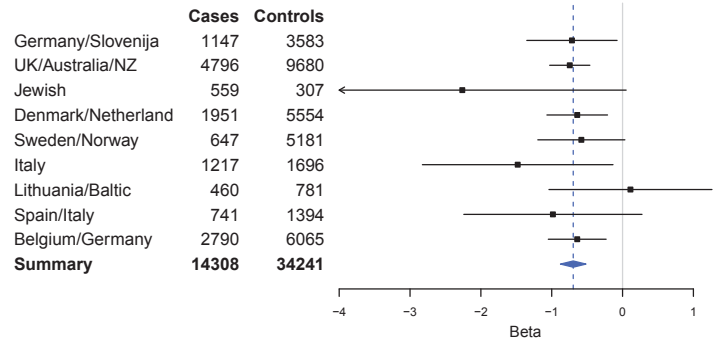
Heterogeneity  $I^2 = 48.29$  ( $p$ -value =  $4.27 \times 10^{-2}$ ) Association  $p$ -value =  $1.85 \times 10^{-29}$

HLA-DRB1\*07:01



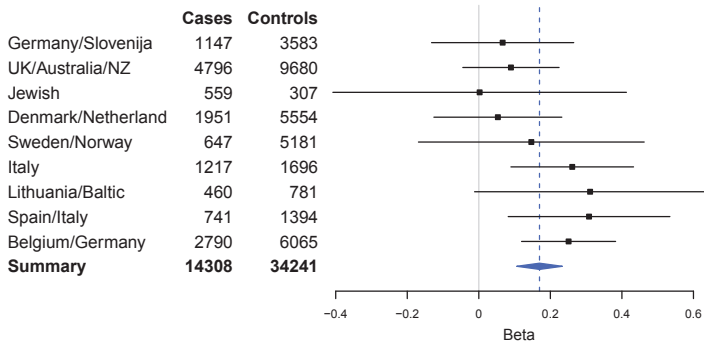
Heterogeneity  $I^2 = 0$  ( $p$ -value =  $7.75 \times 10^{-1}$ ) Association  $p$ -value =  $4.01 \times 10^{-43}$

HLA-DRB1\*09:01



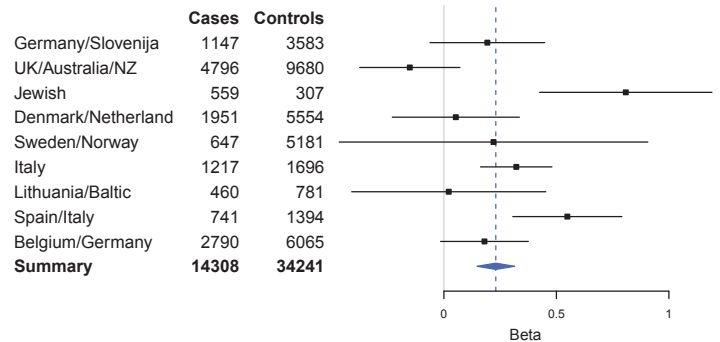
Heterogeneity  $I^2 = 0$  ( $p$ -value =  $7.89 \times 10^{-1}$ ) Association  $p$ -value =  $3.62 \times 10^{-14}$

HLA-DRB1\*11:01

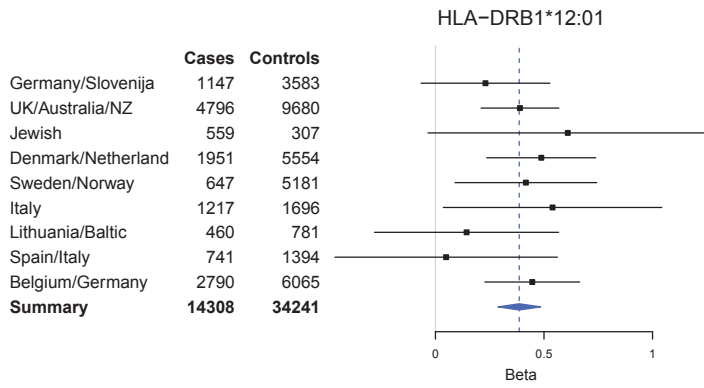


Heterogeneity  $I^2 = 3.44$  ( $p$ -value =  $4.08 \times 10^{-1}$ ) Association  $p$ -value =  $1.78 \times 10^{-7}$

