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## EXTENDED REPORT

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

Chinar Rahmattulla,<sup>1</sup> Antien L Mooyaart,<sup>1</sup> Daphne van Hooven,<sup>1</sup> Jan W Schoones,<sup>2</sup> Jan A Bruijn,<sup>1</sup> Olaf M Dekkers,<sup>3,4,5</sup> European Vasculitis Genetics Consortium, Ingeborg M Bajema<sup>1</sup>

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<sup>1</sup>Department of Pathology, Leiden University Medical Centre, Leiden, The Netherlands

<sup>2</sup>Walaeus Library, Leiden University Medical Centre, Leiden, The Netherlands

<sup>3</sup>Department of Clinical Epidemiology, Leiden University Medical Centre, Leiden, The Netherlands

<sup>4</sup>Department of Medicine, Division Endocrinology, Leiden University Medical Centre, Leiden, The Netherlands

<sup>5</sup>Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

## Correspondence to

Chinar Rahmattulla, Department of Pathology, L1-Q (PO-107), Leiden University Medical Centre, PO Box 9600, Leiden 2300 RC, The Netherlands; C.Rahmattulla@lumc.nl

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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*, *RING11*, *RXR*, *RXR*, *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.

characteristics,<sup>3,4</sup> leading to debate regarding whether these subtypes are part of a single disease spectrum or represent distinct diseases.<sup>5–7</sup> To date, the prevailing concept of a single disease spectrum has resulted in similar treatment strategies in clinical trials<sup>8–10</sup> and to suggestions that genetic studies should consider the subtypes together.<sup>11</sup> 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.<sup>12</sup> Evidence for the role of genetic factors comes from differences in the prevalence of AAV between ethnic groups,<sup>13</sup> familial association studies<sup>14</sup> and genetic associations studies including the two genome-wide association studies (GWAS) performed in AAV.<sup>15,16</sup>

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.<sup>17</sup> These factors are especially relevant in complex diseases such as AAV.<sup>18</sup>

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.<sup>15</sup> Moreover, we conducted stratified analyses based on clinical diagnosis and ANCA serotype to investigate whether these different AAV subtypes have distinct genetic backgrounds.

## 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.<sup>1,2</sup> 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

## 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,<sup>19</sup> American College of Rheumatology criteria,<sup>20</sup> European Medicines Agency algorithm,<sup>21</sup> 1998 Japanese criteria proposed by the Research Committee on Intractable Vasculitides, the Ministry of Health, Labour and Welfare of Japan,<sup>22</sup> 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*,<sup>23</sup> *LEPR*<sup>23</sup> and *TLR9*.<sup>24</sup> 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*<sup>15</sup> 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*<sup>16</sup> 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.<sup>25</sup> Because the HLA serotypes are not completely independent from the HLA alleles, the following HLA variants were collapsed in the analyses: *HLA-DRI*, *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.<sup>26</sup> Egger and Harbord tests were used to assess publication bias.<sup>27</sup> 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 V12 (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*<sup>15</sup> 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-1 $\beta$*  rs1143634, *IL-6* rs1800795, *IL-10* rs1800896, *IRF5* rs10954213, *PTPN22* rs2476601, *RING1/RXR* rs213213, *RXR* rs6531, *RXR* rs9277935, *STAT4* rs7574865, *SERPINA1* Z allele and *TNFA* 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 <sup>2</sup> (%) | 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) <sub>86</sub>      | 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)).

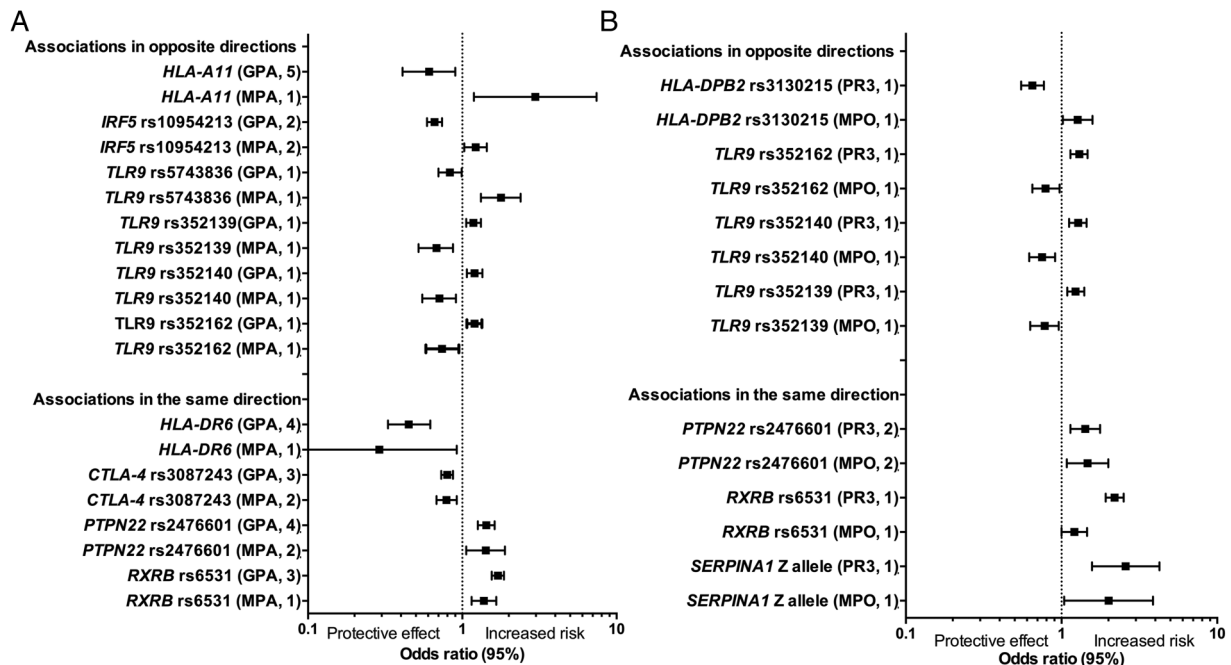
RING1/RXRB rs213213, RXRB rs6531 and RXRB rs9277935 were also significantly associated with AAV with pooled ORs of 1.71 (95% CI 1.57 to 1.86), 1.63 (95% CI 1.50 to 1.77) and 0.44 (95% CI 0.37 to 0.50), respectively.

### 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)<sub>86</sub> 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)<sub>86</sub>, *CTLA-4* (AT)<sub>106</sub> 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.<sup>15</sup> 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 *HLA-DPA1* rs9277341 to be associated with GPA.<sup>16</sup> *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,<sup>15</sup> 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 variants 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<sup>28 29</sup> and type 1 diabetes<sup>30 31</sup> and *PTPN22* rs2476601 in Crohn's disease,<sup>32–34</sup> Behçet's disease,<sup>35</sup> systemic lupus erythematosus<sup>36–38</sup> and giant cell arteritis.<sup>39 40</sup> These findings are in line with the fact that first-degree relatives of patients with AAV have an increased risk of other autoimmune diseases.<sup>41 42</sup> 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.<sup>43</sup> 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.<sup>15 16</sup> 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<sup>3</sup> and clinical outcomes.<sup>4</sup> The results of this meta-analysis indicate that these different AAV subtypes also have distinct genetic backgrounds, as previously shown in a GWAS.<sup>15</sup> 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.<sup>44</sup> 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.<sup>27</sup> To account for heterogeneity, random-effects models were performed where possible.<sup>25</sup> 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.

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## Online supplement

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

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## European Vasculitis Genetics Consortium authors and affiliations

Paul A. Lyons, Tim F. Rayner, Sapna Trivedi, Julia U. Holle, Richard A. Watts, David R.W. Jayne, Bo Baslund, Paul Brenchley, Annette Bruchfeld, Afzal N. Chaudhry, Jan Willem Cohen Tervaert, Conleth Feighery, Wolfgang L. Gross, Loic Guillevin, Iva Gunnarsson, Lorraine Harper, Zdenka Hrušková, Mark A. Little, Davide Martorana, Thomas Neumann, Sophie Ohlsson, Sandosh Padmanabhan, Charles D. Pusey, Alan D. Salama, Jan-Stephan F. Sanders, Caroline O. Savage, Mårten Segelmark, Coen A Stegeman, Vladimír Tesař, Augusto Vaglio, Stefan Wieczorek, Benjamin Wilde, Jochen Zwerina, Andrew J. Rees and Kenneth G.C. Smith.

From the Cambridge Institute for Medical Research (P.A.L., T.F.R., S.T., K.G.C.S.), and Department of Medicine (P.A.L., T.F.R., S.T., D.R.W.J., A.N.C., K.G.C.S.), University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 0XY, UK; Vasculitis and SLE service, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 2QQ (S.T., A.N.C., D.R.W.J., K.G.C.S.); Department of Rheumatology, University Hospital Schleswig-Holstein, Campus Luebeck, Luebeck, Germany (W.L.G.); Department of Rheumatology and Immunology, Klinikum Bad Bramstedt, Bad Bramstedt, Germany (J.U.H., W.L.G.); Department of Rheumatology, Ipswich Hospital NHS Trust, Heath Road, Ipswich, Suffolk, IP4 5PD, and Norwich Medical School, University of East Anglia, Norwich NR7 4TJ, UK (R.A.W.); Department of Rheumatology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark (B.B.); Cardiovascular Research, School of Biomedicine, University of Manchester, UK (P.B.); Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska University Hospital, Karolinska Institute, Stockholm, Sweden (A.B.); Department of Internal Medicine, Division of Clinical & Experimental Immunology, Cardiovascular Research Institute Maastricht, Maastricht University Medical Centre, Maastricht, The Netherlands (J.W.C.T., B.W.); Department of Immunology, Trinity College Dublin, Dublin 2, and St James's Hospital Dublin, Dublin 8, Ireland (C.F.); Hôpital Cochin, Université Paris Descartes, Sorbonne Paris Cité, France (L.G.); Department of Medicine, Unit of Rheumatology, Karolinska University Hospital, Karolinska Institute, Stockholm, Sweden (I.G.); School of Immunity and Infection, University of Birmingham, Edgbaston, Birmingham, UK (L.H., C.O.S.); Department of Nephrology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague, Prague, Czech Republic (Z.H., V.T.); UCL Centre for Nephrology, Royal Free Hospital, London, UK (M.L., A.D.S.); Unit of Molecular Genetics (D.M.) and Unit of Nephrology (A.V.), University Hospital of Parma, Via Gramsci 14, 43126 Parma, Italy; Department of Internal Medicine III, University Hospital Jena, Germany (T.N.); Section of Nephrology, Department of Clinical Sciences, Lund University, Sweden (S.O., M.S.) and the Department of Medical and Health Sciences, Linköping University, Linköping, Sweden (M.S.); Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow G12 8TA, UK (S.P.); Renal Section, Department of Medicine, Imperial College London, London, UK (C.D.P., A.D.S.); Department of Internal

Medicine/Division of Nephrology, University of Groningen, University Medical Center Groningen, The Netherlands (J.F.S., C.A.S.); Human Genetics, Ruhr-University, Bochum, Germany (S.W.); Department of Internal Medicine 3, University of Erlangen-Nuremberg, Germany, and currently Ludwig Boltzmann Institute of Osteology at Hanusch Hospital of WGKK and AUVA Trauma Centre Meidling, 1st Medical Department Hanusch Hospital, Vienna, Austria (J.Z.); and Clinical Institute of Pathology, Medical University of Vienna, Vienna, Austria (A.J.R.).

**Supplementary Table S1. Literature search strategies**

| Database      | Search Strategy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| <b>PubMed</b> | <p><i>Two strategies:</i></p> <p><u>1. AAV and genes</u><br/> ("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])</p> <p><u>2. Vasculitis and genes (excluding AAV)</u><br/> (("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</p> |

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| <b>Embase</b> | <p><i>Two strategies:</i></p> <p><u>1. AAV and genes</u></p> <p>(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</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

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|                       | <p>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/)</p> <p><u>2. Vasculitis and genes (excluding AAV)</u><br/>         ((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/))</p> |
| <b>Web of Science</b> | <p><i>Two strategies:</i></p> <p><u>1. AAV and genes</u><br/>         TS=((("ANCA-associated vasculitis" OR "ANCA associated vasculitis" OR</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

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|  | <p>"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))</p> <p><u>2. Vasculitis and genes (excluding AAV)</u></p> <p>(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)))</p> |
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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       |
| <b>CD226<br/>rs763361<br/>(T)</b>   | Wieczorek et al. 2009 <sup>1**</sup>                            | 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 <sup>2**</sup>                                | 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 <sup>3</sup> | 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) |
| <b>CTLA-4<br/>(AT)<sub>86</sub></b> | Huang et al. 2000 <sup>4</sup>                                  | 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        |
| <b>CTLA-4 (AT)<sub>102</sub></b> | Tsuchiya et al. 2003 <sup>5</sup> | 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 <sup>6</sup>     | 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 <sup>7</sup>  | 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)  |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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 <sup>7</sup>  | 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)  |
| <b>CTLA-4 (AT)<sub>104</sub></b> | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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        |
| <b>CTLA-4 (AT)<sub>106</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)  |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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)  |
| <b>CTLA-4 (AT)<sub>108</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)  |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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)  |
| <b>CTLA-4 (AT)<sub>110</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)  |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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          |
| <b>CTLA-4 (AT)<sub>116</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)    |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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)   |
| <b>CTLA-4 (AT)<sub>118</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)   |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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)    |
| <b>CTLA-4 (AT)<sub>122</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)    |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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          |
| <b>CTLA-4 (AT)<sub>124</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)    |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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)   |
| <b>CTLA-4 (AT)<sub>126</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)    |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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)    |
| <b>CTLA-4 (AT)<sub>128</sub></b> | Persson et al. 2013 <sup>7</sup>  | 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)    |
|                                  | Huang et al. 2000 <sup>4</sup>    | 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 <sup>5</sup> | 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       |
| <b>CTLA-4<br/>rs231775<br/>(G)</b>  | Persson et al. 2013 <sup>7</sup>                                | 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) |
|                                     | Slot et al. 2008 <sup>8</sup>                                   | Case-Control        | The Netherlands | 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 <sup>9</sup>                                 | 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 <sup>3</sup> | 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) |
| <b>CTLA-4<br/>rs3087243<br/>(A)</b> | Kamesh et al. 2009 <sup>9</sup>                                 | 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 <sup>2**</sup>                                | 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       |
| <b>FCAR</b><br><b>rs16986050</b><br><b>(G)</b>  | Previously unpublished Lyons et al. 2012 GWAS data <sup>3</sup> | 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) |
|                                                 | Kelley et al. 2011 <sup>10**</sup>                              | 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 <sup>3</sup> | 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) |
| <b>FCGR2A</b><br><b>rs1801274</b><br><b>(C)</b> | Edberg et al. 1997 <sup>11</sup>                                | 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 <sup>12</sup>                          | 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 <sup>13</sup>                                   | 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 <sup>5</sup>                               | 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       |
| <b>FCGR3A<br/>rs396991<br/>(G)</b> | Previously unpublished Lyons et al. 2012 GWAS data <sup>3</sup> | 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 <sup>7</sup>                                | 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) |
|                                    | Dijstelbloem et al. 1999 <sup>12</sup>                          | 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 <sup>5</sup>                               | 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) |
| <b>FCGR3B<br/>(NA1)</b>            | Dijstelbloem et al. 1999 <sup>12</sup>                          | 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 <sup>14</sup>                                   | 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 <sup>5</sup>                               | 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 <sup>10</sup>                                | 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       |
| <b>GHSR</b><br><b>rs509035</b><br><b>(A)</b> | Wieczorek et al. 2010 <sup>15**</sup><br><br>Previously unpublished Lyons et al. 2012 GWAS data <sup>3</sup> | 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) |
|                                              |                                                                                                              | 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) |
| <b>GHSR</b><br><b>rs519384</b><br><b>(A)</b> | Wieczorek et al. 2010 <sup>15**</sup>                                                                        | 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) |
| <b>GHSR</b><br><b>rs572169</b><br><b>(A)</b> | Wieczorek et al. 2010 <sup>15**</sup>                                                                        | 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) |
| <b>HLA-A1</b>                                | Strimlan et al. 1978 <sup>16</sup>                                                                           | 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 <sup>17</sup>                                                                              | 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 <sup>18</sup>                                                                    | 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       |
| <b>HLA-A2</b> | Stassen et al. 2009 <sup>19</sup>         | 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) |
|               | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany         | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients)                       | NR                                                           | 0.87 (0.48 – 1.58) |
| <b>HLA-A3</b> | Stassen et al. 2009 <sup>19</sup>         | 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) |
|               | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>18</sup> | 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           |
| <b>HLA-A9</b>  | Stassen et al. 2009 <sup>19</sup>  | 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)     |
|                | Strimlan et al. 1978 <sup>16</sup> | 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 <sup>21</sup>     | Case-Control  | USA             | Clinical and histological criteria | Ethnically matched subjects                 | 31/418           | GPA (all patients)                       | NR                                                           | 69.13 (3.28 – 456.19)  |
| <b>HLA-A10</b> | Stassen et al. 2009 <sup>19</sup>  | 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)     |
|                | Strimlan et al. 1978 <sup>16</sup> | 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 <sup>21</sup>     | Case-Control  | USA             | Clinical and histological criteria | Ethnically matched subjects                 | 31/418           | GPA (all patients)                       | NR                                                           | 69.13 (3.28 – 1456.19) |
| <b>HLA-A11</b> | Stassen et al. 2009 <sup>19</sup>  | 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)     |
|                | Strimlan et al. 1978 <sup>16</sup> | 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 <sup>17</sup>    | 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       |
| <b>HLA-A24</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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 <sup>22</sup>   | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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) |
|                | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany         | ACR and CHCC criteria                        | Geographically matched healthy blood donors            | 51/51            | GPA (all patients)                       | NR                                                           | 1.81 (0.51 – 6.37) |
| <b>HLA-A25</b> | Murty et al. 1991 <sup>17</sup>           | 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        |
| <b>HLA-A26</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | Case-Control  | Germany         | ACR and CHCC criteria                        | Geographically matched healthy blood donors            | 51/51            | GPA (all patients)                       | NR                                                           | 2.09 (0.61 – 7.16)  |
|                | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>22</sup>   | Case-Control  | Greece          | Histologically proven AAV                    | Geographically and ethnically matched healthy subjects | 23/405           | MPA (all patients)                       | NR                                                           | 2.49 (1.01 – 6.18)  |
| <b>HLA-A28</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | Case-Control  | Germany         | ACR and CHCC criteria                        | Geographically matched healthy blood donors            | 51/51            | GPA (all patients)                       | NR                                                           | 0.39 (0.07 – 2.05)  |
|                | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>19</sup>         | 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)  |
| <b>HLA-A29</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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        |
| <b>HLA-A30</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 0.66 (0.11 – 4.04)  |
|                | Murty et al. 1991 <sup>17</sup>           | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 2.02 (0.18 – 22.63) |
| <b>HLA-A31</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 0.33 (0.03 – 3.20)  |
| <b>HLA-A32</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>18</sup> | 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       |
| <b>HLA-B5</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>19</sup>         | 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) |
| <b>HLA-B7</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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) |
| <b>HLA-B8</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>21</sup>            | 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 <sup>23</sup>           | 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 <sup>17</sup>           | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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)  |
| <b>HLA-B12</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>19</sup>         | 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)  |
| <b>HLA-B13</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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)  |
| <b>HLA-B14</b> | Strimlan et al. 1978 <sup>16</sup>        | 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         |
| <b>HLA-B15</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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)   |
|                | Von Vietinghoff et al. 2006 <sup>18</sup> | 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 <sup>19</sup>         | 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)   |
| <b>HLA-B18</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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        |
| <b>HLA-B27</b> | Strimlan et al. 1978 <sup>16</sup>        | 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 <sup>17</sup>           | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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) |
| <b>HLA-B35</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>18</sup> | 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 <sup>19</sup>         | 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)  |
| <b>HLA-B37</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | 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 <sup>19</sup>         | 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)   |
| <b>HLA-B39</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany         | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients)                       | NR                                                           | 0.33 (0.01 – 8.20)   |
| <b>HLA-B40</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | 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 <sup>19</sup>         | 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)   |
| <b>HLA-B44</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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 <sup>18</sup> | 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        |
| <b>HLA-B49</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 2.02 (0.18 – 22.63) |
| <b>HLA-B51</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 0.61 (0.19 – 1.92)  |
| <b>HLA-B55</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 0.07 (0.00 – 1.30)  |
| <b>HLA-B57</b> | Murty et al. 1991 <sup>17</sup>           | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 51/51            | GPA (all patients) | NR                    | 1.00 (0.06 – 16.21) |
| <b>HLA-B60</b> | Murty et al. 1991 <sup>17</sup>           | 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       |
| <b>HLA-B62</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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) |
|                | Murty et al. 1991 <sup>17</sup>           | 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 <sup>20</sup>        | 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) |
| <b>HLA-Cw1</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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) |
| <b>HLA-Cw3</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 52/51            | GPA (all patients) | NR                    | 0.98 (0.24 – 4.03) |
|                | Nakamaru et al. 1996 <sup>20</sup>        | 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 <sup>18</sup> | Case-Control  | Germany     | ACR and CHCC criteria                        | Geographically matched healthy blood donors | 52/51            | GPA (all patients) | NR                    | 1.32 (0.62 – 2.81) |
| <b>HLA-Cw7</b> | Nakamaru et al. 1996 <sup>20</sup>        | 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       |
| <b>HLA-DPA1 rs9277341 (C)</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | Case-Control        | Germany     | ACR and CHCC criteria         | Geographically matched healthy blood donors | 52/51            | GPA (all patients)          | NR                                                           | 1.10 (0.62 – 1.96) |
|                               | Heckmann et al. 2008 <sup>24</sup>        | 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 <sup>25**</sup>           | 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) |
| <b>HLA-DPB1*0101</b>          | Zhang et al. 1995 <sup>26</sup>           | 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) |
| <b>HLA-DPB1*0201</b>          | Jagiello et al. 2004 <sup>27</sup>        | 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) |
|                               | Jagiello et al. 2004 <sup>27</sup>        | 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 <sup>28</sup>        | 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 <sup>24</sup>        | 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 <sup>29</sup>       | 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       |
| <b>HLA-DPB1*0301</b> | Zhang et al. 1995 <sup>26</sup>     | 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 <sup>27</sup>  | 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 <sup>24</sup>  | 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 <sup>29</sup> | 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 <sup>30**</sup>  | 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) |
| <b>HLA-DPB1*0401</b> | Zhang et al. 1995 <sup>26</sup>     | 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 <sup>27</sup>  | 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 <sup>24</sup>  | 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 <sup>29</sup> | 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 <sup>30**</sup>  | 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)  |
|                      | <b>HLA-DPB1*0402</b>                | 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 <sup>27</sup>  | 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 <sup>24</sup>  | 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 <sup>29</sup> | Case-Control  | Germany | ACR criteria                  | Geographically matched healthy subjects                    | 102/369          | EGPA (all patients)            | NR                                                           | 1.15 (0.75 – 1.77)  |
| <b>HLA-DPB1*0501</b> | Zhang et al. 1995 <sup>26</sup>     | 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 <sup>27</sup>  | 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)  |
|                      | <b>HLA-DPB1*0601</b>                | 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        |
| <b>HLA-DPB1*0901</b>          | Jagiello et al. 2004 <sup>27</sup>                              | 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)  |
|                               | Zhang et al. 1995 <sup>26</sup>                                 | 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)  |
| <b>HLA-DPB2 rs3130215 (A)</b> | Jagiello et al. 2004 <sup>27</sup>                              | 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) |
|                               | Heckmann et al. 2008 <sup>24</sup>                              | 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 <sup>3</sup> | 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)  |
| <b>HLA-DQB1*02</b>            | Xie et al. 2013 <sup>25</sup>                                   | 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)  |
|                               | Spriewald et al. 2005 <sup>31</sup>                             | 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 <sup>18</sup>                       | Case-Control        | Germany     | ACR and CHCC criteria                                    | Geographically matched healthy blood donors | 51/50            | GPA (all patients)          | NR                                                           | 0.85 (0.41 – 1.77)  |
| <b>HLA-DQB1*0302</b>          | Zhang et al. 1995 <sup>26</sup>                                 | 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         |
| <b>HLA-DQB1*0303</b> | Spriewald et al. 2005 <sup>31</sup>       | 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)   |
|                      | Zhang et al. 1995 <sup>26</sup>           | 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)   |
| <b>HLA-DQB1*04</b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>28</sup>        | 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)   |
|                      | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | Case-Control  | Germany | ACR and CHCC criteria  | Geographically matched healthy blood donors | 51/50            | GPA (all patients)          | NR                                                           | 1.49 (0.24 – 9.08)   |
| <b>HLA-DQB1*0501</b> | Zhang et al. 1995 <sup>26</sup>           | 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)   |
| <b>HLA-DQB1*0602</b> | Spriewald et al. 2005 <sup>31</sup>       | 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)   |
|                      | Zhang et al. 1995 <sup>26</sup>           | 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 <sup>31</sup>       | 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       |
| <b>HLA-DQ7</b> | Zhang et al. 1995 <sup>26</sup>           | 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 <sup>22</sup>   | Case-Control  | Greece  | Histologically proven AAV          | Geographically and ethnically matched healthy subjects | 23/405           | MPA (all patients)                   | NR                                                           | 0.66 (0.34 – 1.30) |
| <b>HLA-DR1</b> | Spriewald et al. 2005 <sup>31</sup>       | 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) |
|                | Elkon et al. 1983 <sup>23</sup>           | 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 <sup>32</sup>          | 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 <sup>26</sup>           | 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 <sup>5</sup>         | 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 <sup>31</sup>       | 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 <sup>18</sup> | 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       |
| <b>HLA-DR2</b> | Wieczorek et al. 2008 <sup>29</sup> | 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 <sup>19</sup>   | 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 <sup>33</sup>       | Case-Control  | USA (96 Caucasians 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 <sup>34</sup>       | 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) |
|                | Elkon et al. 1983 <sup>23</sup>     | 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 <sup>32</sup>    | 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 <sup>26</sup>     | 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       |
| HLA-DR3  | Nakamaru et al. 1996 <sup>20</sup>        | 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 <sup>19</sup>         | 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) |
|          | Elkon et al. 1983 <sup>23</sup>           | 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 <sup>32</sup>          | 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 <sup>26</sup>           | 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 <sup>22</sup>   | 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 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>29</sup>       | 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       |
| HLA-DR4  | Stassen et al. 2009 <sup>19</sup>   | 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 <sup>33</sup>       | Case-Control  | USA (96 Caucasians 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) |
|          | Elkon et al. 1983 <sup>23</sup>     | 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 <sup>17</sup>     | 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 <sup>32</sup>    | 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 <sup>26</sup>      | 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 <sup>20</sup>  | 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 <sup>31</sup> | 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       |
| <b>HLA-DR5</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | 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 <sup>35</sup>          | 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 <sup>29</sup>       | 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 <sup>19</sup>         | 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 <sup>33**</sup>           | Case-Control  | USA (96 Caucasians 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) |
| <b>HLA-DR5</b> | Elkon et al. 1983 <sup>23</sup>           | 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       |
| HLA-DR6  | Papiha et al. 1992 <sup>32</sup>        | 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 <sup>26</sup>          | 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 <sup>22</sup> | 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 <sup>19</sup>       | 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) |
|          | Elkon et al. 1983 <sup>23</sup>         | 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 <sup>32</sup>        | 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 <sup>26</sup>          | 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 <sup>20</sup>      | 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        |
| <b>HLA-DR7</b> | Stassen et al. 2009 <sup>19</sup>         | 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)  |
|                | Elkon et al. 1983 <sup>23</sup>           | 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 <sup>32</sup>          | 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 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>35</sup>          | 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 <sup>29</sup>       | Case-Control  | Germany         | ACR criteria                       | Geographically matched healthy subjects                                                | 102/341          | EGPA (all patients)                      | NR                                                           | 1.58 (1.01 – 2.47)  |
| <b>HLA-DR8</b> | Stassen et al. 2009 <sup>19</sup>         | 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)  |
|                | Elkon et al. 1983 <sup>23</sup>           | 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 <sup>17</sup>           | 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 <sup>26</sup>           | 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 <sup>20</sup>        | 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 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>29</sup>       | 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 <sup>19</sup>         | 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 <sup>33</sup>             | Case-Control  | USA (96 Caucasians 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        |
| <b>HLA-DR9</b> | Elkon et al. 1983 <sup>23</sup>           | 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 <sup>20</sup>        | 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 <sup>36</sup>           | 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 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>35</sup>          | 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 <sup>29</sup>       | 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 <sup>19</sup>         | 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        |
| <b>HLA-DRB1*0401</b> | Cao et al. 2011 <sup>33</sup>      | Case-Control  | USA (96 Caucasians 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 <sup>34</sup>      | 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 <sup>37</sup> | 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)  |
|                      | Tsuchiya et al. 2003 <sup>5</sup>  | 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 <sup>34</sup>      | 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)  |
| <b>HLA-DRB1*0403</b> | Tsuchiya et al. 2003 <sup>5</sup>  | 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 <sup>34</sup>      | 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        |
| <b><i>HLA-DRB1*0405</i></b> | Tsuchiya et al. 2003 <sup>5</sup> | 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 <sup>34</sup>     | 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)  |
| <b><i>HLA-DRB1*0406</i></b> | Tsuchiya et al. 2003 <sup>5</sup> | 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 <sup>34</sup>     | 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)  |
| <b><i>HLA-DRB1*0407</i></b> | Tsuchiya et al. 2003 <sup>5</sup> | 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 <sup>34</sup>     | 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) |
| <b><i>HLA-DRB1*0410</i></b> | Tsuchiya et al. 2003 <sup>5</sup> | 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 <sup>34</sup>     | 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         |
| <b><i>HLA-DRB1*0802</i></b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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)   |
| <b><i>HLA-DRB1*0803</i></b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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)   |
| <b><i>HLA-DRB1*10</i></b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>29</sup>       | 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 <sup>33</sup>             | Case-Control  | USA (96 Caucasians 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)   |
| <b><i>HLA-DRB1*11</i></b>   | Spriewald et al. 2005 <sup>31</sup>       | 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        |
| <b>HLA-DRB1*1101</b> | Von Vietinghoff et al. 2006 <sup>18</sup> | 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 <sup>29</sup>       | 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 <sup>33</sup>             | Case-Control  | USA (96 Caucasians 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)  |
|                      | Luo et al. 2011 <sup>34</sup>             | 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 <sup>37</sup>        | 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)  |
| <b>HLA-DRB1*12</b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>29</sup>       | 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       |
| <b>HLA-DRB1*1201</b> | Cao et al. 2011 <sup>33</sup>             | Case-Control  | USA (96 Caucasians 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) |
|                      | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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) |
| <b>HLA-DRB1*1202</b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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) |
| <b>HLA-DRB1*13</b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | 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        |
| <b>HLA-<br/>DRB1*1302</b> | Vaglio et al. 2007 <sup>35</sup>          | 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 <sup>29</sup>       | Case-Control  | Germany                                      | ACR criteria                    | Geographically matched healthy subjects                                                               | 102/341          | EGPA (all patients)                  | NR                                                            | 0.50 (0.28 – 0.89)  |
|                           | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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)  |
| <b>HLA-<br/>DRB1*14</b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>29</sup>       | 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 <sup>33</sup>             | Case-Control  | USA (96 Caucasians 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       |
| <b><i>HLA-DRB1*1403</i></b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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) |
| <b><i>HLA-DRB1*1405</i></b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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) |
| <b><i>HLA-DRB1*15</i></b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>33**</sup>           | Case-Control  | USA (96 Caucasians 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       |
| <b><i>HLA-DRB1*1501</i></b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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) |
| <b><i>HLA-DRB1*1502</i></b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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) |
| <b><i>HLA-DRB1*16</i></b>   | Spriewald et al. 2005 <sup>31</sup>       | 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 <sup>18</sup> | 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 <sup>33**</sup>           | Case-Control  | USA (96 Caucasians 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) |
| <b>HLA-DRB1*1602</b> | Tsuchiya et al. 2003 <sup>5</sup>         | 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 <sup>34</sup>             | 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)  |
| <b>HLA-DRB3</b>      | Spencer et al. 1992 <sup>38</sup>         | 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 <sup>18</sup> | 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 <sup>35</sup>          | 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 <sup>29</sup>       | Case-Control  | Germany                     | ACR criteria                    | Geographically matched healthy subjects                                                | 102/341          | EGPA (all patients)                  | NR                                                            | 0.61 (0.44 – 0.86)  |
| <b>HLA-DRB4</b>      | Spencer et al. 1992 <sup>38</sup>         | 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       |
| <b>HLA-DRB5</b>             | Von Vietinghoff et al. 2006 <sup>18</sup> | 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 <sup>35</sup>          | 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 <sup>29</sup>       | Case-Control        | Germany     | ACR criteria          | Geographically matched healthy subjects                                                | 102/341          | EGPA (all patients) | NR                                                  | 1.87 (1.34 – 2.61) |
|                             | Spencer et al. 1992 <sup>38</sup>         | 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 <sup>18</sup> | Case-Control        | Germany     | ACR and CHCC criteria | Geographically matched healthy blood donors                                            | 51/51            | GPA (all patients)  | NR                                                  | 1.07 (0.82 – 2.18) |
| <b>HSD17B8 rs421446 (C)</b> | Heckmann et al. 2008 <sup>24</sup>        | 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) |
| <b>IL-1β (A2)</b>           | Xie et al. 2013 <sup>25</sup>             | 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) |
|                             | Huang et al. 2000 <sup>4</sup>            | 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 <sup>39</sup>        | 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        |
| <i>IL1RN*1</i> | Zhou et al. 2004 <sup>6</sup>                                   | 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 <sup>3</sup> | 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)  |
|                | Borgmann et al. 2003 <sup>39</sup>                              | 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 <sup>7</sup>                                | 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)  |
| <i>IL1RN*2</i> | Borgmann et al. 2003 <sup>39</sup>                              | 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 <sup>7</sup>                                | 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)  |
| <i>IL1RN*3</i> | Borgmann et al. 2003 <sup>39</sup>                              | 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 <sup>7</sup>                                | 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)  |
| <i>IL1RN*4</i> | Borgmann et al. 2003 <sup>39</sup>                              | 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        |
| <b><i>IL1RN*5</i></b>                                   | Persson et al. 2013 <sup>7</sup>                                | 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) |
|                                                         | Borgmann et al. 2003 <sup>39</sup>                              | 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 <sup>7</sup>                                | 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) |
| <b><i>IL-6</i><br/><b>rs1800795</b><br/><b>(C)</b></b>  | Zhou et al. 2004 <sup>6</sup>                                   | 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)  |
| <b><i>IL-10</i><br/><b>rs1800872</b><br/><b>(A)</b></b> | Spriewald et al. 2005 <sup>31</sup>                             | 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 <sup>3</sup> | 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 <sup>40</sup>                               | 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)  |
|                                                         | Spriewald et al. 2005 <sup>31</sup>                             | 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 <sup>41</sup>                             | 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       |
| <b><i>IL-10</i><br/>rs1800896<br/>(G)</b> | Murakozy et al. 2001 <sup>42</sup>                              | 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 <sup>43</sup>                               | 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 <sup>31</sup>                             | 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 <sup>41</sup>                             | 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 <sup>3</sup> | 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) |
| <b><i>IRF5</i><br/>rs10954213<br/>(G)</b> | Wieczorek et al. 2010 <sup>44</sup>                             | 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 <sup>3</sup> | 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 <sup>45</sup>                              | 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) |
| <b><i>LEPR</i><br/>rs8179183<br/>(C)</b>  | Wieczorek et al. 2010 <sup>15***</sup>                          | 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       |
| <b>MPO</b><br><b>rs2333227</b><br><b>(A)</b>    | Reynolds et al.<br>2002 <sup>46</sup>  | 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) |
|                                                 |                                        | 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.<br>2004 <sup>47</sup>  | 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.<br>2007 <sup>48</sup>      | 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) |
| <b>PCD1</b><br><b>rs1156882</b><br><b>(A)</b>   | Slot et al.<br>2008 <sup>8</sup>       | Case-Control  | The Netherlands | 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.<br>2009 <sup>49</sup> | Case-Control  | Sweden          | Clinical criteria                       | Geographically and ethnically matched blood donors                             | 66/275           | GPA (all patients)                       | NR                                                                               | 0.78 (0.37 – 1.64) |
| <b>PTPN22</b><br><b>rs2476601</b><br><b>(A)</b> | Jagiello et al.<br>2005 <sup>50</sup>  | 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.<br>2012 <sup>2**</sup>    | 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       |
| <b><i>RING1/RXR B</i> rs213213 (A)</b> |                                                                 | 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 <sup>3</sup> | 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 <sup>51</sup>                             | 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) |
|                                        | Heckmann et al. 2008 <sup>24</sup>                              | 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 <sup>3</sup> | 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 <sup>25</sup>                                   | 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) |
| <b><i>RXRB</i> rs6531 (C)</b>          | Szyld et al. 2006 <sup>52</sup>                                 | 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       |
| <b>RXRB</b><br><b>rs9277935</b><br><b>(T)</b> | Previously unpublished Lyons et al. 2012 GWAS data <sup>3</sup> | 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 <sup>25</sup>                                   | 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) |
|                                               | Wieczorek et al. 2009 <sup>53</sup>                             | 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 <sup>3</sup> | 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 <sup>25</sup>                                   | 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) |
| <b>SERPINA1</b><br><b>S allele</b>            | Lhotta et al. 1994 <sup>54</sup>                                | 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 <sup>55</sup>                              | 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        |
| <b>SERPINA1</b><br><b>Z allele</b> | Mahr et al. 2010 <sup>56</sup>                 | 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 <sup>57</sup>               | 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 <sup>58</sup> | 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) |
|                                    | Lhotta et al. 1994 <sup>54</sup>               | 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 <sup>55</sup>             | 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 <sup>59</sup>               | 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 <sup>60</sup>             | 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       |
| <b>STAT4</b><br><b>rs7574865</b><br><b>(T)</b> | Mahr et al. 2010 <sup>56</sup>                                    | 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 <sup>57</sup>                                  | 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 <sup>3**</sup> | 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 <sup>58</sup>                    | 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) |
|                                                | Wieczorek et al. 2010 <sup>44</sup>                               | 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       |
| <b><i>TGF-β<sub>1</sub></i><br/>rs1800471<br/>(C)</b> | Previously unpublished Lyons et al. 2012 GWAS data <sup>3</sup> | 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 <sup>45</sup>                              | 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) |
|                                                       | Murakozy et al. 2001 <sup>42</sup>                              | 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 <sup>43</sup>                               | 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 <sup>31</sup>                             | 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) |
| <b><i>TNFα</i><br/>rs1800629<br/>(A)</b>              | Mascher et al. 1997 <sup>61</sup>                               | 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 <sup>6</sup>                                   | 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 <sup>31</sup>                             | 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 <sup>3</sup> | 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) |
| <b><i>TNFR11</i> 196R</b>       | Tsuchiya et al. 2003 <sup>5</sup>                               | 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 <sup>6</sup>                                   | 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) |
| <b><i>TLR9</i> rs352162 (T)</b> | Husmann et al. 2014 <sup>40**</sup>                             | 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) |
| <b><i>TLR9</i> rs352140 (T)</b> | Husmann et al. 2014 <sup>40**</sup>                             | 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) |
| <b><i>TLR9</i> rs352139 (T)</b> | Husmann et al. 2014 <sup>40**</sup>                             | 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       |
| <b><i>TLR9</i></b><br><b>rs5743836</b><br><b>(G)</b> | Husmann et al. 2014 <sup>40**</sup> | Case-Control  | 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) |
|                                                      |                                     |               | 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**

