On the pathogenesis and clinical outcome of ANCA-associated vasculitis

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Supplementary table 1. Literature search strategies

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

Supplementary table 1. Literature search strategies (Continued)

Database	Search Strategy
PubMed	2. Vasculitis and genes (excluding AAV) ((“Vasculitis”[majr] OR vasculit*[ti]) AND (“genes”[majr] OR “genes”[ti] OR “gene”[ti] OR “genetic”[ti] OR “genetics”[ti] OR “genetics”[majr] OR “polymorphism, genetic”[majr] OR “polymorphism”[ti] OR “polymorphisms”[ti] OR “dna”[majr] OR “dna”[ti] OR “genome”[majr] OR “genome”[ti] OR “genomes”[ti] OR “genomics”[majr] OR “genomics”[ti] OR “genomic”[ti] OR “Genetic Phenomena”[majr] OR “Genetic Structures”[majr])) NOT ((“Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis”[Mesh] OR “ANCA-associated vasculitis”[all fields] OR “ANCA associated vasculitis”[all fields] OR “Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis”[all fields] OR “Pauci-Immune Vasculitis”[all fields] OR “Pauci Immune Vasculitis”[all fields] OR “Pauci-Immune Vasculitides”[all fields] OR “ANCA-Associated Vasculitides”[all fields] OR “ANCA Associated Vasculitides”[all fields] OR “ANCA-Associated Vasculitide”[all fields] OR (“ANCA”[all fields] AND vasculit*[all fields]) OR (“Anti-Neutrophil”[all fields] AND “Cytoplasmic”[all fields] AND “Antibody-Associated”[all fields] AND vasculit*[all fields]) OR “Churg-Strauss Syndrome”[all fields] OR “Churg Strauss Syndrome”[all fields] OR “Allergic Granulomatous Angiitis”[all fields] OR “Allergic Granulomatous Angiitides”[all fields] OR “Allergic Angiitis”[all fields] OR “Churg-Strauss Vasculitis”[all fields] OR “eosinophilic granulomatosis with polyangiitis”[all fields] OR (“eosinophilic”[all fields] AND “granulomatosis”[all fields] AND “polyangiitis”[all fields]) OR “Microscopic Polyangiitis”[all fields] OR “Microscopic Polyangiitides”[all fields] OR “Wegener Granulomatosis”[all fields] OR “Wegener’s Granulomatosis”[all fields] OR “Wegeners Granulomatosis”[all fields] OR “granulomatosis with polyangiitis”[all fields] OR (“granulomatosis”[all fields] AND “polyangiitis”[all fields]) OR “anca”[tw] OR ((“pr3”[all fields] OR “pr-3”[all fields] OR “mpo”[all fields]) AND (“Vasculitis”[mesh] OR vasculit*[all fields] OR “anca”[tw])) OR “Antibodies, Antineutrophil Cytoplasmic”[Mesh] OR “Antineutrophil Cytoplasmic Antibody”[all fields] OR “Anti-Neutrophil Cytoplasmic Antibody”[all fields] OR “Anti Neutrophil Cytoplasmic Antibody”[all fields] OR “Anti-Neutrophil Cytoplasmic Antibodies”[all fields] OR “Anti Neutrophil Cytoplasmic Antibodies”[all fields] OR “Antineutrophil Cytoplasmic Antibodies”[all fields]) AND (“genes”[mesh] OR “genes”[all fields] OR “gene”[all fields] OR “genetic”[all fields] OR “genetics”[Subheading] OR “genetics”[all fields] OR “genetics”[mesh] OR “polymorphism, genetic”[mesh] OR “polymorphism”[all fields] OR “polymorphisms”[all fields] OR “dna”[mesh] OR “dna”[all fields] OR “genome”[mesh] OR “genome”[all fields] OR “genomes”[all fields] OR “genomics”[mesh] OR “genomics”[all fields] OR “genomic”[all fields] OR “Genetic Phenomena”[mesh] OR “Genetic Structures”[Mesh]))

Supplementary table 1. Literature search strategies (Continued)

Database	Search Strategy
Embase	*Two strategies:* 1. AAV and genes (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/)

Supplementary table 1. Literature search strategies (Continued)

Database	Search Strategy
Embase	2. Vasculitis and genes (excluding AAV) ((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/))

Supplementary table 1. Literature search strategies (Continued)

Database	Search Strategy
Web of Science	*Two strategies:* 1. AAV and genes 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)) 2. Vasculitis and genes (excluding AAV) (TI=((vasculit*) AND (gene OR genes OR genom* OR genetic* OR Polymorphism* OR dna))) NOT (TS=((“ANCA-associated vasculitis” OR “ANCA associated vasculitis” OR “Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis” OR “Pauci-Immune Vasculitis” OR “Pauci Immune Vasculitis” OR “Pauci-Immune Vasculitides” OR “ANCA-Associated Vasculitides” OR “ANCA Associated Vasculitides” OR “ANCA-Associated Vasculitide” OR (“ANCA” AND vasculit*) OR (“Anti-Neutrophil” AND “Cytoplasmic” AND “Antibody-Associated” AND vasculit*) OR “Churg-Strauss Syndrome” OR “Churg Strauss Syndrome” OR “Allergic Granulomatous Angiitis” OR “Allergic Granulomatous Angiitides” OR “Allergic Angiitis” OR “Churg-Strauss Vasculitis” OR “eosinophilic granulomatosis with polyangiitis” OR (“eosinophilic” AND “granulomatosis” AND “polyangiitis”) OR “Microscopic Polyangiitis” OR “Microscopic Polyangiitides” OR “Wegener Granulomatosis” OR “Wegener’s Granulomatosis” OR “Wegeners Granulomatosis” OR “granulomatosis with polyangiitis” OR (“granulomatosis” AND “polyangiitis”) OR “anca” OR ((“pr3” OR “pr-3” OR “mpo”) AND (exp Vasculitis/ OR vasculit* OR “anca”)) OR “neutrophil cytoplasmic antibody” OR “Antineutrophil Cytoplasmic Antibody” OR “Anti-Neutrophil Cytoplasmic Antibody” OR “Anti Neutrophil Cytoplasmic Antibody” OR “Anti-Neutrophil Cytoplasmic Antibodies” OR “Anti Neutrophil Cytoplasmic Antibodies” OR “Antineutrophil Cytoplasmic Antibodies”) AND (gene OR genes OR genom* OR genetic* OR Polymorphism* OR dna)))

Supplementary table 2. Study characteristics of the included studies

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
***CD226* rs763361 (T)**	Wieczorek et al. 2009[1**]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy subjects	761/1226	GPA (642), EGPA (119)	PR3-ANCA (438), MPO-ANCA (32), ANCA negative (43)	1.24 (1.11 – 1.39)
		Case-Control	UK	ACR and CHCC criteria	Geographically matched subjects from the general population	105/9337	GPA (all patients)	NR	1.17 (0.89 – 1.54)
	Chung et al. 2012[2**]	Case-Control	USA	ACR criteria	Geographically matched subjects with no (family) history of autoimmune disease	424/469	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.08 (0.90 – 1.30)
		Case-Control	Canada	ACR criteria	Geographically matched subjects with no history of autoimmune disease	456/1500	GPA (all patients)	NR	1.09 (0.94 – 1.26)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.08 (0.96 – 1.21)
***CTLA-4* $(AT)_{86}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	0.18 (0.10 – 0.35)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	1.31 (0.76 – 2.25)
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	0.38 (0.26 – 0.55)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.72 (0.51 – 1.02)
CTLA-4 **$(AT)_{102}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.71 (0.15 – 19.22)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.89 (0.47 – 1.68)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.73 (0.85 – 3.54)
CTLA-4 **$(AT)_{104}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.74 (0.96 – 3.13)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	1.15 (0.70 – 1.91)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.09 (0.70 – 1.59)
CTLA-4 **$(AT)_{106}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	2.84 (0.74 – 10.91)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.41 (0.14 – 1.22)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	2.63 (1.09 – 6.35)
CTLA-4 **$(AT)_{108}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	0.90 (0.42 – 1.95)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.89 (0.47 – 1.68)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.78 (1.05 – 3.03)
CTLA-4 **$(AT)_{110}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	0.48 (0.02 9.36)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.25 (0.01 – 4.62)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.74 (0.34 – 1.61)
CTLA-4 **$(AT)_{116}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.37 (0.26 – 7.26)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.75 (0.03 – 18.56)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.540 (0.11 – 2.62)
CTLA-4 **$(AT)_{118}$**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	3.44 (0.21 – 55.85)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.75 (0.08 – 7.33)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.27 (0.06 – 1.18)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
CTLA-4 $(AT)_{122}$	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	10.32 (0.42 – 256.50)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	2.32 (0.57 – 9.47)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.47 (0.05 – 4.27)
CTLA-4 $(AT)_{124}$	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	14.47 (1.59 – 131.86)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	2.28 (0.14 – 36.59)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.63 (0.13 – 3.16)
CTLA-4 $(AT)_{126}$	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	4.78 (1.04 – 21.93)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	0.45 (0.05 – 3.88)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	0.81 (0.21 – 3.18)
CTLA-4 $(AT)_{128}$	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.12 (0.05 – 27.93)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	49/111	MPA (all patients)	MPO-ANCA (all patients)	6.98 (0.72 – 67.95)

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	0.89 (0.79 – 0.99)
	Persson et al. 2013[7]	Case-Control	Sweden	ACR and CHCC criteria, EMA algorithm	Blood donors	105/200	GPA (61), MPA (44)	PR3-ANCA (62), MPO-ANCA (43)	1.03 (0.73 – 1.43)
***FCGR3A* rs396991 (G)**	Dijstelbloem et al. 1999[12]	Case-Control	The Netherlands	ACR criteria	Ethnically matched healthy blood donors	91/154	GPA (all patients)	PR3-ANCA (all patients)	1.30 (0.89 – 1.91)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/303	MPA (all patients)	MPO-ANCA (all patients)	0.65 (0.39 – 1.07)
***FCGR3B* (NA1)**	Dijstelbloem et al. 1999[12]	Case-Control	The Netherlands	ACR criteria	Ethnically matched healthy blood donors	91/154	GPA (all patients)	PR3-ANCA (all patients)	1.05 (0.72 – 1.53)
	Tse et al. 2000[14]	Case-Control	UK	CHCC criteria	Ethnically matched healthy subjects	101/100	GPA (45), MPA (52), EGPA (1), PAN (3)	PR3-ANCA (61), MPO-ANCA (30)	1.24 (0.8 – 1.87)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/303	MPA (all patients)	MPO-ANCA (all patients)	1.29 (0.82 – 2.03)
	Kelley et al. 2011[10]	Case-Control	USA	ACR and CHCC criteria	Geographically matched subjects with no (family) history of autoimmune disease	673/413	GPA (all patients)	NR	0.86 (0.72 – 1.03)
***GHSR* rs509035 (A)**	Wieczorek et al. 2010[15]**	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	454/820	GPA (all patients)	NR	1.22 (1.02 – 1.45)
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	179/516	GPA (all patients)	NR	0.94 (0.72 – 1.23)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	914/5259	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	1.00 (0.90 – 1.11)
***GHSR* rs519384 (A)**	Wieczorek et al. 2010[15**]	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	449/813	GPA (all patients)	NR	1.17 (0.98 – 1.40)
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	179/515	GPA (all patients)	NR	1.01 (0.77 – 1.33)
***GHSR* rs572169 (A)**	Wieczorek et al. 2010[15**]	Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	442/812	GPA (all patients)	NR	1.21 (1.01 – 1.44)
		Case-Control	Germany	CHCC criteria	Geographically matched healthy subjects	178/492	GPA (all patients)	NR	0.96 (0.73 – 1.25)
HLA-A1	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.53 (0.81 – 2.87)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.84 (0.47 – 1.52)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.92 (0.42 – 2.03)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.08 (0.87 – 1.35)
HLA-A2	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.78 (0.42 – 1.45)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.04 (0.62 – 1.73)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.90 (0.37 – 2.23)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.87 (0.48 – 1.58)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.98 (0.81 – 1.17)
HLA-A3	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.73 (0.90 –3.31)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.51 (0.86 – 2.66)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.88 (0.89 – 3.98)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.04 (0.84 – 1.31)
HLA-A9	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.09 (0.46 – 2.59)
	Katz et al. 1979[21]	Case-Control	USA	Clinical and histological criteria	Ethnically matched subjects	31/418	GPA (all patients)	NR	69.13 (3.28 – 456.19)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.79 (0.58 – 1.06)
HLA-A10	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.06 (0.32 – 3.48)
	Katz et al. 1979[21]	Case-Control	USA	Clinical and histological criteria	Ethnically matched subjects	31/418	GPA (all patients)	NR	69.13 (3.28 – 1456.19)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.61 (0.33 – 1.12)
HLA-A11	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/607	GPA (all patients)	NR	1.96 (0.81 – 4.72)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.68 (0.24 – 1.90)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.71 (0.17 – 3.03)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	2.97 (1.19 – 7.41)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.43 (0.14 – 1.27)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.62 (0.39 – 0.99)
HLA-A24	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.91 (0.36 – 2.31)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.75 (0.34 – 1.65)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.81 (0.51 – 6.37)
HLA-A25	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.43 (0.33 – 6.17)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.09 (0.61 – 7.16)
HLA-A26	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.68 (0.09 – 5.07)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	2.36 (1.00. – 5.60)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	2.49 (1.01 – 6.18)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.39 (0.07 – 2.05)
HLA-A28	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.40 (0.02 – 6.68)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.32 (0.04 – 2.34)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.88 (0.57 – 1.38)
HLA-A29	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	2.11 (0.68 – 6.57)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.31 (0.04 – 2.25)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.66 (0.11 – 4.04)
HLA-A30	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.68 (0.09 – 5.07)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.02 (0.18 – 22.63)
HLA-A31	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.07 (0.25 – 4.54)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.55 (0.46 – 5.24)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.33 (0.03 – 3.20)
HLA-A32	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	3.73 (1.24 – 11.22)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	2.07 (0.60 – 7.04)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.24 (0.03 – 2.21)
HLA-B5	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.93 (0.28 – 3.02)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.56 (0.35 – 0.89)
HLA-B7	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.54 (0.77 – 3.08)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.74 (1.02 – 2.96)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.07 (0.52 – 2.22)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.00 (0.80 – 1.26)
HLA-B8	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.24 (0.60 – 2.56)
	Katz et al. 1979[21]	Case-Control	USA	Clinical and histological criteria	Ethnically matched subjects	31/418	GPA (all patients)	NR	2.30 (1.18 – 4.50)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	17/113	GPA (all patients)	NR	2.47 (1.01 – 6.05)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.03 (0.55 – 1.93)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	3.27 (1.02 – 10.50)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.11 (0.88 – 1.40)
HLA-B12	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	1.01 (0.47 – 2.15)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.96 (0.74 – 1.24)
HLA-B13	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.87 (0.12 – 6.50)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	2.09 (0.62 – 7.07)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.79 (0.21 – 3.03)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.63 (0.31 – 1.28)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-B14	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/701	GPA (all patients)	NR	0.32 (0.02 – 5.24)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.51 (0.16 – 1.63)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.52 (0.25 – 9.26)
	Stassen et al. 2009[19]	Case-Control	The Nether-lands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.16 (0.63 – 2.14)
HLA-B15	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.38 (0.55 – 3.43)
	Stassen et al. 2009[19]	Case-Control	The Nether-lands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.98 (0.74 – 1.29)
HLA-B18	Strimlan et al. 1978[16]	Case-Control	USA	Histologically proven AAV	Ethnically matched healthy blood donors	31/549	GPA (all patients)	NR	1.16 (0.35 – 3.85)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	0.53 (0.13 – 2.21)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.78 (0.296 – 2.072
	Stassen et al. 2009[19]	Case-Control	The Nether-lands	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

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.07 (0.58 – 1.98)
HLA-B39	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.86 (0.11 – 6.51)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.33 (0.01 – 8.20)
HLA-B40	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.65 (0.52 – 5.23)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5872	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.90 (0.67 – 1.22)
HLA-B44	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.07 (0.58 – 2.00)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	2.50 (0.845 – 7.403
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	3.27 (1.02 – 10.50)
HLA-B49	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	1.27 (0.30 – 5.44)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.02 (0.18 – 22.63)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-B51	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.87 (0.64 – 5.49)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.61 (0.19 – 1.92)
HLA-B55	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	7.35 (2.33 – 23.14)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.07 (0.00 – 1.30)
HLA-B57	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	2.78 (1.05 – 7.32)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.00 (0.06 – 16.21)
HLA-B60	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	3.51 (0.99 – 12.36)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.19 (0.28 – 5.13)
HLA-B62	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/700	GPA (all patients)	NR	2.38 (0.70 – 8.12)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.71 (0.58 – 4.99)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-Cw1	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.45 (0.58 – 3.58)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	52/51	GPA (all patients)	NR	0.98 (0.24 – 4.03)
HLA-Cw3	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.40 (0.65 – 3.01)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	52/51	GPA (all patients)	NR	1.32 (0.62 – 2.81)
HLA-Cw7	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.50 (0.12 – 2.10)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	52/51	GPA (all patients)	NR	1.10 (0.62 – 1.96)
HLA-DPA1 **rs9277341 (C)**	Heckmann et al. 2008 [24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	282/380	GPA (all patients)	ANCA+ (250), ANCA- (27)	0.38 (0.29 – 0.51)
	Xie et al. 2013[25**]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	0.30 (0.24 – 0.37)
		Case-control (GWAS)	USA	ACR criteria	Geographically matched healthy subjects	291/317	GPA (all patients)	c-ANCA (227)	0.43 (0.32 – 0.57)
HLA-DPB1*0101	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.20 (0.53 – 2.75)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.17 (0.05 – 0.63)
HLA-DPB1*0201	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.78 (0.49 – 1.23)
	Tsuchiya et al. 2006[28]	Case-Control	Japan	Japanese 1998 criteria	Geographically matched healthy subjects	50/77	MPA (all patients)	MPO-ANCA (all patients)	0.44 (0.21 – 0.91)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	1.38 (0.75 – 2.52)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.93 (0.57 – 1.51)
HLA-DPB1*0301	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.27 (0.56 – 2.89)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.02 (0.00 – 0.15)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	0.28 (0.14 – 0.55)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.65 (0.38 – 1.11)
	Arning et al. 2011[30**]	Case-Control	Germany	CHCC criteria	Geographically and ethnically matched healthy blood donors	482/356	GPA (389), EGPA (56), MPA (37)	NR	0.30 (0.21 – 0.44)
		Case-Control	UK	CHCC criteria	Geographically and ethnically matched healthy blood donors	193/104	GPA (102), MPA (82), EGPA (9)	NR	0.35 (0.16 – 0.77)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DPB1*0401	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.42 (0.84 – 2.38)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	3.91 (2.62 – 5.84)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	2.15 (1.61 – 2.86)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	1.06 (0.78 – 1.45)
	Arning et al. 2011[30**]	Case-Control	Germany	CHCC criteria	Geographically and ethnically matched healthy blood donors	482/356	GPA (389), EGPA (56), MPA (37)	NR	2.34 (1.92 – 2.85)
		Case-Control	UK	CHCC criteria	Geographically and ethnically matched healthy blood donors	193/104	GPA (102), MPA (82), EGPA (9)	NR	2.02 (1.44 – 2.85)
HLA-DPB1*0402	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.82 (0.38 – 1.78)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	1.11 (0.65 – 1.92)
	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	135/369	GPA (all patients)	ANCA+ (108), ANCA- (27)	1.14 (0.78 – 1.68)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	1.15 (0.75 – 1.77)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DPB1*0501	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.34 (0.26 – 7.02)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.20 (0.01 – 4.93)
HLA-DPB1*0601	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	3.79 (0.19 – 74.15)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	0.60 (0.08 – 4.29)
HLA-DPB1*0901	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.52 (0.15 – 1.84)
	Jagiello et al. 2004[27]	Case-Control	Germany	ACR and CHCC criteria, biopsy	Geographically matched subjects	148/89	GPA (all patients)	PR3-ANCA (all patients)	1.81 (0.07 – 44.73)
HLA-DPB2 **rs3130215 (A)**	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	282/380	GPA (all patients)	ANCA+ (250), ANCA- (27)	2.35 (1.88 – 2.94)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	0.88 (0.79 – 0.99)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	2.44 (2.10 – 2.84)
HLA-DQB1*02	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.98 (0.45 – 2.13)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/50	GPA (all patients)	NR	0.85 (0.41 – 1.77)
HLA-DQB1*0302	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.07 (0.53 – 2.20)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.94 (0.36 – 2.49)
HLA-DQB1*0303	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.84 (0.27 – 2.65)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	2.97 (0.72 – 12.23)
	Tsuchiya et al. 2006[28]	Case-Control	Japan	Japanese 1998 criteria	Geographically matched healthy subjects	50/77	MPA (all patients)	MPO-ANCA (all patients)	2.11 (1.14 – 3.90)
HLA-DQB1*04	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.74 (0.40 – 7.50)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/50	GPA (all patients)	NR	1.49 (0.24 – 9.08)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DQB1*0501	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.77 (0.91 – 3.42)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.77 (0.32 – 1.88)
HLA-DQB1*0602	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.64 (0.29 – 1.42)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	12.86 (2.65 – 62.31)
HLA-DQ7	Zhang et al. 1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/50	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.21 (0.70 – 2.10)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	0.66 (0.34 – 1.30)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.43 (0.16 – 1.16)
HLA-DR1	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	2.17 (0.90 – 5.23)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	4.37 (2.01 – 9.48)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.89 (0.44 – 1.82)
	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.12 (0.48 – 2.64)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	0.68 (0.67 – 1.75)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.56 (0.23 – 1.35)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.71 (0.43 – 1.15)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.67 (0.49 – 0.92)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.53 (0.34 – 0.81)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.79 (0.28 – 2.19)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DR2	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	1.91 (0.97 – 3.75)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	1.20 (0.56 – 2.54)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.19 (0.66 – 2.13)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.33 (0.08 – 1.38)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.97 (0.77 – 1.22)
HLA-DR3	Elkon et al. 1983[23]	Case-Control	UK	Clinical, and histological, criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	1.01 (0.52 – 1.99)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	1.41 (0.59 – 3.36)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.75 (0.43 – 1.30)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	0.16 (0.02 – 1.18)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	2.54 (1.00 – 6.46)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.55 (0.53 – 4.52)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.66 (0.39 – 1.11)
	Stassen et al. 2009[19]	Case-Control	The Nether-lands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.07 (0.84 – 1.35)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched commu-nity-based control frequen-cies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	1.30 (0.86 – 1.95)
HLA-DR4	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histo-logical criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	1.00 (0.52 – 1.92)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/300	GPA (all patients)	NR	0.96 (0.50 – 1.83)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histo-logical criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.81 (0.32 – 2.07)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	1.24 (0.74 – 2.07)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	0.72 (0.27 – 1.88)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.25 (0.54 – 2.90)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.57 (0.61 – 4.01)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	1.73 (0.84 – 3.57)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.87 (1.23 – 2.82)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	1.53 (1.25 – 1.87)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Cao et al. 2011[33]**	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.73 (0.51 – 1.05)
		Case-Control	USA (all African Americans)	Histologically proven AAV	USA African Americans-Bethesda database	16/112	NR	PR3-ANCA (9), MPO-ANCA (4), p-ANCA (2), ANCA negative (1)	0.62 (0.08 – 5.01)
HLA-DR5	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.72 (0.28 – 1.85)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.18 (0.02 – 1.37)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.95 (0.45 – 2.01)
	Papasteriades et al. 1997[22]	Case-Control	Greece	Histologically proven AAV	Geographically and ethnically matched healthy subjects	23/405	MPA (all patients)	NR	1.59 (0.80 – 3.15)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.80 (0.58 – 1.09)
HLA-DR6	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.16 (0.04 – 0.70)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.11 (0.01 – 1.83)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.60 (0.27 – 1.31)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.63 (0.56 – 4.77)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.44 (0.32 – 0.59)
HLA-DR7	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.512 (0.22 – 1.22)
	Papiha et al. 1992[32]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	27/105	GPA (all patients)	NR	0.64 (0.23 – 1.73)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.99 (0.40 – 2.48)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.77 (0.34 – 1.75)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	2.42 (1.47 – 4.00)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.58 (1.01 – 2.47)
	Stassen et al. 2009[19]	Case-Control	The Netherlands	CHCC criteria	Geographically matched healthy blood donors	304/5442	GPA (241), MPA (30), EGPA (12), RVL (21)	PR3-ANCA (218), MPO-ANCA (64), other (4), ANCA negative (18)	0.96 (0.72 – 1.27)
HLA-DR8	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.52 (0.22 – 1.22)
	Murty et al. 1991[17]	Case-Control	Ireland, UK	Histologically proven AAV	Geographically matched healthy subjects	41/300	GPA (all patients)	NR	1.05 (0.21 – 5.14)
	Zhang et al.1995[26]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	2.21 (0.67 – 7.32)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	1.63 (0.66 – 4.05)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.23 (0.31 – 4.91)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.00 (0.12 – 5.08)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	2.03 (1.01 – 4.05)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	UK	CHCC criteria	Geographically matched healthy subjects	94/90	GPA (56), MPA (31), RVL (7)	PR3-ANCA (36), MPO-ANCA (19), PR3- and MPO-ANCA positive (3)	0.95 (0.59 – 1.54)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.76 (0.37 – 1.55)
HLA-DR9	Elkon et al. 1983[23]	Case-Control	UK	Clinical and histological criteria	Geographically matched subjects	46/113	GPA (17), EGPA (14), PAN (15)	NR	0.49 (0.02 – 10.21)
	Nakamaru et al. 1996[20]	Case-Control	Japan	Clinical, histological, serological criteria	Geographically matched healthy subjects	16/472	GPA (all patients)	c-ANCA (all patients)	3.03 (1.40 – 6.56)
	Fujii et al. 2000[36]	Case-Control	Japan	CHCC criteria	Geographically matched healthy subjects	12/472	NR	MPO-ANCA (all patients)	2.75 (1.12 – 6.76)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.94 (0.04 – 23.32)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.66 (0.11 – 4.04)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	1.83 (0.20 – 16.56)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.80 (0.17 – 3.74)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Stassen et al. 2009[19]	Case-Control	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)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.75 (0.208 – 2.72)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.68 (0.43 – 1.06)
	Tsuchiya et al. 2013[37]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	116/265	MPA (96)	MPO-ANCA (all patients)	1.74 (1.18 – 2.57)
HLA-DRB1*0401	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	2.10 (0.52 – 8.50)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.58 (0.18 – 1.90)
HLA-DRB1*0403	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.95 (0.27 – 3.40)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.16 (0.02 – 1.30)
*HLA-DRB1*0405*	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.61 (0.30 – 1.22)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.13 (0.52 – 2.49)
*HLA-DRB1*0406*	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.65 (0.19 – 2.22)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.84 (0.73 – 4.63)
*HLA-DRB1*0407*	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	2.82 (0.78 – 10.14)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.44 (0.02 – 10.77)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
HLA-DRB1*0410	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.67 (0.32 – 8.69)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.44 (0.02 – 10.77)
HLA-DRB1*0802	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.16 (0.42 – 3.18)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.26 (0.01 – 5.47)
HLA-DRB1*0803	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.51 (0.78 – 2.93)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.19 (0.61 – 2.33)
HLA-DRB1*10	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.43 (0.13 – 16.03)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	5.10 (0.24 – 107.55)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.40 (0.02 – 7.44)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.75 (0.21 – 2.72)
HLA-DRB1*11	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.723 (0.26 – 2.04)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.28 (0.48 – 3.38)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.88 (0.53 – 1.48)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	1.09 (0.66 – 1.80)
HLA-DRB1*1101	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.75 (1.02 – 3.00)
	Tsuchiya et al. 2013[37]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	116/265	MPA (96)	MPO-ANCA (all patients)	2.79 (0.84 – 9.23)
HLA-DRB1*12	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	2.97 (0.721 – 2.23)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	6.31 (0.75 – 53.40)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/369	EGPA (all patients)	NR	0.57 (0.17 – 1.93)
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	0.59 (0.17 – 2.06)
HLA-DRB1*1201	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.21 (0.03 – 1.60)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.46 (0.16 – 1.29)
HLA-DRB1*1202	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.37 (0.05 – 2.90)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.70 (0.93 – 3.13)
HLA-DRB1*13	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.56 (0.20 – 1.53)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.65 (0.31 – 1.38)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	0.23 (0.07 – 0.73)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	0.50 (0.28 – 0.89)
HLA-DRB1*1302	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.54 (0.24 – 1.23)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.52 (0.16 – 1.67)
HLA-DRB1*14	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	1.07 (0.27 – 4.16)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	2.02 (0.18 – 22.63)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.83 (0.72 – 4.65)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Cao et al. 2011[33]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	2.82 (1.05 – 7.59)
HLA-DRB1*1403	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	1.25 (0.34 – 4.60)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	1.32 (0.19 – 9.41)
HLA-DRB1*1405	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.11 (0.01 – 1.91)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.96 (0.44 – 2.13)
HLA-DRB1*15	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3 (all patients)	0.79 (0.34 – 1.83)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.13 (0.57 – 2.26)

