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EXTENDED REPORT

Genetic variants in ANCA-associated vasculitis: a meta-analysis

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ABSTRACT

Background Genetic factors may influence the pathogenic pathways leading to antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). We performed a meta-analysis to determine the genetic variants most likely associated with AAV and investigated whether diagnostic and serological subtypes within AAV have distinct genetic backgrounds.

Methods Studies investigating the association between genetic variants and AAV in humans were searched in PubMed, EMBASE and Web of Science. All variants investigated in at least two studies were selected. Subsequently, all studies assessing these variants were included in this meta-analysis. Additionally, data on these variants from the largest genome-wide association studies in AAV were included to increase the validity of this meta-analysis.

Results The literature search yielded 5180 articles. 62 articles investigating 140 genetic variants were included, 33 of which were associated with AAV in a meta-analysis. These genetic variants were in or near the following genes: *CD226*, *CTLA-4*, *FCGR2A*, *HLA-B*, *HLA-DP*, *HLA-DQ*, *HLA-DR*, *HSD17B8*, *IRF5*, *PTPN22*, *RING1/RXRB*, *RXRB*, *STAT4*, *SERPINA1* and *TLR9*. Moreover, we identified genetic distinctions between granulomatosis with polyangiitis and microscopic polyangiitis and between proteinase 3 ANCA vasculitis and myeloperoxidase ANCA vasculitis. In 76% of the genetic variants, subdivision based on ANCA serotype resulted in higher ORs than subdivision based on clinical diagnosis.

Conclusions This meta-analysis identified 33 genetic variants associated with AAV, supporting a role for alpha-1-antitrypsin, the major histocompatibility complex system, and several distinct inflammatory processes in AAV pathogenesis. Our results indicate that subdivision of AAV based on ANCA serotype has a stronger genetic basis than subdivision based on clinical diagnosis.

INTRODUCTION

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic autoimmune disease in which patients often have circulating proteinase 3 (PR3)-ANCA or myeloperoxidase (MPO)-ANCA.[1 2] The clinical syndromes within the spectrum of AAV are granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis.

The subtypes within AAV show significant differences in clinical and epidemiological characteristics,[3 4] leading to debate regarding whether these subtypes are part of a single disease spectrum or represent distinct diseases.[5–7] To date, the prevailing concept of a single disease spectrum has resulted in similar treatment strategies in clinical trials[8–10] and to suggestions that genetic studies should consider the subtypes together.[11] Evidence that these subtypes are pathogenically distinct may lead to the development of syndrome-specific therapeutic strategies.

Both environmental and genetic factors are thought to be involved in the pathogenesis of AAV.[12] Evidence for the role of genetic factors comes from differences in the prevalence of AAV between ethnic groups,[13] familial association studies[14] and genetic associations studies including the two genome-wide association studies (GWAS) performed in AAV.[15 16]

Attempts to replicate findings of genetic association studies performed in AAV have yielded inconsistent outcomes. Small sample sizes and false-positive results arising from the low prior probabilities of genetic associations may be responsible for these inconsistencies.[17] These factors are especially relevant in complex diseases such as AAV.[18]

The aim of this study was to determine the genetic variants associated with AAV. Therefore, we performed a meta-analysis to assess the pooled effect of all genetic variants that have been investigated in AAV in at least two studies. To increase the validity of this meta-analysis, we also included previously unpublished data from the largest GWAS performed in AAV.[15] Moreover, we conducted stratified analyses based on clinical diagnosis and ANCA serotype to investigate whether these different AAV subtypes have distinct genetic backgrounds.

METHODS

Literature search and eligibility

A comprehensive search string was carried out in collaboration with a librarian. PubMed, EMBASE and Web of Science were searched until April 2014 for studies investigating genetic variants in patients with AAV. The search strategy consisted of multiple queries combining 'Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis', 'ANCA', 'vasculitis', 'Granulomatosis with Polyangiitis', 'Wegener's Granulomatosis', 'Microscopic polyangiitis', 'Eosinophilic granulomatosis with polyangiitis',

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'Churg Strauss Syndrome', 'PR3', 'MPO', 'Polymorphisms' or 'Genes'. To minimise the chance of omitting references, a second broader search was performed for genetic variants in vasculitis in general rather than AAV alone (online supplementary table S1). The specific genes and polymorphisms that resulted from the previous searches were added in a next search to minimise the chance of omitting references. To ensure maximum sensitivity, no limits, filters or language restrictions were placed on the searches.

Two observers (CR and DvH) independently reviewed the titles and abstracts of the citations retrieved by the search and read potentially relevant studies independently. Studies that compared genetic variants between patients with AAV and controls without AAV derived from the general population were eligible. Cases had to have an AAV by fulfilling either the Chapel Hill Consensus Conference criteria,[19] American College of Rheumatology criteria,[20] European Medicines Agency algorithm,[21] 1998 Japanese criteria proposed by the Research Committee on Intractable Vasculitides, the Ministry of Health, Labour and Welfare of Japan,[22] or clinical, histological and serological criteria. Definitions of cases and controls in each included study are depicted in online supplementary table S2. All genetic variants investigated in at least two studies were included. Genetic variants investigated in multiple cohorts in one publication were also included. This was the case for genetic variants in *GHSR*,[23] *LEPR*[23] and *TLR9*.[24] For the included genetic variants, all genetic studies were identified to estimate the pooled effect of the genetic variant in a meta-analysis, irrespective of their p values. To increase the validity of this meta-analysis, we also included unpublished data on these genetic variants from the Lyons *et al* [15] GWAS. This was possible for the genetic variants in this meta-analysis that were not human leucocyte antigen (HLA) serotypes or tandem repeats and that were genotyped in the Lyons *et al* GWAS. Moreover, we included data from the stage 1 analysis including all single-nucleotide polymorphisms (SNPs) with a p value $<10^{-4}$ from the Xie *et al* [16] GWAS.

Data extraction

Minor allele frequencies of the included genetic variants were extracted from included studies. Studies investigating the same genetic variant published by the same author(s) were checked for overlapping patient groups, in which case only the study with the largest patient group was included. Studies that reported insufficient data to calculate an OR were excluded.

Statistical analysis

ORs and 95% CIs were calculated at the allele level. To account for potential heterogeneity, random-effects model was performed in all analyses that included at least five studies.[25] Because the HLA serotypes are not completely independent from the HLA alleles, the following HLA variants were collapsed in the analyses: *HLA-DR1*, *HLA-DRB1*01* and *HLA-DRB1*0101*; *HLA-DR3* and *HLA-DRB1*03*; *HLA-DR7* and *HLA-DRB1*07*; *HLA-DR8* and *HLA-DRB1*08*; and *HLA-DR9*, *HLA-DRB1*09* and *HLA-DRB1*0901*. Collapsing other HLA variants was not possible because some studies investigated multiple, closely related, HLA variants in the same patients. If these HLA variants had been collapsed, the same patients would have been included in the same analysis multiple times, increasing their weight in the analysis and introducing a systematic error. To determine whether the disease subtypes within AAV represent parts of a single disease spectrum or distinct clinical entities, we performed pre-specified subgroup analysis stratifying patients according to clinical diagnosis (GPA/MPA) and ANCA serotype (PR3-ANCA/MPO-ANCA and cytoplasmic (c)-ANCA/perinuclear (p)-ANCA), if enough data were available. Moreover, we performed stratified analyses based on ethnicity for all genetic variants investigated in both Caucasian and Asian patients. We assumed difference in effect estimates likely to be present in case subgroups showed significant effects in opposite directions, that is, having a protective effect in one subgroup but leading to an increased risk of AAV in the other subgroup. Heterogeneity within studies was displayed by I^2, which reflects the percentage of total variation across studies beyond chance.[26] Egger and Harbord tests were used to assess publication bias.[27] All of the p values presented are nominal p values and are not corrected for multiple testing. Correction for multiple testing was not performed as the strong linkage disequilibrium between variants tested in the major histocompatibility complex (MHC) region makes calculating an appropriate multiple correction factor impractical. All analyses were performed using STATA V.12 (StataCorp. 2011; Stata Statistical Software: Release 12, College Station, Texas, USA).

RESULTS

Initial search and results

Our literature search yielded 5180 articles, from which we identified 140 genetic variants published in 62 articles. All included studies were case–control studies, two of which were GWAS. These articles were published from 1978 through 2014, and the number of patients with AAV included ranged from 12 to 1445. The characteristics of all included studies are provided in online supplementary table S2. Additionally, previously unpublished data from the Lyons *et al*[15] GWAS were available and included in the meta-analysis for 18 genetic variants: *CD226* rs763361, *CTLA-4* rs231775, *CTLA-4* rs3087243, *FCAR* rs16986050, *FCGR2A* rs1801274, *GHSR* rs509035, *HLA-DPB2* rs3130215, *IL-1β* rs1143634, *IL-6* rs1800795, *IL-10* rs1800896, *IRF5* rs10954213, *PTPN22* rs2476601, *RING1/RXRB* rs213213, *RXRB* rs6531, *RXRB* rs9277935, *STAT4* rs7574865, *SERPINA1* Z allele and *TNFα* rs1800629.

Thirty-three genetic variants were significantly associated with AAV after meta-analysis (table 1 and online supplementary figure S1), and 107 genetic variants were not associated with AAV after meta-analysis (online supplementary table S3). The ORs for the significant associations after meta-analysis ranged from 0.35 to 0.81 for protective genetic variants and from 1.13 to 2.94 for the genetic variants associated with an increased risk of AAV.

AAV is associated with the Z and S alleles of *SERPINA1*

Both the S allele and Z allele of *SERPINA1* were significantly associated with AAV, with pooled ORs of 1.30 (95% CI 1.03 to 1.63) and 2.94 (95% CI 2.22 to 3.88), respectively. Subgroup analysis showed that the association with the *SERPINA1* Z allele was present in both PR3-ANCA (pooled OR 2.58 (95% CI 1.57 to 4.25)) and MPO-ANCA (pooled OR 2.01 (95% CI 1.04 to 3.87)) positive patients and in both c-ANCA (pooled OR 3.53 (95% CI 2.28 to 5.49)) and p-ANCA (pooled OR 3.13 (95% CI 1.21 to 8.13)) positive patients (see online supplementary table S4 and figure S2).

AAV is associated with genetic variants in the MHC region

Seventeen genetic variants in *HLA-B*, *HLA-DP*, *HLA-DQ* and *HLA-DR* remained significantly associated with AAV after meta-analysis (table 1). *HLA-DPA1* rs9277341 had the strongest protective effect (pooled OR 0.35 (95% CI 0.30 to 0.40)), and

Table 1 Genetic variants significantly associated with antibody-associated vasculitis (AAV) after meta-analysis

Variant by gene (minor allele)	Publications (n)	Cases (n)/controls (n)	OR (95% CI)	p Value for meta-analysis	I^2 (%)	p Value for heterogeneity	p Value for funnel plot asymmetry*
CD226 rs763361 (T)	3	2422/17898	1.14 (1.07 to 1.21)	<0.001	0	0.444	0.792
CTLA-4 $(AT)_{86}$	4	303/543	0.54 (0.43 to 0.67)	<0.001	89	<0.001	0.946
CTLA-4 rs231775 (G)	3	1002/6179	1.16 (1.06 to 1.28)	0.002	60	0.080	0.080
CTLA-4 rs3087243 (A)	3	2015/7855	0.81 (0.75 to 0.87)	<0.001	25	0.262	0.122
FCGR2A rs1801274 (C)	6	1239/6209	0.90 (0.82 to 0.99)	0.028	0	0.834	0.788
HLA-B5	2	335/6573	0.59 (0.38 to 0.92)	0.019	0	0.432	N/A
HLA-B8	6	475/7855	1.48 (1.04 to 2.11)	0.028	47	0.096	0.063
HLA-DPA1 rs9277341 (C)	2	1032/2200	0.35 (0.30 to 0.40)	<0.001	54	0.116	0.215
*HLA-DPB1*0301*	5	1154/1337	0.38 (0.21 to 0.69)	0.002	78	<0.001	0.938
*HLA-DPB1*0401*	5	1154/1337	1.99 (1.44 to 2.74)	<0.001	84	<0.001	0.738
HLA-DPB2 rs3130215 (A)	3	1417/7249	1.40 (1.29 to 1.52)	<0.001	99	<0.001	0.446
*HLA-DQB1*0303*	3	176/218	1.82 (1.09 to 3.03)	0.021	17	0.301	0.916
HLA-DR6	5	487/6222	0.50 (0.27 to 0.95)	0.033	55	0.062	0.997
*HLA-DRB1*1101*	2	268/465	1.89 (1.15 to 3.08)	0.011	0	0.487	N/A
*HLA-DRB1*1201*	2	216/465	0.37 (0.15 to 0.91)	0.031	0	0.491	N/A
*HLA-DRB1*13*	4	233/833	0.47 (0.32 to 0.70)	<0.001	0	0.504	0.884
*HLA-DRB1*14*	4	322/862	1.91 (1.07 to 3.42)	0.029	0	0.728	0.700
*HLA-DRB1*15*	3	236/633	1.86 (1.39 to 2.50)	<0.001	69	0.021	0.347
*HLA-DRB1*1501*	2	216/465	1.68 (1.20 to 2.34)	0.002	0	0.925	N/A
HLA-DRB3	4	260/1845	0.62 (0.49 to 0.79)	<0.001	68	0.024	0.689
HLA-DRB4	4	260/1845	1.69 (1.36 to 2.10)	<0.001	61	0.055	0.533
HSD17B8 rs421446 (C)	2	738/1872	0.40 (0.34 to 0.48)	<0.001	0	0.620	N/A
IRF5 rs10954213 (G)	3	1535/6977	0.77 (0.70 to 0.83)	<0.001	99	<0.001	0.948
PTPN22 rs2476601 (A)	4	2099/8678	1.39 (1.24 to 1.56)	<0.001	0	0.693	0.500
RING1/RXRB rs213213 (A)	3	1414/7238	1.71 (1.57 to 1.86)	<0.001	73	0.026	0.187
RXRB rs6531 (C)	3	1557/6955	1.63 (1.50 to 1.77)	<0.001	96	<0.001	0.292
RXRB rs9277935 (T)	3	1417/7233	0.44 (0.37 to 0.50)	<0.001	73	0.025	0.393
SERPINA1 S allele	5	1474/5762	1.30 (1.03 to 1.63)	0.025	0	0.464	0.547
SERPINA1 Z allele	8	3662/8581	2.94 (2.22 to 3.88)	<0.001	41	0.092	0.078
STAT4 rs7574865 (T)	3	1520/6956	1.11 (1.01 to 1.22)	0.029	3	0.357	0.590
TLR9 rs352162 (T)	1	1289/1898	1.58 (1.43 to 1.75)	<0.001	96	<0.001	N/A
TLR9 rs352140 (T)	1	1289/1898	1.13 (1.02 to 1.25)	0.018	0	0.432	N/A
TLR9 rs352139 (T)	1	1289/1898	1.11 (1.00 to 1.23)	0.041	0	0.756	N/A

*Harbord test for funnel plot asymmetry was performed for all genetic variants, except for *CD226* rs763361, *CTLA-4* rs3087243, and *PTPN22* rs2476601. In these cases, the Harbord test was not applicable and the Egger test was performed.

*HLA-DPB1*0401* was the strongest contributor to an increased risk of AAV (pooled OR 1.99 (95% CI 1.44 to 2.74)).

RING1/RXRB rs213213, *RXRB* rs6531 and *RXRB* rs9277935 were also significantly associated with AAV with pooled ORs of 1.71 (95% CI 1.57 to 1.86), 1.63 (95% CI 1.50 to 1.77) and 0.44 (95% CI 0.37 to 0.50), respectively.

AAV is associated with genetic variants involved in inflammatory processes

CTLA-4 rs231775 was associated with an increased risk of AAV (pooled OR of 1.16 (95% CI 1.06 to 1.28)) while *CTLA-4* rs3087243 and *CTLA-4* $(AT)_{86}$ had a protective effect (pooled ORs of 0.81 (95% CI 0.75 to 0.87) and 0.54 (95% CI 0.43 to 0.67), respectively). *PTPN22* rs2476601, *CD226* rs763361 and *IRF5* rs10954213 were also significantly associated with AAV, with pooled ORs of 1.39 (95% CI 1.24 to 1.56), 1.14 (95% CI 1.07 to 1.21) and 0.77 (95% CI 0.70 to 0.83), respectively. Moreover, *TLR9* rs352162 and rs352140 were significantly associated with AAV with pooled ORs of 1.58 (95% CI 1.43 to 1.75) and 1.13 (95% CI 1.02 to 1.25), respectively.

Genetic associations differ for the different diagnostic and serological subtypes of AAV

A significant association with GPA and/or MPA was present for 25 genetic variants, and a significant association with both GPA and MPA was present for 10 genetic variants (online supplementary table S4 and figure S2). In 6 of these 10 genetic variants (60%), the associations were in opposite directions, that is, having a protective effect in one subgroup but leading to an increased risk of AAV in the other subgroup (figure 1). A significant association with PR3-ANCA and/or MPO-ANCA was present for 25 genetic variants, and a genetic association with both PR3-ANCA and MPO-ANCA was present for seven genetic variants. In four of these seven genetic variants (57%), the associations were in opposite directions, that is, having a protective effect in one subgroup but leading to an increased risk of AAV in the other subgroup (figure 1). Moreover, ORs were higher for ANCA serotype than for clinical diagnosis in 76% (16/21) of the genetic variants that were significantly associated with both clinical diagnosis and ANCA serotype.

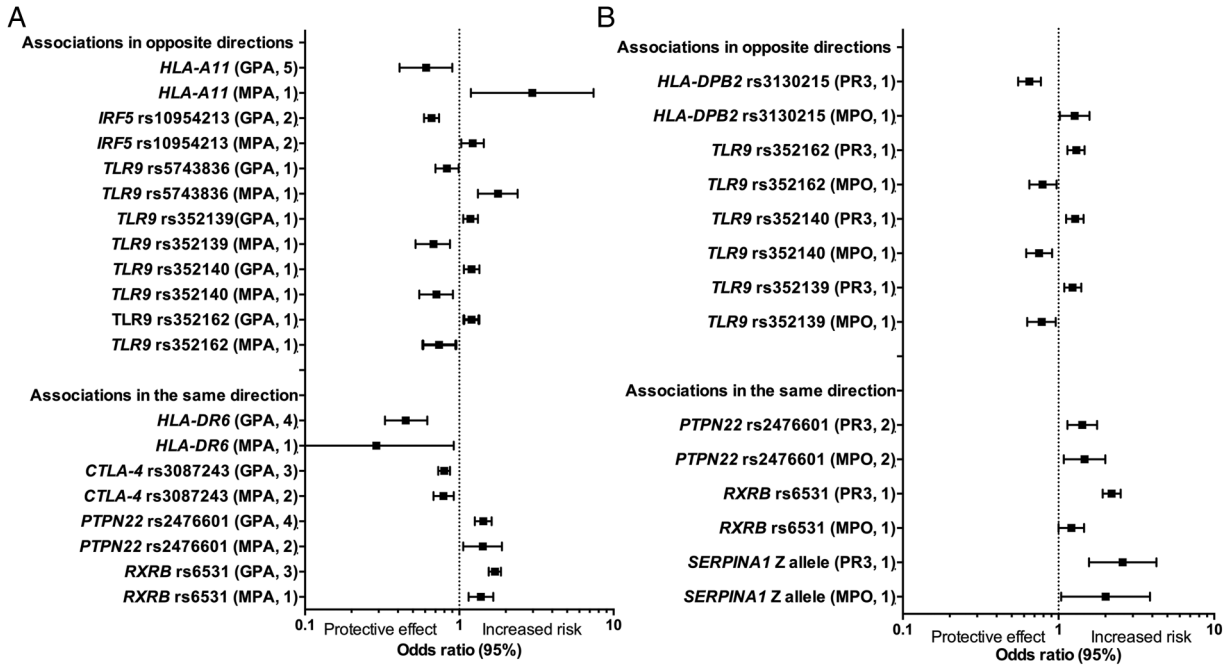

Figure 1 Subgroup analysis based on clinical diagnosis (A) and antineutrophil cytoplasmic antibody (ANCA) serotype (B), with the clinical diagnosis (A) or ANCA serotype (B) and number of included publications depicted between the parentheses. (A) In 6 of the 10 genetic variants (60%) in which there was an association with both granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), the associations were in opposite directions. (B) In four of the seven genetic variants (57%) in which there was an association with both proteinase 3 (PR3)-ANCA vasculitis and myeloperoxidase (MPO)-ANCA vasculitis, the associations were in opposite directions.

Genetic associations differ for AAV patients of Caucasian and Asian origin

The results of the stratified analyses performed for 42 variants investigated in both Caucasian and Asian patients are depicted in online supplementary table S5. CTLA-4 $(AT)_{86}$, CTLA-4 $(AT)_{106}$ and *HLA-DR6* were significantly associated with AAV in the Caucasian patients but not in the Asian patients. Conversely, *HLA-B55* was significantly associated with AAV in the Asian patients but not in the Caucasian patients. Of interest, *IRF5* rs10954213 (G) was significantly associated with AAV in both the Caucasian and Asian patients; however, it had a protective effect in the Caucasian patients while it increased the risk of AAV in the Asian patients. The results of these analyses should be interpreted with caution because each analysis included only one study involving Asian patients.

Genetic variants identified by GWAS

To date, two GWAS have been performed in AAV. The first GWAS included patients with GPA and MPA and found *HLA-DP* rs3117242, *COL11A2* rs3130233, *COL11A2* rs3117016 and *SERPINA1* rs7151526 to be associated with AAV.[15] Moreover, *HLA-DP* rs3117242, *ARHGAP18* rs1705767 and *SERPINA1* rs7151526 were associated with PR3-ANCA vasculitis, and HLA-*DQ* rs5000634 was associated with MPO-ANCA vasculitis. The second GWAS included only patients with GPA and found *HLA-DPB1* rs9277554 and *HL-DPA1* rs9277341 to be associated with GPA.[16] *SEMA6A* rs26595 was associated with GPA at a genome-wide significance level when the results of the two cohorts that were included in this GWAS were combined. However, although *SEMA6A* rs26595 was not genotyped in the first GWAS,[15] data for a large number of proxy SNPs across this locus were available, and these did not reach statistical significance (data not shown).

DISCUSSION

This meta-analysis identified 33 genetic variants, in or near 15 genes, associated with AAV. Twenty of these 33 genetic variants were present in the MHC region. This study provides the first complete and comprehensive overview including all genetic investigated in AAV in at least two studies. Genetic variants in or near *CD226*, *CTLA-4*, *FCGR2A*, *HLA-B*, *HLA-DP*, *HLA-DQ*, *HLA-DR*, *HSD17B8*, *IRF5*, *PTPN22*, *RING1/RXRB*, *RXRB*, *STAT4*, *SERPINA1* and *TLR9* were associated with AAV in this meta-analysis. Of interest, *FCGR2A* and *STAT4* were not associated with AAV in the individual studies, but were significantly associated with AAV after meta-analysis. Moreover, we showed genetic distinctions between the clinical diagnoses GPA and MPA and between the ANCA serotypes PR3-ANCA and MPO-ANCA. Additionally, our results confirm that subdivision of AAV based on ANCA serotype has a stronger genetic basis than subdivision based on clinical diagnosis.

A number of the genetic variants associated with AAV in this meta-analysis have also been associated with other autoimmune diseases, such as *CTLA-4* rs3087243 in rheumatoid arthritis[28 29] and type 1 diabetes[30 31] and *PTPN22* rs2476601 in Crohn's disease,[32–34] Behçet's disease,[35] systemic lupus erythematosus[36–38] and giant cell arteritis.[39 40] These findings are in line with the fact that first-degree relatives of patients with AAV have an increased risk of other autoimmune diseases.[41 42] Overlapping genetic variants may form the basis of a disturbed immune system, and together with environmental factors and other, more distinct genetic factors, form a 'bad hand of cards' that leads to the development of AAV.

The results of this meta-analysis support a role for the intricate relationship among alpha-1-antitrypsin and ANCA, the MHC system and other inflammatory processes in the pathogenesis of AAV. The association between *SERPINA1* and AAV supports the concept that ANCA are important in AAV

pathogenesis. Alpha-1-antitrypsin is coded by *SERPINA1* and is a major inhibitor of PR3. It has been hypothesised that lower levels of alpha-1-antitrypsin, resulting from the presence of the Z and S alleles of *SERPINA1*, lead to increased levels of circulating PR3 and possibly trigger the synthesis of anti-PR3-ANCA.[43] This hypothesis implies that the association of AAV with alpha-1-antitrypsin deficiency is restricted to PR3-ANCA-positive patients; however, in this meta-analysis, the association between the Z allele of *SERPINA1* was present in both PR3-ANCA-positive and MPO-ANCA-positive patients and in both c-ANCA-positive and p-ANCA-positive patients. Another hypothesis is that patients with AAV and alpha-1-antitrypsin deficiency have a reduced ability to bind PR3 released by previously activated neutrophils, thus promoting PR3-mediated proteolytic vessel damage.

As noted, 20 genetic variants in the MHC region were associated with AAV in this meta-analysis. We, therefore, confirm an important role for the MHC region, but because of linkage disequilibrium, were unable to determine the nature of this association, that is, whether it represents single or multiple independent associations. Both GWAS showed that the SNP association signal in the MHC region was fully accounted for by *HLA-DPB1*, dramatically diminishing the associations of other SNPs in this region.[15 16] The results of our meta-analysis also support a role for other inflammatory processes in the pathogenesis of AAV, with the associations with *CTLA-4* and *PTPN22* suggesting a role for a threshold of activation or suppression of T cells.

The different subtypes generally grouped under the umbrella term AAV have profound differences in ANCA specificities[3] and clinical outcomes.[4] The results of this meta-analysis indicate that these different AAV subtypes also have distinct genetic backgrounds, as previously shown in a GWAS.[15] Moreover, we found significant associations in opposite directions for the different AAV subgroups. Significant associations of the same SNP in opposite directions for different types of autoimmune diseases have been described before and could be indicative of different mechanisms of disease.[44] Larger studies are required to investigate this issue further in AAV.

The subdivision of AAV based on ANCA serotype had the stronger genetic basis in our meta-analysis; in 76% of the genetic variants, subdivision based on ANCA serotype resulted in higher ORs than subdivision based on clinical diagnosis. The results of these analyses should, however, be interpreted with caution because of the limited number of studies included in some of the analyses and need to be validated in other studies. Although until now the concept of a single disease spectrum has resulted in similar treatment strategies in patients with AAV, our limited results suggest that syndrome-specific therapeutics based on ANCA serotype strategies may be considered.

Our study has some limitations. First, in some of our analyses, the number of subjects or studies was limited; this limitation was especially the case in the subgroup analyses. Second, publication bias is an issue of concern in all meta-analyses. Authors might omit non-significant genetic associations and report only those associations that reach statistical significance. However, none of the tests performed to assess funnel plot asymmetry in this meta-analysis were significant. Furthermore, the studies included in this meta-analysis show heterogeneity with respect to clinical diagnosis, ANCA serotype, disease characteristics, ethnicity and study design. The clinical heterogeneity was accompanied by statistical heterogeneity for 16 of the 140 included genetic variants. However, there is no fully accepted statistical measure that precisely determines clinical heterogeneity.[27] To account for heterogeneity, random-effects models were performed where possible.[25] Nevertheless, estimates reported in this study should be interpreted with caution, especially when statistical heterogeneity was present or when a small number of studies and/or relatively small groups of participants were included. Finally, it should be kept in mind that the genetic associations identified do not imply causality. While they provide insight into pathogenicity and suggest the involvement of certain pathways, these may not represent therapeutic targets.

In summary, this meta-analysis identified 33 genetic variants, in or near 15 genes, associated with AAV. Moreover, we showed genetic distinctions among the different AAV subtypes, supporting the concept that these subtypes may represent distinct autoimmune syndromes. These subtypes are most likely driven by ANCA serotype and not by clinical diagnosis.

Contributors All authors made substantial contributions to the study conception and design or analysis and interpretation of data and were involved in drafting the manuscript and approved the final version.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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Online supplement

Genetic variants in ANCA-associated vasculitis: a meta-analysis

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Supplementary Table S1. Literature search strategies

Database	Search Strategy
PubMed	*Two strategies:* 1. AAV and genes ("Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis"[Mesh] OR "ANCA-associated vasculitis"[all fields] OR "ANCA associated vasculitis"[all fields] OR "Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis"[all fields] OR "Pauci-Immune Vasculitis"[all fields] OR "Pauci Immune Vasculitis"[all fields] OR "Pauci-Immune Vasculitides"[all fields] OR "ANCA-Associated Vasculitides"[all fields] OR "ANCA Associated Vasculitides"[all fields] OR "ANCA-Associated Vasculitide"[all fields] OR ("ANCA"[all fields] AND vasculit*[all fields]) OR ("Anti-Neutrophil"[all fields] AND "Cytoplasmic"[all fields] AND "Antibody-Associated"[all fields] AND vasculit*[all fields]) OR "Churg-Strauss Syndrome"[all fields] OR "Churg Strauss Syndrome"[all fields] OR "Allergic Granulomatous Angiitis"[all fields] OR "Allergic Granulomatous Angiitides"[all fields] OR "Allergic Angiitis"[all fields] OR "Churg-Strauss Vasculitis"[all fields] OR "eosinophilic granulomatosis with polyangiitis"[all fields] OR ("eosinophilic"[all fields] AND "granulomatosis"[all fields] AND "polyangiitis"[all fields]) OR "Microscopic Polyangiitis"[all fields] OR "Microscopic Polyangiitides"[all fields] OR "Wegener Granulomatosis"[all fields] OR "Wegener's Granulomatosis"[all fields] OR "Wegeners Granulomatosis"[all fields] OR "granulomatosis with polyangiitis"[all fields] OR ("granulomatosis"[all fields] AND "polyangiitis"[all fields]) OR "anca"[tw] OR (("pr3"[all fields] OR "pr-3"[all fields] OR "mpo"[all fields]) AND ("Vasculitis"[mesh] OR vasculit*[all fields] OR "anca"[tw])) OR "Antibodies, Antineutrophil Cytoplasmic"[Mesh] OR "Antineutrophil Cytoplasmic Antibody"[all fields] OR "Anti-Neutrophil Cytoplasmic Antibody"[all fields] OR "Anti Neutrophil Cytoplasmic Antibody"[all fields] OR "Anti-Neutrophil Cytoplasmic Antibodies"[all fields] OR "Anti Neutrophil Cytoplasmic Antibodies"[all fields] OR "Antineutrophil Cytoplasmic Antibodies"[all fields]) AND ("genes"[mesh] OR "genes"[all fields] OR "gene"[all fields] OR "genetic"[all fields] OR "genetics"[Subheading] OR "genetics"[all fields] OR "genetics"[mesh] OR "polymorphism, genetic"[mesh] OR "polymorphism"[all fields] OR "polymorphisms"[all fields] OR "dna"[mesh] OR "dna"[all fields] OR "genome"[mesh] OR "genome"[all fields] OR "genomes"[all fields] OR "genomics"[mesh] OR "genomics"[all fields] OR "genomic"[all fields] OR "Genetic Phenomena"[mesh] OR "Genetic Structures"[Mesh]) 2. Vasculitis and genes (excluding AAV) (("Vasculitis"[majr] OR vasculit*[ti]) AND ("genes"[majr] OR "genes"[ti] OR "gene"[ti] OR "genetic"[ti] OR "genetics"[ti] OR "genetics"[majr] OR "polymorphism, genetic"[majr] OR "polymorphism"[ti] OR "polymorphisms"[ti] OR "dna"[majr] OR "dna"[ti] OR "genome"[majr] OR "genome"[ti] OR "genomes"[ti] OR "genomics"[majr] OR "genomics"[ti] OR "genomic"[ti] OR "Genetic Phenomena"[majr] OR "Genetic

	Structures"[majr])) NOT (("Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis"[Mesh] OR "ANCA-associated vasculitis"[all fields] OR "ANCA associated vasculitis"[all fields] OR "Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis"[all fields] OR "Pauci-Immune Vasculitis"[all fields] OR "Pauci Immune Vasculitis"[all fields] OR "Pauci-Immune Vasculitides"[all fields] OR "ANCA-Associated Vasculitides"[all fields] OR "ANCA Associated Vasculitides"[all fields] OR "ANCA-Associated Vasculitide"[all fields] OR ("ANCA"[all fields] AND vasculit*[all fields]) OR ("Anti-Neutrophil"[all fields] AND "Cytoplasmic"[all fields] AND "Antibody-Associated"[all fields] AND vasculit*[all fields]) OR "Churg-Strauss Syndrome"[all fields] OR "Churg Strauss Syndrome"[all fields] OR "Allergic Granulomatous Angiitis"[all fields] OR "Allergic Granulomatous Angiitides"[all fields] OR "Allergic Angiitis"[all fields] OR "Churg-Strauss Vasculitis"[all fields] OR "eosinophilic granulomatosis with polyangiitis"[all fields] OR ("eosinophilic"[all fields] AND "granulomatosis"[all fields] AND "polyangiitis"[all fields]) OR "Microscopic Polyangiitis"[all fields] OR "Microscopic Polyangiitides"[all fields] OR "Wegener Granulomatosis"[all fields] OR "Wegener's Granulomatosis"[all fields] OR "Wegeners Granulomatosis"[all fields] OR "granulomatosis with polyangiitis"[all fields] OR ("granulomatosis"[all fields] AND "polyangiitis"[all fields]) OR "anca"[tw] OR (("pr3"[all fields] OR "pr-3"[all fields] OR "mpo"[all fields]) AND ("Vasculitis"[mesh] OR vasculit*[all fields] OR "anca"[tw])) OR "Antibodies, Antineutrophil Cytoplasmic"[Mesh] OR "Antineutrophil Cytoplasmic Antibody"[all fields] OR "Anti-Neutrophil Cytoplasmic Antibody"[all fields] OR "Anti Neutrophil Cytoplasmic Antibody"[all fields] OR "Anti-Neutrophil Cytoplasmic Antibodies"[all fields] OR "Anti Neutrophil Cytoplasmic Antibodies"[all fields] OR "Antineutrophil Cytoplasmic Antibodies"[all fields]) AND ("genes"[mesh] OR "genes"[all fields] OR "gene"[all fields] OR "genetic"[all fields] OR "genetics"[Subheading] OR "genetics"[all fields] OR "genetics"[mesh] OR "polymorphism, genetic"[mesh] OR "polymorphism"[all fields] OR "polymorphisms"[all fields] OR "dna"[mesh] OR "dna"[all fields] OR "genome"[mesh] OR "genome"[all fields] OR "genomes"[all fields] OR "genomics"[mesh] OR "genomics"[all fields] OR "genomic"[all fields] OR "Genetic Phenomena"[mesh] OR "Genetic Structures"[Mesh]))
Embase	*Two strategies:* <u>1. AAV and genes</u> (ANCA associated vasculitis/ OR "ANCA-associated vasculitis".mp OR "ANCA associated vasculitis".mp OR "Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis".mp OR "Pauci-Immune Vasculitis".mp OR "Pauci Immune Vasculitis".mp OR "Pauci-Immune Vasculitides".mp OR "ANCA-Associated Vasculitides".mp OR "ANCA Associated Vasculitides".mp OR "ANCA-Associated Vasculitide".mp OR ("ANCA".mp AND vasculit*.mp) OR ("Anti-Neutrophil".mp AND "Cytoplasmic".mp AND "Antibody-Associated".mp AND vasculit*.mp) OR "Churg-Strauss Syndrome".mp OR "Churg Strauss Syndrome".mp OR "Allergic Granulomatous Angiitis".mp OR "Allergic Granulomatous Angiitides".mp OR "Allergic Angiitis".mp OR "Churg-Strauss Vasculitis".mp OR "eosinophilic

	granulomatosis with polyangiitis".mp OR ("eosinophilic".mp AND "granulomatosis".mp AND "polyangiitis".mp) OR "Microscopic Polyangiitis".mp OR "Microscopic Polyangiitides".mp OR "Wegener Granulomatosis".mp OR "Wegener's Granulomatosis".mp OR "Wegeners Granulomatosis".mp OR "granulomatosis with polyangiitis".mp OR ("granulomatosis".mp AND "polyangiitis".mp) OR "anca".mp OR (("pr3".mp OR "pr-3".mp OR "mpo".mp) AND (exp Vasculitis/ OR vasculit*.mp OR "anca".mp)) OR neutrophil cytoplasmic antibody/ OR "Antineutrophil Cytoplasmic Antibody".mp OR "Anti-Neutrophil Cytoplasmic Antibody".mp OR "Anti Neutrophil Cytoplasmic Antibody".mp OR "Anti-Neutrophil Cytoplasmic Antibodies".mp OR "Anti Neutrophil Cytoplasmic Antibodies".mp OR "Antineutrophil Cytoplasmic Antibodies".mp) AND (exp Gene/ OR gene.mp OR genom*.mp OR genes.mp OR exp genetic polymorphism/ OR polymorphism*.mp OR dna.mp OR exp dna/ OR exp *Heredity/) <u>2. Vasculitis and genes (excluding AAV)</u> ((exp *Vasculitis/ OR vasculit*.ti) AND (exp *Gene/ OR gene.ti OR genom*.ti OR genes.ti OR exp *genetic polymorphism/ OR polymorphism*.ti OR dna.ti OR exp *dna/ OR exp *Heredity/)) NOT ((ANCA associated vasculitis/ OR "ANCA-associated vasculitis".mp OR "ANCA associated vasculitis".mp OR "Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis".mp OR "Pauci-Immune Vasculitis".mp OR "Pauci Immune Vasculitis".mp OR "Pauci-Immune Vasculitides".mp OR "ANCA-Associated Vasculitides".mp OR "ANCA Associated Vasculitides".mp OR "ANCA-Associated Vasculitide".mp OR ("ANCA".mp AND vasculit*.mp) OR ("Anti-Neutrophil".mp AND "Cytoplasmic".mp AND "Antibody-Associated".mp AND vasculit*.mp) OR "Churg-Strauss Syndrome".mp OR "Churg Strauss Syndrome".mp OR "Allergic Granulomatous Angiitis".mp OR "Allergic Granulomatous Angiitides".mp OR "Allergic Angiitis".mp OR "Churg-Strauss Vasculitis".mp OR "eosinophilic granulomatosis with polyangiitis".mp OR ("eosinophilic".mp AND "granulomatosis".mp AND "polyangiitis".mp) OR "Microscopic Polyangiitis".mp OR "Microscopic Polyangiitides".mp OR "Wegener Granulomatosis".mp OR "Wegener's Granulomatosis".mp OR "Wegeners Granulomatosis".mp OR "granulomatosis with polyangiitis".mp OR ("granulomatosis".mp AND "polyangiitis".mp) OR "anca".mp OR (("pr3".mp OR "pr-3".mp OR "mpo".mp) AND (exp Vasculitis/ OR vasculit*.mp OR "anca".mp)) OR neutrophil cytoplasmic antibody/ OR "Antineutrophil Cytoplasmic Antibody".mp OR "Anti-Neutrophil Cytoplasmic Antibody".mp OR "Anti Neutrophil Cytoplasmic Antibody".mp OR "Anti-Neutrophil Cytoplasmic Antibodies".mp OR "Anti Neutrophil Cytoplasmic Antibodies".mp OR "Antineutrophil Cytoplasmic Antibodies".mp) AND (exp Gene/ OR gene.mp OR genom*.mp OR genes.mp OR exp genetic polymorphism/ OR polymorphism*.mp OR dna.mp OR exp dna/ OR exp *Heredity/))
Web of Science	*Two strategies:* <u>1. AAV and genes</u> TS=(("ANCA-associated vasculitis" OR "ANCA associated vasculitis" OR

	"Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis" OR "Pauci-Immune Vasculitis" OR "Pauci Immune Vasculitis" OR "Pauci-Immune Vasculitides" OR "ANCA-Associated Vasculitides" OR "ANCA Associated Vasculitides" OR "ANCA-Associated Vasculitide" OR ("ANCA" AND vasculit*) OR ("Anti-Neutrophil" AND "Cytoplasmic" AND "Antibody-Associated" AND vasculit*) OR "Churg-Strauss Syndrome" OR "Churg Strauss Syndrome" OR "Allergic Granulomatous Angiitis" OR "Allergic Granulomatous Angiitides" OR "Allergic Angiitis" OR "Churg-Strauss Vasculitis" OR "eosinophilic granulomatosis with polyangiitis" OR ("eosinophilic" AND "granulomatosis" AND "polyangiitis") OR "Microscopic Polyangiitis" OR "Microscopic Polyangiitides" OR "Wegener Granulomatosis" OR "Wegener's Granulomatosis" OR "Wegeners Granulomatosis" OR "granulomatosis with polyangiitis" OR ("granulomatosis" AND "polyangiitis") OR "anca" OR (("pr3" OR "pr-3" OR "mpo") AND (exp Vasculitis/ OR vasculit* OR "anca")) OR "neutrophil cytoplasmic antibody" OR "Antineutrophil Cytoplasmic Antibody" OR "Anti-Neutrophil Cytoplasmic Antibody" OR "Anti Neutrophil Cytoplasmic Antibody" OR "Anti-Neutrophil Cytoplasmic Antibodies" OR "Anti Neutrophil Cytoplasmic Antibodies" OR "Antineutrophil Cytoplasmic Antibodies") AND (gene OR genes OR genom* OR genetic* OR Polymorphism* OR dna)) <u>2. Vasculitis and genes (excluding AAV)</u> (TI=((vasculit*) AND (gene OR genes OR genom* OR genetic* OR Polymorphism* OR dna))) NOT (TS=(("ANCA-associated vasculitis" OR "ANCA associated vasculitis" OR "Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis" OR "Pauci-Immune Vasculitis" OR "Pauci Immune Vasculitis" OR "Pauci-Immune Vasculitides" OR "ANCA-Associated Vasculitides" OR "ANCA Associated Vasculitides" OR "ANCA-Associated Vasculitide" OR ("ANCA" AND vasculit*) OR ("Anti-Neutrophil" AND "Cytoplasmic" AND "Antibody-Associated" AND vasculit*) OR "Churg-Strauss Syndrome" OR "Churg Strauss Syndrome" OR "Allergic Granulomatous Angiitis" OR "Allergic Granulomatous Angiitides" OR "Allergic Angiitis" OR "Churg-Strauss Vasculitis" OR "eosinophilic granulomatosis with polyangiitis" OR ("eosinophilic" AND "granulomatosis" AND "polyangiitis") OR "Microscopic Polyangiitis" OR "Microscopic Polyangiitides" OR "Wegener Granulomatosis" OR "Wegener's Granulomatosis" OR "Wegeners Granulomatosis" OR "granulomatosis with polyangiitis" OR ("granulomatosis" AND "polyangiitis") OR "anca" OR (("pr3" OR "pr-3" OR "mpo") AND (exp Vasculitis/ OR vasculit* OR "anca")) OR "neutrophil cytoplasmic antibody" OR "Antineutrophil Cytoplasmic Antibody" OR "Anti-Neutrophil Cytoplasmic Antibody" OR "Anti Neutrophil Cytoplasmic Antibody" OR "Anti-Neutrophil Cytoplasmic Antibodies" OR "Anti Neutrophil Cytoplasmic Antibodies" OR "Antineutrophil Cytoplasmic Antibodies") AND (gene OR genes OR genom* OR genetic* OR Polymorphism* OR dna)))