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

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

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

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

| Variant by gene<br>(minor allele)      | Publica-<br>tions (n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value<br>for meta-<br>analysis | I <sup>2</sup><br>(%) | P value for<br>heterogeneity | P value for<br>funnel plot<br>asymmetry |
|----------------------------------------|-----------------------|-----------------------------|--------------------|----------------------------------|-----------------------|------------------------------|-----------------------------------------|
| <i>HLA-DRB5</i>                        | 2                     | 110/1154                    | 1.20 (0.73 – 1.97) | 0.470                            | 0                     | 0.643                        | N/A                                     |
| <i>IL-1β</i> (A2)                      | 4                     | 1172/5687                   | 1.00 (0.90 – 1.12) | 0.995                            | 0                     | 0.805                        | 0.645                                   |
| <i>IL1RN</i> *1                        | 2                     | 214/434                     | 1.06 (0.82 – 1.37) | 0.662                            | 0                     | 0.659                        | N/A                                     |
| <i>IL1RN</i> *2                        | 2                     | 214/434                     | 1.00 (0.77 – 1.31) | 0.980                            | 0                     | 0.956                        | N/A                                     |
| <i>IL1RN</i> *3                        | 2                     | 214/434                     | 0.61 (0.26 – 1.44) | 0.257                            | 45                    | 0.176                        | N/A                                     |
| <i>IL1RN</i> *4                        | 2                     | 214/434                     | 0.85 (0.13 – 5.82) | 0.872                            | 0                     | 0.888                        | N/A                                     |
| <i>IL1RN</i> *5                        | 2                     | 214/434                     | 0.88 (0.13 – 5.94) | 0.892                            | 0                     | 0.796                        | N/A                                     |
| <i>IL-6</i> rs1800795 (C)              | 4                     | 1926/6817                   | 1.01 (0.94 – 1.09) | 0.793                            | 0                     | 0.537                        | 0.584                                   |
| <i>IL-10</i> rs1800872 (A)             | 2                     | 538/598                     | 1.01 (0.83 – 1.22) | 0.963                            | 0                     | 0.795                        | N/A                                     |
| <i>IL-10</i> rs1800896 (G)             | 5                     | 1414/6183                   | 0.90 (0.76 – 1.07) | 0.232                            | 55                    | 0.063                        | 0.285                                   |
| <i>LEPR</i> rs8179183 (C)              | 1                     | 878/2653                    | 0.89 (0.77 – 1.03) | 0.118                            | 89                    | <0.001                       | 0.780                                   |
| <i>MPO</i> rs2333227 (A)               | 3                     | 395/299                     | 0.96 (0.76 – 1.21) | 0.696                            | 0                     | 0.822                        | 0.478                                   |
| <i>PCD1</i> rs1156882 (A)              | 2                     | 168/479                     | 0.88 (0.55 – 1.38) | 0.568                            | 0                     | 0.701                        | N/A                                     |
| <i>TGF-β<sub>1</sub></i> rs1800471 (C) | 3                     | 232/259                     | 1.49 (0.92 – 2.41) | 0.107                            | 0                     | 0.401                        | 0.220                                   |
| <i>TNFα</i> rs1800629 (A)              | 4                     | 860/5691                    | 1.14 (0.88 – 1.45) | 0.327                            | 29                    | 0.236                        | 0.389                                   |
| <i>TNFR2</i> 196R                      | 2                     | 167/385                     | 0.94 (0.66 – 1.34) | 0.749                            | 0                     | 0.317                        | N/A                                     |
| <i>TLR9</i> 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**

| <b>Variant by gene</b>            | <b>Publications<br/>(n)</b> | <b>Cases (n) /<br/>Controls (n)</b> | <b>OR (95% CI)</b> | <b>P value for<br/>meta-analysis</b> |
|-----------------------------------|-----------------------------|-------------------------------------|--------------------|--------------------------------------|
| <i>CD226</i> 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                                |
| <i>CTLA-4</i> (AT) <sub>86</sub>  |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>102</sub> |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>104</sub> |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>106</sub> |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>108</sub> |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>110</sub> |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>116</sub> |                             |                                     |                    |                                      |
| 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                                |
| <i>CTLA-4</i> (AT) <sub>118</sub> |                             |                                     |                    |                                      |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value for<br>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                        |
| <i>CTLA-4</i> (AT) <sub>122</sub> |                     |                             |                    |                              |
| 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                        |
| <i>CTLA-4</i> (AT) <sub>124</sub> |                     |                             |                    |                              |
| 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                        |
| <i>CTLA-4</i> (AT) <sub>126</sub> |                     |                             |                    |                              |
| 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                        |
| <i>CTLA-4</i> (AT) <sub>128</sub> |                     |                             |                    |                              |
| 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                        |
| <i>CTLA-4</i> 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                        |
| <i>CTLA-4</i> 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                        |
| <i>FCAR</i> 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                        |
| <i>FCGR2A</i> 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                        |
| <i>FCGR3A</i> 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value for<br>meta-analysis |
|--------------------------|---------------------|-----------------------------|--------------------|------------------------------|
| MPO-ANCA                 | 1                   | 50/303                      | 0.65 (0.39 – 1.07) | 0.090                        |
| <i>FCGR3B</i> (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                        |
| <i>GHSR</i> 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                        |
| <i>HLA-A2</i>            |                     |                             |                    |                              |
| 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                        |
| <i>HLA-A11</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-A24</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-A26</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-A31</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-A32</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-B35</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-B39</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-B44</i>           |                     |                             |                    |                              |
| 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                        |
| <i>HLA-B51</i>           |                     |                             |                    |                              |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)         | P value for<br>meta-analysis |
|-------------------------------|---------------------|-----------------------------|---------------------|------------------------------|
| <i>HLA-B55</i>                |                     |                             |                     |                              |
| 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                        |
| <i>HLA-B60</i>                |                     |                             |                     |                              |
| 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                        |
| <i>HLA-B62</i>                |                     |                             |                     |                              |
| 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                        |
| <i>HLA-Cw1</i>                |                     |                             |                     |                              |
| 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                        |
| <i>HLA-Cw3</i>                |                     |                             |                     |                              |
| 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                        |
| <i>HLA-Cw7</i>                |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DPA1</i> 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                       |
| <i>HLA-DPB1*0101</i>          |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DPB1*0201</i>          |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DPB1*0301</i>          |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DPB1*0401</i>          |                     |                             |                     |                              |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)          | P value for<br>meta-analysis |
|-------------------------------|---------------------|-----------------------------|----------------------|------------------------------|
| <i>HLA-DPB1*0402</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DPB1*0501</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DPB1*0601</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DPB1*0901</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DPB2 rs3130215 (A)</i> |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DQB1*02</i>            |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DQB1*0302</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DQB1*0303</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DQB1*04</i>            |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DQB1*0501</i>          |                     |                             |                      |                              |
| 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                        |
| <i>HLA-DQB1*0602</i>          |                     |                             |                      |                              |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value for<br>meta-analysis |
|-----------------|---------------------|-----------------------------|--------------------|------------------------------|
| <i>HLA-DQ7</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR1</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR2</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR3</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR4</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR5</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR6</i>  |                     |                             |                    |                              |
| 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                        |
| <i>HLA-DR7</i>  |                     |                             |                    |                              |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)         | P value for<br>meta-analysis |
|----------------------|---------------------|-----------------------------|---------------------|------------------------------|
| <i>HLA-DR8</i>       |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DR9</i>       |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0401</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0403</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0405</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0406</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0407</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0410</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0802</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*0803</i> |                     |                             |                     |                              |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)         | P value for<br>meta-analysis |
|----------------------|---------------------|-----------------------------|---------------------|------------------------------|
| <i>HLA-DRB1*10</i>   |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*11</i>   |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1101</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*12</i>   |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1201</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1202</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*13</i>   |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1302</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*14</i>   |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1403</i> |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1405</i> |                     |                             |                     |                              |
| GPA                  | 1                   | 45/200                      | 1.51 (0.53 – 4.27)  | 0.437                        |

| Variant by gene                    | Publications<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)         | P value for<br>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                        |
| <i>HLA-DRB1*15</i>                 |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1501</i>               |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1502</i>               |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*16</i>                 |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB1*1602</i>               |                     |                             |                     |                              |
| 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                        |
| <i>HLA-DRB3</i>                    |                     |                             |                     |                              |
| GPA                                | 1                   | 51/51                       | 1.41 (0.76 – 2.60)  | 0.276                        |
| EGPA                               | 2                   | 150/691                     | 0.58 (0.45 – 0.76)  | <0.001                       |
| <i>HLA-DRB4</i>                    |                     |                             |                     |                              |
| GPA                                | 1                   | 51/51                       | 0.89 (0.46 – 1.72)  | 0.738                        |
| EGPA                               | 2                   | 150/691                     | 2.06 (1.57 – 2.69)  | <0.001                       |
| <i>IL-1<math>\beta</math> (A2)</i> |                     |                             |                     |                              |
| 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                        |
| <i>IL1RN*1</i>                     |                     |                             |                     |                              |
| 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                        |
| <i>IL1RN*2</i>                     |                     |                             |                     |                              |
| 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                        |
| <i>IL1RN*3</i>                     |                     |                             |                     |                              |
| GPA                                | 1                   | 61/200                      | 0.72 (0.15 – 3.40)  | 0.682                        |

| Variant by gene             | Publications<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)         | P value for<br>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                        |
| <i>IL1RN</i> *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                        |
| <i>IL1RN</i> *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                        |
| <i>IL-6</i> 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                        |
| <i>IL-10</i> 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                        |
| <i>IL-10</i> 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                        |
| <i>IRF5</i> 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                        |
| <i>LEPR</i> 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                        |
| <i>MPO</i> 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                        |
| <i>PTPN22</i> 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value for<br>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                        |
| <i>RING1/RXR</i> B 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                        |
| <i>RXR</i> B 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                        |
| <i>RXR</i> B 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                        |
| <i>SERPINA1</i> 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                        |
| <i>SERPINA1</i> 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                        |
| <i>STAT4</i> 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                        |
| <i>TGF-<math>\beta_1</math></i> 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                        |
| <i>TNF<math>\alpha</math></i> 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                        |
| <i>TNFR</i> II 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value for<br>meta-analysis |
|---------------------------|---------------------|-----------------------------|--------------------|------------------------------|
| <i>TLR9</i> 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                        |
| <i>TLR9</i> 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                        |
| <i>TLR9</i> 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                        |
| <i>TLR9</i> 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**

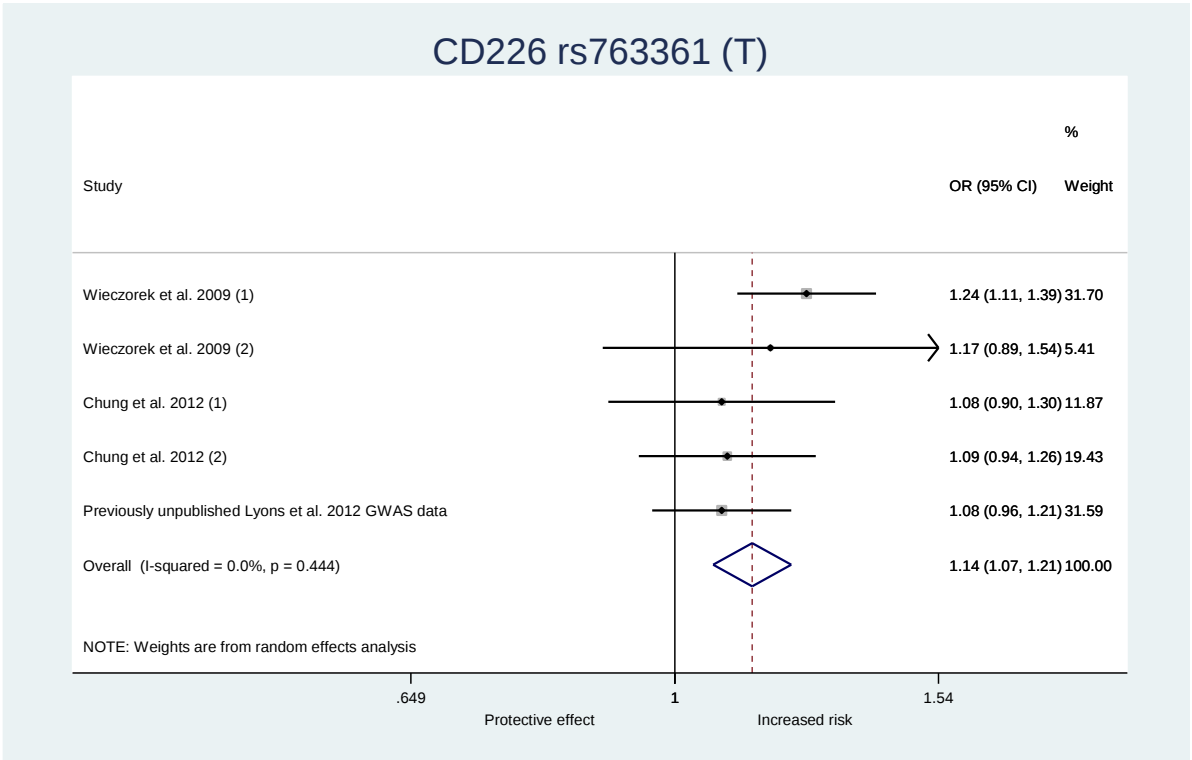
| <b>Variant by gene</b>            | <b>Publications<br/>(n)</b> | <b>Cases (n) /<br/>Controls (n)</b> | <b>OR (95% CI)</b>  | <b>P value for<br/>meta-analysis</b> |
|-----------------------------------|-----------------------------|-------------------------------------|---------------------|--------------------------------------|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

| <b>Variant by gene</b>      | <b>Publications<br/>(n)</b> | <b>Cases (n) /<br/>Controls (n)</b> | <b>OR (95% CI)</b> | <b>P value for<br/>meta-analysis</b> |
|-----------------------------|-----------------------------|-------------------------------------|--------------------|--------------------------------------|
| <i>FCGR2A</i> 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                                |
| <i>FCGR3A</i> 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                                |
| <i>FCGR3B</i> (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                                |
| <i>HLA-A2</i>               |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 0.90 (0.37 – 2.23) | 0.826                                |
| Caucasian                   | 4                           | 427/7324                            | 0.96 (0.81 – 1.13) | 0.595                                |
| <i>HLA-A11</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 0.71 (0.17 – 3.03) | 0.644                                |
| Caucasian                   | 5                           | 450/7635                            | 1.01 (0.50 – 2.05) | 0.978                                |
| <i>HLA-A24</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 0.75 (0.34 – 1.65) | 0.476                                |
| Caucasian                   | 2                           | 92/751                              | 1.16 (0.57 – 2.38) | 0.683                                |
| <i>HLA-A26</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 2.36 (1.00 – 5.60) | 0.051                                |
| Caucasian                   | 3                           | 115/1156                            | 1.21 (0.58 – 2.55) | 0.612                                |
| <i>HLA-A31</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 1.55 (0.46 – 5.24) | 0.479                                |
| Caucasian                   | 2                           | 92/751                              | 0.73 (0.21 – 2.52) | 0.613                                |
| <i>HLA-A32</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 2.07 (0.61 – 7.04) | 0.246                                |
| Caucasian                   | 2                           | 92/751                              | 1.41 (0.52 – 3.84) | 0.500                                |
| <i>HLA-B35</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 0.80 (0.17 – 3.40) | 0.757                                |
| Caucasian                   | 3                           | 396/6623                            | 0.78 (0.58 – 1.06) | 0.115                                |
| <i>HLA-B39</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 0.86 (0.11 – 6.51) | 0.887                                |
| Caucasian                   | 1                           | 51/51                               | 0.33 (0.01 – 8.20) | 0.499                                |
| <i>HLA-B44</i>              |                             |                                     |                    |                                      |
| Asian                       | 1                           | 16/472                              | 2.50 (0.85 – 7.40) | 0.098                                |
| Caucasian                   | 2                           | 92/751                              | 1.41(0.85 – 2.35)  | 0.188                                |

| <b>Variant by gene</b> | <b>Publications<br/>(n)</b> | <b>Cases (n) /<br/>Controls (n)</b> | <b>OR (95% CI)</b>  | <b>P value for<br/>meta-analysis</b> |
|------------------------|-----------------------------|-------------------------------------|---------------------|--------------------------------------|
| <i>HLA-B51</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 1.87 (0.64 – 5.49)  | 0.255                                |
| Caucasian              | 1                           | 51/51                               | 0.61 (0.19 – 1.92)  | 0.394                                |
| <i>HLA-B55</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 7.35 (2.34 – 23.14) | 0.001                                |
| Caucasian              | 1                           | 51/51                               | 0.07 (0.00 – 1.30)  | 0.075                                |
| <i>HLA-B60</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 1.19 (0.28 – 5.13)  | 0.814                                |
| Caucasian              | 1                           | 41/700                              | 3.51 (0.99 – 12.36) | 0.051                                |
| <i>HLA-B62</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 1.71 (0.58 – 4.99)  | 0.331                                |
| Caucasian              | 1                           | 41/700                              | 2.38 (0.70 – 8.12)  | 0.166                                |
| <i>HLA-Cw1</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 1.45 (0.58 – 3.58)  | 0.426                                |
| Caucasian              | 1                           | 52/51                               | 0.98 (0.24 – 4.03)  | 0.978                                |
| <i>HLA-Cw3</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 1.40 (0.66 – 3.01)  | 0.384                                |
| Caucasian              | 1                           | 52/51                               | 1.32 (0.62 – 2.81)  | 0.479                                |
| <i>HLA-Cw7</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 0.50 (0.12 – 2.10)  | 0.340                                |
| Caucasian              | 1                           | 52/51                               | 1.10 (0.62 – 1.96)  | 0.735                                |
| <i>HLA-DPB1*0201</i>   |                             |                                     |                     |                                      |
| Asian                  | 1                           | 50/77                               | 1.38 (0.75 – 2.52)  | 0.298                                |
| Caucasian              | 3                           | 385/827                             | 0.76 (0.56 – 1.03)  | 0.073                                |
| <i>HLA-DQB1*0303</i>   |                             |                                     |                     |                                      |
| Asian                  | 1                           | 50/77                               | 2.11 (1.14 – 3.90)  | 0.018                                |
| Caucasian              | 2                           | 126/141                             | 1.35 (0.55 – 3.33)  | 0.515                                |
| <i>HLA-DR1</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 64/265                              | 1.12 (0.48 – 2.64)  | 0.793                                |
| Caucasian              | 9                           | 945/6840                            | 0.91 (0.61 – 1.36)  | 0.651                                |
| <i>HLA-DR2</i>         |                             |                                     |                     |                                      |
| Asian                  | 1                           | 16/472                              | 0.33 (0.08 – 1.38)  | 0.128                                |
| Caucasian              | 4                           | 471/5750                            | 1.06 (0.87 – 1.29)  | 0.565                                |
| <i>HLA-DR4</i>         |                             |                                     |                     |                                      |
| 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<br>(n) | Cases (n) /<br>Controls (n) | OR (95% CI)        | P value for<br>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                        |
| <i>IRF5</i> 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                       |
| <i>STAT4</i> 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                        |
| <i>TNFR2</i> 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                        |

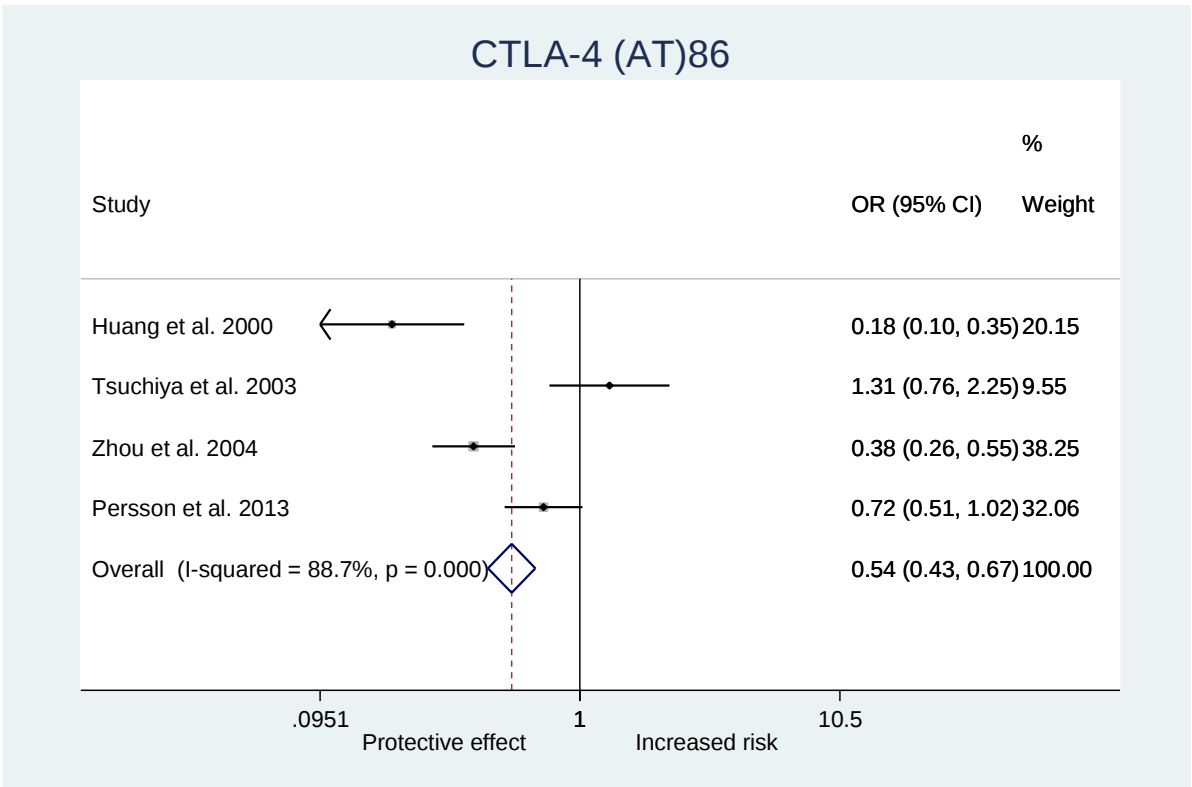
Supplementary Figure S1. Forest plots



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

References

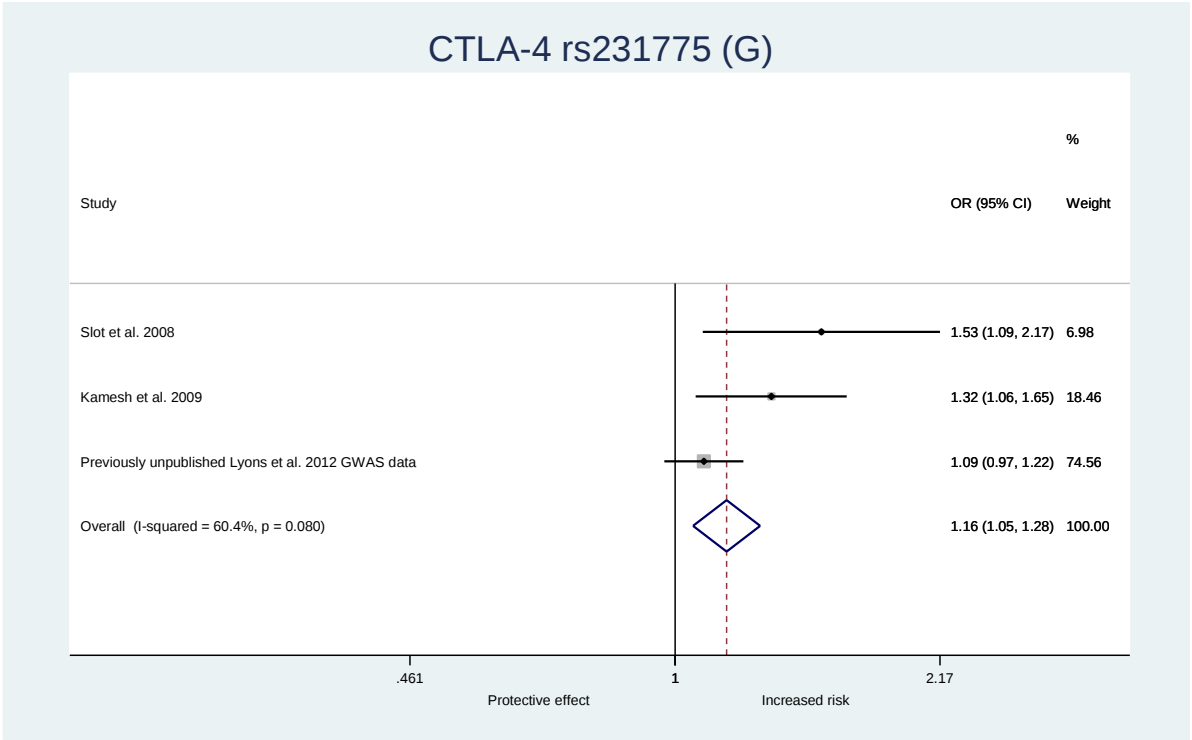
<sup>1\*\*</sup>, <sup>2\*\*</sup>, <sup>3</sup>



CTLA-4 (AT)<sub>86</sub> forest plot. Harbold test:  $p=0.946$ , Egger test:  $p=0.788$ .

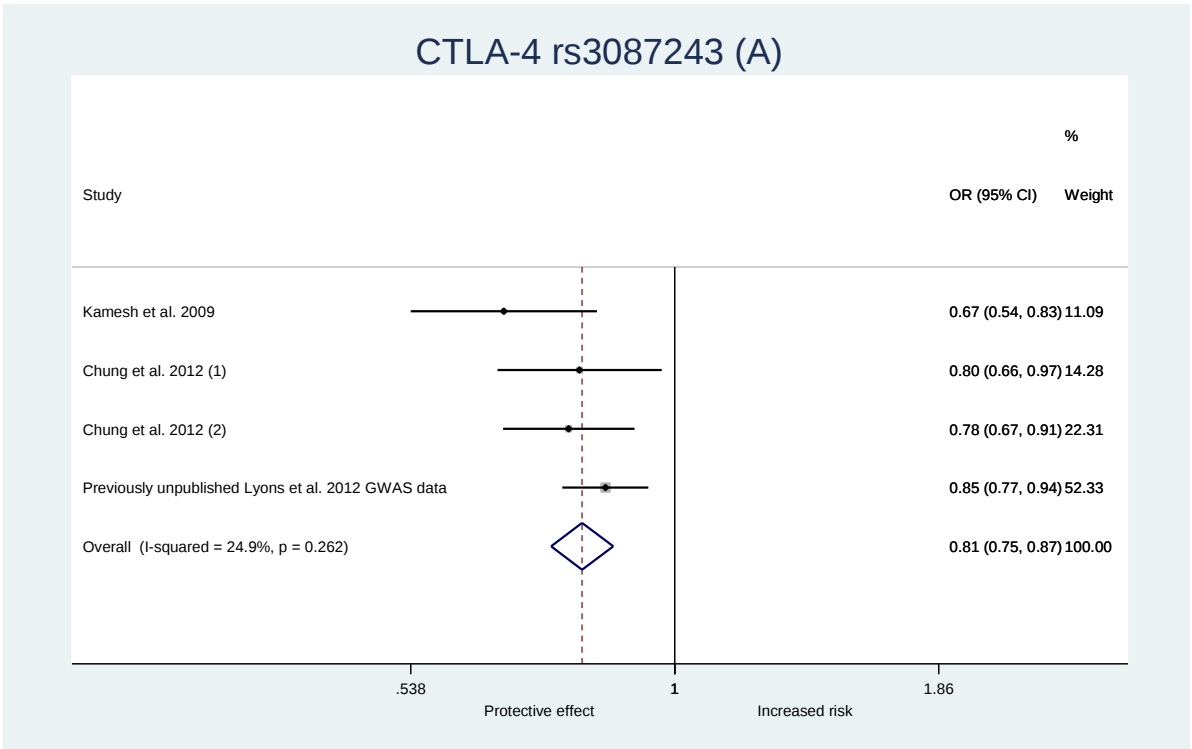
References

<sup>4</sup>, <sup>5</sup>, <sup>6</sup>, <sup>7</sup>



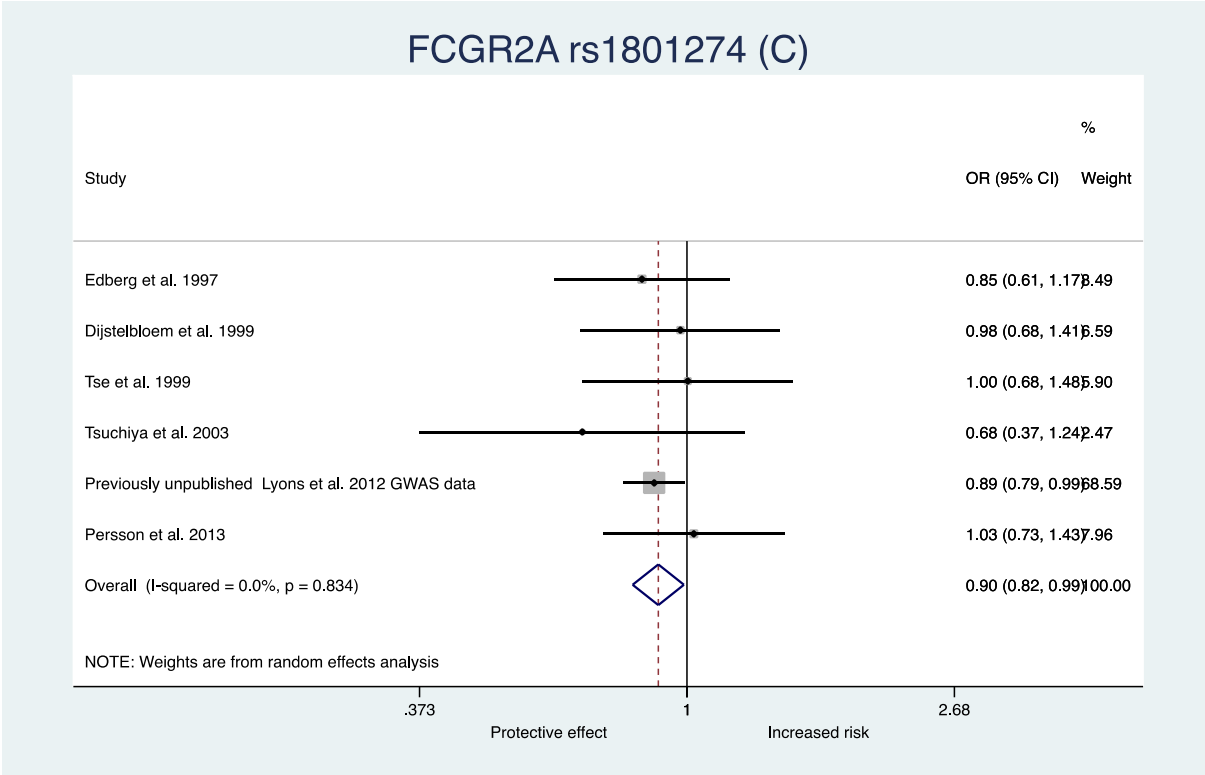
CTLA-4 rs231775 (G) forest plot. Harbold test:  $p=0.080$ , Egger test:  $p=0.081$ .