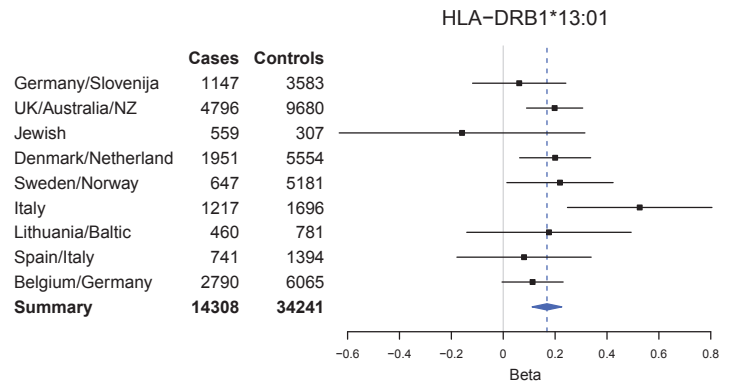
HLA-DRB1\*11:04



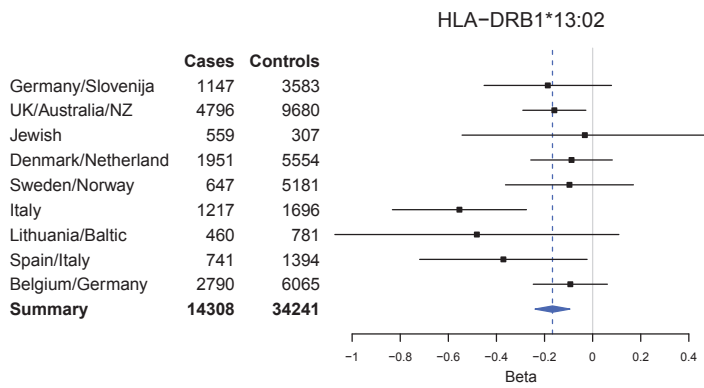
Heterogeneity  $I^2 = 70.35$  ( $p$ -value =  $3.81 \times 10^{-4}$ ) Association  $p$ -value =  $5.86 \times 10^{-8}$



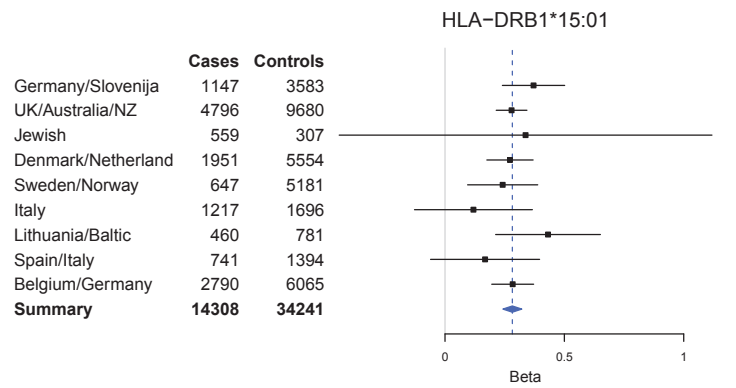
Heterogeneity  $I^2 = 0$  ( $p$ -value =  $7.71 \times 10^{-1}$ ) Association  $p$ -value =  $1.47 \times 10^{-14}$



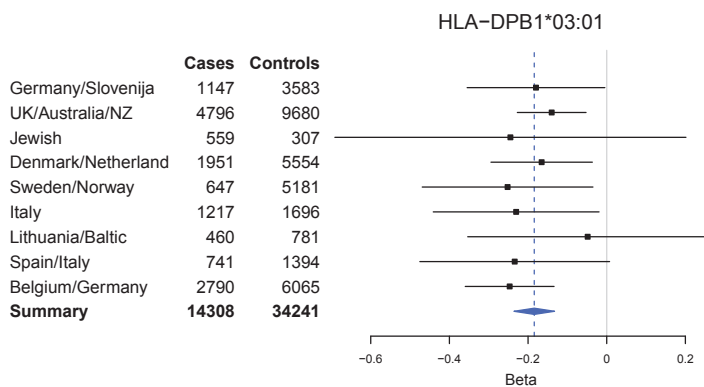
Heterogeneity  $I^2 = 21.27$  ( $p$ -value =  $2.47 \times 10^{-1}$ ) Association  $p$ -value =  $8.02 \times 10^{-9}$