Supplementary Table S2. Study characteristics of the included studies

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
***CD226* rs763361 (T)**	Wieczorek et al. 2009[1**]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy subjects	761/1226	GPA (642), EGPA (119)	PR3-ANCA (438), MPO-ANCA (32), ANCA negative (43)	1.24 (1.11 – 1.39)
		Case-Control	UK	ACR and CHCC criteria	Geographically matched subjects from the general population	105/9337	GPA (all patients)	NR	1.17 (0.89 – 1.54)
	Chung et al. 2012[2**]	Case-Control	USA	ACR criteria	Geographically matched subjects with no (family) history of autoimmune disease	424/469	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.08 (0.90 – 1.30)
		Case-Control	Canada	ACR criteria	Geographically matched subjects with no history of autoimmune disease	456/1500	GPA (all patients)	NR	1.09 (0.94 – 1.26)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.08 (0.96 – 1.21)
***CTLA-4* $(AT)_{86}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	0.18 (0.10 – 0.35)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	1.31 (0.76 – 2.25)
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	0.38 (0.26 – 0.55)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.72 (0.51 – 1.02)
***CTLA-4* $(AT)_{102}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.71 (0.15 – 19.22)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.89 (0.47 – 1.68)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.73 (0.85 – 3.54)
***CTLA-4* $(AT)_{104}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.74 (0.96 – 3.13)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	1.15 (0.70 – 1.91)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.09 (0.70 – 1.59)
***CTLA-4* $(AT)_{106}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	2.84 (0.74 – 10.91)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.41 (0.14 – 1.22)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	2.63 (1.09 – 6.35)
***CTLA-4* $(AT)_{108}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	0.90 (0.42 – 1.95)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.89 (0.47 – 1.68)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.78 (1.05 – 3.03)
***CTLA-4* $(AT)_{110}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	0.48 (0.02 9.36)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.25 (0.01 – 4.62)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.74 (0.34 – 1.61)
***CTLA-4* (AT)$_{116}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.37 (0.26 – 7.26)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.75 (0.03 – 18.56)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.540 (0.11 – 2.62)
***CTLA-4* (AT)$_{118}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	3.44 (0.21 – 55.85)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.75 (0.08 – 7.33)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.27 (0.06 – 1.18)
***CTLA-4* (AT)$_{122}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	10.32 (0.42 – 256.50)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	2.32 (0.57 – 9.47)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.47 (0.05 – 4.27)
***CTLA-4* (AT)$_{124}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	14.47 (1.59 – 131.86)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	2.28 (0.14 – 36.59)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.63 (0.13 – 3.16)
***CTLA-4* (AT)$_{126}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	4.78 (1.04 – 21.93)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.45 (0.05 – 3.88)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.81 (0.21 – 3.18)
***CTLA-4* (AT)$_{128}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.12 (0.05 – 27.93)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	6.98 (0.72 – 67.95)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.69 (0.22 – 2.18)
***CTLA-4* rs231775 (G)**	Slot et al. 2008[8]	Case-Control	The Nether-lands	CHCC criteria	Geographically and ethnically matched healthy subjects	104/185	GPA (50), MPA (24), EGPA (7), RLV (21)	PR3-ANCA (49), MPO-ANCA (34), PR3- and MPO-ANCA positive (2), ANCA negative (17)	1.53 (1.09 – 2.17)
	Kamesh et al. 2009[9]	Case-Control	UK	CHCC criteria	Ethnically matched healthy subjects with no (family) history of autoimmune disease	222/629	GPA (116), MPA (96)	NR	1.32 (1.06 – 1.65)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.09 (0.97 – 1.22)
***CTLA-4* rs3087243 (A)**	Kamesh et al. 2009[9]	Case-Control	UK	CHCC criteria	Ethnically matched healthy subjects with no (family) history of autoimmune disease	222/629	GPA (116), MPA (96)	NR	0.67 (0.54 – 0.83)
	Chung et al. 2012[2**]	Case-Control	USA	ACR criteria	Geographically matched subjects with no (family) history of autoimmune disease	424/469	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	0.80 (0.66 – 0.97)
		Case-Control	Canada	ACR criteria	Geographically matched subjects with no history of autoimmune disease	456/1500	GPA (all patients)	NR	0.78 (0.67 – 0.91)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	913/5257	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	0.85 (0.77 - 0.94)
***FCAR* rs16986050 (G)**	Kelley et al. 2011[10**]	Case-Control	USA	ACR and CHCC criteria	Geographically matched subjects with no (family) history of autoimmune disease	445/413	GPA (all patients)	NR	0.65 (0.50 – 0.83)
		Case-Control	USA, Canada	ACR and CHCC criteria	HapMap Caucasians	190/113	GPA (all patients)	NR	0.79 (0.52 – 1.21)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.07 (0.93 – 1.24)
***FCGR2A* rs1801274 (C)**	Edberg et al. 1997[11]	Case-Control	USA, Chile, Germany, Canada	ACR and CHCC criteria	Ethnically matched healthy volunteers	147/149	GPA (all patients)	NR	0.85 (0.61 – 1.17)
	Dijstelbloem et al. 1999[12]	Case-Control	The Netherlands	ACR criteria	Ethnically matched healthy blood donors	91/154	GPA (all patients)	PR3-ANCA (all patients)	0.98 (0.68 – 1.41)
	Tse et al. 1999[13]	Case-Control	UK	CHCC criteria	Ethnically matched healthy subjects	107/100	GPA (48), MPA (54), EGPA (1), PAN (4)	PR3-ANCA (75), MPO-ANCA (32)	1.00 (0.68 – 1.48)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/303	MPA (all patients)	MPO-ANCA (all patients)	0.68 (0.37 – 1.24)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	0.89 (0.79 – 0.99)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.03 (0.73 – 1.43)
***FCGR3A* rs396991 (G)**	Dijstelbloem et al. 1999[12]	Case-Control	The Netherlands	ACR criteria	Ethnically matched healthy blood donors	91/154	GPA (all patients)	PR3-ANCA (all patients)	1.30 (0.89 – 1.91)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/303	MPA (all patients)	MPO-ANCA (all patients)	0.65 (0.39 – 1.07)
***FCGR3B* (NA1)**	Dijstelbloem et al. 1999[12]	Case-Control	The Netherlands	ACR criteria	Ethnically matched healthy blood donors	91/154	GPA (all patients)	PR3-ANCA (all patients)	1.05 (0.72 – 1.53)
	Tse et al. 2000[14]	Case-Control	UK	CHCC criteria	Ethnically matched healthy subjects	101/100	GPA (45), MPA (52), EGPA (1), PAN (3)	PR3-ANCA (61), MPO-ANCA (30)	1.24 (0.8 – 1.87)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/303	MPA (all patients)	MPO-ANCA (all patients)	1.29 (0.82 – 2.03)
	Kelley et al. 2011[10]	Case-Control	USA	ACR and CHCC criteria	Geographically matched subjects with no (family) history of autoimmune disease	673/413	GPA (all patients)	NR	0.86 (0.72 – 1.03)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
***GHSR* rs509035 (A)**	Wieczorek et al. 2010[15]**	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	454/820	GPA (all patients)	NR	1.22 (1.02 – 1.45)
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	179/516	GPA (all patients)	NR	0.94 (0.72 – 1.23)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	914/5259	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	1.00 (0.90 – 1.11)
***GHSR* rs519384 (A)**	Wieczorek et al. 2010[15**]	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	449/813	GPA (all patients)	NR	1.17 (0.98 – 1.40)
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	179/515	GPA (all patients)	NR	1.01 (0.77 – 1.33)
***GHSR* rs572169 (A)**	Wieczorek et al. 2010[15**]	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	442/812	GPA (all patients)	NR	1.21 (1.01 – 1.44)
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	178/492	GPA (all patients)	NR	0.96 (0.73 – 1.25)
HLA-A1	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.53 (0.81 – 2.87)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.84 (0.47 – 1.52)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.92 (0.42 – 2.03)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.08 (0.87 – 1.35)
HLA-A2	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.78 (0.42 – 1.45)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.04 (0.62 – 1.73)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.90 (0.37 – 2.23)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.87 (0.48 – 1.58)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.98 (0.81 – 1.17)
HLA-A3	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.73 (0.90 –3.31)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.51 (0.86 – 2.66)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.88 (0.89 – 3.98)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.04 (0.84 – 1.31)
HLA-A9	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.09 (0.46 – 2.59)
	Katz et al. 1979[21]	Case-Control	USA	Clinical and histological criteria	Ethnically matched subjects	31/418	GPA (all patients)	NR	69.13 (3.28 – 456.19)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.79 (0.58 – 1.06)
HLA-A10	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.06 (0.32 – 3.48)
	Katz et al. 1979[21]	Case-Control	USA	Clinical and histological criteria	Ethnically matched subjects	31/418	GPA (all patients)	NR	69.13 (3.28 – 1456.19)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.61 (0.33 – 1.12)
HLA-A11	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/607	GPA (all patients)	NR	1.96 (0.81 – 4.72)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.68 (0.24 – 1.90)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.71 (0.17 – 3.03)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	2.97 (1.19 – 7.41)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.43 (0.14 – 1.27)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.62 (0.39 – 0.99)
HLA-A24	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.91 (0.36 – 2.31)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.75 (0.34 – 1.65)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.81 (0.51 – 6.37)
HLA-A25	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.43 (0.33 – 6.17)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.09 (0.61 – 7.16)
HLA-A26	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.68 (0.09 – 5.07)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	2.36 (1.00. – 5.60)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	2.49 (1.01 – 6.18)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.39 (0.07 – 2.05)
HLA-A28	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.40 (0.02 – 6.68)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.32 (0.04 – 2.34)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.88 (0.57 – 1.38)
HLA-A29	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	2.11 (0.68 – 6.57)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.31 (0.04 – 2.25)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.66 (0.11 – 4.04)
HLA-A30	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.68 (0.09 – 5.07)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.02 (0.18 – 22.63)
HLA-A31	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.07 (0.25 – 4.54)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.55 (0.46 – 5.24)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.33 (0.03 – 3.20)
HLA-A32	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	3.73 (1.24 – 11.22)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	2.07 (0.60 – 7.04)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.24 (0.03 – 2.21)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-B5	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.93 (0.28 – 3.02)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.56 (0.35 – 0.89)
HLA-B7	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.54 (0.77 – 3.08)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.74 (1.02 – 2.96)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.07 (0.52 – 2.22)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.00 (0.80 – 1.26)
HLA-B8	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.24 (0.60 – 2.56)
	Katz et al. 1979[21]	Case-Control	USA	Clinical and histological criteria	Ethnically matched subjects	31/418	GPA (all patients)	NR	2.30 (1.18 – 4.50)
	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	17/113	GPA (all patients)	NR	2.47 (1.01 – 6.05)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.03 (0.55 – 1.93)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	3.27 (1.02 – 10.50)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.11 (0.88 – 1.40)
HLA-B12	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.01 (0.47 – 2.15)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.96 (0.74 – 1.24)
HLA-B13	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.87 (0.12 – 6.50)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	2.09 (0.62 – 7.07)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.79 (0.21 – 3.03)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.63 (0.31 – 1.28)
HLA-B14	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.32 (0.02 – 5.24)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.51 (0.16 – 1.63)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.52 (0.25 – 9.26)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.16 (0.63 – 2.14)
HLA-B15	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.38 (0.55 – 3.43)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.98 (0.74 – 1.29)
HLA-B18	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/549	GPA (all patients)	NR	1.16 (0.35 – 3.85)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.53 (0.13 – 2.21)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.78 (0.296 – 2.072
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.75 (0.435 – 1.283

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-B27	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/600	GPA (all patients)	NR	0.74 (0.18 – 3.093
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.60 (0.14 – 2.503
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.06 (0.00 – 1.102
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.77 (0.48 – 1.247
HLA-B35	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.45 (0.11 – 1.86)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.80 (0.187 – 3.40)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.85 (0.28 – 2.62)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.81 (0.59 – 1.12)
HLA-B37	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.14 (0.01 – 2.72)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.07 (0.58 – 1.98)
HLA-B39	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.86 (0.11 – 6.51)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.33 (0.01 – 8.20)
HLA-B40	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.65 (0.52 – 5.23)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.90 (0.67 – 1.22)
HLA-B44	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.07 (0.58 – 2.00)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	2.50 (0.845 – 7.403
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	3.27 (1.02 – 10.50)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-B49	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.27 (0.30 – 5.44)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.02 (0.18 – 22.63)
HLA-B51	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.87 (0.64 – 5.49)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.61 (0.19 – 1.92)
HLA-B55	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	7.35 (2.33 – 23.14)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.07 (0.00 – 1.30)
HLA-B57	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	2.78 (1.05 – 7.32)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.00 (0.06 – 16.21)
HLA-B60	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	3.51 (0.99 – 12.36)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.19 (0.28 – 5.13)
HLA-B62	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	2.38 (0.70 – 8.12)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.71 (0.58 – 4.99)
HLA-Cw1	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.45 (0.58 – 3.58)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	52/51	GPA (all patients)	NR	0.98 (0.24 – 4.03)
HLA-Cw3	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.40 (0.65 – 3.01)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	52/51	GPA (all patients)	NR	1.32 (0.62 – 2.81)
HLA-Cw7	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.50 (0.12 – 2.10)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	52/51	GPA (all patients)	NR	1.10 (0.62 – 1.96)
***HLA-DPA1* rs9277341 (C)**	Heckmann et al. 2008 [24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	282/380	GPA (all patients)	ANCA+ (250), ANCA- (27)	0.38 (0.29 – 0.51)
	Xie et al. 2013[25**]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	0.30 (0.24 – 0.37)
		Case-control (GWAS)	USA	ACR criteria	Geographically matched healthy subjects	291/317	GPA (all patients)	c-ANCA (227)	0.43 (0.32 – 0.57)
HLA-DPB1*0101	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.20 (0.53 – 2.75)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.17 (0.05 – 0.63)
HLA-DPB1*0201	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.78 (0.49 – 1.23)
	Tsuchiya et al. 2006[28]	Case-Control	Japan	Japanese 1998 criteria	Geographically matched healthy subjects	50/77	MPA (all patients)	MPO-ANCA (all patients)	0.44 (0.21 – 0.91)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	1.38 (0.75 – 2.52)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.93 (0.57 – 1.51)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
***HLA-DPB1**0301**	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.27 (0.56 – 2.89)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.02 (0.00 – 0.15)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	0.28 (0.14 – 0.55)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.65 (0.38 – 1.11)
	Arning et al. 2011[30**]	Case-Control	Germany	CHCC criteria	Geographically and ethnically matched healthy blood donors	482/356	GPA (389), EGPA (56), MPA (37)	NR	0.30 (0.21 – 0.44)
		Case-Control	UK	CHCC criteria	Geographically and ethnically matched healthy blood donors	193/104	GPA (102), MPA (82), EGPA (9)	NR	0.35 (0.16 – 0.77)
***HLA-DPB1**0401**	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.42 (0.84 – 2.38)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	3.91 (2.62 – 5.84)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	2.15 (1.61 – 2.86)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	1.06 (0.78 – 1.45)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Arning et al. 2011[30**]	Case-Control	Germany	CHCC criteria	Geographically and ethnically matched healthy blood donors	482/356	GPA (389), EGPA (56), MPA (37)	NR	2.34 (1.92 – 2.85)
		Case-Control	UK	CHCC criteria	Geographically and ethnically matched healthy blood donors	193/104	GPA (102), MPA (82), EGPA (9)	NR	2.02 (1.44 – 2.85)
HLA-DPB1*0402	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.82 (0.38 – 1.78)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	1.11 (0.65 – 1.92)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	1.14 (0.78 – 1.68)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	1.15 (0.75 – 1.77)
HLA-DPB1*0501	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.34 (0.26 – 7.02)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.20 (0.01 – 4.93)
HLA-DPB1*0601	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	3.79 (0.19 – 74.15)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.60 (0.08 – 4.29)
HLA-DPB1*0901	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.52 (0.15 – 1.84)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	1.81 (0.07 – 44.73)
***HLA-DPB2* rs3130215 (A)**	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	282/380	GPA (all patients)	ANCA+ (250), ANCA- (27)	2.35 (1.88 – 2.94)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	0.88 (0.79 – 0.99)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	2.44 (2.10 – 2.84)
HLA-DQB1*02	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.98 (0.45 – 2.13)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/50	GPA (all patients)	NR	0.85 (0.41 – 1.77)
HLA-DQB1*0302	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.07 (0.53 – 2.20)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.94 (0.36 – 2.49)
HLA-DQB1*0303	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.84 (0.27 – 2.65)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	2.97 (0.72 – 12.23)
	Tsuchiya et al. 2006[28]	Case-Control	Japan	Japanese 1998 criteria	Geographically matched healthy subjects	50/77	MPA (all patients)	MPO-ANCA (all patients)	2.11 (1.14 – 3.90)
HLA-DQB1*04	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.74 (0.40 – 7.50)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/50	GPA (all patients)	NR	1.49 (0.24 – 9.08)
HLA-DQB1*0501	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.77 (0.91 – 3.42)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.77 (0.32 – 1.88)
HLA-DQB1*0602	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.64 (0.29 – 1.42)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	12.86 (2.65 – 62.31)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DQ7	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.21 (0.70 – 2.10)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	0.66 (0.34 – 1.30)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.43 (0.16 – 1.16)
HLA-DR1	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	2.17 (0.90 – 5.23)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	4.37 (2.01 – 9.48)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.89 (0.44 – 1.82)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.12 (0.48 – 2.64)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.68 (0.67 – 1.75)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.56 (0.23 – 1.35)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.71 (0.43 – 1.15)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.67 (0.49 – 0.92)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.53 (0.34 – 0.81)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.79 (0.28 – 2.19)
HLA-DR2	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	1.91 (0.97 – 3.75)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	1.20 (0.56 – 2.54)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.19 (0.66 – 2.13)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.33 (0.08 – 1.38)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.97 (0.77 – 1.22)
HLA-DR3	Elkon et al. 1983[23]	Case-Control	UK	Clinical, and histological, criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	1.01 (0.52 – 1.99)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	1.41 (0.59 – 3.36)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.75 (0.43 – 1.30)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	0.16 (0.02 – 1.18)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	2.54 (1.00 – 6.46)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.55 (0.53 – 4.52)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.66 (0.39 – 1.11)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.07 (0.84 – 1.35)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	1.30 (0.86 – 1.95)
HLA-DR4	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	1.00 (0.52 – 1.92)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/300	GPA (all patients)	NR	0.96 (0.50 – 1.83)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.81 (0.32 – 2.07)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.24 (0.74 – 2.07)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.72 (0.27 – 1.88)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.25 (0.54 – 2.90)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.57 (0.61 – 4.01)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	1.73 (0.84 – 3.57)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.87 (1.23 – 2.82)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.53 (1.25 – 1.87)
	Cao et al. 2011[33]**	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.73 (0.51 – 1.05)
		Case-Control	USA (all African Americans)	Histologically proven AAV	USA African Americans-Bethesda database	16/112	NR	PR3-ANCA (9), MPO-ANCA (4), p-ANCA (2), ANCA negative (1)	0.62 (0.08 – 5.01)
HLA-DR5	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.72 (0.28 – 1.85)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.18 (0.02 – 1.37)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.95 (0.45 – 2.01)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	1.59 (0.80 – 3.15)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.80 (0.58 – 1.09)
HLA-DR6	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.16 (0.04 – 0.70)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.11 (0.01 – 1.83)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.60 (0.27 – 1.31)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.63 (0.56 – 4.77)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.44 (0.32 – 0.59)
HLA-DR7	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.512 (0.22 – 1.22)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.64 (0.23 – 1.73)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.99 (0.40 – 2.48)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.77 (0.34 – 1.75)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	2.42 (1.47 – 4.00)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.58 (1.01 – 2.47)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.96 (0.72 – 1.27)
HLA-DR8	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.52 (0.22 – 1.22)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/300	GPA (all patients)	NR	1.05 (0.21 – 5.14)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	2.21 (0.67 – 7.32)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.63 (0.66 – 4.05)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.23 (0.31 – 4.91)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.00 (0.12 – 5.08)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	2.03 (1.01 – 4.05)
	Stassen et al. 2009[19]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.95 (0.59 – 1.54)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.76 (0.37 – 1.55)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DR9	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.49 (0.02 – 10.21)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	3.03 (1.40 – 6.56)
	Fujii et al. 2000[36]	Case-Control	Japan	CHCC criteria	Geographically matched healthy subjects	12/472	NR	MPO-ANCA (all patients)	2.75 (1.12 – 6.76)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.94 (0.04 – 23.32)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.66 (0.11 – 4.04)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	1.83 (0.20 – 16.56)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.80 (0.17 – 3.74)
	Stassen et al. 2009[19]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.35 (0.11 – 1.09)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.75 (0.208 – 2.72)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.68 (0.43 – 1.06)
	Tsuchiya et al. 2013[37]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	116/265	MPA (96)	MPO-ANCA (all patients)	1.74 (1.18 – 2.57)
HLA-DRB1*0401	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	2.10 (0.52 – 8.50)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.58 (0.18 – 1.90)
HLA-DRB1*0403	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.95 (0.27 – 3.40)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.16 (0.02 – 1.30)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DRB1*0405	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.61 (0.30 – 1.22)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.13 (0.52 – 2.49)
HLA-DRB1*0406	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.65 (0.19 – 2.22)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.84 (0.73 – 4.63)
HLA-DRB1*0407	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	2.82 (0.78 – 10.14)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.44 (0.02 – 10.77)
HLA-DRB1*0410	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.67 (0.32 – 8.69)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.44 (0.02 – 10.77)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DRB1*0802	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.16 (0.42 – 3.18)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.26 (0.01 – 5.47)
HLA-DRB1*0803	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.51 (0.78 – 2.93)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.19 (0.61 – 2.33)
HLA-DRB1*10	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.43 (0.13 – 16.03)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	5.10 (0.24 – 107.55)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.40 (0.02 – 7.44)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.75 (0.21 – 2.72)
HLA-DRB1*11	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.723 (0.26 – 2.04)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.28 (0.48 – 3.38)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.88 (0.53 – 1.48)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	1.09 (0.66 – 1.80)
HLA-DRB1*1101	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.75 (1.02 – 3.00)
	Tsuchiya et al. 2013[37]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	116/265	MPA (96)	MPO-ANCA (all patients)	2.79 (0.84 – 9.23)
HLA-DRB1*12	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	2.97 (0.721 – 2.23)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	6.31 (0.75 – 53.40)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.57 (0.17 – 1.93)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.59 (0.17 – 2.06)
HLA-DRB1*1201	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.21 (0.03 – 1.60)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.46 (0.16 – 1.29)
HLA-DRB1*1202	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.37 (0.05 – 2.90)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.70 (0.93 – 3.13)
HLA-DRB1*13	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.56 (0.20 – 1.53)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.65 (0.31 – 1.38)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	0.23 (0.07 – 0.73)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	0.50 (0.28 – 0.89)
HLA-DRB1*1302	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.54 (0.24 – 1.23)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.52 (0.16 – 1.67)
HLA-DRB1*14	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.07 (0.27 – 4.16)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.02 (0.18 – 22.63)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.83 (0.72 – 4.65)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	2.82 (1.05 – 7.59)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DRB1*1403	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.25 (0.34 – 4.60)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.32 (0.19 – 9.41)
HLA-DRB1*1405	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.11 (0.01 – 1.91)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.96 (0.44 – 2.13)
HLA-DRB1*15	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.79 (0.34 – 1.83)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.13 (0.57 – 2.26)
	Cao et al. 2011[33**]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	2.72 (1.84 – 4.03)
		Case-Control	USA (all African Americans)	Histologically proven AAV	USA African Americans-Bethesda database	16/112	NR	PR3-ANCA (9), MPO-ANCA (4), p-ANCA (2), ANCA negative (1)	2.08 (0.86 – 5.03)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DRB1*1501	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.62 (0.79 – 3.35)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.69 (1.16 – 2.46)
HLA-DRB1*1502	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.67 (0.32 – 1.39)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.35 (0.10 – 1.27)
HLA-DRB1*16	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.40 (0.02 – 7.80)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.14 (0.01 – 2.72)
	Cao et al. 2011[33**]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor- North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	1.39 (0.34 – 5.59)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
		Case-Control	USA (all African Americans)	Histologically proven AAV	USA African Americans-Bethesda database	16/112	NR	PR3-ANCA (9), MPO-ANCA (4), p-ANCA (2), ANCA negative (1)	2.42 (0.47 – 12.55)
HLA-DRB1*1602	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.24 (0.01 – 4.171)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.12 (0.01 – 2.14)
HLA-DRB3	Spencer et al. 1992[38]	Case-Control	UK	Clinical criteria	Geographically and ethnically matched subjects	59/1103	GPA (34), MPA (25)	c-ANCA (47), p-ANCA (10), ANCA negative (2)	0.29 (0.11 – 0.79)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.41 (0.76 – 2.60)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	0.54 (0.35 – 0.84)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	0.61 (0.44 – 0.86)
HLA-DRB4	Spencer et al. 1992[38]	Case-Control	UK	Clinical criteria	Geographically and ethnically matched subjects	59/1103	GPA (34), MPA (25)	c-ANCA (47), p-ANCA (10), ANCA negative (2)	1.38 (0.89 – 2.13)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.89 (0.46 – 1.72)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	2.49 (1.58 – 3.90)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.87 (1.34 – 2.61)
HLA-DRB5	Spencer et al. 1992[38]	Case-Control	UK	Clinical criteria	Geographically and ethnically matched subjects	59/1103	GPA (34), MPA (25)	c-ANCA (47), p-ANCA (10), ANCA negative (2)	1.35 (0.69 – 2.63)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.07 (0.82 – 2.18)
***HSD17B8* rs421446 (C)**	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	282/369	GPA (all patients)	ANCA+ (250), ANCA- (27)	0.43 (0.32 – 0.57)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	0.39 (0.32 – 0.48)
***IL-1β* (A2)**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.21 (0.55 – 2.63)
	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/196	NR	PR3-ANCA (79), MPO-ANCA (30)	0.89 (0.61 – 1.29)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	1.16 (0.72 – 1.85)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	914/5259	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	1.00 (0.89 – 1.12)
***IL1RN**1**	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/234	NR	PR3-ANCA (79), MPO-ANCA (30)	1.12 (0.79 –1.59)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.00 (0.69 – 1.44)
***IL1RN**2**	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/234	NR	PR3-ANCA (79), MPO-ANCA (30)	1.00 (0.69 – 1.43)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.01 (0.69 – 1.48)
***IL1RN**3**	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/234	NR	PR3-ANCA (79), MPO-ANCA (30)	0.30 (0.07 – 1.33)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.06 (0.35 – 3.20)
***IL1RN**4**	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/234	NR	PR3-ANCA (79), MPO-ANCA (30)	0.71 (0.03 – 17.58)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.95 (0.09 – 10.56)
***IL1RN**5**	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/234	NR	PR3-ANCA (79), MPO-ANCA (30)	1.07 (0.10 – 11.91)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.63 (0.03 – 15.60)
***IL-6* rs1800795 (C)**	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	1.00 (0.70 – 1.44)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.37 (0.76 – 2.48)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	914/5259	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	1.04 (0.94 – 1.15)
	Husmann et al. 2014[40]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	0.95 (0.85 – 1.08)
***IL-10* rs1800872 (A)**	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.10 (0.55 – 2.12)
	Wieczorek et al. 2008[41]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	506/507	GPA (403), EGPA (103)	ANCA+ (389), ANCA- (110)	1.00 (0.81 – 1.23)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
***IL-10* rs1800896 (G)**	Murakozy et al. 2001[42]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	39/72	GPA (all patients)	NR	0.59 (0.34 – 1.03)
	Bartfai et al. 2003[43]	Case-Control	Caucasian patients	ACR and CHCC criteria	Ethnically matched blood donors	161/153	GPA (125), MPA (36)	NR	0.74 (0.54 – 1.02)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.18 (0.67 – 2.10)
	Wieczorek et al. 2008[41]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	506/507	GPA (403), EGPA (103)	ANCA+ (389), ANCA- (110)	0.88 (0.74 – 1.05)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5360	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.04 (0.93 – 1.17)
***IRF5* rs10954213 (G)**	Wieczorek et al. 2010[44]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	627/902	GPA (all patients)	NR	0.31 (0.26 – 0.37)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.04 (0.93 – 1.17)
	Kawasaki et al. 2013[45]	Case-Control	Japan	EMA algorithm	Geographically matched healthy, unrelated subjects	232/710	GPA (28), MPA (177), EGPA (15), unclassified (12)	MPO (all patients)	1.28 (1.04 – 1.58)
***LEPR* rs8179183 (C)**	Wieczorek et al. 2010[15***]	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	456/818	GPA (all patients)	NR	0.72 (0.58 – 0.90)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	226/508	GPA (all patients)	NR	0.71 (0.52 – 0.97)
		Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	196/1327	EGPA (all patients)	NR	1.41 (1.10 – 1.81)
***MPO* rs2333227 (A)**	Reynolds et al. 2002[46]	Case-Control	The Netherlands	CHCC criteria	Ethnically matched healthy subjects	142/192	GPA (96), MPA (26), EGPA (8), iRPGN (12)	PR3-ANCA (92), MPO-ANCA (50)	1.07 (0.70 – 1.63)
	Fiebeler et al. 2004[47]	Case-Control	Germany	Clinical criteria	Geographically matched healthy subjects	119/270	GPA (63), MPA (56)	PR3-ANCA (71), MPO-ANCA (48)	0.90 (0.62 – 1.32)
	Rajp et al. 2007[48]	Case-Control	UK	CHCC criteria and histological criteria	Ethnically matched healthy subjects	134/150	GPA (69), MPA (65)	PR3-ANCA (91), MPO-ANCA (43)	0.92 (0.61 – 1.39)
***PCD1* rs1156882 (A)**	Slot et al. 2008[8]	Case-Control	The Nether-lands	CHCC criteria	Geographically and ethnically matched healthy subjects	102/204	GPA (50), MPA (24), EGPA (7), RLV (21)	PR3-ANCA (49), MPO-ANCA (34), PR3- and MPO-ANCA positive (2), ANCA negative (17)	0.94 (0.52 – 1.70)
	Sakthivel et al. 2009[49]	Case-Control	Sweden	Clinical criteria	Geographically and ethnically matched blood donors	66/275	GPA (all patients)	NR	0.78 (0.37 – 1.64)
***PTPN22* rs2476601 (A)**	Jagiello et al. 2005[50]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy subjects	199/399	GPA (all patients)	c-ANCA+ (168), p-ANCA+ (1), ANCA negative (30)	1.75 (1.23 – 2.49)
	Chung et al. 2012[2**]	Case-Control	USA	ACR criteria	Geographically matched subjects with no (family) history of autoimmune disease	424/469	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.25 (0.91 – 1.71)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
		Case-Control	Canada	ACR criteria	Geographically matched subjects with no history of autoimmune disease	456/1500	GPA (all patients)	NR	1.40 (1.11 – 1.78)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.35 (1.14 – 1.60)
	Martorana et al. 2012[51]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no history of autoimmune disease	344/945	GPA (143), EGPA (99), MPA (102)	c-ANCA (126), p-ANCA (163), ANCA negative (39)	1.40 (0.97 – 2.04)
***RING1/RXRB* rs213213 (A)**	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	279/369	GPA (all patients)	ANCA+ (250), ANCA- (27)	2.13 (1.70 – 2.67)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.55 (1.38 – 1.74)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	1.83 (1.57 – 2.13)
***RXRB* rs6531 (C)**	Szyld et al. 2006[52]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy subjects	187/201	GPA (all patients)	ANCA+ (151), ANCA- (36)	0.60 (0.45 – 0.80)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	911/5251	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	1.79 (1.61 – 1.98)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	1.81 (1.55 – 2.11)
***RXRB* rs9277935 (T)**	Wieczorek et al. 2009[53]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	282/380	GPA (all patients)	NR	0.39 (0.29 – 0.54)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5350	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	0.51 (0.43 – 0.61)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	0.34 (0.27 – 0.44)
***SERPINA1* S allele**	Lhotta et al. 1994[54]	Case-Control	Austria	ACR	Geographically matched healthy subjects	32/868	GPA (29), MPA (2), iRPGN (1)	c-ANCA (all patients)	0.69 (0.09 – 5.11)
	Griffith et al. 1996[55]	Case-Control	UK	CHCC criteria	Geographically and ethnically matched unrelated subjects	102/2310	GPA (51), MPA (29), EGPA (9), PAN (2), iRPGN (11)	c-ANCA (70), p-ANCA (32)	1.42 (0.79 – 2.52)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Mahr et al. 2010[56]	Case-Control	USA	ACR criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	433/421	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.68 (1.08 – 2.63)
	Morris et al. 2011[57]	Case-Control	Germany (531), France (81), UK (244)	CHCC criteria	Geographically and ethnically matched healthy subjects with no (family) history of autoimmune disease	856/1505	GPA (723), MPA (133)	c-ANCA (605), p-ANCA (150), ANCA negative (54)	1.11 (0.81 – 1.51)
	Chorostowska-Wynimko et al. 2013[58]	Case-Control	Poland	Clinical, histological, and serological criteria	Geographically matched neonates born alive	51/658	GPA (all patients)	c-ANCA (43), p-ANCA (2), ANCA negative (4)	2.61 (0.56 – 12.08)
***SERPINA1* Z allele**	Lhotta et al. 1994[54]	Case-Control	Austria	ACR criteria	Geographically matched healthy subjects	32/868	GPA (29), MPA (2), iRPGN (1)	c-ANCA (all patients)	8.76 (3.63 – 21.17)
	Griffith et al. 1996[55]	Case-Control	UK	CHCC criteria	Geographically and ethnically matched unrelated subjects	102/2310	GPA (51), MPA (29), EGPA (9), PAN (2), iRPGN (11)	c-ANCA (70), p-ANCA (32)	2.20 (1.05 – 4.62)
	Callea et al. 1997[59]	Case-Control	Italy	CHCC criteria	Healthy blood donors	84/200	GPA (33), MPA (28), iRPGN (23)	c-ANCA (38), p-ANCA (46)	4.90 (1.21 – 19.83)
	Borgmann et al. 2001[60]	Case-Control	Germany	ACR and CHCC criteria	Geographically and ethnically matched healthy, unrelated subjects	97/752	GPA (all patients)	c-ANCA (all patients)	3.36 (1.45 – 7.79)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Mahr et al. 2010[56]	Case-Control	USA	ACR criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	433/421	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.99 (1.12 – 3.52)
	Morris et al. 2011[57]	Case-Control	Germany (531), France (81), UK (244)	CHCC criteria	Geographically and ethnically matched healthy subjects with no (family) history of autoimmune disease	856/1505	GPA (723), MPA (133)	c-ANCA (605), p-ANCA (150), ANCA negative (54)	2.25 (1.60 – 3.18)
	Previously unpublished Lyons et al. 2012 GWAS data[3**]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	562/805	GPA (391), MPA (143)	PR3-ANCA (322), MPO-ANCA (166)	2.59 (1.66 – 4.02)
		Case-control (GWAS)	Europe	EMA algorithm, supported by either serology or histology	Geographically matched subjects	1445/1062	NR	NR	4.19 (2.62 – 6.69)
	Chorostowska-Wynimko et al. 2013[58]	Case-Control	Poland	Clinical, histological, serological criteria	Geographically matched neonates born alive	51/658	GPA (all patients)	c-ANCA (43), p-ANCA (2), ANCA negative (4)	2.19 (0.63 – 7.55)
***STAT4* rs7574865 (T)**	Wieczorek et al. 2010[44]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	612/880	GPA (all patients)	NR	1.01 (0.85 – 1.20)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.18 (1.04 – 1.35)
	Kawasaki et al. 2013[45]	Case-Control	Japan	EMA algorithm	Geographically matched healthy, unrelated subjects	232/710	GPA (28), MPA (177), EGPA (15), unclassified (12)	MPO (all patients)	1.10 (0.89 – 1.37)
***TGF-β_1* rs1800471 (C)**	Murakozy et al. 2001[42]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	39/72	GPA (all patients)	NR	2.20 (0.89 – 5.44)
	Bartfai et al. 2003[43]	Case-Control	Caucasian patients	ACR and CHCC criteria	Ethnically matched blood donors	161/96	GPA (125), MPA (36)	NR	1.06 (0.52 – 2.14)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.86 (0.73 – 4.71)
***TNFα* rs1800629 (A)**	Mascher et al. 1997[61]	Case-Control	Germany	ACR and CHCC criteria	Healthy blood donors	35/111	GPA (all patients)	c-ANCA (32), p-ANCA (1), ANCA negative (1)	1.54 (0.77 – 3.10)
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	0.88 (0.52 – 1.50)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	2.22 (0.93 – 5.29)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.06 (0.92 – 1.23)
***TNFRII* 196R**	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/262	MPA (all patients)	MPO-ANCA (all patients)	0.67 (0.31 – 1.45)
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	1.05 (0.70 – 1.57)
***TLR9* rs352162 (T)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	1.89 (1.67 – 2.14)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.07 (0.90 – 1.28)
***TLR9* rs352140 (T)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	1.16 (1.03 – 1.31)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.06 (0.89 – 1.27)
***TLR9* rs352139 (T)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	1.12 (0.99 – 1.27)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.08 (0.91 – 1.30)
***TLR9* rs5743836 (G)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	0.82 (0.69 – 0.98)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.22 (0.94 – 1.58)

ACR, American College of Rheumatology; ANCA, anti-neutrophil cytoplasm antibody; AAV, ANCA-associated vasculitis; c-ANCA, cytoplasmic ANCA; CHCC, Chapel Hill Consensus Conference; EGPA, eosinophilic granulomatosis with polyangiitis; EMA, European Medicines Agency; GPA, granulomatosis with polyangiitis; GWAS, genome-wide association study; iRPGN, idiopathic rapidly progressive glomerulonephritis; MPA, microscopic polyangiitis; MPO-ANCA, myeloperoxidase ANCA; NR, not reported; PAN, polyarteritis nodosa; p-ANCA, perinuclear ANCA; NR, not reported; RLV, renal limited vasculitis; PR3-ANCA, proteinase 3 ANCA; UK, United Kingdom; USA, United States of America. **Two cohorts described in the same publication; ***Three cohorts described in the same publication.

Supplementary Table 3. Genetic variants not associated with AAV after meta-analysis

Variant by gene (minor allele)	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
CTLA-4 $(AT)_{102}$	3	186/420	1.20 (0.75 – 1.90)	0.449	0	0.375	0.986
CTLA-4 $(AT)_{104}$	3	186/420	1.21 (0.92 – 1.60)	0.180	0	0.390	0.227
CTLA-4 $(AT)_{106}$	3	186/420	1.30 (0.74 – 2.29)	0.359	75	0.018	0.674
CTLA-4 $(AT)_{108}$	3	186/420	0.88 (0.50 – 1.56)	0.963	0	0.963	0.473
CTLA-4 $(AT)_{110}$	3	186/420	0.74 (0.34 – 1.61)	0.441	0	0.667	0.171
CTLA-4 $(AT)_{116}$	3	186/420	0.80 (0.27 – 2.33)	0.677	0	0.724	0.786
CTLA-4 $(AT)_{118}$	3	186/420	0.46 (0.16 – 1.35)	0.158	26	0.258	0.155
CTLA-4 $(AT)_{122}$	3	186/420	1.70 (0.62 – 4.71)	0.304	26	0.260	0.557
CTLA-4 $(AT)_{124}$	3	186/420	1.97 (0.73 – 5.31)	0.178	61	0.080	0.637
CTLA-4 $(AT)_{126}$	3	186/420	1.25 (0.53 – 2.94)	0.609	53	0.121	0.701
CTLA-4 $(AT)_{128}$	3	186/420	1.15 (0.47 – 2.82)	0.760	37	0.204	0.826
FCAR rs16986050 (G)	2	1311/5891	0.93 (0.82 – 1.05)	0.211	84	0.002	0.523
FCGR3A rs396991 (G)	2	141/457	1.00 (0.74 – 1.34)	0.978	79	0.030	N/A
FCGR3B (NA1)	4	982/970	0.96 (0.84 – 1.11)	0.590	37	0.191	0.210
GHSR rs509035 (A)	2	1547/6595	1.04 (0.96 – 1.14)	0.342	52	0.123	0.874
GHSR rs519384 (A)	1	628/1328	1.12 (0.96 – 1.30)	0.140	0	0.389	N/A
GHSR rs572169 (A)	1	620/1304	1.12 (0.97 – 1.30)	0.118	50	0.158	N/A
HLA-A1	4	427/7324	1.07 (0.89 – 1.30)	0.455	0	0.567	0.996
HLA-A2	5	443/7796	0.96 (0.82 – 1.12)	0.582	0	0.956	0.335
HLA-A3	4	427/7324	1.18 (0.97 – 1.42)	0.092	35	0.201	0.273
HLA-A9	3	366/6991	0.85 (0.65 – 1.13)	0.266	77	0.014	0.311

Variant by gene (minor allele)	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
HLA-A10	3	366/6991	0.79 (0.48 – 1.30)	0.356	78	0.010	0.273
HLA-A11	6	466/8107	0.97 (0.52 – 1.81)	0.924	65	0.013	0.273
HLA-A24	3	108/1223	0.94 (0.56 – 1.60)	0.830	0	0.510	0.090
HLA-A25	2	92/751	1.82 (0.72 – 4.58)	0.206	0	0.699	N/A
HLA-A26	4	131/1628	1.56 (0.89 – 2.74)	0.124	43	0.154	0.143
HLA-A28	3	376/6962	0.80 (0.52 – 1.23)	0.302	0	0.538	0.066
HLA-A29	3	123/988	0.88 (0.38 – 2.03)	0.760	42	0.178	0.801
HLA-A30	2	92/751	1.03 (0.25 – 4.28)	0.964	0	0.496	N/A
HLA-A31	3	108/1223	1.02 (0.43 – 2.44)	0.969	0	0.482	0.169
HLA-A32	3	108/1223	1.62 (0.74 – 3.54)	0.231	62	0.074	0.996
HLA-B7	4	427/7324	1.11 (0.91 – 1.35)	0.294	30	0.232	0.234
HLA-B12	2	335/6573	0.97 (0.76 – 1.23)	0.775	0	0.911	N/A
HLA-B13	4	427/7324	0.78 (0.46 – 1.34)	0.373	0	0.413	0.319
HLA-B14	4	427/7324	0.90 (0.54 – 1.49)	0.676	0	0.487	0.615
HLA-B15	2	355/5923	1.01 (0.77 – 1.31)	0.955	0	0.482	N/A
HLA-B18	4	427/7172	0.76 (0.50 – 1.16)	0.204	0	0.865	0.756
HLA-B27	4	412/7223	0.67 (0.44 – 1.02)	0.061	1	0.388	0.336
HLA-B35	4	412/7095	0.78 (0.58 – 1.06)	0.108	0	0.885	0.527
HLA-B37	2	355/5923	0.93 (0.51 – 1.70)	0.814	44	0.182	N/A
HLA-B39	2	67/523	0.65 (0.11 – 3.68)	0.622	0	0.619	N/A
HLA-B40	2	355/5923	0.94 (0.70 – 1.25)	0.652	0	0.319	N/A
HLA-B44	3	108/1223	1.53 (0.96 – 2.44)	0.072	46	0.157	0.225
HLA-B49	2	92/751	1.46 (0.43 – 4.92)	0.542	0	0.747	N/A

Variant by gene (minor allele)	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
HLA-B51	2	67/523	1.03 (0.46 – 2.32)	0.943	50	0.158	N/A
HLA-B55	2	67/523	1.07 (0.40 – 2.88)	0.887	93	<0.001	N/A
HLA-B57	2	92/751	2.37 (0.92 – 6.11)	0.075	0	0.493	N/A
HLA-B60	2	57/1172	1.98 (0.77 – 5.09)	0.154	20	0.263	N/A
HLA-B62	2	57/1172	1.95 (0.87 – 4.37)	0.107	0	0.688	N/A
HLA-Cw1	2	68/523	1.28 (0.59 – 2.77)	0.534	0	0.650	N/A
HLA-Cw3	2	68/523	1.36 (0.79 – 2.33)	0.267	0	0.907	N/A
HLA-Cw7	2	68/523	0.96 (0.57 – 1.62)	0.877	3	0.309	N/A
*HLA-DPB1*0101*	2	242/139	0.65 (0.34 – 1.22)	0.178	84	0.013	N/A
*HLA-DPB1*0201*	4	435/904	0.85 (0.65 – 1.12)	0.241	49	0.118	0.708
*HLA-DPB1*0402*	4	479/877	1.10 (0.87 – 1.40)	0.433	0	0.893	0.074
*HLA-DPB1*0501*	2	242/139	0.86 (0.22 – 3.33)	0.823	7	0.300	N/A
*HLA-DPB1*0601*	2	242/139	1.25 (0.28 – 5.67)	0.769	7	0.300	N/A
*HLA-DPB1*0901*	2	242/139	0.63 (0.20 – 2.01)	0.438	0	0.476	N/A
*HLA-DQB1*02*	2	83/141	0.91 (0.53 – 1.55)	0.720	0	0.796	N/A
*HLA-DQB1*0302*	2	126/141	1.03 (0.58 – 1.82)	0.931	0	0.832	N/A
*HLA-DQB1*04*	2	83/141	1.63 (0.52 – 5.11)	0.404	0	0.893	N/A
*HLA-DQB1*0501*	2	209/282	1.32 (0.79 – 2.20)	0.287	53	0.143	N/A
*HLA-DQB1*0602*	2	126/141	1.36 (0.70 – 2.64)	0.360	91	0.001	N/A
HLA-DQ7	3	149/546	0.82 (0.56 – 1.20)	0.302	49	0.142	0.252
HLA-DR1	10	1009/7105	0.93 (0.64 – 1.34)	0.684	70	<0.001	0.105
HLA-DR2	5	487/6222	1.10 (0.80 – 1.54)	0.554	37	0.176	0.757
HLA-DR3	9	816/7045	1.05 (0.81 – 1.36)	0.740	41	0.096	0.946

Variant by gene (minor allele)	Publica-tions (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
HLA-DR4	11	914/7696	1.19 (0.95 – 1.50)	0.132	47	0.037	0.342
HLA-DR5	5	494/6155	0.90 (0.61 – 1.31)	0.570	32	0.206	0.965
HLA-DR7	7	610/6493	1.08 (0.73 – 1.60)	0.164	66	0.007	0.932
HLA-DR8	9	823/7157	1.10 (0.80 – 1.51)	0.552	15	0.307	0.375
HLA-DR9	11	1016/8204	1.16 (0.71 – 1.90)	0.560	60	0.005	0.925
*HLA-DRB1*0401*	2	216/465	0.93 (0.38 – 2.28)	0.869	48	0.167	N/A
*HLA-DRB1*0403*	2	216/465	0.49 (0.17 – 1.42)	0.190	53	0.144	N/A
*HLA-DRB1*0405*	2	216/465	0.78 (0.47 – 1.30)	0.344	27	0.242	N/A
*HLA-DRB1*0406*	2	216/465	1.22 (0.61 – 2.5)	0.580	44	0.182	N/A
*HLA-DRB1*0407*	2	216/465	1.95 (0.61 – 6.29)	0.263	13	0.283	N/A
*HLA-DRB1*0410*	2	216/465	1.17 (0.27 – 5.05)	0.832	0	0.463	N/A
*HLA-DRB1*0802*	2	216/465	0.94 (0.36 – 2.43)	0.897	0	0.359	N/A
*HLA-DRB1*0803*	2	216/465	1.33 (0.83 – 2.14)	0.236	0	0.622	N/A
*HLA-DRB1*10*	4	322/890	0.98 (0.39 – 2.46)	0.969	0	0.627	0.596
*HLA-DRB1*11*	4	322/890	0.98 (0.71 – 1.34)	0.818	0	0.818	1.000
*HLA-DRB1*12*	4	322/890	1.12 (0.60 – 2.09)	0.712	54	0.088	0.121
*HLA-DRB1*1302*	2	216/465	0.54 (0.27 – 1.05)	0.068	0	0.952	N/A
*HLA-DRB1*1202*	2	216/465	1.42 (0.81 – 2.49)	0.219	49	0.160	N/A
*HLA-DRB1*1403*	2	216/465	1.27 (0.43 – 3.76)	0.666	0	0.964	N/A
*HLA-DRB1*1405*	2	216/465	0.66 (0.32 – 1.37)	0.265	57	0.125	N/A
*HLA-DRB1*1502*	2	216/465	0.57 (0.30 – 1.07)	0.079	0	0.398	N/A
*HLA-DRB1*16*	3	236/633	0.91 (0.37 – 2.27)	0.842	15	0.315	0.436
*HLA-DRB1*1602*	2	216/465	0.17 (0.02 – 1.29)	0.086	0	0.734	N/A

Variant by gene (minor allele)	**Publications (n)**	**Cases (n) / Controls (n)**	**OR (95% CI)**	**P value for meta-analysis**	**I^2 (%)**	**P value for heterogeneity**	**P value for funnel plot asymmetry**
HLA-DRB5	2	110/1154	1.20 (0.73 – 1.97)	0.470	0	0.643	N/A
IL-1β (A2)	4	1172/5687	1.00 (0.90 – 1.12)	0.995	0	0.805	0.645
*IL1RN**1	2	214/434	1.06 (0.82 – 1.37)	0.662	0	0.659	N/A
*IL1RN**2	2	214/434	1.00 (0.77 – 1.31)	0.980	0	0.956	N/A
*IL1RN**3	2	214/434	0.61 (0.26 – 1.44)	0.257	45	0.176	N/A
*IL1RN**4	2	214/434	0.85 (0.13 – 5.82)	0.872	0	0.888	N/A
*IL1RN**5	2	214/434	0.88 (0.13 – 5.94)	0.892	0	0.796	N/A
IL-6 rs1800795 (C)	4	1926/6817	1.01 (0.94 – 1.09)	0.793	0	0.537	0.584
IL-10 rs1800872 (A)	2	538/598	1.01 (0.83 – 1.22)	0.963	0	0.795	N/A
IL-10 rs1800896 (G)	5	1414/6183	0.90 (0.76 – 1.07)	0.232	55	0.063	0.285
LEPR rs8179183 (C)	1	878/2653	0.89 (0.77 – 1.03)	0.118	89	<0.001	0.780
MPO rs2333227 (A)	3	395/299	0.96 (0.76 – 1.21)	0.696	0	0.822	0.478
PCD1 rs1156882 (A)	2	168/479	0.88 (0.55 – 1.38)	0.568	0	0.701	N/A
TGF-β_1 rs1800471 (C)	3	232/259	1.49 (0.92 – 2.41)	0.107	0	0.401	0.220
TNFα rs1800629 (A)	4	860/5691	1.14 (0.88 – 1.45)	0.327	29	0.236	0.389
TNFRII 196R	2	167/385	0.94 (0.66 – 1.34)	0.749	0	0.317	N/A
TLR9 rs5743836 (G)	1	1289/1898	0.93 (0.81 – 1.08)	0.343	83	0.014	N/A

Supplementary Table S4. Results of the meta-analyses stratified by diagnostic and serologic subgroups