**References**  
8 9 3  
, ,



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

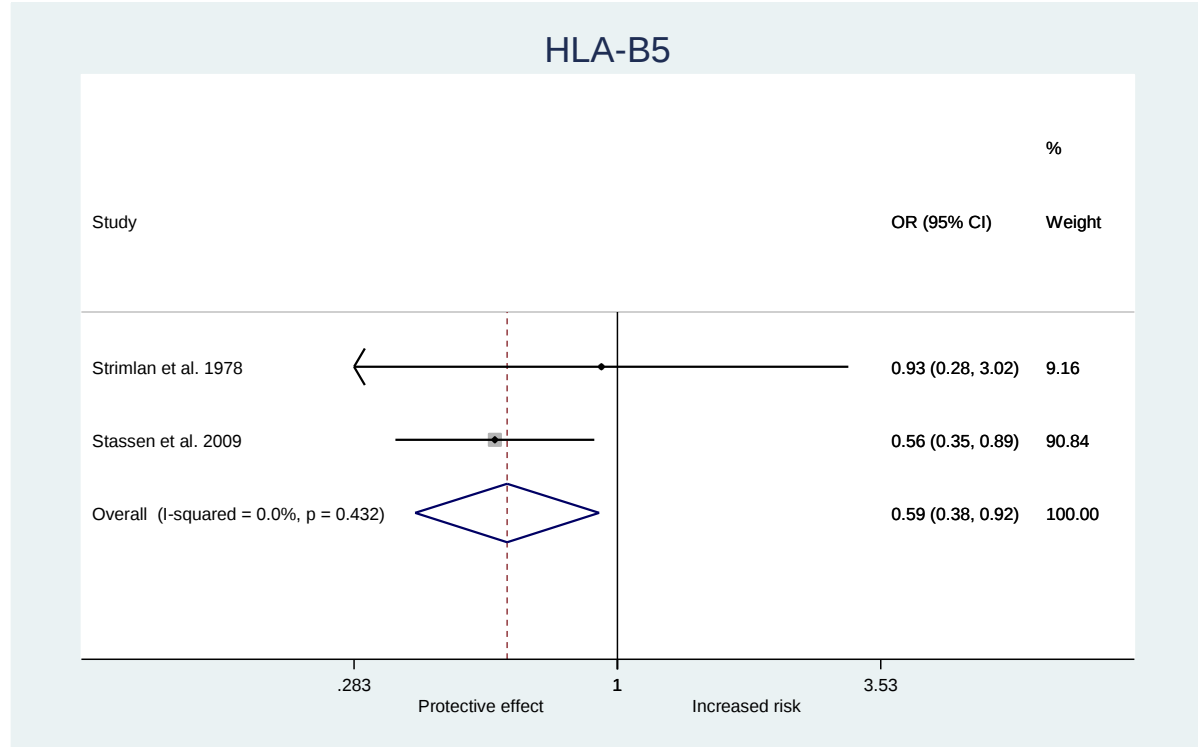
**References**  
9 2\*\* 3  
, \*\*, ,



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

**References**

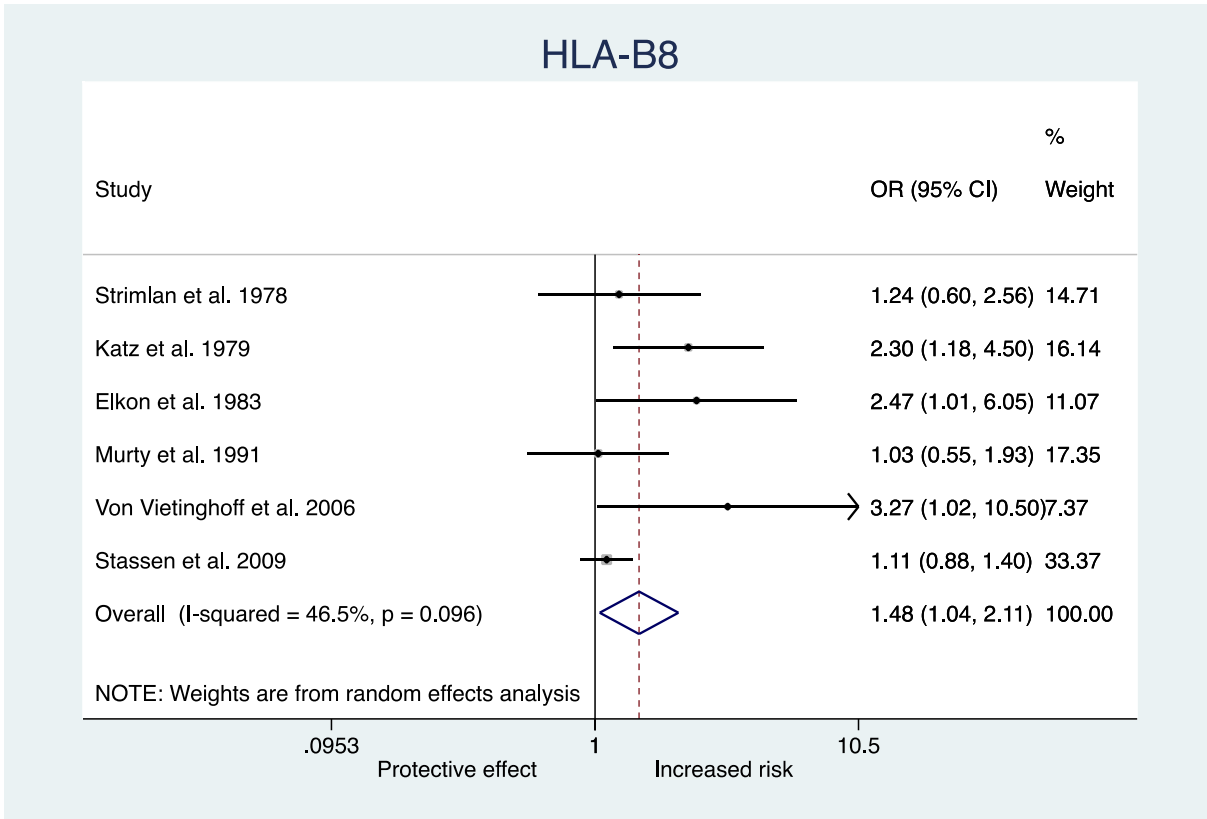
11 12 13 5 7 3  
, , , , ,



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

**References**

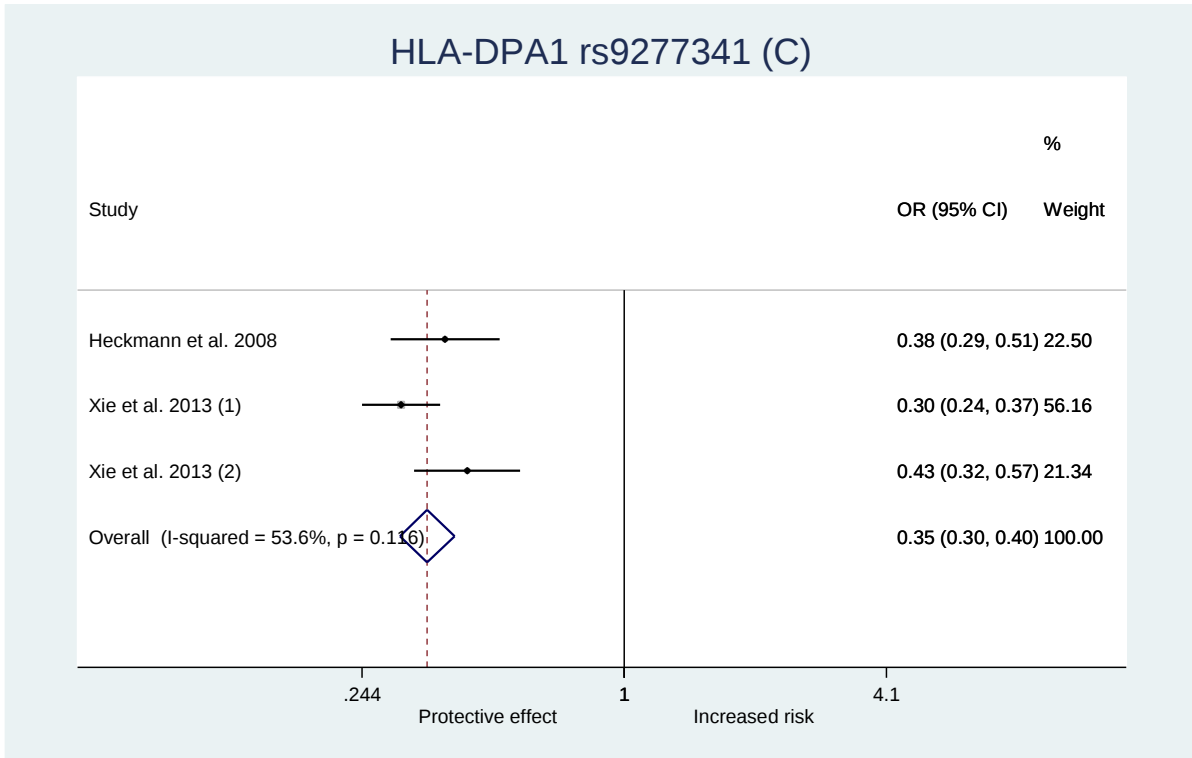
16 19  
,



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

#### References

<sup>16</sup> , <sup>21</sup> , <sup>23</sup> , <sup>17</sup> , <sup>18</sup> , <sup>19</sup> ,

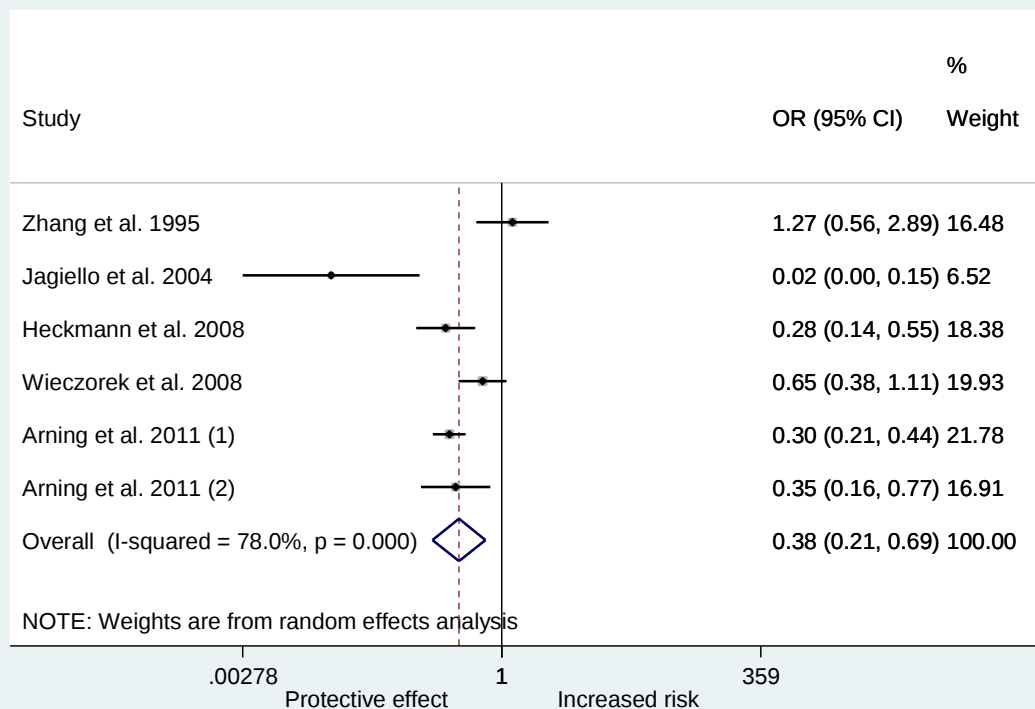


HLA-DPA1 rs9277341 (C) forest plot. Harbold test:  $p=0.215$ , Egger test:  $p=0.219$ .

#### References

<sup>24</sup> , <sup>25</sup> \*\*,

## HLA-DPB1\*0301

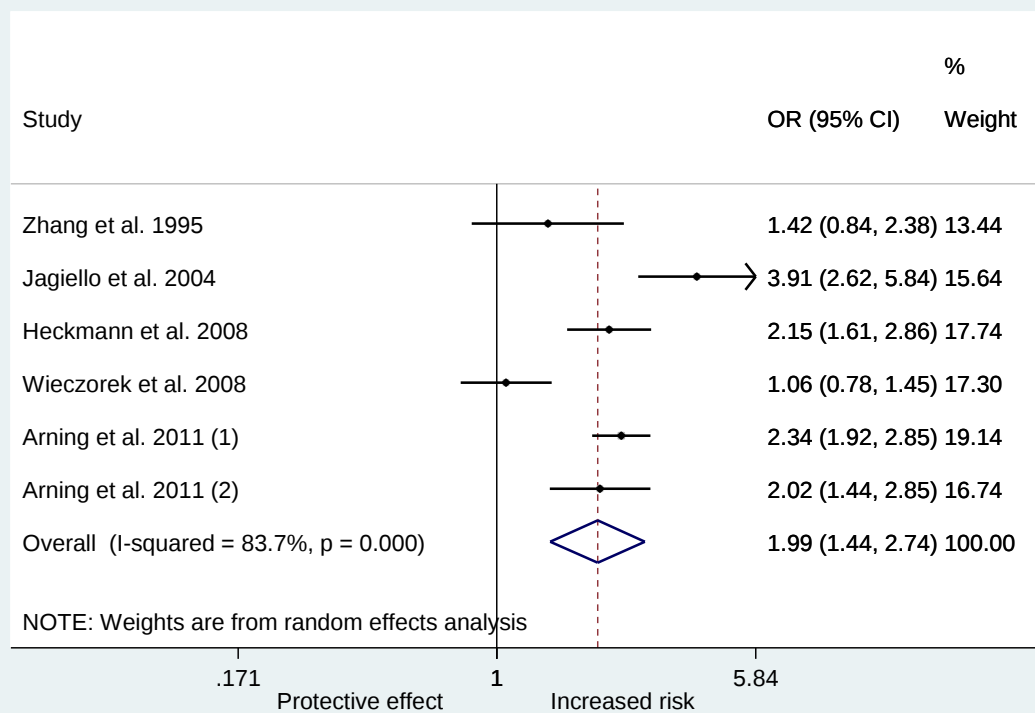


HLA-DPB1\*0301 forest plot. Harbold test:  $p=0.938$ , Egger test:  $p=0.744$ .

### References

<sup>26</sup>, <sup>27</sup>, <sup>24</sup>, <sup>29</sup>, <sup>30</sup>\*\*

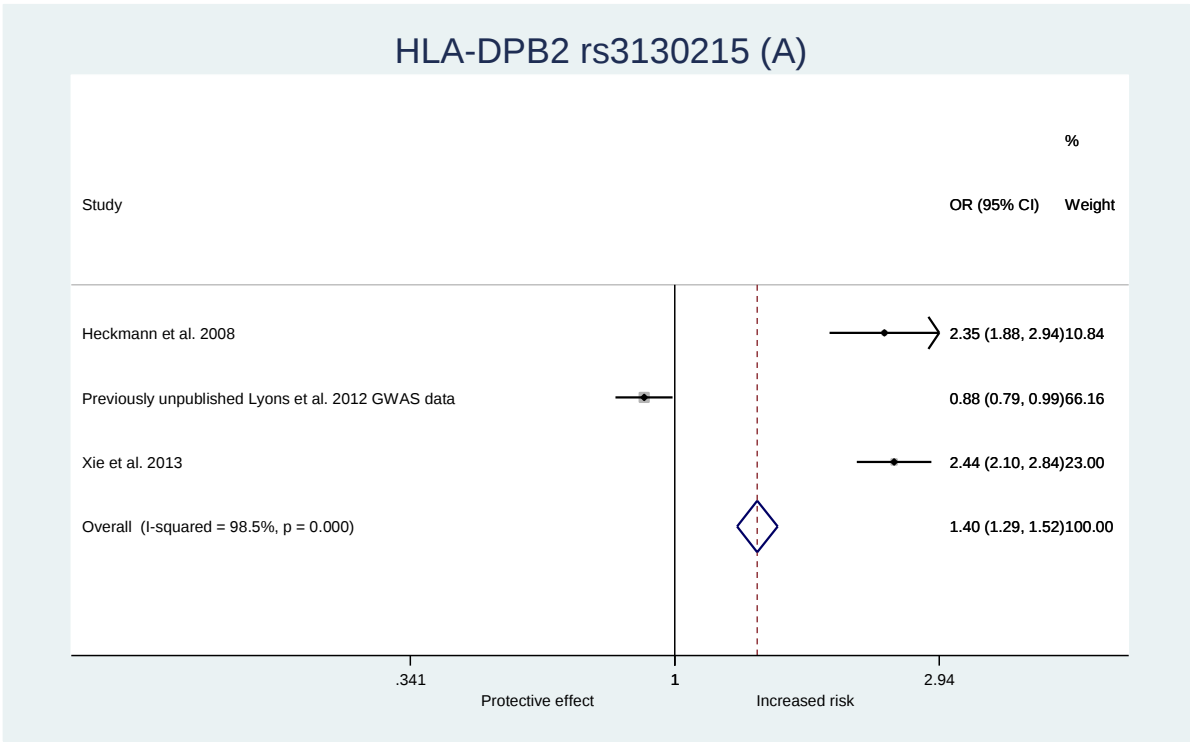
## HLA-DPB1\*0401



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

### References

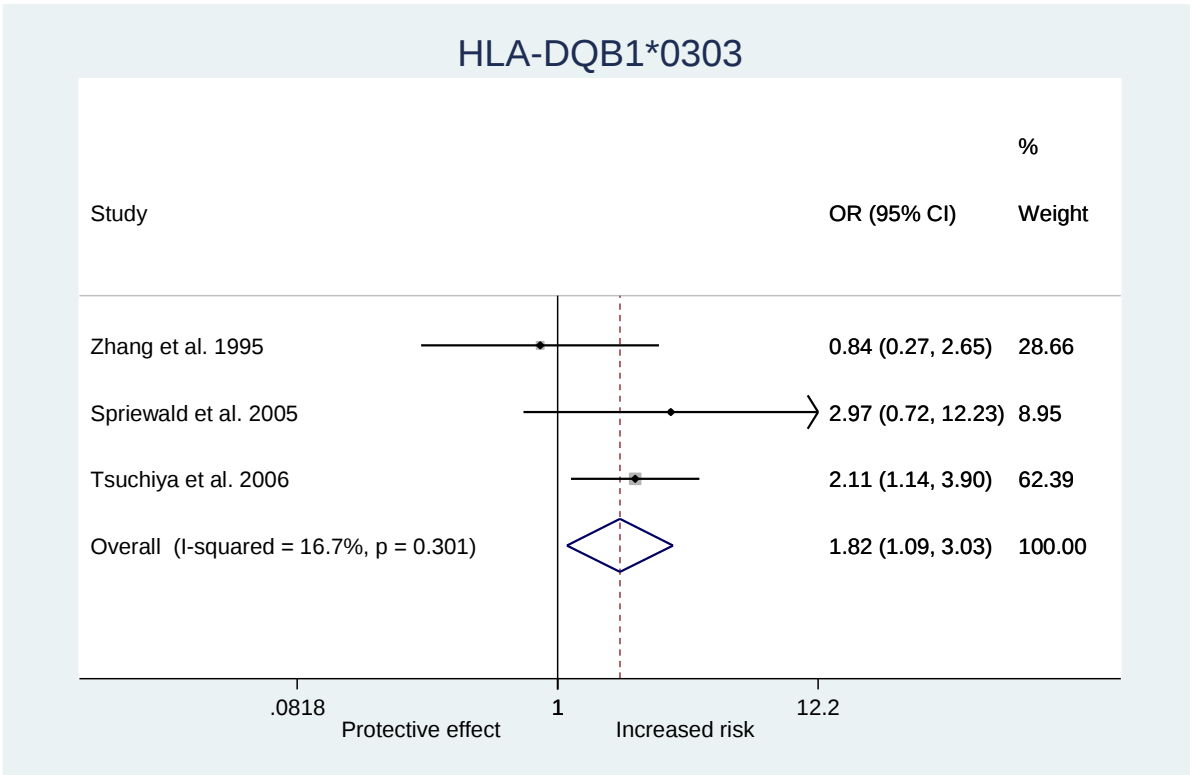
<sup>26</sup>, <sup>27</sup>, <sup>24</sup>, <sup>29</sup>, <sup>30</sup>\*\*



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

**References**

24 3 25  
, ,

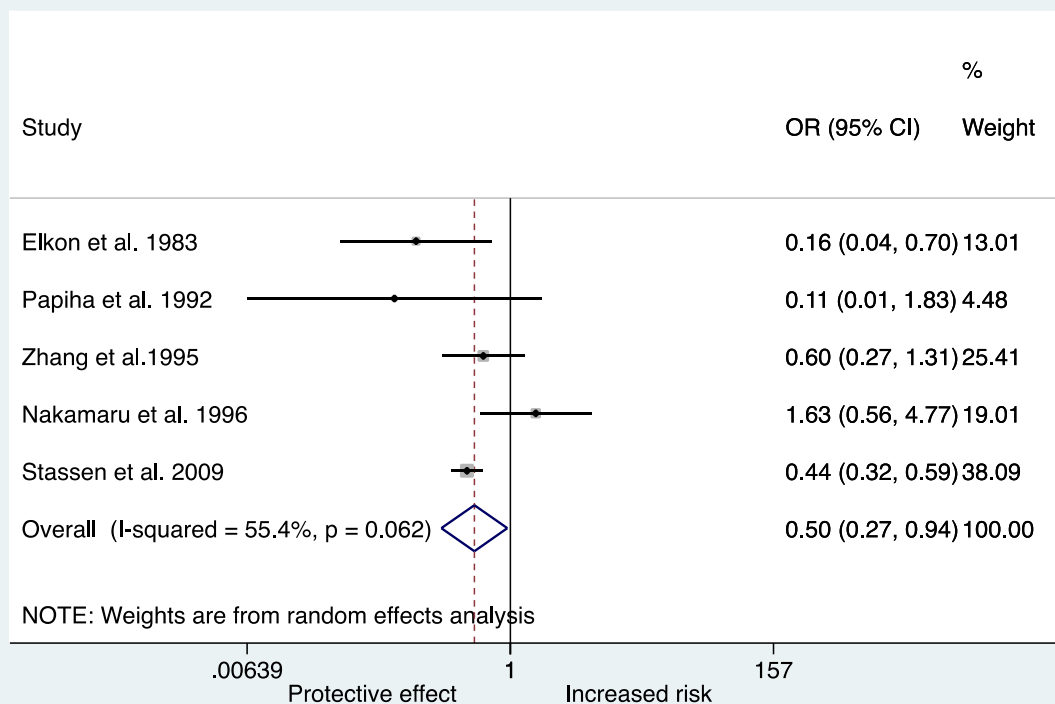


HLA-DQB1\*0303 forest plot. Harbold test:  $p=0.916$ , Egger test:  $p=0.834$ .

**References**

26 31 28  
, ,

## HLA-DR6

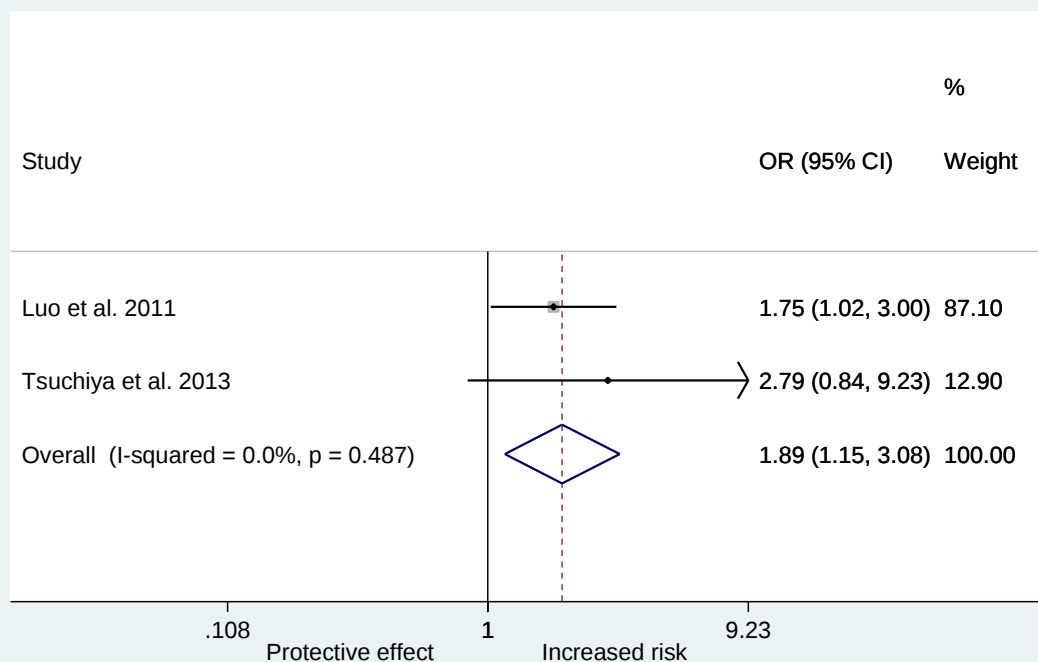


HLA-DR6 forest plot. Harbold test:  $p=0.997$ , Egger test:  $p=0.989$ .

## References

23 32 26 20 19  
, , , ,

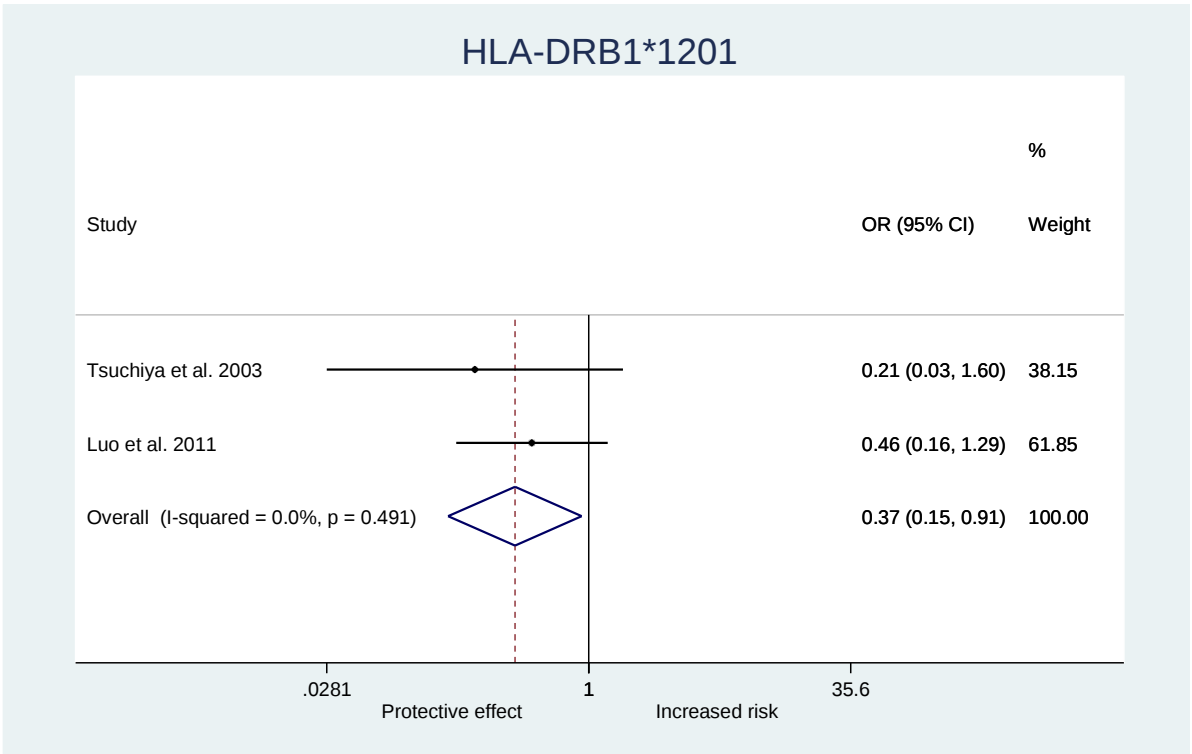
## HLA-DRB1\*1101



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

## References

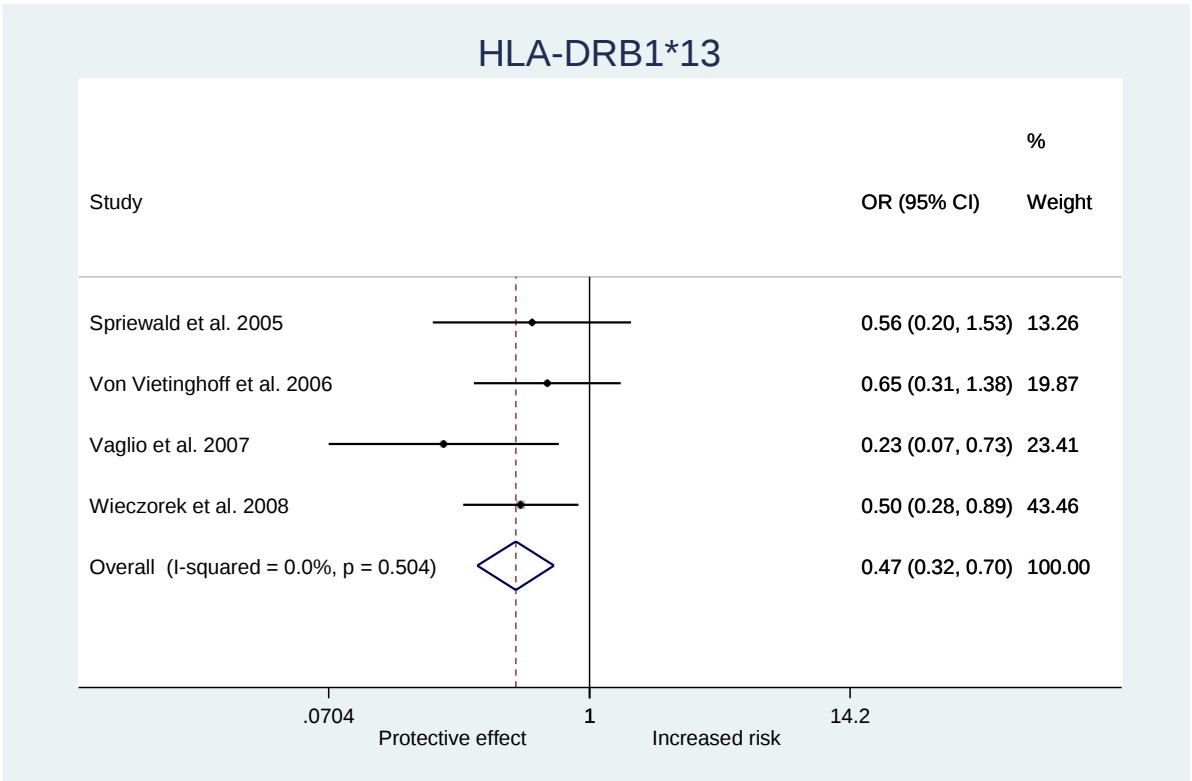
34 37  
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HLA-DRB1\*1201 forest plot. Harbold test: N/A, Egger test: N/A.

**References**

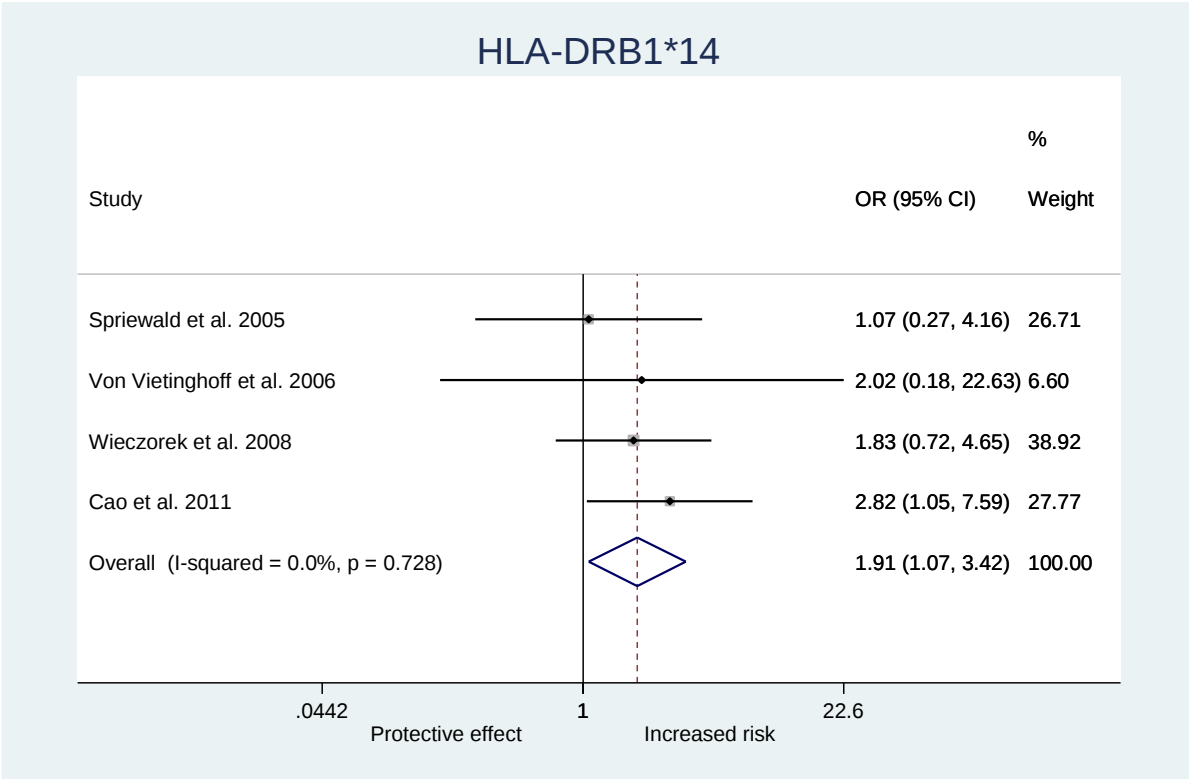
5 34 ,



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

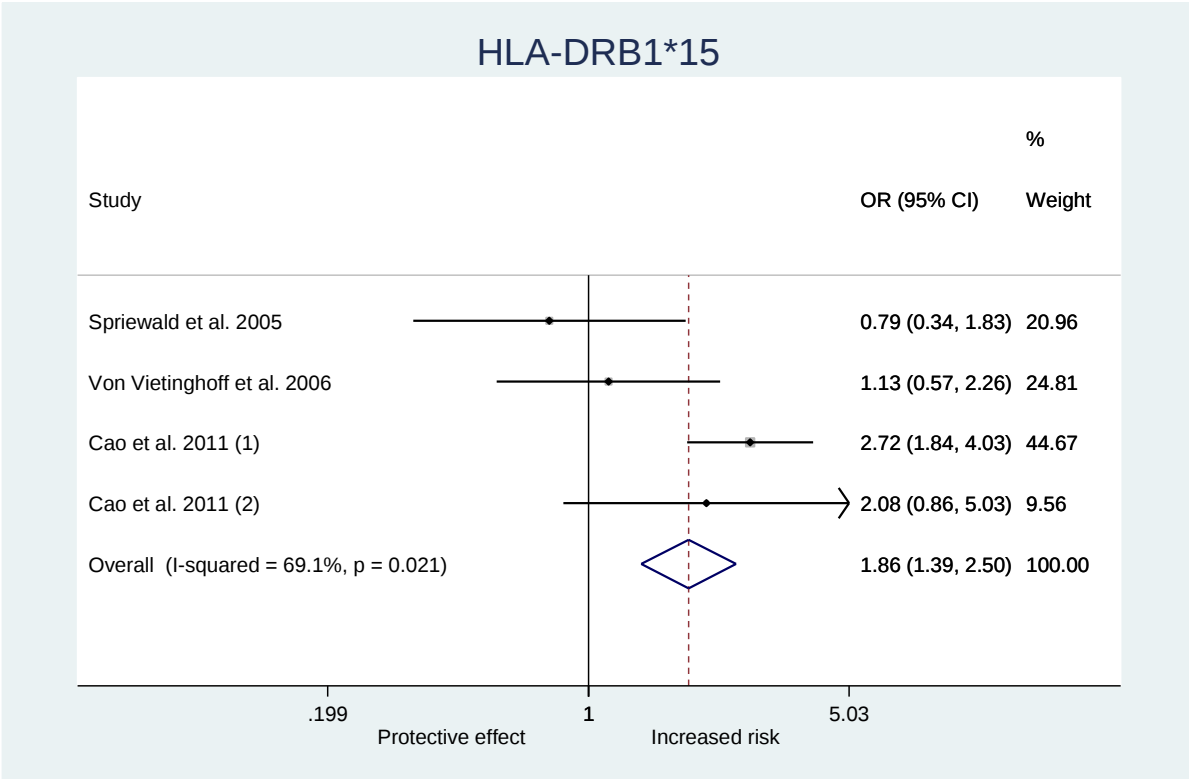
**References**

31 18 35 29 , , ,



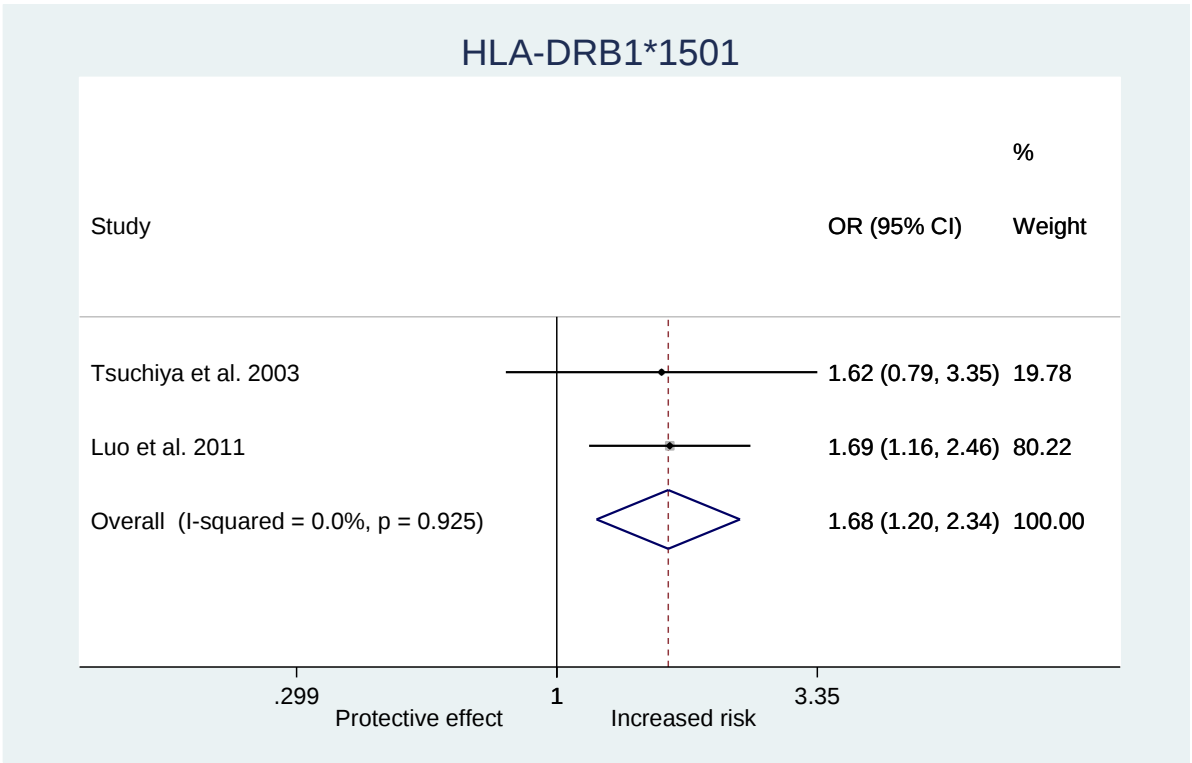
*HLA-DRB1\*14* forest plot. Harbold test:  $p=0.700$ , Egger test:  $p=0.706$ .