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.14 (0.01 – 2.72)
	Cao et al. 2011[33**]	Case-Control	USA (96 Caucarians and 41 African Americans)	Histologically proven AAV	Ethnically matched community-based control frequencies (Healthy Organ Donor-North Carolina Services)	137/379	NR	PR3-ANCA (90), MPO-ANCA (47)	1.39 (0.34 – 5.59)
		Case-Control	USA (all African Americans)	Histologically proven AAV	USA African Americans-Bethesda database	16/112	NR	PR3-ANCA (9), MPO-ANCA (4), p-ANCA (2), ANCA negative (1)	2.42 (0.47 – 12.55)
HLA-DRB1*1602	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	64/265	GPA (3), MPA (50), EGPA (8), PAN (3)	MPO-ANCA (all patients)	0.24 (0.01 – 4.171)
	Luo et al. 2011[34]	Case-Control	China	EMA algorithm	Ethnically matched healthy blood donors	152/200	GPA (45), MPA (107)	PR3-ANCA (19), MPO-ANCA (130), PR3- and MPO-ANCA positive (3)	0.12 (0.01 – 2.14)
HLA-DRB3	Spencer et al. 1992[38]	Case-Control	UK	Clinical criteria	Geographically and ethnically matched subjects	59/1103	GPA (34), MPA (25)	c-ANCA (47), p-ANCA (10), ANCA negative (2)	0.29 (0.11 – 0.79)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.41 (0.76 – 2.60)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	0.54 (0.35 – 0.84)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	0.61 (0.44 – 0.86)
HLA-DRB4	Spencer et al. 1992[38]	Case-Control	UK	Clinical criteria	Geographically and ethnically matched subjects	59/1103	GPA (34), MPA (25)	c-ANCA (47), p-ANCA (10), ANCA negative (2)	1.38 (0.89 – 2.13)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	0.89 (0.46 – 1.72)
	Vaglio et al. 2007[35]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	48/350	EGPA (all patients)	MPO-ANCA (18), ANCA negative (26), undetermined (4)	2.49 (1.58 – 3.90)
	Wieczorek et al. 2008[29]	Case-Control	Germany	ACR criteria	Geographically matched healthy subjects	102/341	EGPA (all patients)	NR	1.87 (1.34 – 2.61)
HLA-DRB5	Spencer et al. 1992[38]	Case-Control	UK	Clinical criteria	Geographically and ethnically matched subjects	59/1103	GPA (34), MPA (25)	c-ANCA (47), p-ANCA (10), ANCA negative (2)	1.35 (0.69 – 2.63)
	Von Vietinghoff et al. 2006[18]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	51/51	GPA (all patients)	NR	1.07 (0.82 – 2.18)
HSD17B8 **rs421446 (C)**	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	282/369	GPA (all patients)	ANCA+ (250), ANCA- (27)	0.43 (0.32 – 0.57)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	0.39 (0.32 – 0.48)
IL-1β **(A2)**	Huang et al. 2000[4]	Case-Control	Sweden	ACR criteria	Geographically and ethnically matched healthy subjects	32/109	GPA (all patients)	PR3-ANCA (29)	1.21 (0.55 – 2.63)
	Borgmann et al. 2003[39]	Case-Control	Germany	CHCC criteria	Geographically matched healthy, unrelated subjects	109/196	NR	PR3-ANCA (79), MPO-ANCA (30)	0.89 (0.61 – 1.29)

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

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

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
		Case-Control	Canada	ACR criteria	Geographically matched subjects with no history of autoimmune disease	456/1500	GPA (all patients)	NR	1.40 (1.11 – 1.78)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5365	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.35 (1.14 – 1.60)
	Martorana et al. 2012[51]	Case-Control	Italy	ACR and CHCC criteria	Geographically matched healthy subjects with no history of autoimmune disease	344/945	GPA (143), EGPA (99), MPA (102)	c-ANCA (126), p-ANCA (163), ANCA negative (39)	1.40 (0.97 – 2.04)
***RING1/ RXRB* rs213213 (A)**	Heckmann et al. 2008[24]	Case-Control	Germany	ACR criteria	Geographically matched healthy blood donors	279/369	GPA (all patients)	ANCA+ (250), ANCA- (27)	2.13 (1.70 – 2.67)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.55 (1.38 – 1.74)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	1.83 (1.57 – 2.13)
***RXRB* rs6531 (C)**	Szyld et al. 2006[52]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy subjects	187/201	GPA (all patients)	ANCA+ (151), ANCA- (36)	0.60 (0.45 – 0.80)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	911/5251	GPA (565), MPA (262)	PR3-ANCA (478), MPO-ANCA (264)	1.79 (1.61 – 1.98)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	1.81 (1.55 – 2.11)
***RXRB* rs9277935 (T)**	Wieczorek et al. 2009[53]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	282/380	GPA (all patients)	NR	0.39 (0.29 – 0.54)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5350	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	0.51 (0.43 – 0.61)
	Xie et al. 2013[25]	Case-control (GWAS)	Canada, USA	ACR criteria	Geographically matched healthy subjects	459/1503	GPA (all patients)	c-ANCA (351)	0.34 (0.27 – 0.44)
***SERPINA1* S allele**	Lhotta et al. 1994[54]	Case-Control	Austria	ACR	Geographically matched healthy subjects	32/868	GPA (29), MPA (2), iRPGN (1)	c-ANCA (all patients)	0.69 (0.09 – 5.11)
	Griffith et al. 1996[55]	Case-Control	UK	CHCC criteria	Geographically and ethnically matched unrelated subjects	102/2310	GPA (51), MPA (29), EGPA (9), PAN (2), iRPGN (11)	c-ANCA (70), p-ANCA (32)	1.42 (0.79 – 2.52)
	Mahr et al. 2010[56]	Case-Control	USA	ACR criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	433/421	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.68 (1.08 – 2.63)
	Morris et al. 2011[57]	Case-Control	Germany (531), France (81), UK (244)	CHCC criteria	Geographically and ethnically matched healthy subjects with no (family) history of autoimmune disease	856/1505	GPA (723), MPA (133)	c-ANCA (605), p-ANCA (150), ANCA negative (54)	1.11 (0.81 – 1.51)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Chorostowska-Wynimko et al. 2013[58]	Case-Control	Poland	Clinical, histological, and serological criteria	Geographically matched neonates born alive	51/658	GPA (all patients)	c-ANCA (43), p-ANCA (2), ANCA negative (4)	2.61 (0.56 – 12.08)
***SERPINA1* Z allele**	Lhotta et al. 1994[54]	Case-Control	Austria	ACR criteria	Geographically matched healthy subjects	32/868	GPA (29), MPA (2), iRPGN (1)	c-ANCA (all patients)	8.76 (3.63 – 21.17)
	Griffith et al. 1996[55]	Case-Control	UK	CHCC criteria	Geographically and ethnically matched unrelated subjects	102/2310	GPA (51), MPA (29), EGPA (9), PAN (2), iRPGN (11)	c-ANCA (70), p-ANCA (32)	2.20 (1.05 – 4.62)
	Callea et al. 1997[59]	Case- Control	Italy	CHCC criteria	Healthy blood donors	84/200	GPA (33), MPA (28), iRPGN (23)	c-ANCA (38), p-ANCA (46)	4.90 (1.21 – 19.83)
	Borgmann et al. 2001[60]	Case-Control	Germany	ACR and CHCC criteria	Geographically and ethnically matched healthy, unrelated subjects	97/752	GPA (all patients)	c-ANCA (all patients)	3.36 (1.45 – 7.79)
	Mahr et al. 2010[56]	Case-Control	USA	ACR criteria	Geographically matched healthy subjects with no (family) history of autoimmune disease	433/421	GPA (all patients)	PR3-ANCA (339), MPO-ANCA (44), ANCA negative (39)	1.99 (1.12 – 3.52)
	Morris et al. 2011[57]	Case-Control	Germany (531), France (81), UK (244)	CHCC criteria	Geographically and ethnically matched healthy subjects with no (family) history of autoimmune disease	856/1505	GPA (723), MPA (133)	c-ANCA (605), p-ANCA (150), ANCA negative (54)	2.25 (1.60 – 3.18)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Previously unpublished Lyons et al. 2012 GWAS data[3**]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	562/805	GPA (391), MPA (143)	PR3-ANCA (322), MPO-ANCA (166)	2.59 (1.66 – 4.02)
		Case-control (GWAS)	Europe	EMA algorithm, supported by either serology or histology	Geographically matched subjects	1445/1062	NR	NR	4.19 (2.62 – 6.69)
	Chorostowska-Wynimko et al. 2013[58]	Case-Control	Poland	Clinical, histological, serological criteria	Geographically matched neonates born alive	51/658	GPA (all patients)	c-ANCA (43), p-ANCA (2), ANCA negative (4)	2.19 (0.63 – 7.55)
***STAT4* rs7574865 (T)**	Wieczorek et al. 2010[44]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	612/880	GPA (all patients)	NR	1.01 (0.85 – 1.20)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.18 (1.04 – 1.35)
	Kawasaki et al. 2013[45]	Case-Control	Japan	EMA algorithm	Geographically matched healthy, unrelated subjects	232/710	GPA (28), MPA (177), EGPA (15), unclassified (12)	MPO (all patients)	1.10 (0.89 – 1.37)
***TGF*-β_1 rs1800471 (C)**	Murakozy et al. 2001[42]	Case-Control	Germany	ACR and CHCC criteria	Geographically matched healthy blood donors	39/72	GPA (all patients)	NR	2.20 (0.89 – 5.44)
	Bartfai et al. 2003[43]	Case-Control	Caucasian patients	ACR and CHCC criteria	Ethnically matched blood donors	161/96	GPA (125), MPA (36)	NR	1.06 (0.52 – 2.14)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	1.86 (0.73 – 4.71)
***TNFα* rs1800629 (A)**	Mascher et al. 1997[61]	Case-Control	Germany	ACR and CHCC criteria	Healthy blood donors	35/111	GPA (all patients)	c-ANCA (32), p-ANCA (1), ANCA negative (1)	1.54 (0.77 – 3.10)
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	0.88 (0.52 – 1.50)
	Spriewald et al. 2005[31]	Case-Control	Germany	ACR and CHCC criteria	Ethnically matched healthy subjects	32/91	GPA (all patients)	PR3-ANCA (all patients)	2.22 (0.93 – 5.29)
	Previously unpublished Lyons et al. 2012 GWAS data[3]	Case-control (GWAS)	UK	EMA algorithm, supported by either serology or histology	Wellcome Trust Case Control Consortium (UK)	676/5366	GPA (394), MPA (156)	PR3-ANCA (326), MPO-ANCA (167)	1.06 (0.92 – 1.23)
***TNFRII* 196R**	Tsuchiya et al. 2003[5]	Case-Control	Japan	CHCC and Japanese 1998 criteria	Geographically matched healthy subjects	50/262	MPA (all patients)	MPO-ANCA (all patients)	0.67 (0.31 – 1.45)

Supplementary table 2. Study characteristics of the included studies (Continued)

Variants	Article	Study details		Definitions		Participants (n)			OR (95% CI)
		Design	Setting	Cases	Controls	Cases / Controls	Diagnoses	ANCA serotype	Allele level
	Zhou et al. 2004[6]	Case-Control	USA	ACR criteria	Geographically and ethnically matched healthy, unrelated subjects	117/123	GPA (all patients)	PR3-ANCA (82), MPO-ANCA (5), PR3- and MPO-ANCA positive (2), ANCA negative (25)	1.05 (0.70 – 1.57)
***TLR9* rs352162 (T)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	1.89 (1.67 – 2.14)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.07 (0.90 – 1.28)
***TLR9* rs352140 (T)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	1.16 (1.03 – 1.31)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.06 (0.89 – 1.27)
***TLR9* rs352139 (T)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	1.12 (0.99 – 1.27)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.08 (0.91 – 1.30)
***TLR9* rs5743836 (G)**	Husmann et al. 2014[40**]	Case-Control	Germany	EMA algorithm	Geographically matched healthy blood donors	863/1344	GPA (646), MPA (53), EGPA (164)	NR	0.82 (0.69 – 0.98)
			The Netherlands, UK	EMA algorithm	Geographically and ethnically matched healthy subjects	426/554	GPA (273), MPA (100), EGPA (53)	NR	1.22 (0.94 – 1.58)

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

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

Variant by gene (minor allele)	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
CTLA-4 $(AT)_{102}$	3	186/420	1.20 (0.75 – 1.90)	0.449	0	0.375	0.986
CTLA-4 $(AT)_{104}$	3	186/420	1.21 (0.92 – 1.60)	0.180	0	0.390	0.227
CTLA-4 $(AT)_{106}$	3	186/420	1.30 (0.74 – 2.29)	0.359	75	0.018	0.674
CTLA-4 $(AT)_{108}$	3	186/420	0.88 (0.50 – 1.56)	0.963	0	0.963	0.473
CTLA-4 $(AT)_{110}$	3	186/420	0.74 (0.34 – 1.61)	0.441	0	0.667	0.171
CTLA-4 $(AT)_{116}$	3	186/420	0.80 (0.27 – 2.33)	0.677	0	0.724	0.786
CTLA-4 $(AT)_{118}$	3	186/420	0.46 (0.16 – 1.35)	0.158	26	0.258	0.155
CTLA-4 $(AT)_{122}$	3	186/420	1.70 (0.62 – 4.71)	0.304	26	0.260	0.557
CTLA-4 $(AT)_{124}$	3	186/420	1.97 (0.73 – 5.31)	0.178	61	0.080	0.637
CTLA-4 $(AT)_{126}$	3	186/420	1.25 (0.53 – 2.94)	0.609	53	0.121	0.701
CTLA-4 $(AT)_{128}$	3	186/420	1.15 (0.47 – 2.82)	0.760	37	0.204	0.826
FCAR rs16986050 (G)	2	1311/5891	0.93 (0.82 – 1.05)	0.211	84	0.002	0.523
FCGR3A rs396991 (G)	2	141/457	1.00 (0.74 – 1.34)	0.978	79	0.030	N/A
FCGR3B (NA1)	4	982/970	0.96 (0.84 – 1.11)	0.590	37	0.191	0.210
GHSR rs509035 (A)	2	1547/6595	1.04 (0.96 – 1.14)	0.342	52	0.123	0.874
GHSR rs519384 (A)	1	628/1328	1.12 (0.96 – 1.30)	0.140	0	0.389	N/A
GHSR rs572169 (A)	1	620/1304	1.12 (0.97 – 1.30)	0.118	50	0.158	N/A
HLA-A1	4	427/7324	1.07 (0.89 – 1.30)	0.455	0	0.567	0.996
HLA-A2	5	443/7796	0.96 (0.82 – 1.12)	0.582	0	0.956	0.335
HLA-A3	4	427/7324	1.18 (0.97 – 1.42)	0.092	35	0.201	0.273
HLA-A9	3	366/6991	0.85 (0.65 – 1.13)	0.266	77	0.014	0.311
HLA-A10	3	366/6991	0.79 (0.48 – 1.30)	0.356	78	0.010	0.273

Supplementary table 3. Genetic variants not associated with AAV after meta-analysis (Continued)

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

Supplementary table 3. Genetic variants not associated with AAV after meta-analysis (Continued)

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

Supplementary table 3. Genetic variants not associated with AAV after meta-analysis (Continued)

Variant by gene (minor allele)	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
HLA-DR3	9	816/7045	1.05 (0.81 – 1.36)	0.740	41	0.096	0.946
HLA-DR4	11	914/7696	1.19 (0.95 – 1.50)	0.132	47	0.037	0.342
HLA-DR5	5	494/6155	0.90 (0.61 – 1.31)	0.570	32	0.206	0.965
HLA-DR7	7	610/6493	1.08 (0.73 – 1.60)	0.164	66	0.007	0.932
HLA-DR8	9	823/7157	1.10 (0.80 – 1.51)	0.552	15	0.307	0.375
HLA-DR9	11	1016/8204	1.16 (0.71 – 1.90)	0.560	60	0.005	0.925
*HLA-DRB1*0401*	2	216/465	0.93 (0.38 – 2.28)	0.869	48	0.167	N/A
*HLA-DRB1*0403*	2	216/465	0.49 (0.17 – 1.42)	0.190	53	0.144	N/A
*HLA-DRB1*0405*	2	216/465	0.78 (0.47 – 1.30)	0.344	27	0.242	N/A
*HLA-DRB1*0406*	2	216/465	1.22 (0.61 – 2.5)	0.580	44	0.182	N/A
*HLA-DRB1*0407*	2	216/465	1.95 (0.61 – 6.29)	0.263	13	0.283	N/A
*HLA-DRB1*0410*	2	216/465	1.17 (0.27 – 5.05)	0.832	0	0.463	N/A
*HLA-DRB1*0802*	2	216/465	0.94 (0.36 – 2.43)	0.897	0	0.359	N/A
*HLA-DRB1*0803*	2	216/465	1.33 (0.83 – 2.14)	0.236	0	0.622	N/A
*HLA-DRB1*10*	4	322/890	0.98 (0.39 – 2.46)	0.969	0	0.627	0.596
*HLA-DRB1*11*	4	322/890	0.98 (0.71 – 1.34)	0.818	0	0.818	1.000
*HLA-DRB1*12*	4	322/890	1.12 (0.60 – 2.09)	0.712	54	0.088	0.121
*HLA-DRB1*1302*	2	216/465	0.54 (0.27 – 1.05)	0.068	0	0.952	N/A
*HLA-DRB1*1202*	2	216/465	1.42 (0.81 – 2.49)	0.219	49	0.160	N/A
*HLA-DRB1*1403*	2	216/465	1.27 (0.43 – 3.76)	0.666	0	0.964	N/A
*HLA-DRB1*1405*	2	216/465	0.66 (0.32 – 1.37)	0.265	57	0.125	N/A
*HLA-DRB1*1502*	2	216/465	0.57 (0.30 – 1.07)	0.079	0	0.398	N/A

Supplementary table 3. Genetic variants not associated with AAV after meta-analysis (Continued)

Variant by gene (minor allele)	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis	I^2 (%)	P value for heterogeneity	P value for funnel plot asymmetry
*HLA-DRB1*16*	3	236/633	0.91 (0.37 – 2.27)	0.842	15	0.315	0.436
*HLA-DRB1*1602*	2	216/465	0.17 (0.02 – 1.29)	0.086	0	0.734	N/A
HLA-DRB5	2	110/1154	1.20 (0.73 – 1.97)	0.470	0	0.643	N/A
*IL-1*β (A2)	4	1172/5687	1.00 (0.90 – 1.12)	0.995	0	0.805	0.645
*IL1RN*1*	2	214/434	1.06 (0.82 – 1.37)	0.662	0	0.659	N/A
*IL1RN*2*	2	214/434	1.00 (0.77 – 1.31)	0.980	0	0.956	N/A
*IL1RN*3*	2	214/434	0.61 (0.26 – 1.44)	0.257	45	0.176	N/A
*IL1RN*4*	2	214/434	0.85 (0.13 – 5.82)	0.872	0	0.888	N/A
*IL1RN*5*	2	214/434	0.88 (0.13 – 5.94)	0.892	0	0.796	N/A
IL-6 rs1800795 (C)	4	1926/6817	1.01 (0.94 – 1.09)	0.793	0	0.537	0.584
IL-10 rs1800872 (A)	2	538/598	1.01 (0.83 – 1.22)	0.963	0	0.795	N/A
IL-10 rs1800896 (G)	5	1414/6183	0.90 (0.76 – 1.07)	0.232	55	0.063	0.285
LEPR rs8179183 (C)	1	878/2653	0.89 (0.77 – 1.03)	0.118	89	<0.001	0.780
MPO rs2333227 (A)	3	395/299	0.96 (0.76 – 1.21)	0.696	0	0.822	0.478
PCD1 rs1156882 (A)	2	168/479	0.88 (0.55 – 1.38)	0.568	0	0.701	N/A
TGF-β_1 rs1800471 (C)	3	232/259	1.49 (0.92 – 2.41)	0.107	0	0.401	0.220
*TNF*α rs1800629 (A)	4	860/5691	1.14 (0.88 – 1.45)	0.327	29	0.236	0.389
TNFRII 196R	2	167/385	0.94 (0.66 – 1.34)	0.749	0	0.317	N/A
TLR9 rs5743836 (G)	1	1289/1898	0.93 (0.81 – 1.08)	0.343	83	0.014	N/A

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups

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

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
CTLA-4 $(AT)_{116}$				
GPA	2	93/309	0.66 (0.17 – 2.60)	0.553
MPA	2	93/311	0.41 (0.05 – 3.38)	0.408
PR3-ANCA	1	62/200	0.21 (0.01 – 3.72)	0.288
MPO-ANCA	2	92/311	0.69 (0.12 – 3.98)	0.673
CTLA-4 $(AT)_{118}$				
GPA	2	93/309	0.32 (0.06 – 1.68)	0.176
MPA	2	93/311	0.31 (0.06 – 1.69)	0.175
PR3-ANCA	1	62/200	0.11 (0.01 – 1.81)	0.121
MPO-ANCA	2	92/311	0.44 (0.10 – 1.97)	0.283
CTLA-4 $(AT)_{122}$				
GPA	2	93/309	1.32 (0.26 – 6.80)	0.742
MPA	2	93/311	1.57 (0.48 – 5.19)	0.456
PR3-ANCA	1	62/200	0.35 (0.02 – 6.62)	0.487
MPO-ANCA	2	92/311	3.69 (1.40 – 9.71)	0.008
CTLA-4 $(AT)_{124}$				
GPA	2	93/309	1.69 (0.67 – 4.25)	0.264
MPA	2	93/311	0.64 (0.28 – 1.46)	0.287
PR3-ANCA	1	62/200	1.83 (0.60 – 5.55)	0.289
MPO-ANCA	2	92/311	0.53 (0.22 – 1.30)	0.168
CTLA-4 $(AT)_{126}$				
GPA	2	93/309	1.43 (0.47 – 4.35)	0.526
MPA	2	93/311	0.38 (0.08 – 2.11)	0.266
PR3-ANCA	1	62/200	0.21 (0.01 – 3.72)	0.288
MPO-ANCA	2	92/311	0.54 (0.12 – 2.46)	0.428
CTLA-4 $(AT)_{128}$				
GPA	2	93/309	0.39 (0.07 – 2.14)	0.278
MPA	2	93/311	1.27 (0.39 – 4.20)	0.694
PR3-ANCA	1	62/200	0.29 (0.04 – 2.25)	0.235
MPO-ANCA	2	92/311	1.29 (0.39 – 4.28)	0.674
CTLA-4 rs231775 (G)				
GPA	2	510/5994	1.05 (0.92 – 1.20)	0.430
MPA	2	252/5994	1.17 (0.97 – 1.40)	0.100
PR3-ANCA	1	326/5365	1.00 (0.85 – 1.18)	0.983
MPO-ANCA	1	167/5365	0.96 (0.77 – 1.21)	0.747

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
CTLA-4 rs3087243 (A)				
GPA	3	1561/7855	0.80 (0.73 – 0.87)	<0.001
MPA	2	358/5886	0.79 (0.68 – 0.92)	0.003
PR3-ANCA	1	478/5257	0.81 (0.71 – 0.93)	0.003
MPO-ANCA	1	264/5257	0.96 (0.80 – 1.15)	0.658
FCAR rs16986050 (G)				
GPA	2	1029/5891	0.92 (0.80 – 1.05)	0.214
MPA	1	394/5365	0.93 (0.69 – 1.26)	0.647
PR3-ANCA	1	326/5365	1.13 (0.93 – 1.38)	0.211
MPO-ANCA	1	167/5365	1.00 (0.75 – 1.33)	0.988
FCGR2A rs1801274 (C)				
GPA	5	1082/5969	0.99 (0.94 – 1.05)	0.827
MPA	4	800/5766	0.97 (0.81 – 1.15)	0.698
PR3-ANCA	4	883/5820	0.91 (0.79 – 1.03)	0.138
MPO-ANCA	4	844/5969	0.80 (0.67 – 0.95)	0.011
FCGR3A rs396991 (G)				
GPA	1	91/154	1.30 (0.89 – 1.91)	0.172
MPA	1	50/303	0.65 (0.39 – 1.07)	0.090
PR3-ANCA	1	91/154	1.30 (0.89 – 1.91)	0.172
MPO-ANCA	1	50/303	0.65 (0.39 – 1.07)	0.090
FCGR3B (NA1)				
GPA	3	865/667	0.93 (0.80 – 1.08)	0.343
MPA	2	75/200	1.52 (1.03 – 2.25)	0.035
PR3-ANCA	2	143/254	1.07 (0.79 – 1.45)	0.664
MPO-ANCA	2	121/403	1.19 (0.86 – 1.64)	0.287
GHSR rs509035 (A)				
GPA	2	1198/6595	1.05 (0.96 – 1.16)	0.292
MPA	1	262/5259	1.00 (0.82 – 1.20)	0.966
PR3-ANCA	1	478/5259	1.05 (0.91 – 1.21)	0.521
MPO-ANCA	1	264/5259	0.83 (0.68 – 1.01)	0.057
HLA-A2				
GPA	5	380/7796	0.96 (0.81 – 1.14)	0.633
c-ANCA	1	16/96	0.90 (0.37 – 2.23)	0.826
HLA-A11				
GPA	5	380/7702	0.61 (0.41 – 0.90)	0.014