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
CD226 rs763361 (T)				
GPA	3	2021/17898	1.19 (1.11 – 1.28)	<0.001
MPA	1	156/5366	1.04 (0.83 – 1.31)	0.739
EGPA	1	119/1226	1.19 (0.91 – 1.56)	0.208
PR3-ANCA	2	764/6592	1.22 (1.09 – 1.36)	<0.001
MPO-ANCA	2	199/6592	1.20 (0.99 – 1.46)	0.066
CTLA-4 $(AT)_{86}$				
GPA	3	210/432	0.44 (0.34 – 0.57)	<0.001
MPA	2	93/311	0.87 (0.60 – 1.25)	0.450
PR3-ANCA	1	62/200	0.71 (0.47 – 1.09)	0.122
MPO-ANCA	2	92/311	0.94 (0.65 – 1.35)	0.733
CTLA-4 $(AT)_{102}$				
GPA	2	93/309	0.94 (0.45 – 1.94)	0.856
MPA	2	93/311	0.86 (0.51 – 1.45)	0.574
PR3-ANCA	1	62/200	0.87 (0.41 – 1.87)	0.722
MPO-ANCA	2	92/311	0.69 (0.26 – 1.81)	0.456
CTLA-4 $(AT)_{104}$				
GPA	2	93/309	0.84 (0.55 – 1.27)	0.398
MPA	2	93/311	0.87 (0.58 – 1.29)	0.474
PR3-ANCA	1	62/200	0.42 (0.22 – 0.79)	0.007
MPO-ANCA	2	92/311	0.85 (0.57 – 1.26)	0.412
CTLA-4 $(AT)_{106}$				
GPA	2	93/309	1.69 (0.67 – 4.25)	0.264
MPA	2	93/311	0.64 (0.28 – 1.46)	0.287
PR3-ANCA	1	62/200	1.83 (0.60 – 5.55)	0.289
MPO-ANCA	2	92/311	0.53 (0.22 – 1.30)	0.168
CTLA-4 $(AT)_{108}$				
GPA	2	93/309	0.40 (0.12 – 1.35)	0.141
MPA	2	93/311	0.75 (0.36 – 1.54)	0.431
PR3-ANCA	1	62/200	0.30 (0.07 – 1.28)	0.103
MPO-ANCA	2	92/311	0.66 (0.31 – 1.41)	0.291
CTLA-4 $(AT)_{110}$				
GPA	2	93/309	0.55 (0.18 – 1.74)	0.311
MPA	2	93/311	0.26 (0.05 – 1.36)	0.109
PR3-ANCA	1	62/200	0.56 (0.16 – 1.94)	0.359
MPO-ANCA	2	92/311	0.26 (0.05 – 1.38)	0.113
CTLA-4 $(AT)_{116}$				
GPA	2	93/309	0.66 (0.17 – 2.60)	0.553
MPA	2	93/311	0.41 (0.05 – 3.38)	0.408
PR3-ANCA	1	62/200	0.21 (0.01 – 3.72)	0.288
MPO-ANCA	2	92/311	0.69 (0.12 – 3.98)	0.673
CTLA-4 $(AT)_{118}$				
GPA	2	93/309	0.32 (0.06 – 1.68)	0.176
MPA	2	93/311	0.31 (0.06 – 1.69)	0.175

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
PR3-ANCA	1	62/200	0.11 (0.01 – 1.81)	0.121
MPO-ANCA	2	92/311	0.44 (0.10 – 1.97)	0.283
CTLA-4 $(AT)_{122}$				
GPA	2	93/309	1.32 (0.26 – 6.80)	0.742
MPA	2	93/311	1.57 (0.48 – 5.19)	0.456
PR3-ANCA	1	62/200	0.35 (0.02 – 6.62)	0.487
MPO-ANCA	2	92/311	3.69 (1.40 – 9.71)	0.008
CTLA-4 $(AT)_{124}$				
GPA	2	93/309	1.69 (0.67 – 4.25)	0.264
MPA	2	93/311	0.64 (0.28 – 1.46)	0.287
PR3-ANCA	1	62/200	1.83 (0.60 – 5.55)	0.289
MPO-ANCA	2	92/311	0.53 (0.22 – 1.30)	0.168
CTLA-4 $(AT)_{126}$				
GPA	2	93/309	1.43 (0.47 – 4.35)	0.526
MPA	2	93/311	0.38 (0.08 – 2.11)	0.266
PR3-ANCA	1	62/200	0.21 (0.01 – 3.72)	0.288
MPO-ANCA	2	92/311	0.54 (0.12 – 2.46)	0.428
CTLA-4 $(AT)_{128}$				
GPA	2	93/309	0.39 (0.07 – 2.14)	0.278
MPA	2	93/311	1.27 (0.39 – 4.20)	0.694
PR3-ANCA	1	62/200	0.29 (0.04 – 2.25)	0.235
MPO-ANCA	2	92/311	1.29 (0.39 – 4.28)	0.674
CTLA-4 rs231775 (G)				
GPA	2	510/5994	1.05 (0.92 – 1.20)	0.430
MPA	2	252/5994	1.17 (0.97 – 1.40)	0.100
PR3-ANCA	1	326/5365	1.00 (0.85 – 1.18)	0.983
MPO-ANCA	1	167/5365	0.96 (0.77 – 1.21)	0.747
CTLA-4 rs3087243 (A)				
GPA	3	1561/7855	0.80 (0.73 – 0.87)	<0.001
MPA	2	358/5886	0.79 (0.68 – 0.92)	0.003
PR3-ANCA	1	478/5257	0.81 (0.71 – 0.93)	0.003
MPO-ANCA	1	264/5257	0.96 (0.80 – 1.15)	0.658
FCAR rs16986050 (G)				
GPA	2	1029/5891	0.92 (0.80 – 1.05)	0.214
MPA	1	394/5365	0.93 (0.69 – 1.26)	0.647
PR3-ANCA	1	326/5365	1.13 (0.93 – 1.38)	0.211
MPO-ANCA	1	167/5365	1.00 (0.75 – 1.33)	0.988
FCGR2A rs1801274 (C)				
GPA	5	1082/5969	0.99 (0.94 – 1.05)	0.827
MPA	4	800/5766	0.97 (0.81 – 1.15)	0.698
PR3-ANCA	4	883/5820	0.91 (0.79 – 1.03)	0.138
MPO-ANCA	4	844/5969	0.80 (0.67 – 0.95)	0.011
FCGR3A rs396991 (G)				
GPA	1	91/154	1.30 (0.89 – 1.91)	0.172
MPA	1	50/303	0.65 (0.39 – 1.07)	0.090
PR3-ANCA	1	91/154	1.30 (0.89 – 1.91)	0.172

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPO-ANCA	1	50/303	0.65 (0.39 – 1.07)	0.090
FCGR3B (NA1)				
GPA	3	865/667	0.93 (0.80 – 1.08)	0.343
MPA	2	75/200	1.52 (1.03 – 2.25)	0.035
PR3-ANCA	2	143/254	1.07 (0.79 – 1.45)	0.664
MPO-ANCA	2	121/403	1.19 (0.86 – 1.64)	0.287
GHSR rs509035 (A)				
GPA	2	1198/6595	1.05 (0.96 – 1.16)	0.292
MPA	1	262/5259	1.00 (0.82 – 1.20)	0.966
PR3-ANCA	1	478/5259	1.05 (0.91 – 1.21)	0.521
MPO-ANCA	1	264/5259	0.83 (0.68 – 1.01)	0.057
HLA-A2				
GPA	5	380/7796	0.96 (0.81 – 1.14)	0.633
c-ANCA	1	16/96	0.90 (0.37 – 2.23)	0.826
HLA-A11				
GPA	5	380/7702	0.61 (0.41 – 0.90)	0.014
MPA	1	23/405	2.97 (1.19 – 7.41)	0.020
c-ANCA	1	16/472	0.71 (0.17 – 3.03)	0.644
HLA-A24				
GPA	3	108/1223	0.94 (0.56 – 1.60)	0.830
c-ANCA	1	16/472	0.75 (0.34 – 1.65)	0.476
HLA-A26				
GPA	3	108/1223	1.24 (0.61 – 2.54)	0.550
MPA	1	23/405	2.49 (1.00 – 6.18)	0.049
c-ANCA	1	16/472	2.36 (1.00 – 5.60)	0.051
HLA-A31				
GPA	3	108/1223	1.02 (0.43 – 2.44)	0.969
c-ANCA	1	16/472	1.55 (0.46 – 5.24)	0.479
HLA-A32				
GPA	3	108/1223	1.62 (0.74 – 3.54)	0.231
c-ANCA	1	16/472	2.07 (0.61 – 7.04)	0.246
HLA-B35				
GPA	4	349/7095	0.62 (0.44 – 0.89)	0.010
c-ANCA	1	16/472	0.80 (0.19 – 3.40)	0.757
HLA-B39				
GPA	2	67/523	0.65 (0.11 – 3.68)	0.622
c-ANCA	1	16/472	0.86 (0.11 – 6.51)	0.887
HLA-B44				
GPA	3	108/1223	1.53 (0.96 – 2.44)	0.072
c-ANCA	1	16/472	2.50 (0.85 – 7.40)	0.098
HLA-B51				
GPA	2	67/523	1.03 (0.46 – 2.32)	0.943
c-ANCA	1	16/472	1.87 (0.64 – 5.49)	0.255

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
HLA-B55				
GPA	2	67/523	1.07 (0.40 – 2.88)	0.887
c-ANCA	1	16/472	7.35 (2.33 – 23.14)	0.001
HLA-B60				
GPA	2	57/1172	1.98 (0.77 – 5.09)	0.154
c-ANCA	1	16/472	1.19 (0.28 – 5.13)	0.814
HLA-B62				
GPA	2	57/1172	2.27 (1.05 – 4.90)	0.036
c-ANCA	1	16/472	2.21 (0.83 – 5.91)	0.114
HLA-Cw1				
GPA	2	68/523	1.28 (0.59 – 2.77)	0.534
c-ANCA	1	16/472	1.45 (0.58 – 3.58)	0.426
HLA-Cw3				
GPA	2	68/523	1.36 (0.79 – 2.33)	0.267
c-ANCA	1	16/472	1.40 (0.65 – 3.01)	0.384
HLA-Cw7				
GPA	2	68/523	0.96 (0.57 – 1.62)	0.877
c-ANCA	1	16/472	0.50 (0.12 – 2.10)	0.340
HLA-DPA1 rs9277341 (C)				
GPA	2	1032/2200	0.35 (0.30 – 0.41)	<0.001
c-ANCA	1	578/1820	0.27 (0.22 – 0.33)	<0.001
*HLA-DPB1*0101*				
GPA	1	148/89	0.17 (0.05 – 0.63)	0.008
PR3-ANCA	2	183/139	0.45 (0.20 – 0.99)	0.048
MPO-ANCA	1	22/50	1.01 (0.29 – 3.48)	0.986
*HLA-DPB1*0201*				
GPA	2	283/458	0.67 (0.45 – 0.99)	0.042
MPA	1	50/77	1.38 (0.75 – 2.52)	0.298
EGPA	1	102/369	0.93 (0.57 – 1.51)	0.759
PR3-ANCA	1	148/89	0.44 (0.21 – 0.91)	0.027
MPO-ANCA	1	50/77	1.38 (0.75 – 2.52)	0.298
*HLA-DPB1*0301*				
GPA	3	774/918	0.23 (0.16 – 0.32)	<0.001
MPA	1	119/460	0.67 (0.37 – 1.21)	0.186
EGPA	2	167/829	0.47 (0.29 – 0.75)	0.001
PR3-ANCA	2	183/139	0.19 (0.09 – 0.39)	<0.001
MPO-ANCA	1	22/50	1.71 (0.74 – 3.94)	0.210
ANCA negative	1	27/369	0.58 (0.21 – 1.65)	0.311
*HLA-DPB1*0401*				
GPA	3	774/918	2.89 (2.50 – 3.35)	<0.001
MPA	1	119/460	1.09 (0.80 – 1.49)	0.597
EGPA	2	167/829	1.08 (0.85 – 1.36)	0.548
PR3-ANCA	2	183/139	3.93 (2.75 – 5.62)	<0.001
MPO-ANCA	1	22/50	1.43 (0.67 – 3.02)	0.351
ANCA negative	1	27/369	1.26 (0.73 – 2.20)	0.407

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
*HLA-DPB1*0402*				
GPA	2	283/458	1.13 (0.82 – 1.55)	0.439
EGPA	1	102/369	1.15 (0.75 – 1.75)	0.533
PR3-ANCA	2	183/139	1.11 (0.69 – 1.77)	0.674
MPO-ANCA	1	22/50	0.94 (0.31 – 2.85)	0.913
*HLA-DPB1*0501*				
GPA	1	148/89	0.20 (0.01 – 4.93)	0.324
PR3-ANCA	2	183/139	1.11 (0.26 – 4.76)	0.886
MPO-ANCA	1	22/50	1.14 (0.10 – 12.91)	0.916
*HLA-DPB1*0601*				
GPA	1	148/89	0.60 (0.08 – 4.29)	0.610
PR3-ANCA	2	183/139	1.12 (0.23 – 5.51)	0.887
MPO-ANCA	1	22/50	6.93 (0.28 – 173.53)	0.239
*HLA-DPB1*0901*				
GPA	1	148/89	1.81 (0.07 – 44.73)	0.716
PR3-ANCA	2	183/139	0.98 (0.27 – 3.62)	0.978
MPO-ANCA	1	22/50	0.91 (0.17 – 4.85)	0.907
HLA-DPB2 rs3130215 (A)				
GPA	3	1135/7249	1.37 (0.88 – 2.13)	0.160
MPA	1	156/5366	1.33(1.06 – 1.66)	0.013
PR3-ANCA	1	326/5366	0.65 (0.55 – 0.77)	<0.001
MPO-ANCA	1	167/5366	1.27 (1.02 – 1.58)	0.032
*HLA-DQB1*02*				
GPA	2	83/141	0.91 (0.53 – 1.55)	0.720
PR3-ANCA	1	32/91	0.98 (0.45 – 2.14)	0.954
*HLA-DQB1*0302*				
GPA	1	32/91	0.94 (0.36 – 2.49)	0.905
PR3-ANCA	2	67/141	1.03 (0.54 – 1.98)	0.924
MPO-ANCA	1	22/50	1.06 (0.37 – 2.99)	0.917
*HLA-DQB1*0303*				
GPA	1	32/91	2.97 (0.72 – 12.23)	0.132
MPA	1	50/77	2.11 (1.14 – 3.90)	0.018
PR3-ANCA	2	67/141	0.79 (0.31 – 2.05)	0.634
MPO-ANCA	2	72/127	1.91 (1.12 – 3.26)	0.017
*HLA-DQB1*04*				
GPA	2	83/141	1.63 (0.52 – 5.11)	0.404
PR3-ANCA	1	32/91	1.74 (0.40 – 7.50)	0.457
*HLA-DQB1*0501*				
GPA	1	32/91	0.77 (0.32 – 1.88)	0.568
PR3-ANCA	2	67/141	1.05 (0.58 – 1.91)	0.865
MPO-ANCA	1	22/50	2.05 (0.84 – 4.97)	0.113
*HLA-DQB1*0602*				
GPA	1	32/91	0.89 (0.38 – 2.05)	0.779
PR3-ANCA	2	67/141	0.80 (0.42 – 1.54)	0.504
MPO-ANCA	1	22/50	0.35 (0.08 – 1.63)	0.181

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
HLA-DQ7				
GPA	1	32/91	0.43 (0.16 – 1.16)	0.095
MPA	1	23/405	0.66 (0.34 – 1.30)	0.234
PR3-ANCA	2	67/141	0.98 (0.58 – 1.66)	0.940
MPO-ANCA	1	22/50	1.26 (0.57 – 2.77)	0.569
HLA-DR1				
GPA	6	413/6002	0.76 (0.58 – 1.00)	0.054
MPA	4	223/6020	1.12 (0.72 – 1.74)	0.612
EGPA	3	128/5924	0.82 (0.53 – 1.26)	0.360
PR3-ANCA	3	157/560	0.57 (0.38 – 0.86)	0.008
MPO-ANCA	3	133/734	0.78 (0.49 – 1.25)	0.297
HLA-DR2				
GPA	4	301/6132	1.36 (1.08 – 1.72)	0.010
EGPA	1	14/113	1.40 (0.45 – 4.39)	0.561
PR3-ANCA	1	35/90	1.34 (0.63 – 2.86)	0.442
MPO-ANCA	1	22/90	1.03 (0.39 – 2.69)	0.958
c-ANCA	1	16/472	0.33 (0.08 – 1.38)	0.128
HLA-DR3				
GPA	5	368/5802	1.24 (1.00 – 1.56)	0.056
MPA	2	38/518	0.45 (0.17 – 1.14)	0.092
EGPA	2	116/482	0.70 (0.43 – 1.13)	0.139
PR3-ANCA	3	157/560	1.29 (0.90 – 1.86)	0.170
MPO-ANCA	2	69/469	0.85 (0.49 – 1.48)	0.574
HLA-DR4				
GPA	7	425/6424	1.32 (1.09 – 1.60)	0.004
MPA	2	66/5555	1.50 (0.98 – 2.30)	0.060
EGPA	4	176/6246	1.70 (1.23 – 2.34)	0.001
PR3-ANCA	3	157/560	0.98 (0.71 – 1.36)	0.917
MPO-ANCA	2	69/202	2.51 (1.46 – 4.32)	0.001
c-ANCA	1	16/472	0.72 (0.27 – 1.88)	0.498
HLA-DR5				
GPA	3	285/5660	0.76 (0.54 – 1.06)	0.102
MPA	1	23/405	1.59 (0.80 – 3.15)	0.182
EGPA	1	14/113	1.24 (0.34 – 4.46)	0.746
PR3-ANCA	1	35/90	0.85 (0.30 – 2.42)	0.756
MPO-ANCA	1	22/90	0.52 (0.12 – 2.38)	0.402
HLA-DR6				
GPA	4	301/6132	0.45 (0.33 – 0.62)	<0.001
MPA	1	30/5442	0.29 (0.09 – 0.92)	0.035
EGPA	2	26/5555	0.19 (0.04 – 0.95)	0.043
PR3-ANCA	1	35/90	0.28 (0.06 – 1.25)	0.096
MPO-ANCA	1	22/90	0.70 (0.20 – 2.51)	0.586
c-ANCA	1	16/472	1.63 (0.56 – 4.77)	0.371
HLA-DR7				
GPA	5	368/5802	0.92 (0.71 – 1.19)	0.508
MPA	1	15/113	0.70 (0.20 – 2.44)	0.575
EGPA	3	164/804	1.71 (1.24 – 2.37)	0.001
PR3-ANCA	1	32/91	1.00 (0.40 – 2.48)	0.991

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
HLA-DR8				
GPA	5	381/6206	0.89 (0.57 – 1.39)	0.610
MPA	1	51/5442	0.31 (0.04 – 2.21)	0.242
EGPA	2	114/5811	3.08 (1.75 – 5.41)	<0.001
PR3-ANCA	3	157/560	0.68 (0.33 – 1.42)	0.308
MPO-ANCA	2	69/469	1.70 (0.80 – 3.60)	0.170
c-ANCA	1	16/472	1.63 (0.66 – 4.05)	0.291
HLA-DR9				
GPA	6	402/6369	0.90 (0.58 – 1.39)	0.623
MPA	3	218/578	1.14 (0.83 – 1.56)	0.423
EGPA	3	164/832	1.07 (0.33 – 3.42)	0.915
PR3-ANCA	2	122/470	0.47 (0.09 – 2.58)	0.383
MPO-ANCA	3	175/1116	1.83 (1.29 – 2.60)	0.001
c-ANCA	1	16/472	3.03 (1.40 – 6.56)	0.005
*HLA-DRB1*0401*				
GPA	1	45/200	0.49 (0.06 – 3.90)	0.499
MPA	2	157/465	1.42 (0.60 – 3.41)	0.426
MPO-ANCA	1	64/265	2.10 (0.52 – 8.50)	0.300
*HLA-DRB1*0403*				
GPA	1	45/200	0.26 (0.02 – 4.46)	0.349
MPA	2	157/465	0.48 (0.14 – 1.59)	0.227
MPO-ANCA	1	64/265	0.95 (0.27 – 3.40)	0.943
*HLA-DRB1*0405*				
GPA	1	45/200	0.15 (0.01 – 2.49)	0.184
MPA	2	157/465	0.95 (0.56 – 1.62)	0.862
MPO-ANCA	1	64/265	0.61 (0.30 – 1.22)	0.159
*HLA-DRB1*0406*				
GPA	1	45/200	2.28 (0.67 – 7.74)	0.187
MPA	2	157/465	1.31 (0.62 – 2.78)	0.483
MPO-ANCA	1	64/265	0.65 (0.19 – 2.22)	0.487
*HLA-DRB1*0407*				
GPA	1	45/200	1.47 (0.06 – 36.42)	0.813
MPA	2	157/465	1.95 (0.54 – 6.99)	0.306
MPO-ANCA	1	64/265	2.82 (0.78 – 10.14)	0.113
*HLA-DRB1*0410*				
GPA	1	45/200	1.47 (0.06 – 36.42)	0.813
MPA	2	157/465	1.53 (0.35 – 6.64)	0.569
MPO-ANCA	1	64/265	1.67 (0.32 – 8.69)	0.544
*HLA-DRB1*0802*				
GPA	1	45/200	0.88 (0.04 – 18.50)	0.935
MPA	2	157/465	0.99 (0.35 – 2.79)	0.984
MPO-ANCA	1	64/265	1.16 (0.42 – 3.18)	0.778
*HLA-DRB1*0803*				
GPA	1	45/200	1.18 (0.43 – 3.25)	0.749
MPA	2	157/465	1.25 (0.73 – 2.13)	0.413
MPO-ANCA	1	64/265	1.51 (0.78 – 2.93)	0.226

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
*HLA-DRB1*10*				
GPA	2	83/142	2.61 (0.45 – 15.24)	0.286
EGPA	1	102/369	0.40 (0.02 – 7.44)	0.538
PR3-ANCA	2	122/470	0.59 (0.13 – 2.65)	0.487
MPO-ANCA	1	47/379	1.48 (0.32 – 6.76)	0.616
*HLA-DRB1*11*				
GPA	2	83/142	0.97 (0.49 – 1.94)	0.932
EGPA	1	102/369	0.88 (0.53 – 1.48)	0.632
PR3-ANCA	2	122/470	0.97 (0.58 – 1.62)	0.908
MPO-ANCA	1	47/379	1.10 (0.51 – 2.38)	0.805
*HLA-DRB1*1101*				
GPA	1	45/200	0.16 (0.02 – 1.21)	0.076
MPA	2	223/465	2.57 (1.56 – 4.23)	<0.001
MPO-ANCA	1	116/265	2.79 (0.84 – 9.23)	0.093
*HLA-DRB1*12*				
GPA	2	83/142	4.06 (1.27 – 12.99)	0.018
EGPA	1	102/369	0.57 (0.17 – 1.93)	0.362
PR3-ANCA	2	122/470	1.01 (0.36 – 2.81)	0.983
MPO-ANCA	1	47/379	1.16 (0.26 – 5.16)	0.850
*HLA-DRB1*1201*				
GPA	1	45/200	0.15 (0.01 – 2.49)	0.184
MPA	2	157/465	0.51 (0.21 – 1.26)	0.146
MPO-ANCA	1	64/265	0.21 (0.03 – 1.60)	0.132
*HLA-DRB1*1202*				
GPA	1	45/200	2.92 (1.37 – 6.23)	0.005
MPA	2	157/465	1.07 (0.55 – 2.09)	0.838
PR3-ANCA	1	19/200	1.63 (0.46 – 5.75)	0.449
MPO-ANCA	2	89/465	1.00 (0.38 – 2.61)	1.000
*HLA-DRB1*13*				
GPA	2	83/142	0.61 (0.34 – 1.12)	0.111
EGPA	2	150/691	0.40 (0.24 – 0.68)	0.001
PR3-ANCA	1	32/91	0.56 (0.20 – 1.53)	0.257
*HLA-DRB1*1302*				
GPA	1	45/200	0.89 (0.19 – 4.12)	0.878
MPA	2	157/465	0.46 (0.20 – 1.02)	0.055
MPO-ANCA	1	64/265	0.54 (0.24 – 1.23)	0.142
*HLA-DRB1*14*				
GPA	2	83/142	1.26 (0.40 – 4.01)	0.698
EGPA	1	102/341	1.83 (0.72 – 4.65)	0.205
PR3-ANCA	2	122/470	2.00 (0.87 – 4.56)	0.101
MPO-ANCA	1	47/379	2.04 (0.43 – 9.74)	0.372
*HLA-DRB1*1403*				
GPA	1	45/200	2.24 (0.20 – 24.93)	0.513
MPA	2	157/465	0.81 (0.21 – 3.19)	0.767
MPO-ANCA	1	64/265	1.25 (0.34 – 4.60)	0.739
*HLA-DRB1*1405*				
GPA	1	45/200	1.51 (0.53 – 4.27)	0.437

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPA	2	157/465	0.45 (0.18 – 1.15)	0.096
MPO-ANCA	1	64/265	0.11 (0.01 – 1.91)	0.131
*HLA-DRB1*15*				
GPA	2	83/142	0.97 (0.57 – 1.65)	0.921
PR3-ANCA	2	131/582	2.82 (2.00 – 3.96)	<0.001
MPO-ANCA	1	51/491	0.80 (0.37 – 1.73)	0.566
*HLA-DRB1*1501*				
GPA	1	45/200	1.70 (0.98 – 2.94)	0.059
MPA	2	157/465	1.65 (1.14 – 2.38)	0.007
PR3-ANCA	1	19/200	0.98 (0.40 – 2.45)	0.973
MPO-ANCA	2	89/465	2.03 (1.26 – 3.29)	0.004
*HLA-DRB1*1502*				
GPA	1	45/200	0.80 (0.18 – 3.69)	0.779
MPA	2	157/465	0.60 (0.30 – 1.21)	0.154
MPO-ANCA	1	64/265	0.67 (0.32 – 1.39)	0.279
*HLA-DRB1*16*				
GPA	2	83/142	0.23 (0.03 – 1.85)	0.166
PR3-ANCA	2	131/582	1.00 (0.29 – 3.41)	0.996
MPO-ANCA	1	51/491	3.55 (1.02 – 12.38)	0.047
*HLA-DRB1*1602*				
GPA	1	45/200	0.40 (0.02 – 7.25)	0.533
MPA	2	157/465	0.23 (0.03 – 1.72)	0.151
MPO-ANCA	1	64/265	0.24 (0.01 – 4.17)	0.327
HLA-DRB3				
GPA	1	51/51	1.41 (0.76 – 2.60)	0.276
EGPA	2	150/691	0.58 (0.45 – 0.76)	<0.001
HLA-DRB4				
GPA	1	51/51	0.89 (0.46 – 1.72)	0.738
EGPA	2	150/691	2.06 (1.57 – 2.69)	<0.001
IL-1β (A2)				
GPA	3	714/5491	1.07 (0.93 – 1.22)	0.336
MPA	1	262/5259	0.89 (0.72 – 1.10)	0.286
PR3-ANCA	2	557/5455	1.01 (0.87 – 1.17)	0.930
MPO-ANCA	2	294/5455	1.00 (0.82 – 1.21)	0.971
*IL1RN**1				
GPA	1	61/200	0.88 (0.57 – 1.37)	0.573
MPA	1	105/200	1.21 (0.83 – 1.77)	0.325
PR3-ANCA	2	122/434	1.12 (0.82 – 1.54)	0.476
MPO-ANCA	2	92/434	0.98 (0.69 – 1.40)	0.916
*IL1RN**2				
GPA	1	61/200	1.22 (0.78 – 1.92)	0.380
MPA	1	105/200	0.77 (0.52 – 1.16)	0.212
PR3-ANCA	2	122/434	0.95 (0.68 – 1.31)	0.748
MPO-ANCA	2	92/434	1.02 (0.71 – 1.47)	0.921
*IL1RN**3				
GPA	1	61/200	0.72 (0.15 – 3.40)	0.682

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPA	1	105/200	1.50 (0.55 – 4.08)	0.429
PR3-ANCA	2	122/434	0.61 (0.21 – 1.76)	0.358
MPO-ANCA	2	92/434	0.71 (0.22 – 2.29)	0.571
*IL1RN**4				
GPA	1	61/200	0.65 (0.03 – 13.64)	0.782
MPA	1	105/200	1.91 (0.27 – 13.68)	0.518
PR3-ANCA	2	122/434	0.95 (0.11 – 8.63)	0.964
MPO-ANCA	2	92/434	3.08 (0.58 – 16.42)	0.188
*IL1RN**5				
GPA	1	61/200	1.09 (0.04 – 26.86)	0.959
MPA	1	105/200	0.63 (0.03 – 15.60)	0.779
PR3-ANCA	2	122/434	0.87 (0.10 – 7.74)	0.901
MPO-ANCA	2	92/434	2.18 (0.32 – 14.79)	0.424
IL-6 rs1800795 (C)				
GPA	4	1360/1558	0.99 (0.94 – 1.04)	0.750
MPA	2	315/6593	0.98 (0.84 – 1.16)	0.829
EGPA	1	426/6593	0.96 (0.76 – 1.21)	0.730
PR3-ANCA	3	NR/6694	0.98 (0.89 – 1.09)	0.751
MPO-ANCA	2	NR/6603	1.04 (0.90 – 1.20)	0.616
IL-10 rs1800872 (A)				
GPA	2	435/598	1.03 (0.84 – 1.27)	0.762
EGPA	1	103/507	0.89 (0.62 – 1.27)	0.512
PR3-ANCA	1	32/91	1.10 (0.55 – 2.20)	0.793
IL-10 rs1800896 (G)				
GPA	5	993/6183	0.95 (0.85 – 1.05)	0.293
MPA	2	192/5513	0.95 (0.78 – 1.17)	0.655
EGPA	1	103/507	0.68 (0.50 – 0.92)	0.012
PR3-ANCA	2	358/5451	1.05 (0.90 – 1.22)	0.527
MPO-ANCA	1	167/5360	0.96 (0.77 – 1.19)	0.693
IRF5 rs10954213 (G)				
GPA	2	1021/6267	0.66 (0.59 – 0.74)	<0.001
MPA	2	333/6075	1.22 (1.03 – 1.44)	0.018
PR3-ANCA	1	326/5365	1.09 (0.93 – 1.28)	0.293
MPO-ANCA	2	399/6075	1.12 (0.96 – 1.31)	0.142
LEPR rs8179183 (C)				
GPA	1	682/1326	0.72 (0.60 – 0.86)	<0.001
EGPA	1	196/1327	1.41 (1.10 – 1.81)	0.007
MPO rs2333227 (A)				
GPA	1	69/150	0.70 (0.41 – 1.21)	0.204
MPA	1	65/150	1.18 (0.72 – 1.93)	0.523
PR3-ANCA	3	258/549	1.00 (0.77 – 1.31)	0.977
MPO-ANCA	3	141/549	0.94 (0.68 – 1.31)	0.719
PTPN22 rs2476601 (A)				
GPA	4	1616/8678	1.43 (1.26 – 1.62)	<0.001
MPA	2	258/6310	1.42 (1.06 – 1.89)	0.018
EGPA	1	99/945	0.52 (0.21 – 1.29)	0.158

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
PR3-ANCA	2	419/6310	1.42 (1.14 – 1.77)	0.002
MPO-ANCA	2	183/6310	1.47 (1.08 – 2.00)	0.014
RING1/RXRB rs213213 (A)				
GPA	3	1132/7238	1.91 (1.73 – 2.10)	<0.001
MPA	1	156/5366	1.15 (0.90 – 1.45)	0.264
PR3-ANCA	1	326/5366	2.06 (1.75 – 2.41)	<0.001
MPO-ANCA	1	167/5366	1.05 (0.83 – 1.32)	0.687
RXRB rs6531 (C)				
GPA	3	1211/6955	1.70 (1.55 – 1.86)	<0.001
MPA	1	262/5251	1.38 (1.15 – 1.66)	0.001
PR3-ANCA	1	478/5251	2.19 (1.92 – 2.51)	<0.001
MPO-ANCA	1	264/5251	1.21 (1.00 – 1.46)	0.046
ANCA negative	1	36/201	1.02 (0.59 – 1.74)	0.948
RXRB rs9277935 (T)				
GPA	3	1135/7233	0.37 (0.31 – 0.43)	<0.001
MPA	1	156/5350	0.93 (0.70 – 1.24)	0.629
PR3-ANCA	1	326/5350	0.24 (0.17 – 0.33)	<0.001
MPO-ANCA	1	167/5350	1.18 (0.92 – 1.53)	0.193
SERPINA1 S allele				
GPA	2	484/1079	1.72 (1.12 – 2.66)	0.014
c-ANCA	3	145/3836	1.92 (1.12 – 3.29)	0.017
SERPINA1 Z allele				
GPA	4	972/2636	2.40 (1.73 - 3.33)	<0.001
MPA	1	143/805	1.60 (0.76 - 3.39)	0.218
PR3-ANCA	1	322/805	2.58 (1.57 - 4.25)	<0.001
MPO-ANCA	1	166/805	2.01 (1.04 - 3.87)	0.037
c-ANCA	5	280/4788	3.53 (2.28 – 5.49)	<0.001
p-ANCA	2	78/2510	3.13 (1.21 – 8.13)	0.019
STAT4 rs7574865 (T)				
GPA	2	1288/6246	1.06 (0.94 – 1.20)	0.331
MPA	1	676/5366	1.12 (0.86 – 1.46)	0.392
PR3-ANCA	1	676/5366	1.06 (0.88 – 1.28)	0.547
MPO-ANCA	2	908/6076	1.24 (1.05 – 1.46)	0.009
TGF-β_1 rs1800471 (C)				
GPA	3	196/259	1.52 (0.93 – 2.48)	0.096
MPA	1	36/96	1.03 (0.35 – 2.99)	0.960
PR3-ANCA	1	32/91	1.86 (0.73 – 4.71)	0.193
TNFα rs1800629 (A)				
GPA	4	578/5691	1.15 (0.98 – 1.35)	0.098
MPA	1	156/5366	1.13 (0.95 – 1.35)	0.182
PR3-ANCA	2	357/5457	1.21 (0.93 – 1.57)	0.149
MPO-ANCA	1	167/5366	0.88 (0.66 – 1.17)	0.375
TNFRII 196R				
GPA	1	177/123	1.05 (0.70 – 1.57)	0.819
MPA	1	50/262	0.67 (0.31 – 1.45)	0.313
MPO-ANCA	1	50/262	0.67 (0.31 – 1.45)	0.313

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
TLR9 rs352162 (T)				
GPA	1	919/1898	1.20 (1.07 – 1.34)	0.001
MPA	1	153/1898	0.74 (0.58 – 0.95)	0.020
EGPA	1	217/1898	1.28 (1.05 – 1.57)	0.015
PR3-ANCA	1	NR/NR	1.30 (1.14 – 1.47)	<0.001
MPO-ANCA	1	NR/NR	0.79 (0.65 – 0.97)	0.028
ANCA negative	1	NR/NR	1.22 (0.99 – 1.50)	0.060
TLR9 rs352140 (T)				
GPA	1	919/1898	1.20 (1.07 – 1.35)	0.001
MPA	1	153/1898	0.71 (0.55 – 0.91)	0.006
EGPA	1	217/1898	1.17 (0.96 – 1.43)	0.129
PR3-ANCA	1	NR/NR	1.28 (1.12 – 1.45)	<0.001
MPO-ANCA	1	NR/NR	0.75 (0.62 – 0.91)	0.004
ANCA negative	1	NR/NR	1.19 (0.97 – 1.47)	0.097
TLR9 rs352139 (T)				
GPA	1	919/1898	1.18 (1.06 – 1.32)	0.003
MPA	1	153/1898	0.68 (0.52 – 0.87)	0.003
EGPA	1	217/1898	1.21 (0.99 – 1.47)	0.057
PR3-ANCA	1	NR/NR	1.23 (1.09 – 1.40)	0.001
MPO-ANCA	1	NR/NR	0.78 (0.63 – 0.96)	0.017
ANCA negative	1	NR/NR	1.20 (0.98 – 1.47)	0.086
TLR9 rs5743836 (G)				
GPA	1	919/1898	0.83 (0.70 – 0.99)	0.037
MPA	1	153/1898	1.78 (1.32 – 2.39)	<0.001
EGPA	1	217/1898	0.90 (0.68 – 1.21)	0.499
PR3-ANCA	1	NR/NR	0.83 (0.70 – 1.00)	0.045
MPO-ANCA	1	NR/NR	1.20 (0.91 – 1.58)	0.207
ANCA negative	1	NR/NR	0.99 (0.74 – 1.34)	0.970

Supplementary Table S5. Results of the meta-analyses stratified by ethnic subgroups

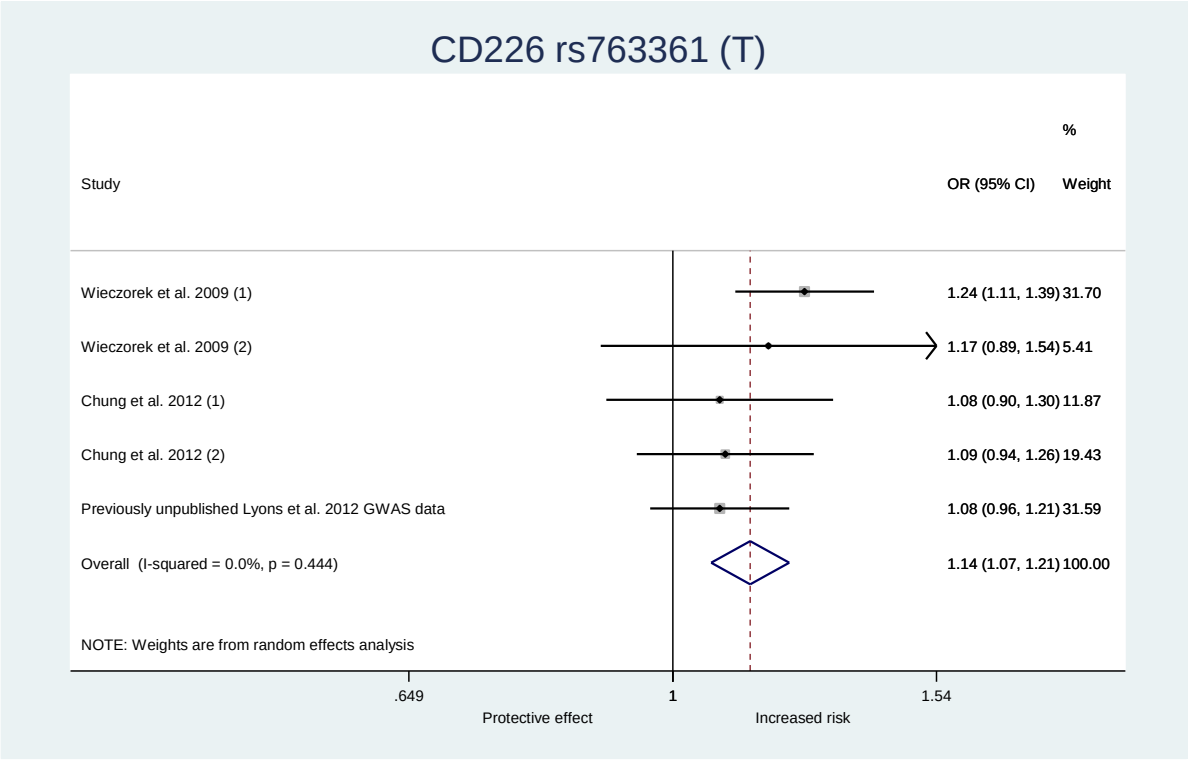
Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
CTLA-4 $(AT)_{86}$				
Asian	1	49/111	1.31 (0.76 – 2.25)	0.333
Caucasian	3	254/432	0.46 (0.36 – 0.58)	<0.001
CTLA-4 $(AT)_{102}$				
Asian	1	49/111	0.89 (0.47 – 1.68)	0.714
Caucasian	2	137/309	1.73 (0.87 – 3.44)	0.117
CTLA-4 $(AT)_{104}$				
Asian	1	49/111	1.15 (0.70 – 1.91)	0.578
Caucasian	2	137/309	1.24 (0.88 – 1.73)	0.215
CTLA-4 $(AT)_{106}$				
Asian	1	49/111	0.41 (0.14 – 1.22)	0.109
Caucasian	2	137/309	2.69 (1.28 – 5.63)	0.009
CTLA-4 $(AT)_{108}$				
Asian	1	49/111	0.82 (0.33 – 2.02)	0.670
Caucasian	2	137/309	0.92 (0.44 – 1.92)	0.831
CTLA-4 $(AT)_{110}$				
Asian	1	49/111	0.25 (0.01 – 4.62)	0.349
Caucasian	2	137/309	0.84 (0.37 – 1.91)	0.679
CTLA-4 $(AT)_{116}$				
Asian	1	49/111	0.75 (0.03 – 18.56)	0.860
Caucasian	2	137/309	0.80 (0.26 – 2.50)	0.705
CTLA-4 $(AT)_{118}$				
Asian	1	49/111	0.75 (0.08 – 7.33)	0.807
Caucasian	2	137/309	0.41 (0.12 – 1.39)	0.152
CTLA-4 $(AT)_{122}$				
Asian	1	49/111	2.32 (0.57 – 9.45)	0.241
Caucasian	2	137/309	1.22 (0.27 – 5.49)	0.799
CTLA-4 $(AT)_{124}$				
Asian	1	49/111	2.28 (0.14 – 36.80)	0.562
Caucasian	2	137/309	1.94 (0.67 – 5.58)	0.222
CTLA-4 $(AT)_{126}$				
Asian	1	49/111	0.45 (0.05 – 3.88)	0.466
Caucasian	2	137/309	1.65 (0.63 – 4.32)	0.305
CTLA-4 $(AT)_{128}$				
Asian	1	49/111	6.98 (0.72 – 67.95)	0.094
Caucasian	2	137/309	0.72 (0.24 – 2.15)	0.560

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
FCGR2A rs1801274 (C)				
Asian	1	50/303	0.68 (0.37 – 1.24)	0.208
Caucasian	5	1126/5969	0.91 (0.82 – 1.00)	0.043
FCGR3A rs396991 (G)				
Asian	1	50/303	0.65 (0.39 – 1.07)	0.090
Caucasian	1	91/154	1.30 (0.89 – 1.91)	0.172
FCGR3B (NA1)				
Asian	1	50/303	1.29 (0.82 – 2.03)	0.267
Caucasian	3	865/667	0.93 (0.80 – 1.08)	0.343
HLA-A2				
Asian	1	16/472	0.90 (0.37 – 2.23)	0.826
Caucasian	4	427/7324	0.96 (0.81 – 1.13)	0.595
HLA-A11				
Asian	1	16/472	0.71 (0.17 – 3.03)	0.644
Caucasian	5	450/7635	1.01 (0.50 – 2.05)	0.978
HLA-A24				
Asian	1	16/472	0.75 (0.34 – 1.65)	0.476
Caucasian	2	92/751	1.16 (0.57 – 2.38)	0.683
HLA-A26				
Asian	1	16/472	2.36 (1.00 – 5.60)	0.051
Caucasian	3	115/1156	1.21 (0.58 – 2.55)	0.612
HLA-A31				
Asian	1	16/472	1.55 (0.46 – 5.24)	0.479
Caucasian	2	92/751	0.73 (0.21 – 2.52)	0.613
HLA-A32				
Asian	1	16/472	2.07 (0.61 – 7.04)	0.246
Caucasian	2	92/751	1.41 (0.52 – 3.84)	0.500
HLA-B35				
Asian	1	16/472	0.80 (0.17 – 3.40)	0.757
Caucasian	3	396/6623	0.78 (0.58 – 1.06)	0.115
HLA-B39				
Asian	1	16/472	0.86 (0.11 – 6.51)	0.887
Caucasian	1	51/51	0.33 (0.01 – 8.20)	0.499
HLA-B44				
Asian	1	16/472	2.50 (0.85 – 7.40)	0.098
Caucasian	2	92/751	1.41(0.85 – 2.35)	0.188

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
HLA-B51				
Asian	1	16/472	1.87 (0.64 – 5.49)	0.255
Caucasian	1	51/51	0.61 (0.19 – 1.92)	0.394
HLA-B55				
Asian	1	16/472	7.35 (2.34 – 23.14)	0.001
Caucasian	1	51/51	0.07 (0.00 – 1.30)	0.075
HLA-B60				
Asian	1	16/472	1.19 (0.28 – 5.13)	0.814
Caucasian	1	41/700	3.51 (0.99 – 12.36)	0.051
HLA-B62				
Asian	1	16/472	1.71 (0.58 – 4.99)	0.331
Caucasian	1	41/700	2.38 (0.70 – 8.12)	0.166
HLA-Cw1				
Asian	1	16/472	1.45 (0.58 – 3.58)	0.426
Caucasian	1	52/51	0.98 (0.24 – 4.03)	0.978
HLA-Cw3				
Asian	1	16/472	1.40 (0.66 – 3.01)	0.384
Caucasian	1	52/51	1.32 (0.62 – 2.81)	0.479
HLA-Cw7				
Asian	1	16/472	0.50 (0.12 – 2.10)	0.340
Caucasian	1	52/51	1.10 (0.62 – 1.96)	0.735
*HLA-DPB1*0201*				
Asian	1	50/77	1.38 (0.75 – 2.52)	0.298
Caucasian	3	385/827	0.76 (0.56 – 1.03)	0.073
*HLA-DQB1**0303				
Asian	1	50/77	2.11 (1.14 – 3.90)	0.018
Caucasian	2	126/141	1.35 (0.55 – 3.33)	0.515
HLA-DR1				
Asian	1	64/265	1.12 (0.48 – 2.64)	0.793
Caucasian	9	945/6840	0.91 (0.61 – 1.36)	0.651
HLA-DR2				
Asian	1	16/472	0.33 (0.08 – 1.38)	0.128
Caucasian	4	471/5750	1.06 (0.87 – 1.29)	0.565
HLA-DR4				
Asian	1	16/472	0.72 (0.27 – 1.88)	0.498
Caucasian	10	882/7262	1.23 (0.97 – 1.57)	0.088

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
HLA-DR6				
Asian	1	16/472	1.63 (0.56 – 4.77)	0.371
Caucasian	4	471/5750	0.43 (0.30 – 0.61)	<0.001
HLA-DR8				
Asian	1	16/472	1.63 (0.66 – 4.05)	0.291
Caucasian	8	597/1483	1.05 (0.75 – 1.49)	0.768
HLA-DR9				
Asian	4	296/1409	1.67 (0.83 – 3.34)	0.148
Caucasian	7	510/1443	0.63 (0.34 – 1.19)	0.152
IRF5 rs10954213 (G)				
Asian	1	232/710	1.28 (1.04 – 1.58)	0.022
Caucasian	2	1303/6267	0.69 (0.63 – 0.76)	<0.001
STAT4 rs7574865 (T)				
Asian	1	232/710	1.10 (0.89 – 1.37)	0.388
Caucasian	2	1288/6246	1.11 (1.00 – 1.24)	0.044
TNFRII 196R				
Asian	1	50/262	0.67 (0.31 – 1.45)	0.313
Caucasian	1	117/123	1.05 (0.70 – 1.57)	0.819

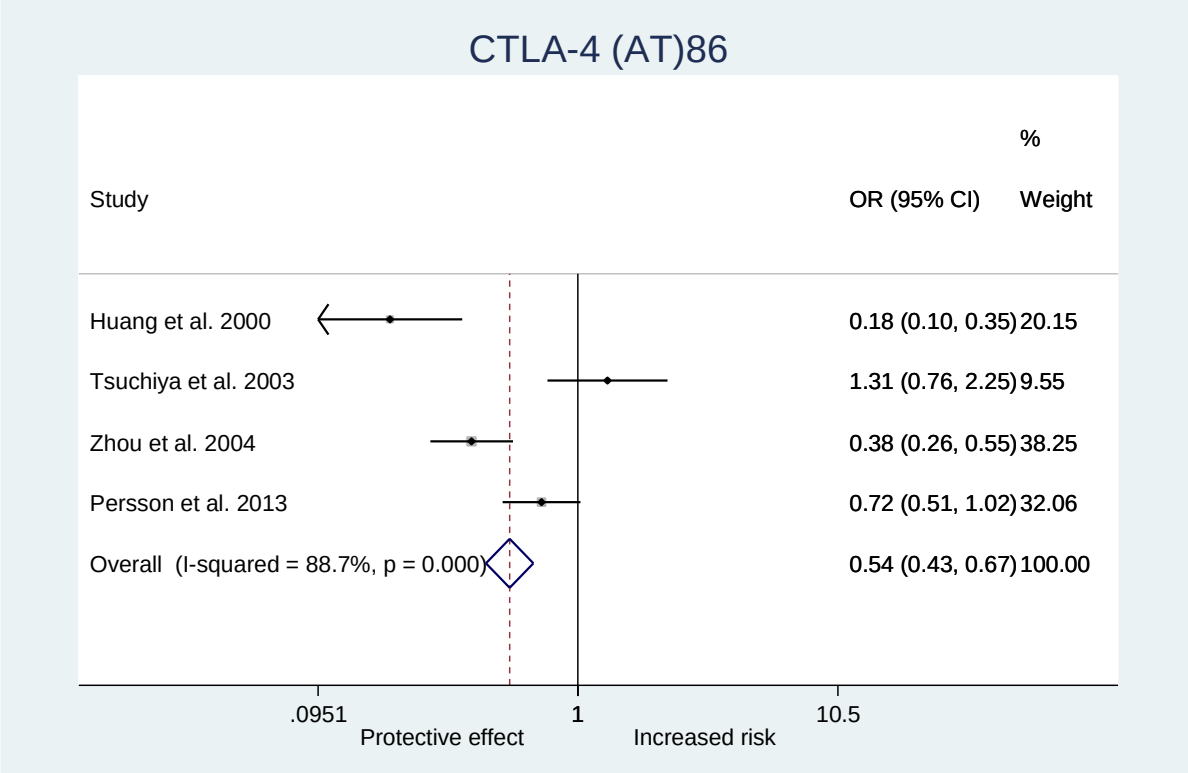
Supplementary Figure S1. Forest plots



CD226 rs763361 (T) forest plot. Harbold test: N/A, Egger test: p=0.792.