**References**  
31 18 29 33  
, , ,



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

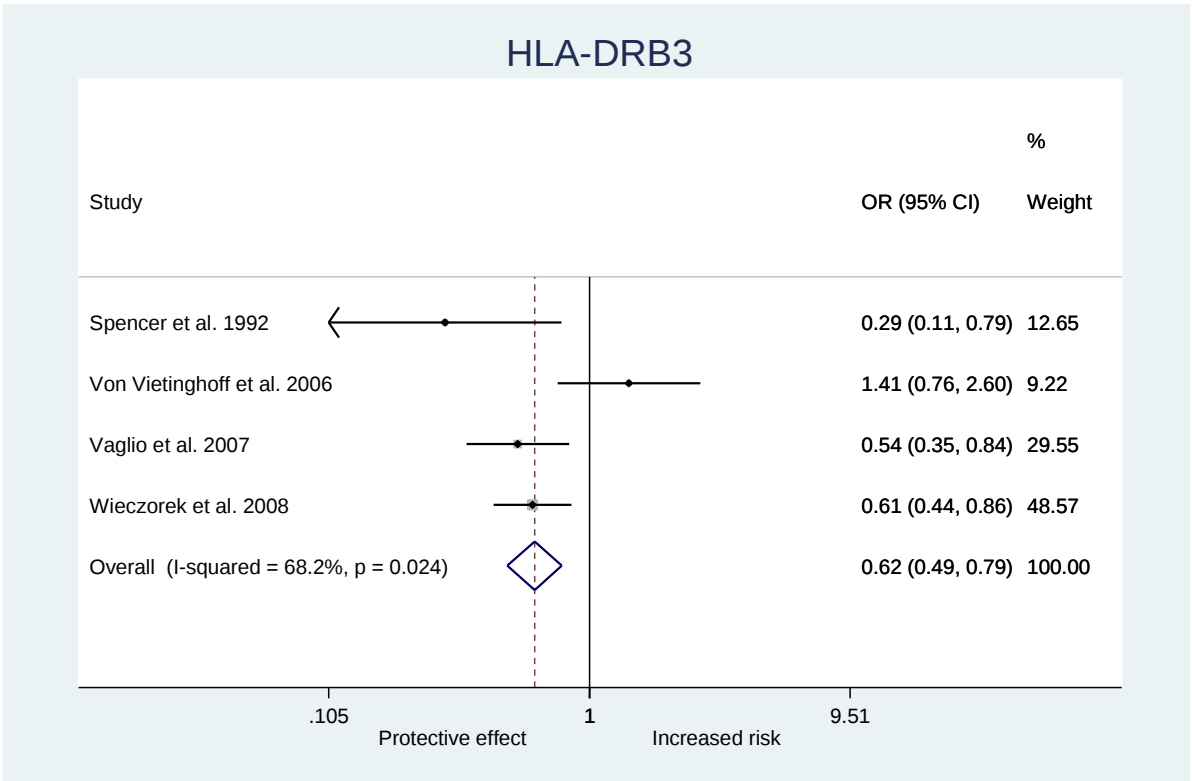
**References**  
31 18 33\*\*  
, ,



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

**References**

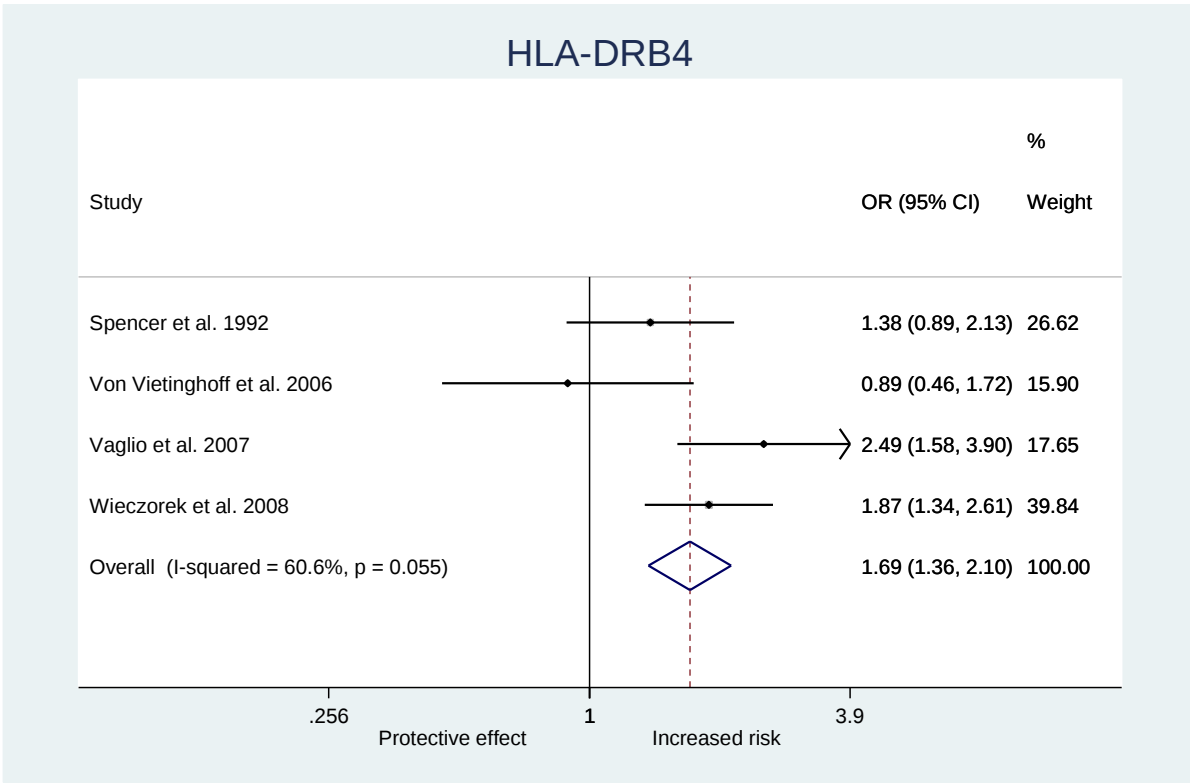
5 34  
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*HLA-DRB3* forest plot. Harbold test:  $p=0.689$ , Egger test:  $p=0.958$ .

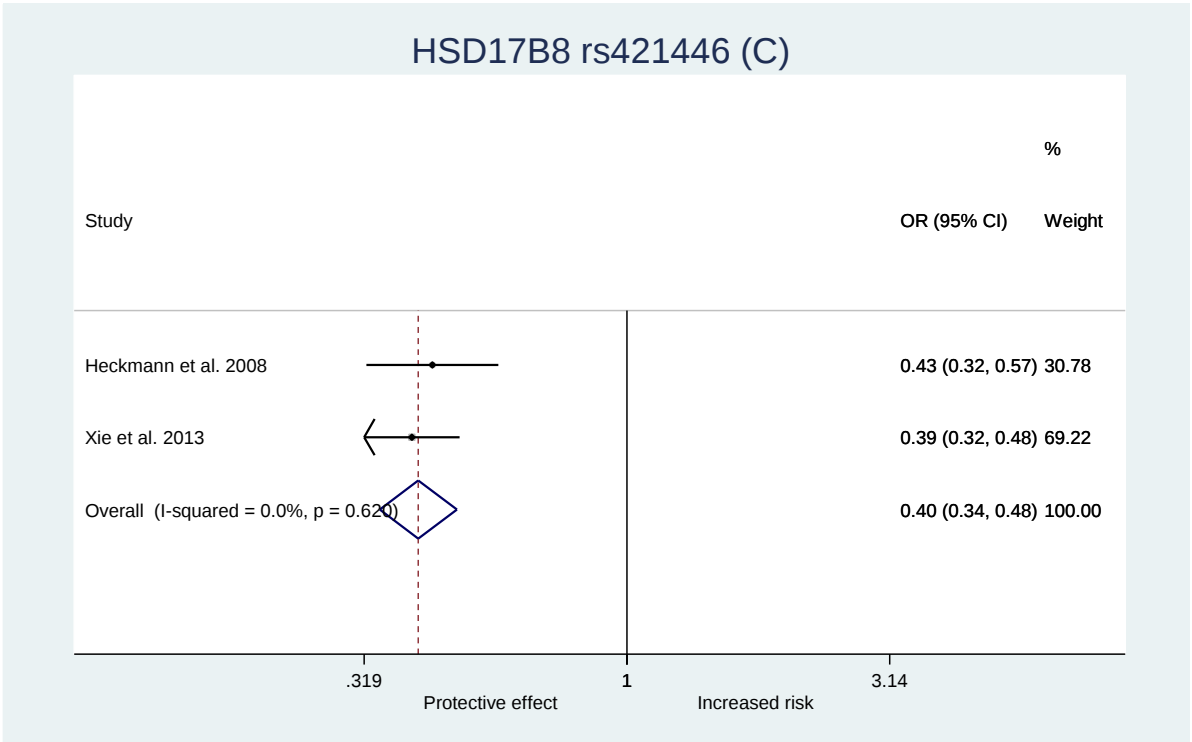
**References**

38 18 35 29  
, , ,



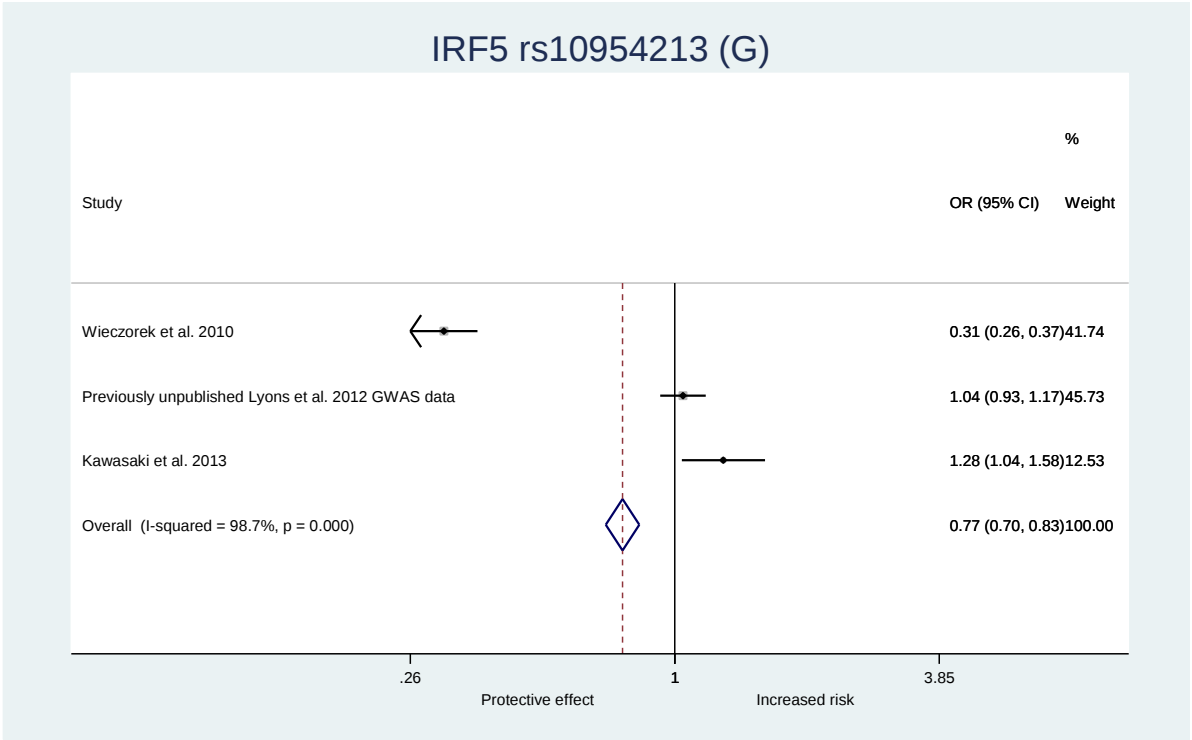
*HLA-DRB4* forest plot. Harbold test:  $p=0.533$ , Egger test:  $p=0.388$ .

**References**  
38 18 35 29  
, , ,



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

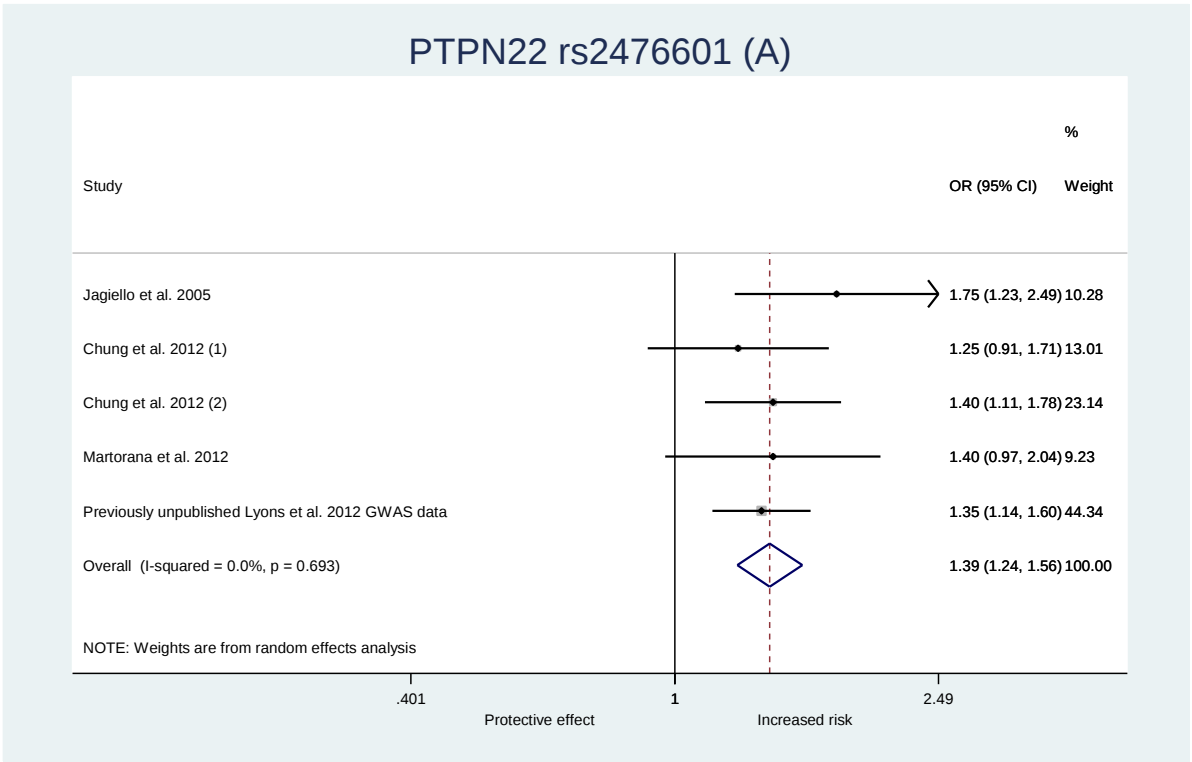
**References**  
24 25  
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*IRF5* rs10954213 (G) forest plot. Harbold test:  $p=0.948$ , Egger test:  $p=0.833$ .

**References**

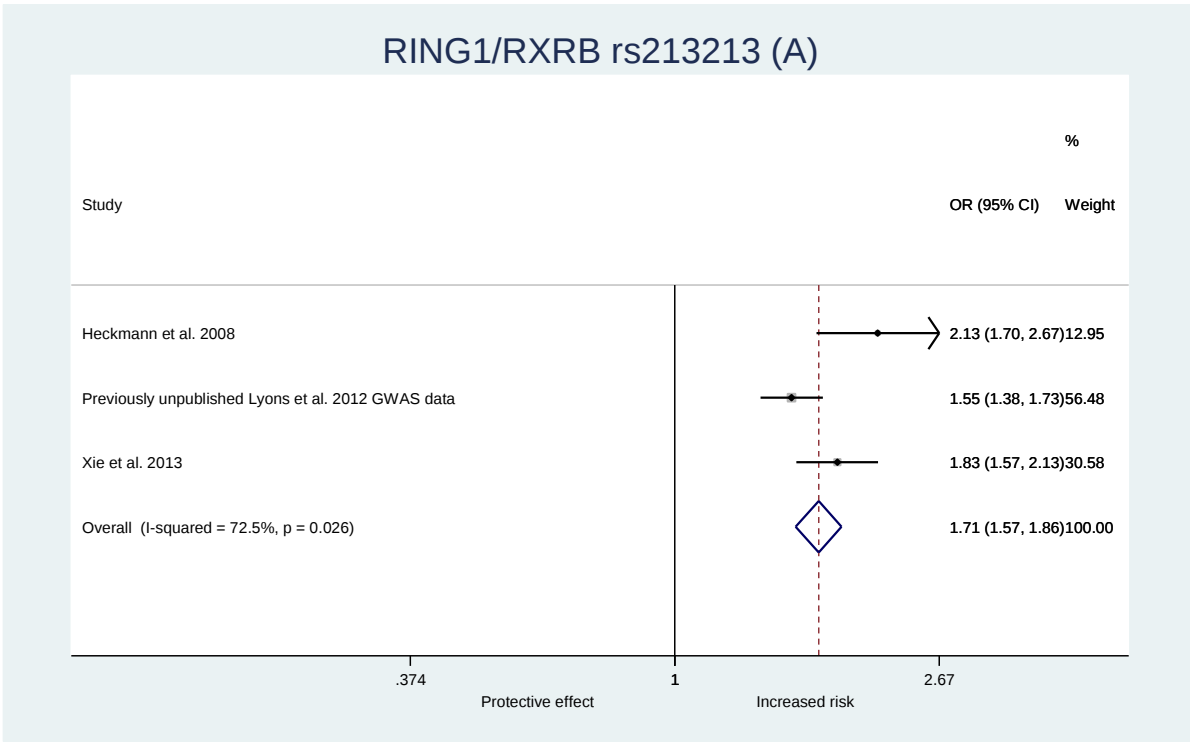
44 3 45  
, ,



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

**References**

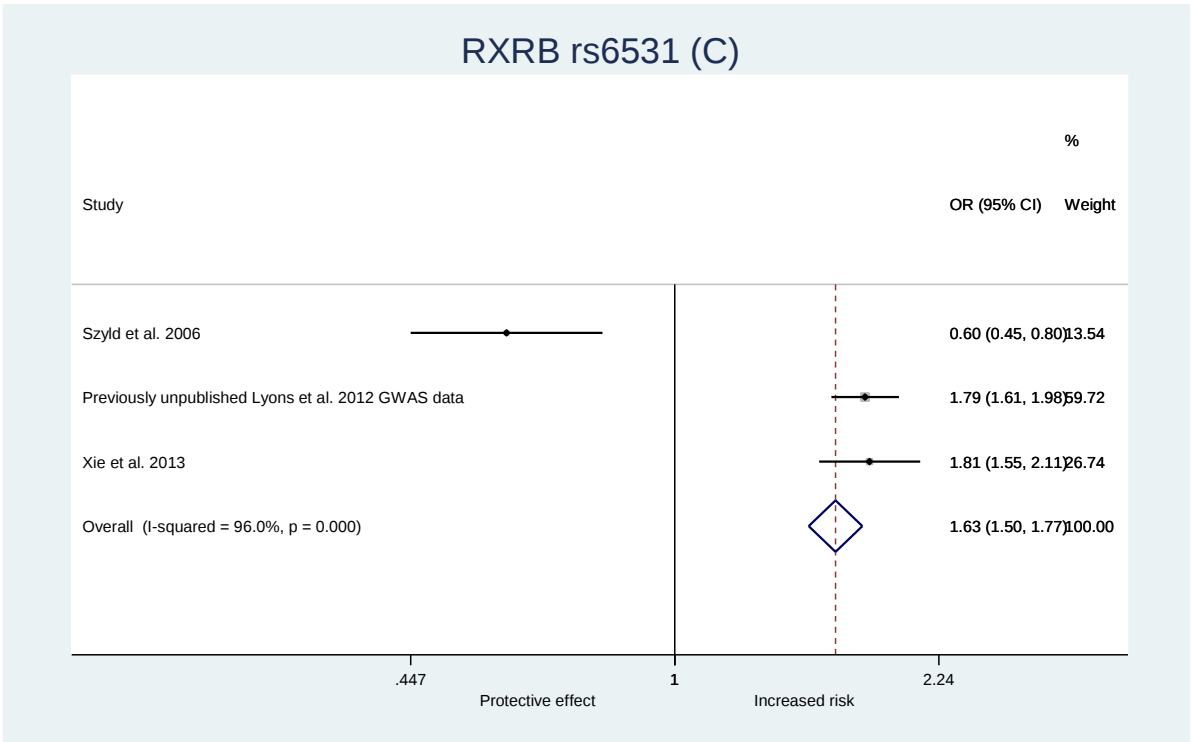
50 2\*\* 51 3  
, \*\*, ,



*RING1/RXR $\beta$*  rs213213 (A) forest plot. Harbold test:  $p=0.187$ , Egger test:  $p=0.169$ .

**References**

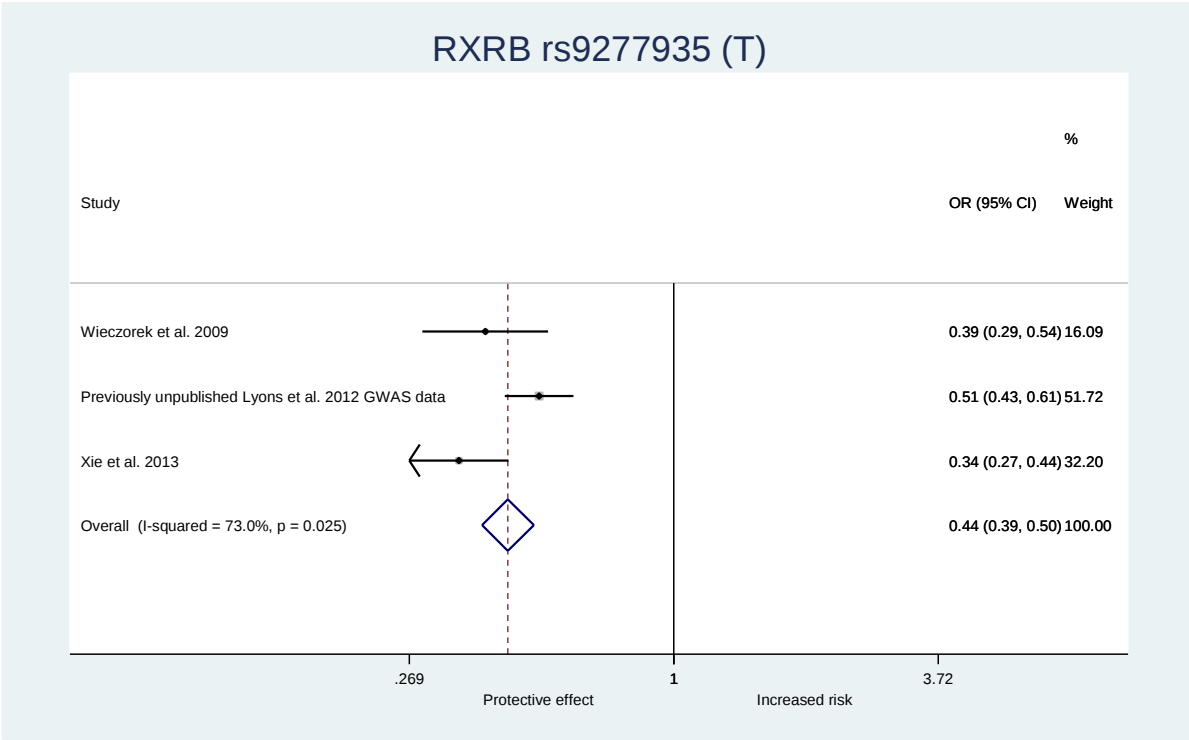
24 3 25  
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*RXR $\beta$*  rs6531 (C) forest plot. Harbold test:  $p=0.292$ , Egger test:  $p=0.301$ .

**References**

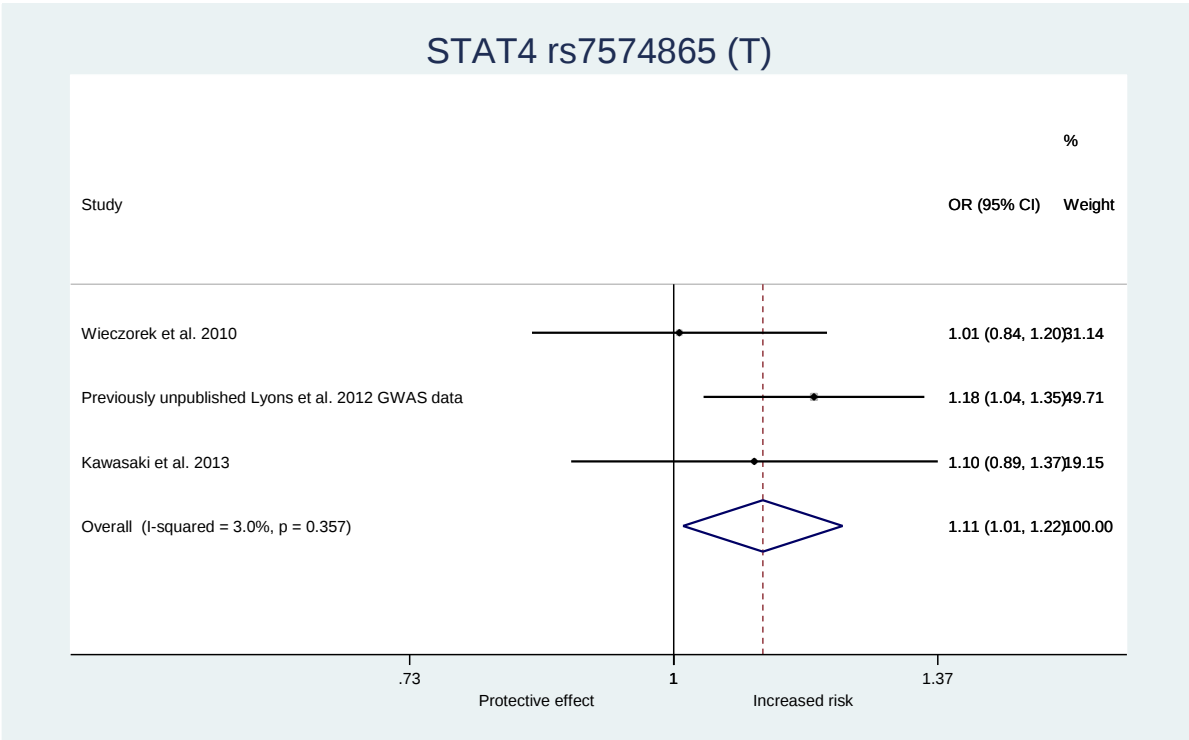
52 3 25  
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*RXRB* rs9277935 (T) forest plot. Harbold test:  $p=0.393$ , Egger test:  $p=0.406$ .