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPA	1	23/405	2.97 (1.19 – 7.41)	0.020
c-ANCA	1	16/472	0.71 (0.17 – 3.03)	0.644
HLA-A24				
GPA	3	108/1223	0.94 (0.56 – 1.60)	0.830
c-ANCA	1	16/472	0.75 (0.34 – 1.65)	0.476
HLA-A26				
GPA	3	108/1223	1.24 (0.61 – 2.54)	0.550
MPA	1	23/405	2.49 (1.00 – 6.18)	0.049
c-ANCA	1	16/472	2.36 (1.00 – 5.60)	0.051
HLA-A31				
GPA	3	108/1223	1.02 (0.43 – 2.44)	0.969
c-ANCA	1	16/472	1.55 (0.46 – 5.24)	0.479
HLA-A32				
GPA	3	108/1223	1.62 (0.74 – 3.54)	0.231
c-ANCA	1	16/472	2.07 (0.61 – 7.04)	0.246
HLA-B35				
GPA	4	349/7095	0.62 (0.44 – 0.89)	0.010
c-ANCA	1	16/472	0.80 (0.19 – 3.40)	0.757
HLA-B39				
GPA	2	67/523	0.65 (0.11 – 3.68)	0.622
c-ANCA	1	16/472	0.86 (0.11 – 6.51)	0.887
HLA-B44				
GPA	3	108/1223	1.53 (0.96 – 2.44)	0.072
c-ANCA	1	16/472	2.50 (0.85 – 7.40)	0.098
HLA-B51				
GPA	2	67/523	1.03 (0.46 – 2.32)	0.943
c-ANCA	1	16/472	1.87 (0.64 – 5.49)	0.255
HLA-B55				
GPA	2	67/523	1.07 (0.40 – 2.88)	0.887
c-ANCA	1	16/472	7.35 (2.33 – 23.14)	0.001
HLA-B60				
GPA	2	57/1172	1.98 (0.77 – 5.09)	0.154
c-ANCA	1	16/472	1.19 (0.28 – 5.13)	0.814
HLA-B62				
GPA	2	57/1172	2.27 (1.05 – 4.90)	0.036

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

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

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
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
*HLA-DPB1*0402*				
GPA	2	283/458	1.13 (0.82 – 1.55)	0.439
EGPA	1	102/369	1.15 (0.75 – 1.75)	0.533
PR3-ANCA	2	183/139	1.11 (0.69 – 1.77)	0.674
MPO-ANCA	1	22/50	0.94 (0.31 – 2.85)	0.913
*HLA-DPB1*0501*				
GPA	1	148/89	0.20 (0.01 – 4.93)	0.324
PR3-ANCA	2	183/139	1.11 (0.26 – 4.76)	0.886
MPO-ANCA	1	22/50	1.14 (0.10 – 12.91)	0.916
*HLA-DPB1*0601*				
GPA	1	148/89	0.60 (0.08 – 4.29)	0.610
PR3-ANCA	2	183/139	1.12 (0.23 – 5.51)	0.887
MPO-ANCA	1	22/50	6.93 (0.28 – 173.53)	0.239
*HLA-DPB1*0901*				
GPA	1	148/89	1.81 (0.07 – 44.73)	0.716
PR3-ANCA	2	183/139	0.98 (0.27 – 3.62)	0.978
MPO-ANCA	1	22/50	0.91 (0.17 – 4.85)	0.907
HLA-DPB2 rs3130215 (A)				
GPA	3	1135/7249	1.37 (0.88 – 2.13)	0.160
MPA	1	156/5366	1.33(1.06 – 1.66)	0.013
PR3-ANCA	1	326/5366	0.65 (0.55 – 0.77)	<0.001
MPO-ANCA	1	167/5366	1.27 (1.02 – 1.58)	0.032
*HLA-DQB1*02*				
GPA	2	83/141	0.91 (0.53 – 1.55)	0.720
PR3-ANCA	1	32/91	0.98 (0.45 – 2.14)	0.954
*HLA-DQB1*0302*				
GPA	1	32/91	0.94 (0.36 – 2.49)	0.905
PR3-ANCA	2	67/141	1.03 (0.54 – 1.98)	0.924
MPO-ANCA	1	22/50	1.06 (0.37 – 2.99)	0.917
*HLA-DQB1*0303*				
GPA	1	32/91	2.97 (0.72 – 12.23)	0.132

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPA	1	50/77	2.11 (1.14 – 3.90)	0.018
PR3-ANCA	2	67/141	0.79 (0.31 – 2.05)	0.634
MPO-ANCA	2	72/127	1.91 (1.12 – 3.26)	0.017
*HLA-DQB1*04*				
GPA	2	83/141	1.63 (0.52 – 5.11)	0.404
PR3-ANCA	1	32/91	1.74 (0.40 – 7.50)	0.457
*HLA-DQB1*0501*				
GPA	1	32/91	0.77 (0.32 – 1.88)	0.568
PR3-ANCA	2	67/141	1.05 (0.58 – 1.91)	0.865
MPO-ANCA	1	22/50	2.05 (0.84 – 4.97)	0.113
*HLA-DQB1*0602*				
GPA	1	32/91	0.89 (0.38 – 2.05)	0.779
PR3-ANCA	2	67/141	0.80 (0.42 – 1.54)	0.504
MPO-ANCA	1	22/50	0.35 (0.08 – 1.63)	0.181
HLA-DQ7				
GPA	1	32/91	0.43 (0.16 – 1.16)	0.095
MPA	1	23/405	0.66 (0.34 – 1.30)	0.234
PR3-ANCA	2	67/141	0.98 (0.58 – 1.66)	0.940
MPO-ANCA	1	22/50	1.26 (0.57 – 2.77)	0.569
HLA-DR1				
GPA	6	413/6002	0.76 (0.58 – 1.00)	0.054
MPA	4	223/6020	1.12 (0.72 – 1.74)	0.612
EGPA	3	128/5924	0.82 (0.53 – 1.26)	0.360
PR3-ANCA	3	157/560	0.57 (0.38 – 0.86)	0.008
MPO-ANCA	3	133/734	0.78 (0.49 – 1.25)	0.297
HLA-DR2				
GPA	4	301/6132	1.36 (1.08 – 1.72)	0.010
EGPA	1	14/113	1.40 (0.45 – 4.39)	0.561
PR3-ANCA	1	35/90	1.34 (0.63 – 2.86)	0.442
MPO-ANCA	1	22/90	1.03 (0.39 – 2.69)	0.958
c-ANCA	1	16/472	0.33 (0.08 – 1.38)	0.128
HLA-DR3				
GPA	5	368/5802	1.24 (1.00 – 1.56)	0.056
MPA	2	38/518	0.45 (0.17 – 1.14)	0.092
EGPA	2	116/482	0.70 (0.43 – 1.13)	0.139

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
PR3-ANCA	3	157/560	1.29 (0.90 – 1.86)	0.170
MPO-ANCA	2	69/469	0.85 (0.49 – 1.48)	0.574
HLA-DR4				
GPA	7	425/6424	1.32 (1.09 – 1.60)	0.004
MPA	2	66/5555	1.50 (0.98 – 2.30)	0.060
EGPA	4	176/6246	1.70 (1.23 – 2.34)	0.001
PR3-ANCA	3	157/560	0.98 (0.71 – 1.36)	0.917
MPO-ANCA	2	69/202	2.51 (1.46 – 4.32)	0.001
c-ANCA	1	16/472	0.72 (0.27 – 1.88)	0.498
HLA-DR5				
GPA	3	285/5660	0.76 (0.54 – 1.06)	0.102
MPA	1	23/405	1.59 (0.80 – 3.15)	0.182
EGPA	1	14/113	1.24 (0.34 – 4.46)	0.746
PR3-ANCA	1	35/90	0.85 (0.30 – 2.42)	0.756
MPO-ANCA	1	22/90	0.52 (0.12 – 2.38)	0.402
HLA-DR6				
GPA	4	301/6132	0.45 (0.33 – 0.62)	<0.001
MPA	1	30/5442	0.29 (0.09 – 0.92)	0.035
EGPA	2	26/5555	0.19 (0.04 – 0.95)	0.043
PR3-ANCA	1	35/90	0.28 (0.06 – 1.25)	0.096
MPO-ANCA	1	22/90	0.70 (0.20 – 2.51)	0.586
c-ANCA	1	16/472	1.63 (0.56 – 4.77)	0.371
HLA-DR7				
GPA	5	368/5802	0.92 (0.71 – 1.19)	0.508
MPA	1	15/113	0.70 (0.20 – 2.44)	0.575
EGPA	3	164/804	1.71 (1.24 – 2.37)	0.001
PR3-ANCA	1	32/91	1.00 (0.40 – 2.48)	0.991
HLA-DR8				
GPA	5	381/6206	0.89 (0.57 – 1.39)	0.610
MPA	1	51/5442	0.31 (0.04 – 2.21)	0.242
EGPA	2	114/5811	3.08 (1.75 – 5.41)	<0.001
PR3-ANCA	3	157/560	0.68 (0.33 – 1.42)	0.308
MPO-ANCA	2	69/469	1.70 (0.80 – 3.60)	0.170
c-ANCA	1	16/472	1.63 (0.66 – 4.05)	0.291
HLA-DR9				

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
GPA	6	402/6369	0.90 (0.58 – 1.39)	0.623
MPA	3	218/578	1.14 (0.83 – 1.56)	0.423
EGPA	3	164/832	1.07 (0.33 – 3.42)	0.915
PR3-ANCA	2	122/470	0.47 (0.09 – 2.58)	0.383
MPO-ANCA	3	175/1116	1.83 (1.29 – 2.60)	0.001
c-ANCA	1	16/472	3.03 (1.40 – 6.56)	0.005
*HLA-DRB1*0401*				
GPA	1	45/200	0.49 (0.06 – 3.90)	0.499
MPA	2	157/465	1.42 (0.60 – 3.41)	0.426
MPO-ANCA	1	64/265	2.10 (0.52 – 8.50)	0.300
*HLA-DRB1*0403*				
GPA	1	45/200	0.26 (0.02 – 4.46)	0.349
MPA	2	157/465	0.48 (0.14 – 1.59)	0.227
MPO-ANCA	1	64/265	0.95 (0.27 – 3.40)	0.943
*HLA-DRB1*0405*				
GPA	1	45/200	0.15 (0.01 – 2.49)	0.184
MPA	2	157/465	0.95 (0.56 – 1.62)	0.862
MPO-ANCA	1	64/265	0.61 (0.30 – 1.22)	0.159
*HLA-DRB1*0406*				
GPA	1	45/200	2.28 (0.67 – 7.74)	0.187
MPA	2	157/465	1.31 (0.62 – 2.78)	0.483
MPO-ANCA	1	64/265	0.65 (0.19 – 2.22)	0.487
*HLA-DRB1*0407*				
GPA	1	45/200	1.47 (0.06 – 36.42)	0.813
MPA	2	157/465	1.95 (0.54 – 6.99)	0.306
MPO-ANCA	1	64/265	2.82 (0.78 – 10.14)	0.113
*HLA-DRB1*0410*				
GPA	1	45/200	1.47 (0.06 – 36.42)	0.813
MPA	2	157/465	1.53 (0.35 – 6.64)	0.569
MPO-ANCA	1	64/265	1.67 (0.32 – 8.69)	0.544
*HLA-DRB1*0802*				
GPA	1	45/200	0.88 (0.04 – 18.50)	0.935
MPA	2	157/465	0.99 (0.35 – 2.79)	0.984
MPO-ANCA	1	64/265	1.16 (0.42 – 3.18)	0.778
*HLA-DRB1*0803*				

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
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
*HLA-DRB1*10*				
GPA	2	83/142	2.61 (0.45 – 15.24)	0.286
EGPA	1	102/369	0.40 (0.02 – 7.44)	0.538
PR3-ANCA	2	122/470	0.59 (0.13 – 2.65)	0.487
MPO-ANCA	1	47/379	1.48 (0.32 – 6.76)	0.616
*HLA-DRB1*11*				
GPA	2	83/142	0.97 (0.49 – 1.94)	0.932
EGPA	1	102/369	0.88 (0.53 – 1.48)	0.632
PR3-ANCA	2	122/470	0.97 (0.58 – 1.62)	0.908
MPO-ANCA	1	47/379	1.10 (0.51 – 2.38)	0.805
*HLA-DRB1*1101*				
GPA	1	45/200	0.16 (0.02 – 1.21)	0.076
MPA	2	223/465	2.57 (1.56 – 4.23)	<0.001
MPO-ANCA	1	116/265	2.79 (0.84 – 9.23)	0.093
*HLA-DRB1*12*				
GPA	2	83/142	4.06 (1.27 – 12.99)	0.018
EGPA	1	102/369	0.57 (0.17 – 1.93)	0.362
PR3-ANCA	2	122/470	1.01 (0.36 – 2.81)	0.983
MPO-ANCA	1	47/379	1.16 (0.26 – 5.16)	0.850
*HLA-DRB1*1201*				
GPA	1	45/200	0.15 (0.01 – 2.49)	0.184
MPA	2	157/465	0.51 (0.21 – 1.26)	0.146
MPO-ANCA	1	64/265	0.21 (0.03 – 1.60)	0.132
*HLA-DRB1*1202*				
GPA	1	45/200	2.92 (1.37 – 6.23)	0.005
MPA	2	157/465	1.07 (0.55 – 2.09)	0.838
PR3-ANCA	1	19/200	1.63 (0.46 – 5.75)	0.449
MPO-ANCA	2	89/465	1.00 (0.38 – 2.61)	1.000
*HLA-DRB1*13*				
GPA	2	83/142	0.61 (0.34 – 1.12)	0.111
EGPA	2	150/691	0.40 (0.24 – 0.68)	0.001
PR3-ANCA	1	32/91	0.56 (0.20 – 1.53)	0.257

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
*HLA-DRB1*1302*				
GPA	1	45/200	0.89 (0.19 – 4.12)	0.878
MPA	2	157/465	0.46 (0.20 – 1.02)	0.055
MPO-ANCA	1	64/265	0.54 (0.24 – 1.23)	0.142
*HLA-DRB1*14*				
GPA	2	83/142	1.26 (0.40 – 4.01)	0.698
EGPA	1	102/341	1.83 (0.72 – 4.65)	0.205
PR3-ANCA	2	122/470	2.00 (0.87 – 4.56)	0.101
MPO-ANCA	1	47/379	2.04 (0.43 – 9.74)	0.372
*HLA-DRB1*1403*				
GPA	1	45/200	2.24 (0.20 – 24.93)	0.513
MPA	2	157/465	0.81 (0.21 – 3.19)	0.767
MPO-ANCA	1	64/265	1.25 (0.34 – 4.60)	0.739
*HLA-DRB1*1405*				
GPA	1	45/200	1.51 (0.53 – 4.27)	0.437
MPA	2	157/465	0.45 (0.18 – 1.15)	0.096
MPO-ANCA	1	64/265	0.11 (0.01 – 1.91)	0.131
*HLA-DRB1*15*				
GPA	2	83/142	0.97 (0.57 – 1.65)	0.921
PR3-ANCA	2	131/582	2.82 (2.00 – 3.96)	<0.001
MPO-ANCA	1	51/491	0.80 (0.37 – 1.73)	0.566
*HLA-DRB1*1501*				
GPA	1	45/200	1.70 (0.98 – 2.94)	0.059
MPA	2	157/465	1.65 (1.14 – 2.38)	0.007
PR3-ANCA	1	19/200	0.98 (0.40 – 2.45)	0.973
MPO-ANCA	2	89/465	2.03 (1.26 – 3.29)	0.004
*HLA-DRB1*1502*				
GPA	1	45/200	0.80 (0.18 – 3.69)	0.779
MPA	2	157/465	0.60 (0.30 – 1.21)	0.154
MPO-ANCA	1	64/265	0.67 (0.32 – 1.39)	0.279
*HLA-DRB1*16*				
GPA	2	83/142	0.23 (0.03 – 1.85)	0.166
PR3-ANCA	2	131/582	1.00 (0.29 – 3.41)	0.996
MPO-ANCA	1	51/491	3.55 (1.02 – 12.38)	0.047
*HLA-DRB1*1602*				

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
GPA	1	45/200	0.40 (0.02 – 7.25)	0.533
MPA	2	157/465	0.23 (0.03 – 1.72)	0.151
MPO-ANCA	1	64/265	0.24 (0.01 – 4.17)	0.327
HLA-DRB3				
GPA	1	51/51	1.41 (0.76 – 2.60)	0.276
EGPA	2	150/691	0.58 (0.45 – 0.76)	<0.001
HLA-DRB4				
GPA	1	51/51	0.89 (0.46 – 1.72)	0.738
EGPA	2	150/691	2.06 (1.57 – 2.69)	<0.001
*IL-1*β (A2)				
GPA	3	714/5491	1.07 (0.93 – 1.22)	0.336
MPA	1	262/5259	0.89 (0.72 – 1.10)	0.286
PR3-ANCA	2	557/5455	1.01 (0.87 – 1.17)	0.930
MPO-ANCA	2	294/5455	1.00 (0.82 – 1.21)	0.971
*IL1RN**1				
GPA	1	61/200	0.88 (0.57 – 1.37)	0.573
MPA	1	105/200	1.21 (0.83 – 1.77)	0.325
PR3-ANCA	2	122/434	1.12 (0.82 – 1.54)	0.476
MPO-ANCA	2	92/434	0.98 (0.69 – 1.40)	0.916
*IL1RN**2				
GPA	1	61/200	1.22 (0.78 – 1.92)	0.380
MPA	1	105/200	0.77 (0.52 – 1.16)	0.212
PR3-ANCA	2	122/434	0.95 (0.68 – 1.31)	0.748
MPO-ANCA	2	92/434	1.02 (0.71 – 1.47)	0.921
*IL1RN**3				
GPA	1	61/200	0.72 (0.15 – 3.40)	0.682
MPA	1	105/200	1.50 (0.55 – 4.08)	0.429
PR3-ANCA	2	122/434	0.61 (0.21 – 1.76)	0.358
MPO-ANCA	2	92/434	0.71 (0.22 – 2.29)	0.571
*IL1RN**4				
GPA	1	61/200	0.65 (0.03 – 13.64)	0.782
MPA	1	105/200	1.91 (0.27 – 13.68)	0.518
PR3-ANCA	2	122/434	0.95 (0.11 – 8.63)	0.964
MPO-ANCA	2	92/434	3.08 (0.58 – 16.42)	0.188
*IL1RN**5				

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

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

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPA	2	258/6310	1.42 (1.06 – 1.89)	0.018
EGPA	1	99/945	0.52 (0.21 – 1.29)	0.158
PR3-ANCA	2	419/6310	1.42 (1.14 – 1.77)	0.002
MPO-ANCA	2	183/6310	1.47 (1.08 – 2.00)	0.014
RING1/RXRB rs213213 (A)				
GPA	3	1132/7238	1.91 (1.73 – 2.10)	<0.001
MPA	1	156/5366	1.15 (0.90 – 1.45)	0.264
PR3-ANCA	1	326/5366	2.06 (1.75 – 2.41)	<0.001
MPO-ANCA	1	167/5366	1.05 (0.83 – 1.32)	0.687
RXRB rs6531 (C)				
GPA	3	1211/6955	1.70 (1.55 – 1.86)	<0.001
MPA	1	262/5251	1.38 (1.15 – 1.66)	0.001
PR3-ANCA	1	478/5251	2.19 (1.92 – 2.51)	<0.001
MPO-ANCA	1	264/5251	1.21 (1.00 – 1.46)	0.046
ANCA negative	1	36/201	1.02 (0.59 – 1.74)	0.948
RXRB rs9277935 (T)				
GPA	3	1135/7233	0.37 (0.31 – 0.43)	<0.001
MPA	1	156/5350	0.93 (0.70 – 1.24)	0.629
PR3-ANCA	1	326/5350	0.24 (0.17 – 0.33)	<0.001
MPO-ANCA	1	167/5350	1.18 (0.92 – 1.53)	0.193
SERPINA1 S allele				
GPA	2	484/1079	1.72 (1.12 – 2.66)	0.014
c-ANCA	3	145/3836	1.92 (1.12 – 3.29)	0.017
SERPINA1 Z allele				
GPA	4	972/2636	2.40 (1.73 - 3.33)	<0.001
MPA	1	143/805	1.60 (0.76 - 3.39)	0.218
PR3-ANCA	1	322/805	2.58 (1.57 - 4.25)	<0.001
MPO-ANCA	1	166/805	2.01 (1.04 - 3.87)	0.037
c-ANCA	5	280/4788	3.53 (2.28 – 5.49)	<0.001
p-ANCA	2	78/2510	3.13 (1.21 – 8.13)	0.019
STAT4 rs7574865 (T)				
GPA	2	1288/6246	1.06 (0.94 – 1.20)	0.331
MPA	1	676/5366	1.12 (0.86 – 1.46)	0.392
PR3-ANCA	1	676/5366	1.06 (0.88 – 1.28)	0.547

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
MPO-ANCA	2	908/6076	1.24 (1.05 – 1.46)	0.009
TGF-β_1 rs1800471 (C)				
GPA	3	196/259	1.52 (0.93 – 2.48)	0.096
MPA	1	36/96	1.03 (0.35 – 2.99)	0.960
PR3-ANCA	1	32/91	1.86 (0.73 – 4.71)	0.193
*TNF*α rs1800629 (A)				
GPA	4	578/5691	1.15 (0.98 – 1.35)	0.098
MPA	1	156/5366	1.13 (0.95 – 1.35)	0.182
PR3-ANCA	2	357/5457	1.21 (0.93 – 1.57)	0.149
MPO-ANCA	1	167/5366	0.88 (0.66 – 1.17)	0.375
TNFRII 196R				
GPA	1	177/123	1.05 (0.70 – 1.57)	0.819
MPA	1	50/262	0.67 (0.31 – 1.45)	0.313
MPO-ANCA	1	50/262	0.67 (0.31 – 1.45)	0.313
TLR9 rs352162 (T)				
GPA	1	919/1898	1.20 (1.07 – 1.34)	0.001
MPA	1	153/1898	0.74 (0.58 – 0.95)	0.020
EGPA	1	217/1898	1.28 (1.05 – 1.57)	0.015
PR3-ANCA	1	NR/NR	1.30 (1.14 – 1.47)	<0.001
MPO-ANCA	1	NR/NR	0.79 (0.65 – 0.97)	0.028
ANCA negative	1	NR/NR	1.22 (0.99 – 1.50)	0.060
TLR9 rs352140 (T)				
GPA	1	919/1898	1.20 (1.07 – 1.35)	0.001
MPA	1	153/1898	0.71 (0.55 – 0.91)	0.006
EGPA	1	217/1898	1.17 (0.96 – 1.43)	0.129
PR3-ANCA	1	NR/NR	1.28 (1.12 – 1.45)	<0.001
MPO-ANCA	1	NR/NR	0.75 (0.62 – 0.91)	0.004
ANCA negative	1	NR/NR	1.19 (0.97 – 1.47)	0.097
TLR9 rs352139 (T)				
GPA	1	919/1898	1.18 (1.06 – 1.32)	0.003
MPA	1	153/1898	0.68 (0.52 – 0.87)	0.003
EGPA	1	217/1898	1.21 (0.99 – 1.47)	0.057
PR3-ANCA	1	NR/NR	1.23 (1.09 – 1.40)	0.001
MPO-ANCA	1	NR/NR	0.78 (0.63 – 0.96)	0.017
ANCA negative	1	NR/NR	1.20 (0.98 – 1.47)	0.086

Supplementary table 4. Results of the meta-analyses stratified by diagnostic and serologic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
TLR9 rs5743836 (G)				
GPA	1	919/1898	0.83 (0.70 – 0.99)	0.037
MPA	1	153/1898	1.78 (1.32 – 2.39)	<0.001
EGPA	1	217/1898	0.90 (0.68 – 1.21)	0.499
PR3-ANCA	1	NR/NR	0.83 (0.70 – 1.00)	0.045
MPO-ANCA	1	NR/NR	1.20 (0.91 – 1.58)	0.207
ANCA negative	1	NR/NR	0.99 (0.74 – 1.34)	0.970

Supplementary table 5. Results of the meta-analyses stratified by ethnic subgroups

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
CTLA-4 $(AT)_{86}$				
Asian	1	49/111	1.31 (0.76 – 2.25)	0.333
Caucasian	3	254/432	0.46 (0.36 – 0.58)	<0.001
CTLA-4 $(AT)_{102}$				
Asian	1	49/111	0.89 (0.47 – 1.68)	0.714
Caucasian	2	137/309	1.73 (0.87 – 3.44)	0.117
CTLA-4 $(AT)_{104}$				
Asian	1	49/111	1.15 (0.70 – 1.91)	0.578
Caucasian	2	137/309	1.24 (0.88 – 1.73)	0.215
CTLA-4 $(AT)_{106}$				
Asian	1	49/111	0.41 (0.14 – 1.22)	0.109
Caucasian	2	137/309	2.69 (1.28 – 5.63)	0.009
CTLA-4 $(AT)_{108}$				
Asian	1	49/111	0.82 (0.33 – 2.02)	0.670
Caucasian	2	137/309	0.92 (0.44 – 1.92)	0.831
CTLA-4 $(AT)_{110}$				
Asian	1	49/111	0.25 (0.01 – 4.62)	0.349
Caucasian	2	137/309	0.84 (0.37 – 1.91)	0.679
CTLA-4 $(AT)_{116}$				
Asian	1	49/111	0.75 (0.03 – 18.56)	0.860
Caucasian	2	137/309	0.80 (0.26 – 2.50)	0.705
CTLA-4 $(AT)_{118}$				
Asian	1	49/111	0.75 (0.08 – 7.33)	0.807
Caucasian	2	137/309	0.41 (0.12 – 1.39)	0.152

Supplementary table 5. Results of the meta-analyses stratified by ethnic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
CTLA-4 $(AT)_{122}$				
Asian	1	49/111	2.32 (0.57 – 9.45)	0.241
Caucasian	2	137/309	1.22 (0.27 – 5.49)	0.799
CTLA-4 $(AT)_{124}$				
Asian	1	49/111	2.28 (0.14 – 36.80)	0.562
Caucasian	2	137/309	1.94 (0.67 – 5.58)	0.222
CTLA-4 $(AT)_{126}$				
Asian	1	49/111	0.45 (0.05 – 3.88)	0.466
Caucasian	2	137/309	1.65 (0.63 – 4.32)	0.305
CTLA-4 $(AT)_{128}$				
Asian	1	49/111	6.98 (0.72 – 67.95)	0.094
Caucasian	2	137/309	0.72 (0.24 – 2.15)	0.560
FCGR2A rs1801274 (C)				
Asian	1	50/303	0.68 (0.37 – 1.24)	0.208
Caucasian	5	1126/5969	0.91 (0.82 – 1.00)	0.043
FCGR3A rs396991 (G)				
Asian	1	50/303	0.65 (0.39 – 1.07)	0.090
Caucasian	1	91/154	1.30 (0.89 – 1.91)	0.172
FCGR3B (NA1)				
Asian	1	50/303	1.29 (0.82 – 2.03)	0.267
Caucasian	3	865/667	0.93 (0.80 – 1.08)	0.343
HLA-A2				
Asian	1	16/472	0.90 (0.37 – 2.23)	0.826
Caucasian	4	427/7324	0.96 (0.81 – 1.13)	0.595
HLA-A11				
Asian	1	16/472	0.71 (0.17 – 3.03)	0.644
Caucasian	5	450/7635	1.01 (0.50 – 2.05)	0.978
HLA-A24				
Asian	1	16/472	0.75 (0.34 – 1.65)	0.476
Caucasian	2	92/751	1.16 (0.57 – 2.38)	0.683
HLA-A26				
Asian	1	16/472	2.36 (1.00 – 5.60)	0.051
Caucasian	3	115/1156	1.21 (0.58 – 2.55)	0.612
HLA-A31				
Asian	1	16/472	1.55 (0.46 – 5.24)	0.479
Caucasian	2	92/751	0.73 (0.21 – 2.52)	0.613