References

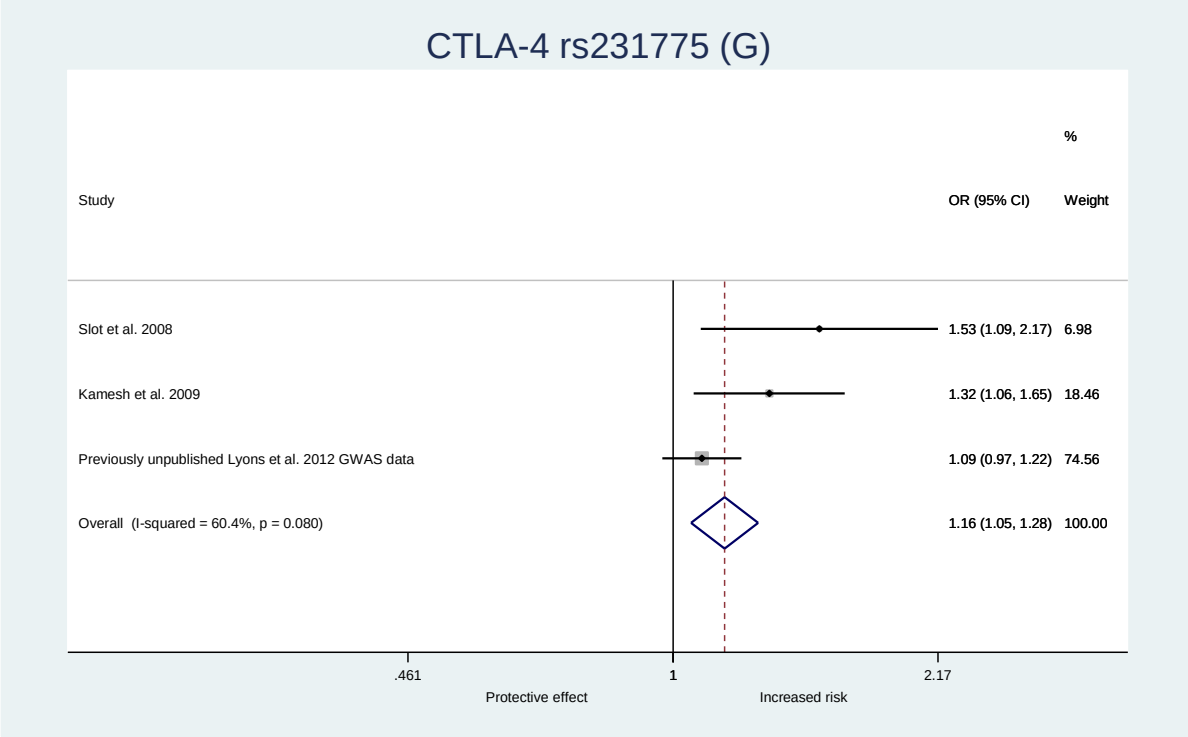
[1]**, [2]**, [3]



CTLA-4 $(AT)_{86}$ forest plot. Harbold test: p=0.946, Egger test: p=0.788.

References

[4] [5] [6] [7]



CTLA-4 rs231775 (G) forest plot. Harbold test: p=0.080, Egger test: p=0.081.

References

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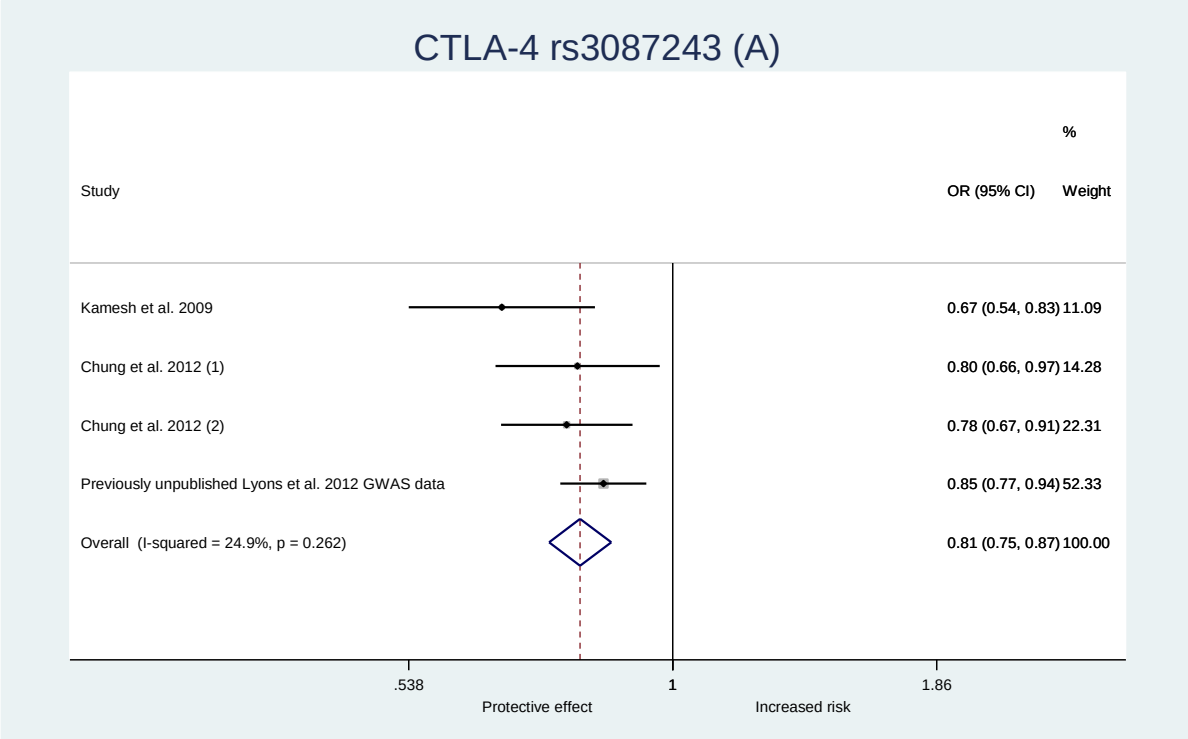

CTLA-4 rs3087243 (A) forest plot. Harbold test: N/A, Egger test: p=0.122.

References

9 2** 3
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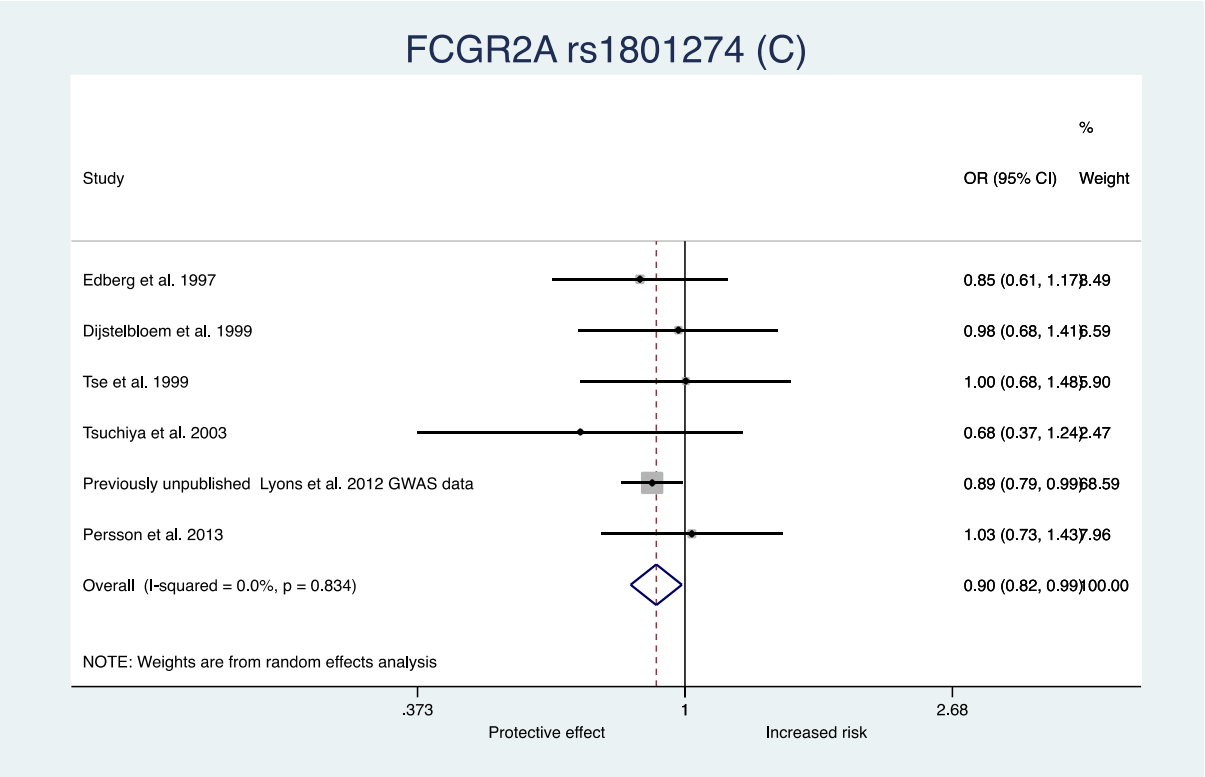
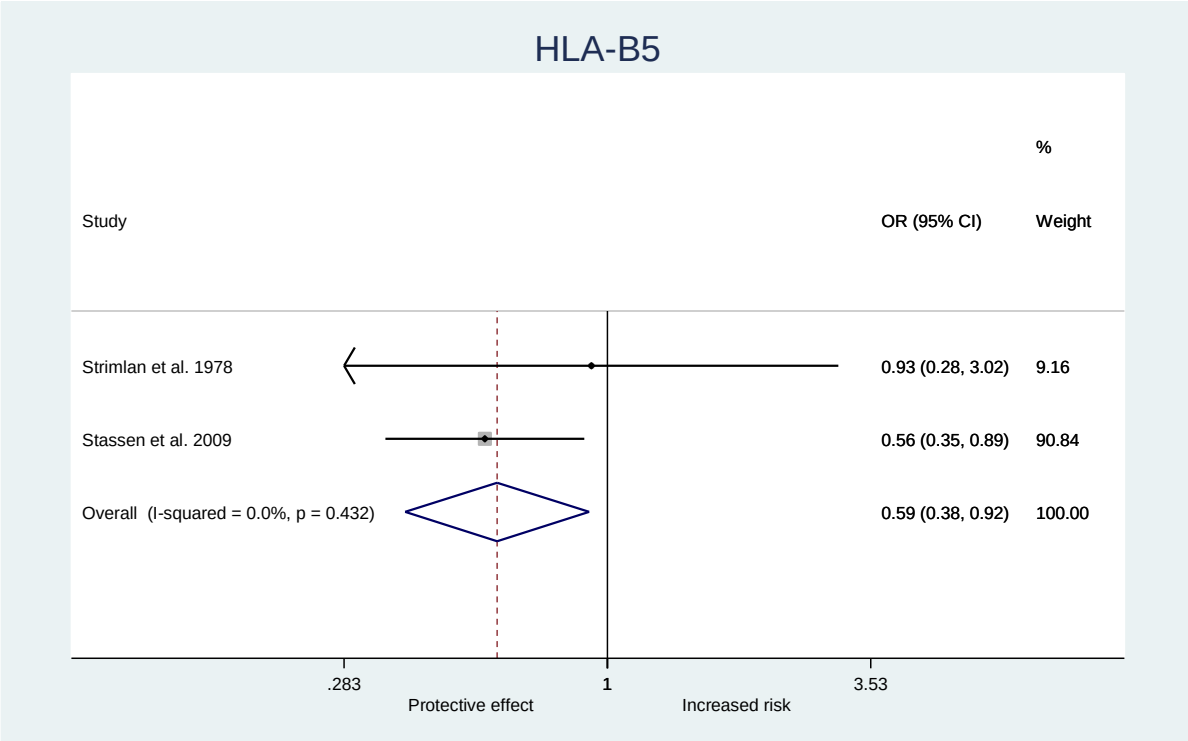


FCGR2A rs1801274 (C) forest plot. Harbold test: p=0.788, Egger test: p=0.829.

References

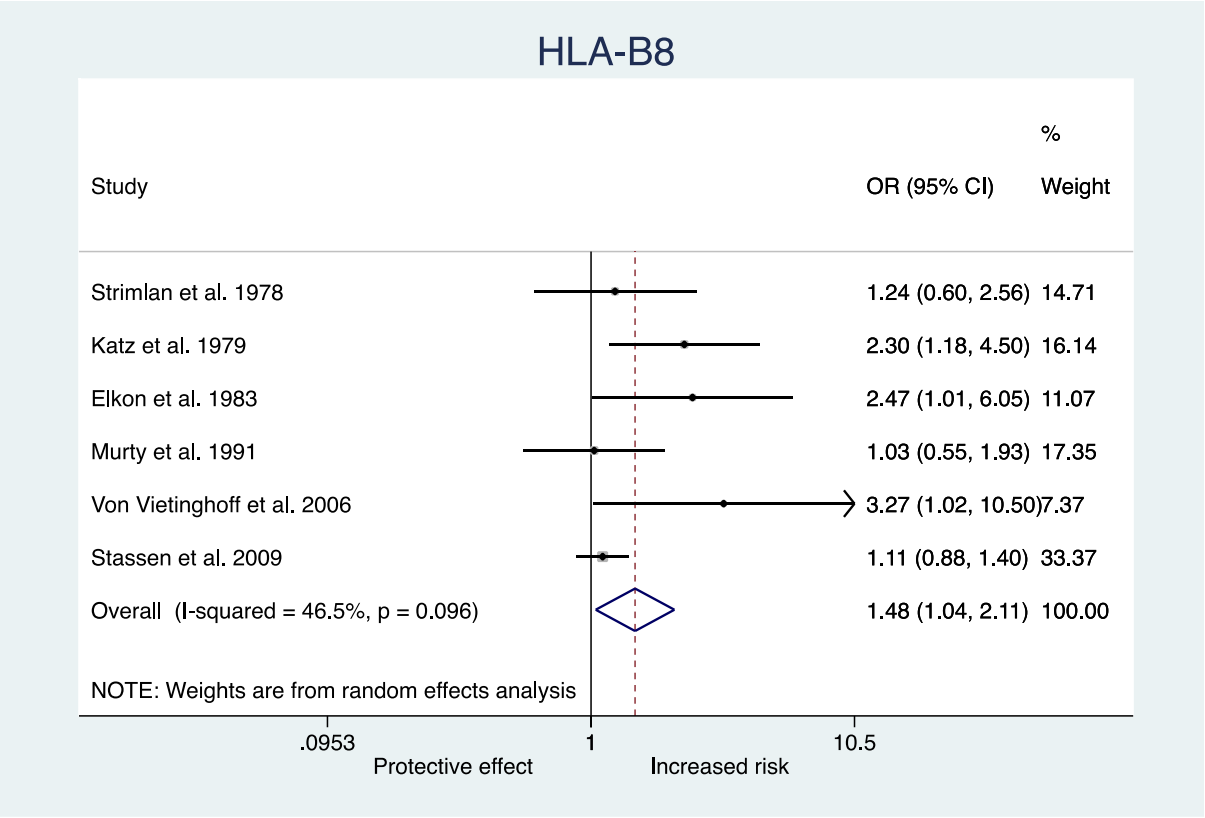
11, 12, 13, 5, 7, 3



HLA-B5 forest plot. Harbold test: N/A, Egger test: N/A.

References

16, 19



HLA-B8 forest plot. Harbold test: p=0.063, Egger test: p=0.077.

References

16 21 23 17 18 19
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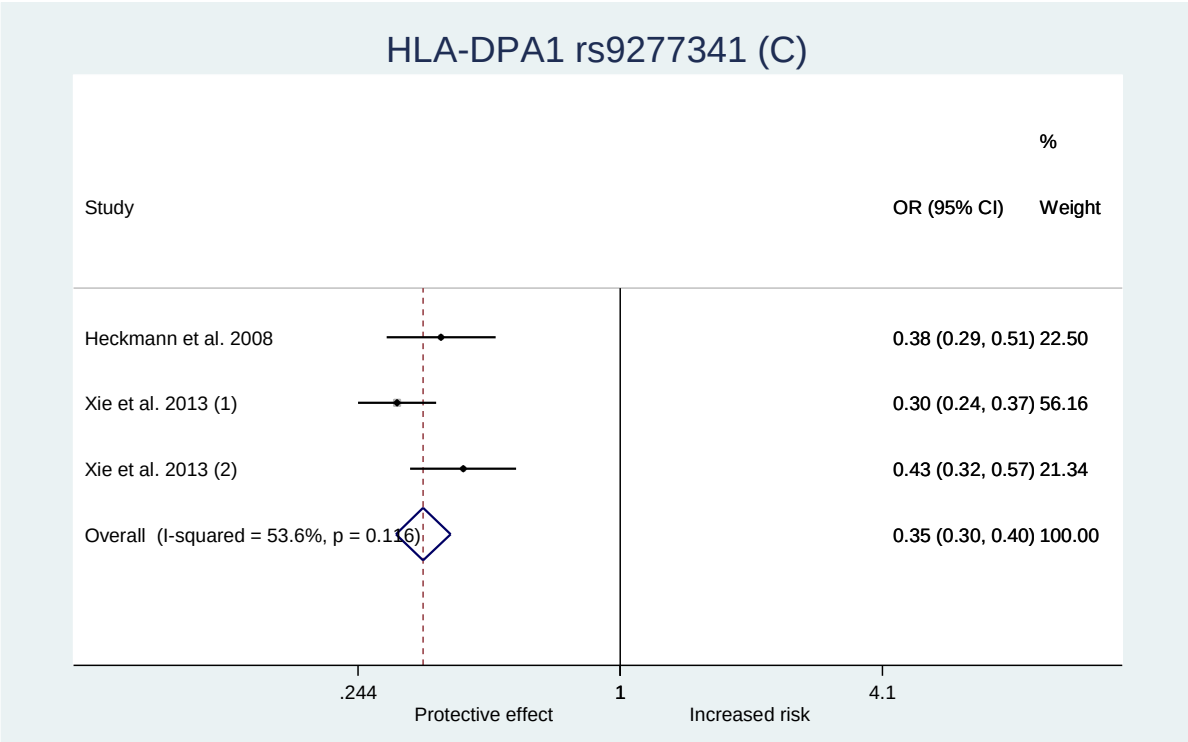

HLA-DPA1 rs9277341 (C) forest plot. Harbold test: p=0.215, Egger test: p=0.219.

References

24 25**
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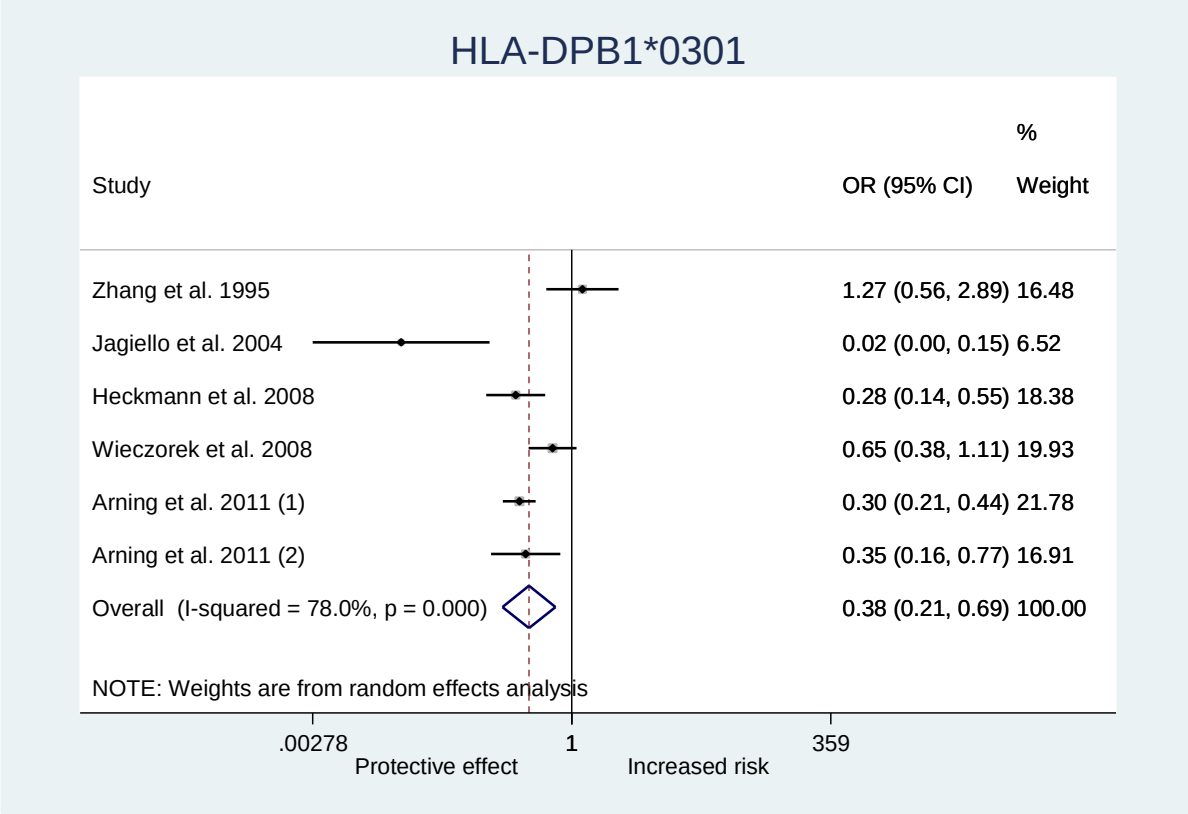
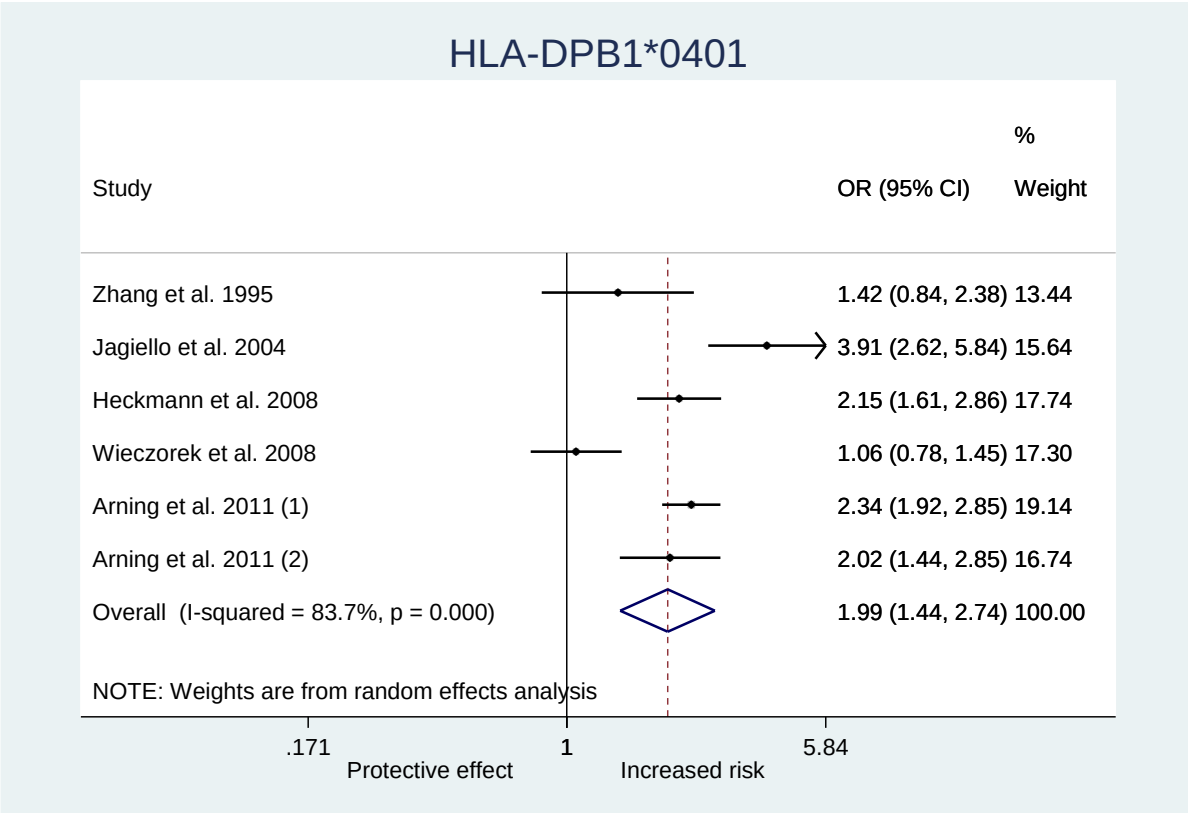


*HLA-DPB1*0301* forest plot. Harbold test: p=0.938, Egger test: p=0.744.

References

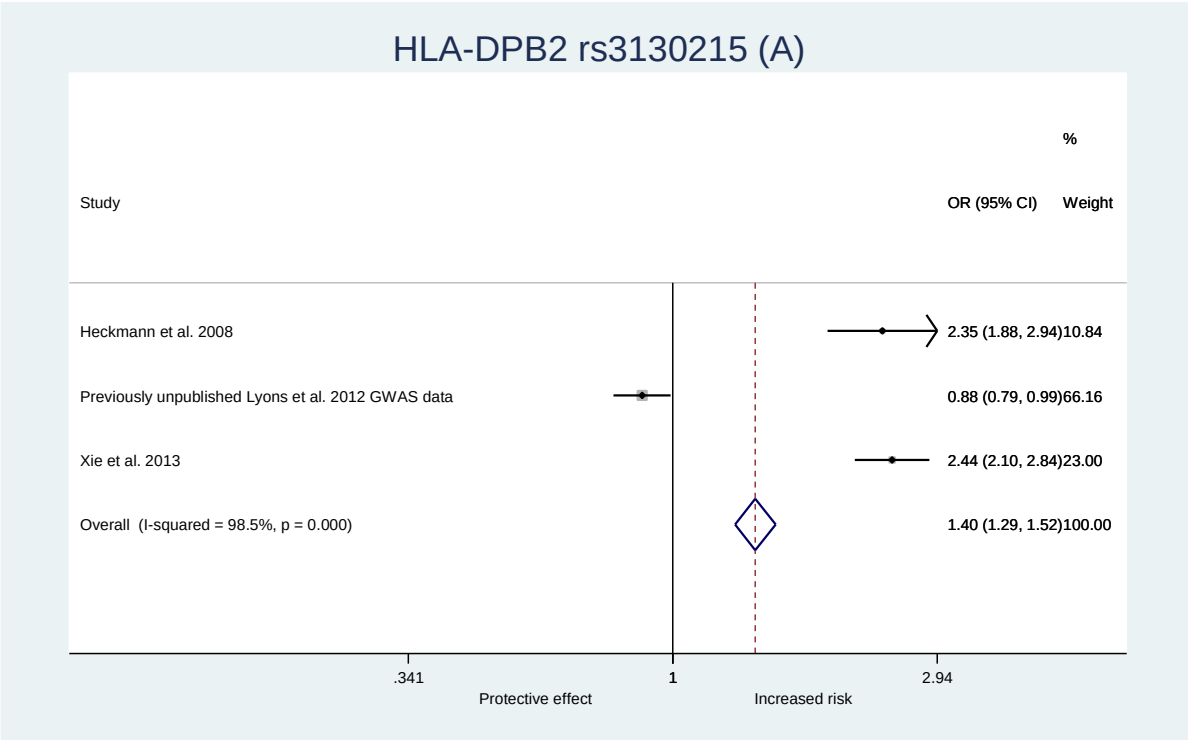
[26, 27, 24, 29, 30]**



*HLA-DPB1*0401* forest plot. Harbold test: p=0.738, Egger test: p=0.759.

References

[26, 27, 24, 29, 30]**



HLA-DPB2 rs3130215 (A) forest plot. Harbold test: p=0.446, Egger test: p=0.431.

References

24 3 25
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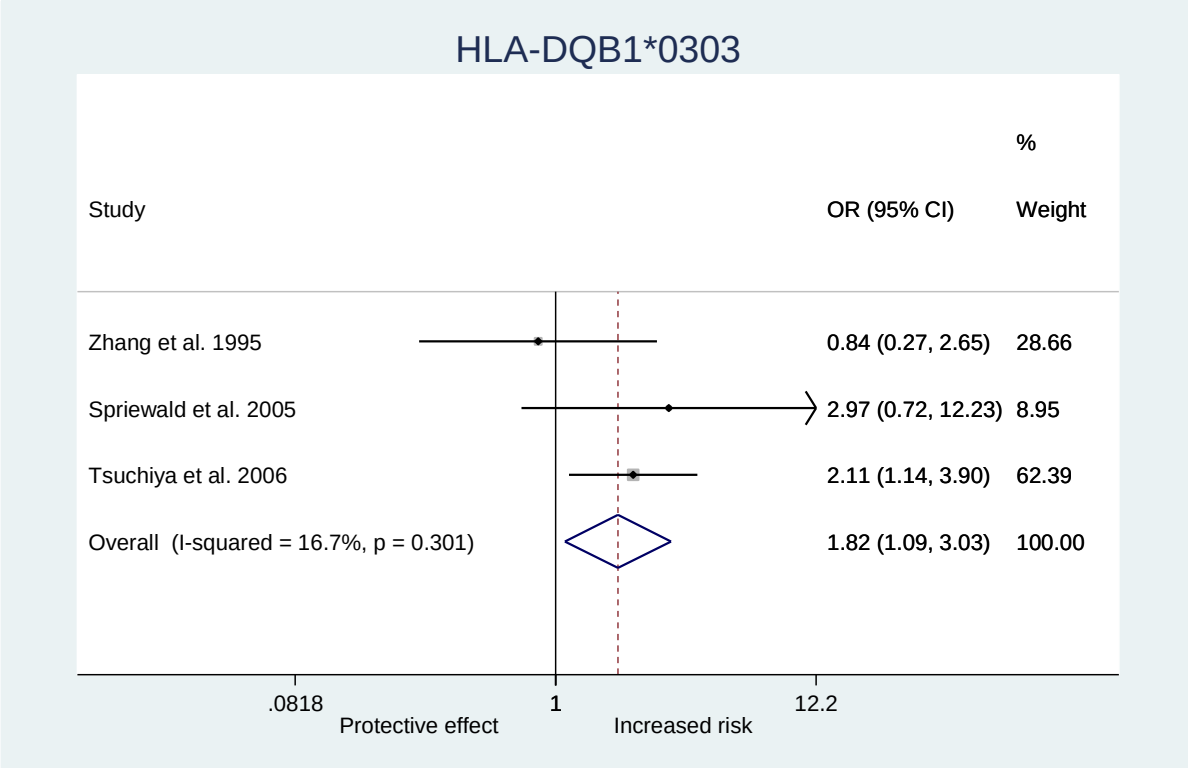

*HLA-DQB1*0303* forest plot. Harbold test: p=0.916, Egger test: p=0.834.

References

26 31 28
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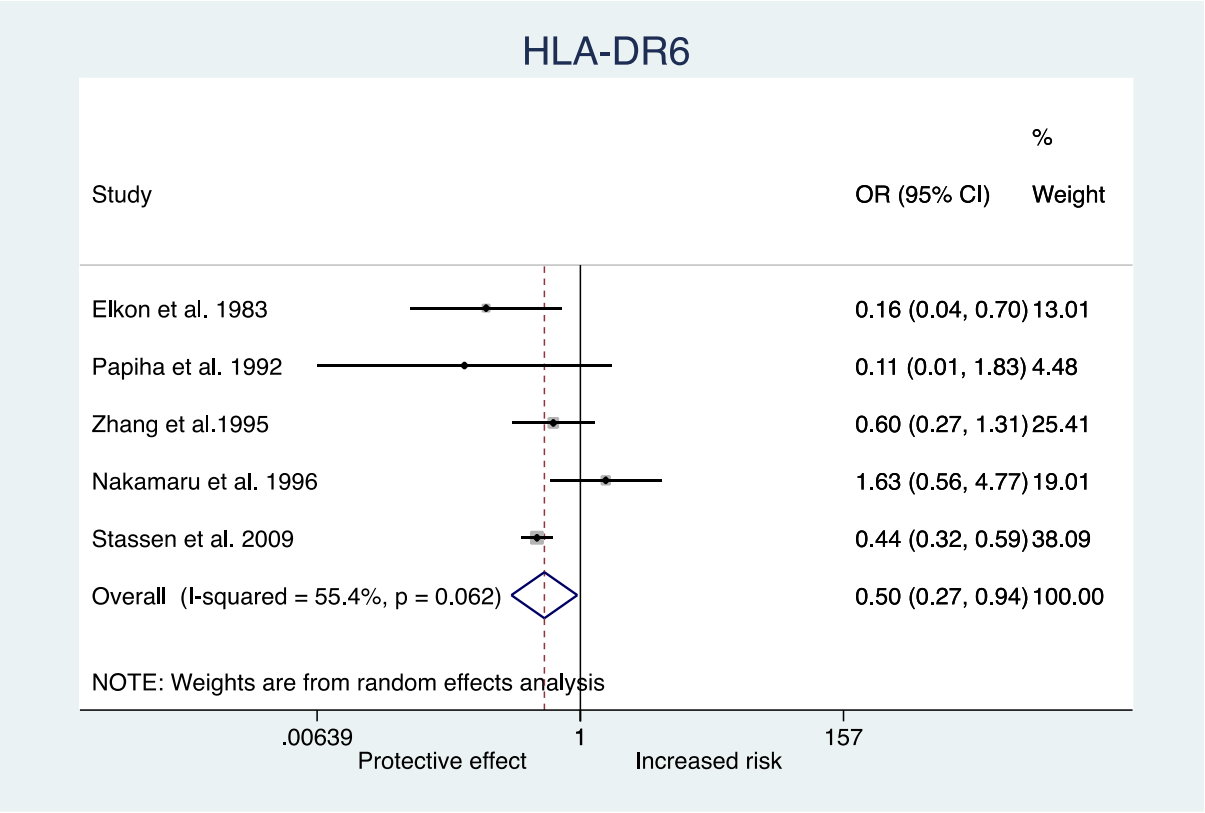
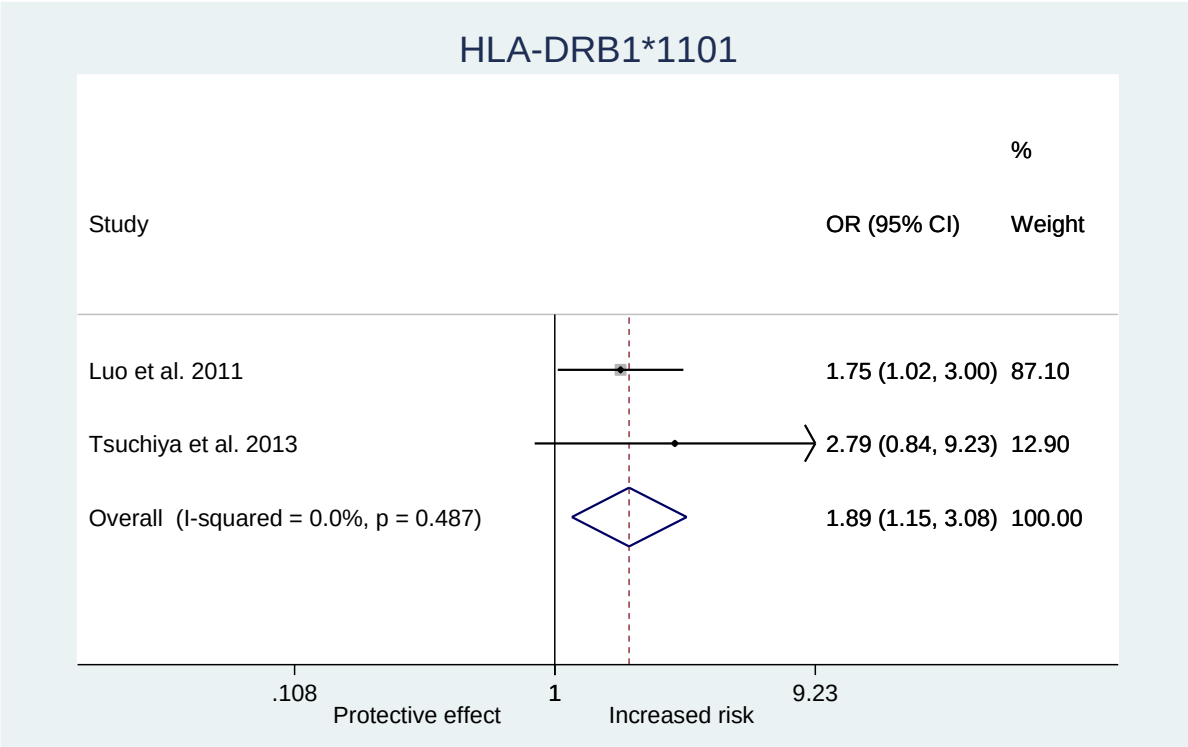


HLA-DR6 forest plot. Harbold test: p=0.997, Egger test: p=0.989.

References

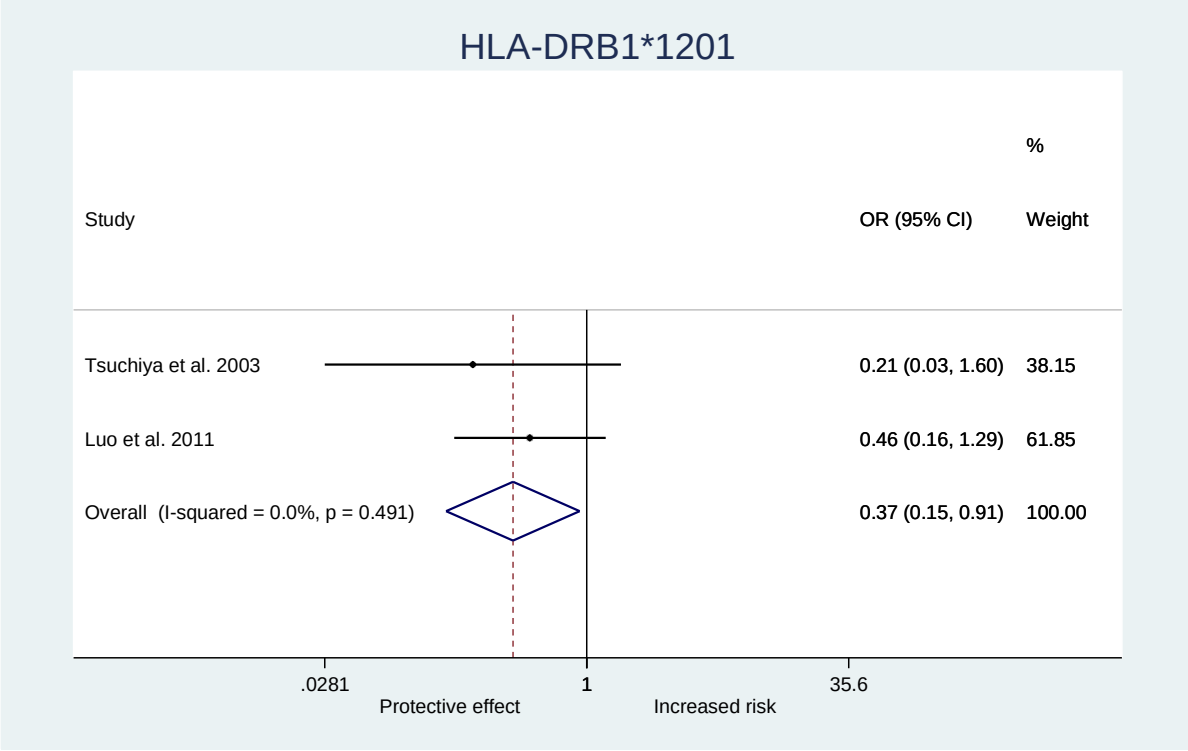
23, 32, 26, 20, 19



*HLA-DRB1*1101* forest plot. Harbold test: N/A, Egger test: N/A.

References

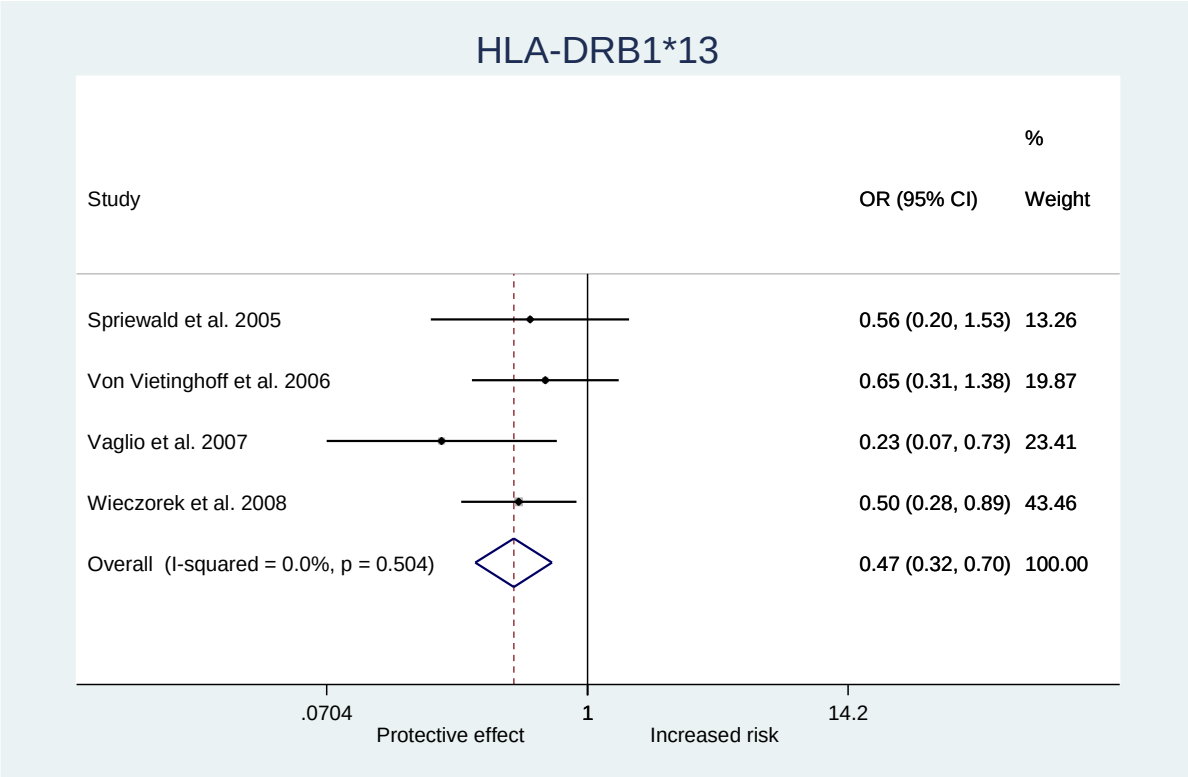
34, 37



*HLA-DRB1*1201* forest plot. Harbold test: N/A, Egger test: N/A.

References

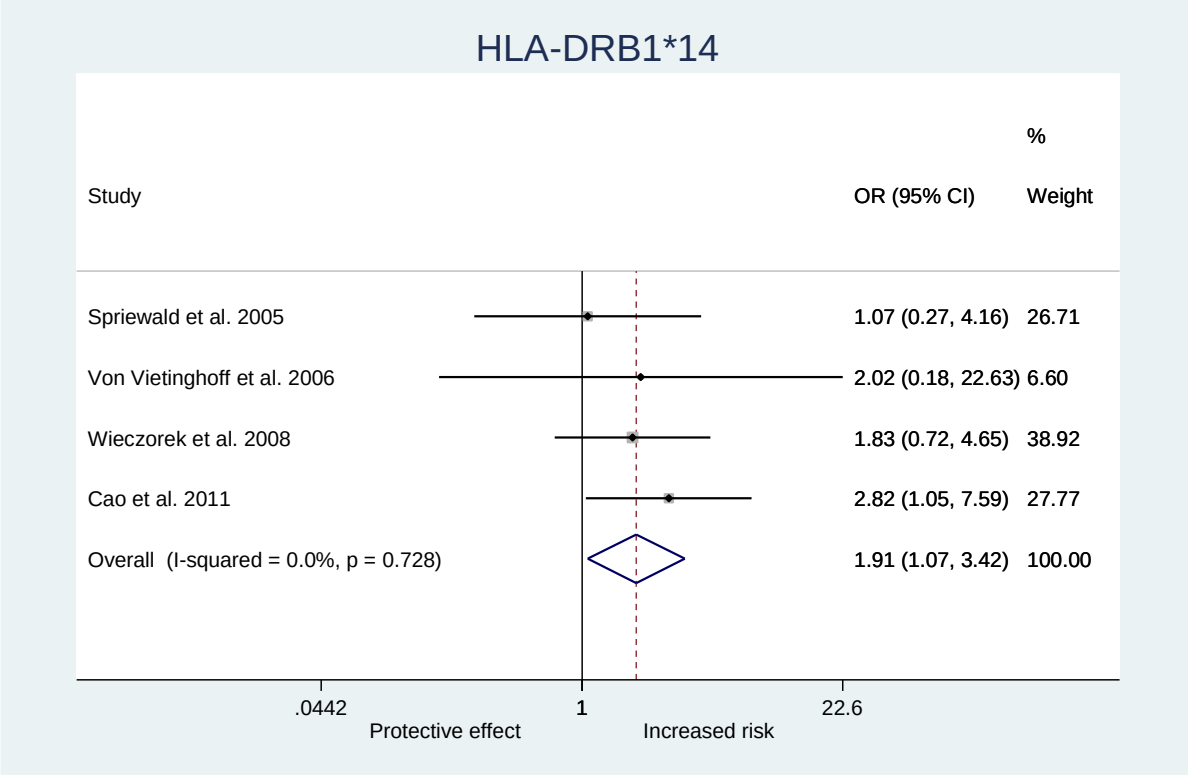
[5, 34]



*HLA-DRB1*13* forest plot. Harbold test: p=0.884, Egger test: p=0.467.