**References**

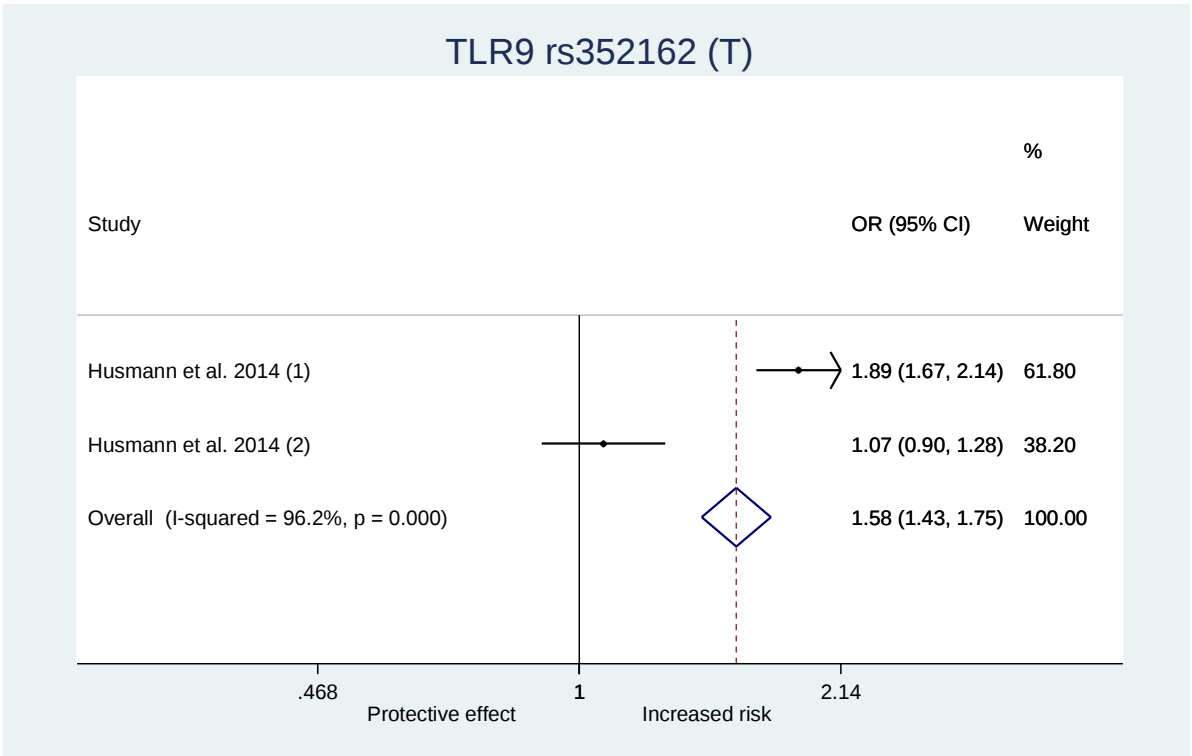
53 3 25  
, ,



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

**References**

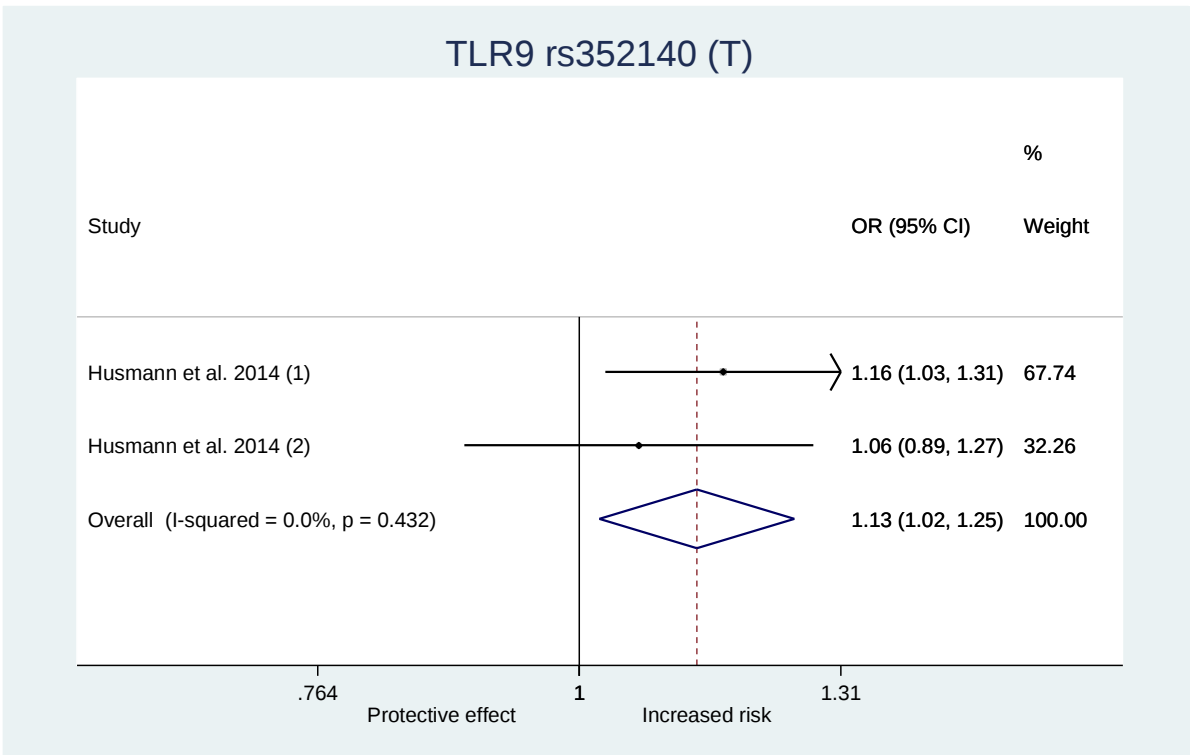
44 45 3  
, ,



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

**References**

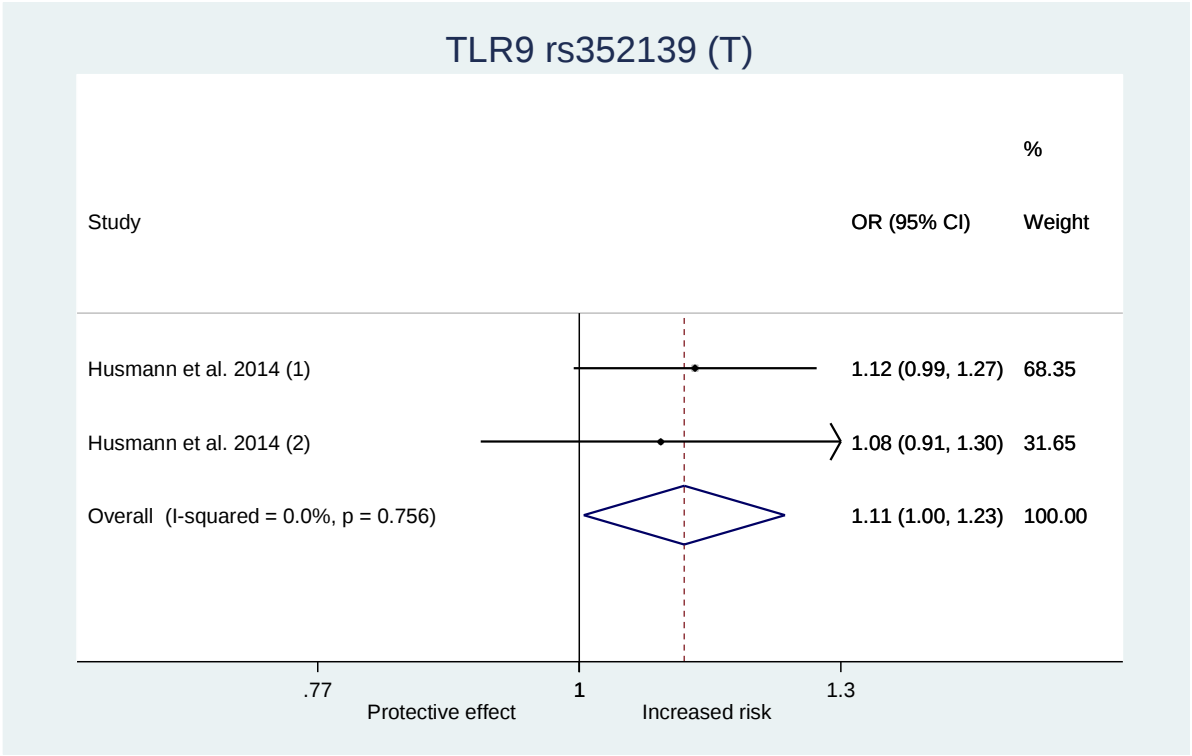
40\*\*



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

**References**

40\*\*



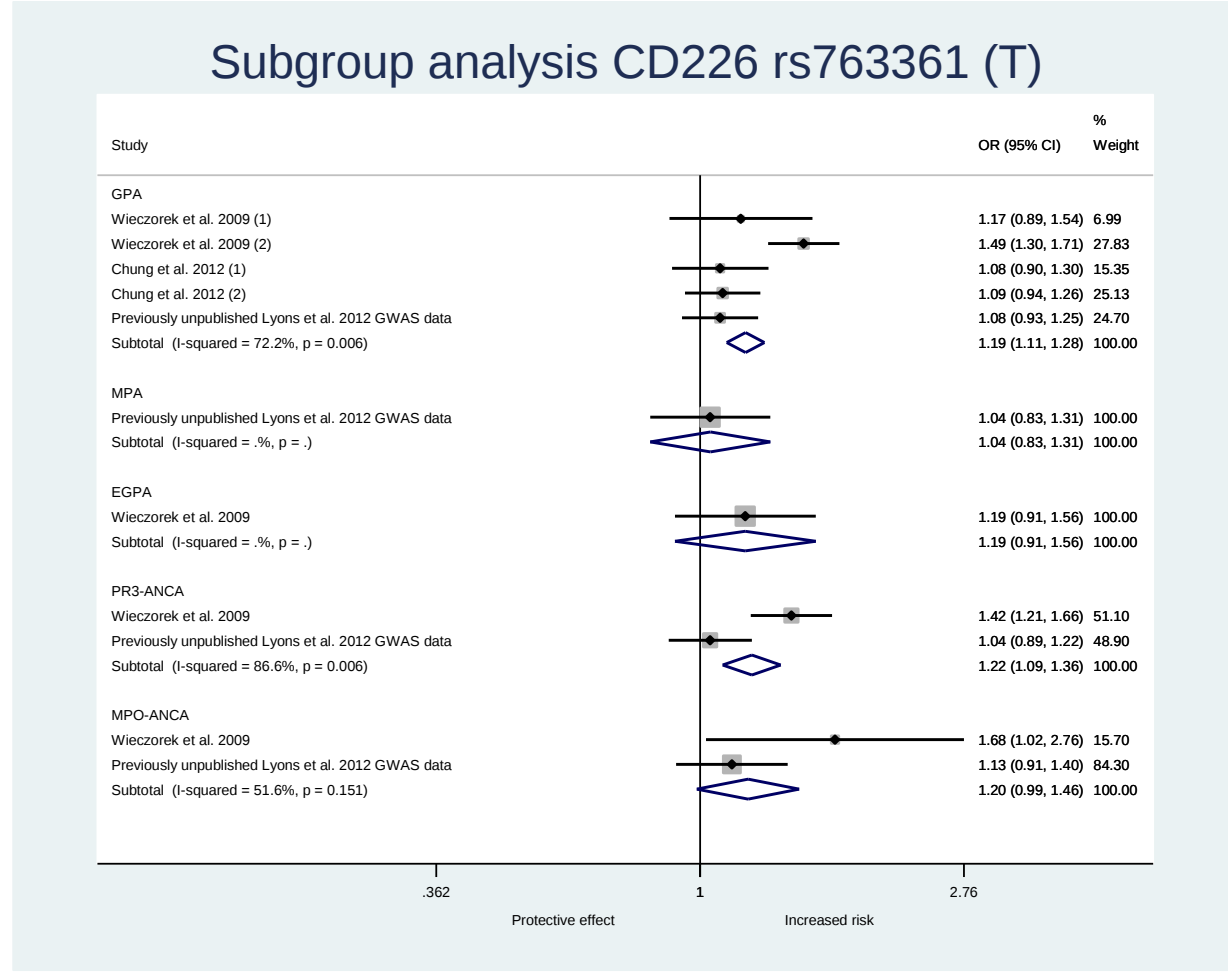
TLR9 rs352139 (T) forest plot. Harbold test: N/A, Egger test: N/A.

**References**

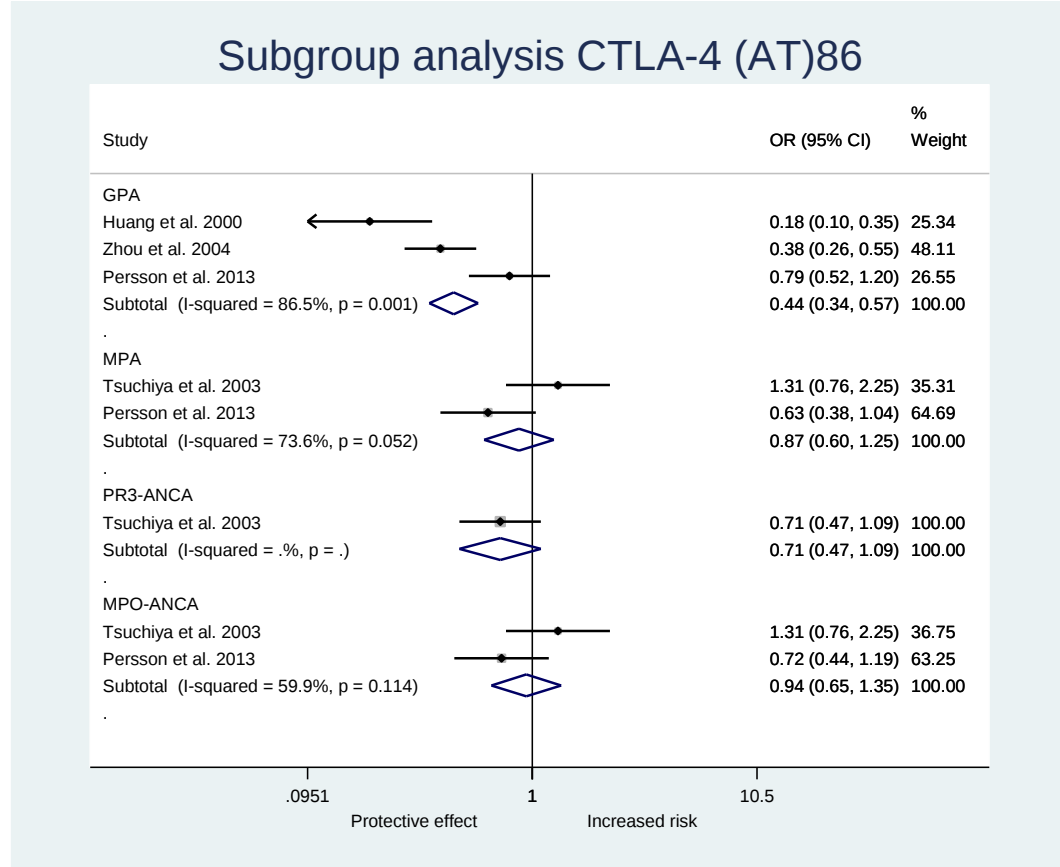
40\*\*

\*\*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

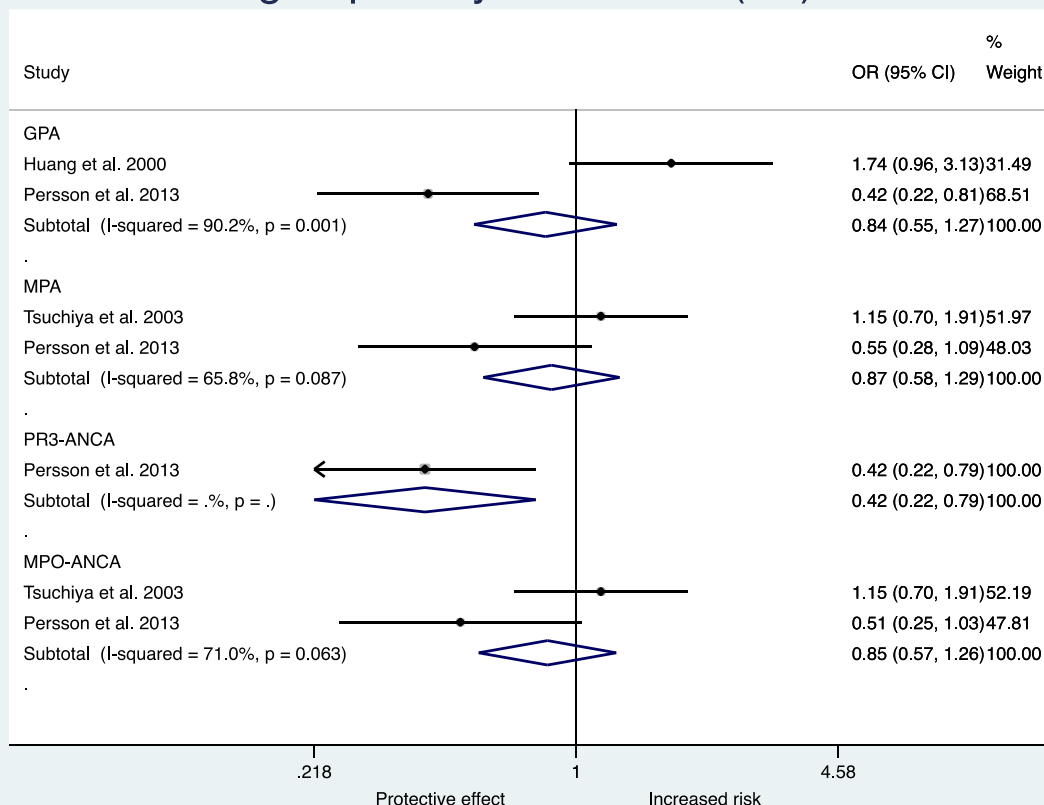


References: <sup>1\*\*</sup>, <sup>2\*\*</sup>, <sup>3</sup>



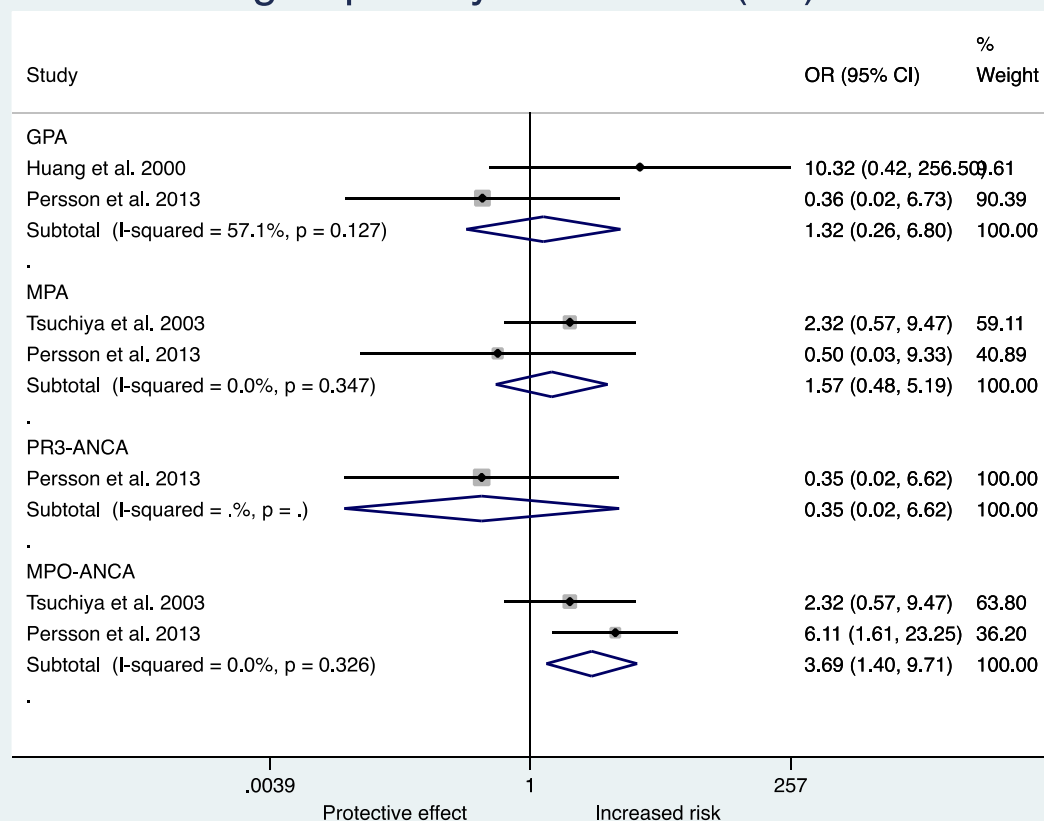
References: <sup>4</sup>, <sup>5</sup>, <sup>6</sup>, <sup>7</sup>

## Subgroup analysis CTLA-4 (AT)104



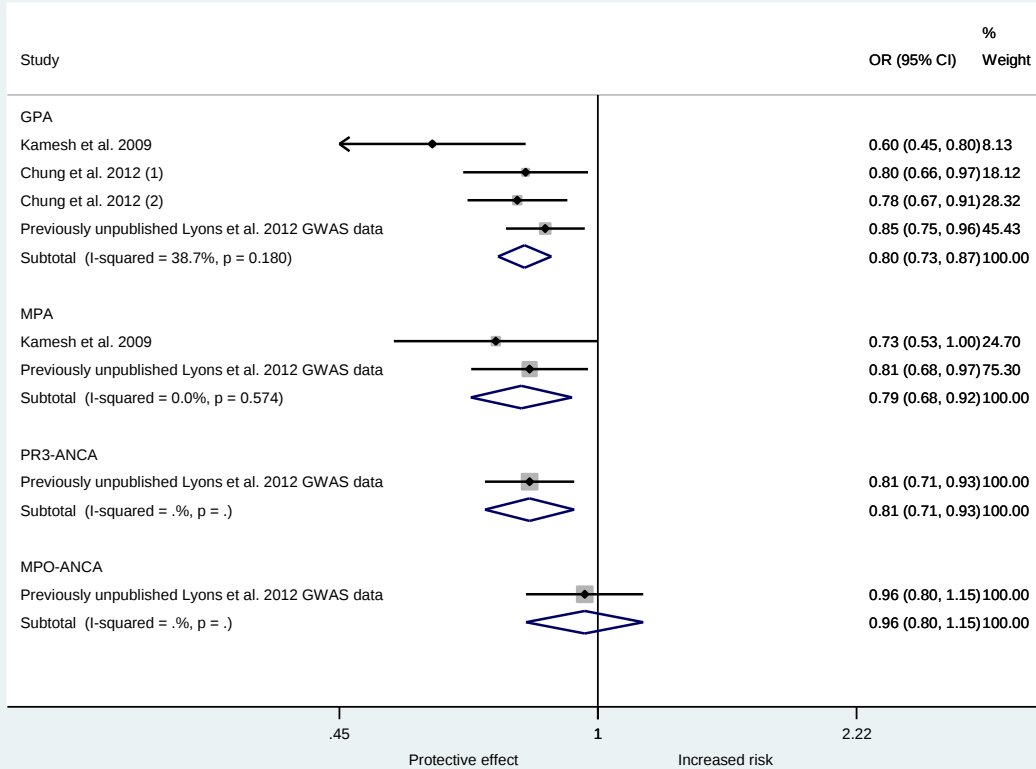
References: <sup>4</sup>, <sup>7</sup>, <sup>5</sup>

## Subgroup analysis CTLA-4 (AT)122



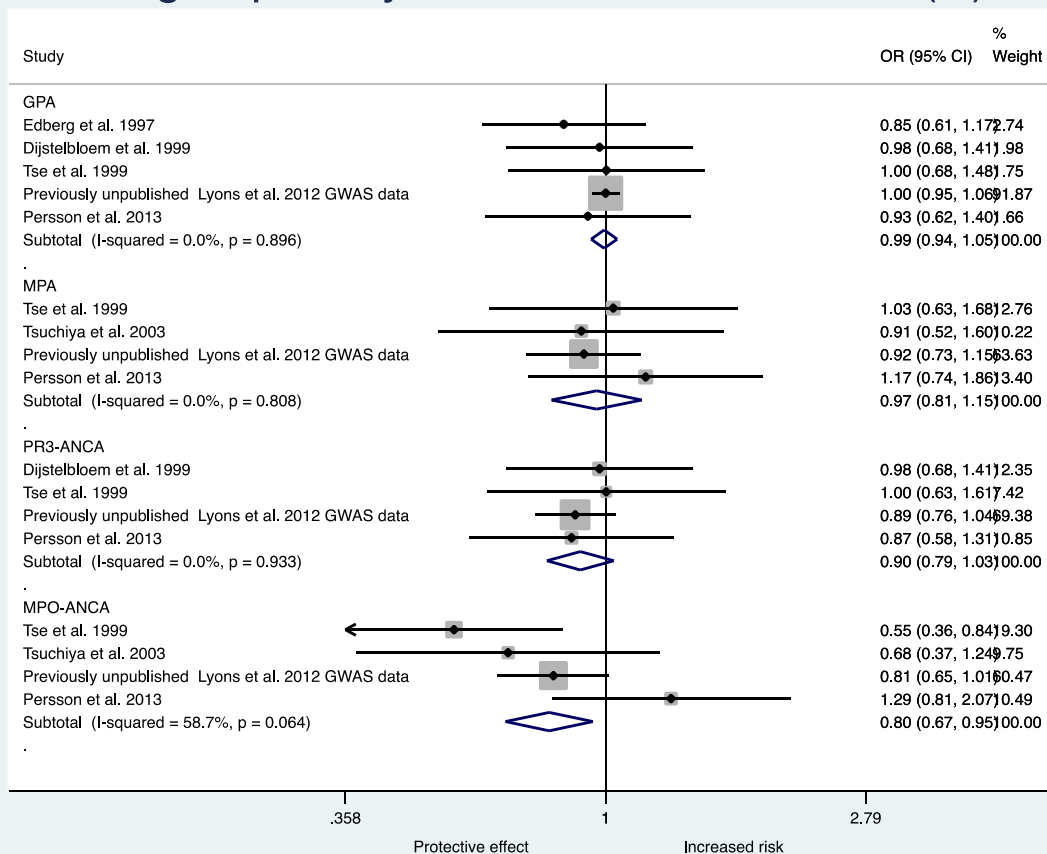
References: <sup>4</sup>, <sup>7</sup>, <sup>5</sup>

## Subgroup analysis CTLA-4 rs3087243 (A)



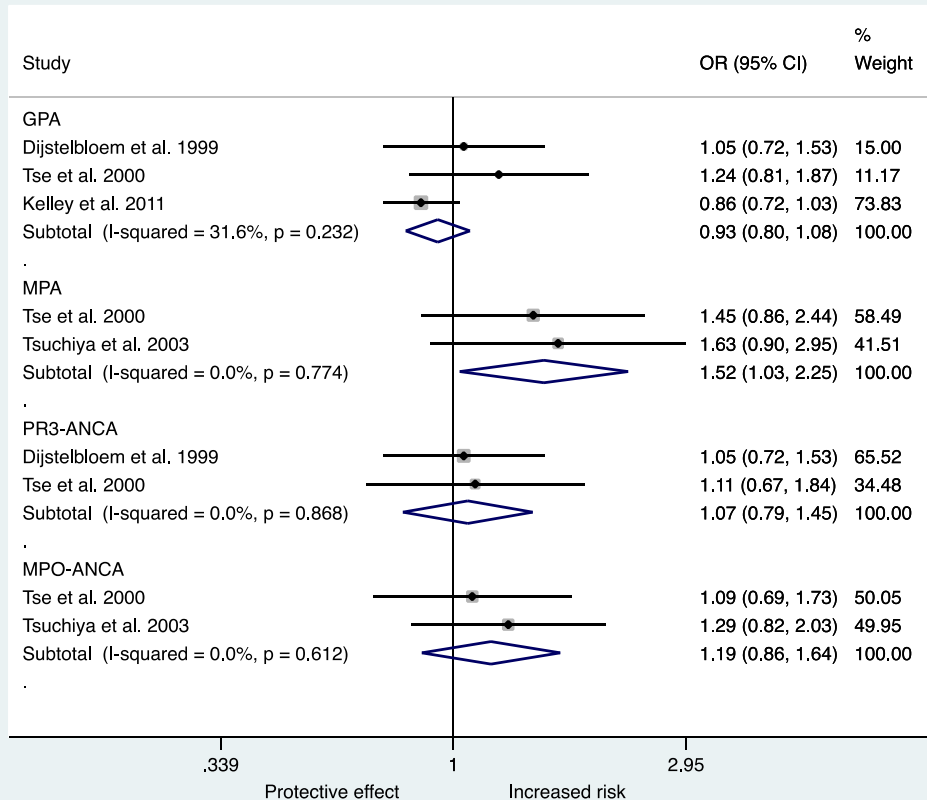
References: <sup>9</sup>, <sup>2\*\*</sup>, <sup>3</sup>

## Subgroup analysis FCGR2A rs1801274 (C)



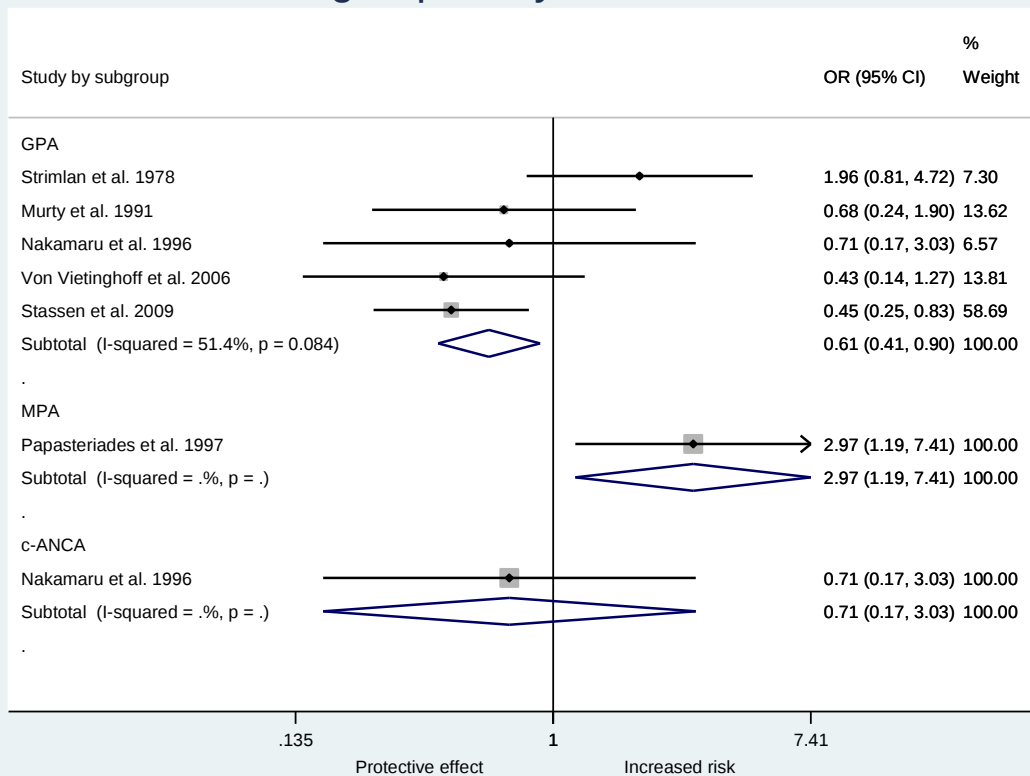
References: <sup>11</sup>, <sup>12</sup>, <sup>13</sup>, <sup>5</sup>, <sup>7</sup>, <sup>3</sup>

## Subgroup analysis FCGR3B (NA1)



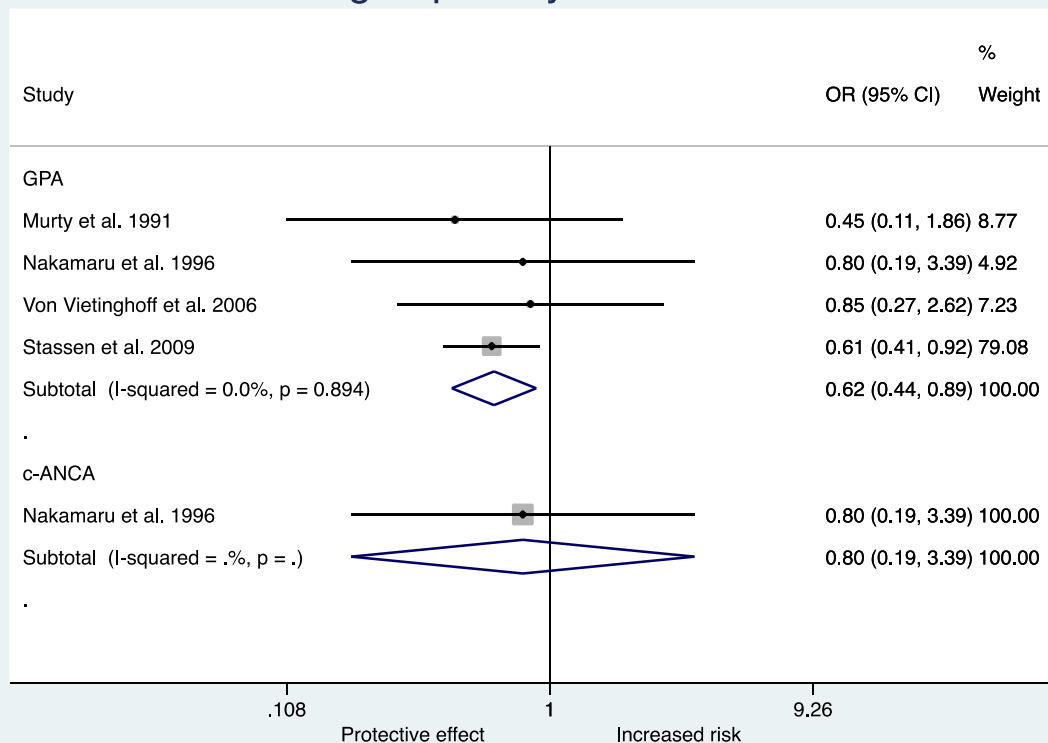
References: <sup>12</sup>, <sup>14</sup>, <sup>10</sup>, <sup>5</sup>

## Subgroup analysis HLA-A11



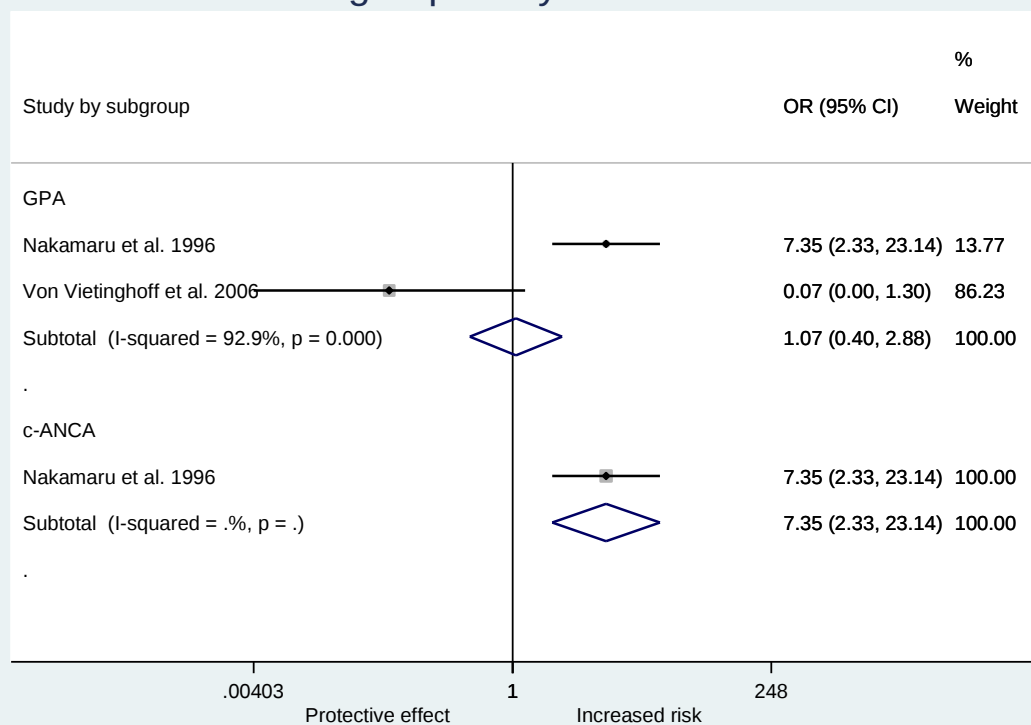
References: <sup>16</sup>, <sup>17</sup>, <sup>20</sup>, <sup>22</sup>, <sup>18</sup>, <sup>19</sup>

## Subgroup analysis HLA-B35



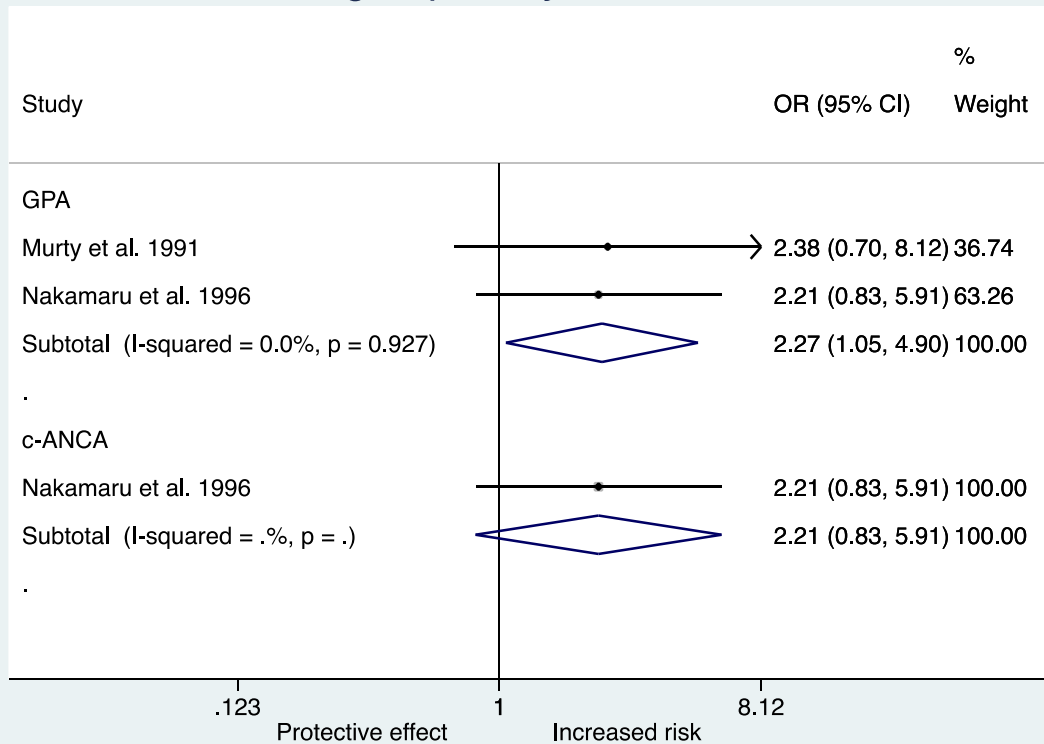
References: <sup>17</sup>, <sup>20</sup>, <sup>18</sup>, <sup>19</sup>