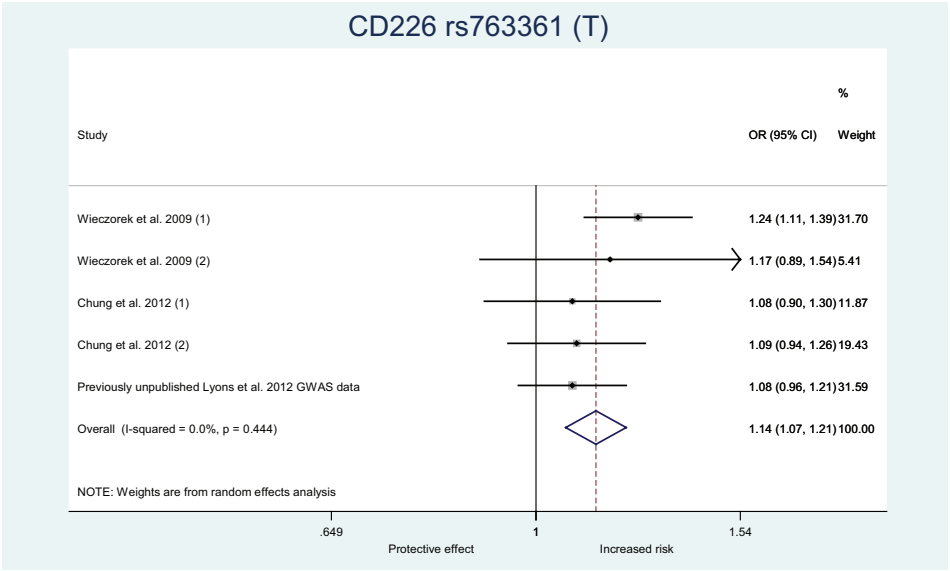
Supplementary table 5. Results of the meta-analyses stratified by ethnic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
HLA-A32				
Asian	1	16/472	2.07 (0.61 – 7.04)	0.246
Caucasian	2	92/751	1.41 (0.52 – 3.84)	0.500
HLA-B35				
Asian	1	16/472	0.80 (0.17 – 3.40)	0.757
Caucasian	3	396/6623	0.78 (0.58 – 1.06)	0.115
HLA-B39				
Asian	1	16/472	0.86 (0.11 – 6.51)	0.887
Caucasian	1	51/51	0.33 (0.01 – 8.20)	0.499
HLA-B44				
Asian	1	16/472	2.50 (0.85 – 7.40)	0.098
Caucasian	2	92/751	1.41(0.85 – 2.35)	0.188
HLA-B51				
Asian	1	16/472	1.87 (0.64 – 5.49)	0.255
Caucasian	1	51/51	0.61 (0.19 – 1.92)	0.394
HLA-B55				
Asian	1	16/472	7.35 (2.34 – 23.14)	0.001
Caucasian	1	51/51	0.07 (0.00 – 1.30)	0.075
HLA-B60				
Asian	1	16/472	1.19 (0.28 – 5.13)	0.814
Caucasian	1	41/700	3.51 (0.99 – 12.36)	0.051
HLA-B62				
Asian	1	16/472	1.71 (0.58 – 4.99)	0.331
Caucasian	1	41/700	2.38 (0.70 – 8.12)	0.166
HLA-Cw1				
Asian	1	16/472	1.45 (0.58 – 3.58)	0.426
Caucasian	1	52/51	0.98 (0.24 – 4.03)	0.978
HLA-Cw3				
Asian	1	16/472	1.40 (0.66 – 3.01)	0.384
Caucasian	1	52/51	1.32 (0.62 – 2.81)	0.479
HLA-Cw7				
Asian	1	16/472	0.50 (0.12 – 2.10)	0.340
Caucasian	1	52/51	1.10 (0.62 – 1.96)	0.735
*HLA-DPB1*0201*				
Asian	1	50/77	1.38 (0.75 – 2.52)	0.298
Caucasian	3	385/827	0.76 (0.56 – 1.03)	0.073

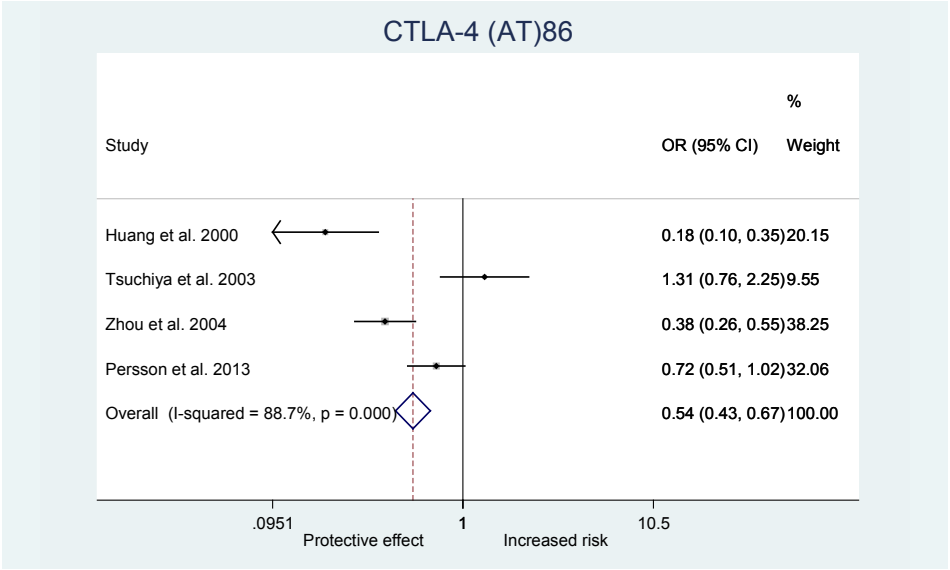
Supplementary table 5. Results of the meta-analyses stratified by ethnic subgroups (Continued)

Variant by gene	Publications (n)	Cases (n) / Controls (n)	OR (95% CI)	P value for meta-analysis
*HLA-DQB1**0303				
Asian	1	50/77	2.11 (1.14 – 3.90)	0.018
Caucasian	2	126/141	1.35 (0.55 – 3.33)	0.515
HLA-DR1				
Asian	1	64/265	1.12 (0.48 – 2.64)	0.793
Caucasian	9	945/6840	0.91 (0.61 – 1.36)	0.651
HLA-DR2				
Asian	1	16/472	0.33 (0.08 – 1.38)	0.128
Caucasian	4	471/5750	1.06 (0.87 – 1.29)	0.565
HLA-DR4				
Asian	1	16/472	0.72 (0.27 – 1.88)	0.498
Caucasian	10	882/7262	1.23 (0.97 – 1.57)	0.088
HLA-DR6				
Asian	1	16/472	1.63 (0.56 – 4.77)	0.371
Caucasian	4	471/5750	0.43 (0.30 – 0.61)	<0.001
HLA-DR8				
Asian	1	16/472	1.63 (0.66 – 4.05)	0.291
Caucasian	8	597/1483	1.05 (0.75 – 1.49)	0.768
HLA-DR9				
Asian	4	296/1409	1.67 (0.83 – 3.34)	0.148
Caucasian	7	510/1443	0.63 (0.34 – 1.19)	0.152
IRF5 rs10954213 (G)				
Asian	1	232/710	1.28 (1.04 – 1.58)	0.022
Caucasian	2	1303/6267	0.69 (0.63 – 0.76)	<0.001
STAT4 rs7574865 (T)				
Asian	1	232/710	1.10 (0.89 – 1.37)	0.388
Caucasian	2	1288/6246	1.11 (1.00 – 1.24)	0.044
TNFRII 196R				
Asian	1	50/262	0.67 (0.31 – 1.45)	0.313
Caucasian	1	117/123	1.05 (0.70 – 1.57)	0.819

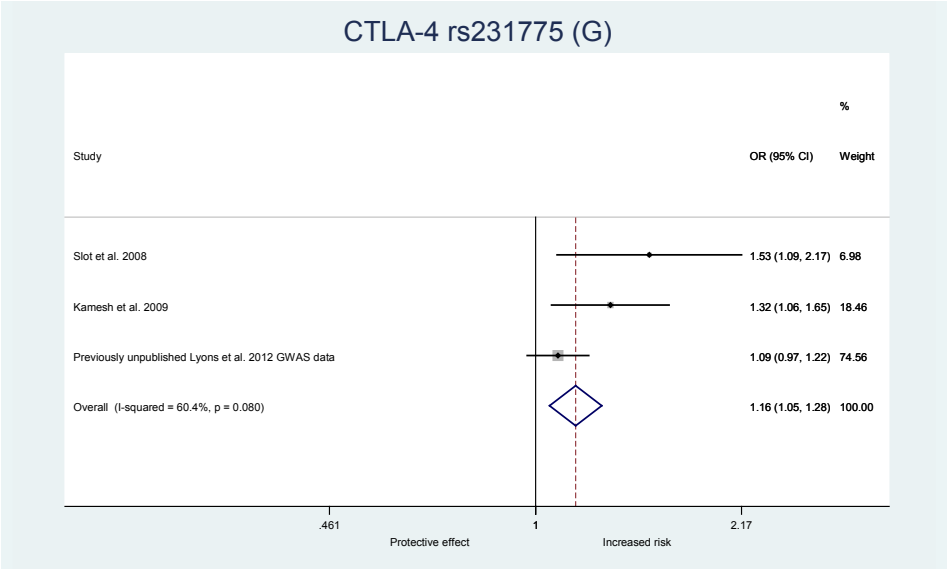
Supplementary figure 1. Forest plots



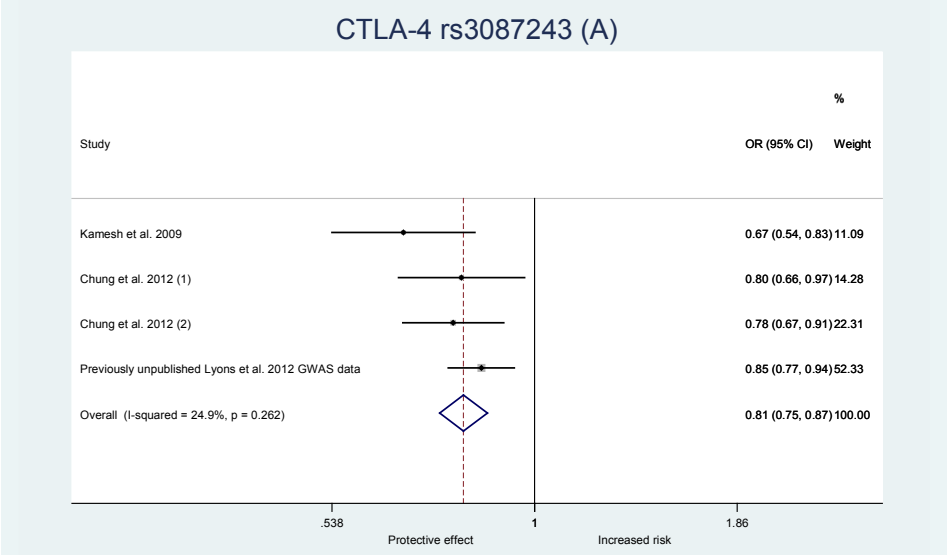
CD226 rs763361 (T) forest plot. Harbold test: N/A, Egger test: p=0.792.
References: [1]**, [2]**, [3]



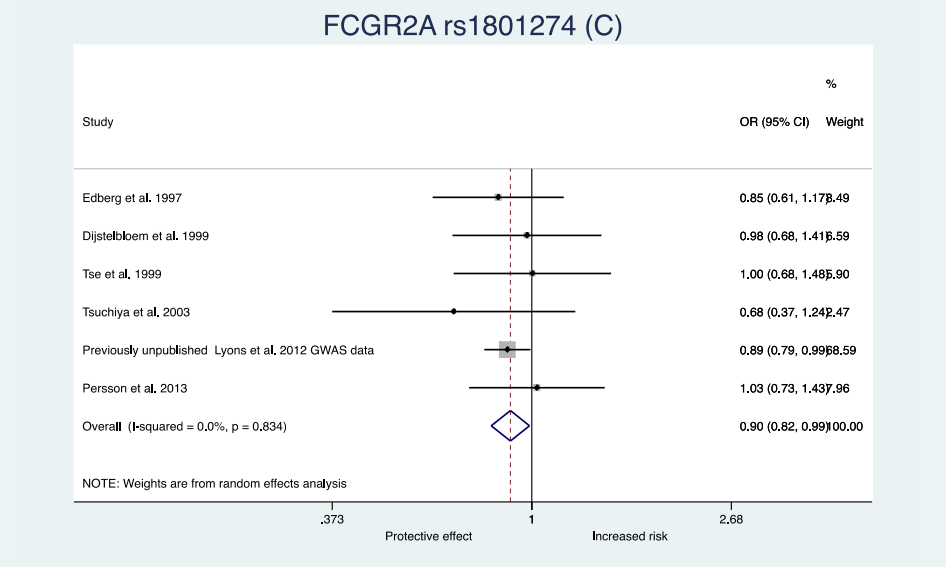
CTLA-4 $(AT)_{86}$ forest plot. Harbold test: p=0.946, Egger test: p=0.788.
References: [4], [5], [6], [7]



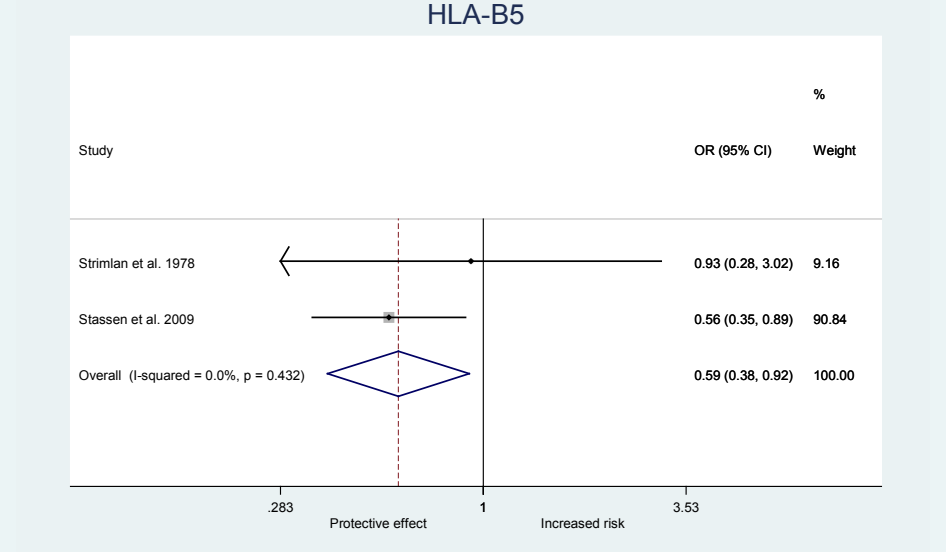
CTLA-4 rs231775 (G) forest plot. Harbold test: p=0.080, Egger test: p=0.081.
References: [8], [9], [3]



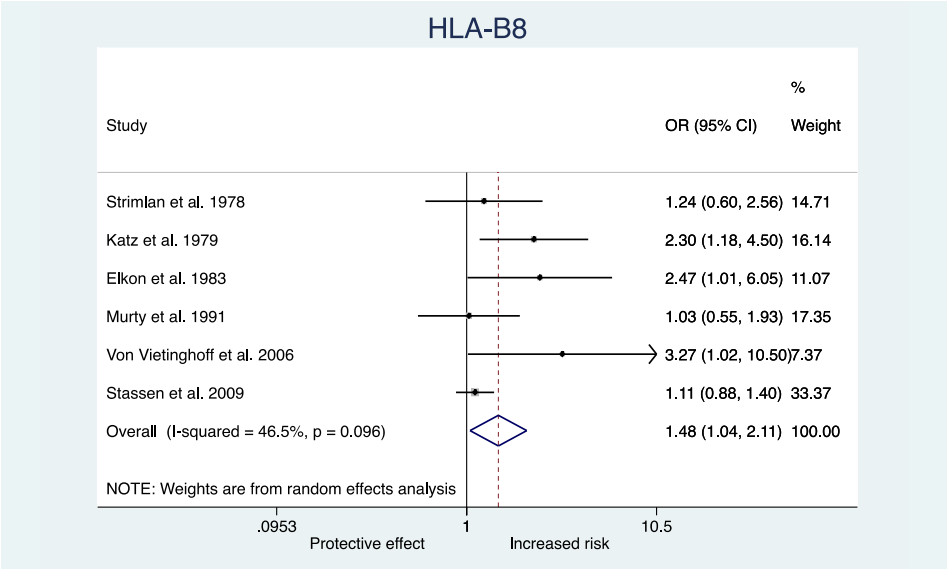
CTLA-4 rs3087243 (A) forest plot. Harbold test: N/A, Egger test: p=0.122.
References: [9], [2]**, [3]



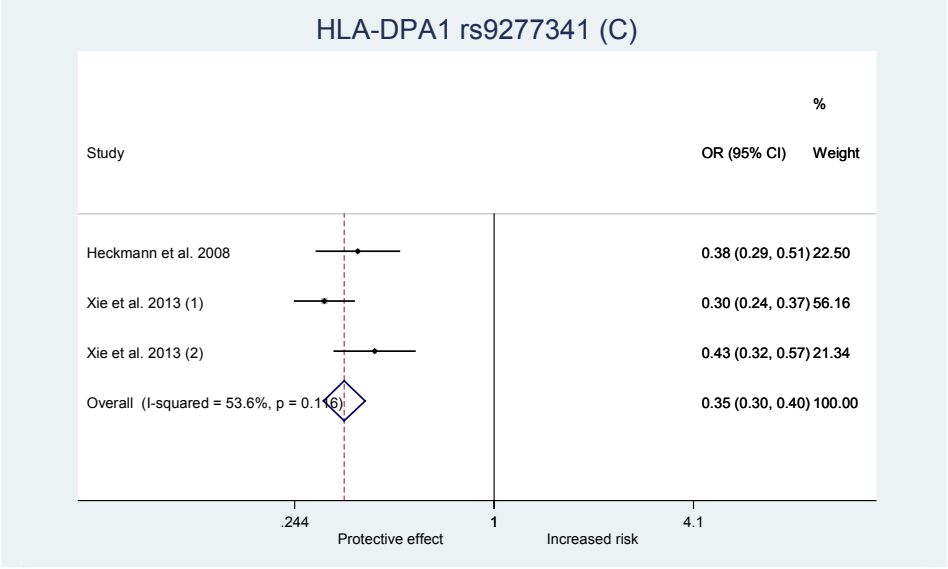
FCGR2A rs1801274 (C) forest plot. Harbold test: p=0.788, Egger test: p=0.829.
References: [11], [12], [13], [5], [7], [3]



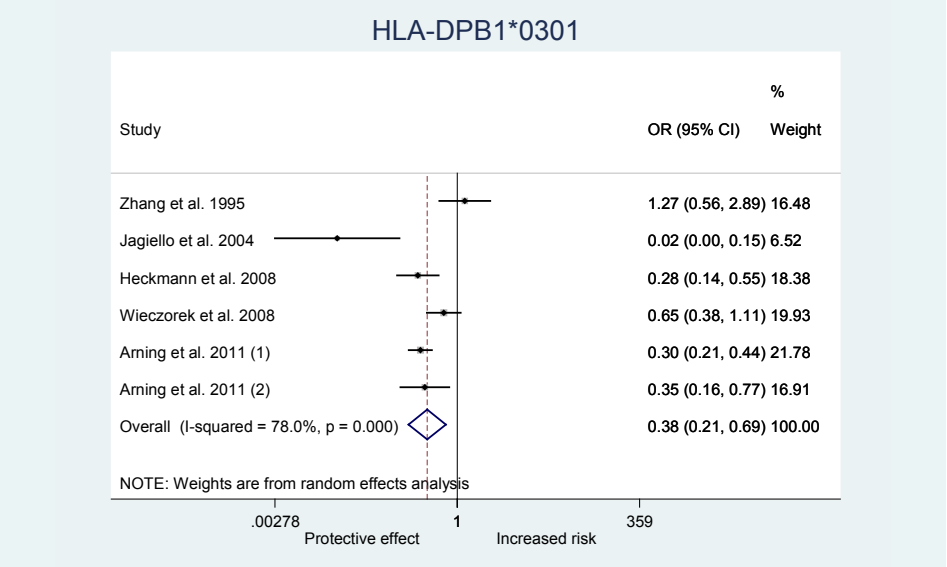
HLA-B5 forest plot. Harbold test: N/A, Egger test: N/A.
References: [16], [19]



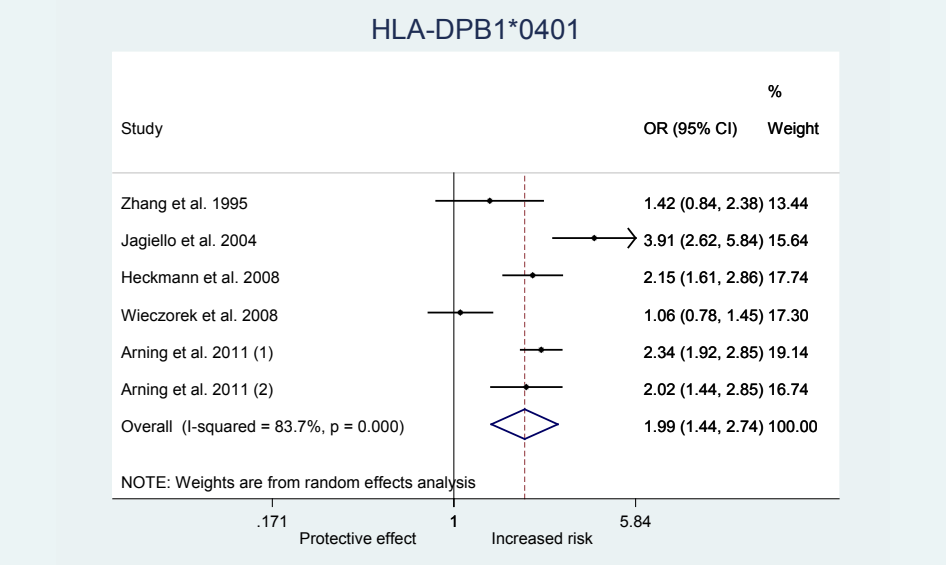
HLA-B8 forest plot. Harbold test: p=0.063, Egger test: p=0.077.
References: [16], [21], [23], [17], [18], [19]



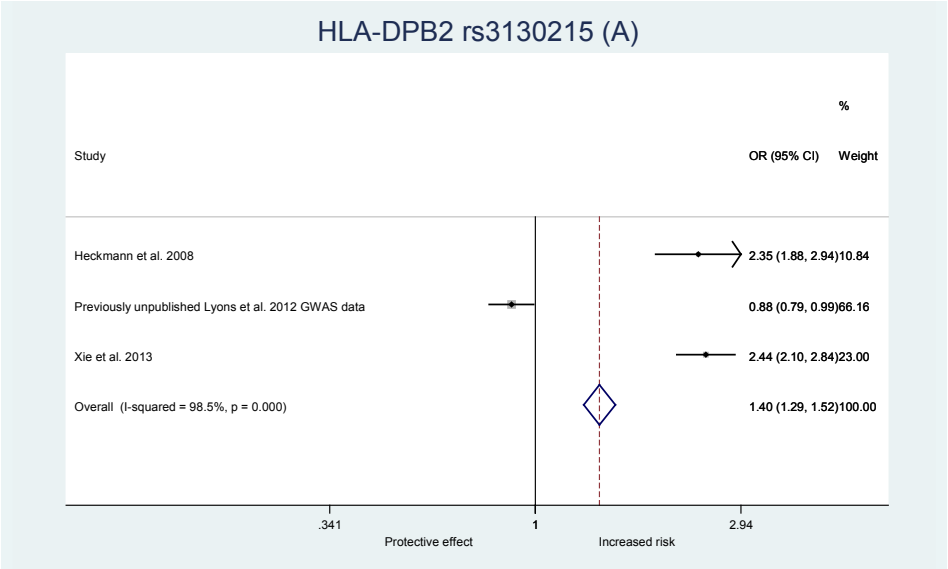
HLA-DPA1 rs9277341 (C) forest plot. Harbold test: p=0.215, Egger test: p=0.219.
References: [24], [25]**



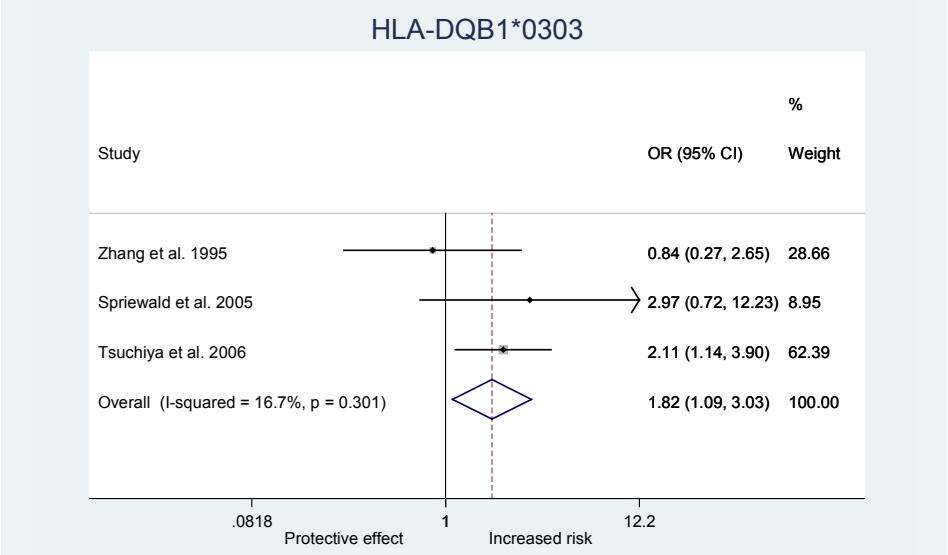
*HLA-DPB1*0301* forest plot. Harbold test: p=0.938, Egger test: p=0.744.
References: [26], [27], [24], [29], [30]**



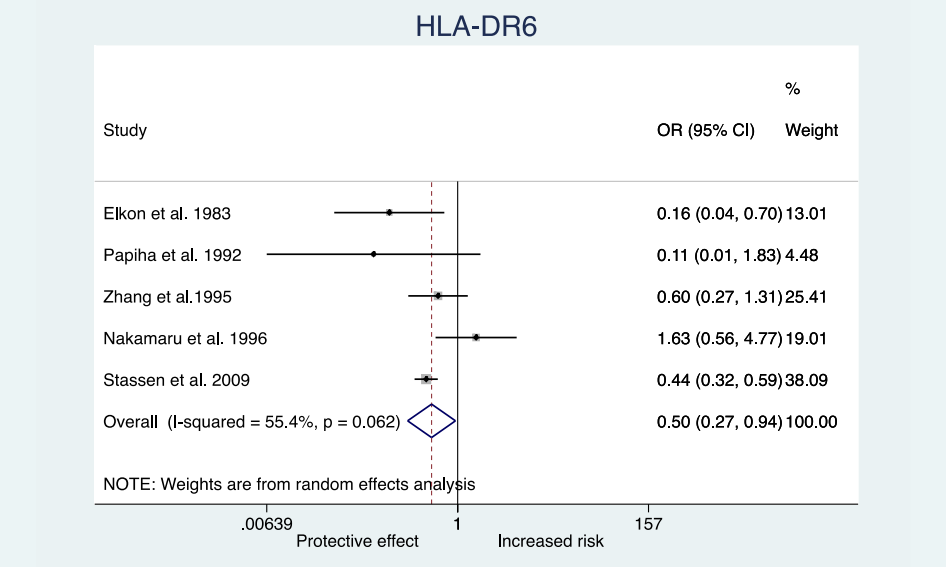
*HLA-DPB1*0401* forest plot. Harbold test: p=0.738, Egger test: p=0.759.
References: [26], [27], [24], [29], [30]**