References

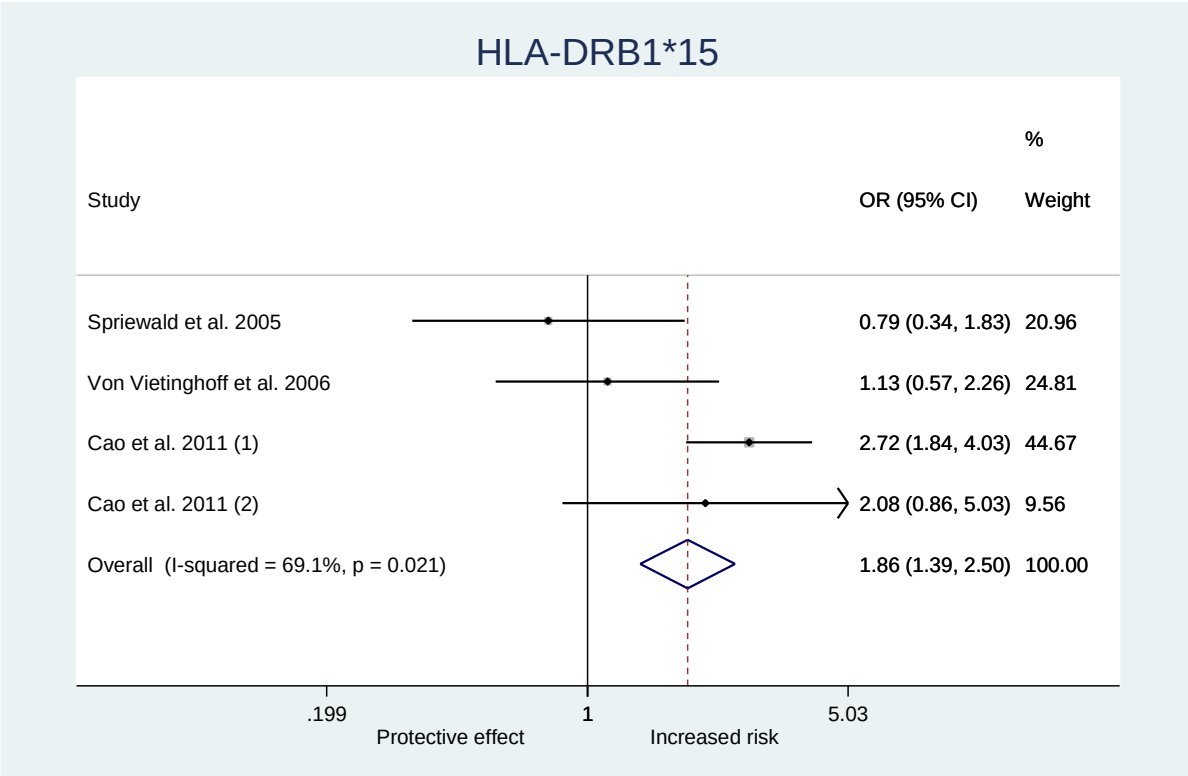
[31, 18, 35, 29]



*HLA-DRB1*14* forest plot. Harbold test: p=0.700, Egger test: p=0.706.

References

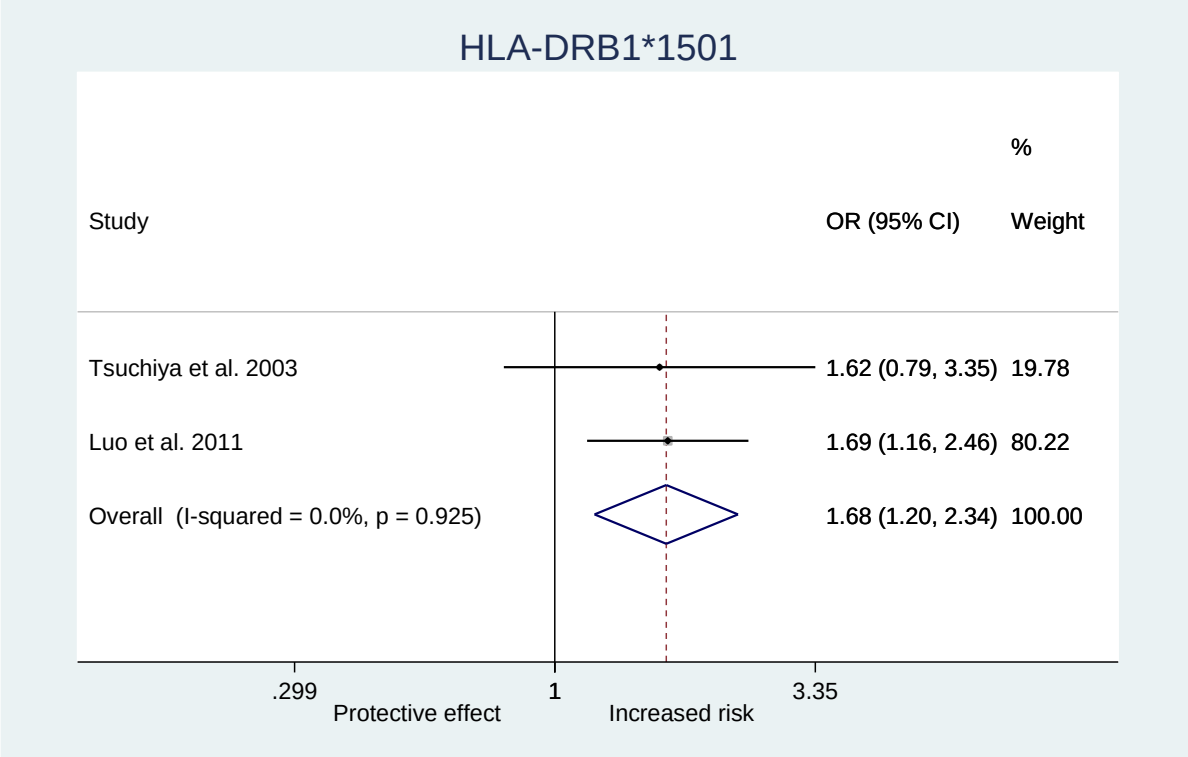
[31], [18], [29], [33]



*HLA-DRB1*15* forest plot. Harbold test: p=0.347, Egger test: p=0.214.

References

[31], [18], [33]**



*HLA-DRB1*1501* forest plot. Harbold test: N/A, Egger test: N/A.

References

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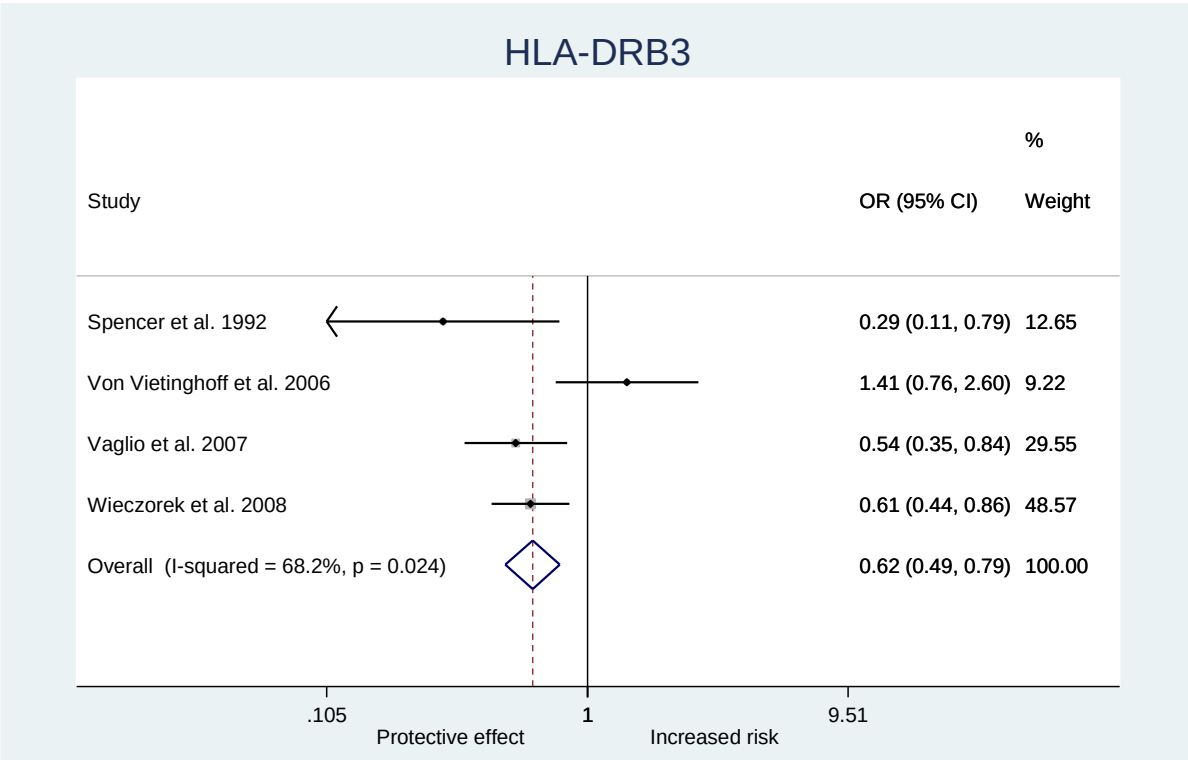

HLA-DRB3 forest plot. Harbold test: p=0.689, Egger test: p=0.958.

References

38 18 35 29
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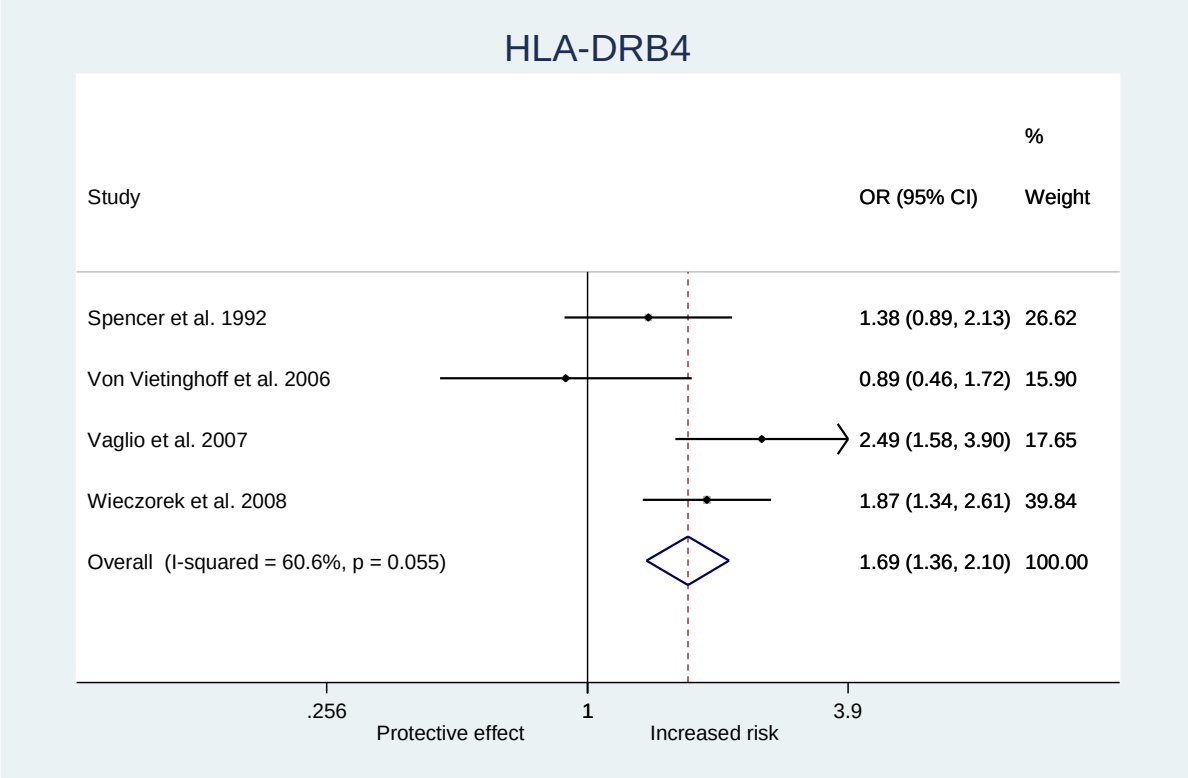
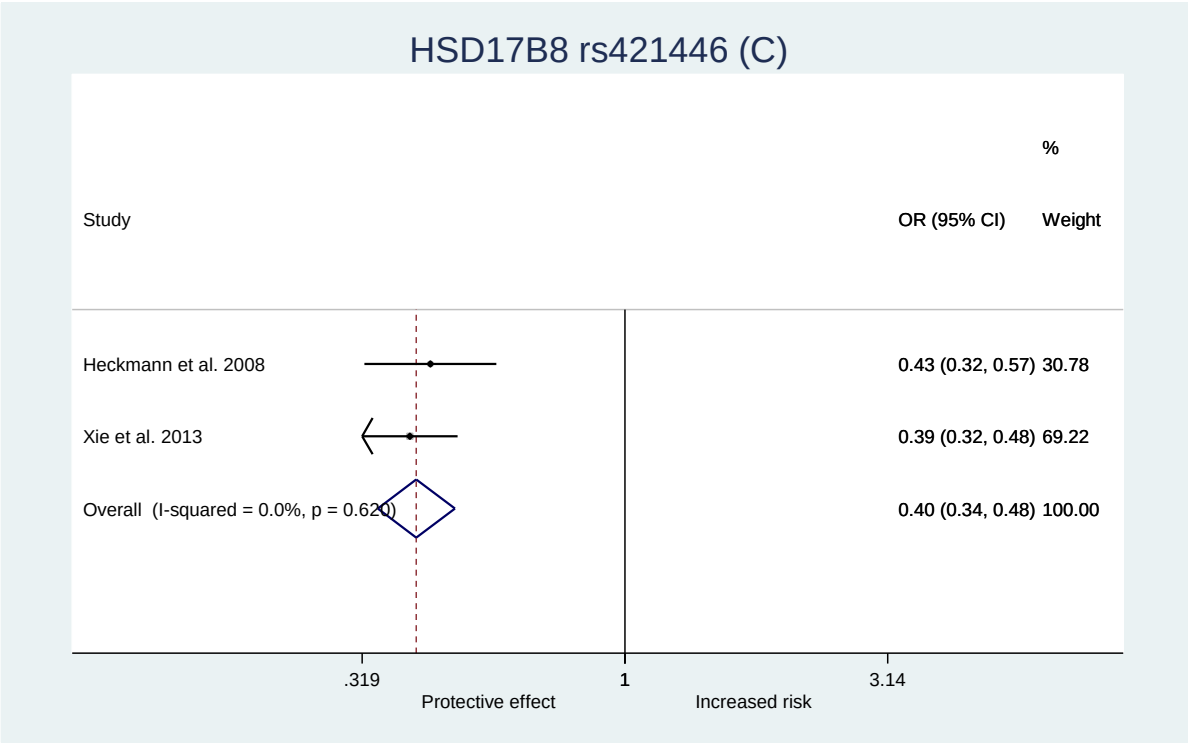


HLA-DRB4 forest plot. Harbold test: p=0.533, Egger test: p=0.388.

References

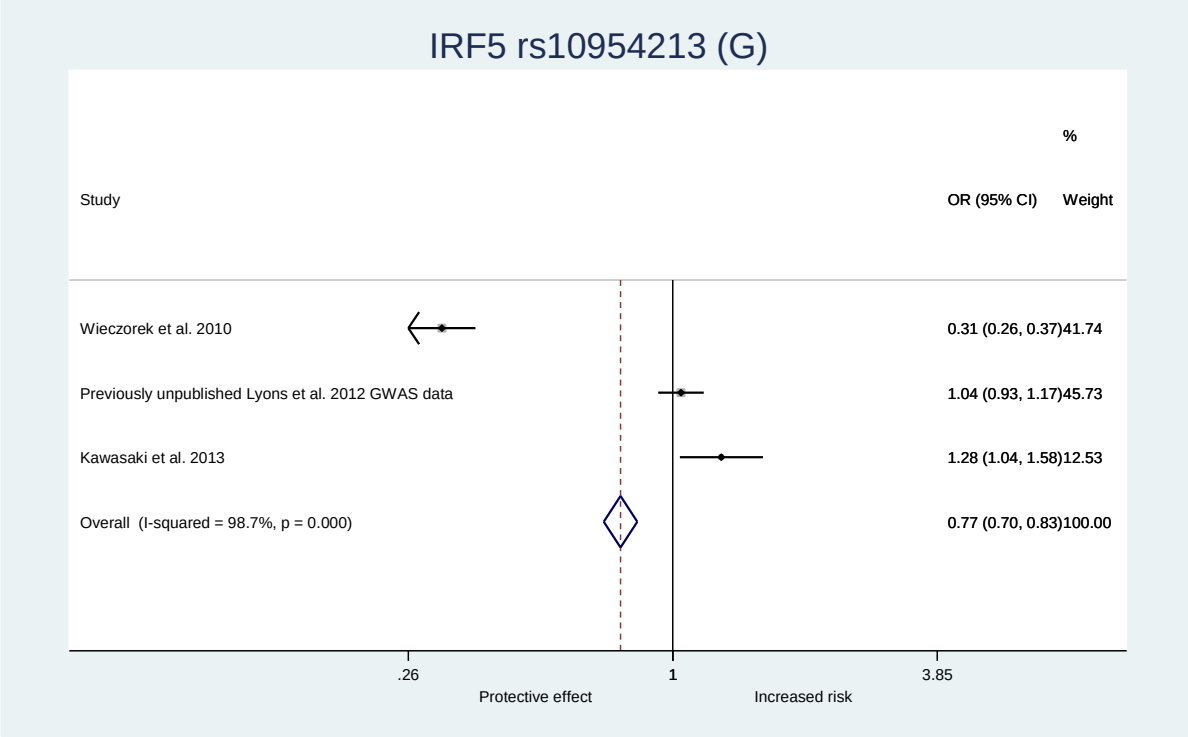
38 , 18 , 35 , 29



HSD17B8 rs421446 (C) forest plot. Harbold test: N/A, Egger test: N/A.

References

24 , 25



IRF5 rs10954213 (G) forest plot. Harbold test: p=0.948, Egger test: p=0.833.

References

44 3 45
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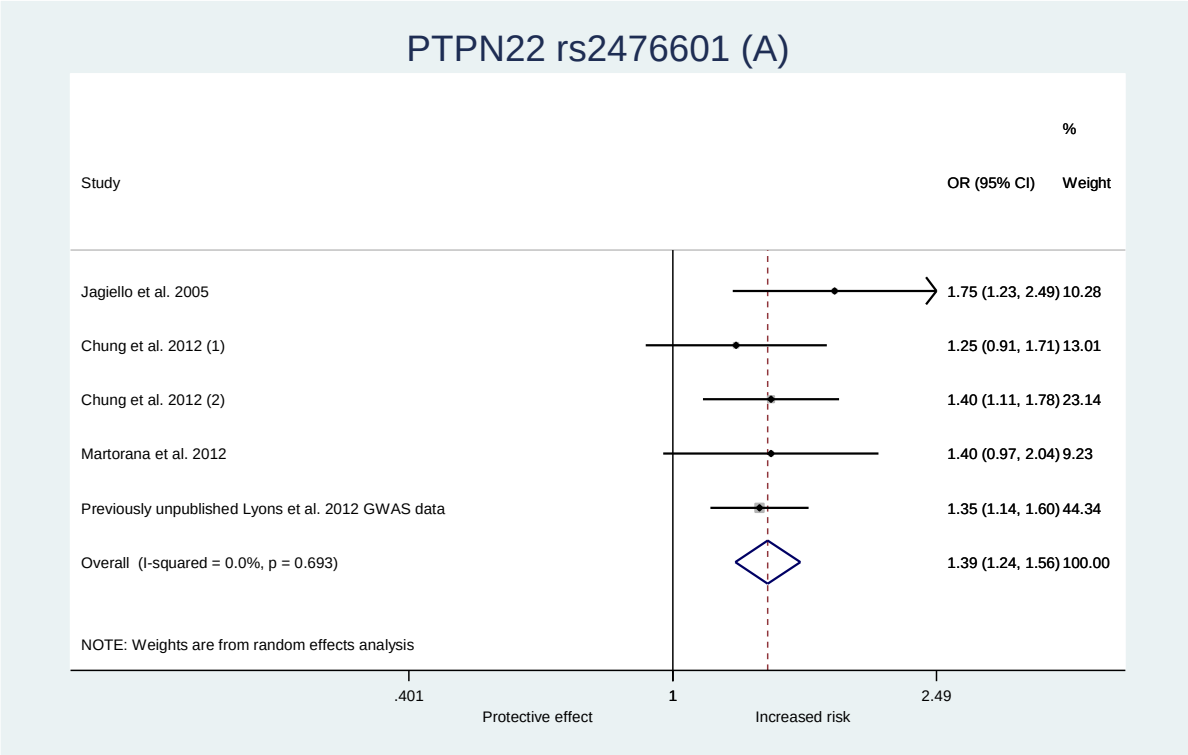

PTPN22 rs2476601 (A) forest plot. Harbold test: N/A, Egger test: p=0.500.

References

50 2** 51 3
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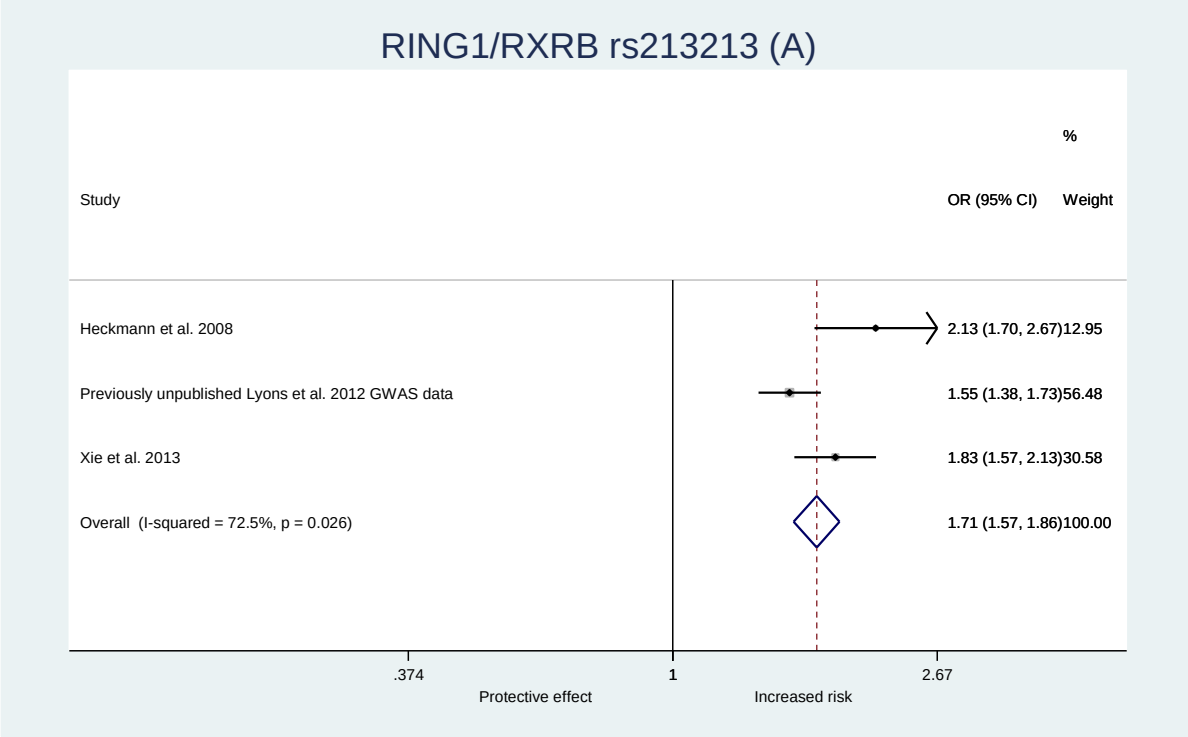

RING1/RXRB rs213213 (A) forest plot. Harbold test: p=0.187, Egger test: p=0.169.

References

24 3 25
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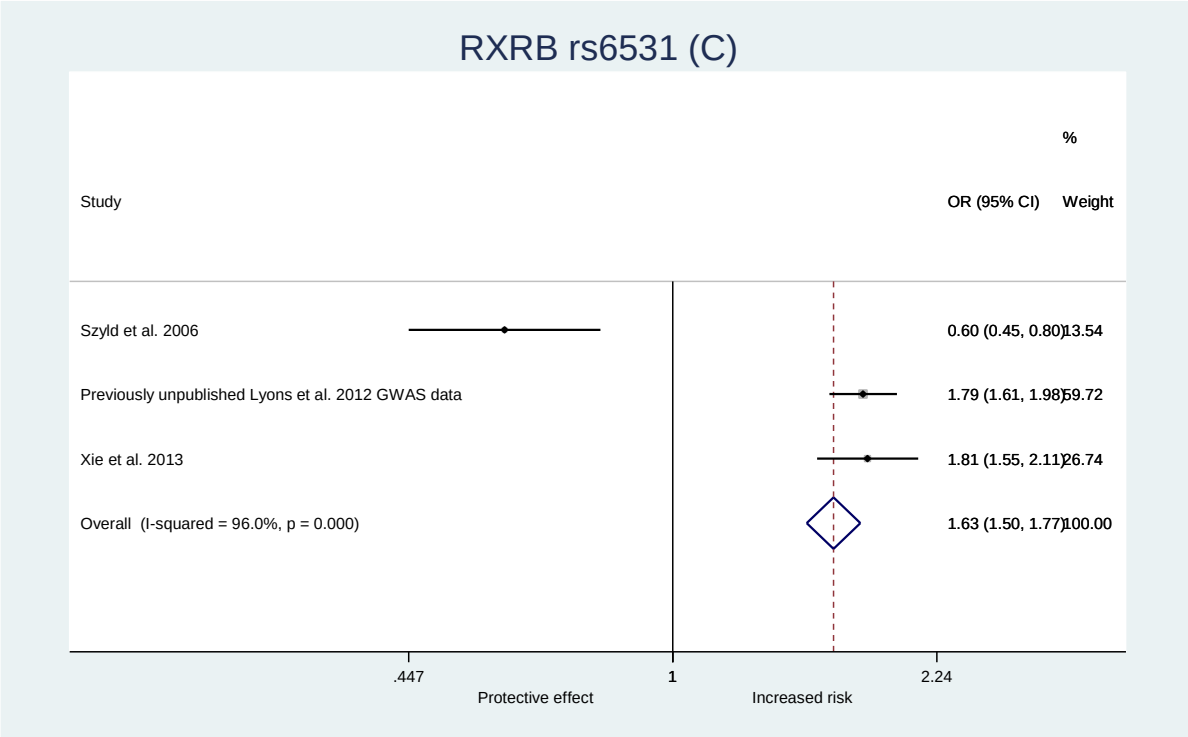

RXRB rs6531 (C) forest plot. Harbold test: p=0.292, Egger test: p=0.301.

References

52 3 25
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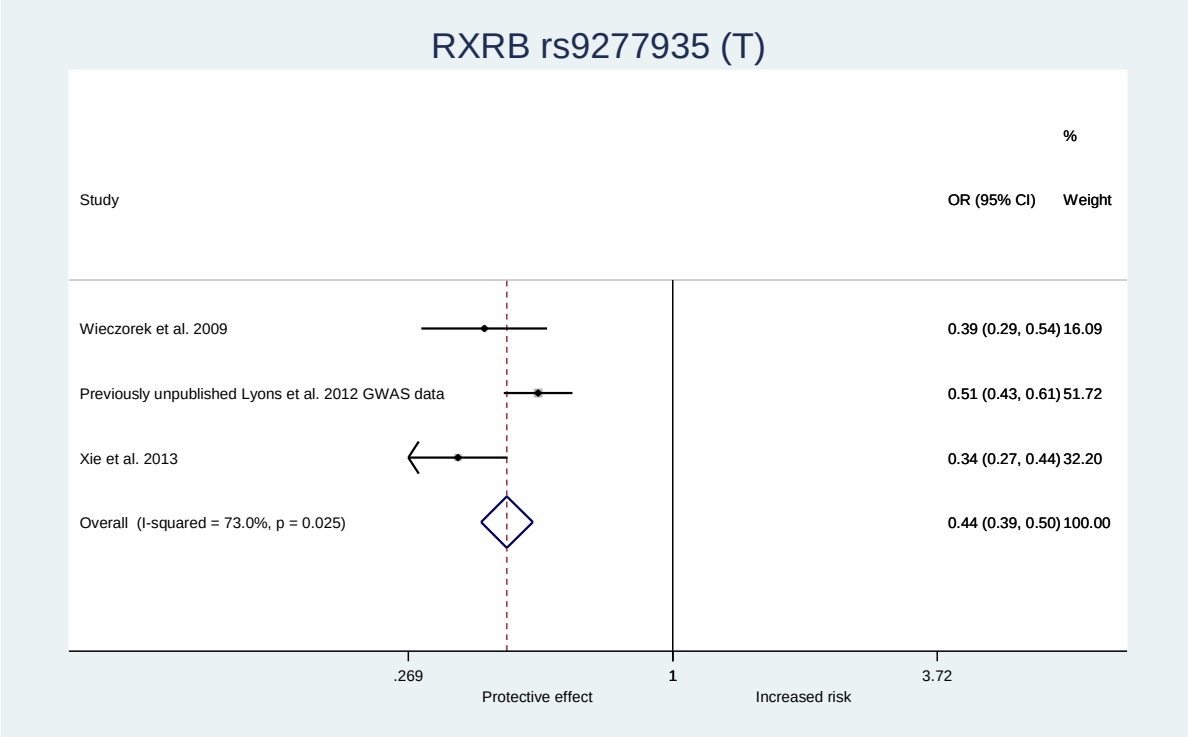

RXRB rs9277935 (T) forest plot. Harbold test: p=0.393, Egger test: p=0.406.

References

53 3 25
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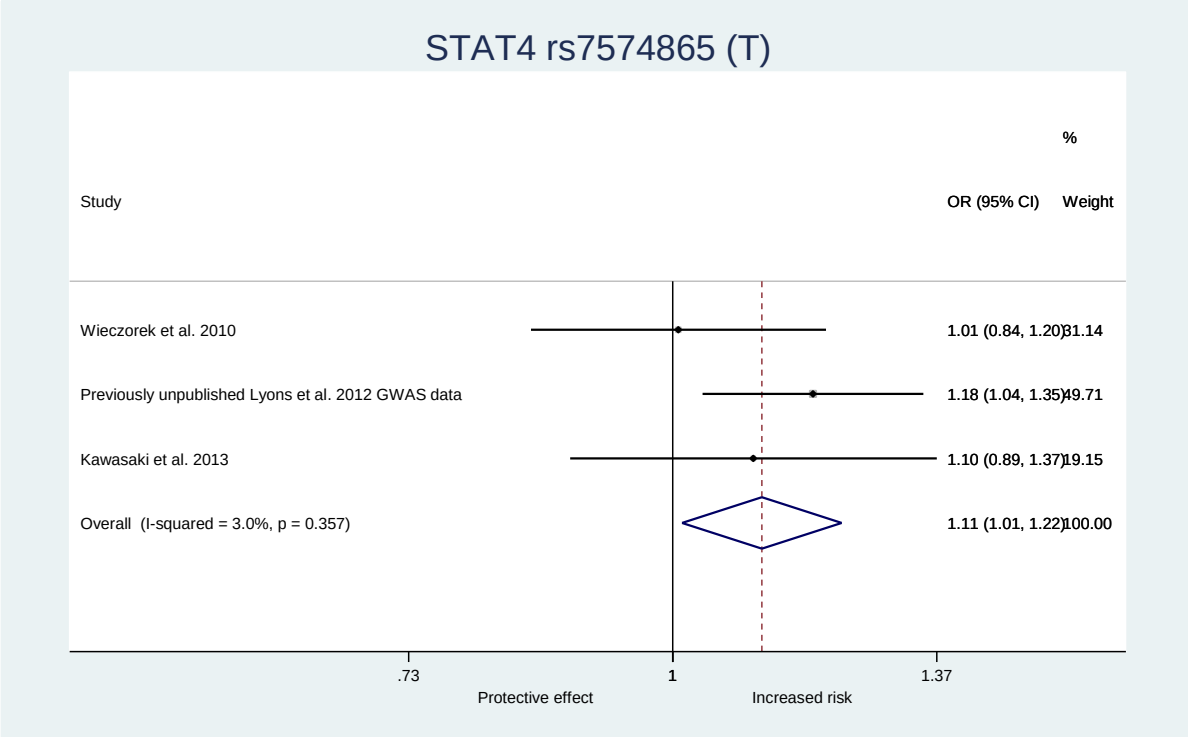

STAT4 rs7574865 (T) forest plot. Harbold test: p=0.590, Egger test: p=0.567.

References

44 45 3
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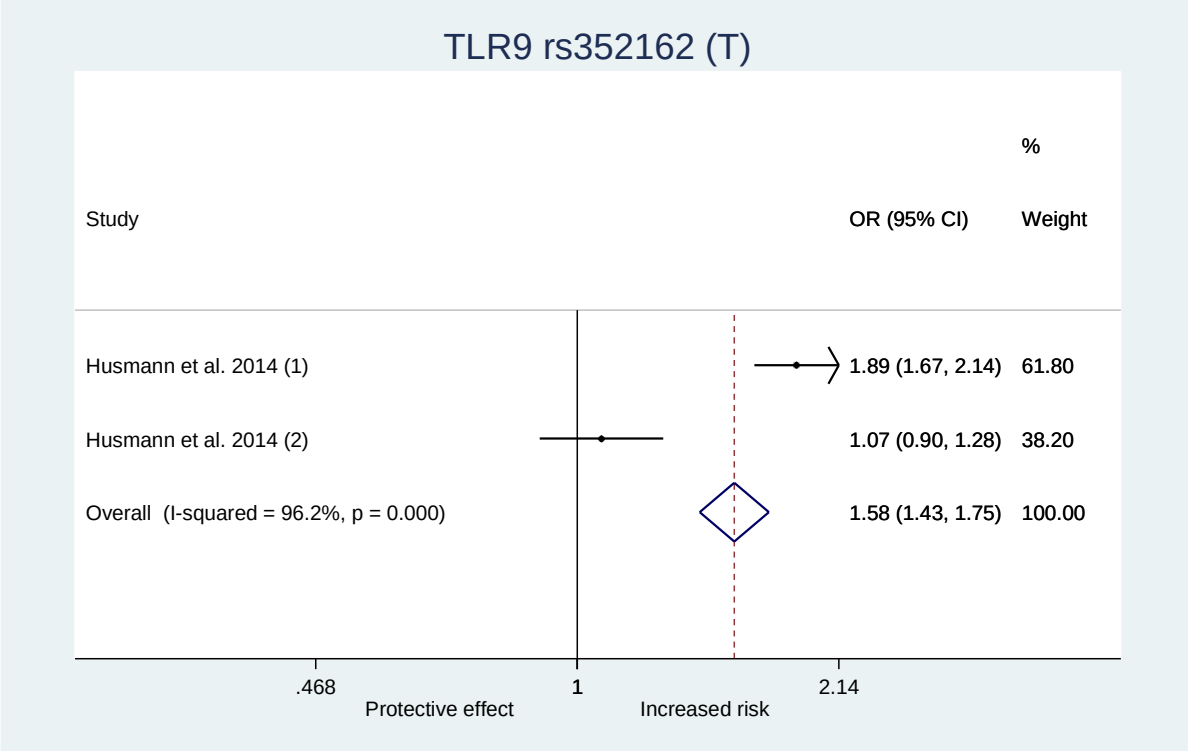
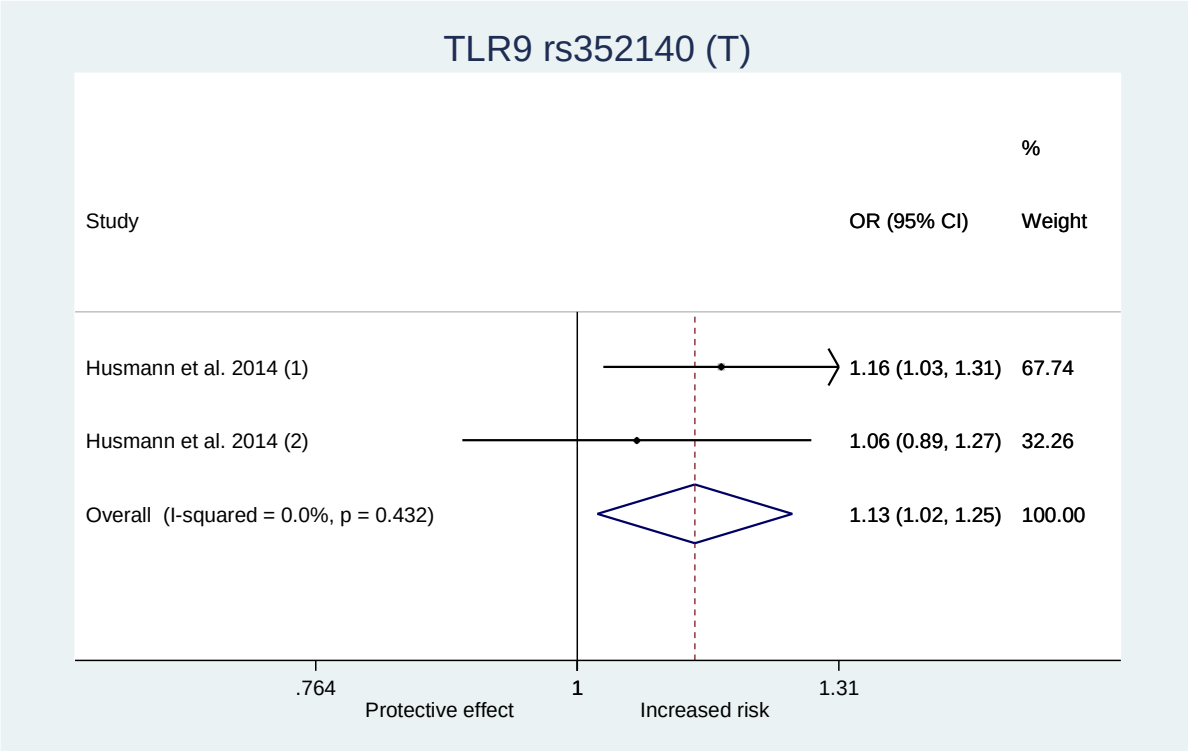


TLR9 rs352162 (T) forest plot. Harbold test: N/A, Egger test: N/A.

References

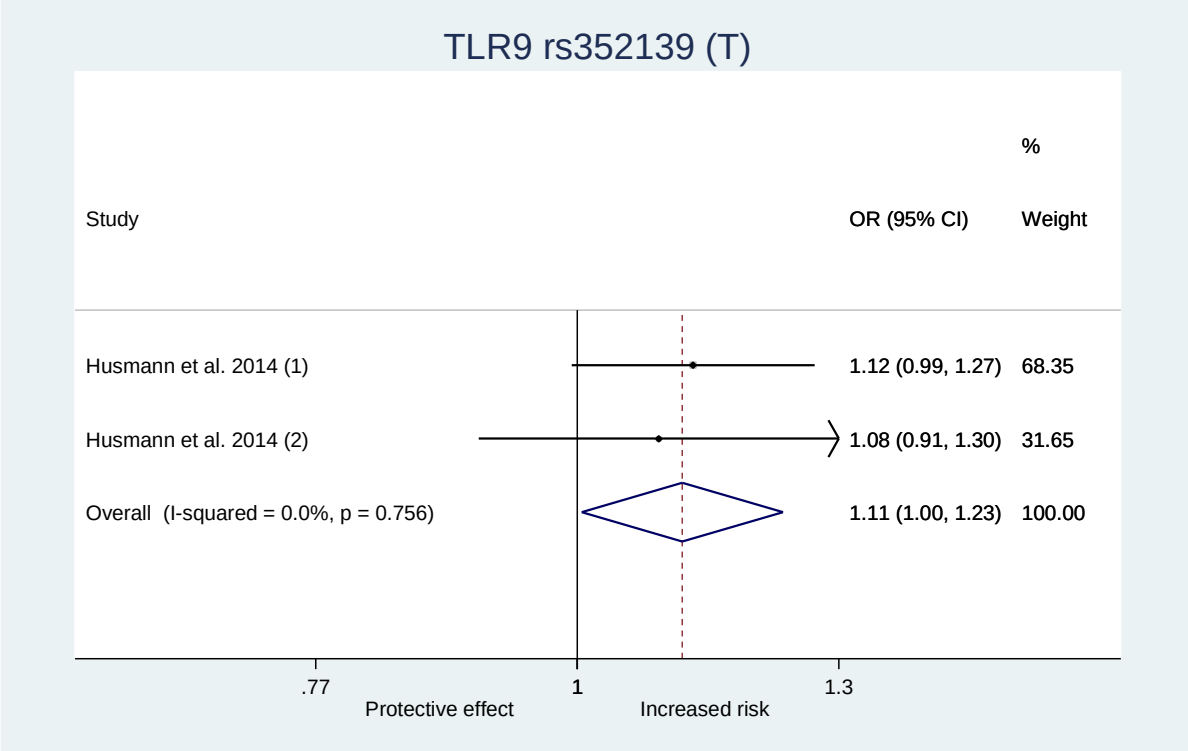
[40]**



TLR9 rs352140 (T) forest plot. Harbold test: N/A, Egger test: N/A.

References

[40]**



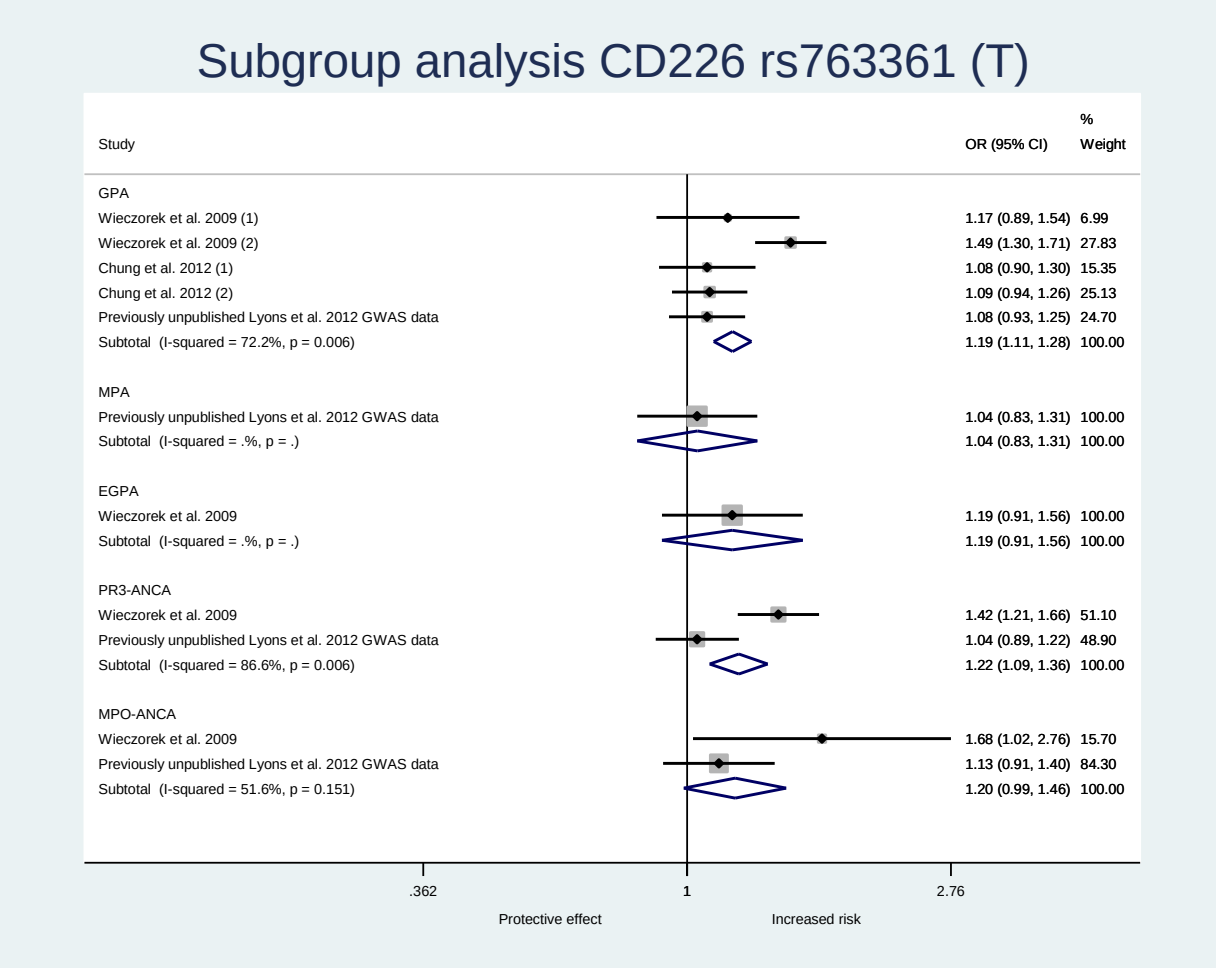
TLR9 rs352139 (T) forest plot. Harbold test: N/A, Egger test: N/A.