## Subgroup analysis HLA-B55



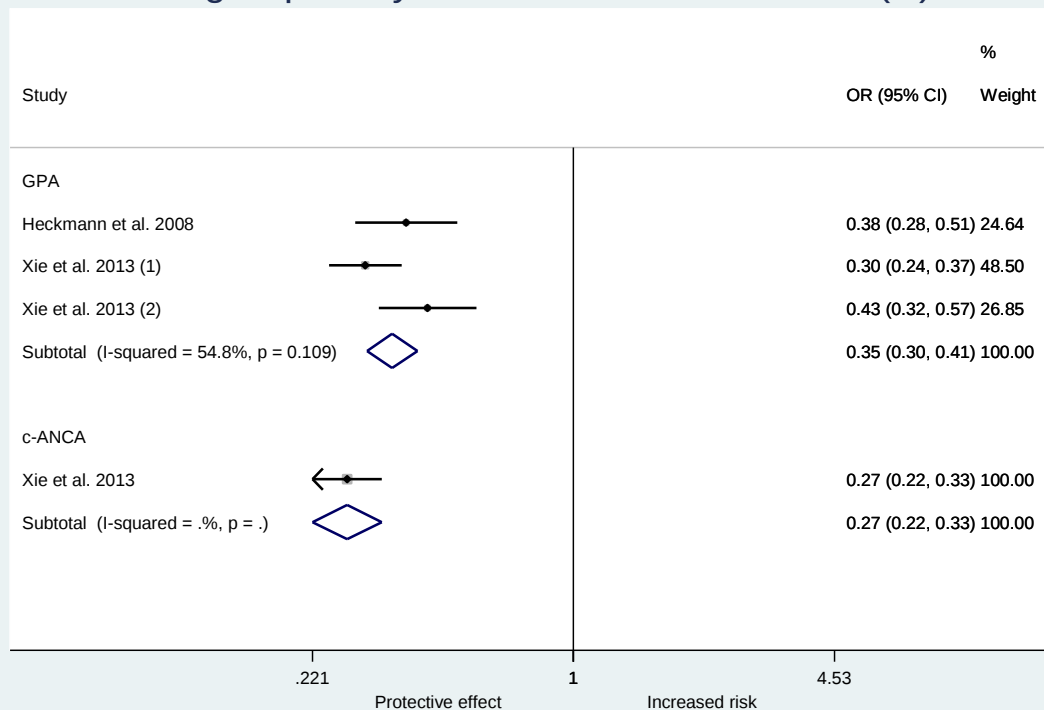
References: <sup>20</sup>, <sup>18</sup>

## Subgroup analysis HLA-B62



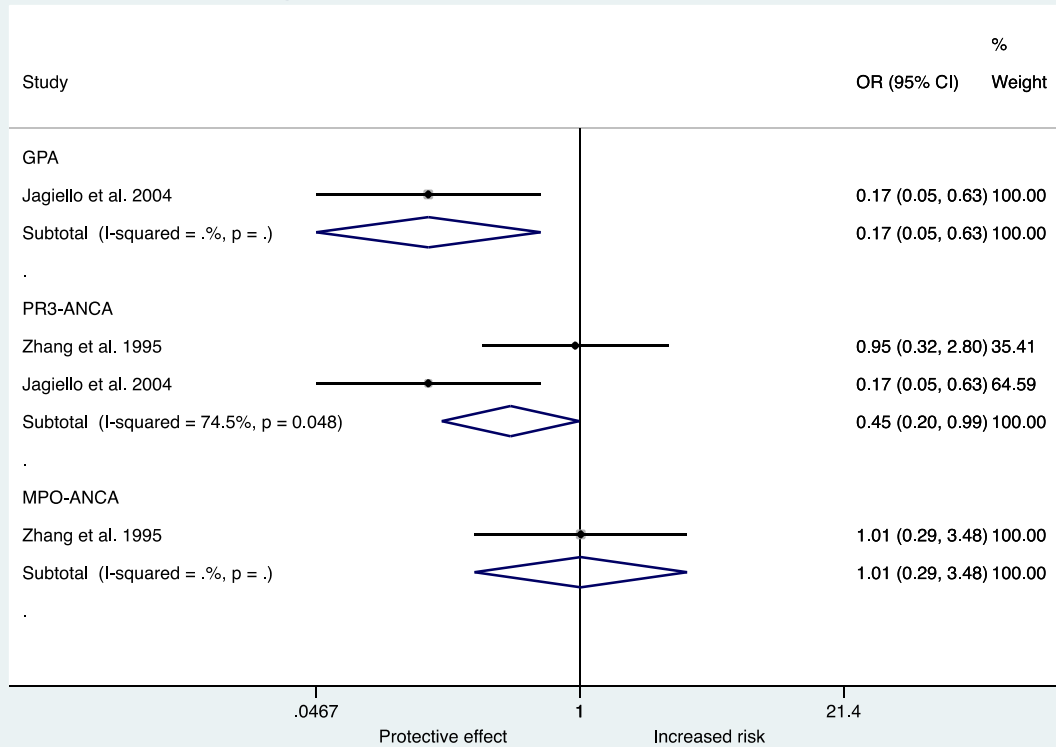
References: <sup>17</sup>, <sup>20</sup>

## Subgroup analysis HLA-DPA1 rs9277341 (C)



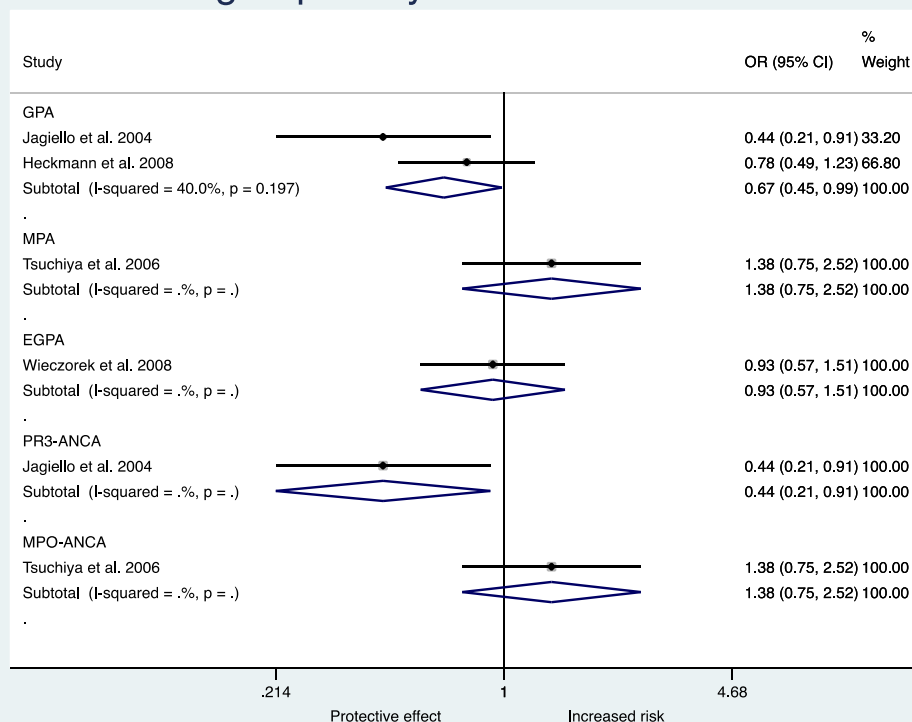
References: <sup>24</sup>, <sup>25\*\*</sup>

## Subgroup analysis HLA-DPB1\*0101



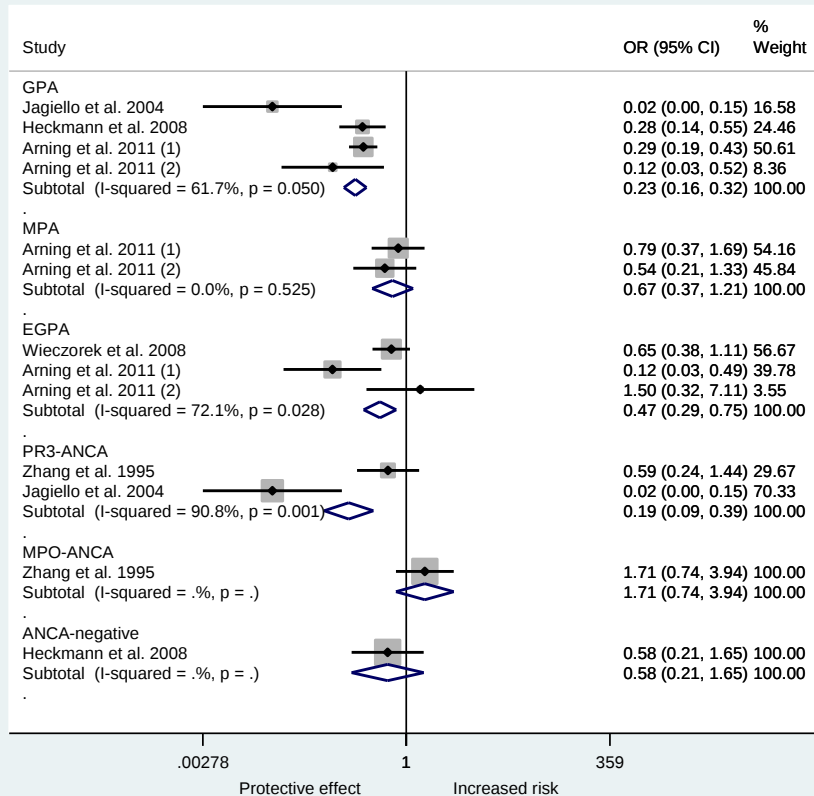
References: <sup>27</sup>, <sup>26</sup>

## Subgroup analysis HLA-DPB1\*0201



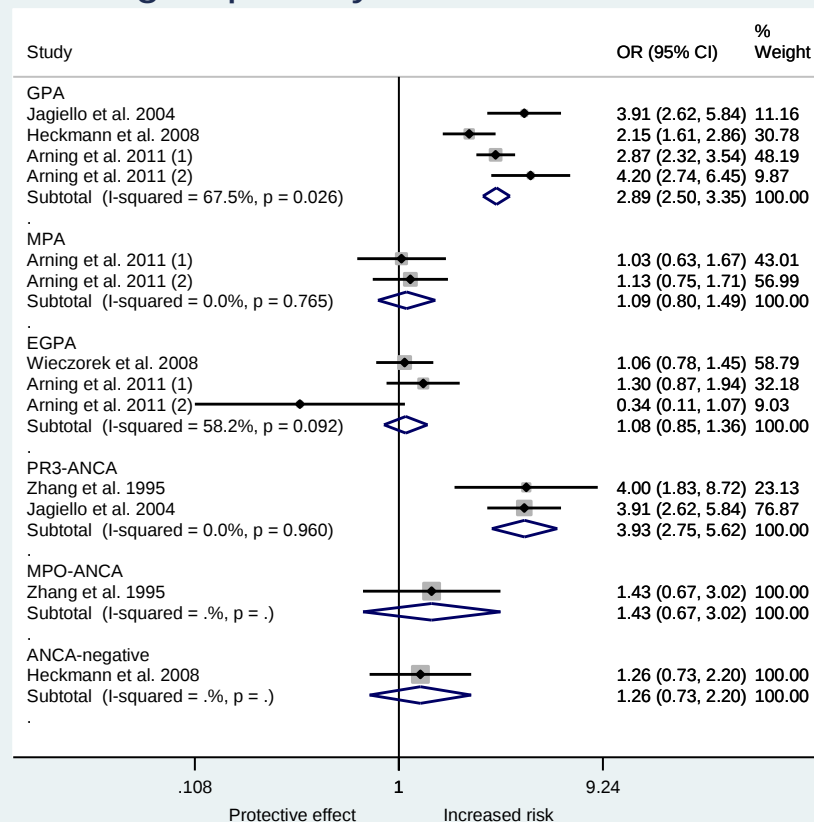
References: <sup>27</sup>, <sup>24</sup>, <sup>28</sup>, <sup>29</sup>

## Subgroup analysis HLA-DPB1\*0301



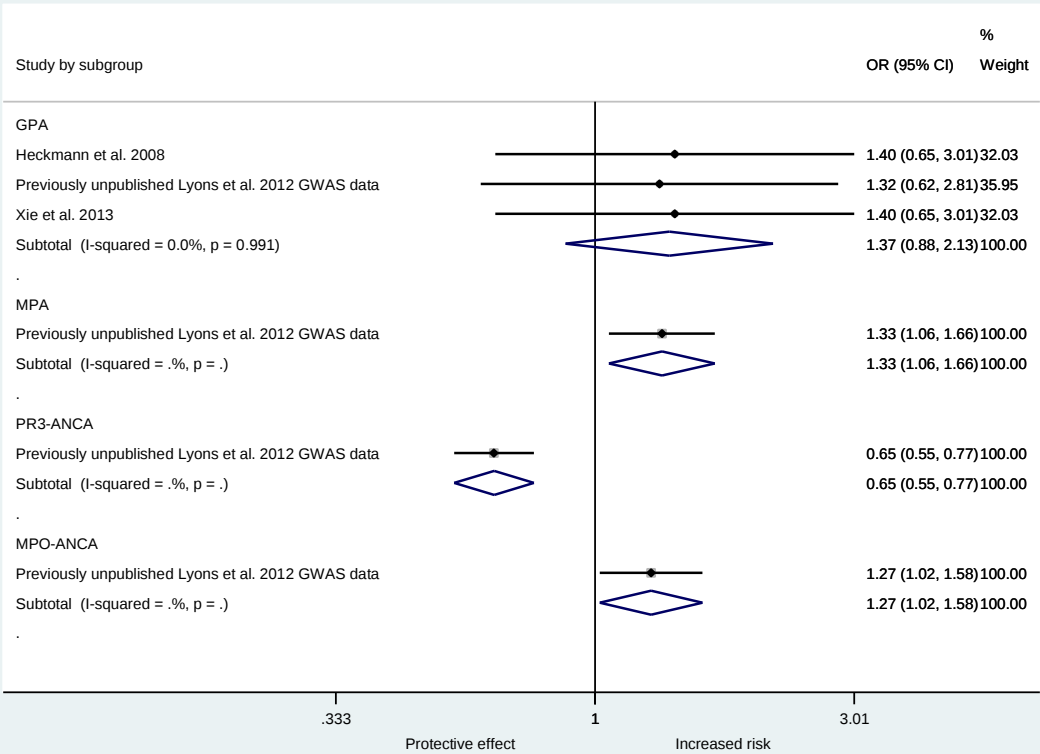
References: <sup>26</sup>, <sup>27</sup>, <sup>24</sup>, <sup>29</sup>, <sup>30</sup>\*\*

## Subgroup analysis HLA-DPB1\*0401



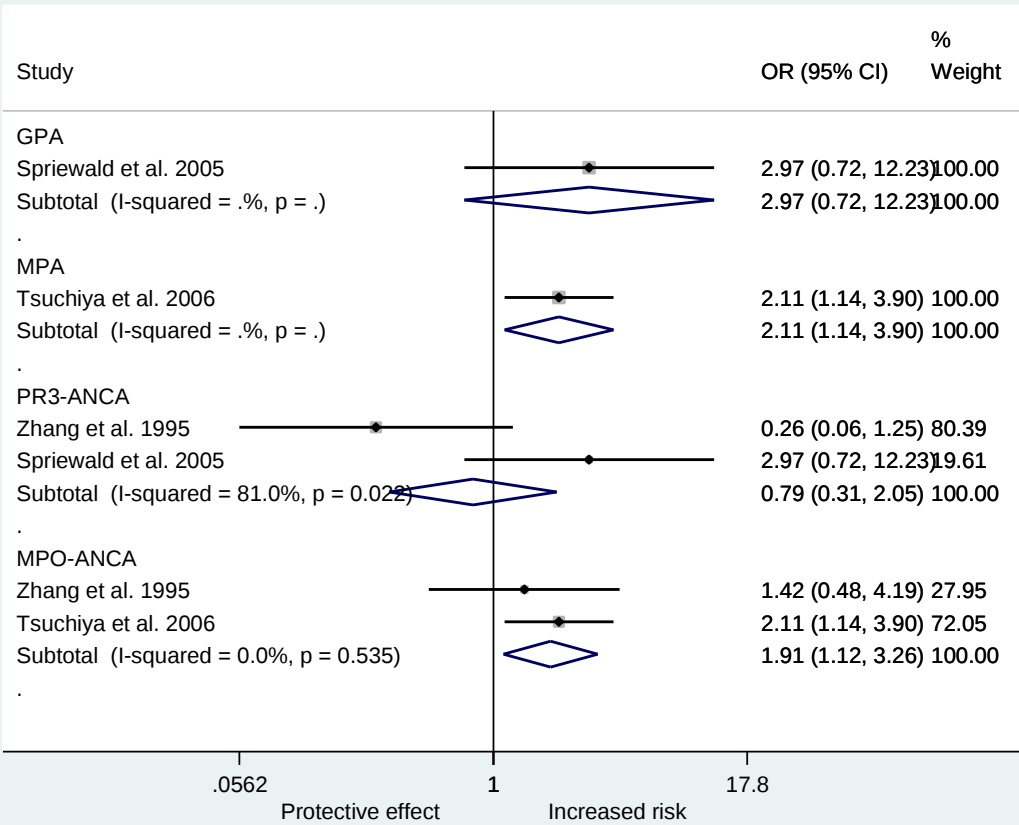
References: <sup>26</sup>, <sup>27</sup>, <sup>24</sup>, <sup>29</sup>, <sup>30</sup>\*\*

# Subgroup analysis HLA-DPB2 rs3130215 (A)



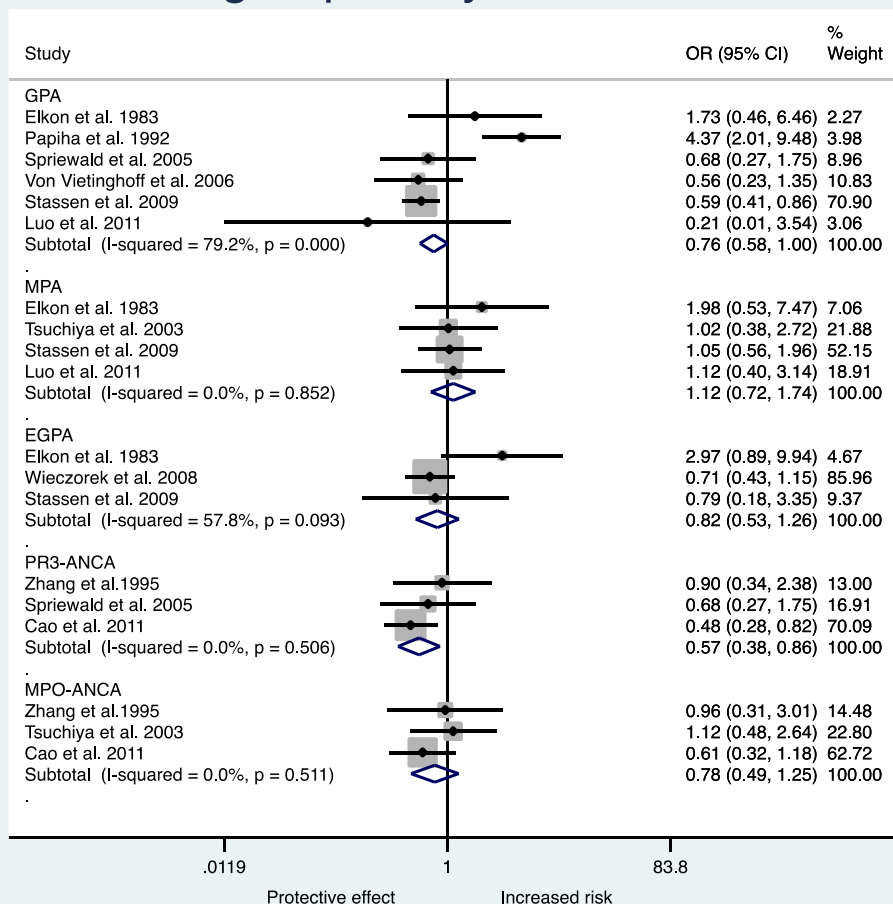
References: <sup>24</sup>, <sup>3</sup>, <sup>25</sup>

# Subgroup analysis HLA-DQB1\*0303



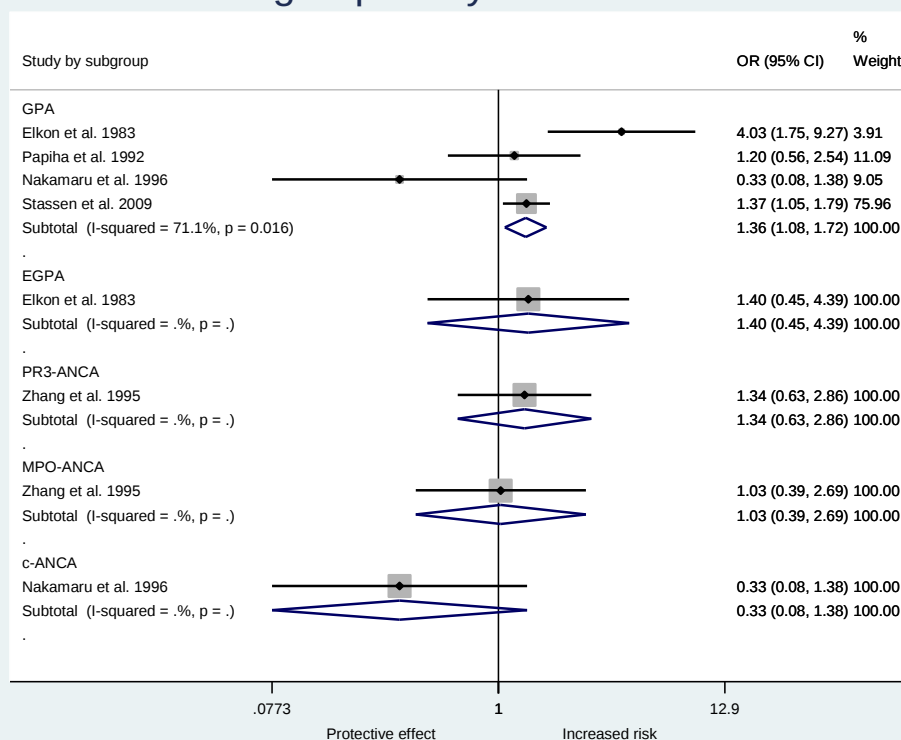
References: <sup>26</sup>, <sup>31</sup>, <sup>28</sup>

## Subgroup analysis HLA-DR1



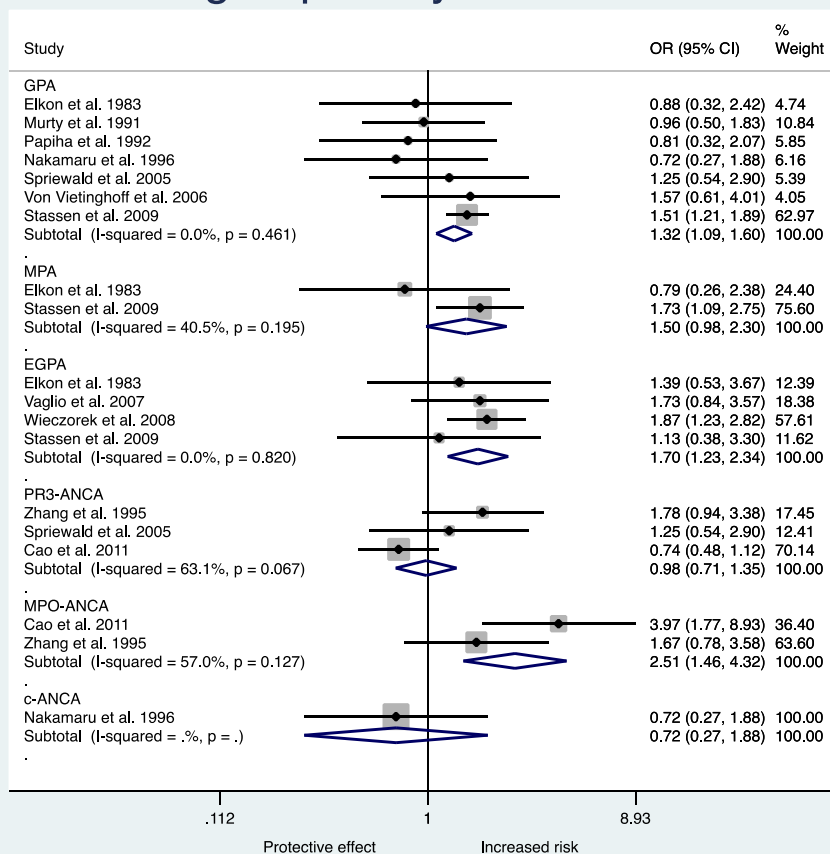
References: 23, 32, 31, 18, 19, 34, 5, 29, 26, 33

## Subgroup analysis HLA-DR2



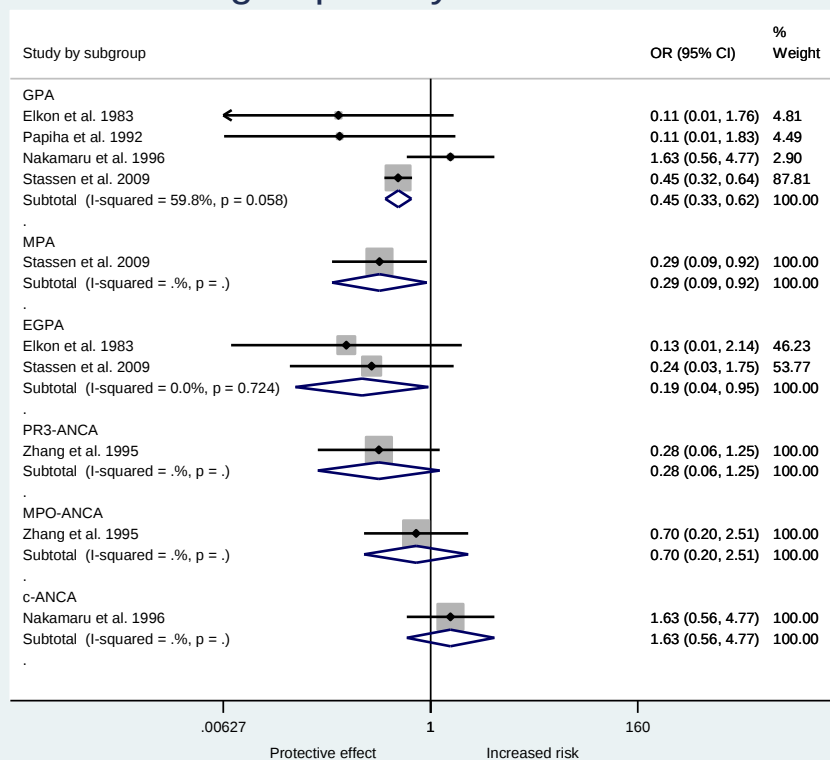
References: 23, 32, 26, 20, 19

## Subgroup analysis HLA-DR4



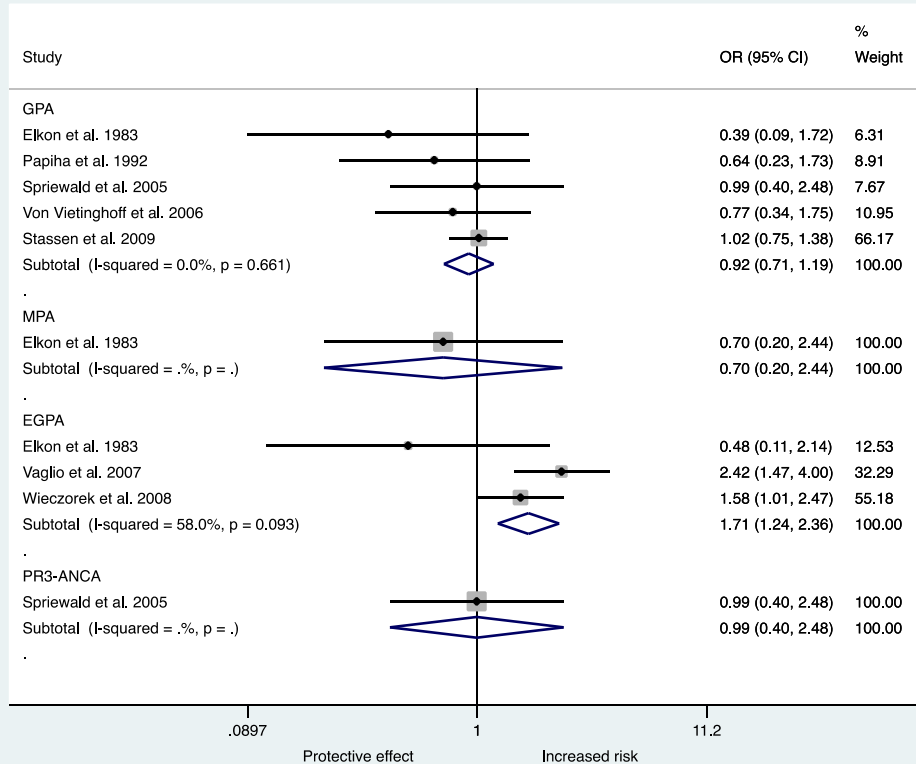
References: 23, 17, 32, 20, 31, 18, 19, 35, 29, 26, 33

## Subgroup analysis HLA-DR6



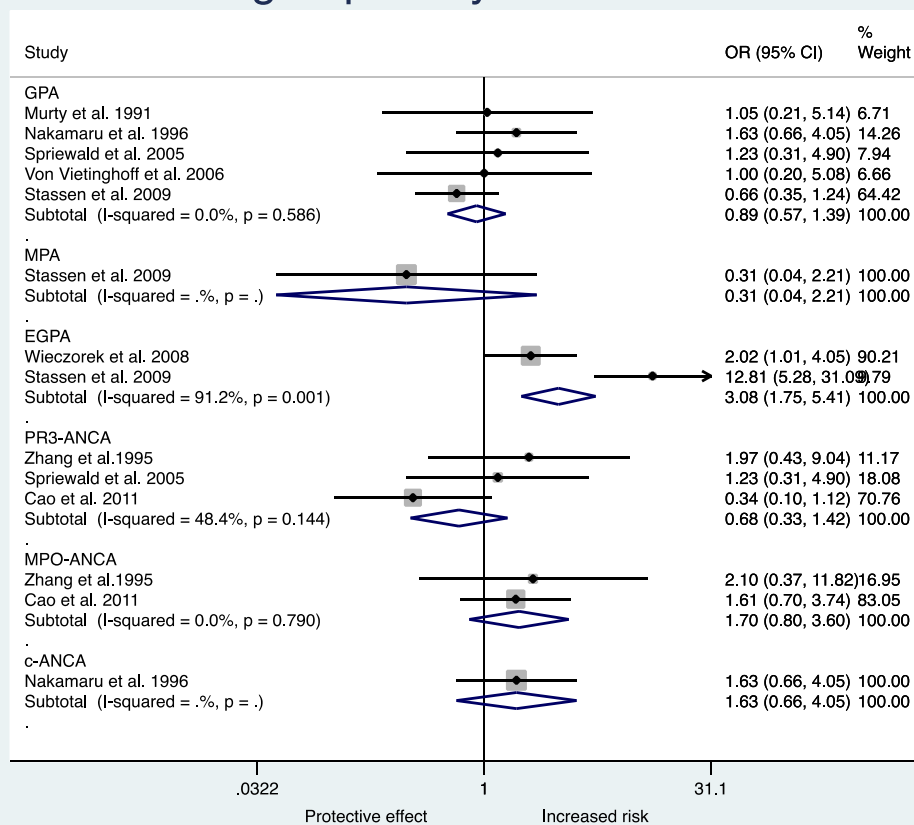
References: 23, 32, 26, 20, 19

## Subgroup analysis HLA-DR7



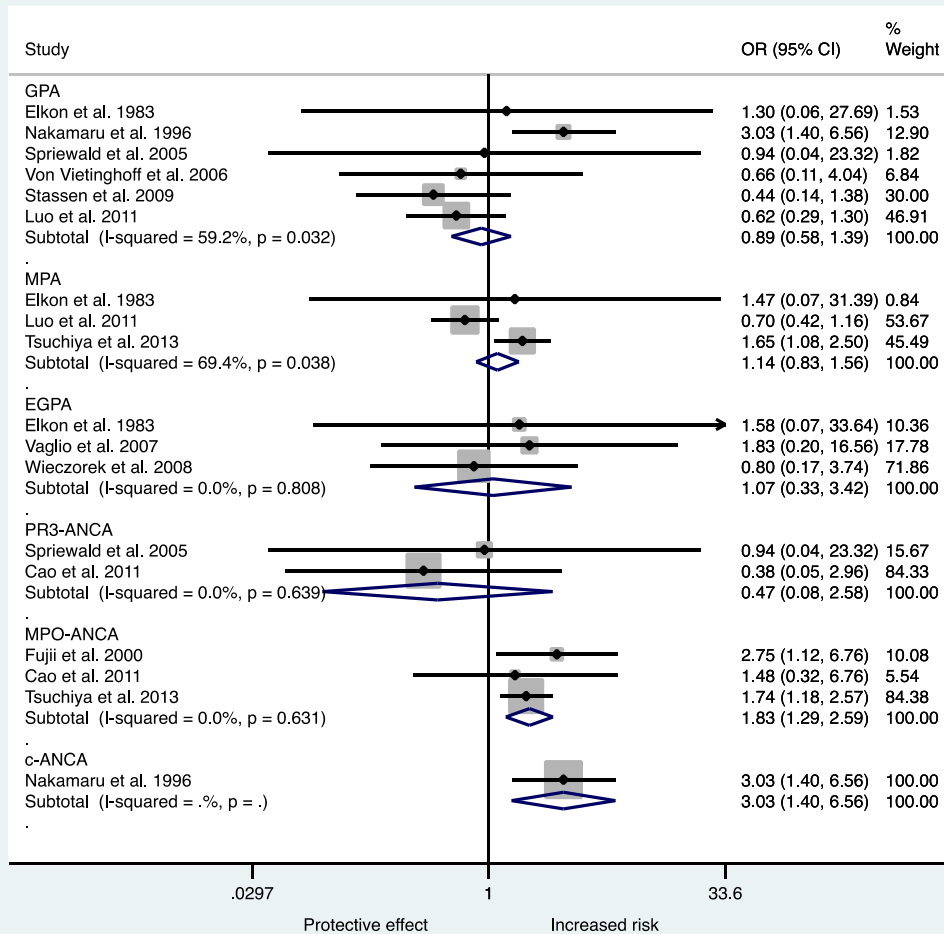
References: 23, 32, 31, 18, 19, 35, 29

## Subgroup analysis HLA-DR8



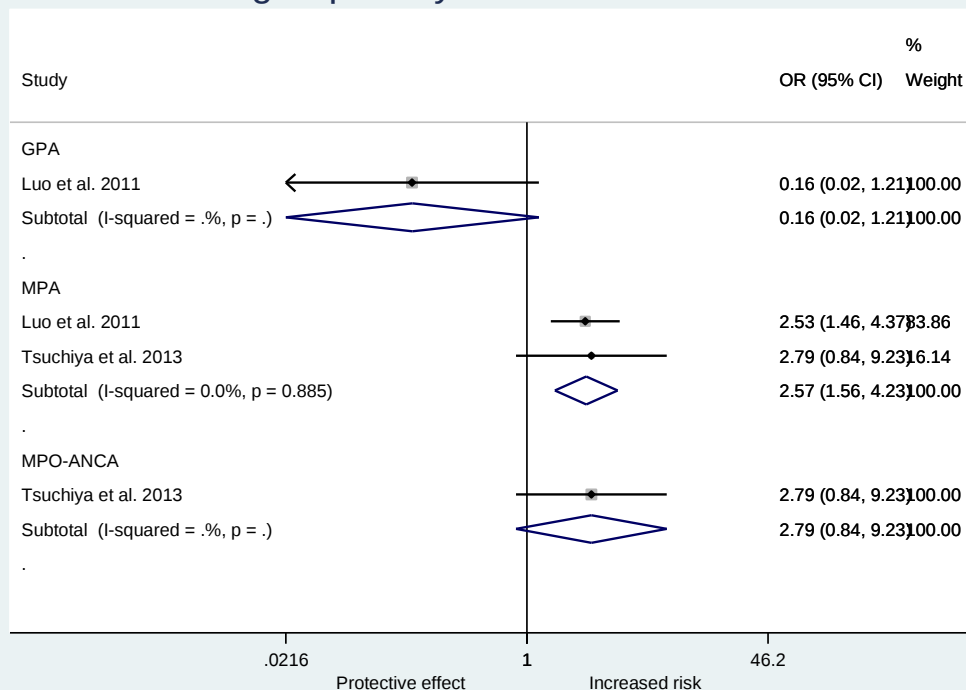
References: 17, 20, 31, 18, 19, 29, 26, 33