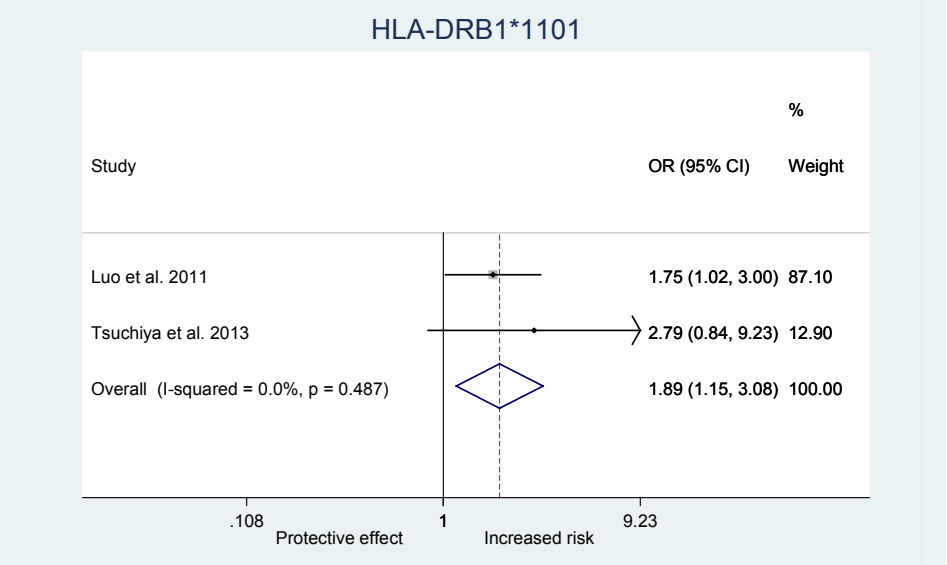
HLA-DPB2 rs3130215 (A) forest plot. Harbold test: p=0.446, Egger test: p=0.431.
References: [24], [3], [25]



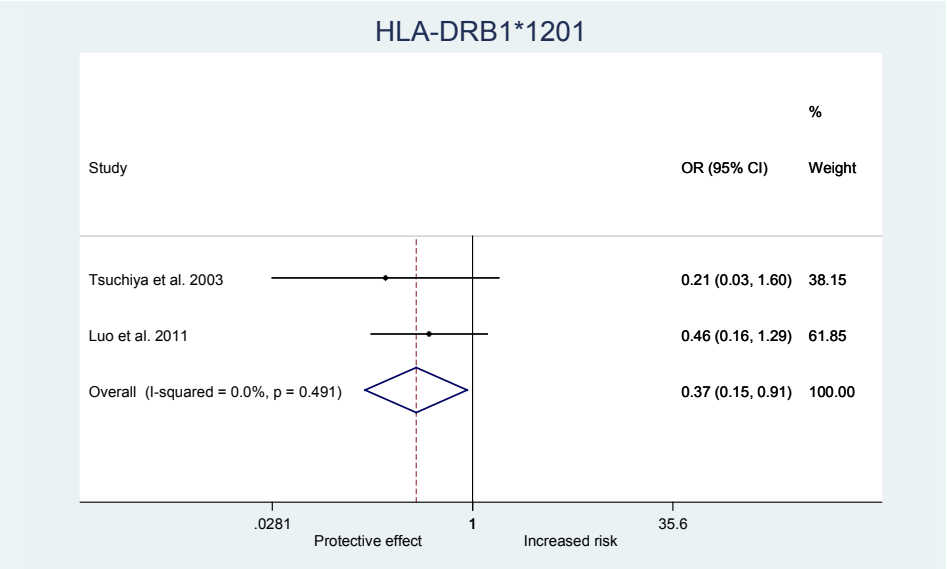
*HLA-DQB1*0303* forest plot. Harbold test: p=0.916, Egger test: p=0.834.
References: [26], [31], [28]



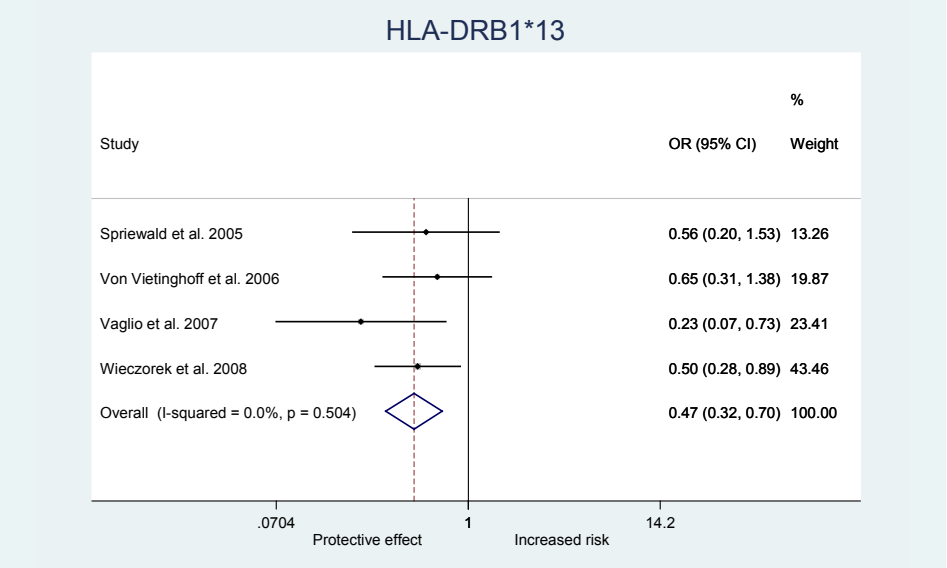
HLA-DR6 forest plot. Harbold test: p=0.997, Egger test: p=0.989.
References: [23], [32], [26], [20], [19]



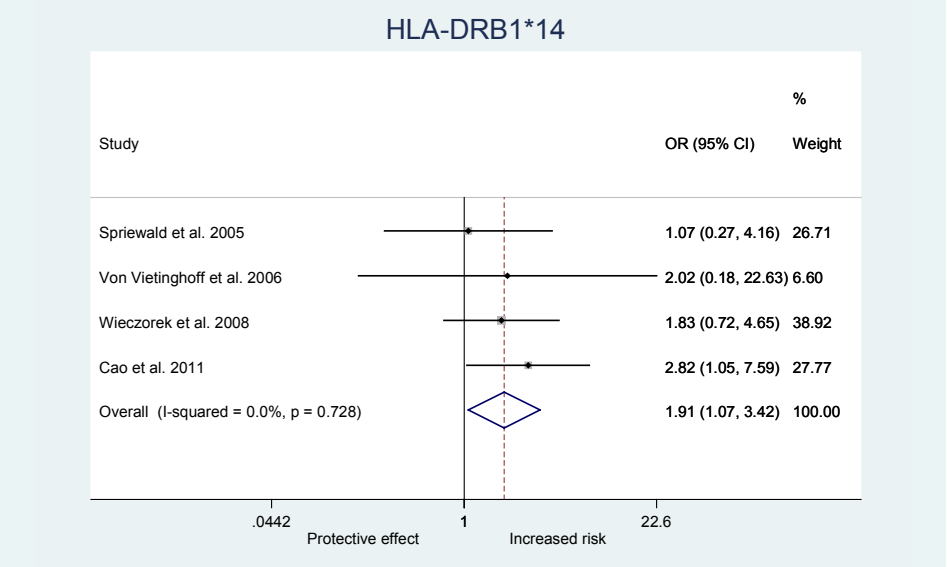
*HLA-DRB1*1101* forest plot. Harbold test: N/A, Egger test: N/A.
References: [34], [37]



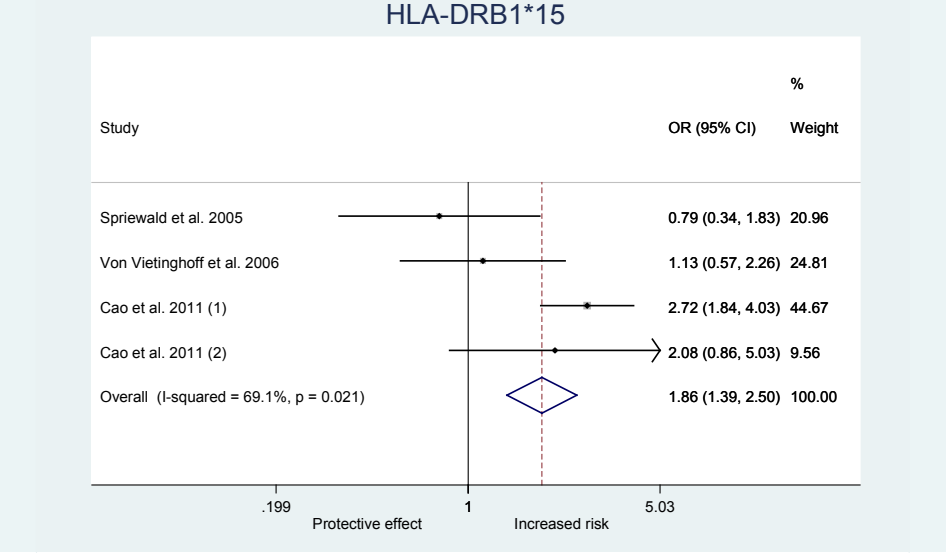
*HLA-DRB1*1201* forest plot. Harbold test: N/A, Egger test: N/A.
References: [5], [34]



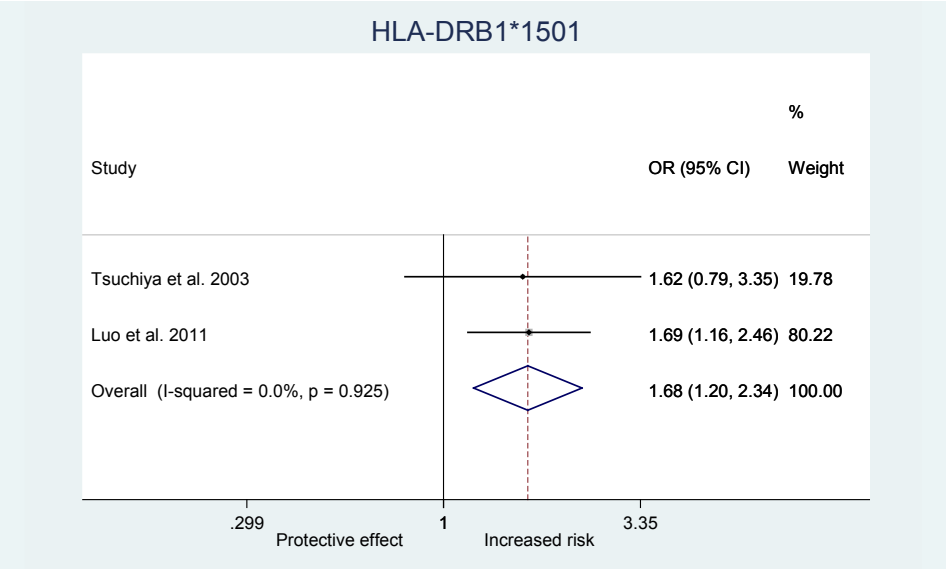
*HLA-DRB1*13* forest plot. Harbold test: p=0.884, Egger test: p=0.467.
References: [31], [18], [35], [29]



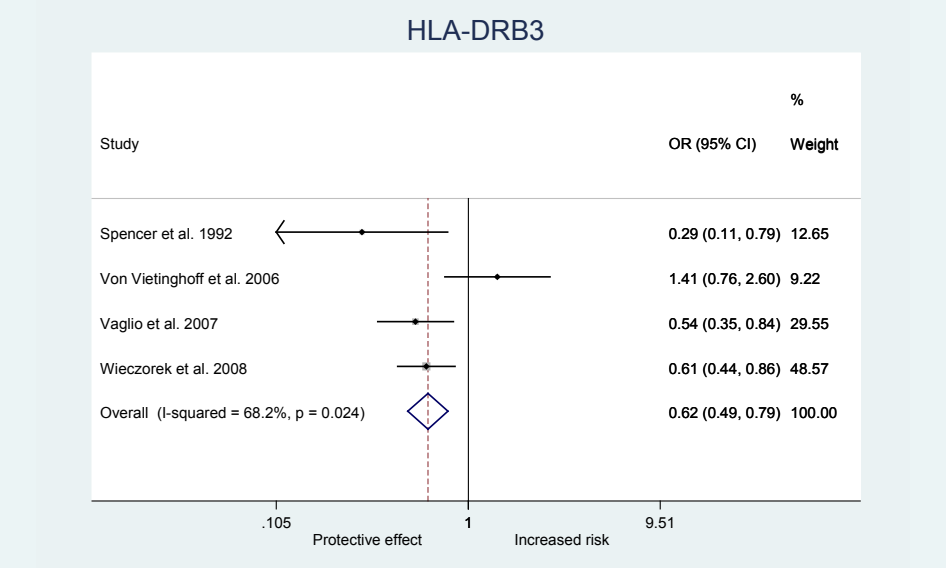
*HLA-DRB1*14* forest plot. Harbold test: p=0.700, Egger test: p=0.706.
References: [31], [18], [29], [33]



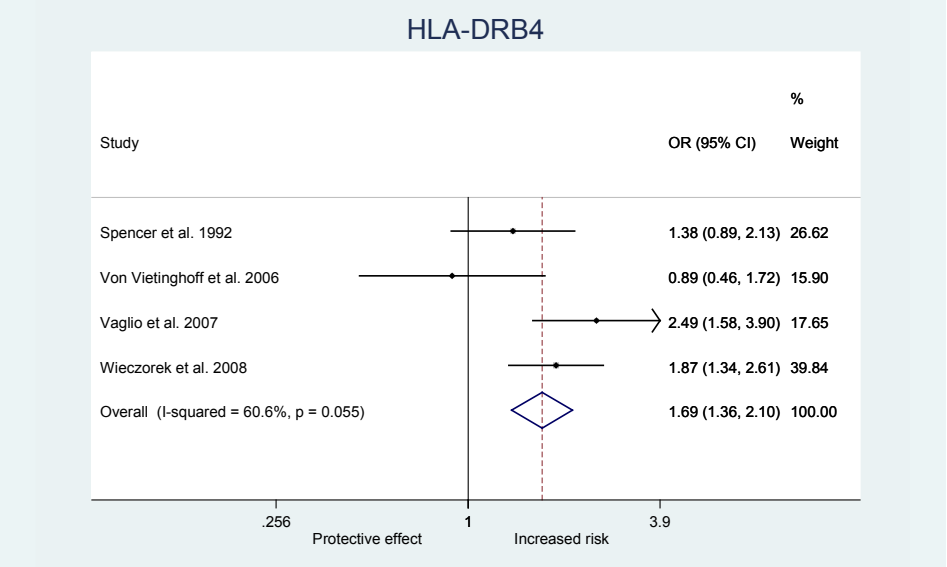
*HLA-DRB1*15* forest plot. Harbold test: p=0.347, Egger test: p=0.214.
References: [31], [18], [33]**



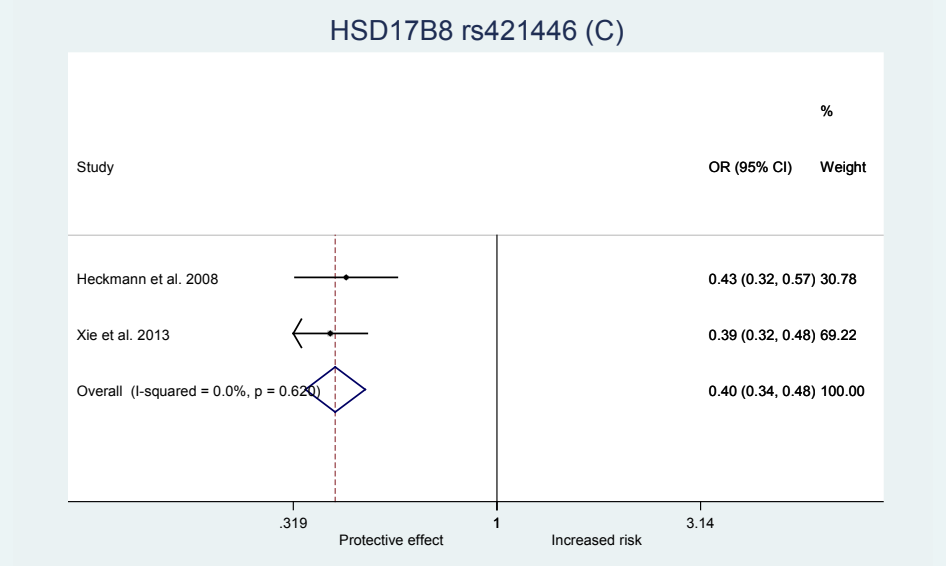
*HLA-DRB1*1501* forest plot. Harbold test: N/A, Egger test: N/A.
References: [5], [34]



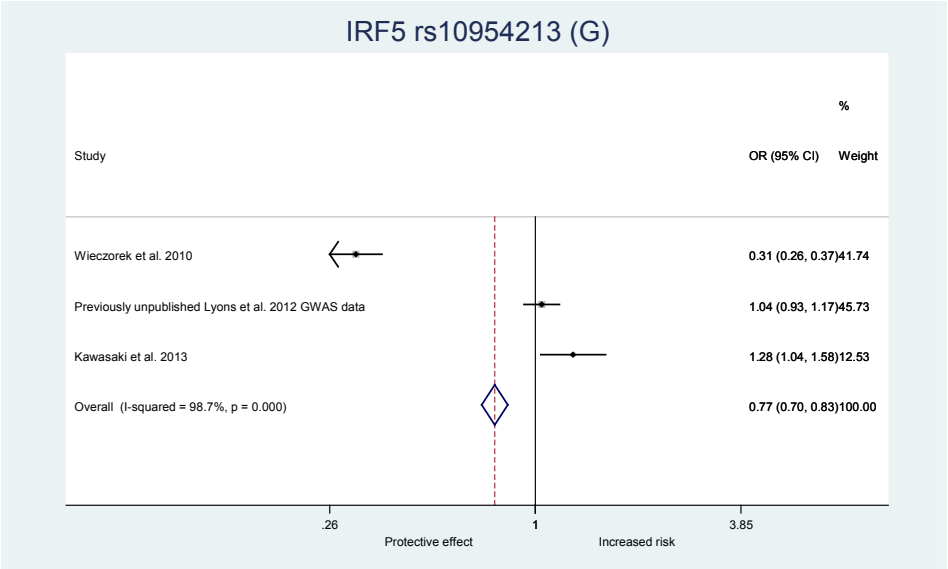
HLA-DRB3 forest plot. Harbold test: p=0.689, Egger test: p=0.958.
References: [38], [18], [35], [29]



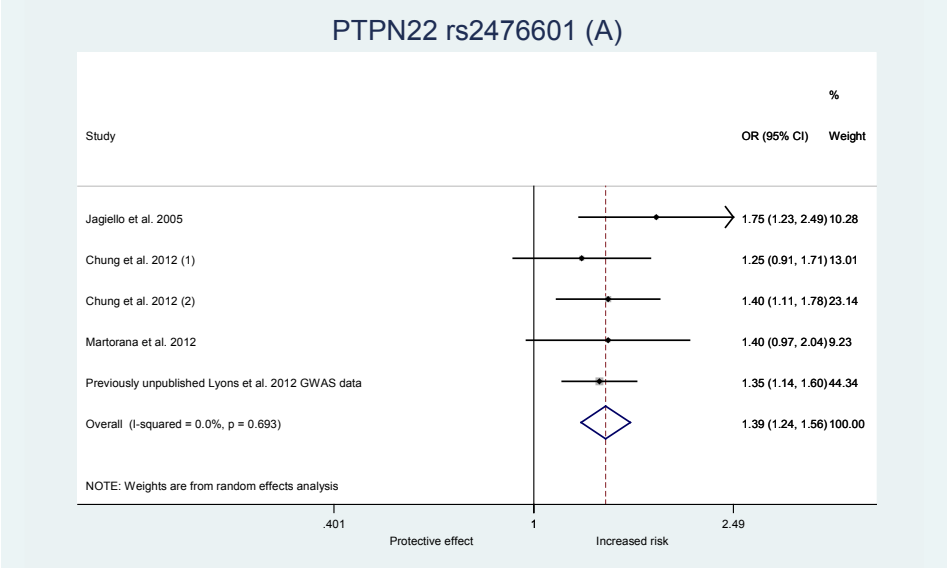
HLA-DRB4 forest plot. Harbold test: p=0.533, Egger test: p=0.388.
References: [38], [18], [35], [29]



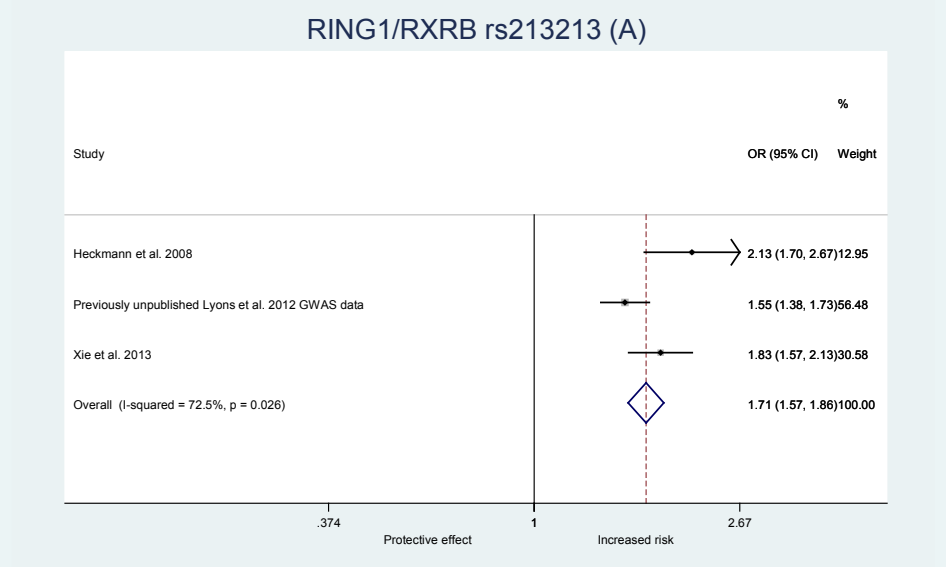
HSD17B8 rs421446 (C) forest plot. Harbold test: N/A, Egger test: N/A.
References: [24], [25]



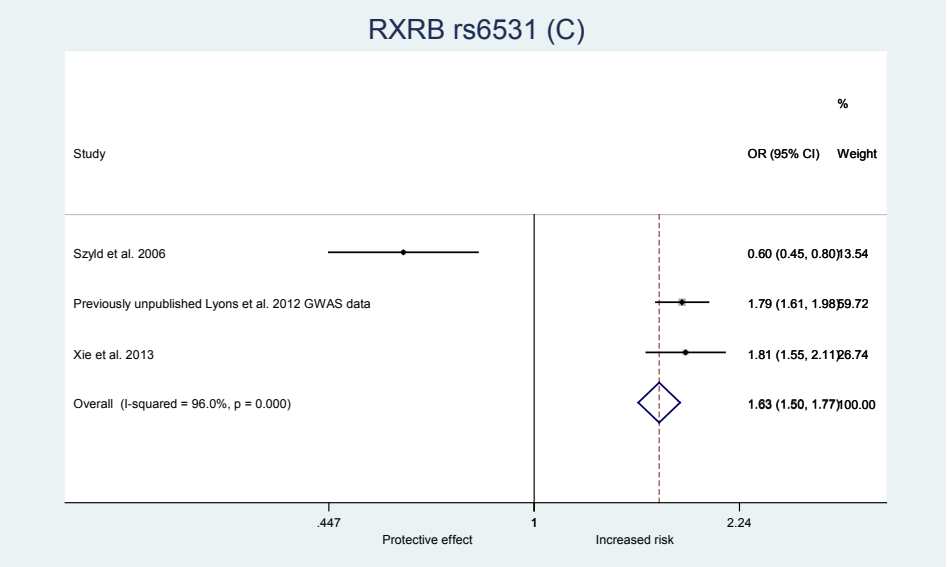
IRF5 rs10954213 (G) forest plot. Harbold test: p=0.948, Egger test: p=0.833.
References: [44], [3], [45]



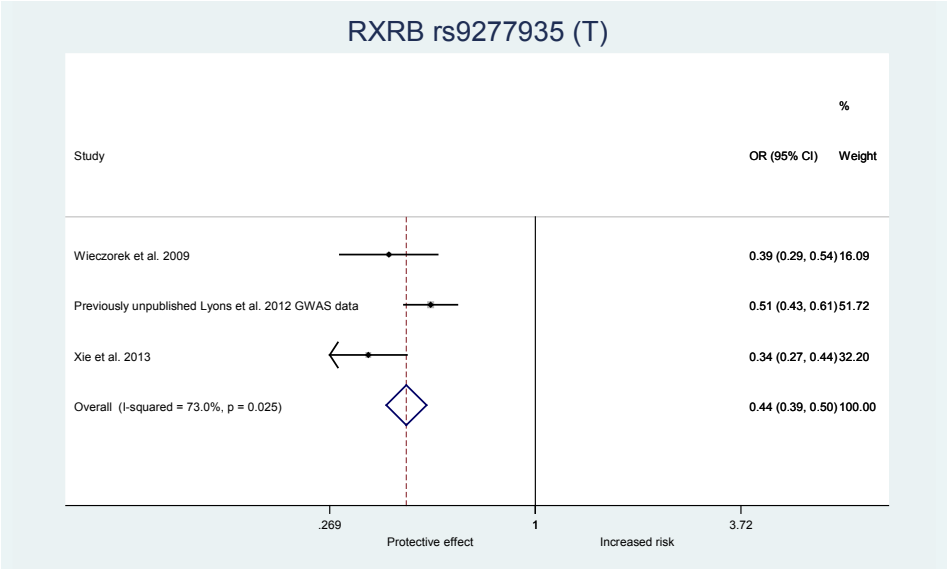
PTPN22 rs2476601 (A) forest plot. Harbold test: N/A, Egger test: p=0.500.
References: [50], [2**], [51], [3]



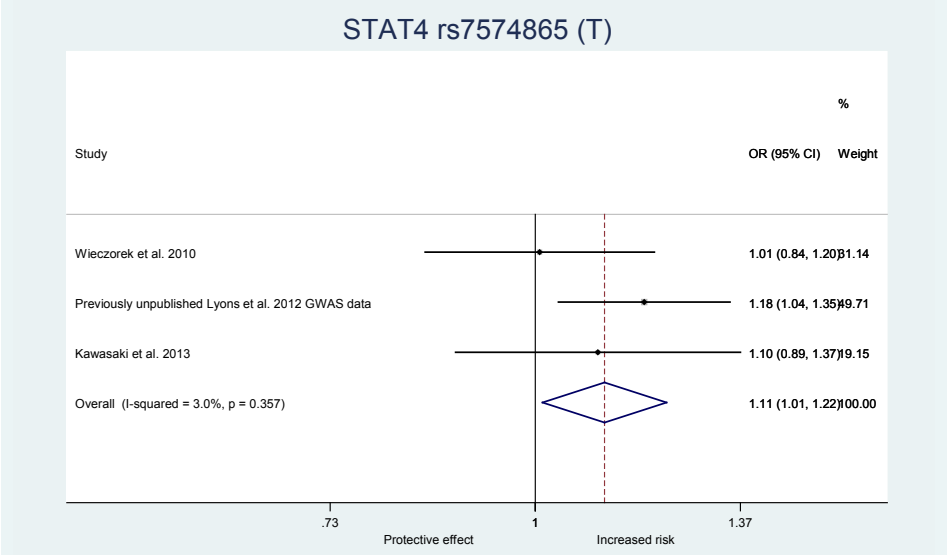
RING1/RXRB rs213213 (A) forest plot. Harbold test: p=0.187, Egger test: p=0.169.
References: [24], [3], [25]