References

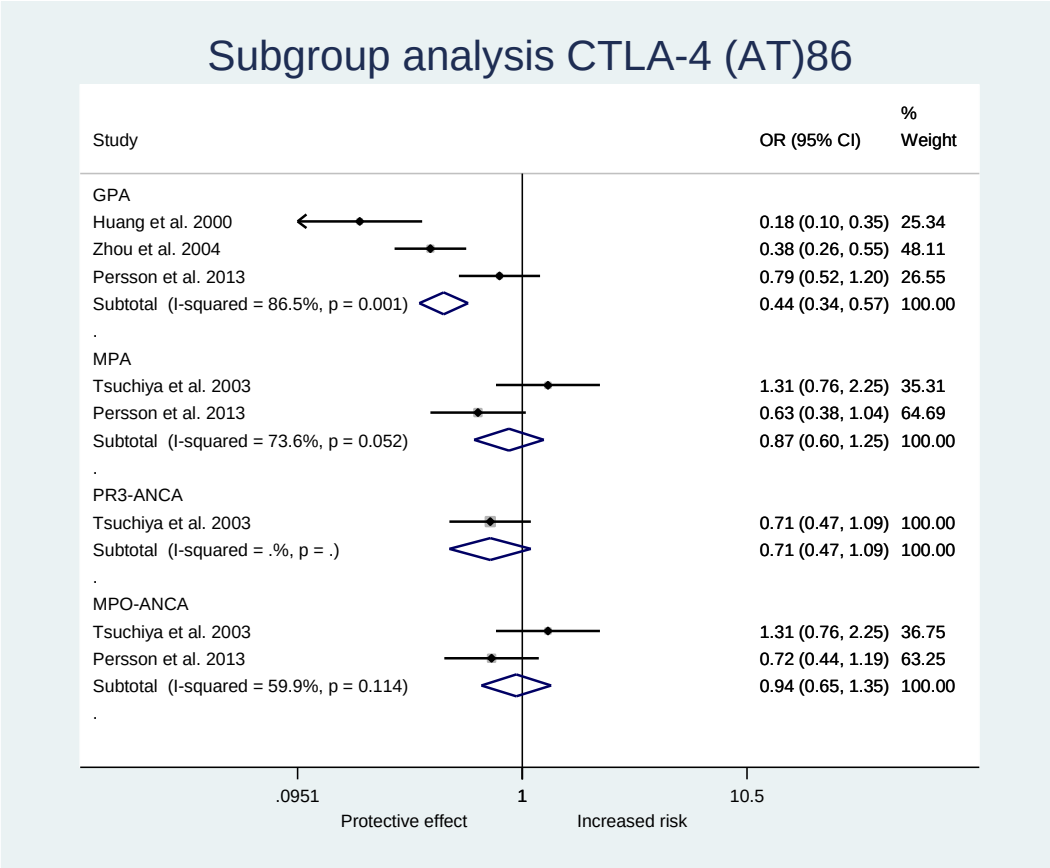
[40]**

**Two cohorts described in the same publication.
***Three cohorts described in the same publication.
N/A, not applicable

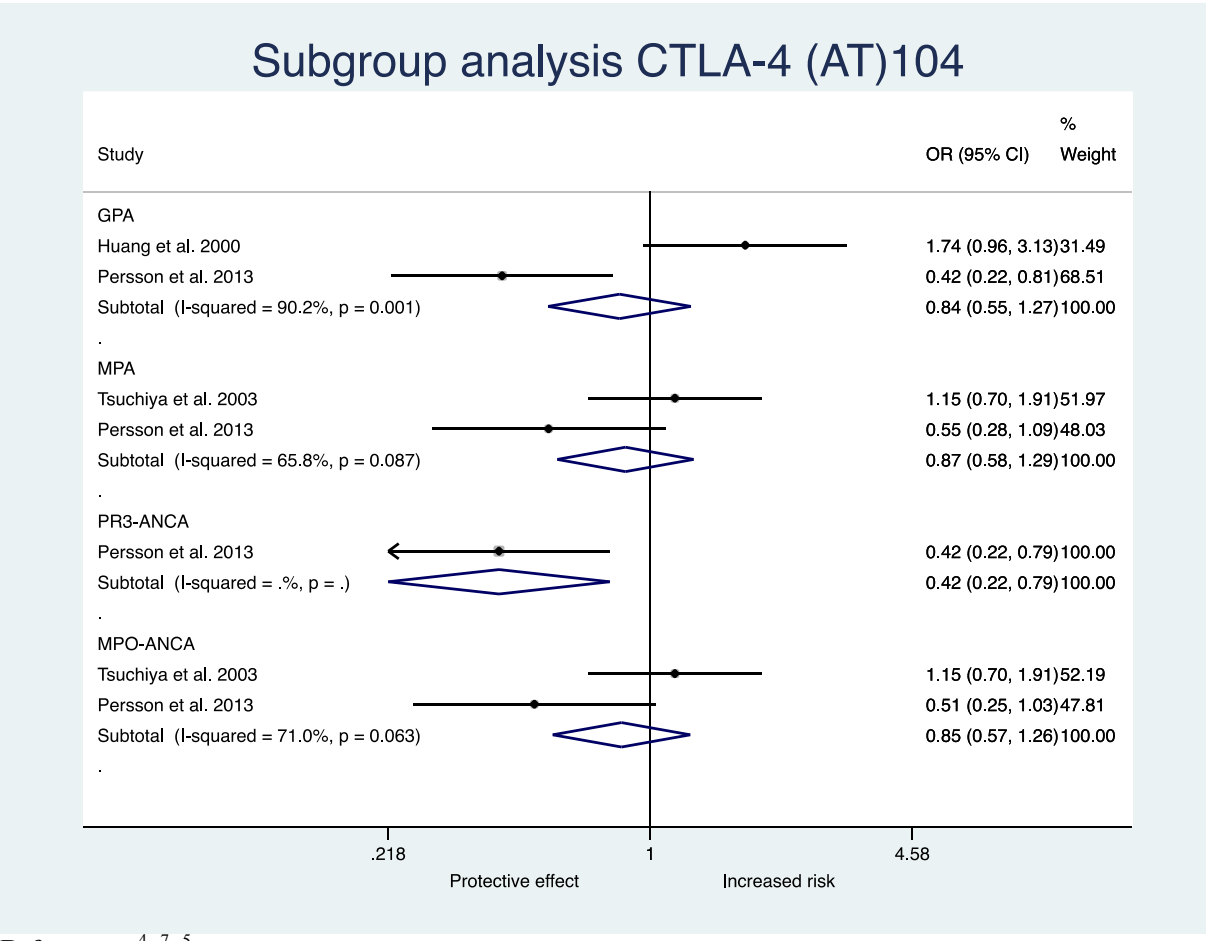
Supplementary Figure S2. Forest plots by diagnostic and serologic subgroups



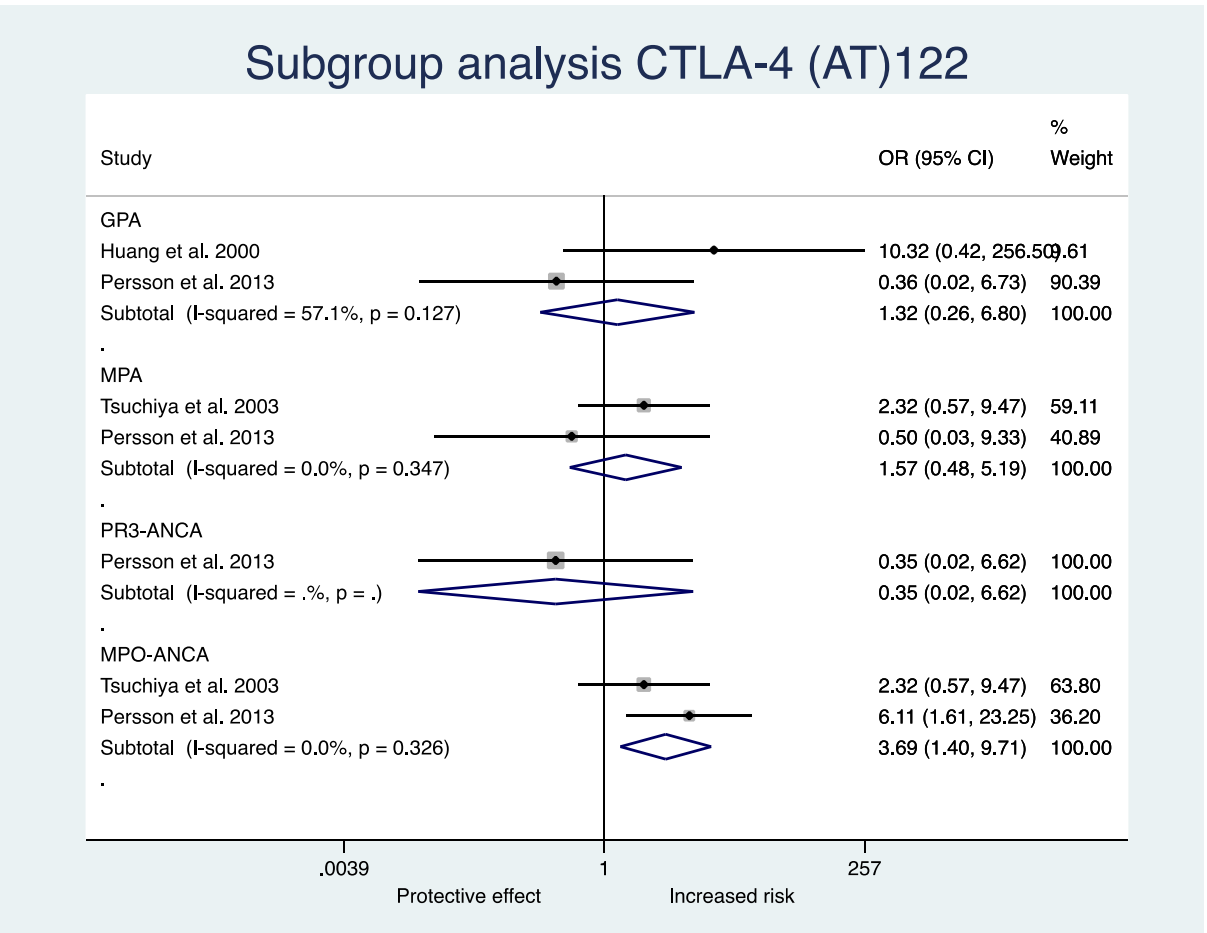
References: [1]**, [2]**, [3]



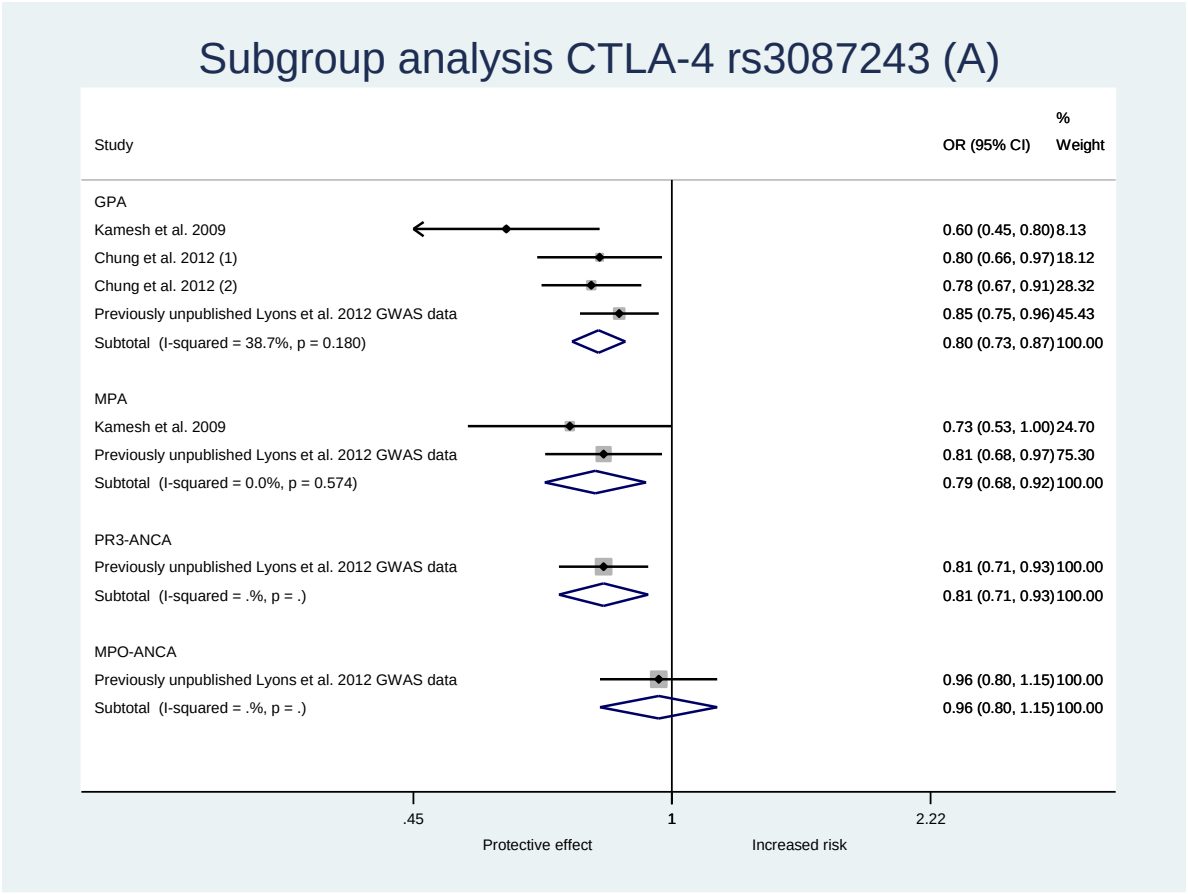
References: [4], [5], [6], [7]



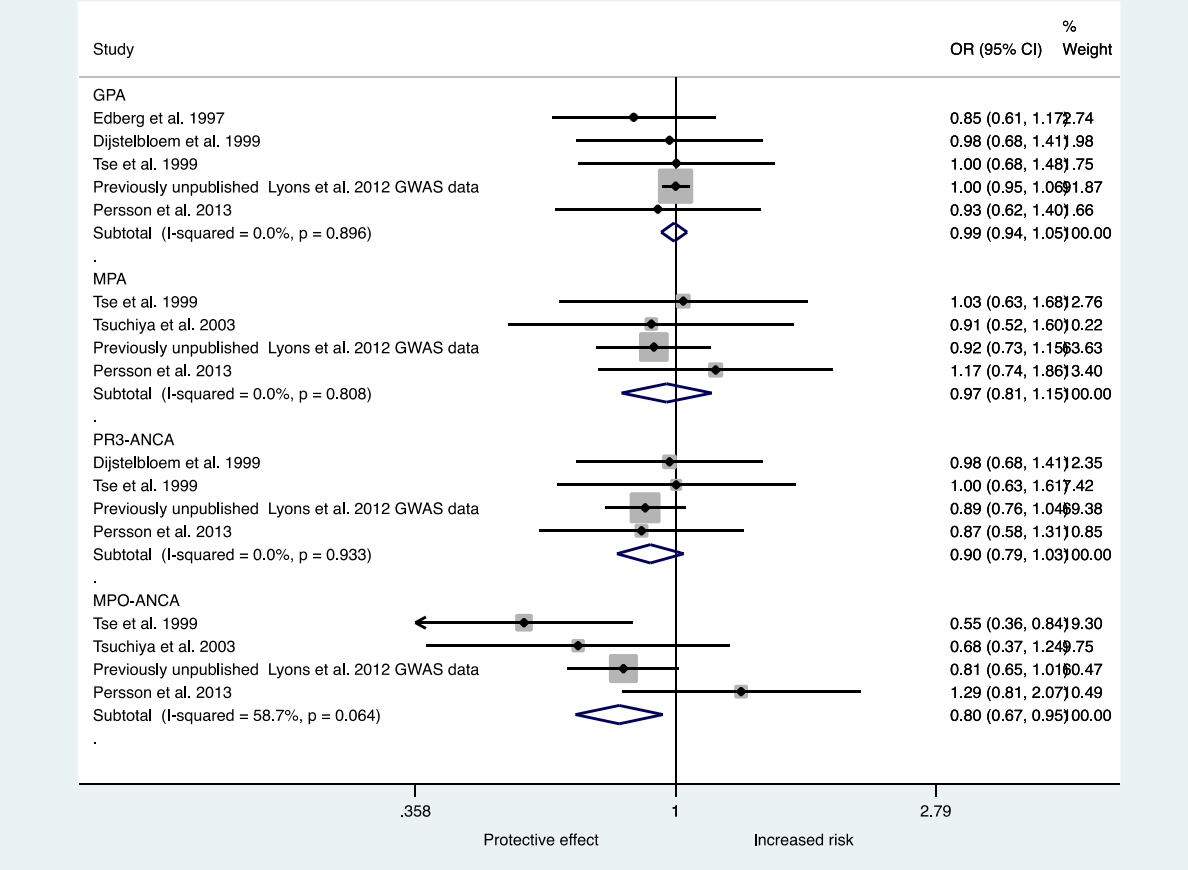
References: [4], [7], [5]



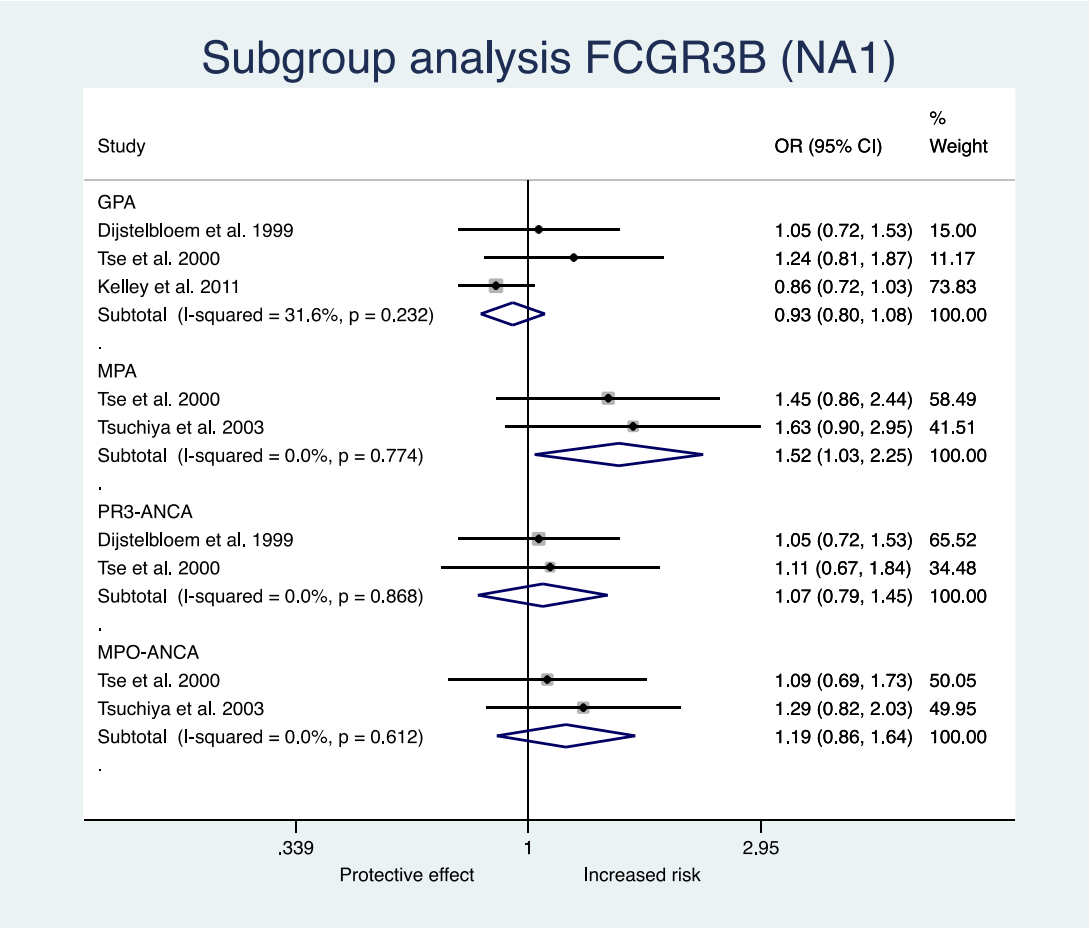
References: [4], [7], [5]



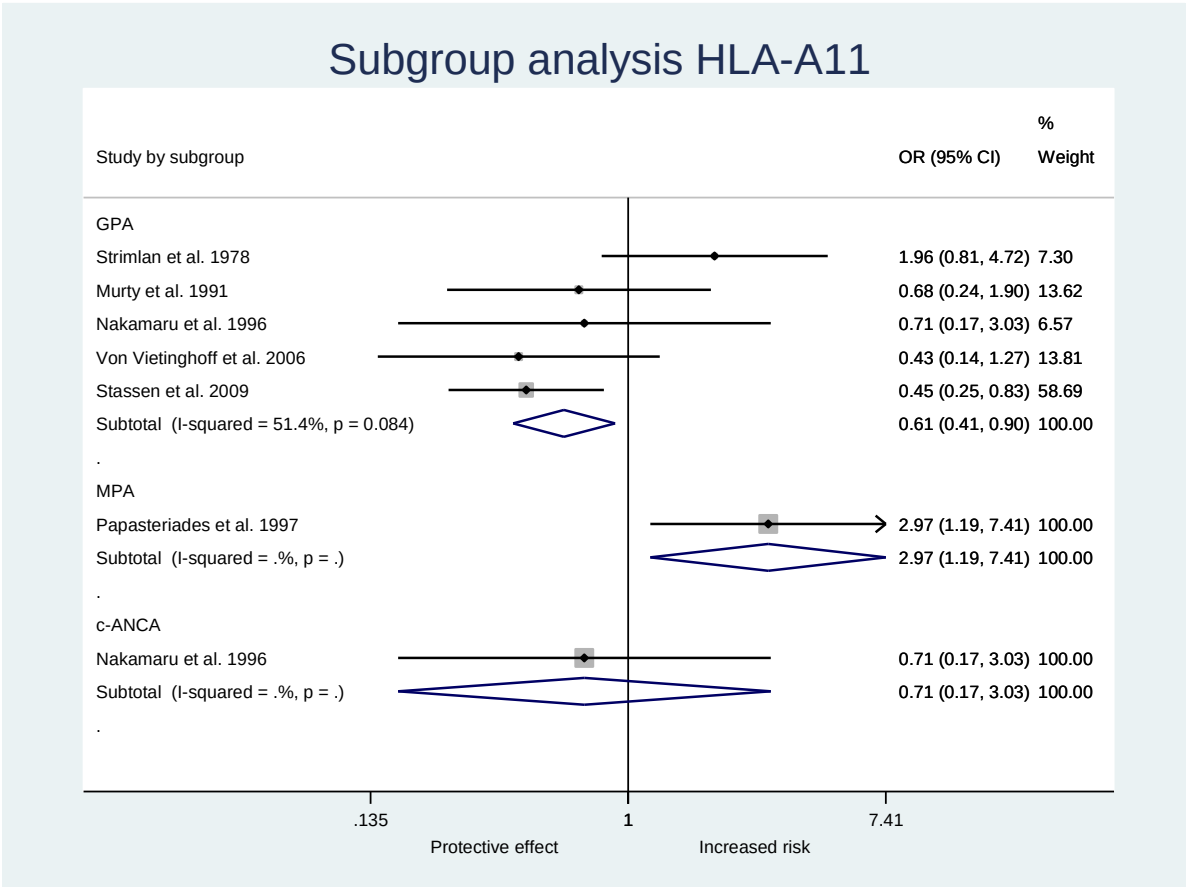
References: [9], [2]**, [3]



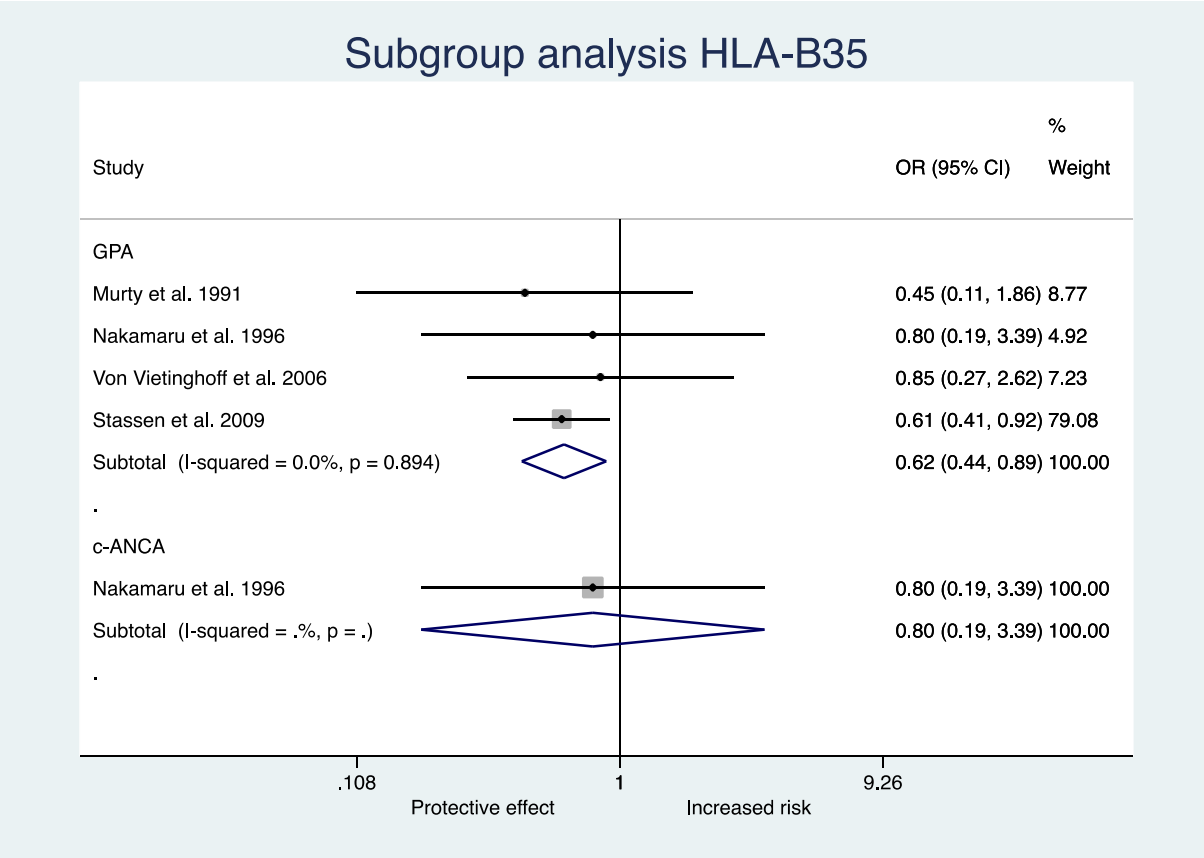
References: [11], [12], [13], [5], [7], [3]



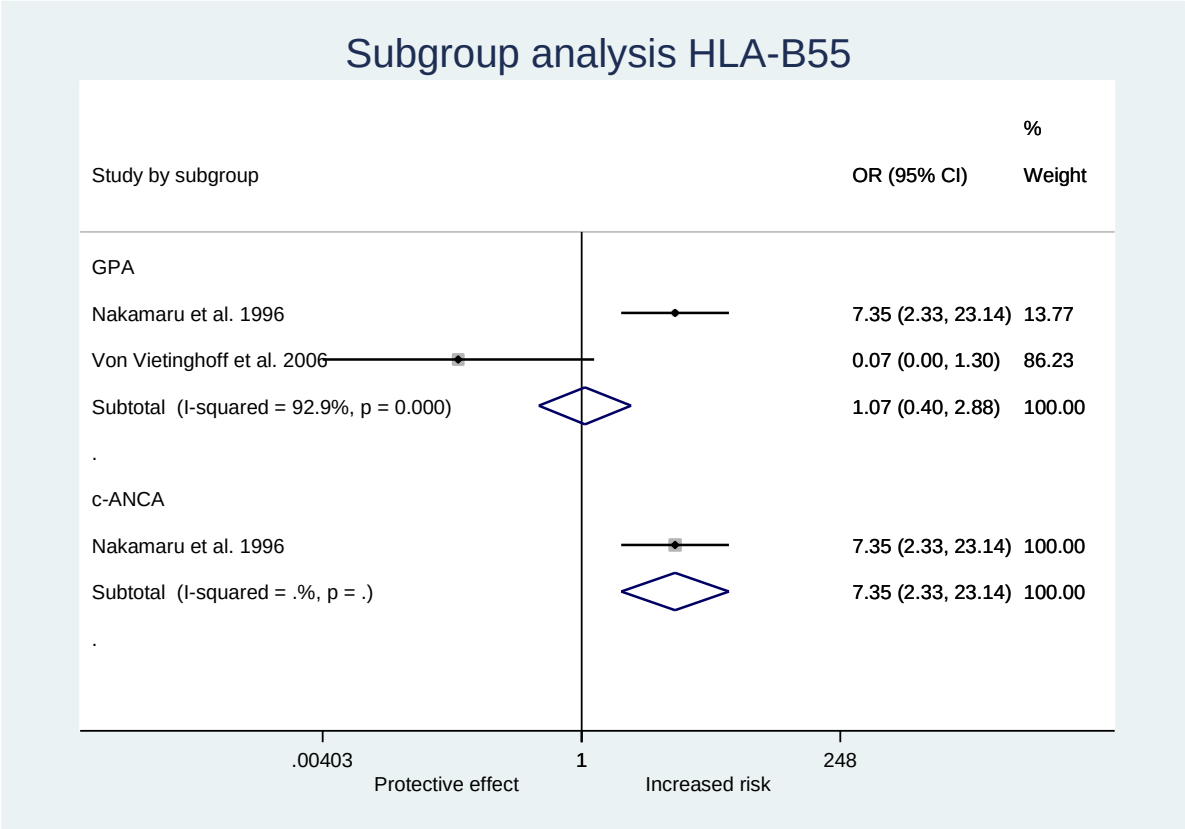
References: [12], [14], [10], [5]



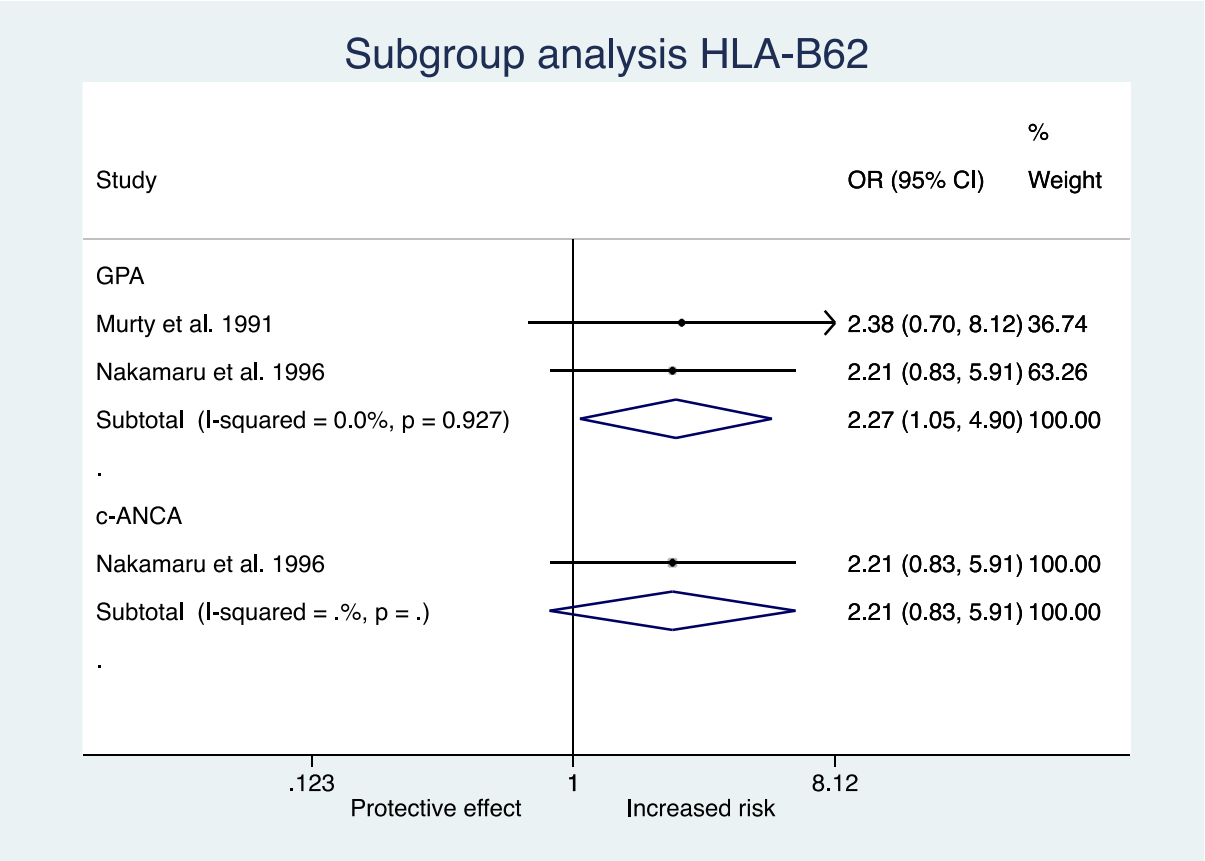
References: [16], [17], [20], [22], [18], [19]



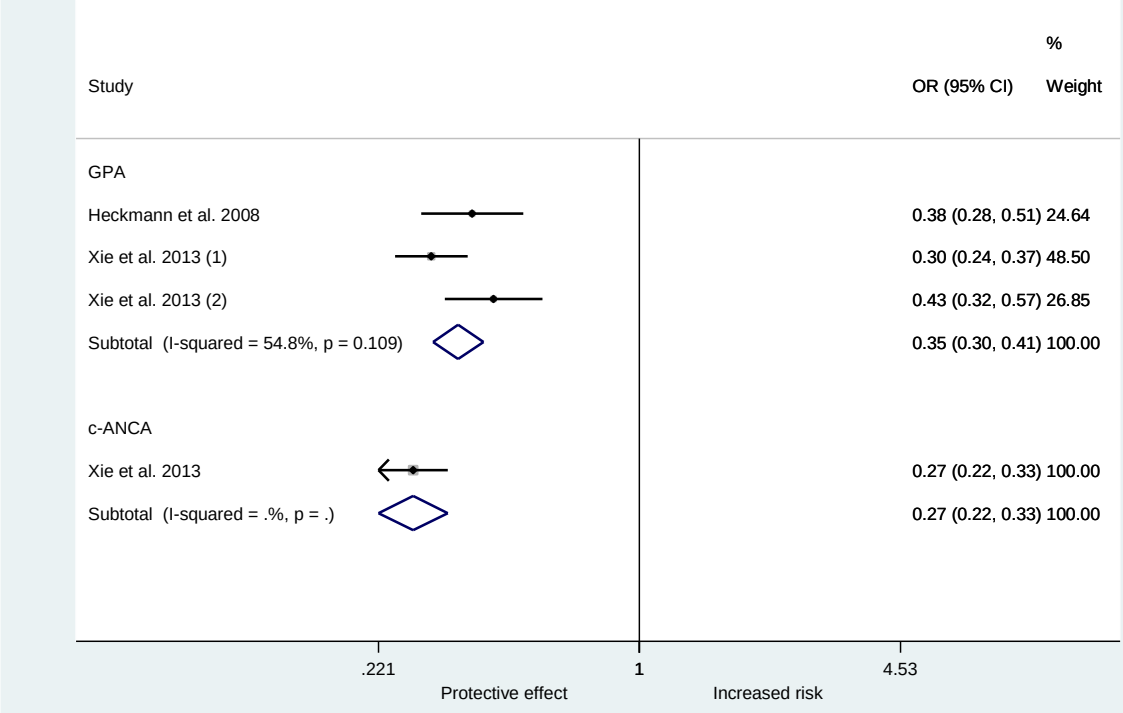
References: [17], [20], [18], [19]



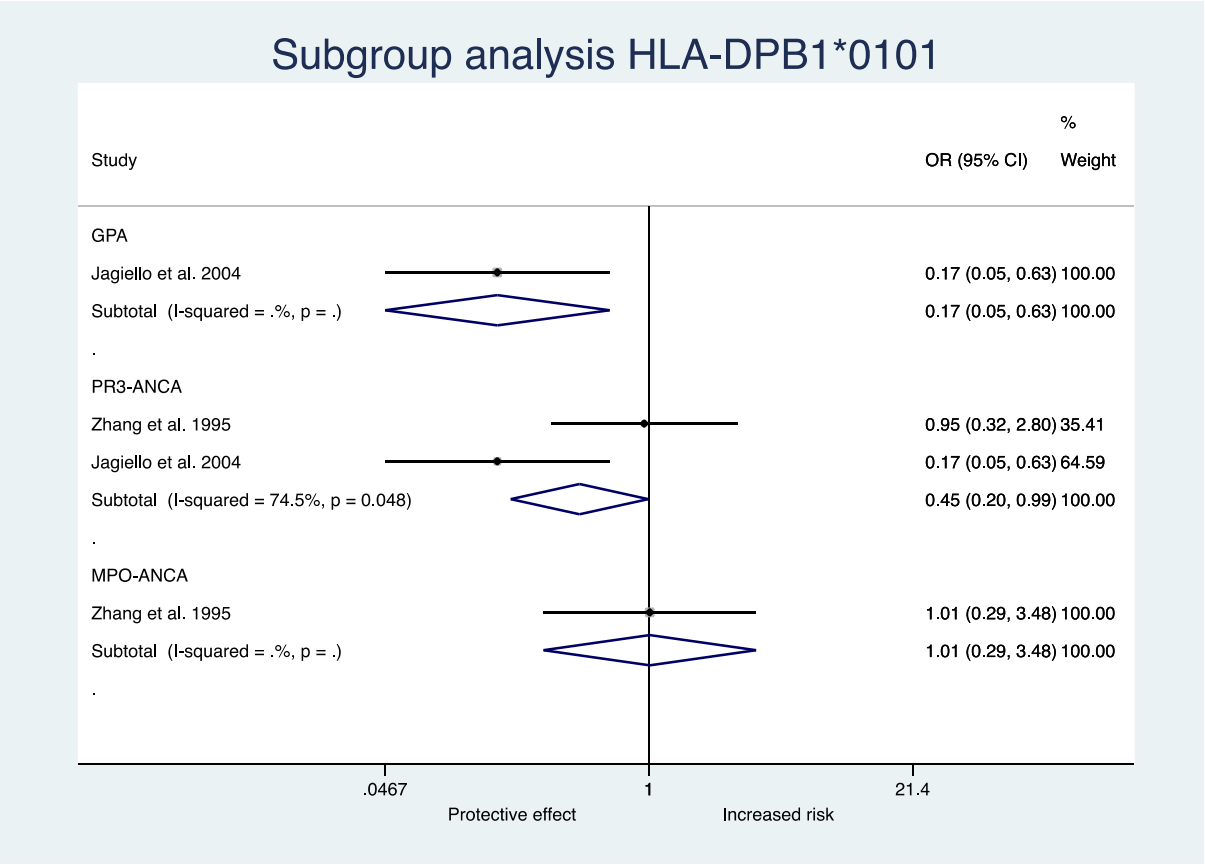
References: [20], [18]



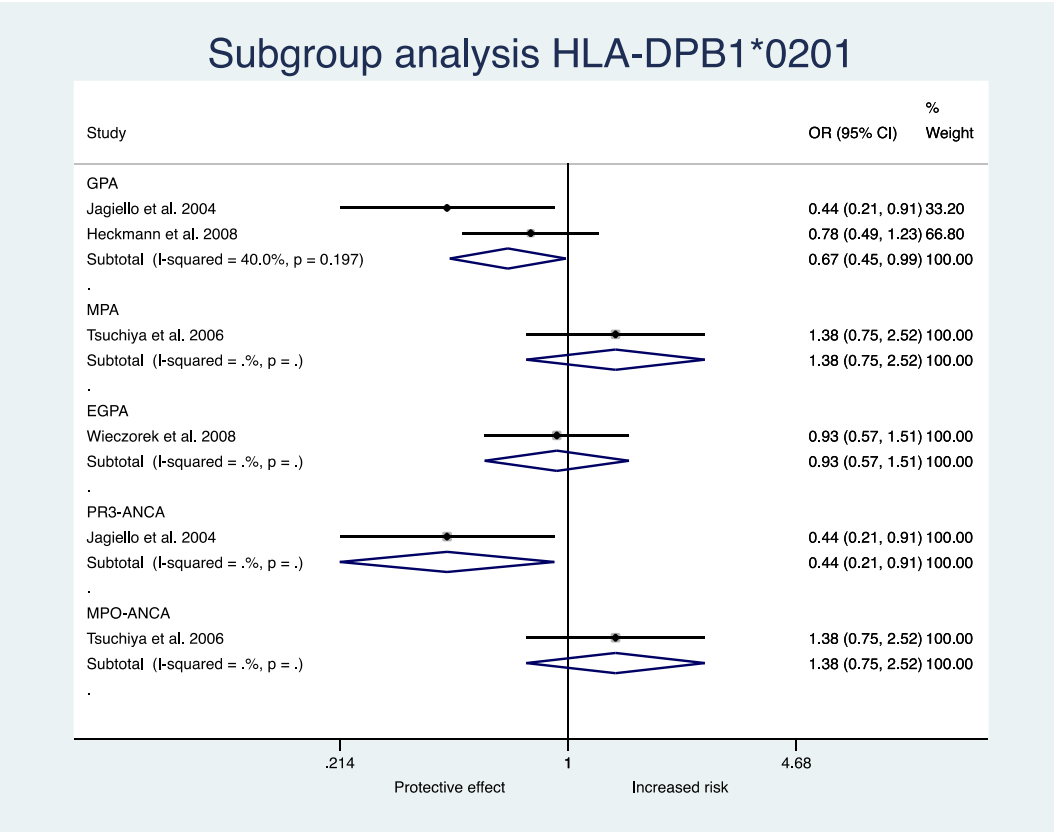
References: [17], [20]



References: [24], [25]**

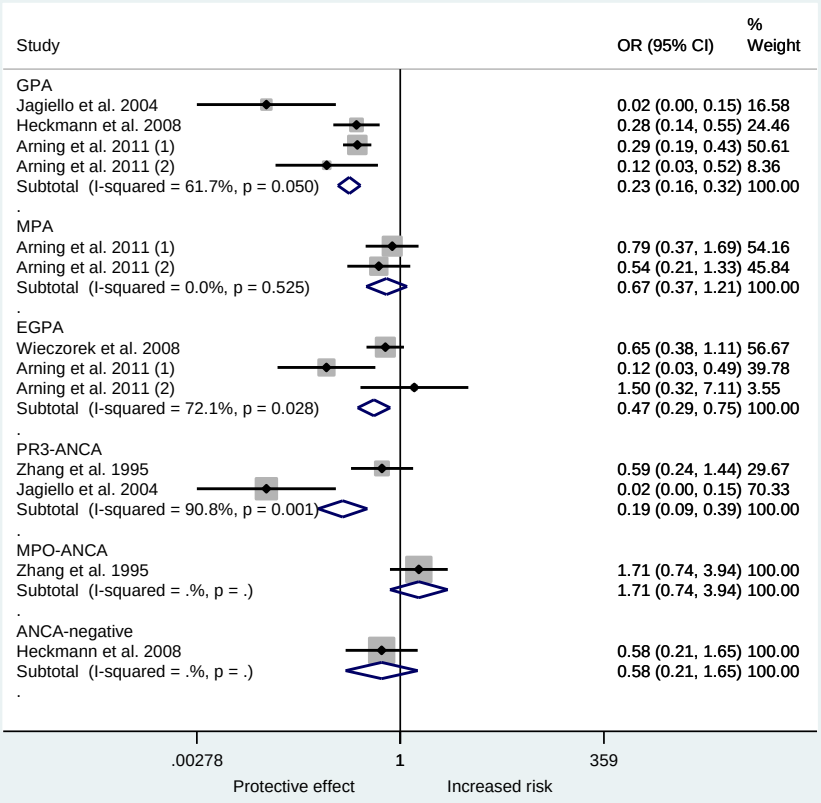


References: [27], [26]



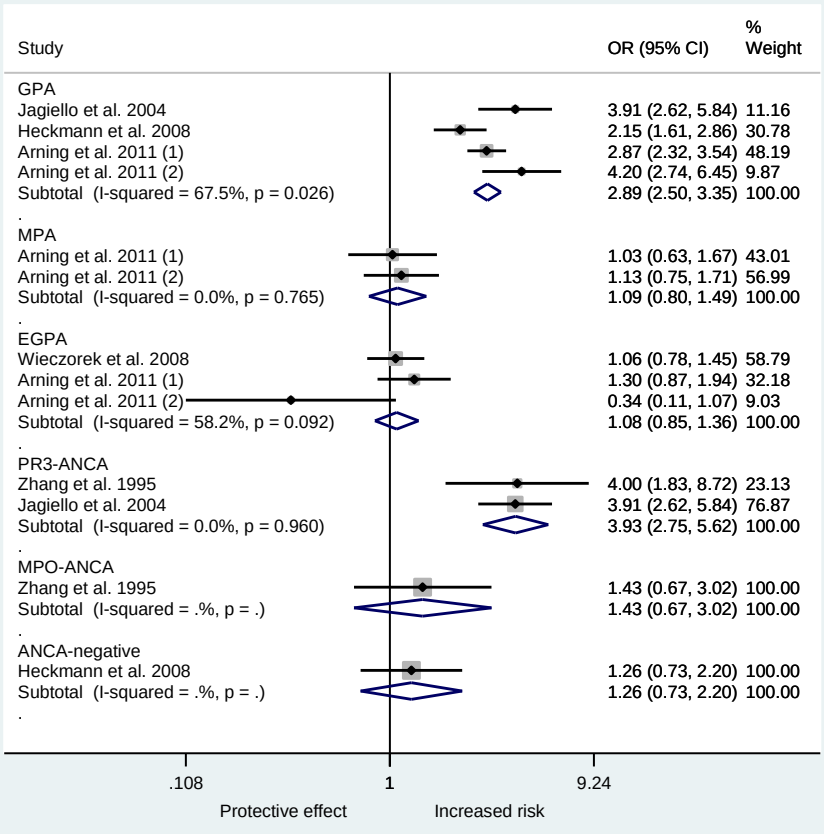
References: [27], [24], [28], [29]

Subgroup analysis HLA-DPB1*0301



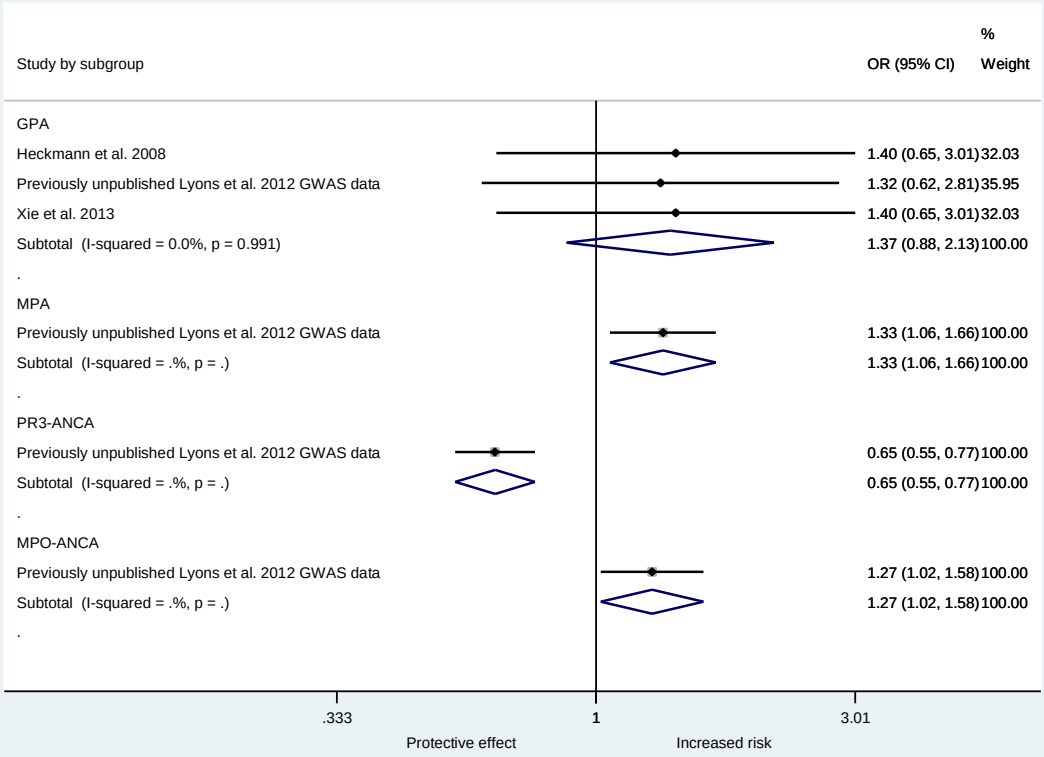
References: [26], [27], [24], [29], [30]**

Subgroup analysis HLA-DPB1*0401



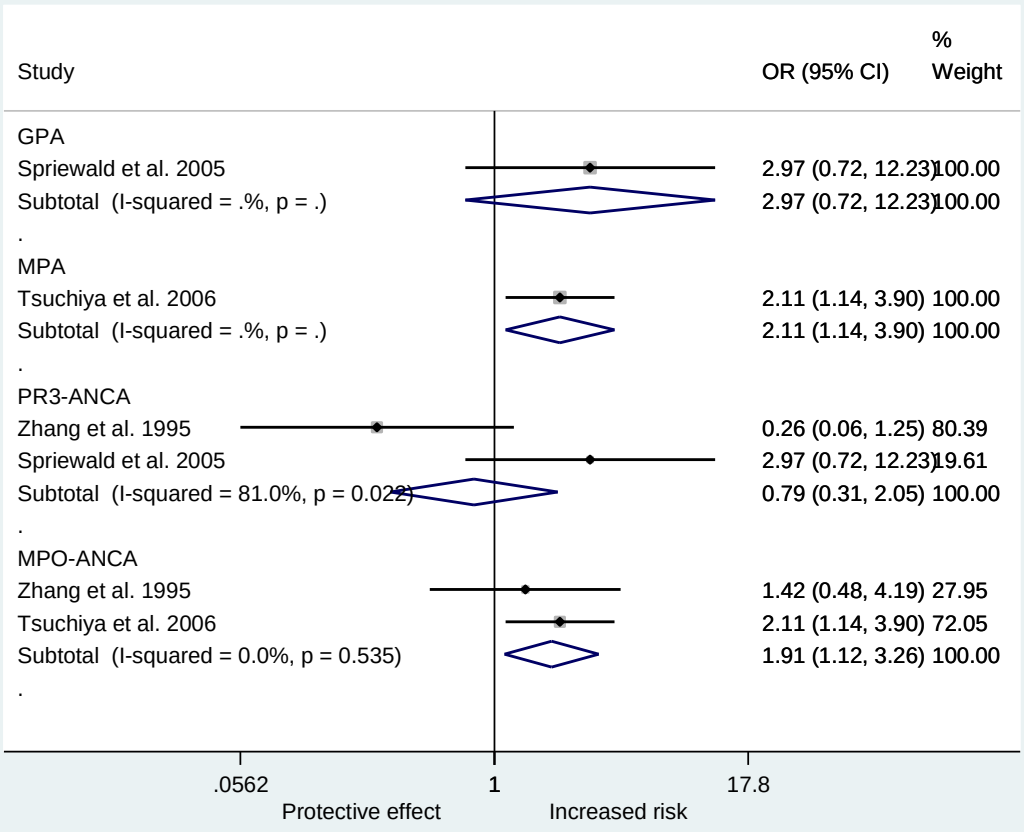
References: [26], [27], [24], [29], [30]**