## Subgroup analysis HLA-DR9



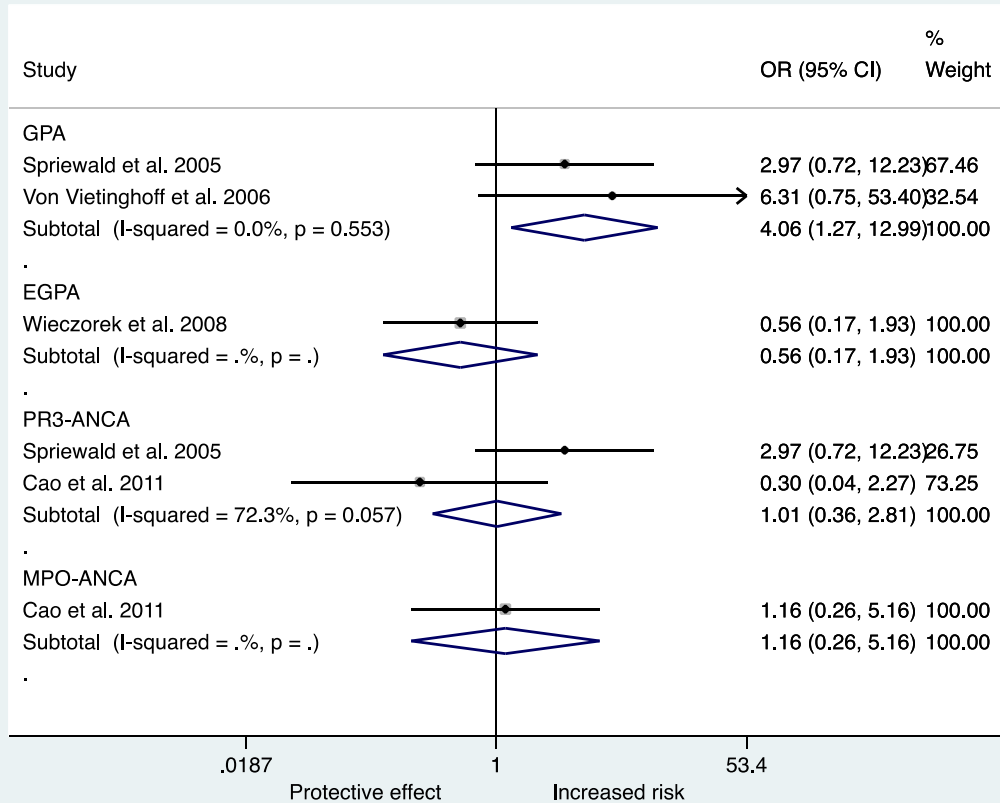
References: 23, 20, 31, 18, 19, 34, 37, 35, 29, 33, 36

## Subgroup analysis HLA-DRB1\*1101



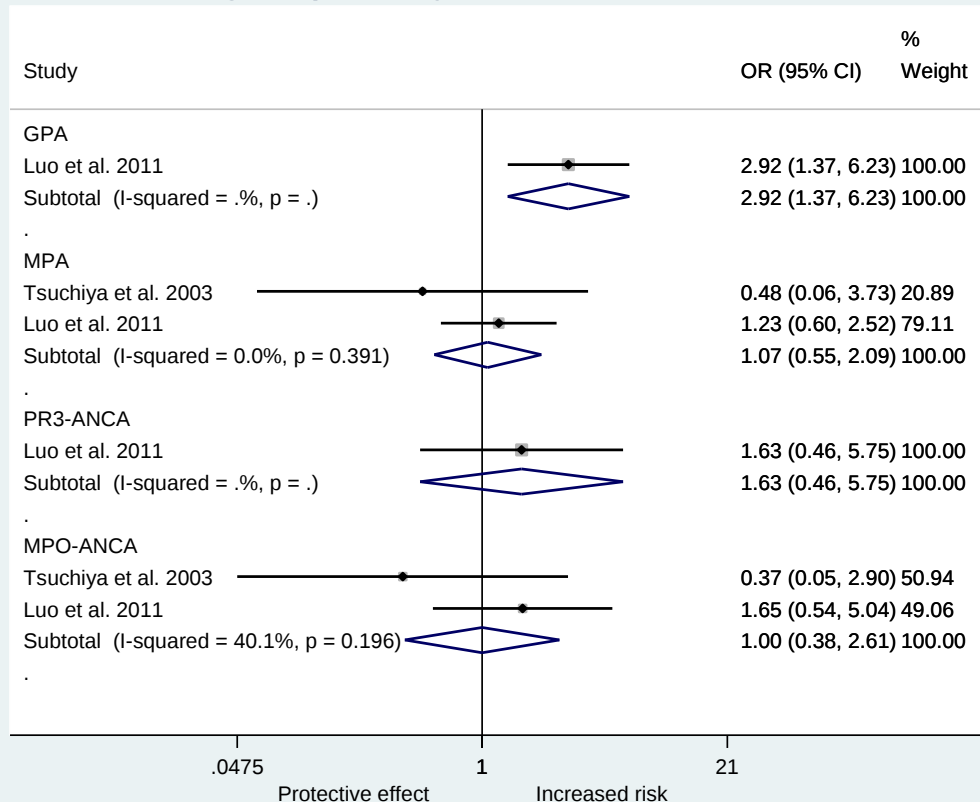
References: 34, 37

## Subgroup analysis HLA-DRB1\*12



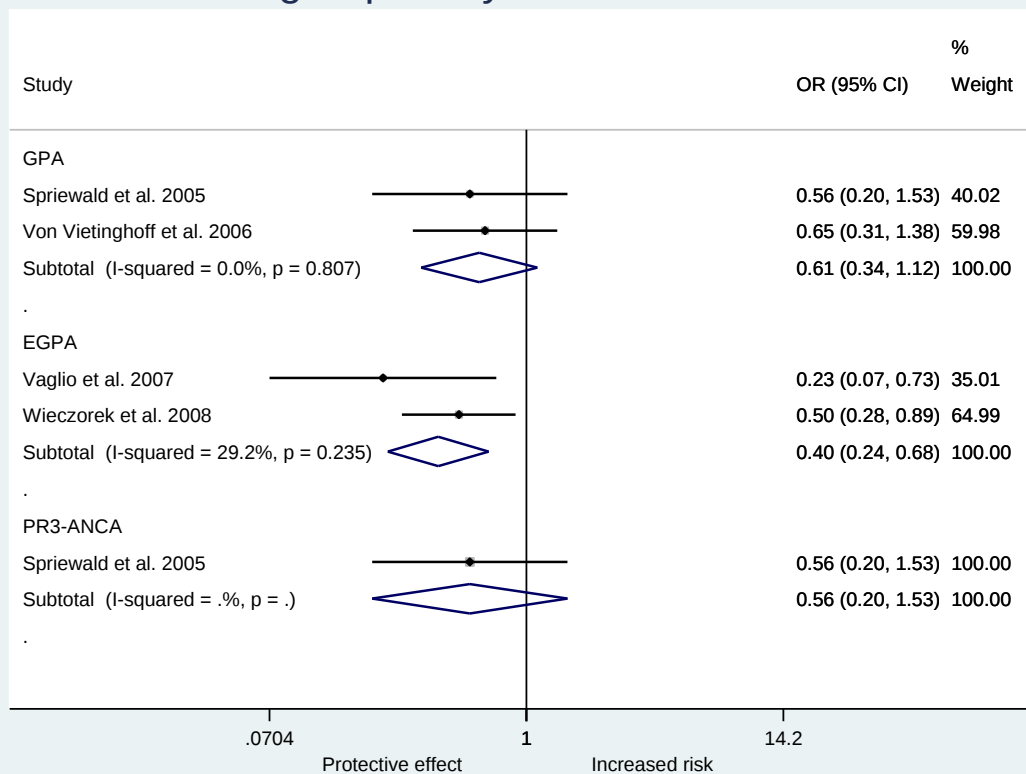
References: <sup>31</sup>, <sup>18</sup>, <sup>29</sup>, <sup>33</sup>

## Subgroup analysis HLA-DRB1\*1202



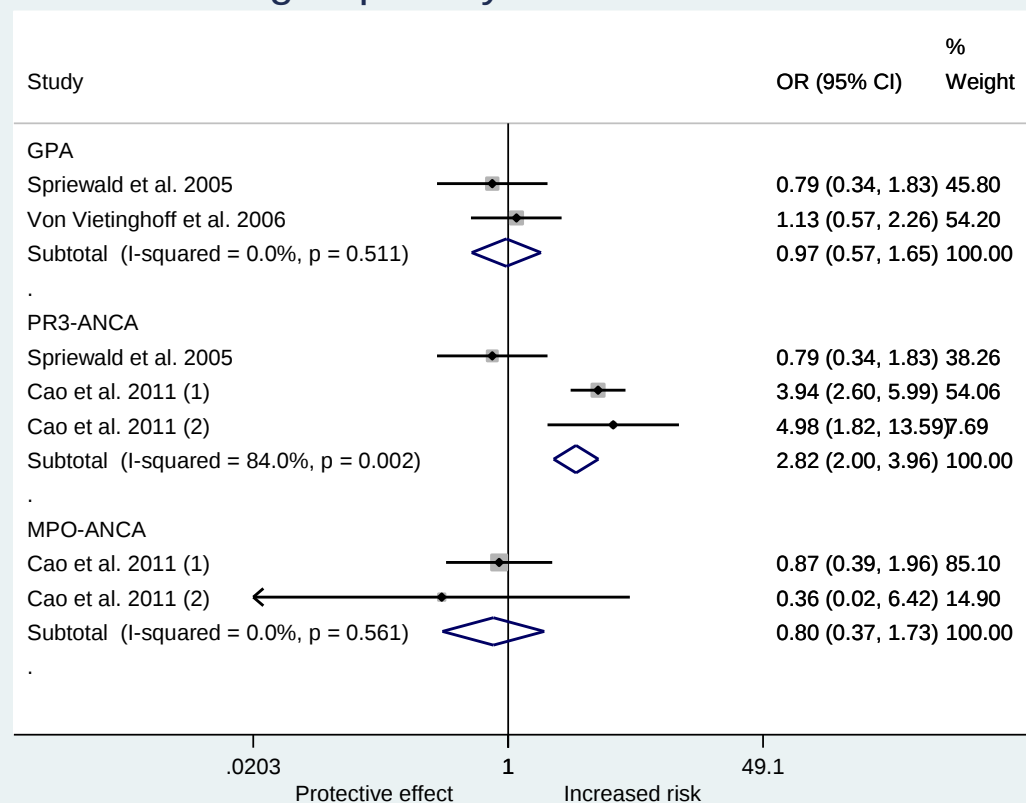
References: <sup>5</sup>, <sup>34</sup>

## Subgroup analysis HLA-DRB1\*13



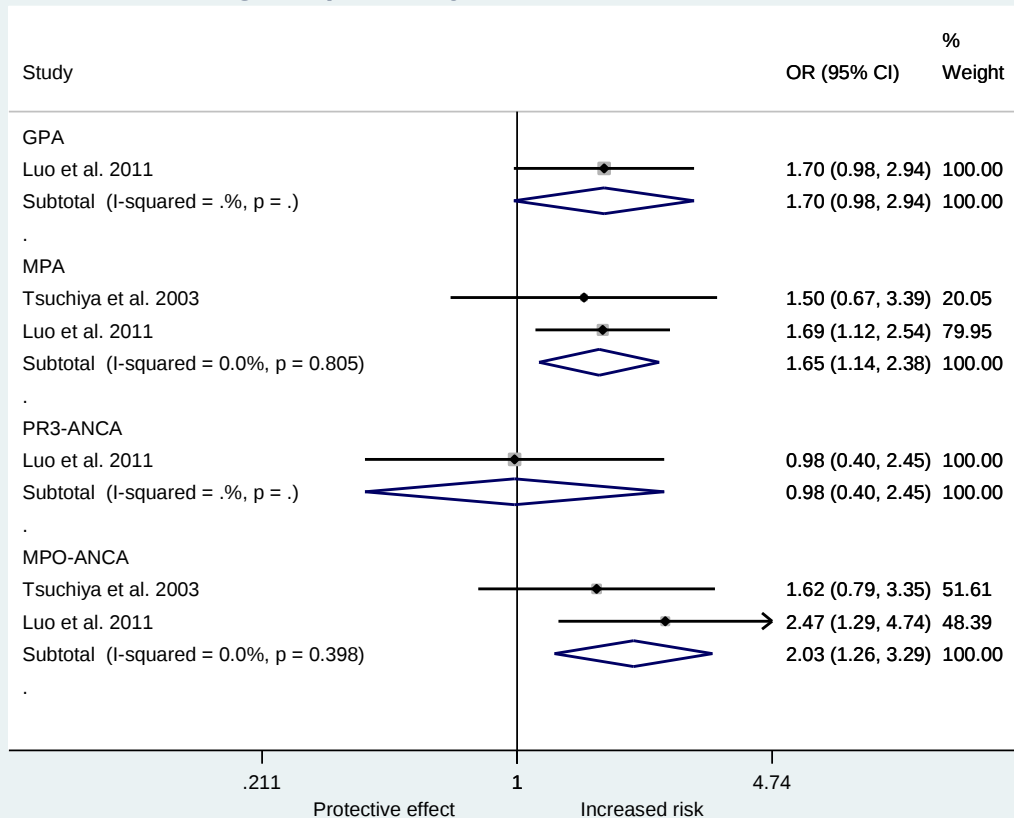
References: <sup>31</sup>, <sup>18</sup>, <sup>35</sup>, <sup>29</sup>

## Subgroup analysis HLA-DRB1\*15



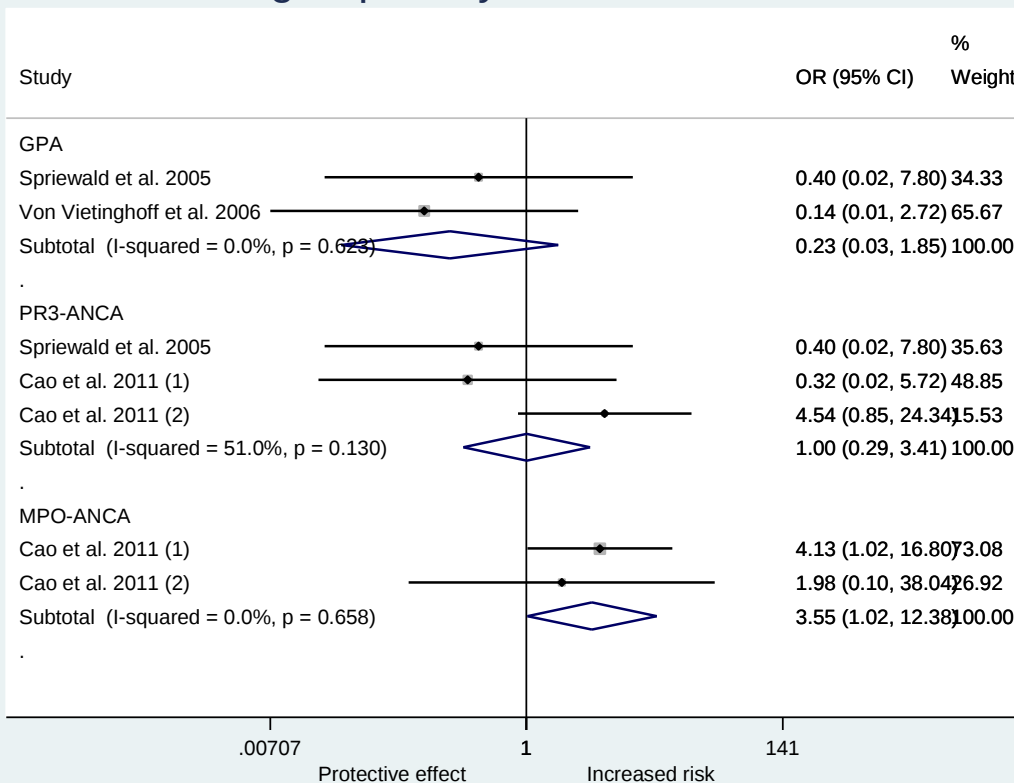
References: <sup>31</sup>, <sup>18</sup>, <sup>33\*\*</sup>

## Subgroup analysis HLA-DRB1\*1501



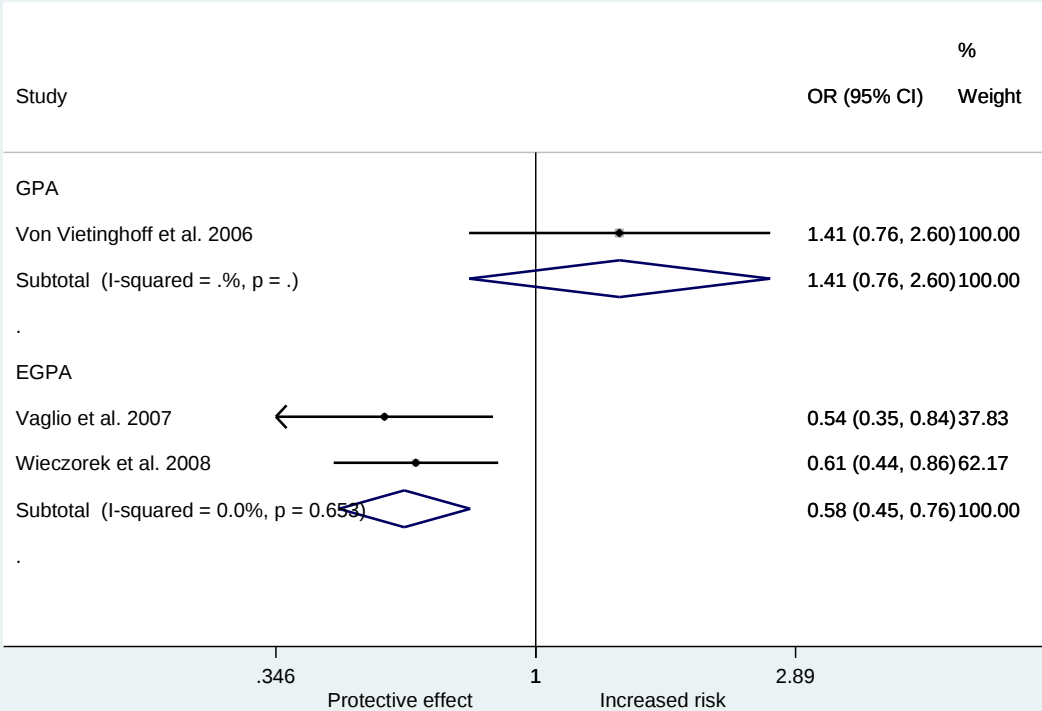
References: <sup>5</sup>, <sup>34</sup>

## Subgroup analysis HLA-DRB1\*16



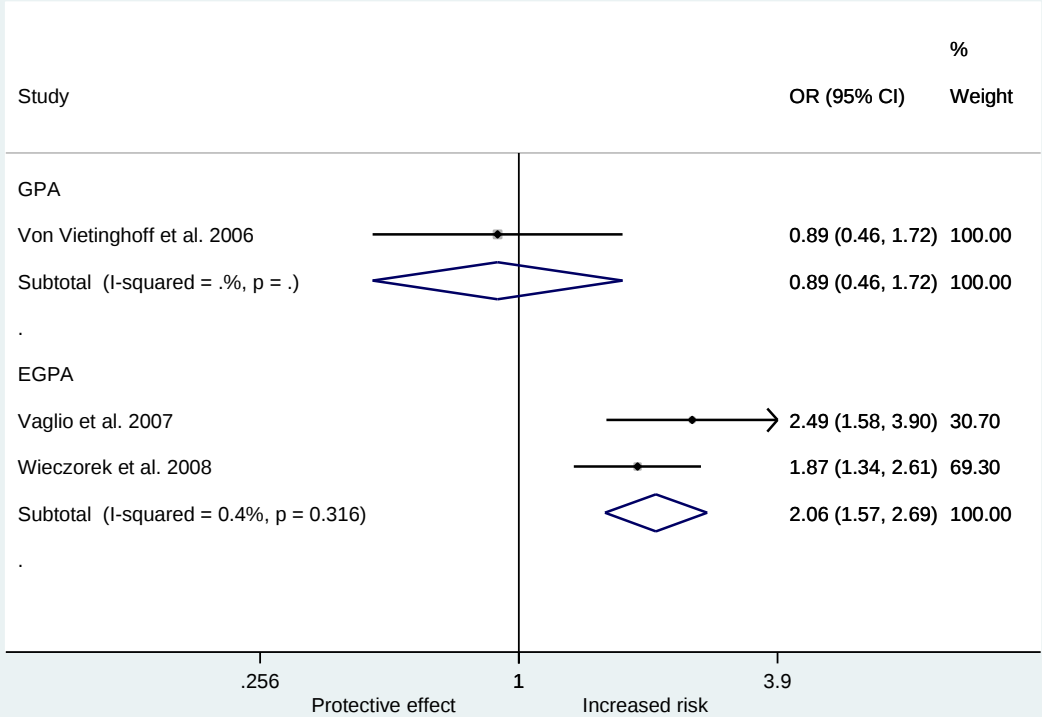
References: <sup>31</sup>, <sup>18</sup>, <sup>33</sup>\*\*

## Subgroup analysis HLA-DRB3



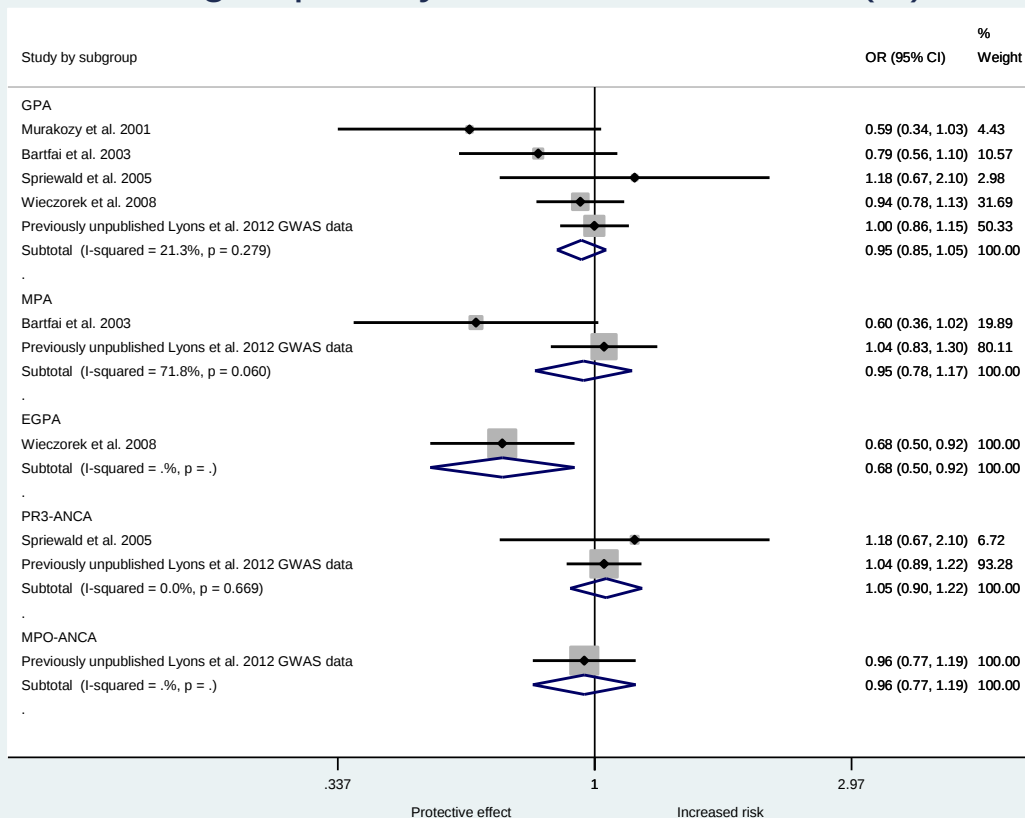
References: <sup>18</sup>, <sup>35</sup>, <sup>29</sup>

## Subgroup analysis HLA-DRB4



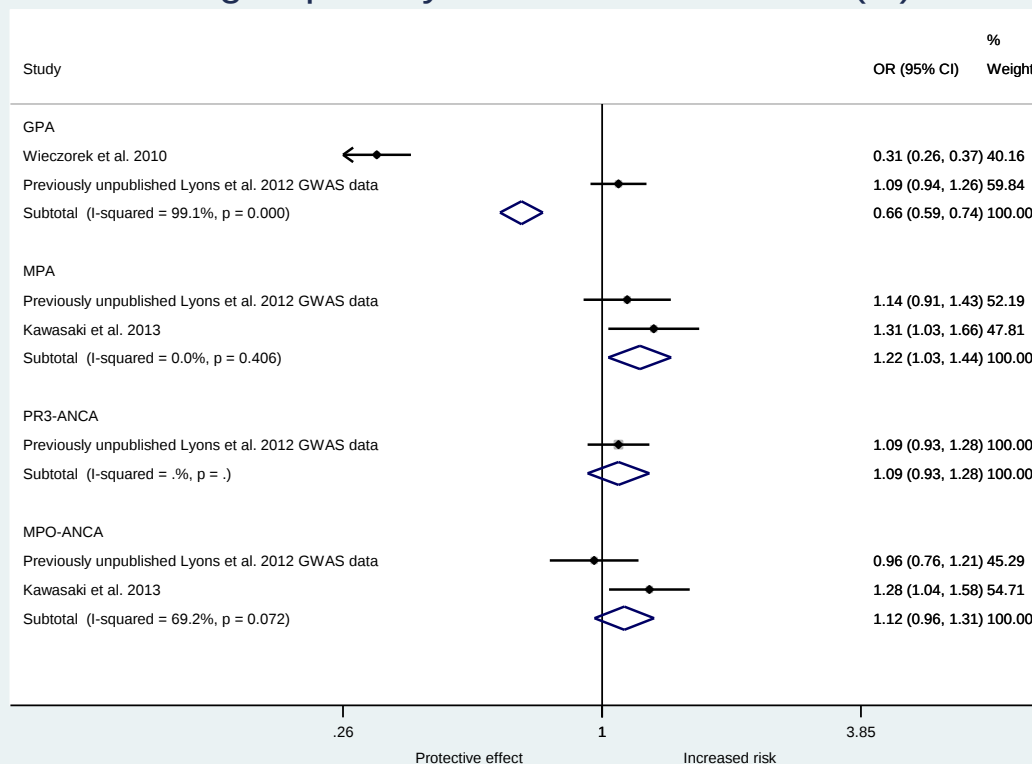
References: <sup>18</sup>, <sup>35</sup>, <sup>29</sup>

## Subgroup analysis IL-10 rs1800896 (G)



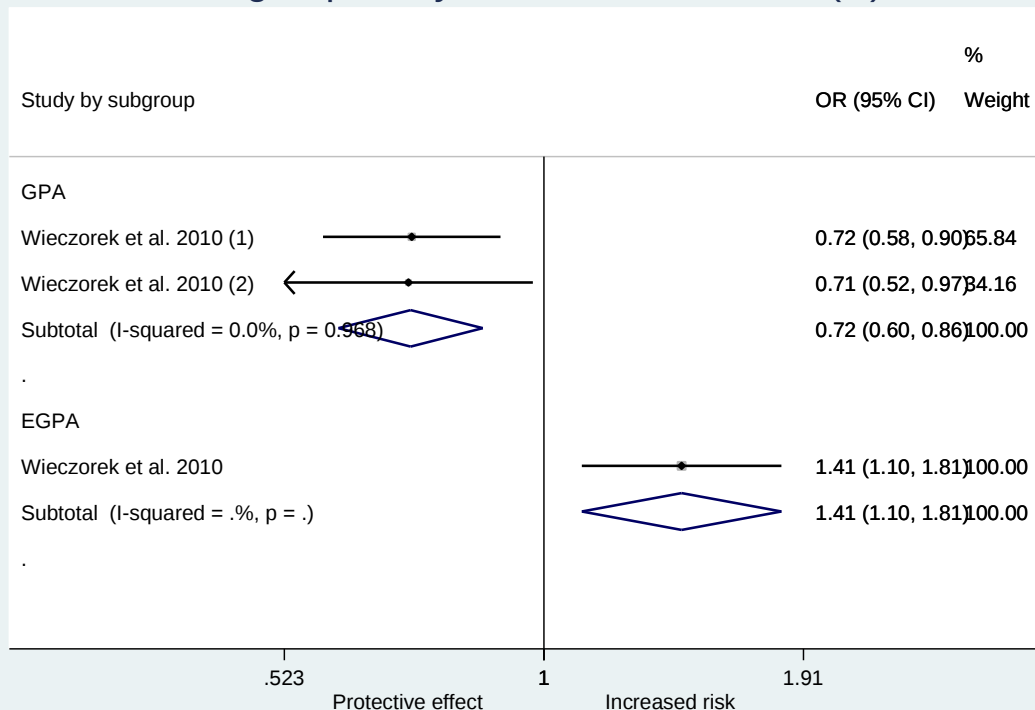
References: 42, 43, 31, 41, 3

## Subgroup analysis IRF5 rs10954213 (G)



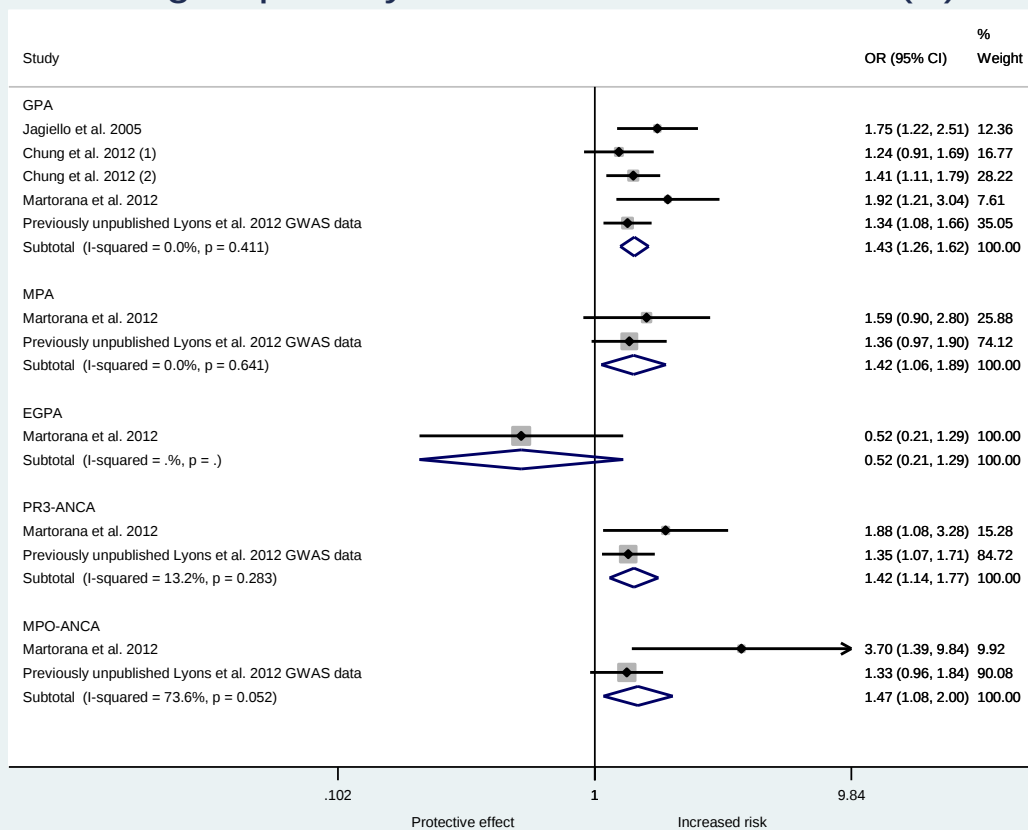
References: 44, 3, 45

## Subgroup analysis LEPR rs8179183 (C)



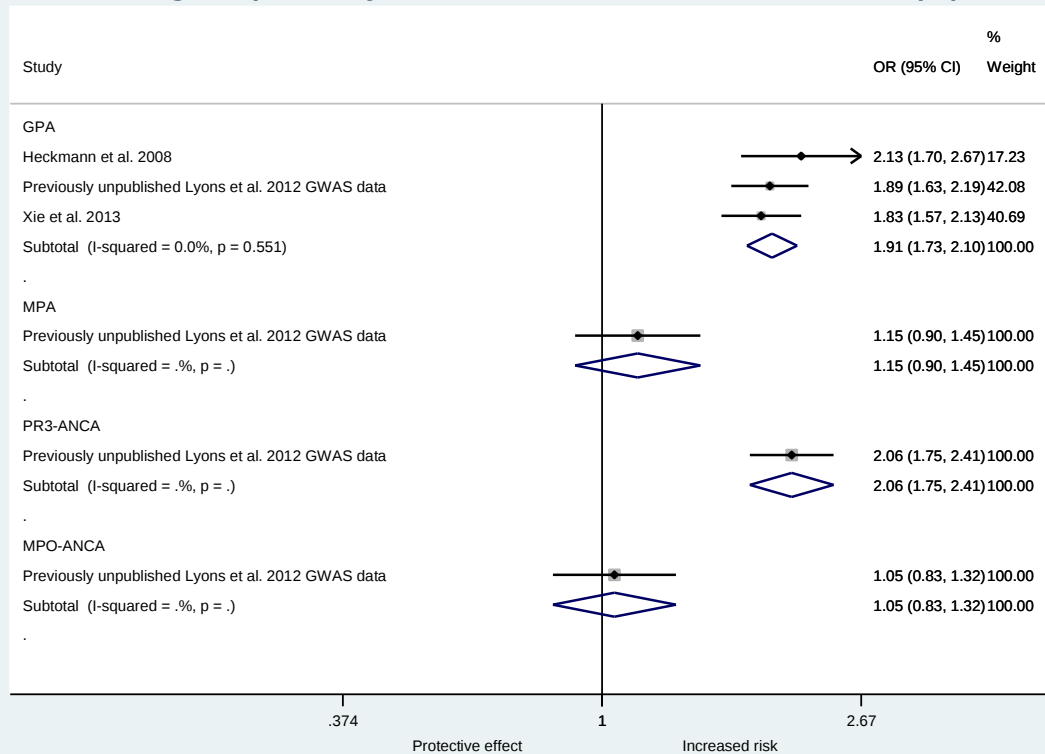
References: 15\*\*

## Subgroup analysis PTPN22 rs2476601 (A)



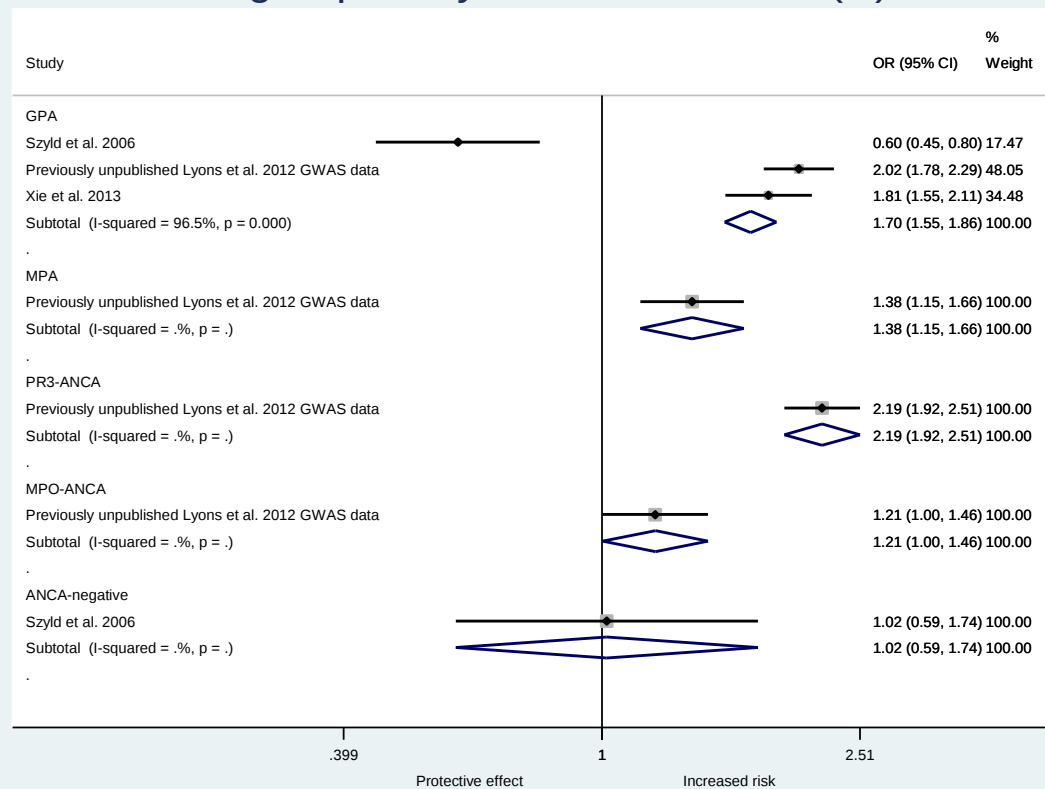
References: 50, 2\*\*, 51, 3

## Subgroup analysis RING1/RXRB rs213213 (A)



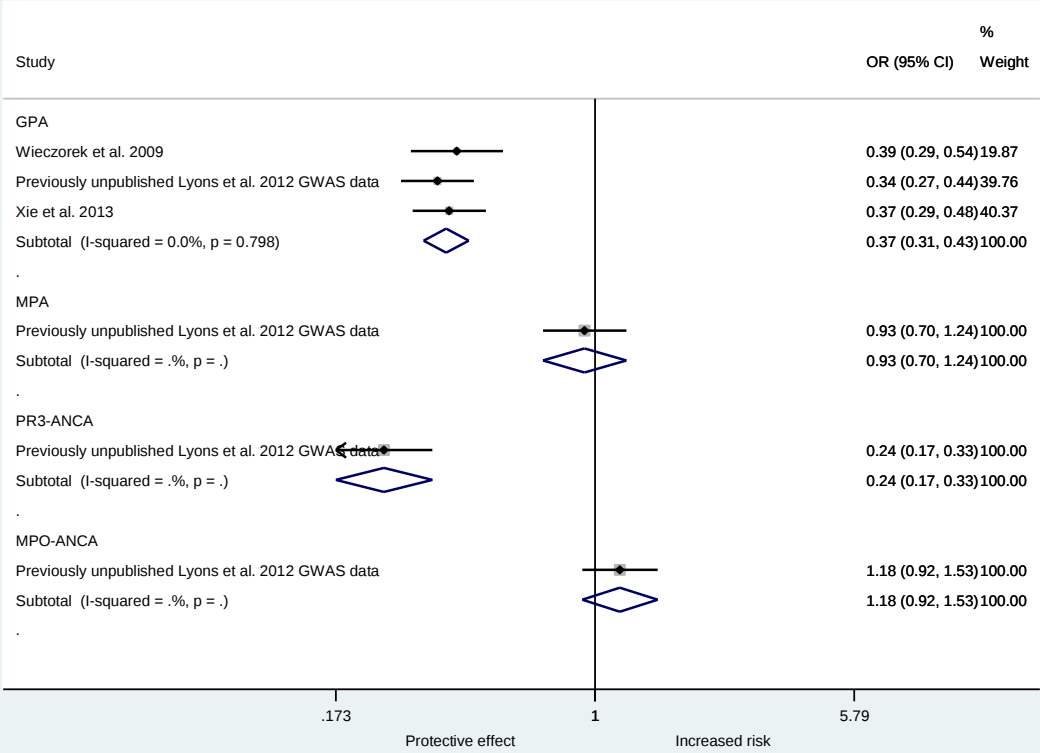
References: <sup>24</sup>, <sup>3</sup>, <sup>25</sup>