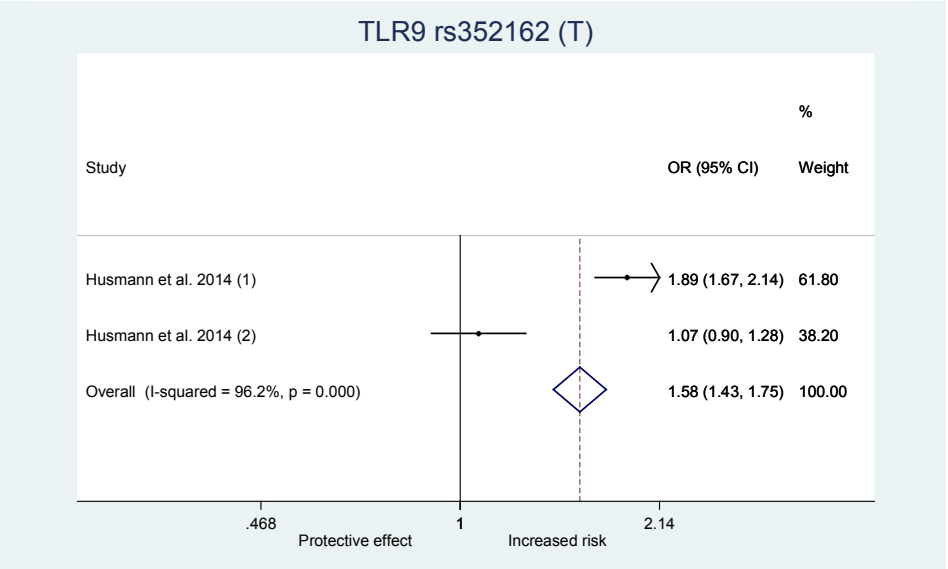
RXRB rs6531 (C) forest plot. Harbold test: p=0.292, Egger test: p=0.301.
References: [52], [3], [25]



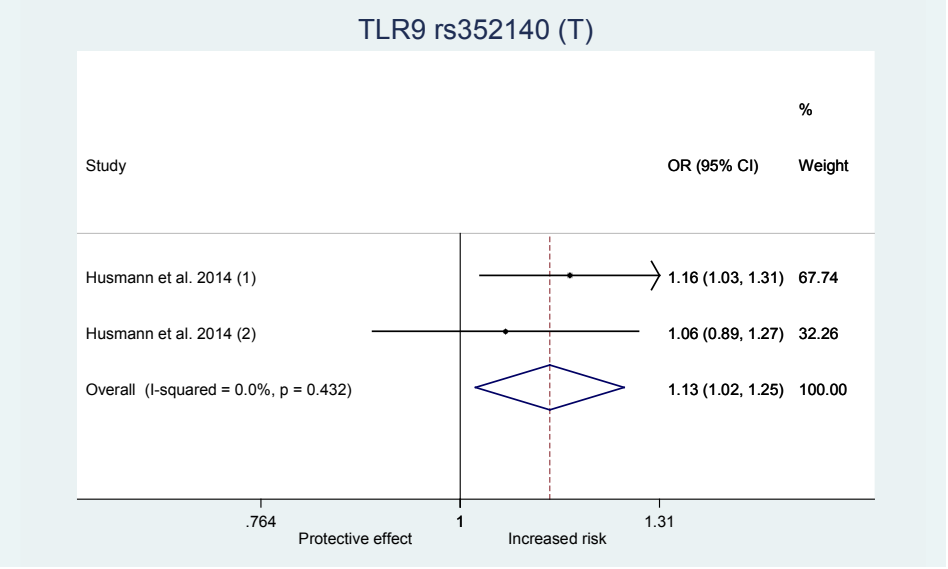
RXRB rs9277935 (T) forest plot. Harbold test: p=0.393, Egger test: p=0.406.
References: [53], [3], [25]



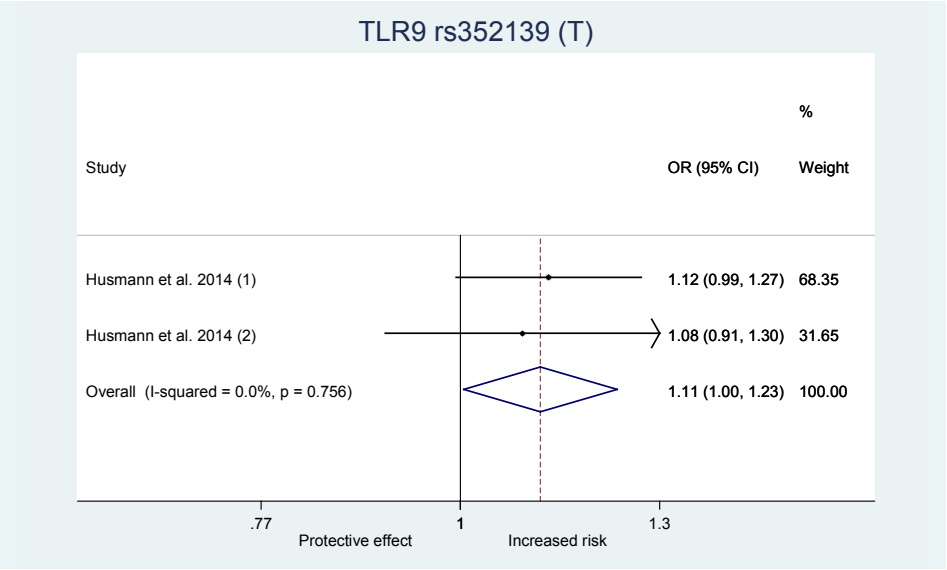
STAT4 rs7574865 (T) forest plot. Harbold test: p=0.590, Egger test: p=0.567.
References: [44], [45], [3]



TLR9 rs352162 (T) forest plot. Harbold test: N/A, Egger test: N/A.
References: [40]**



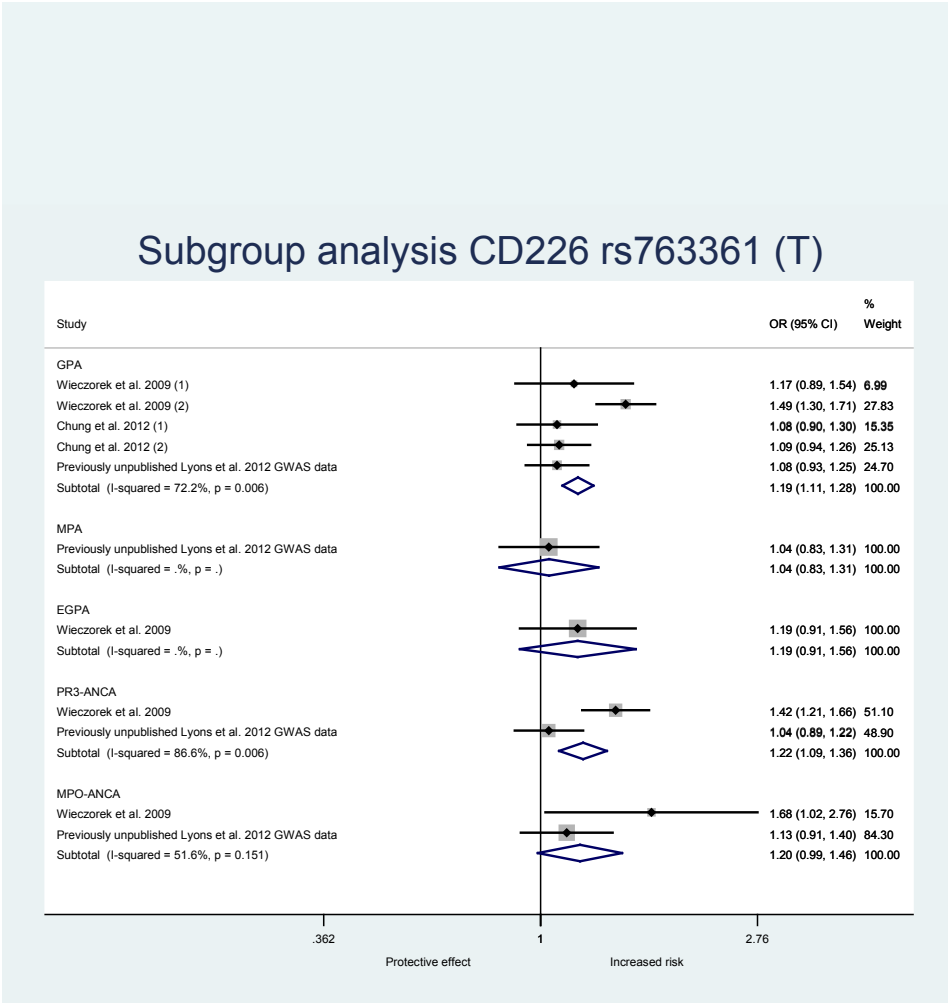
TLR9 rs352140 (T) forest plot. Harbold test: N/A, Egger test: N/A.
References: [40]**



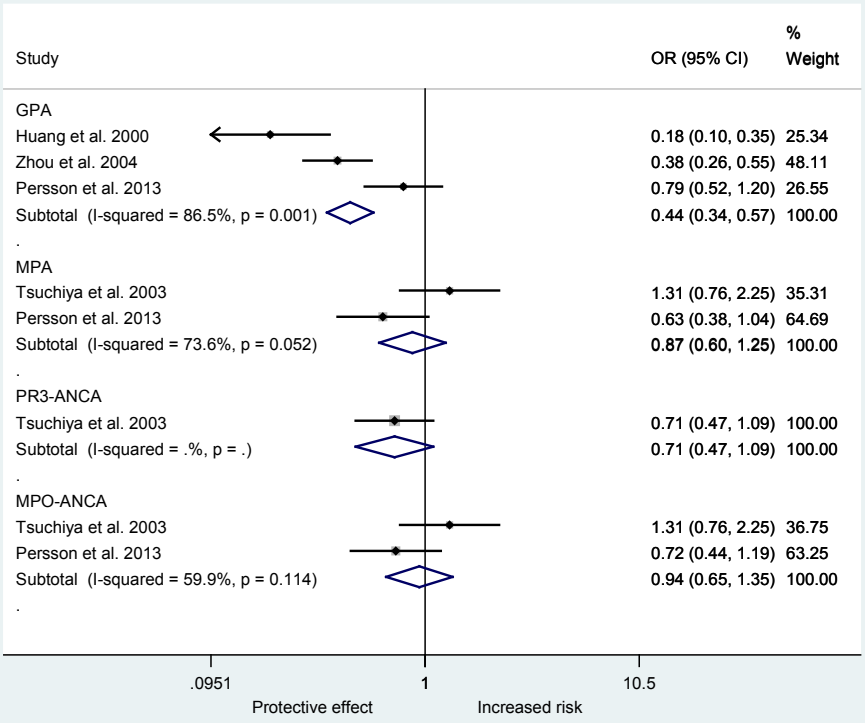
TLR9 rs352139 (T) forest plot. Harbold test: N/A, Egger test: N/A.
References: [40]**

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

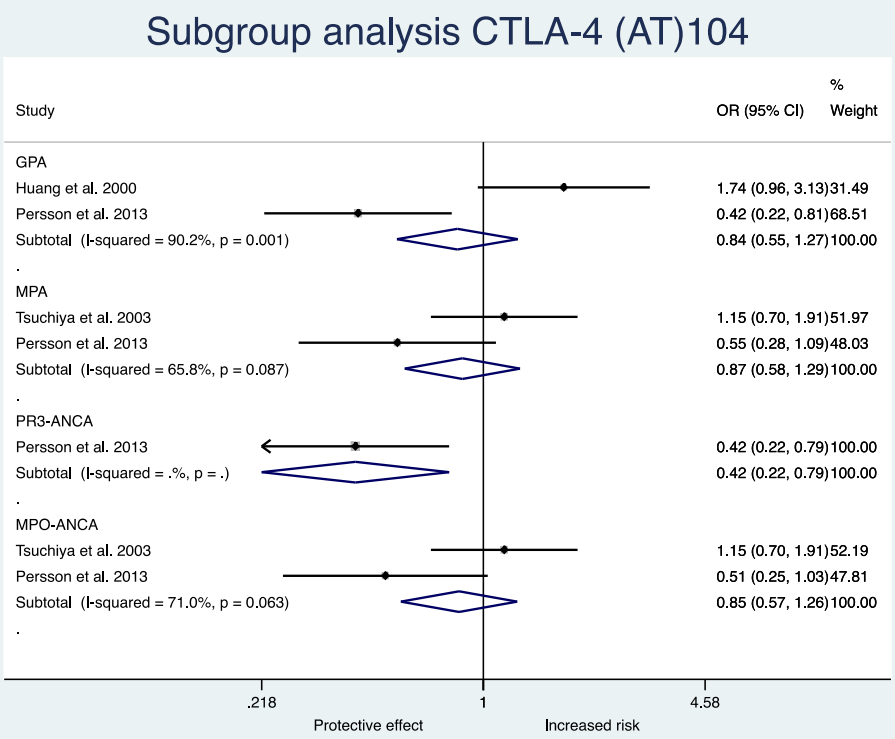
Supplementary figure 2. Forest plots by diagnostic and serologic subgroups



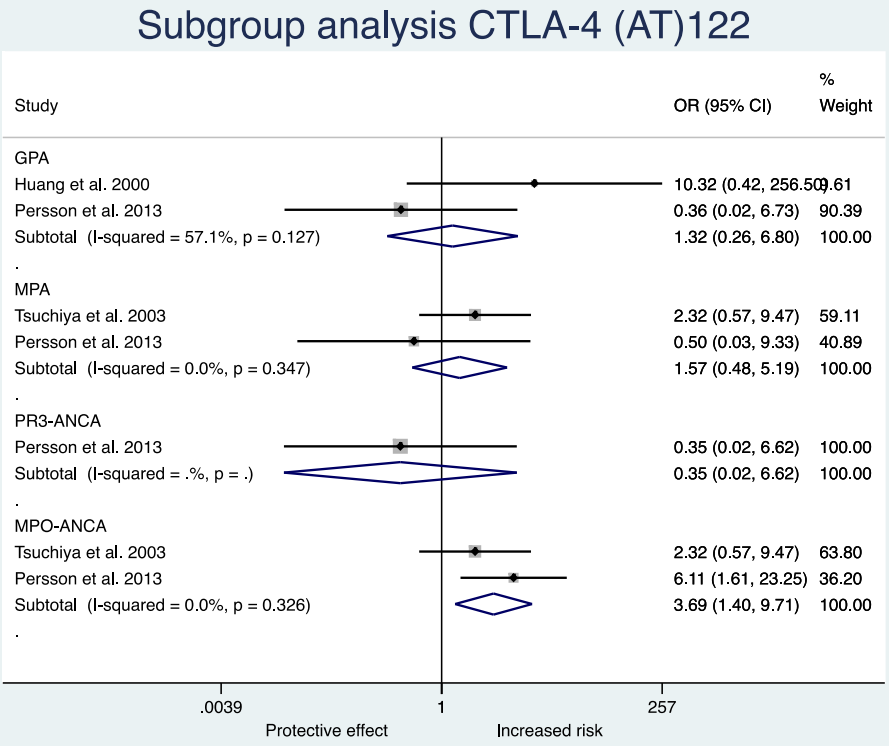
References: [1]**, [2]**, [3]



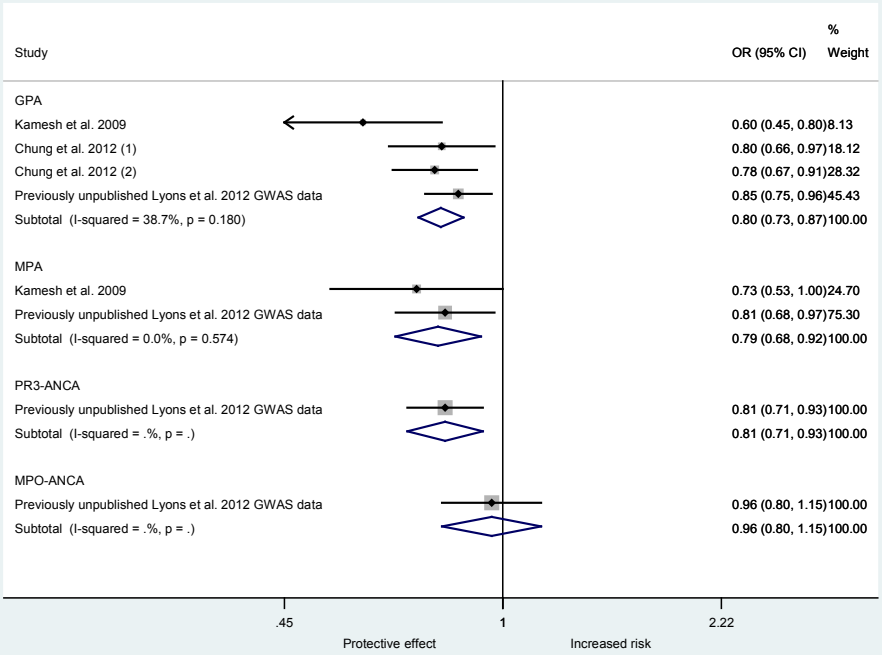
References: [4], [5], [6], [7]



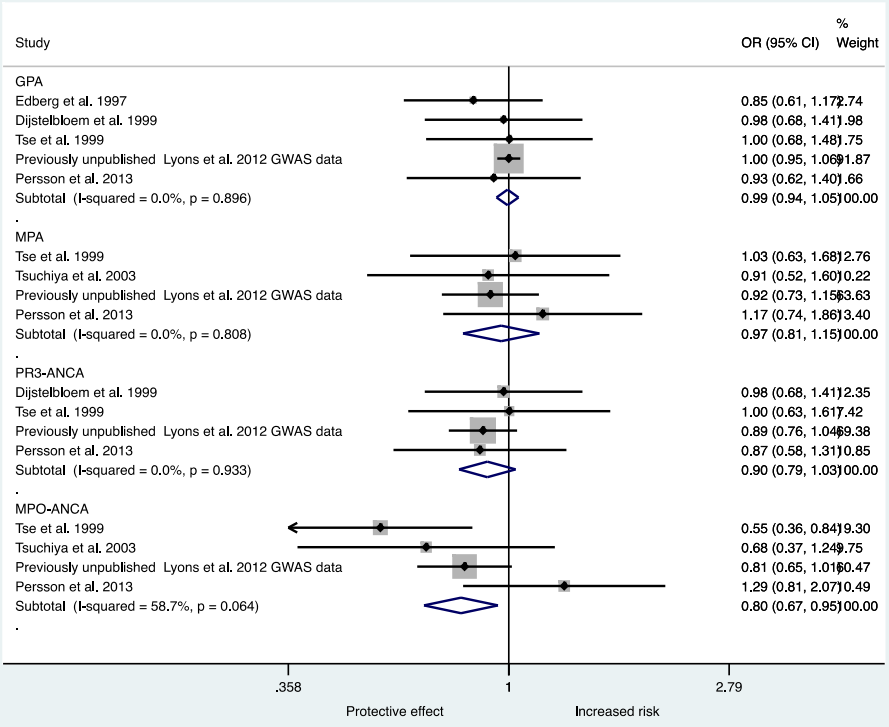
References: [4], [7], [5]



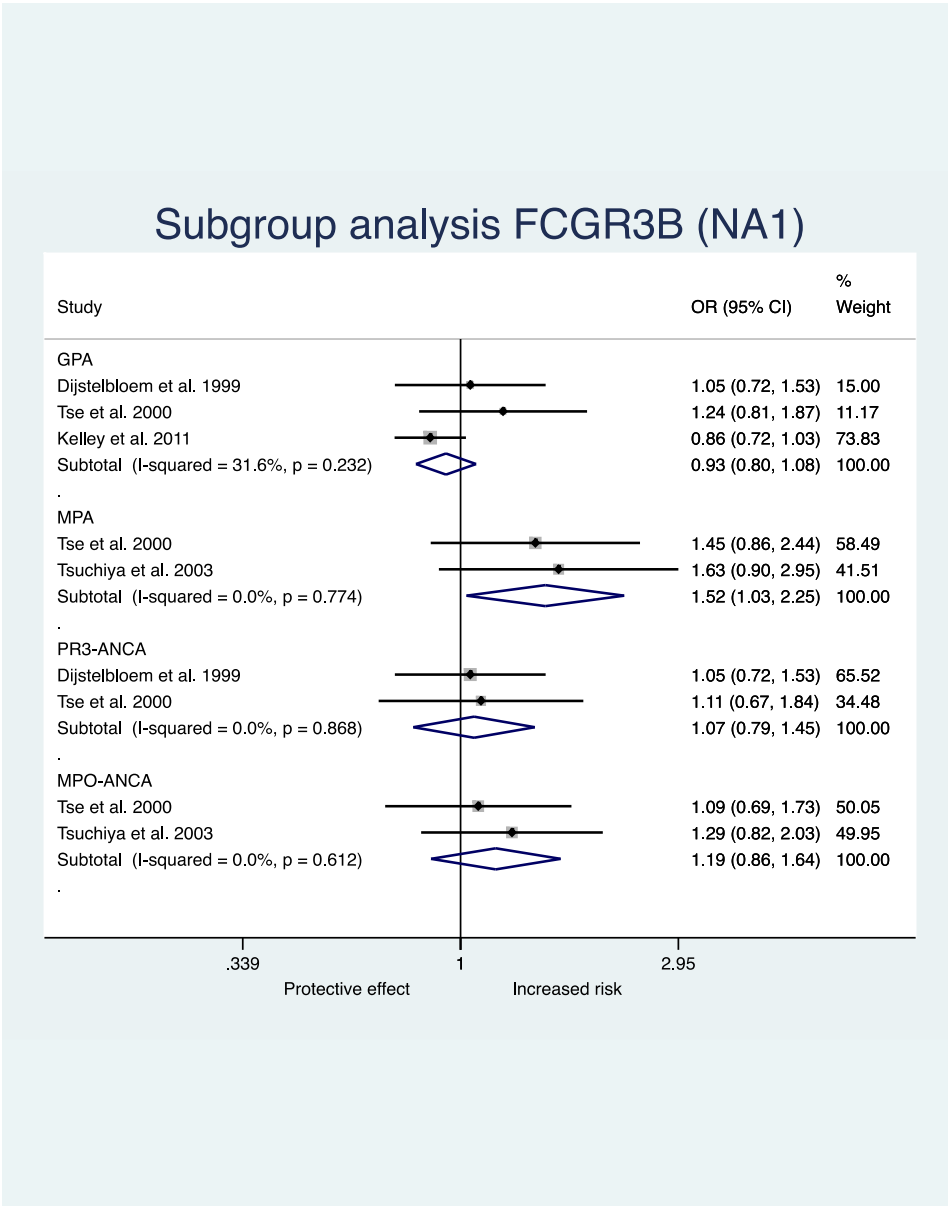
References: [4], [7], [5]



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

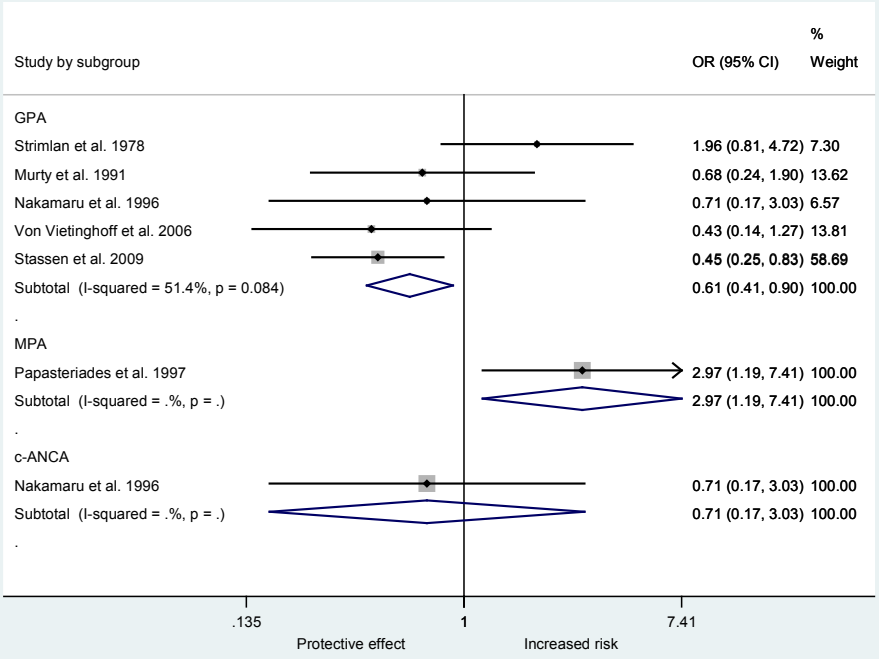


References: [11], [12], [13], [5], [7], [3]

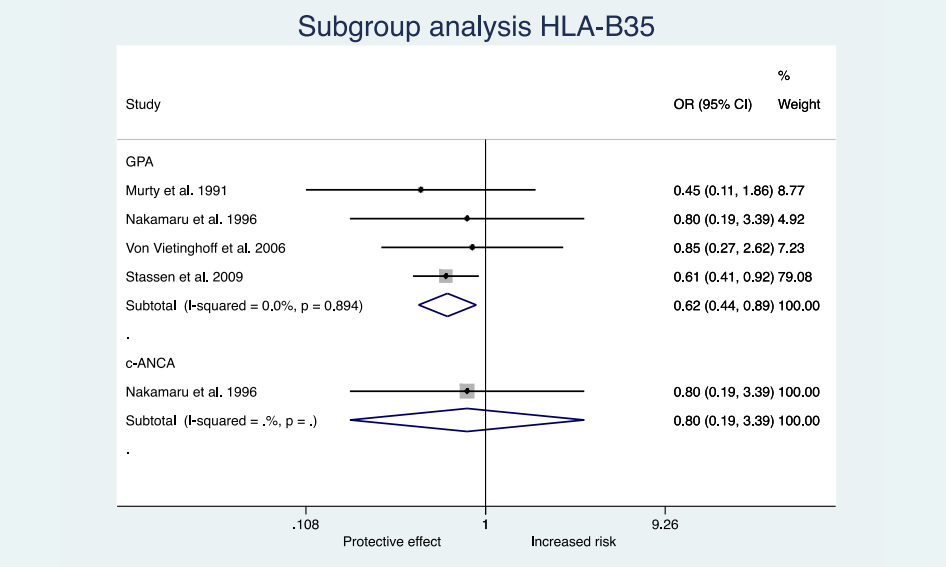


References: [12], [14], [10], [5]