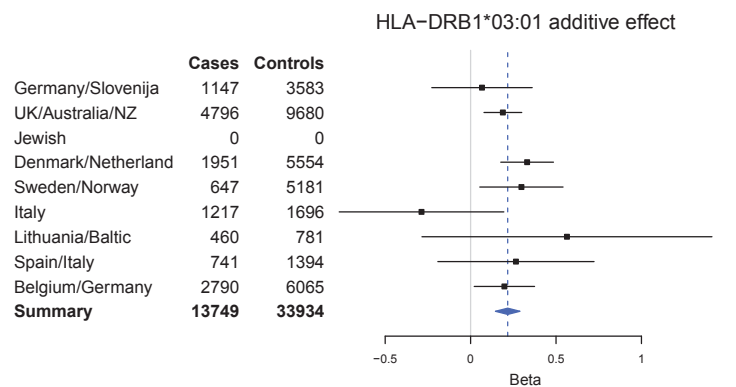
Heterogeneity  $I^2 = 24.98$  ( $p$ -value =  $2.13 \times 10^{-1}$ ) Association  $p$ -value =  $6.65 \times 10^{-6}$



Heterogeneity  $I^2 = 0$  ( $p$ -value =  $6.9 \times 10^{-1}$ ) Association  $p$ -value =  $4.31 \times 10^{-44}$

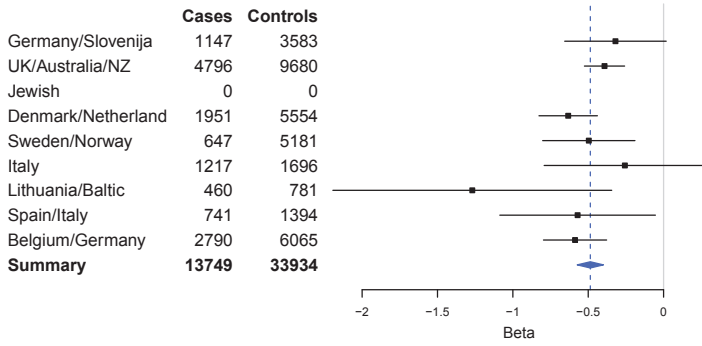


Heterogeneity  $I^2 = 0$  ( $p$ -value =  $9.26 \times 10^{-1}$ ) Association  $p$ -value =  $2.66 \times 10^{-12}$



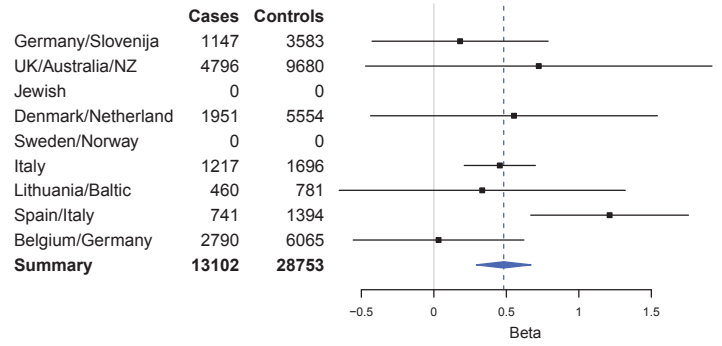
Heterogeneity  $I^2 = 7.1$  ( $p$ -value =  $3.76 \times 10^{-1}$ ) Association  $p$ -value =  $3.48 \times 10^{-9}$

HLA-DRB1\*03:01 dominance effect



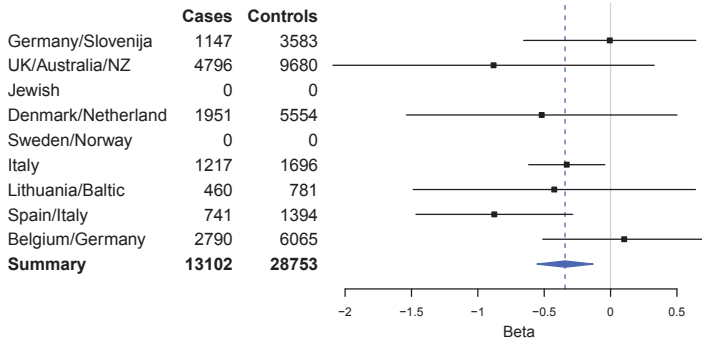
Heterogeneity  $I^2 = 15.1$  ( $p\text{-value} = 3.08 \times 10^{-1}$ ) Association  $p\text{-value} = 6.75 \times 10^{-28}$

HLA-DRB1\*11:04 additive effect



Heterogeneity  $I^2 = 32.07$  ( $p\text{-value} = 1.72 \times 10^{-1}$ ) Association  $p\text{-value} = 5.73 \times 10^{-7}$

HLA-DRB1\*11:04 dominance effect



Heterogeneity  $I^2 = 0.41$  ( $p\text{-value} = 4.26 \times 10^{-1}$ ) Association  $p\text{-value} = 1.48 \times 10^{-3}$