Subgroup analysis HLA-DPB2 rs3130215 (A)



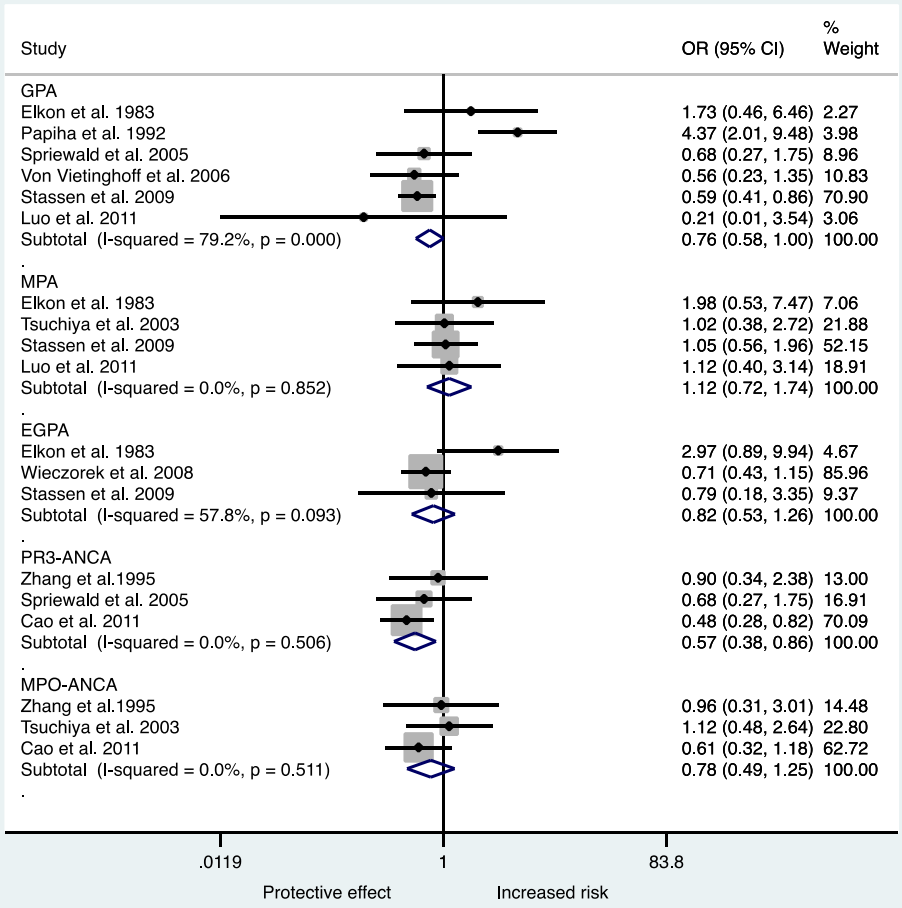
References: [24], [3], [25]

Subgroup analysis HLA-DQB1*0303



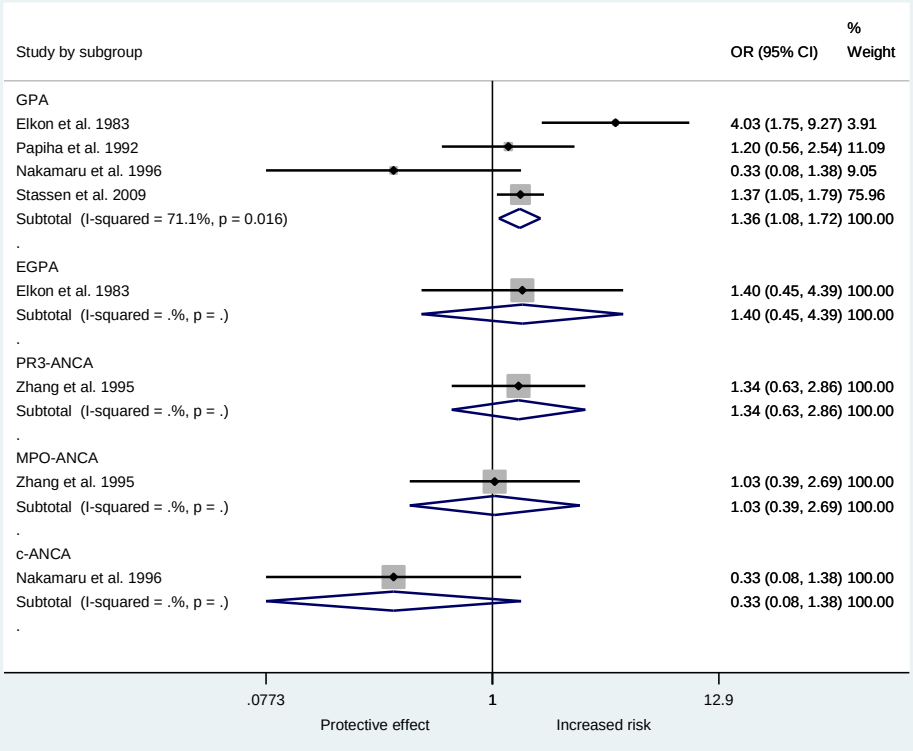
References: [26], [31], [28]

Subgroup analysis HLA-DR1



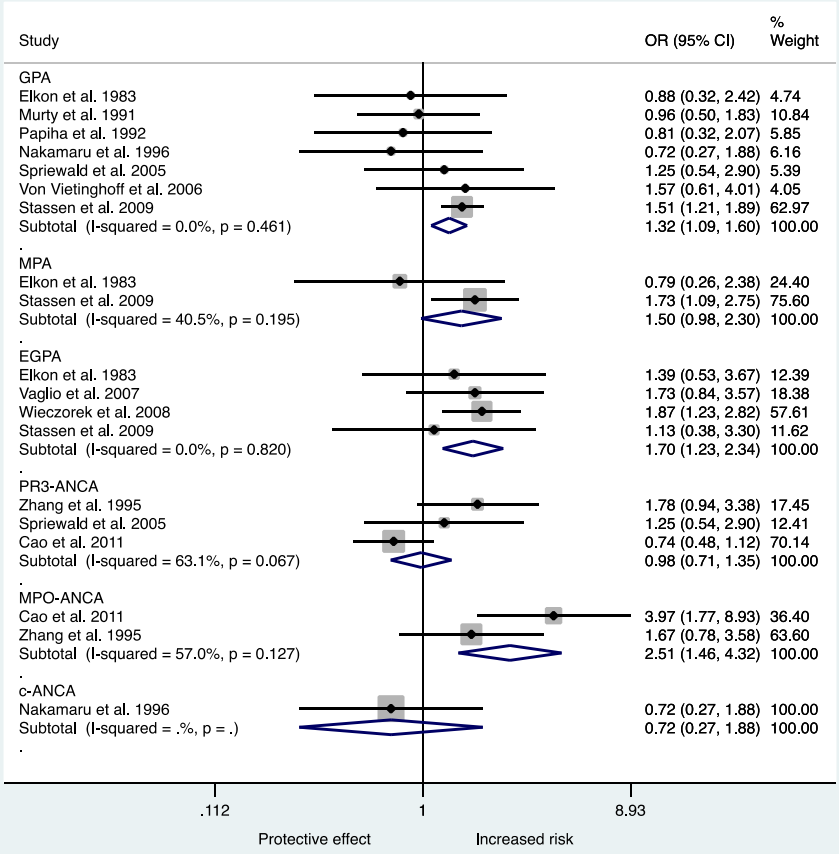
References: [23], [32], [31], [18], [19], [34], [5], [29], [26], [33]

Subgroup analysis HLA-DR2



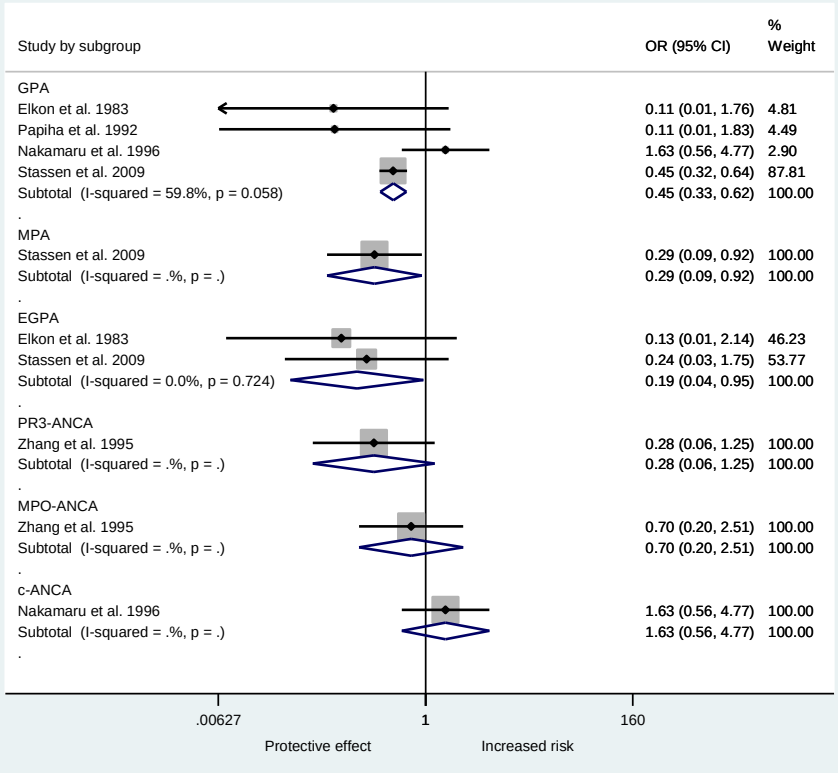
References: [23], [32], [26], [20], [19]

Subgroup analysis HLA-DR4



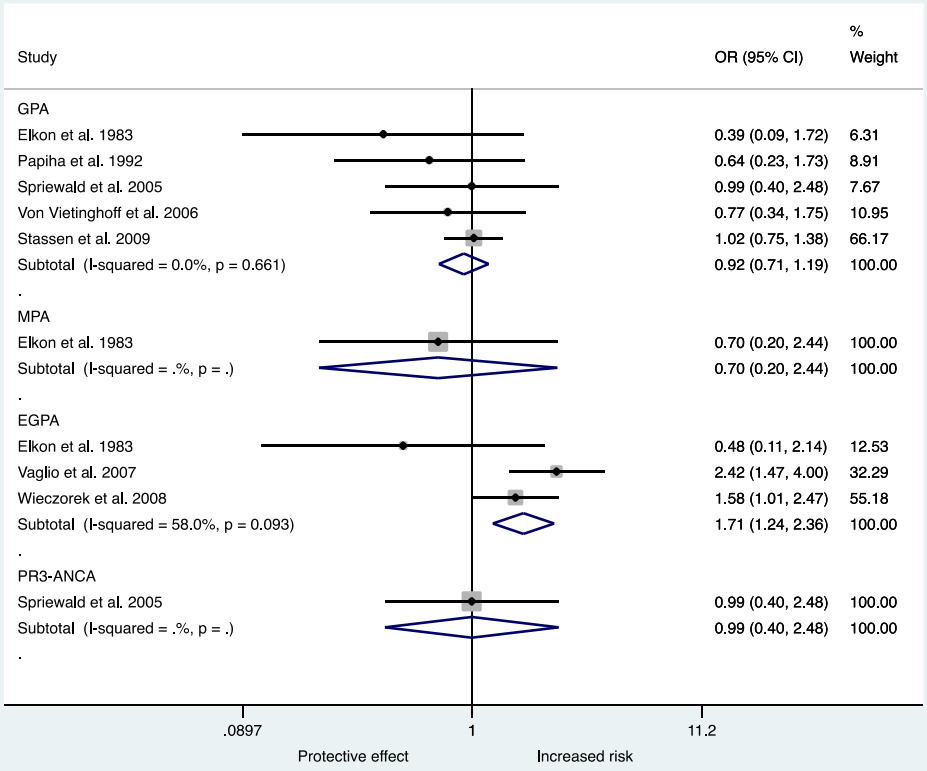
References: [23], [17], [32], [20], [31], [18], [19], [35], [29], [26], [33]

Subgroup analysis HLA-DR6



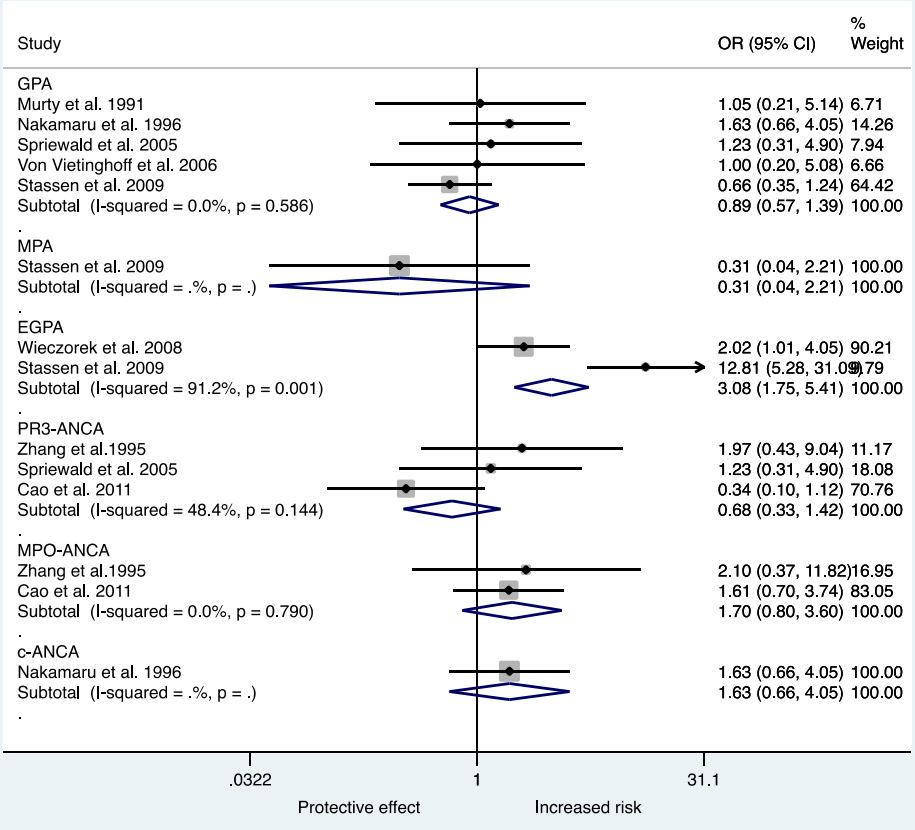
References: [23], [32], [26], [20], [19]

Subgroup analysis HLA-DR7



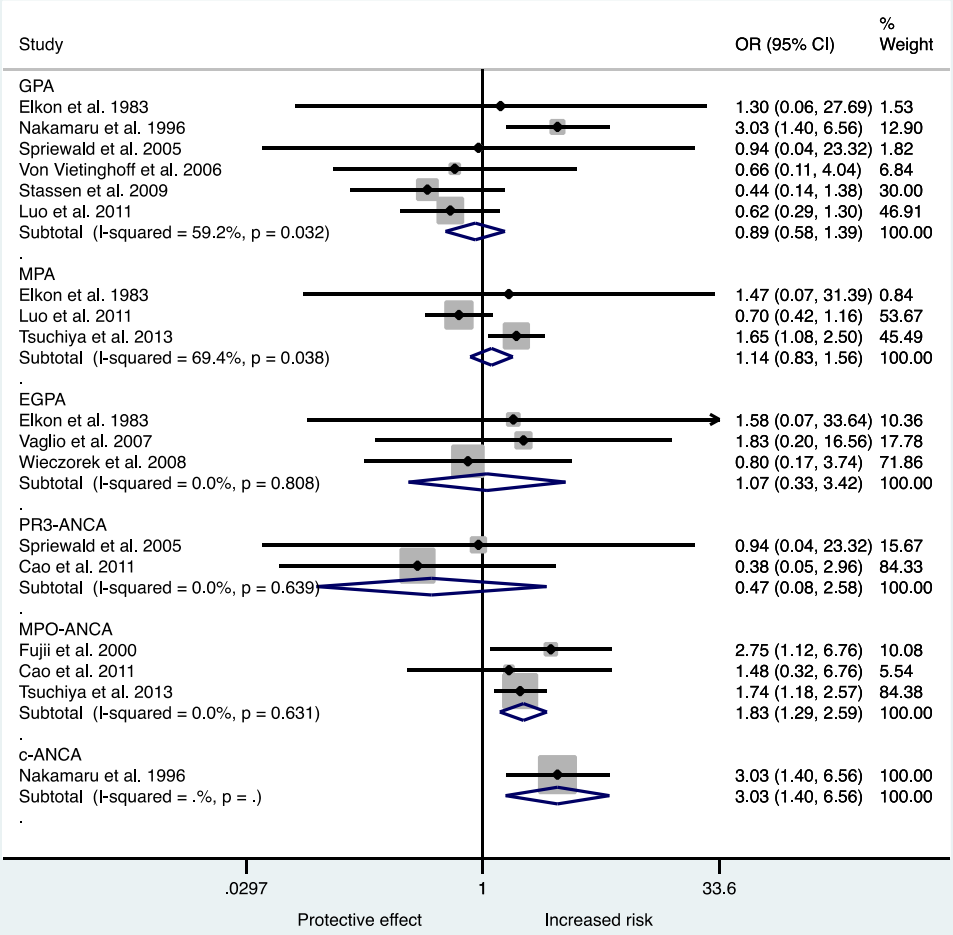
References: [23], [32], [31], [18], [19], [35], [29]

Subgroup analysis HLA-DR8



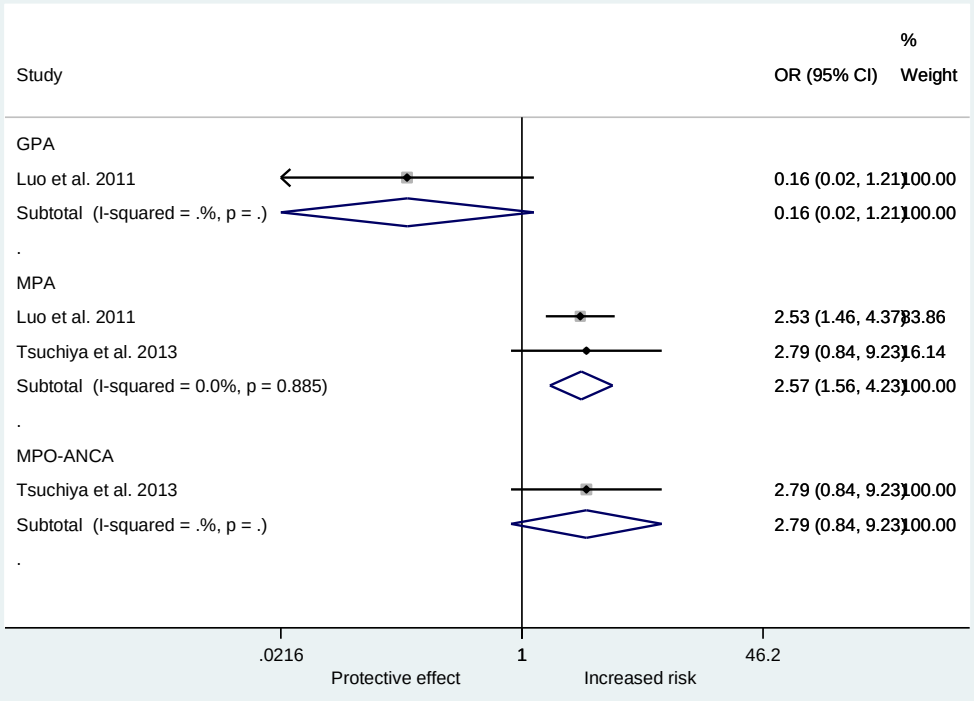
References: [17], [20], [31], [18], [19], [29], [26], [33]

Subgroup analysis HLA-DR9



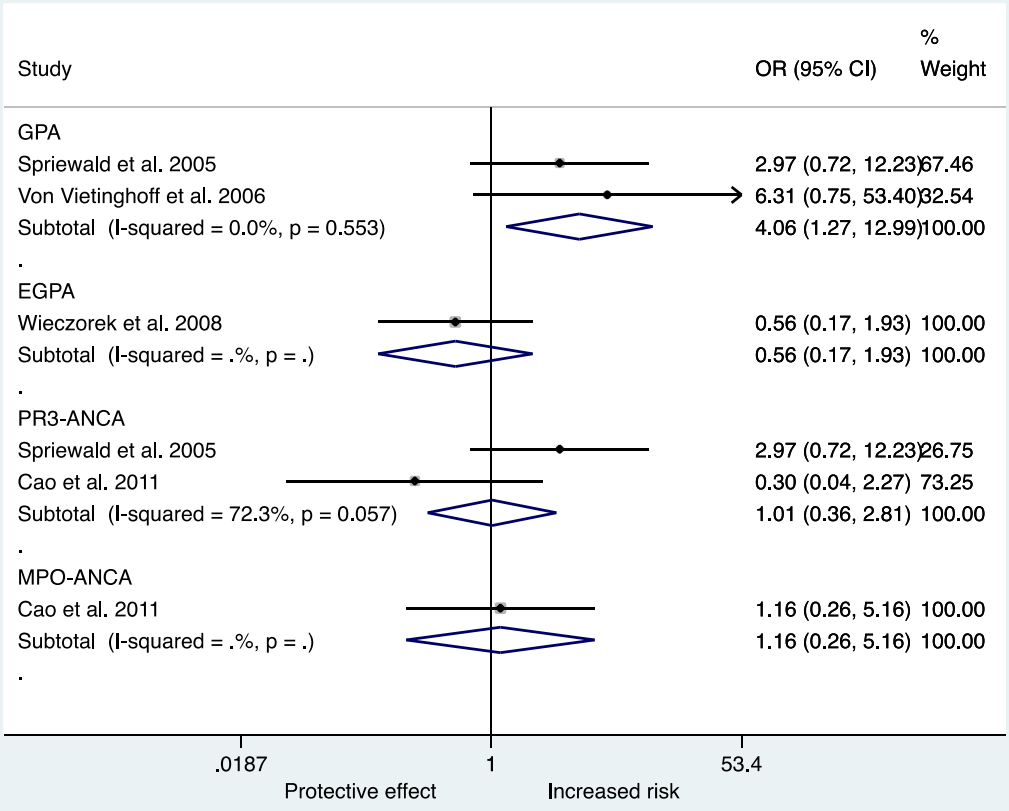
References: [23], [20], [31], [18], [19], [34], [37], [35], [29], [33], [36]

Subgroup analysis HLA-DRB1*1101



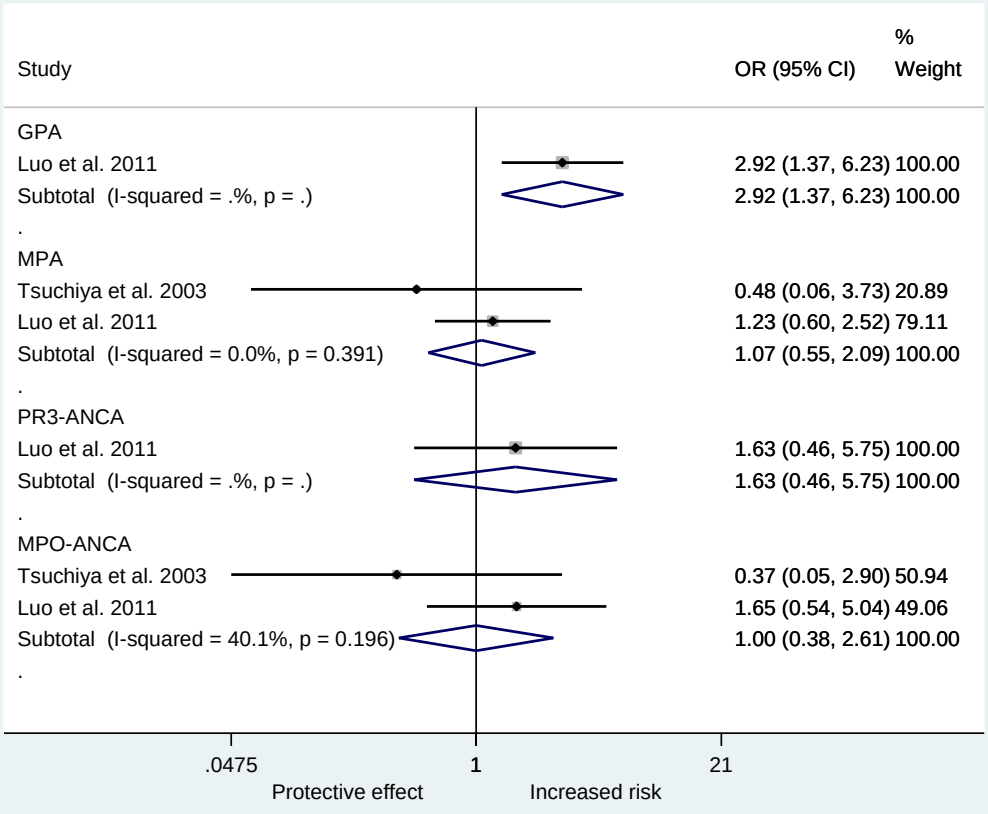
References: [34], [37]

Subgroup analysis HLA-DRB1*12



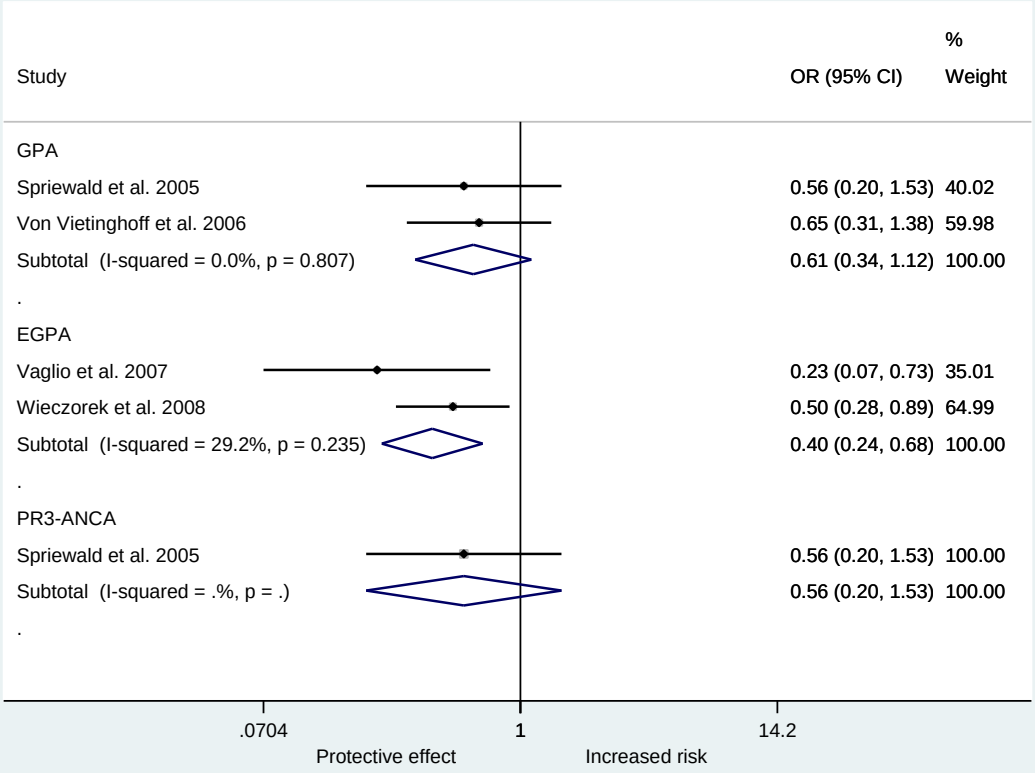
References: [31], [18], [29], [33]

Subgroup analysis HLA-DRB1*1202



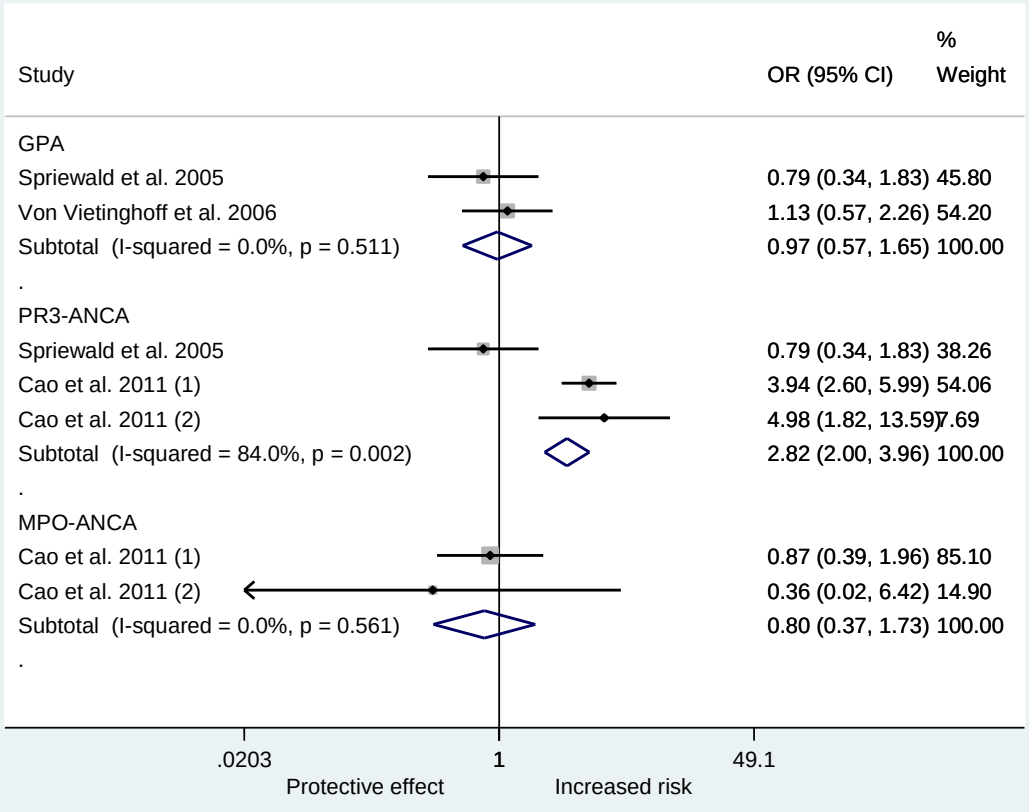
References: [5], [34]

Subgroup analysis HLA-DRB1*13



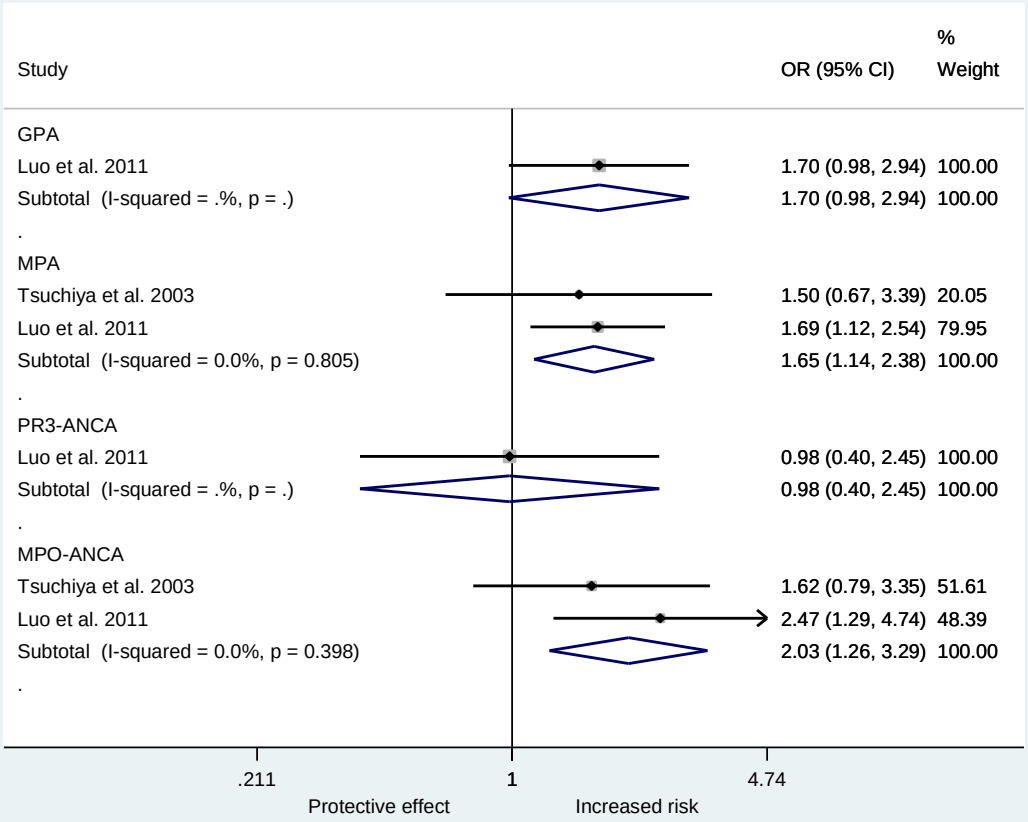
References: [31], [18], [35], [29]

Subgroup analysis HLA-DRB1*15



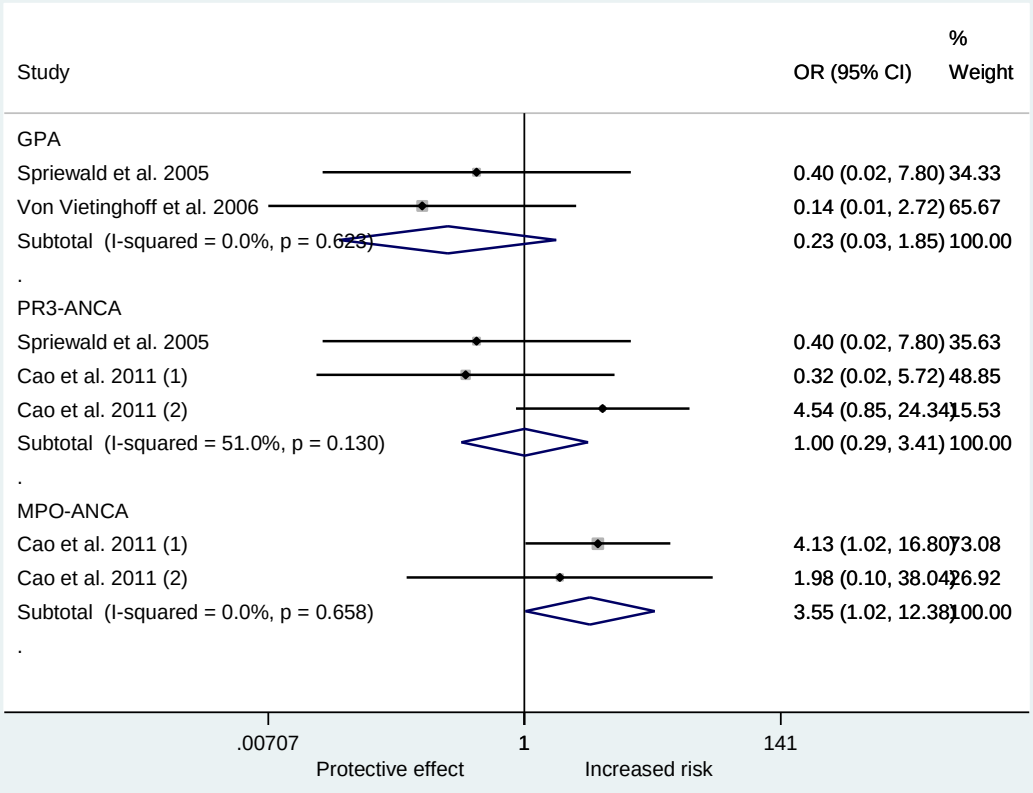
References: [31], [18], [33]**

Subgroup analysis HLA-DRB1*1501

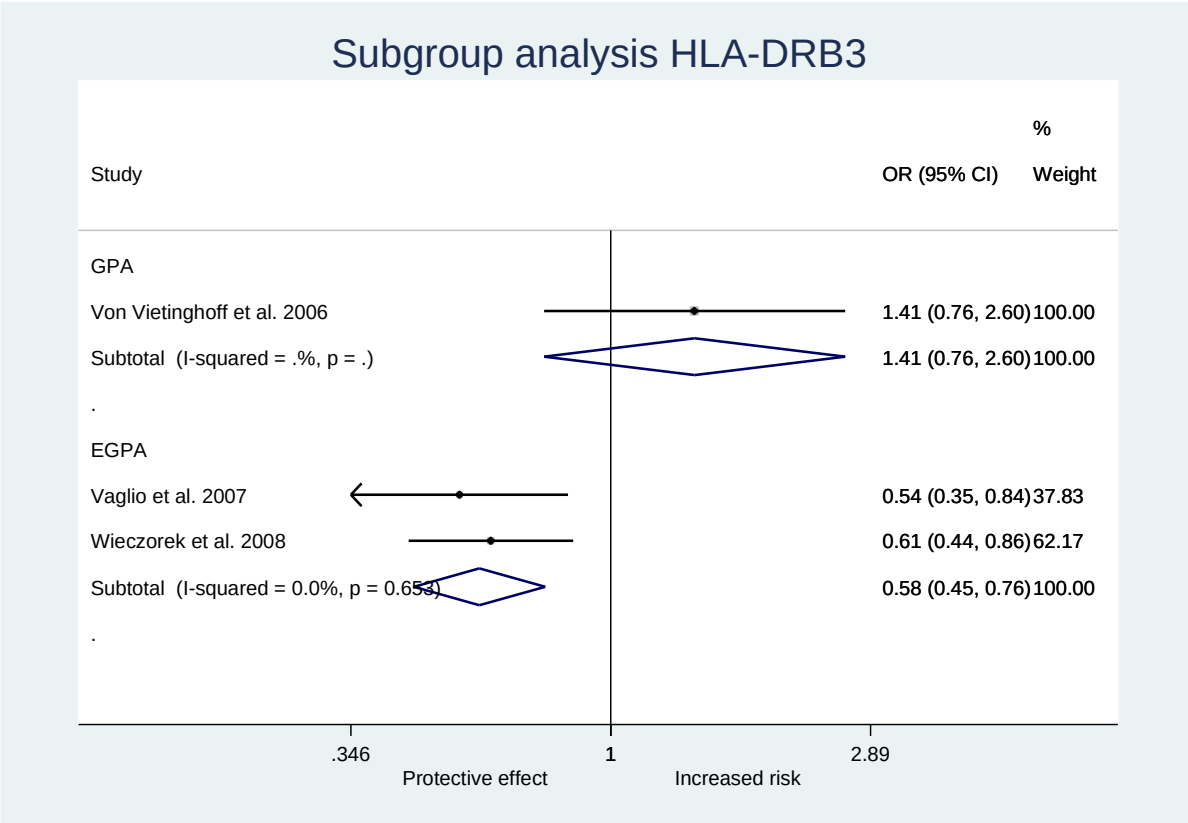


References: [5], [34]

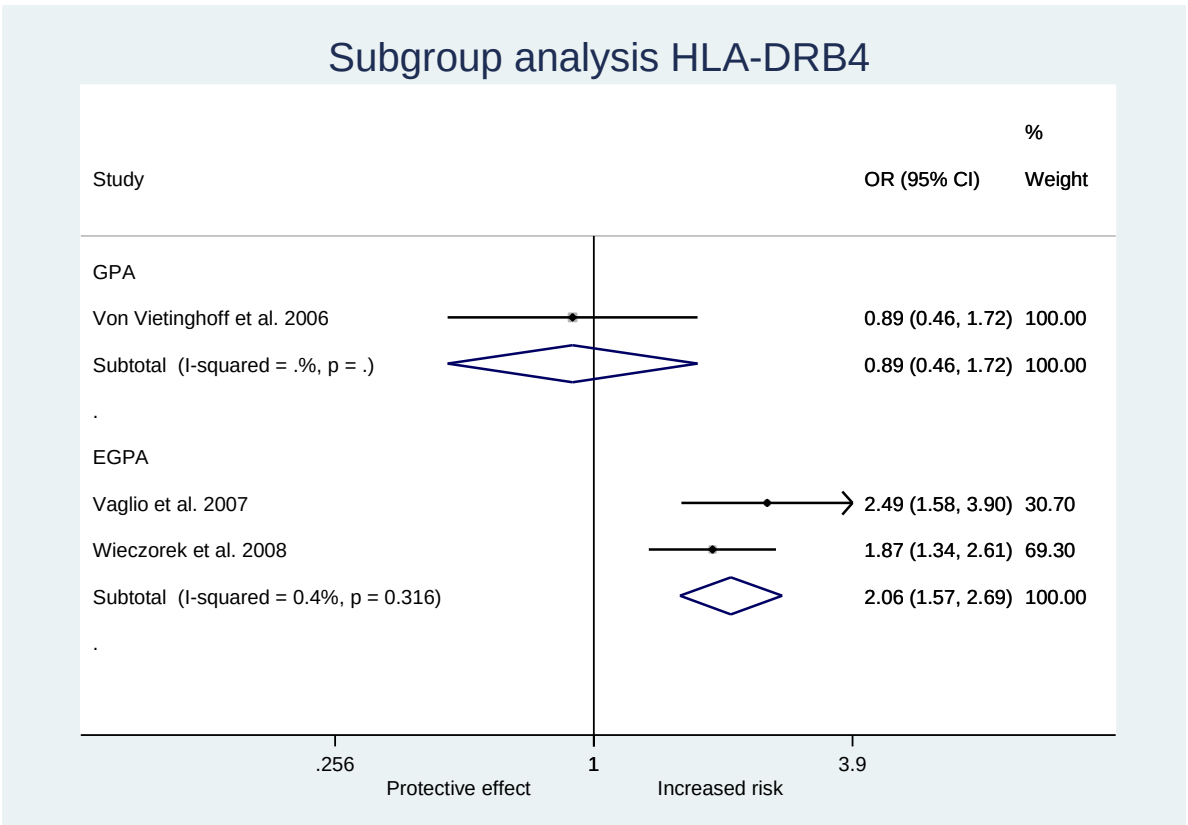
Subgroup analysis HLA-DRB1*16



References: [31], [18], [33]**

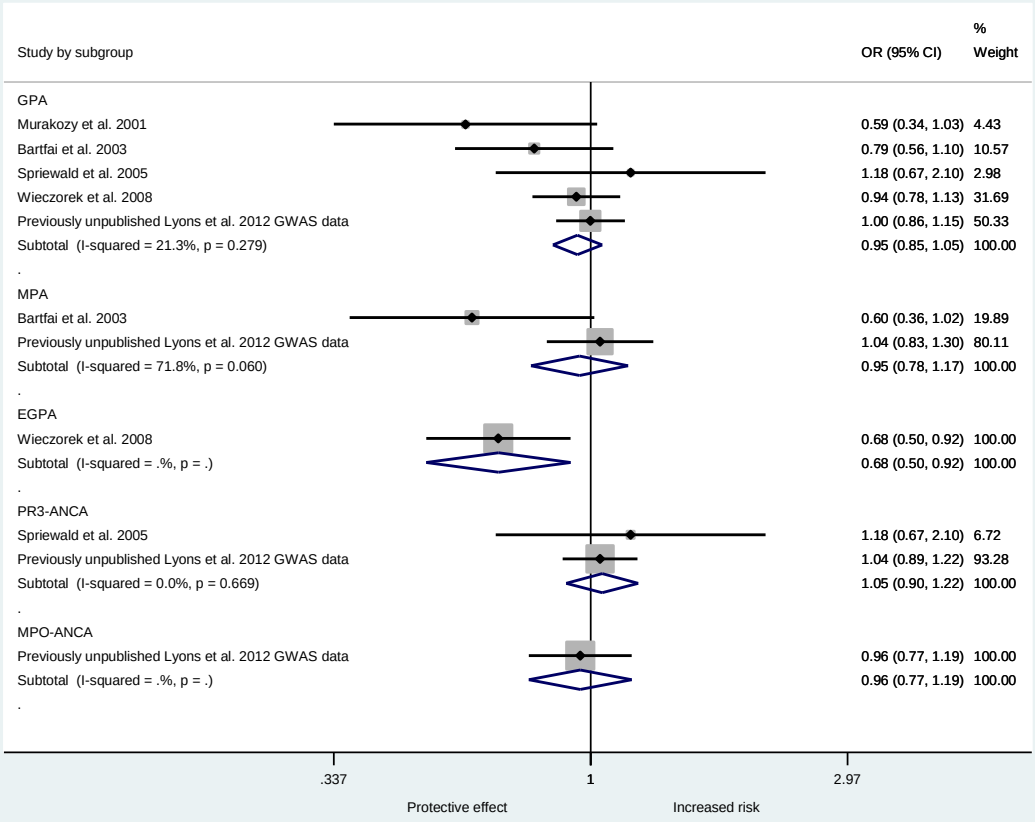


References: [18], [35], [29]



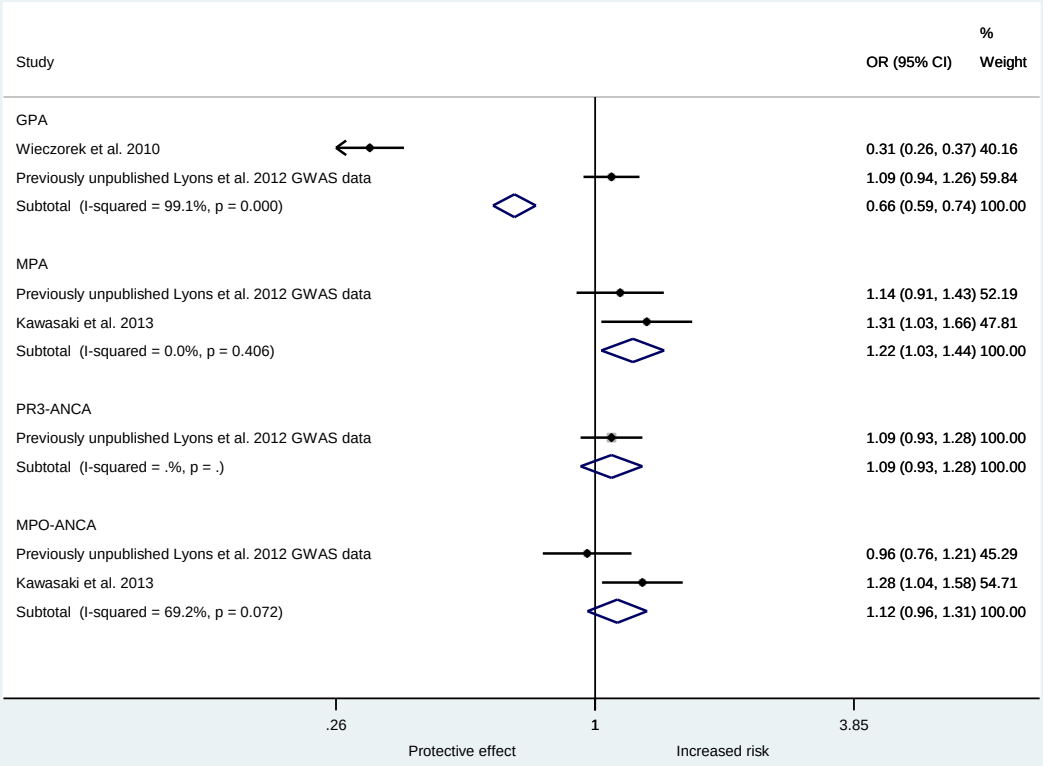
References: [18], [35], [29]