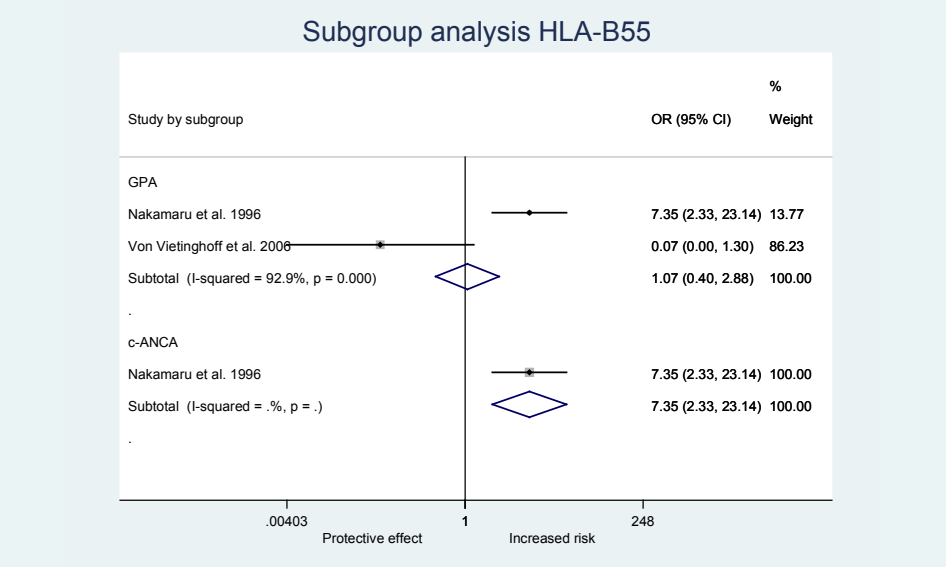
Subgroup analysis HLA-A11



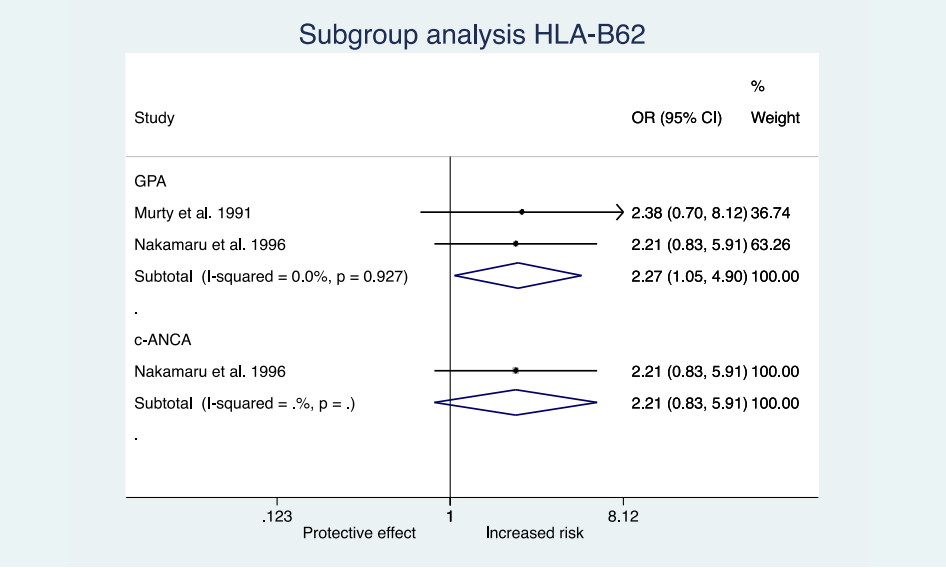
References: [16], [17], [20], [22], [18], [19]



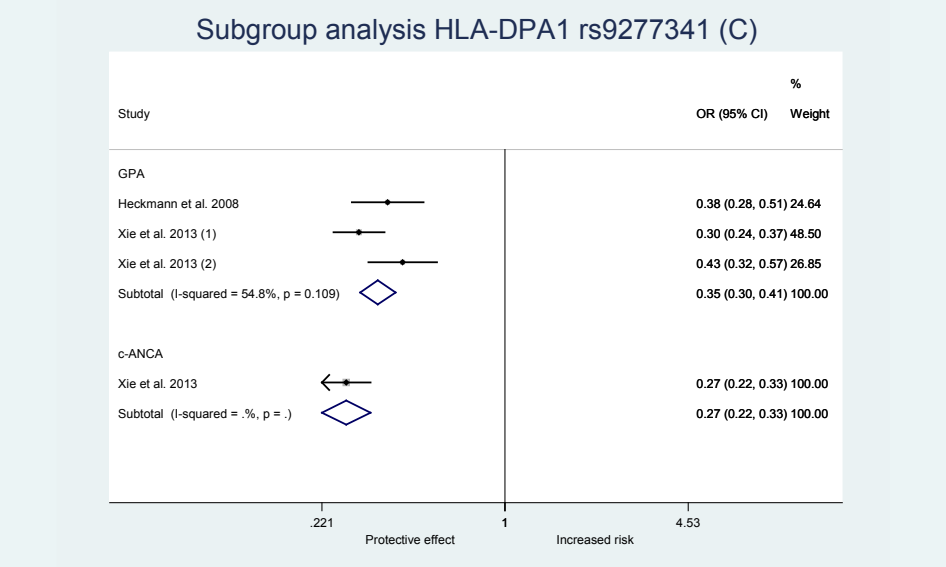
References: [17], [20], [18], [19]



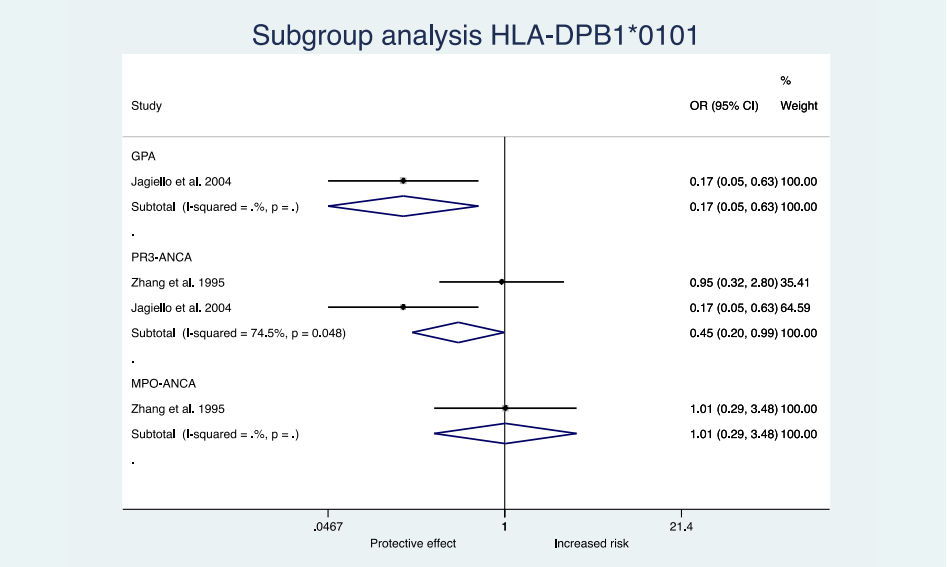
References: [20], [18]



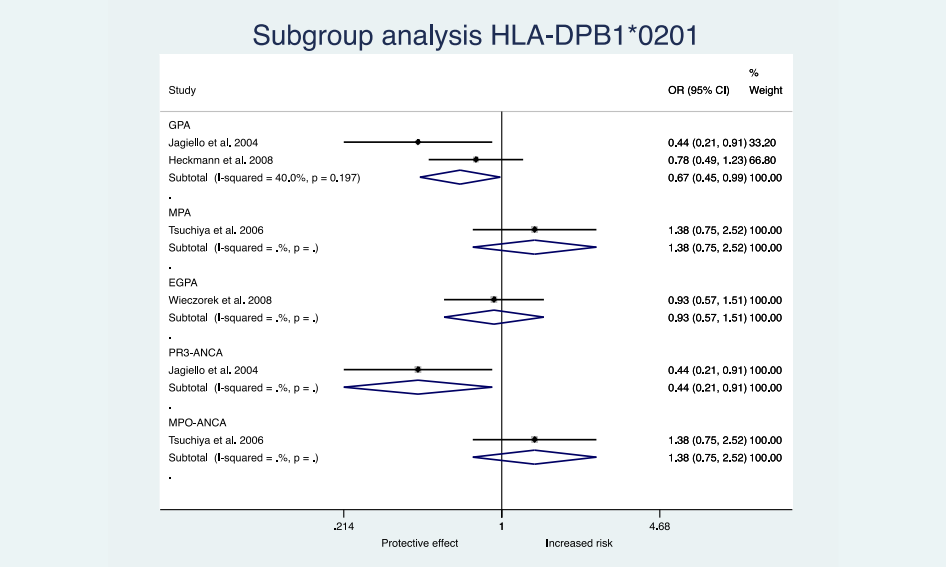
References: [17], [20]



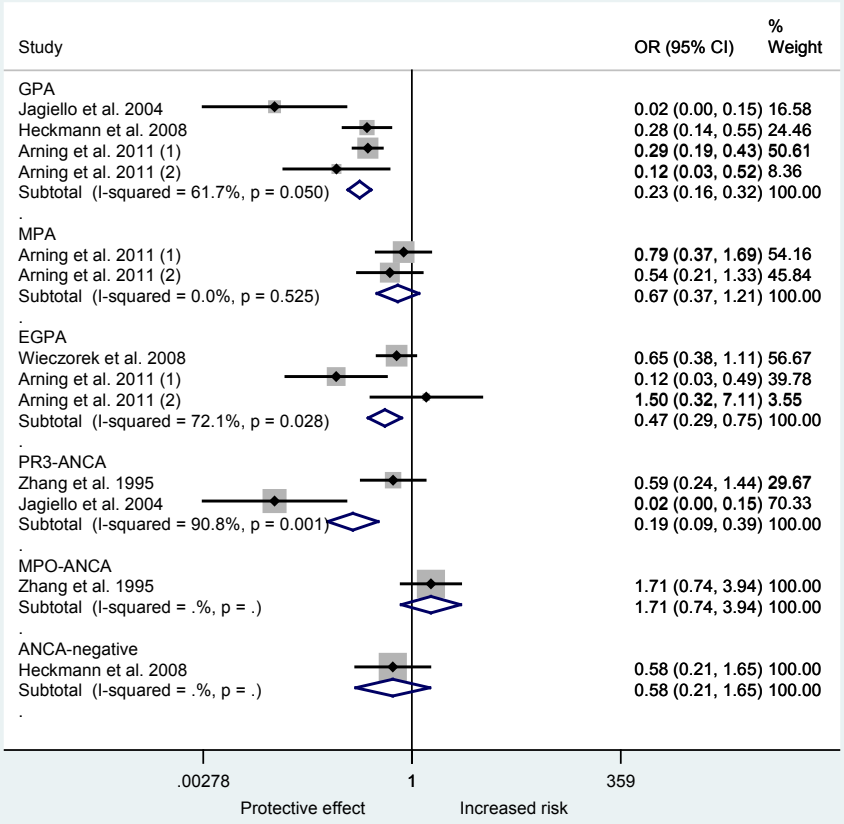
References: [24], [25]**



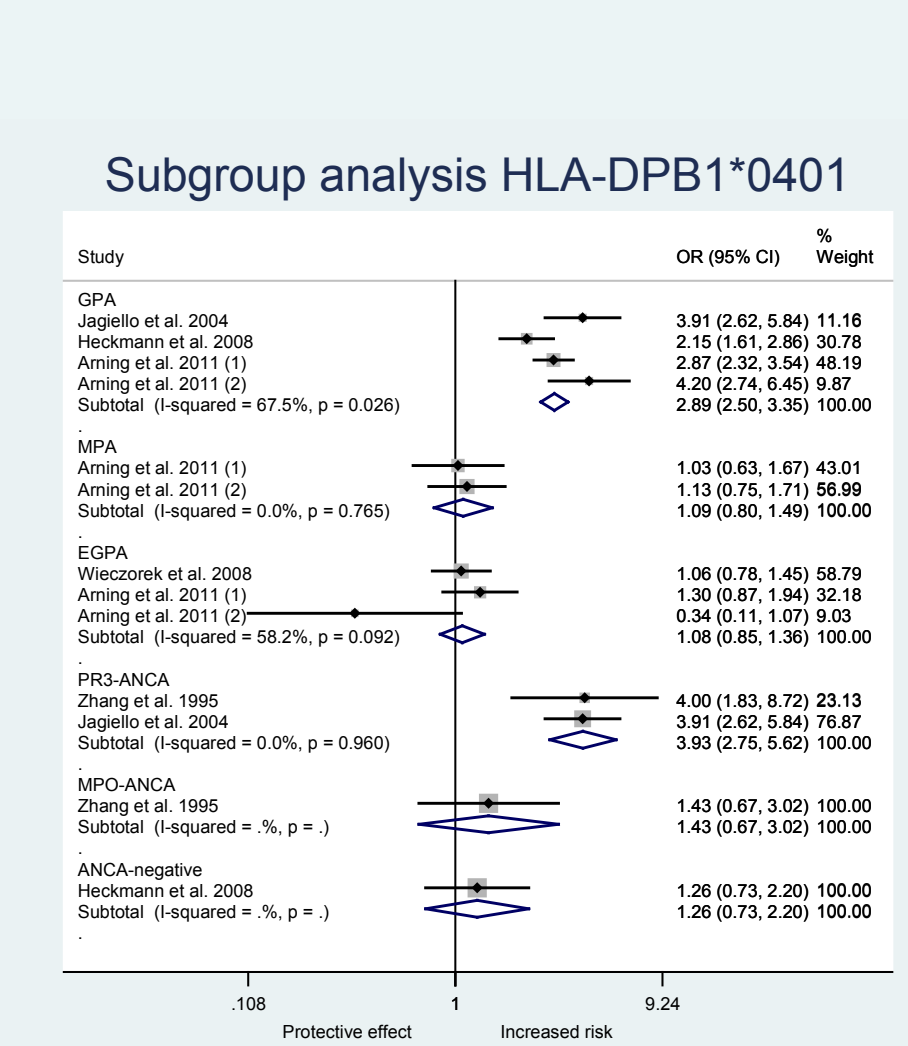
References: [27], [26]



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



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



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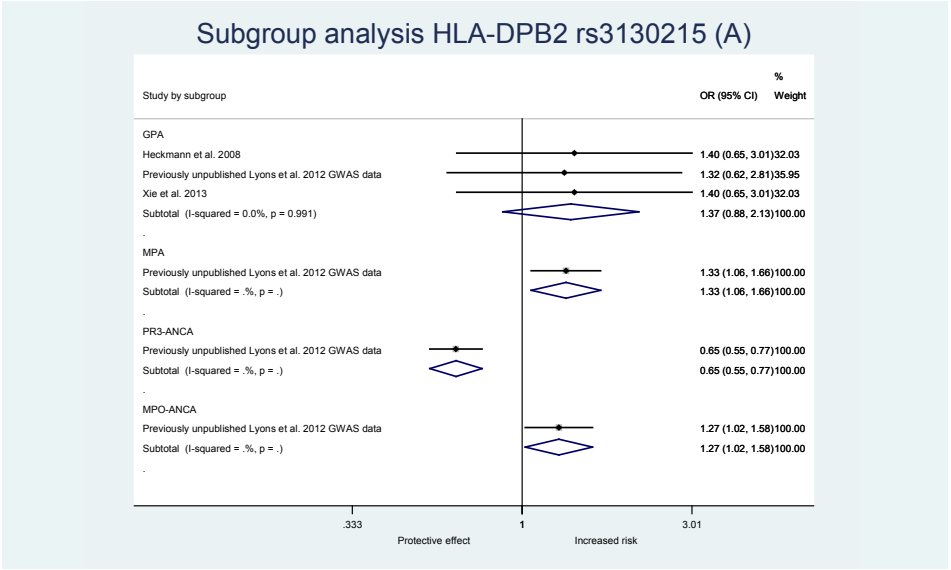
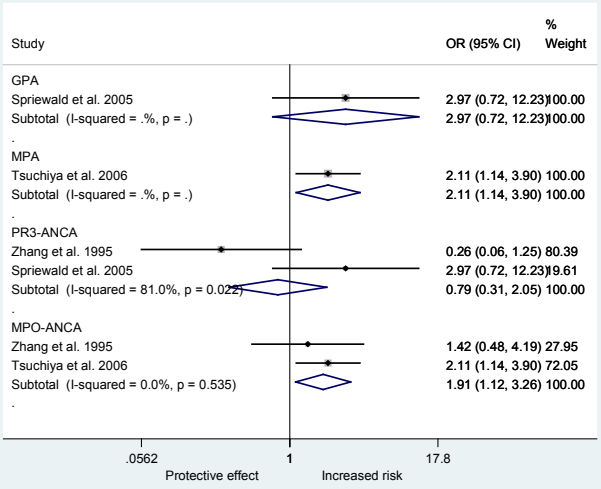
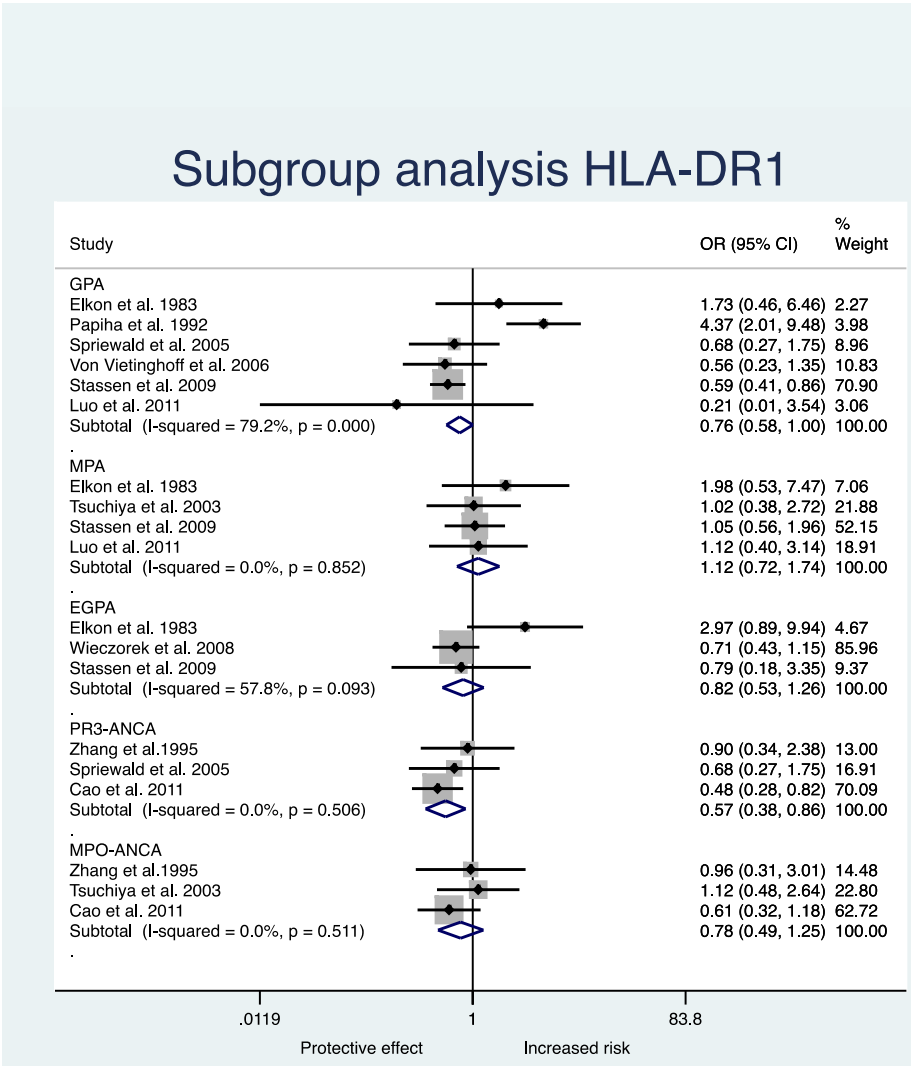


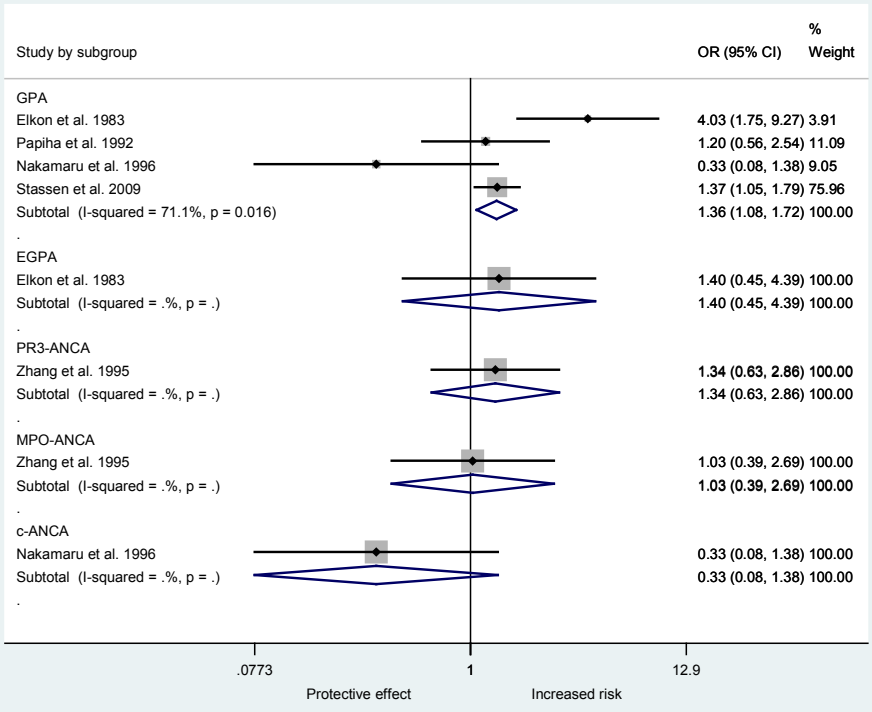
References: [24], [3], [25]



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

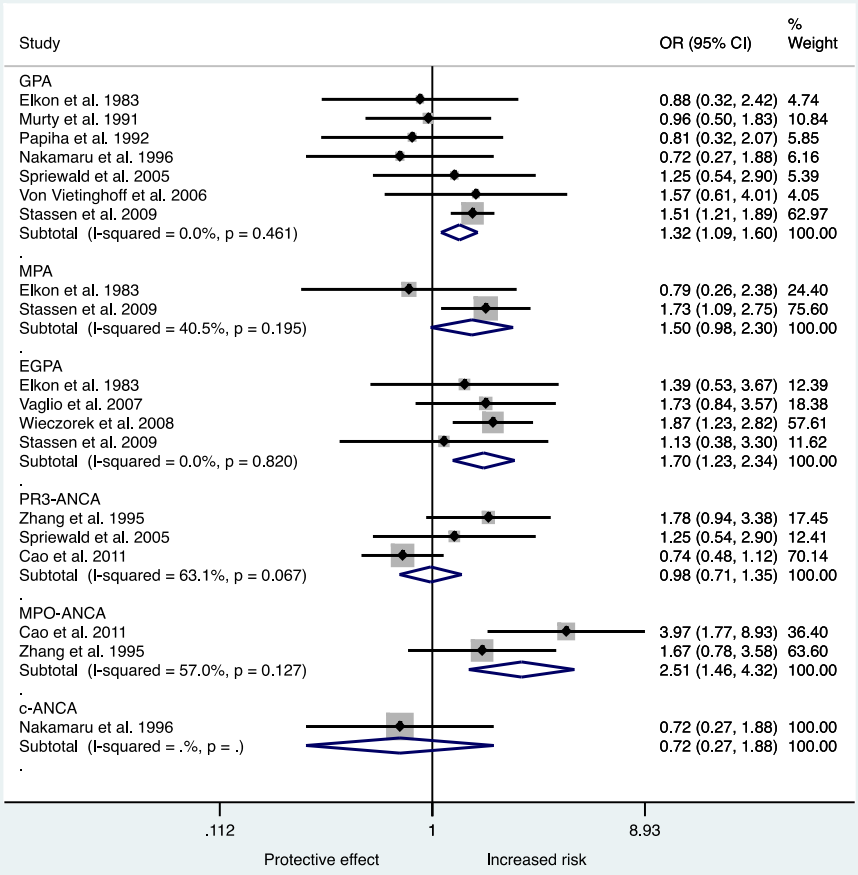


References: [23], [32], [31], [18], [19], [34], [5], [29], [26], [33]



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

Subgroup analysis HLA-DR4



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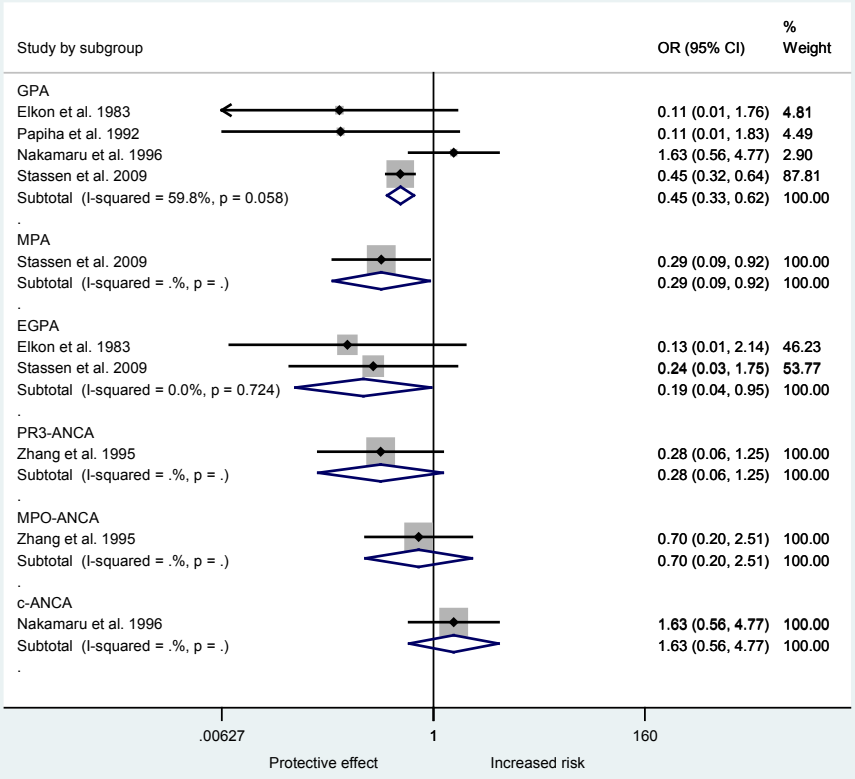
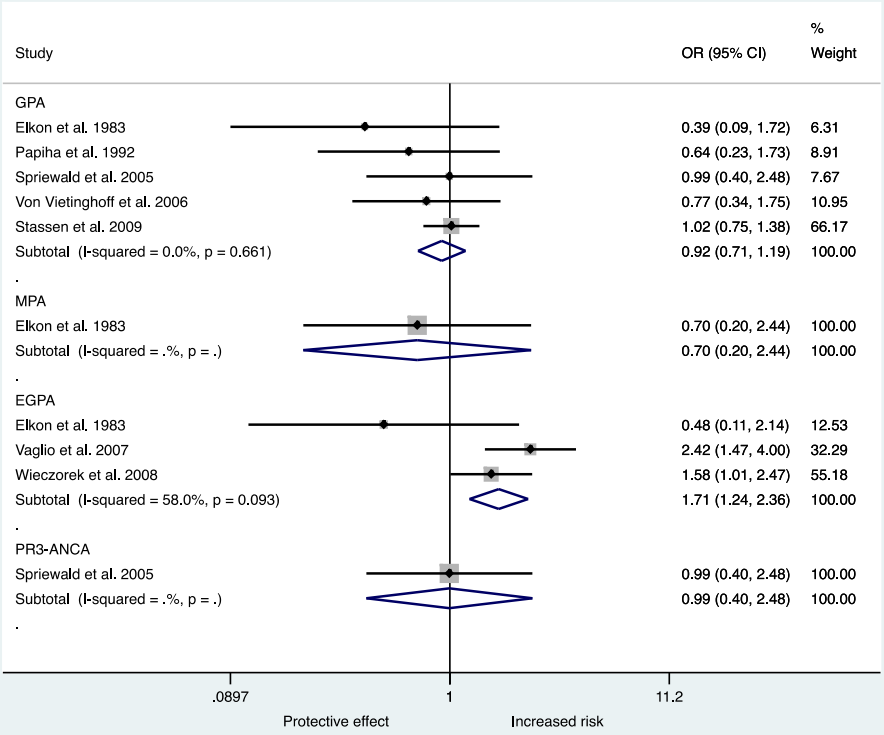
Subgroup analysis HLA-DR6