## Subgroup analysis RXRB rs6531 (C)



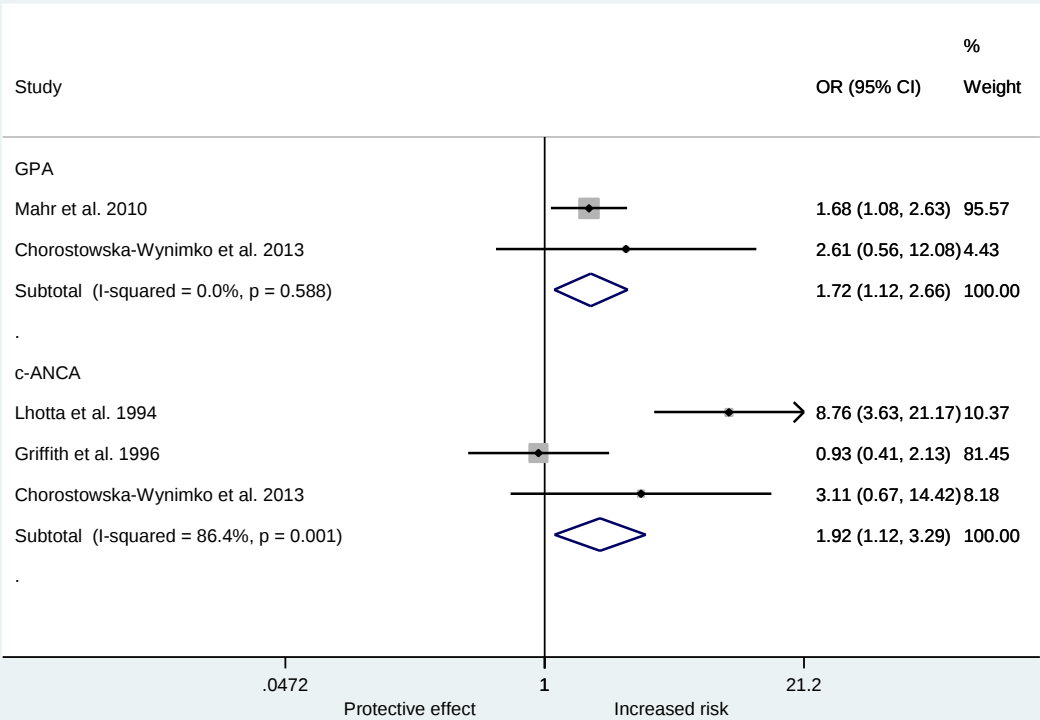
References: <sup>52</sup>, <sup>3</sup>, <sup>25</sup>

# Subgroup analysis RXRB rs9277935 (T)



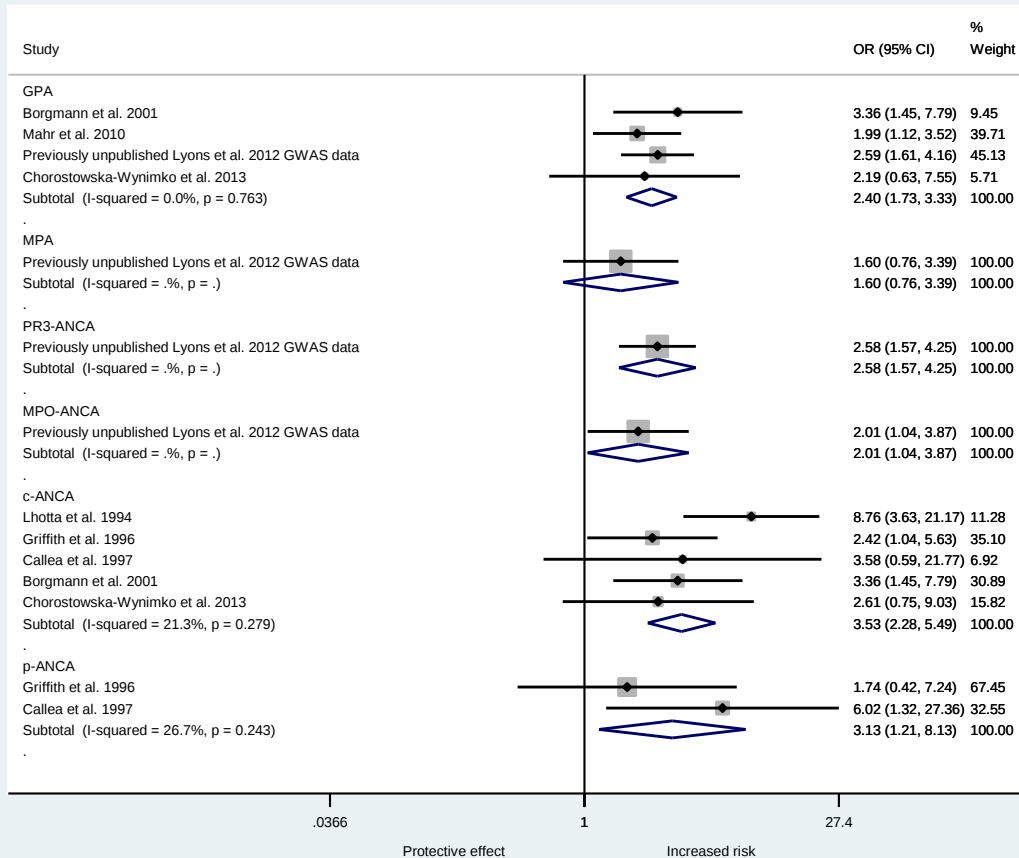
References: 53, 3, 25

# Subgroup analysis SERPINA1 S allele



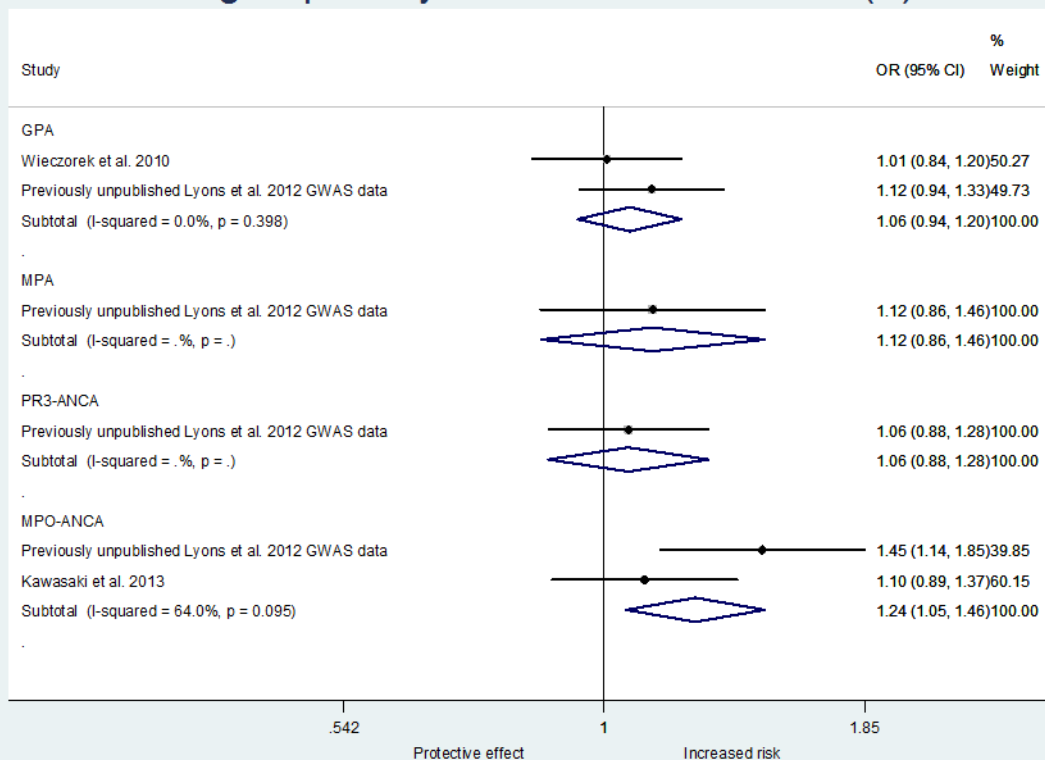
References: 54, 55, 56, 58

## Subgroup analysis SERPINA1 Z allele



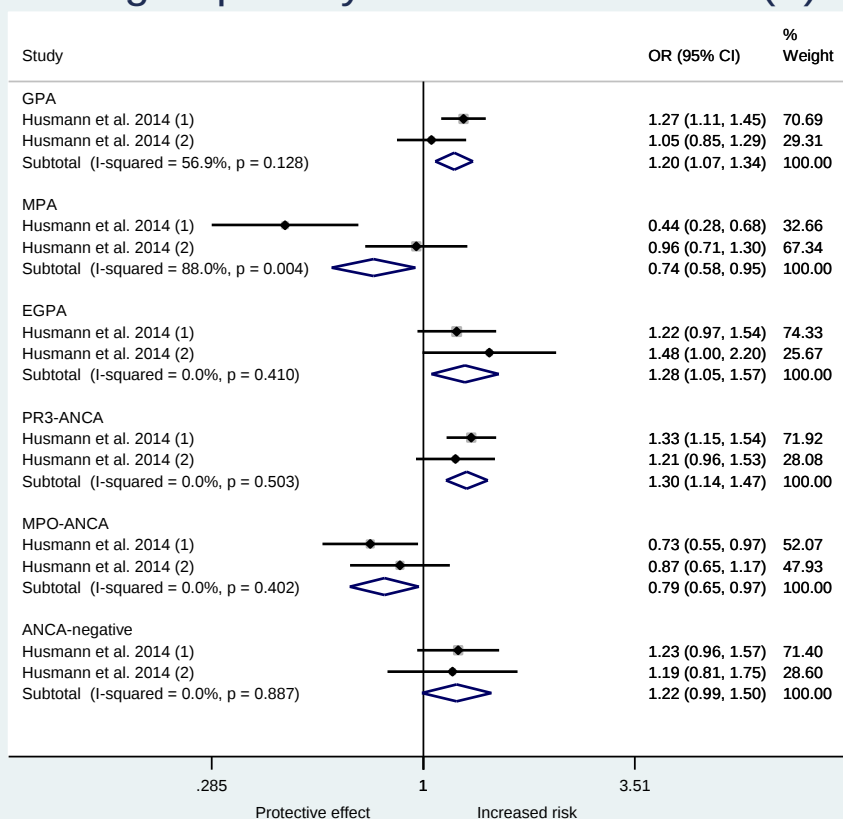
References: 54, 55, 59, 60, 56, 3, 58

## Subgroup analysis STAT4 rs7574865 (T)



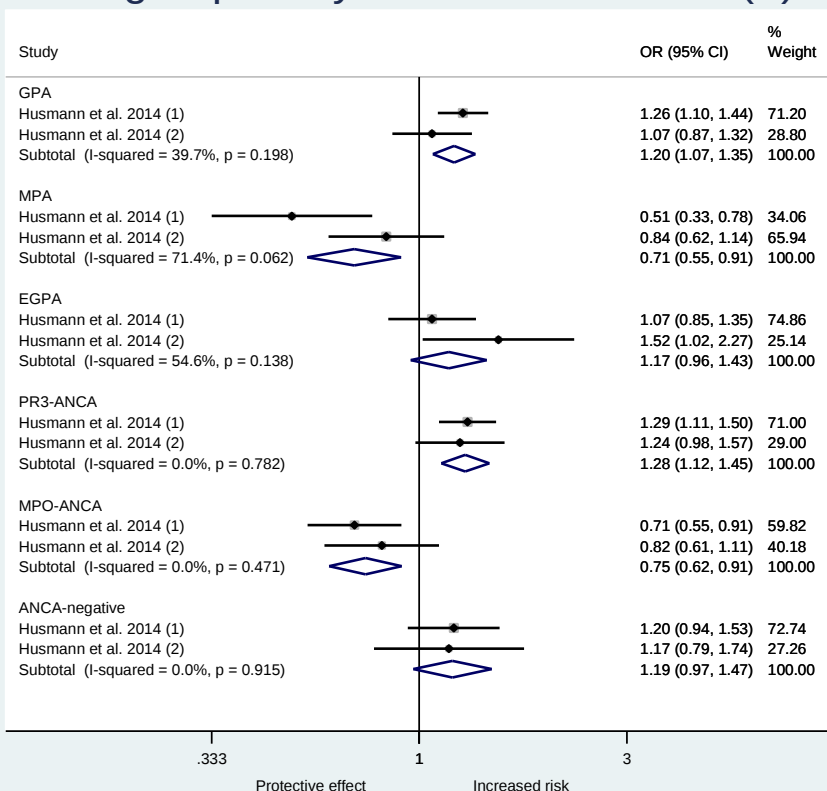
References: 44, 45

## Subgroup analysis TLR9 rs352162 (T)



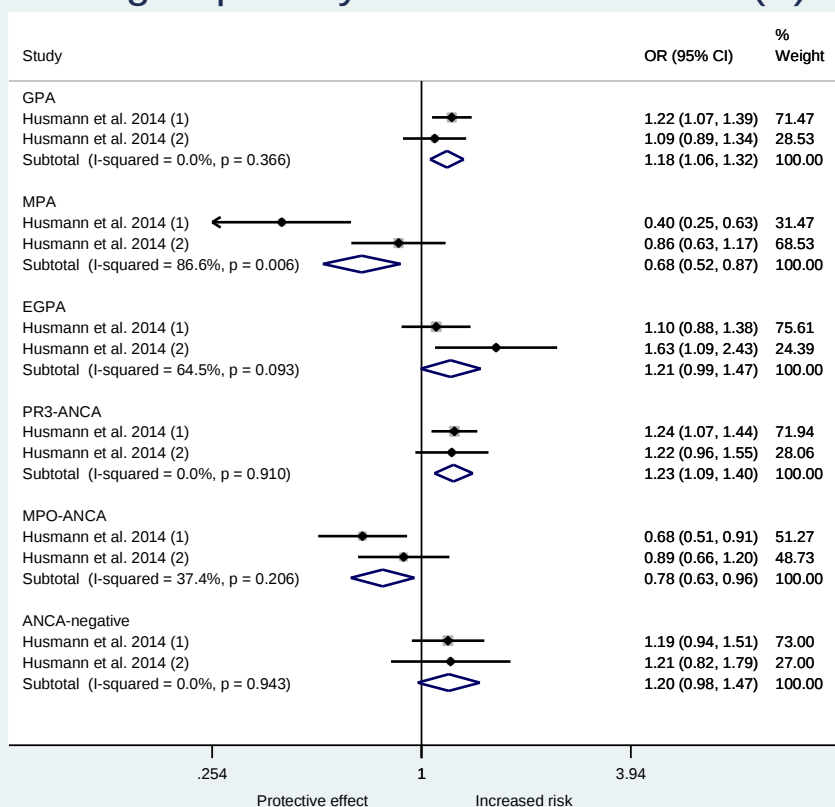
References: <sup>40\*\*</sup>

## Subgroup analysis TLR9 rs352140 (T)



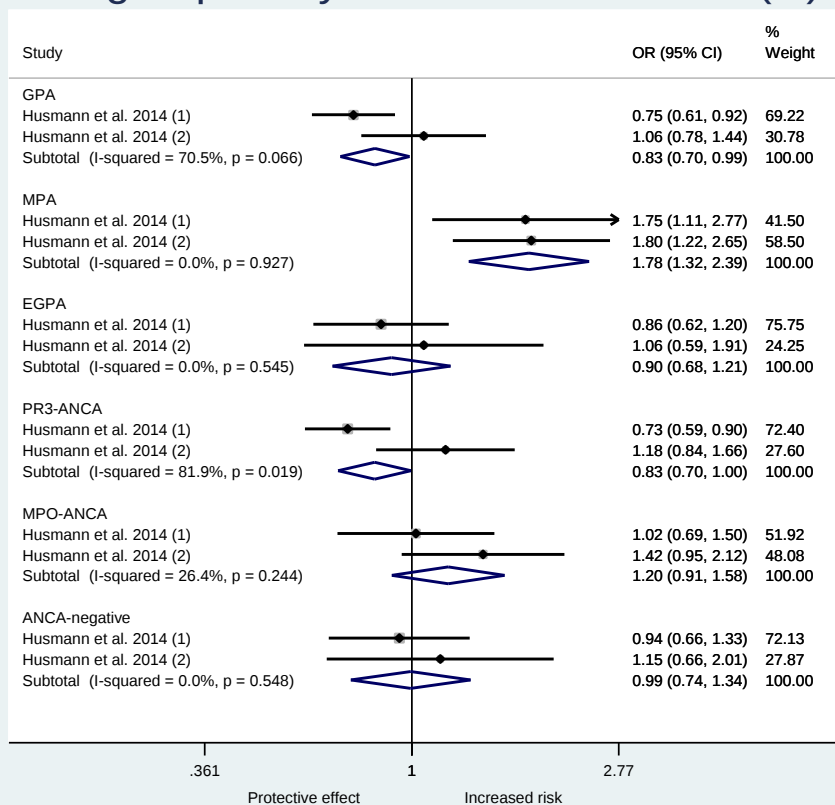
References: <sup>40\*\*</sup>

## Subgroup analysis TLR9 rs352139 (T)



References: <sup>40\*\*</sup>

## Subgroup analysis TLR9 rs5743836 (G)

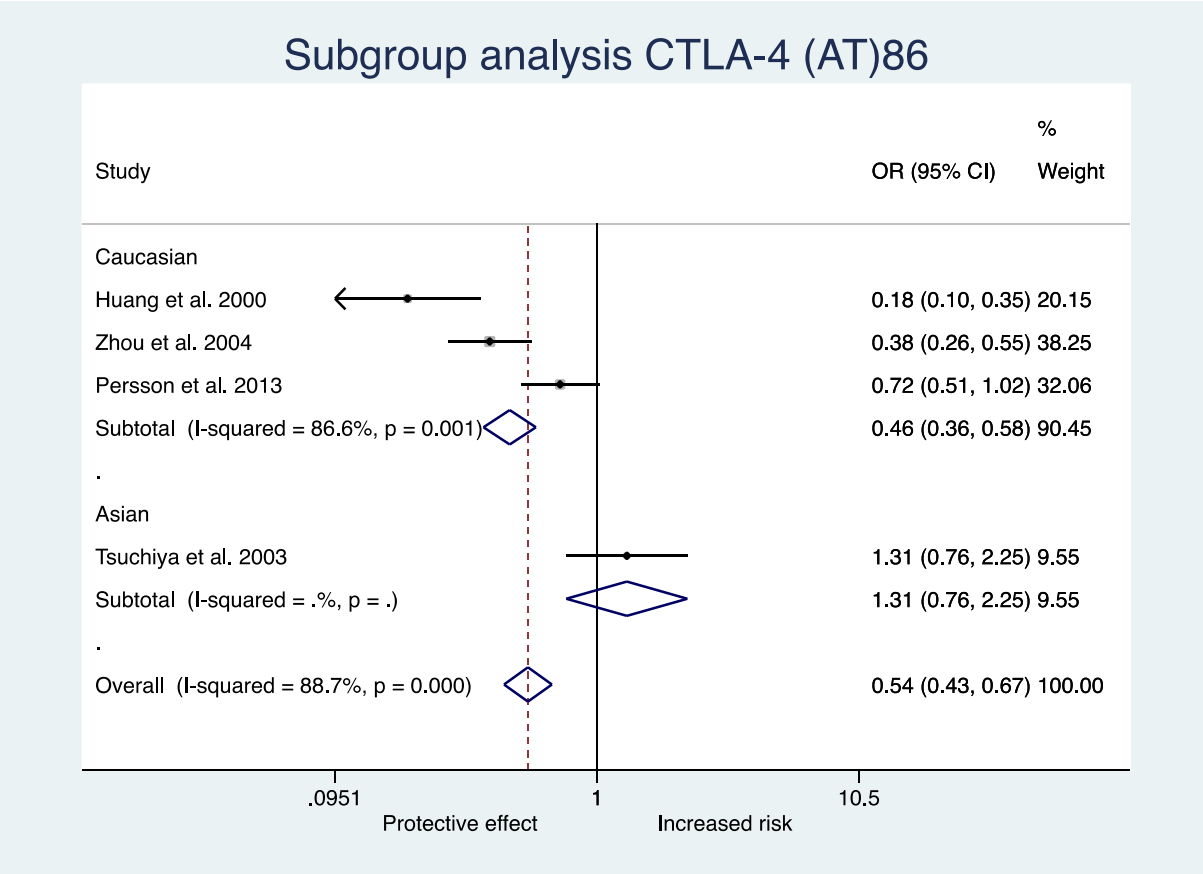


References: <sup>40\*\*</sup>

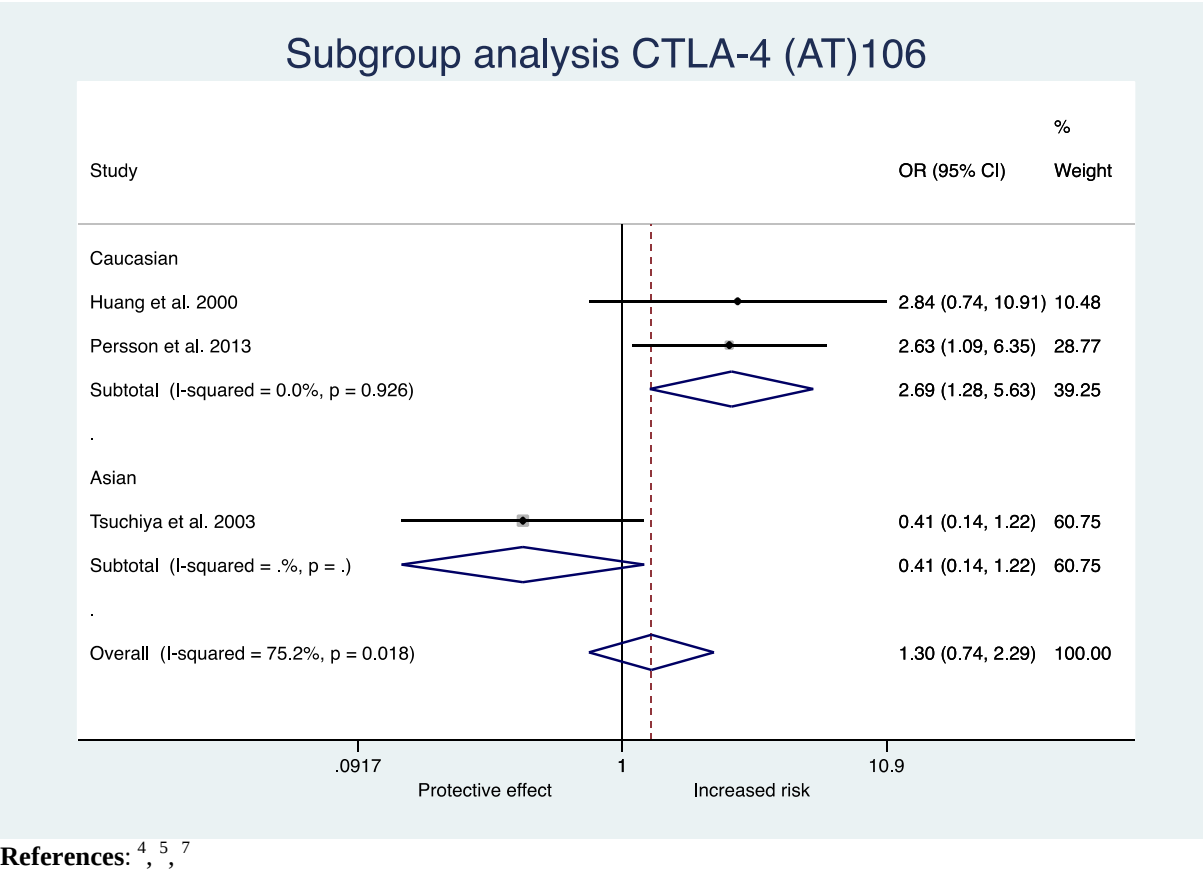
\*\*Two cohorts described in the same publication.

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

Supplementary Figure S3. Forest plots by ethnic subgroups

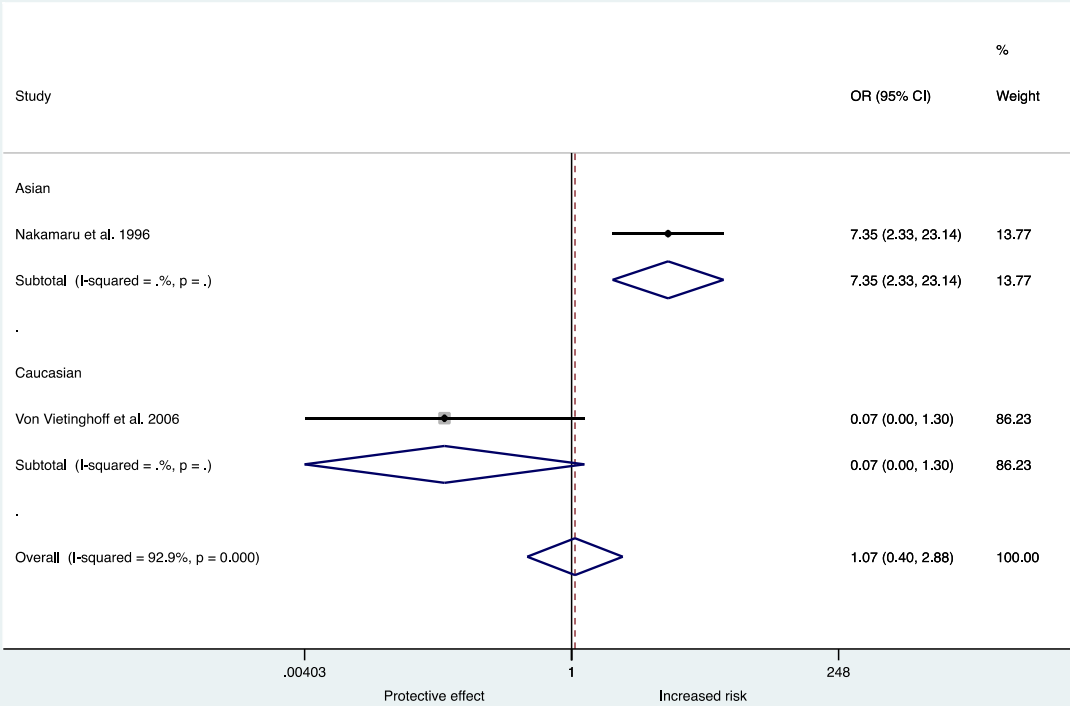


References: <sup>4</sup>, <sup>5</sup>, <sup>6</sup>, <sup>7</sup>



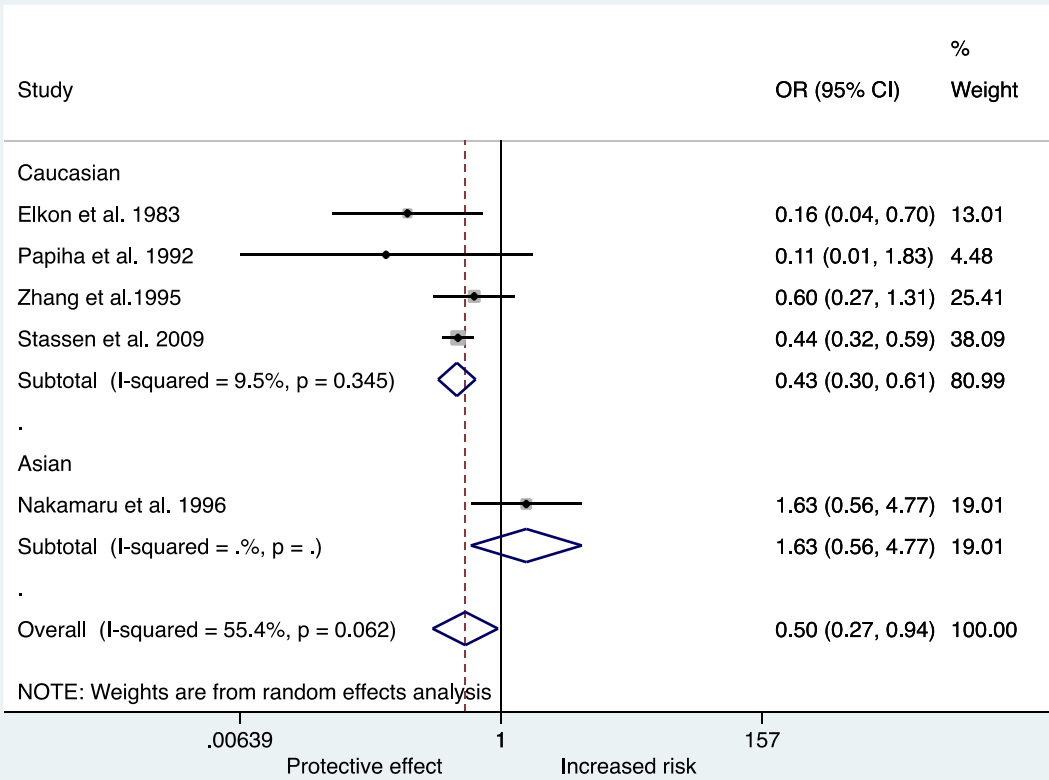
References: <sup>4</sup>, <sup>5</sup>, <sup>7</sup>

Subgroup analysis HLA-B55



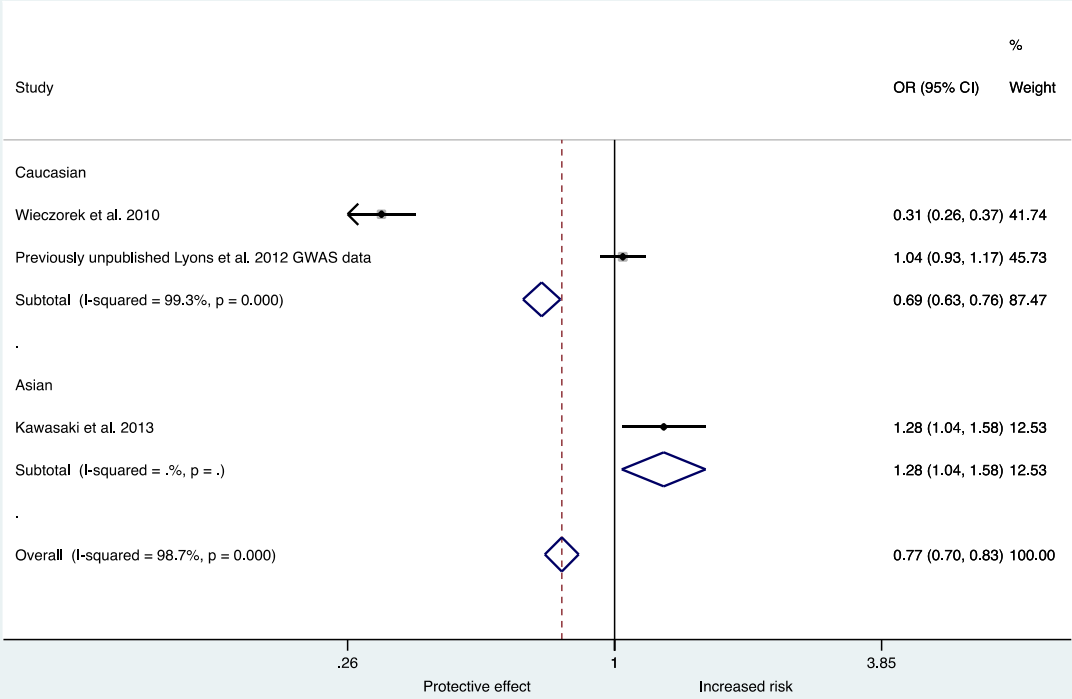
References: 20, 18,

Subgroup analysis HLA-DR6



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

Subgroup analysis IRF5 rs10954213 (G)



References: <sup>44</sup>, <sup>3</sup>, <sup>45</sup>

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