Subgroup analysis IL-10 rs1800896 (G)



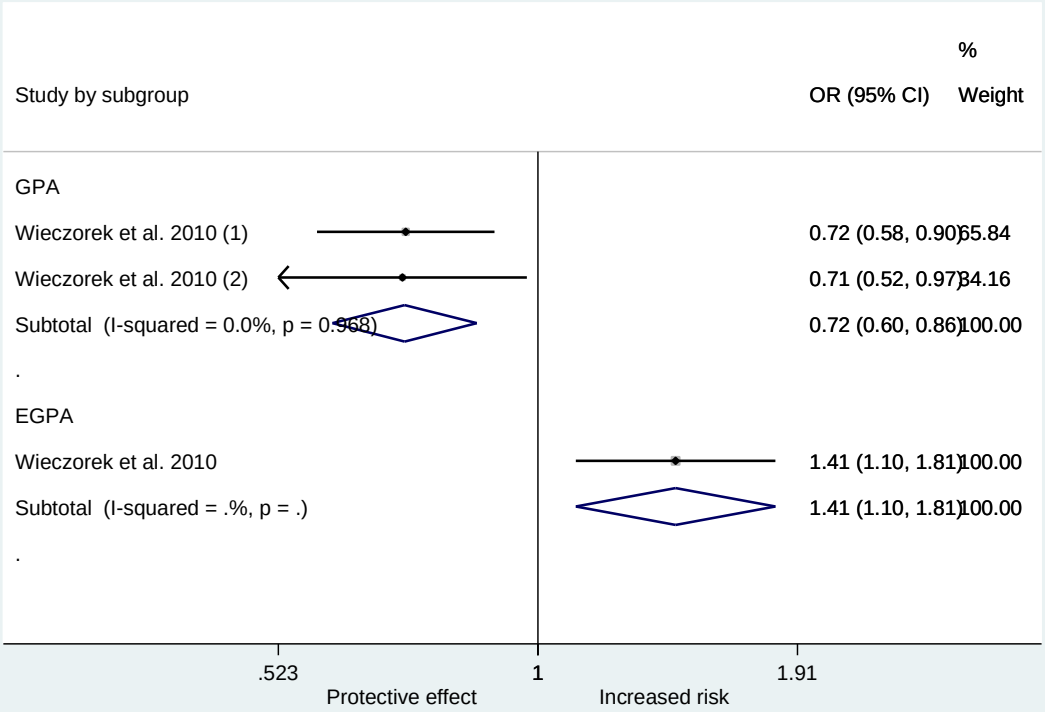
References: [42], [43], [31], [41], [3]

Subgroup analysis IRF5 rs10954213 (G)



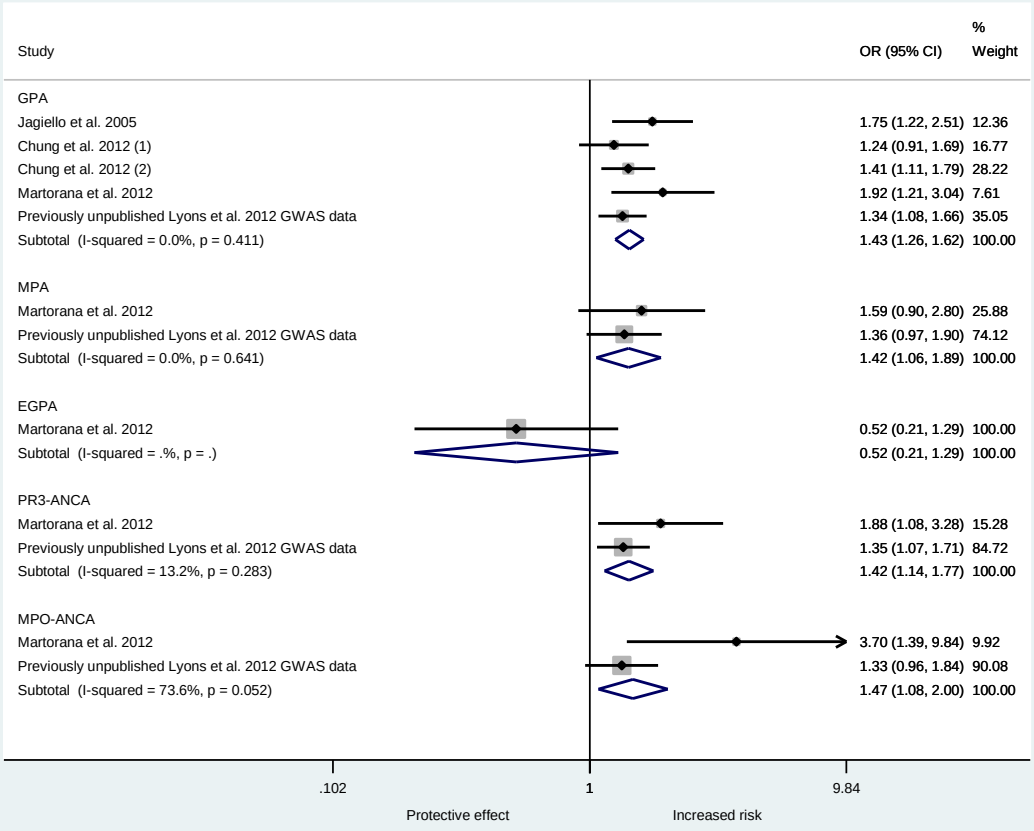
References: [44], [3], [45]

Subgroup analysis LEPR rs8179183 (C)



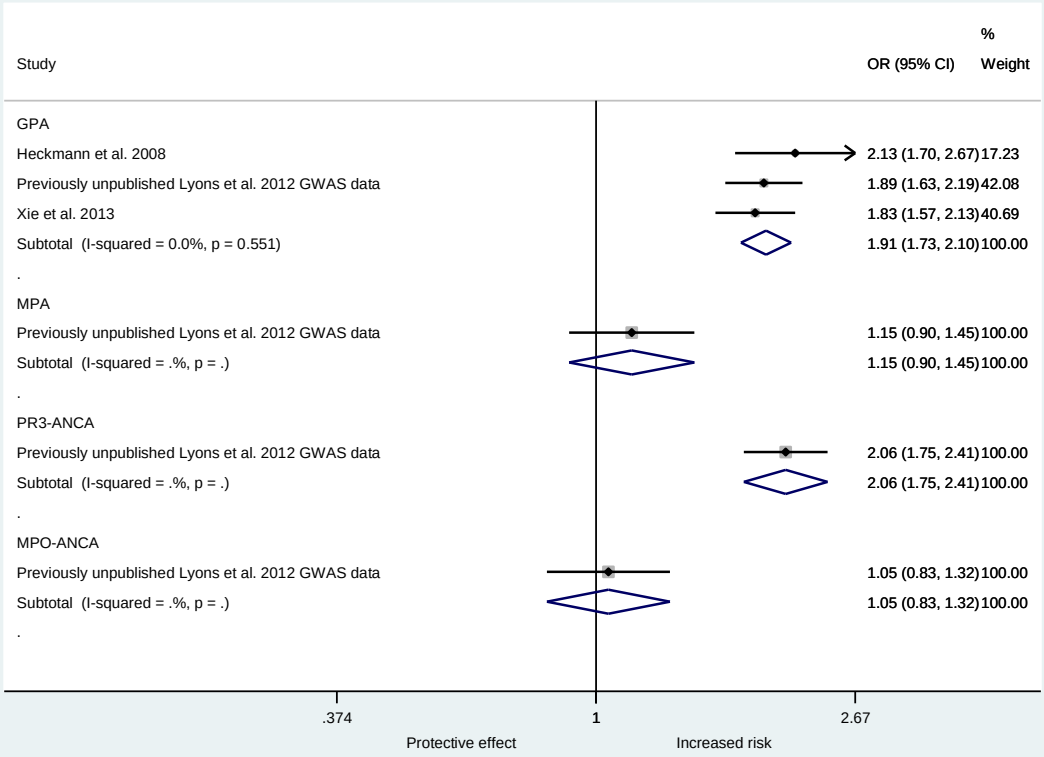
References: [15]**

Subgroup analysis PTPN22 rs2476601 (A)



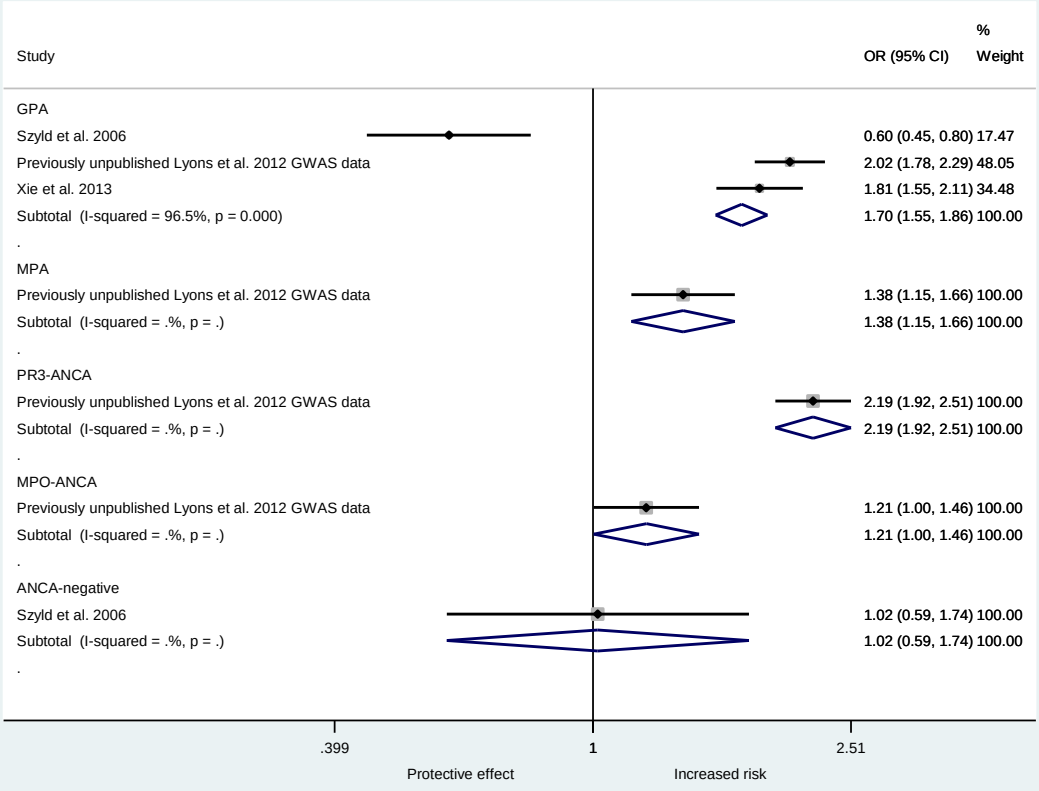
References: [50], [2]**, [51], [3]

Subgroup analysis RING1/RXRB rs213213 (A)



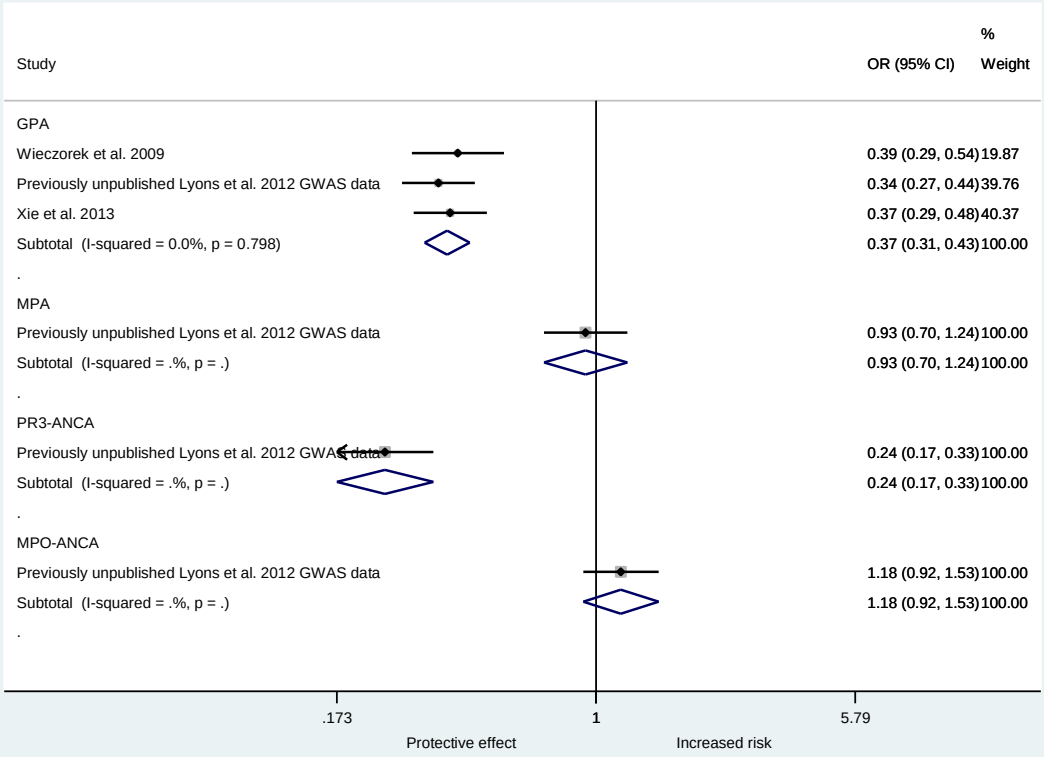
References: [24], [3], [25]

Subgroup analysis RXRB rs6531 (C)



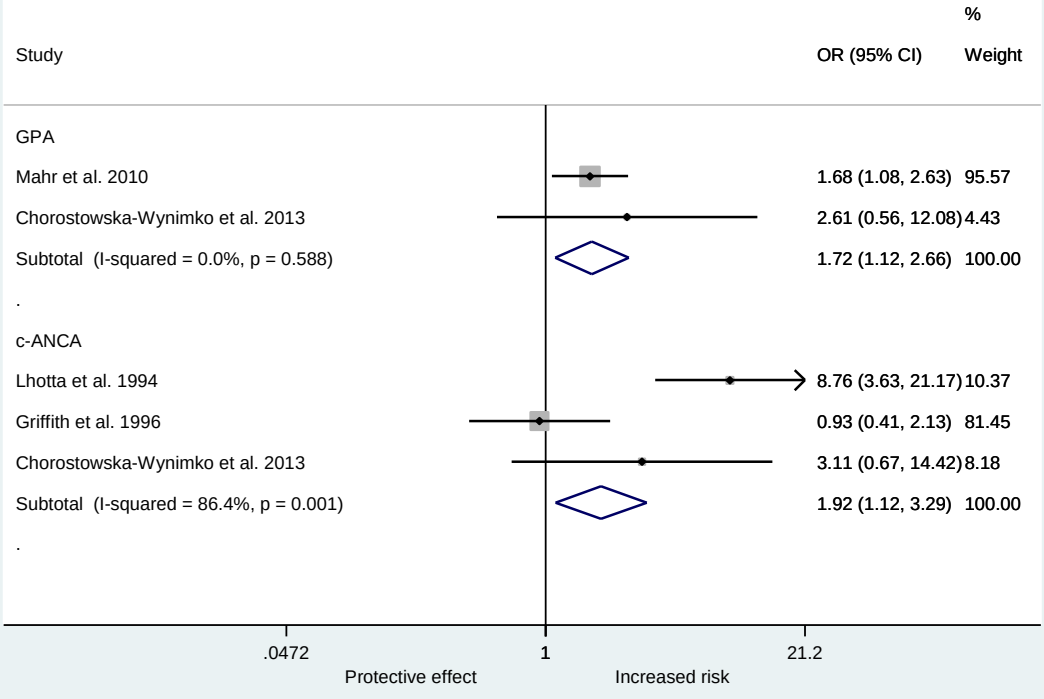
References: [52], [3], [25]

Subgroup analysis RXRB rs9277935 (T)



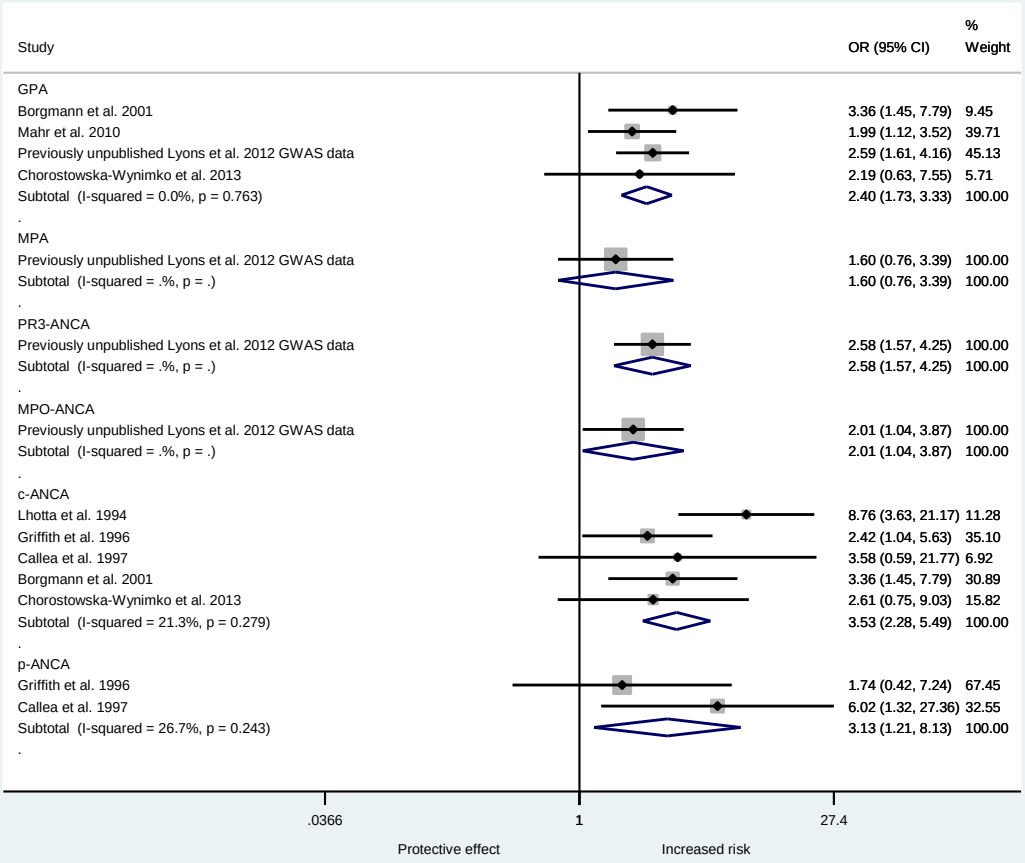
References: [53], [3], [25]

Subgroup analysis SERPINA1 S allele



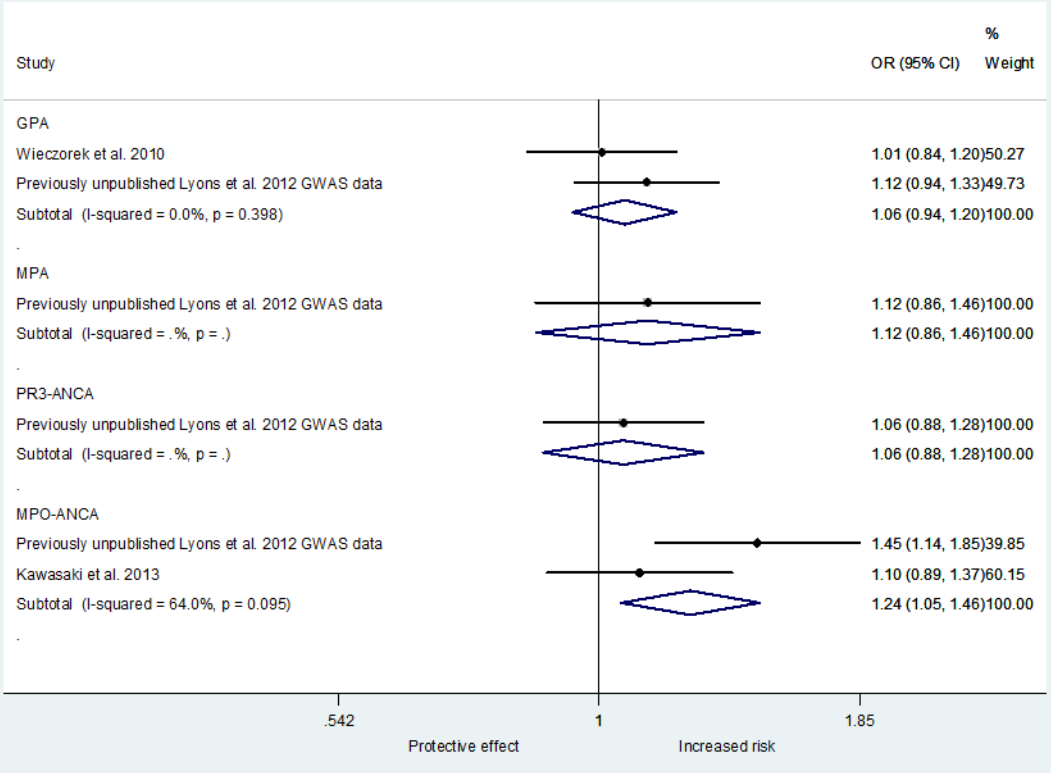
References: [54], [55], [56], [58]

Subgroup analysis SERPINA1 Z allele



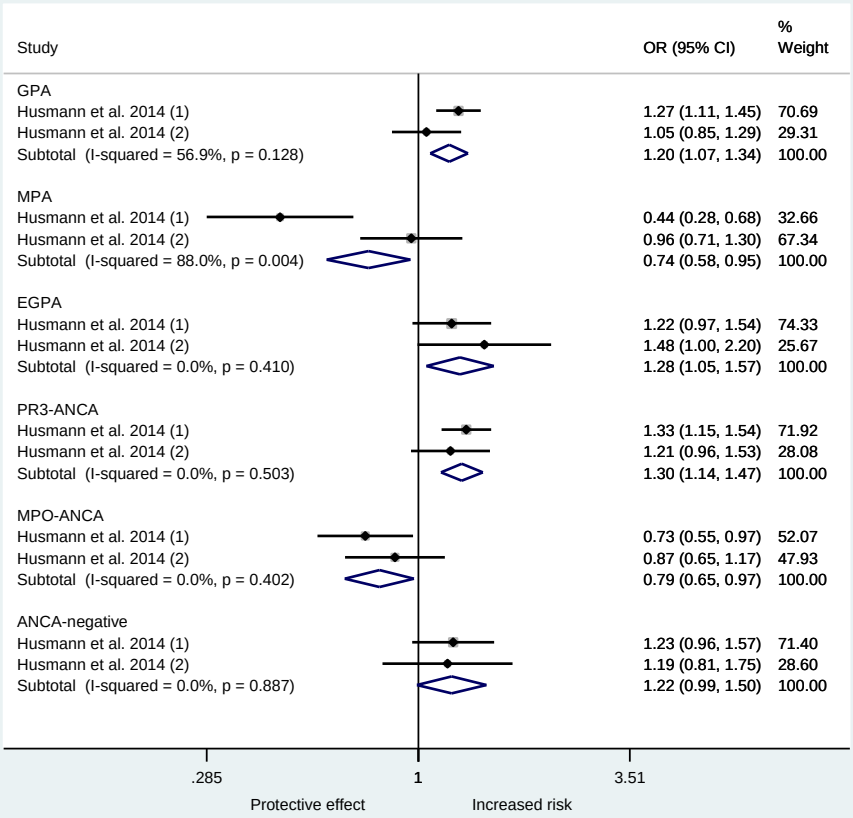
References: [54], [55], [59], [60], [56], [3], [58]

Subgroup analysis STAT4 rs7574865 (T)



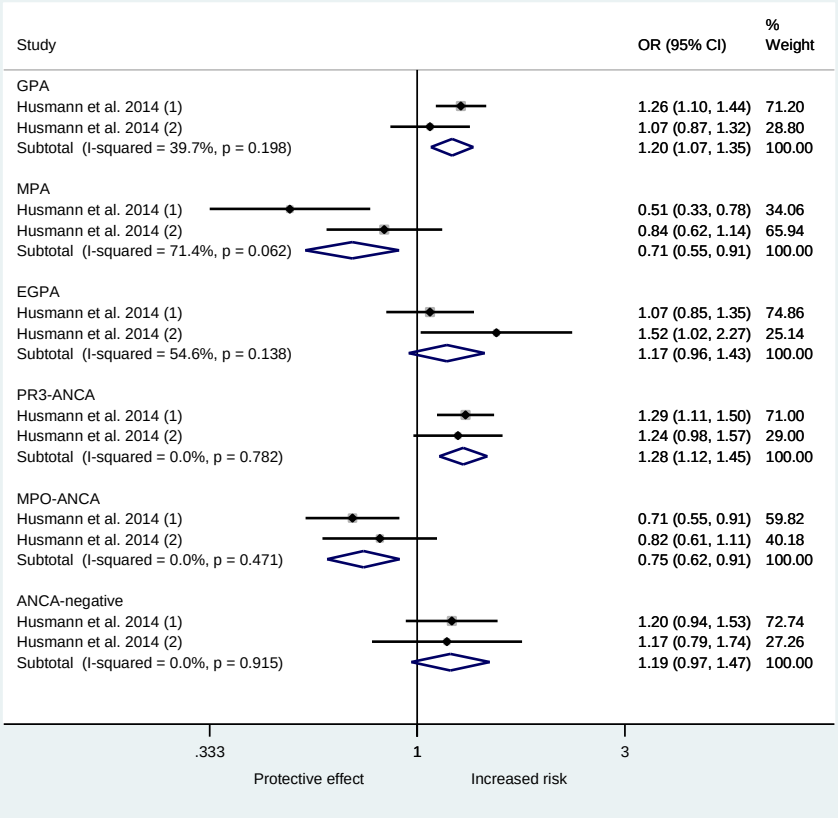
References: [44], [45]

Subgroup analysis TLR9 rs352162 (T)

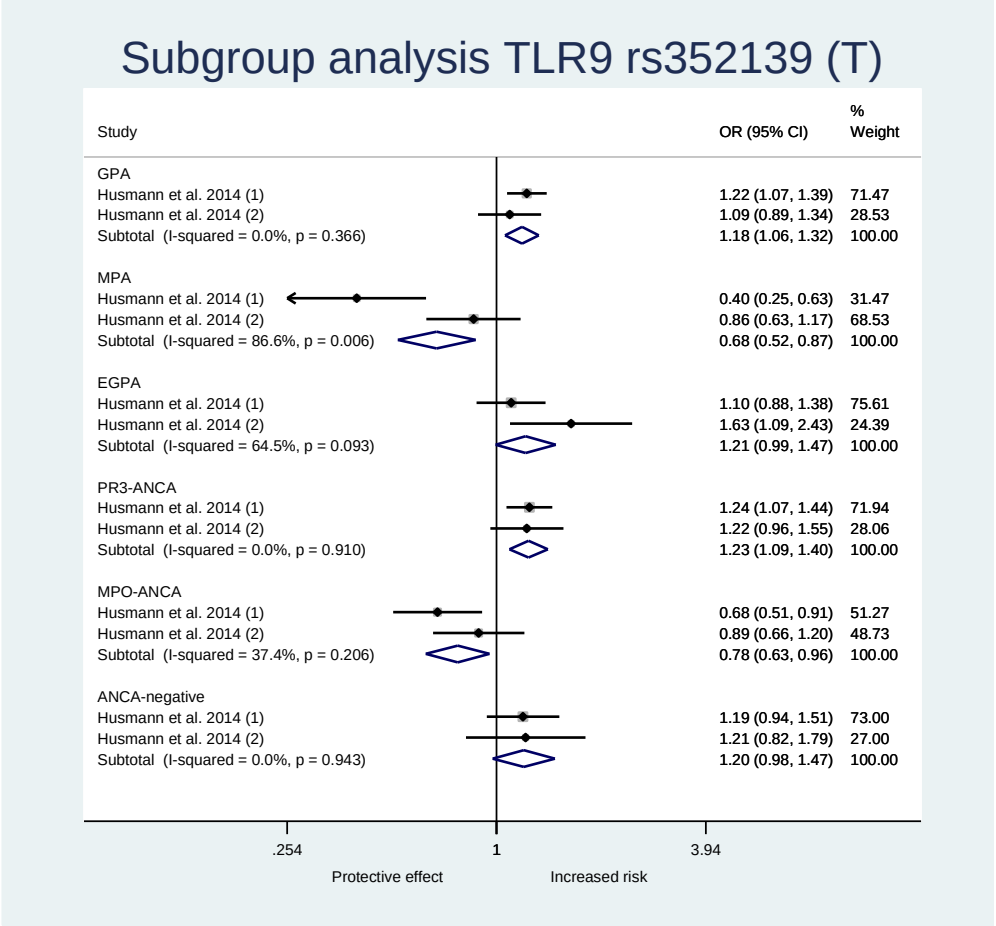


References: [40]**

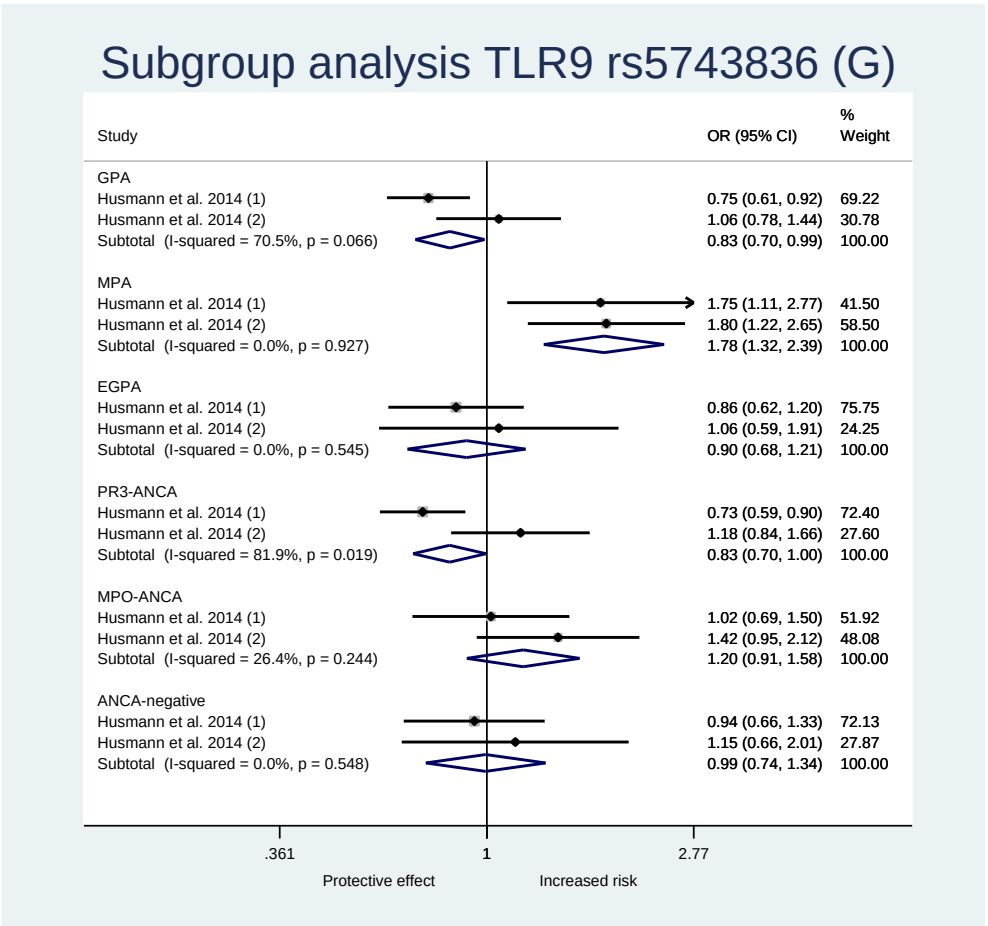
Subgroup analysis TLR9 rs352140 (T)



References: [40]**



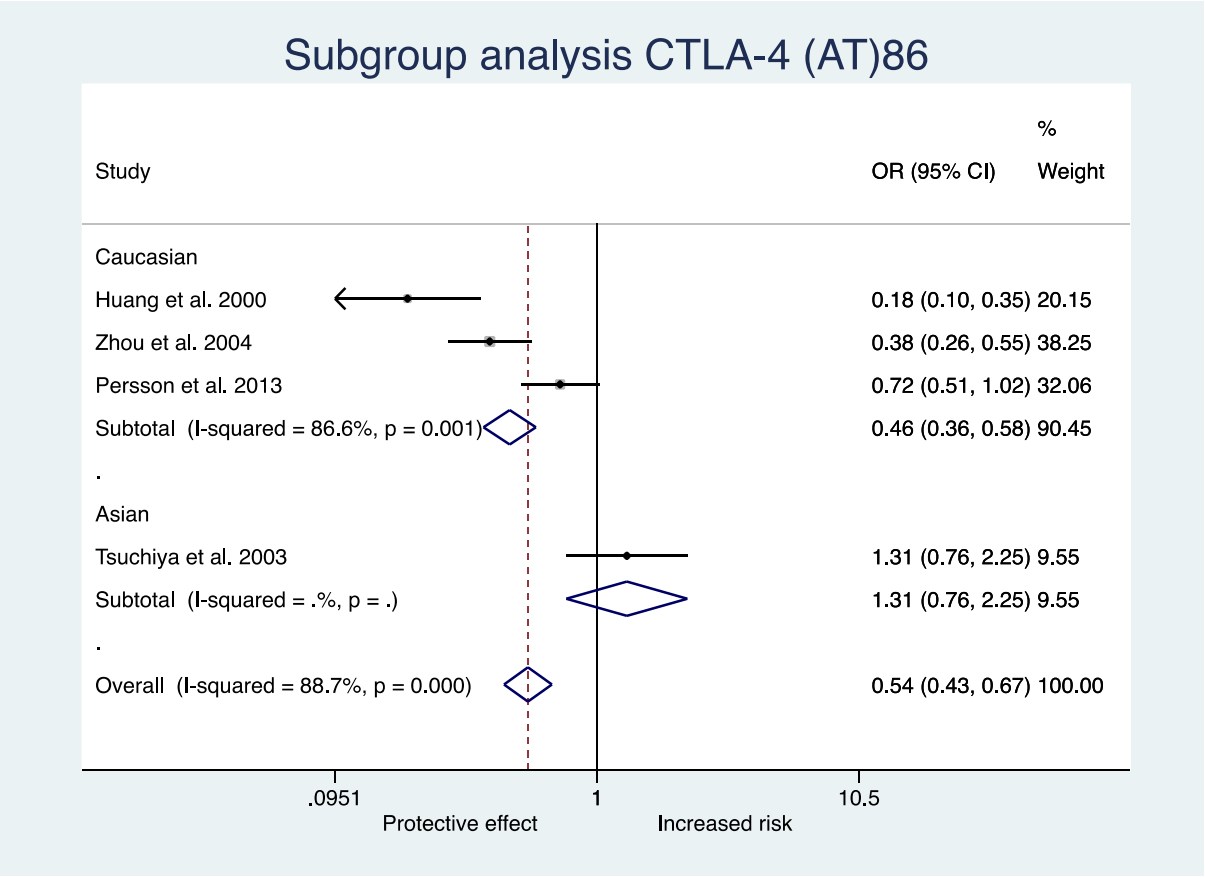
References: [40]**



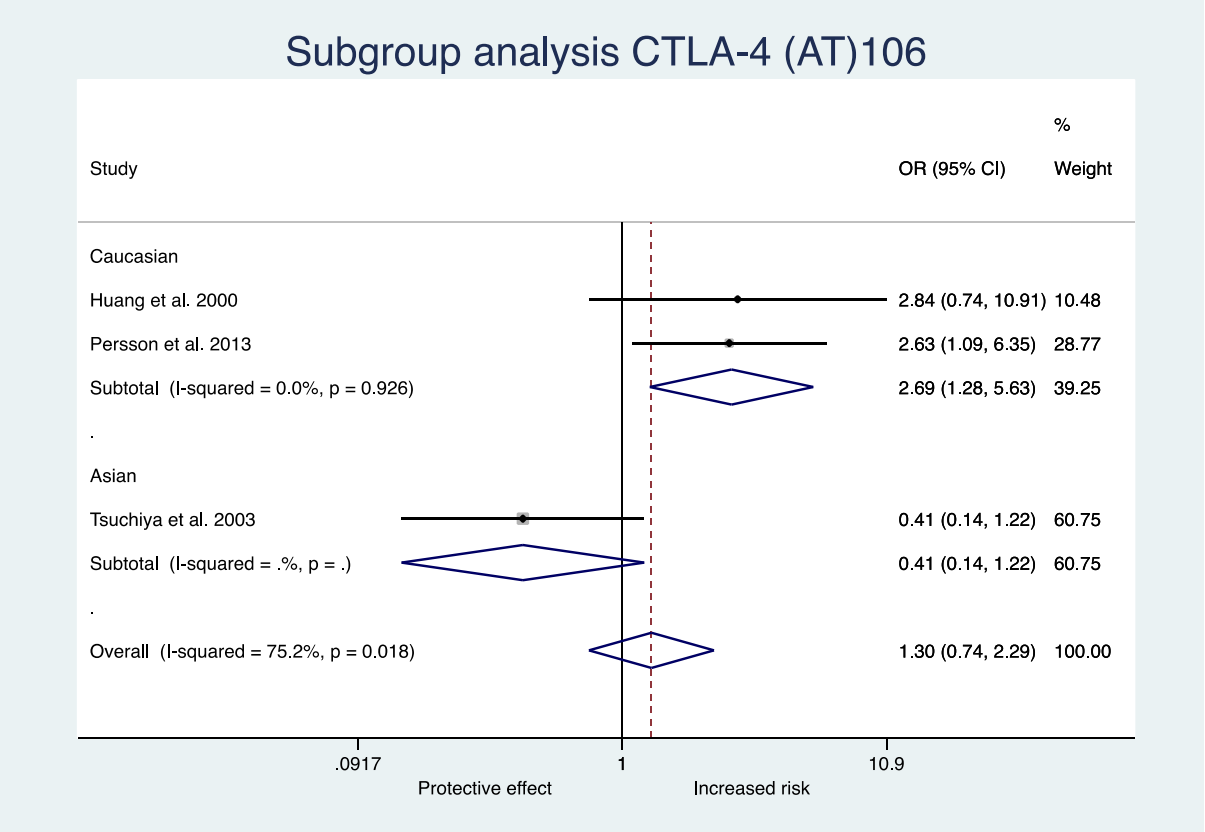
References: [40]**

**Two cohorts described in the same publication.
***Three cohorts described in the same publication.

Supplementary Figure S3. Forest plots by ethnic subgroups

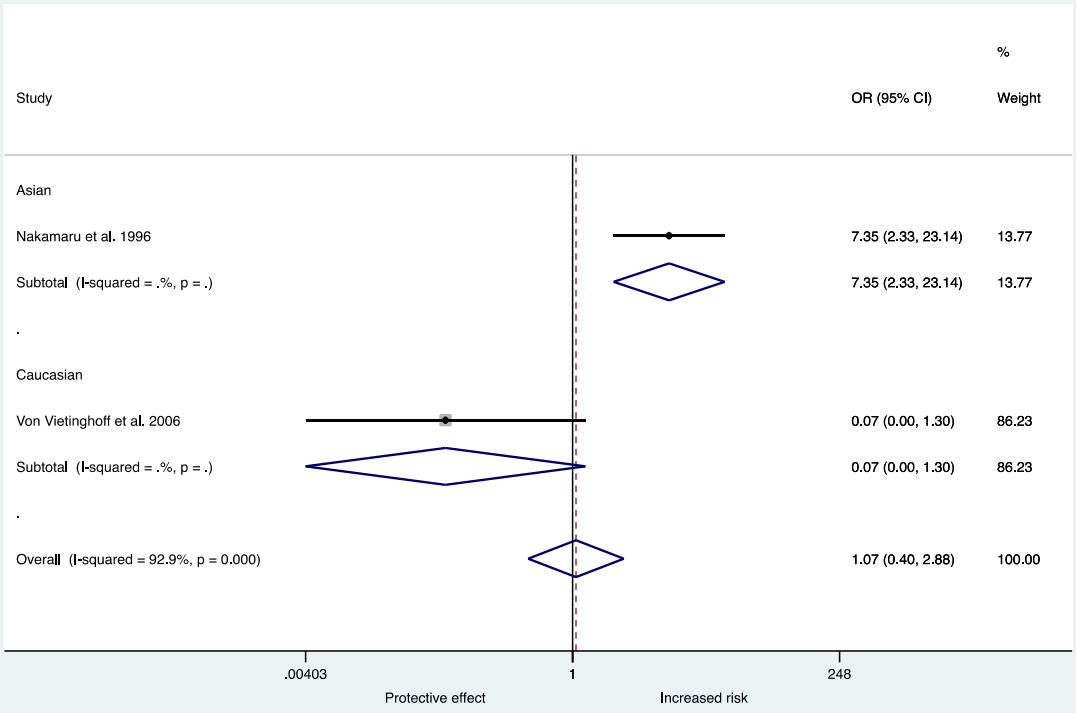


References; [4], [5], [6], [7]



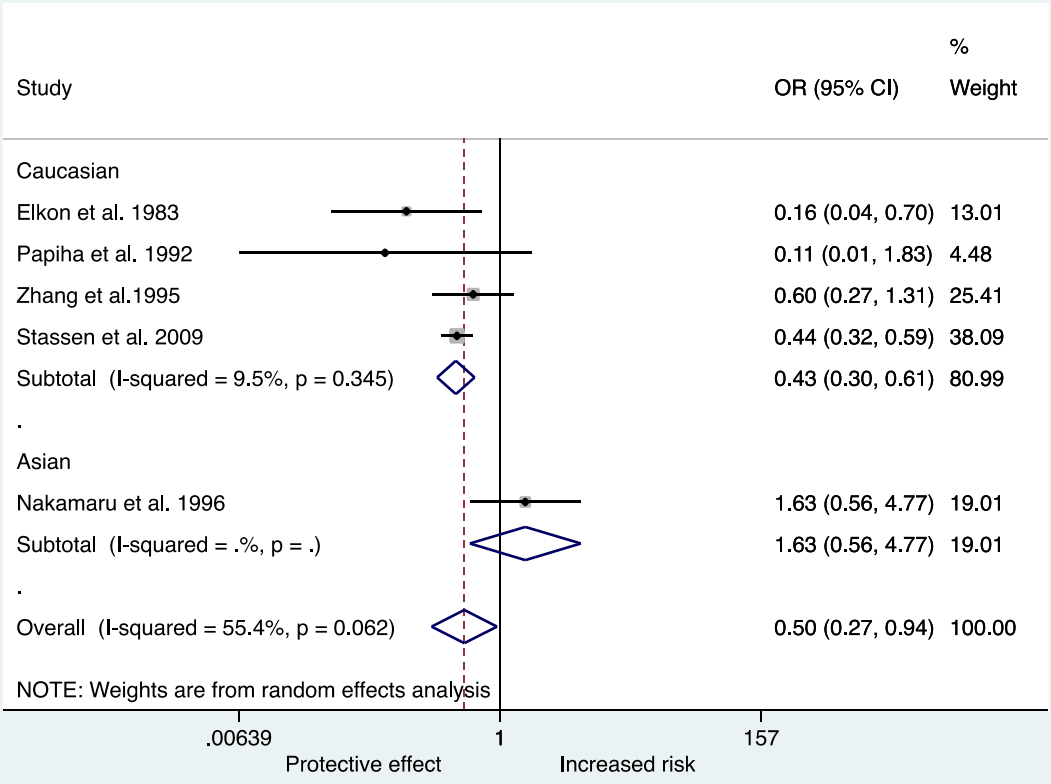
References: [4], [5], [7]

Subgroup analysis HLA-B55

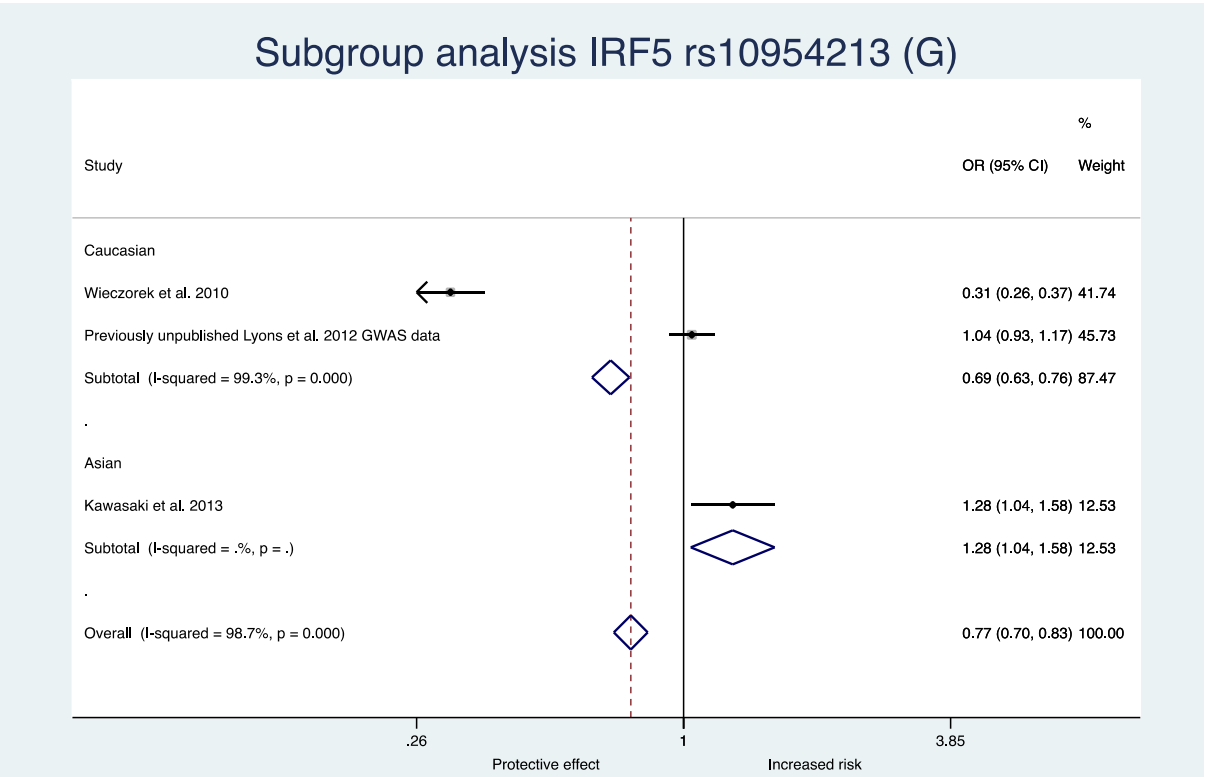


References: [20], [18]

Subgroup analysis HLA-DR6



References: [23], [32], [26], [20], [19]



References: [44], [3], [45]

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