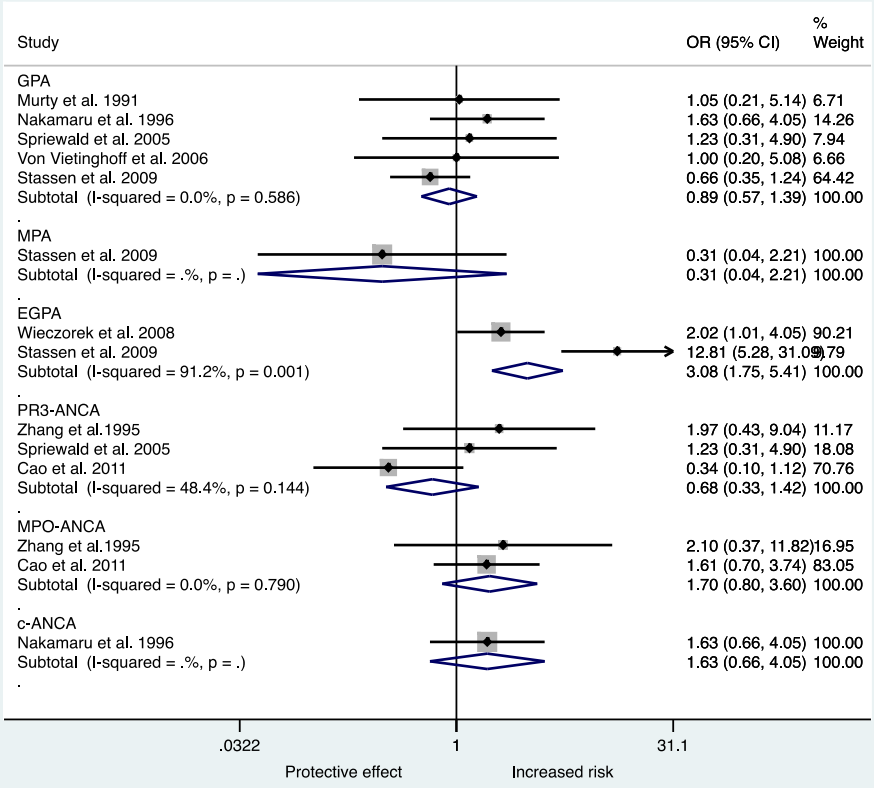
References: [23], [32], [26], [20], [19]

Subgroup analysis HLA-DR7

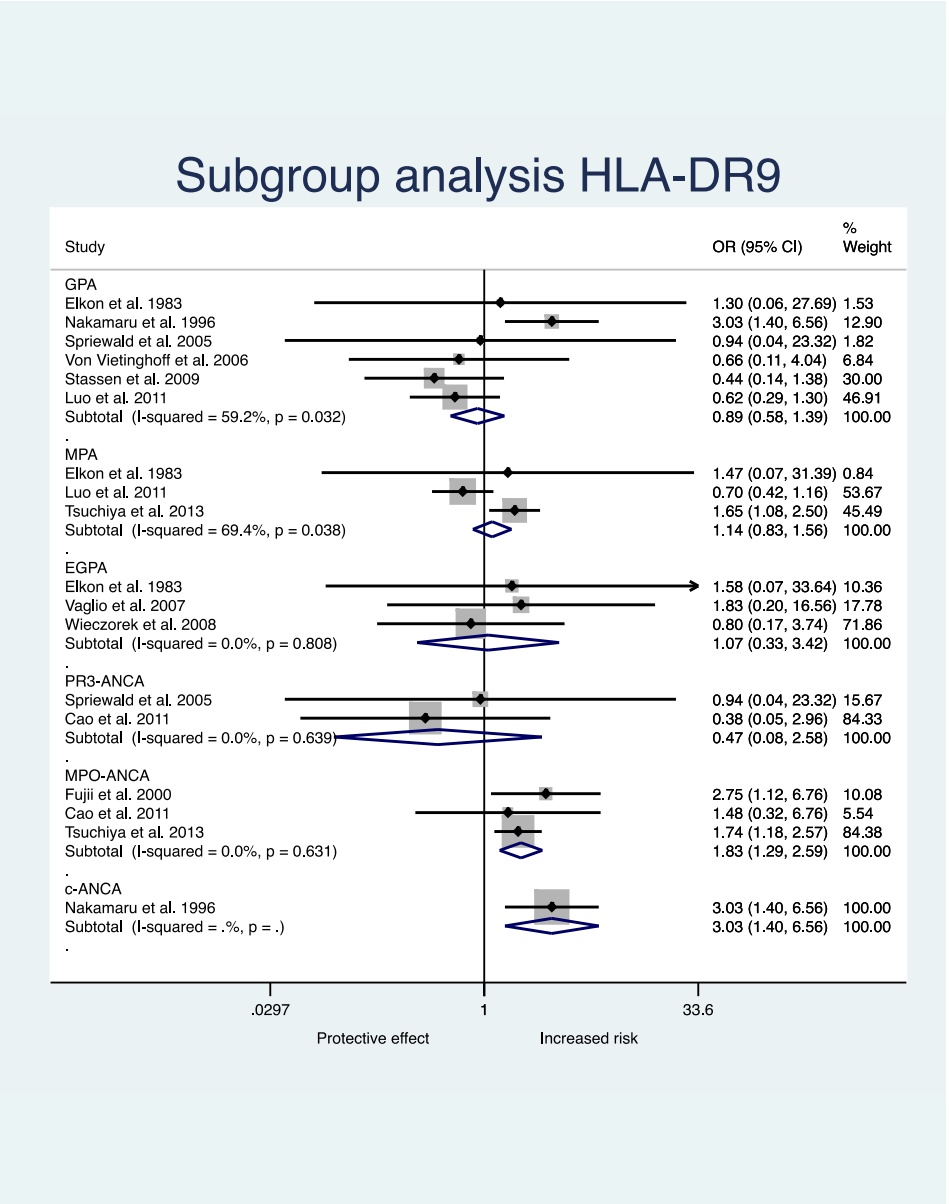


References: [23], [32], [31], [18], [19], [35], [29]

Subgroup analysis HLA-DR8



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



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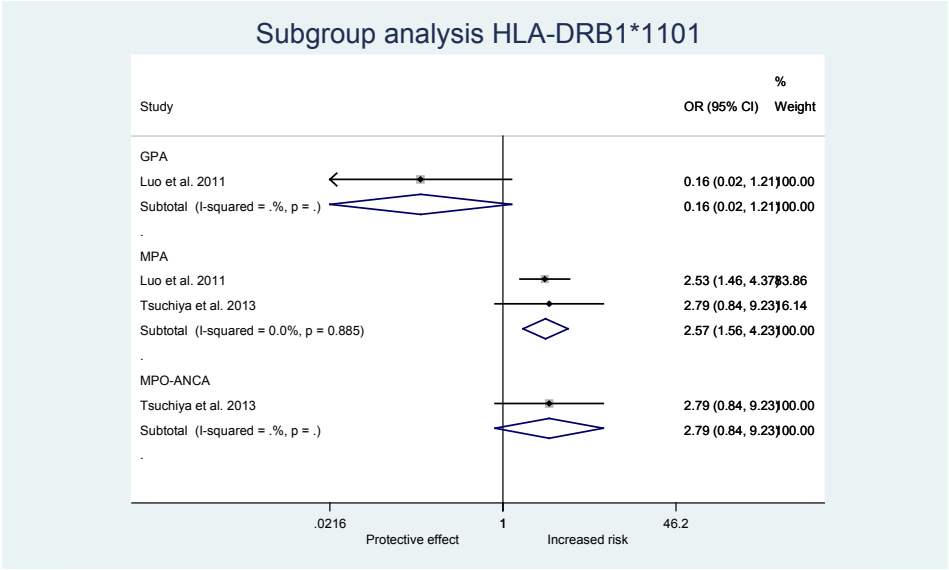

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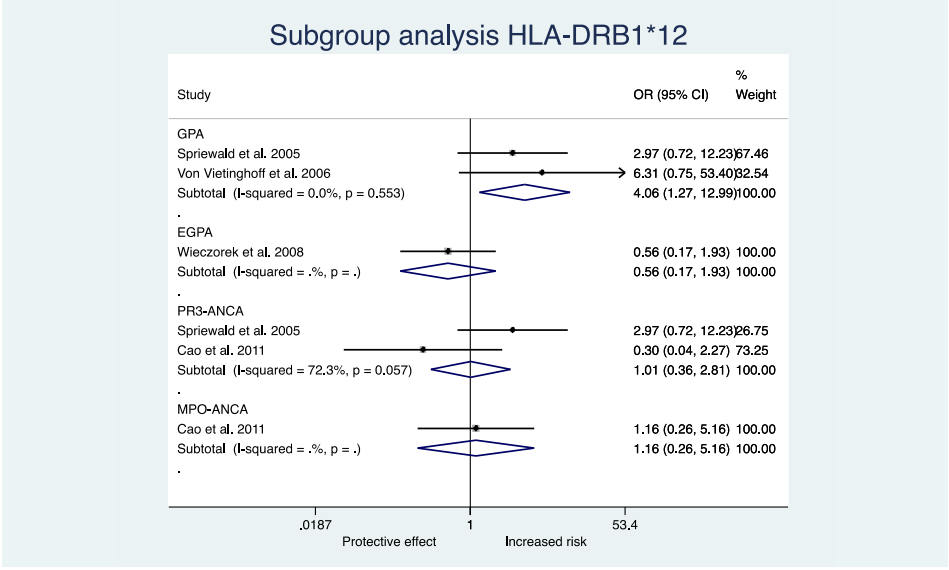
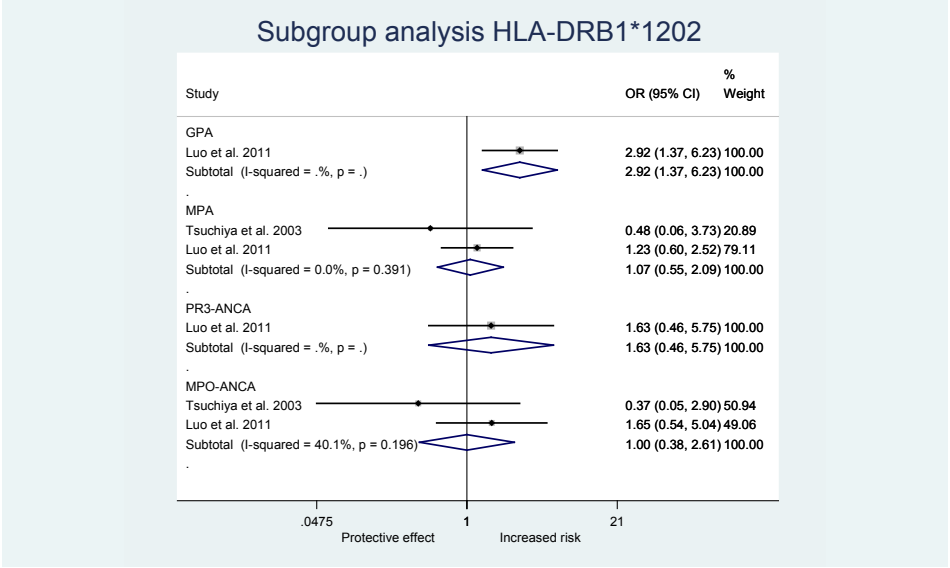
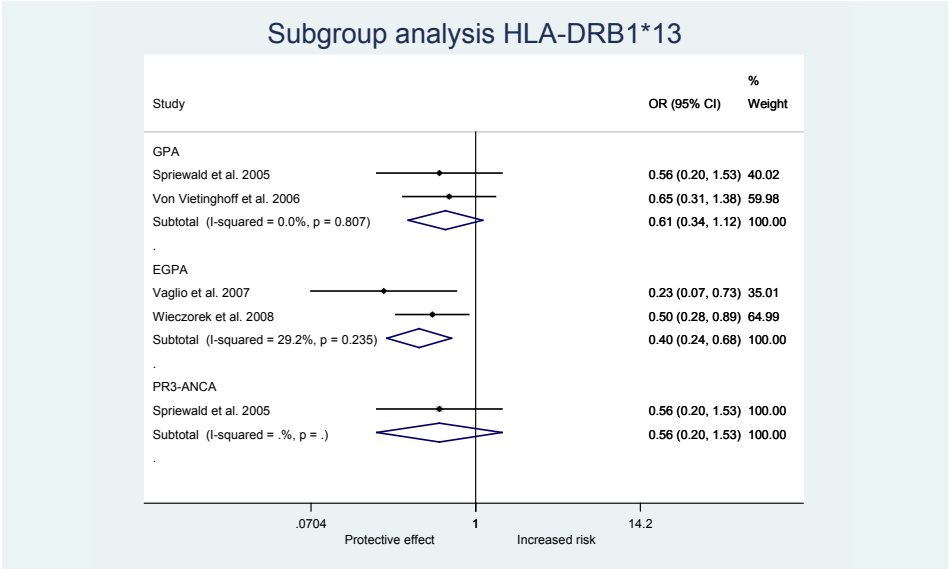


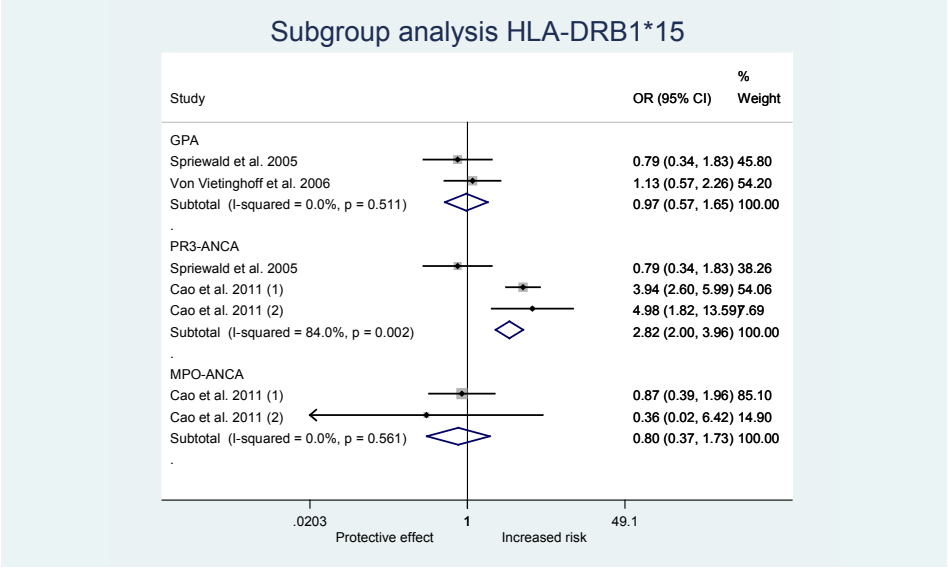
References: [31], [18], [29], [33]



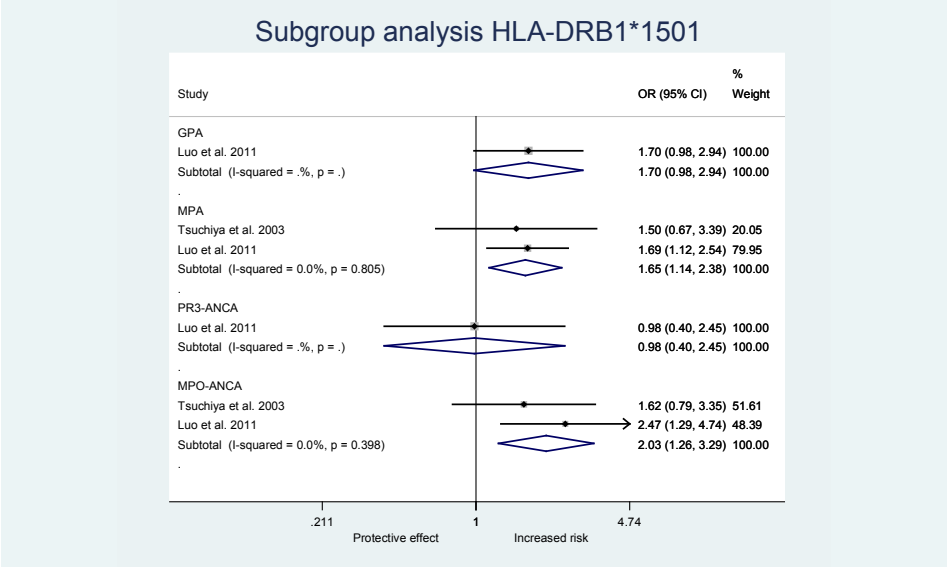
References: [5], [34]



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



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



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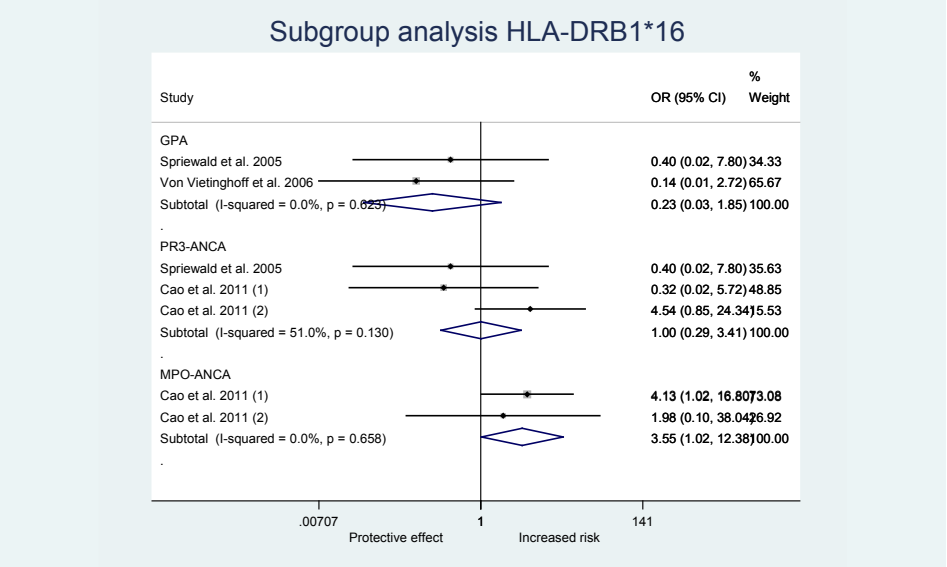
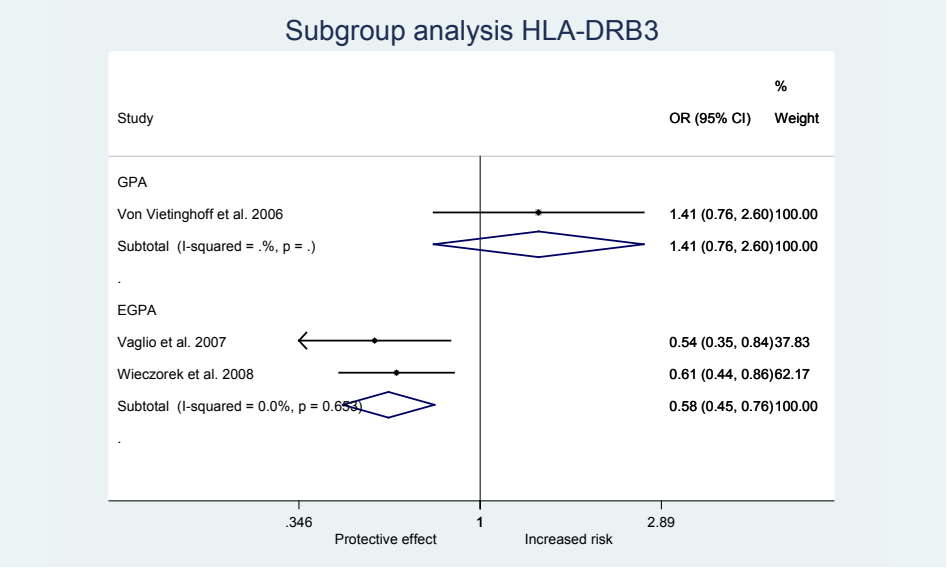
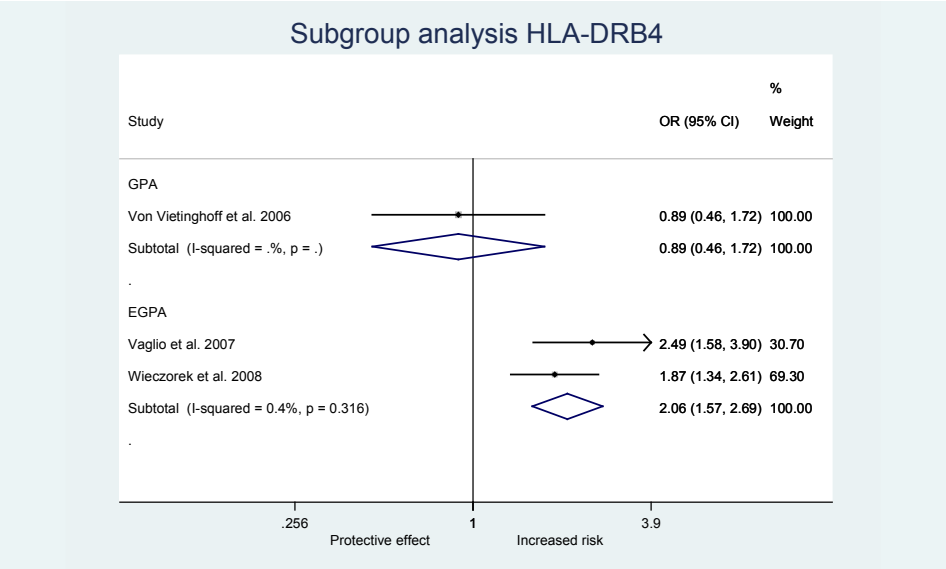


References: [31], [18], [33]**

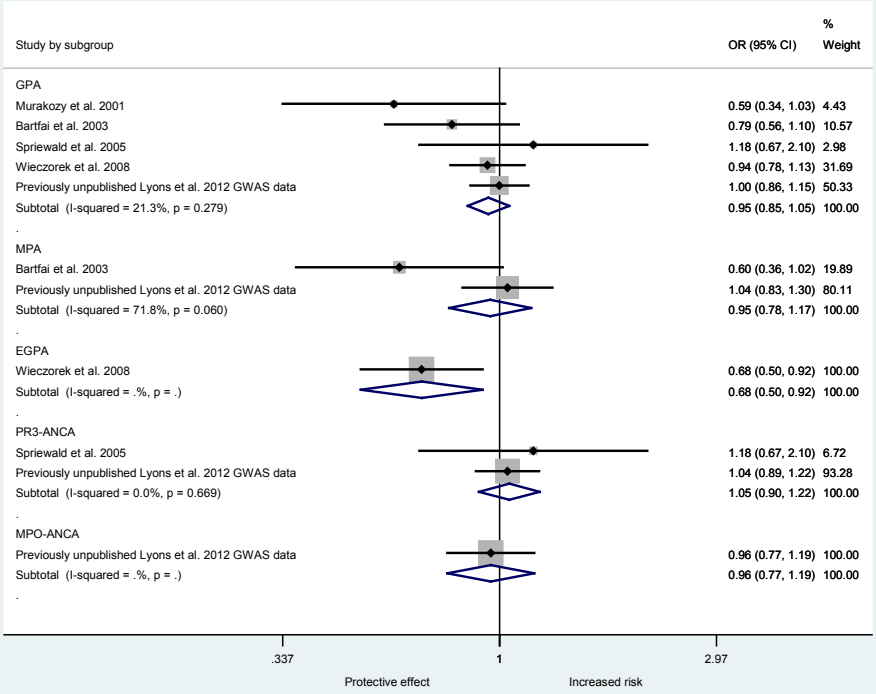


References: [18], [35], [29]

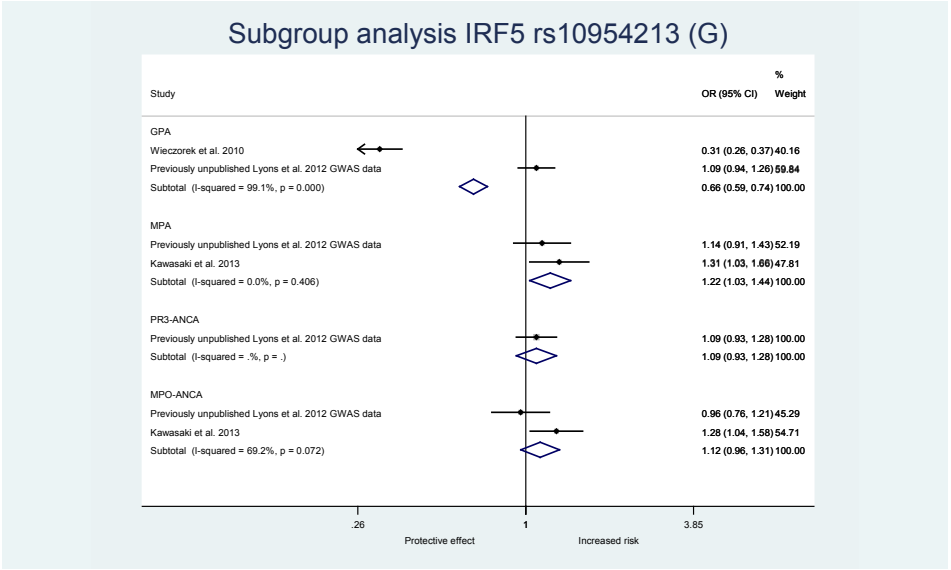


References: [18], [35], [29]

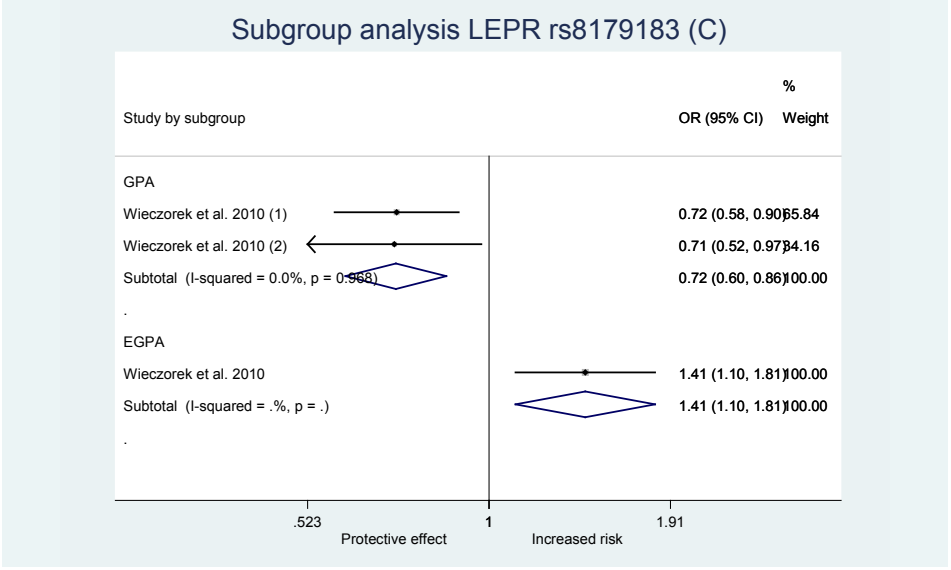
Subgroup analysis IL-10 rs1800896 (G)



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

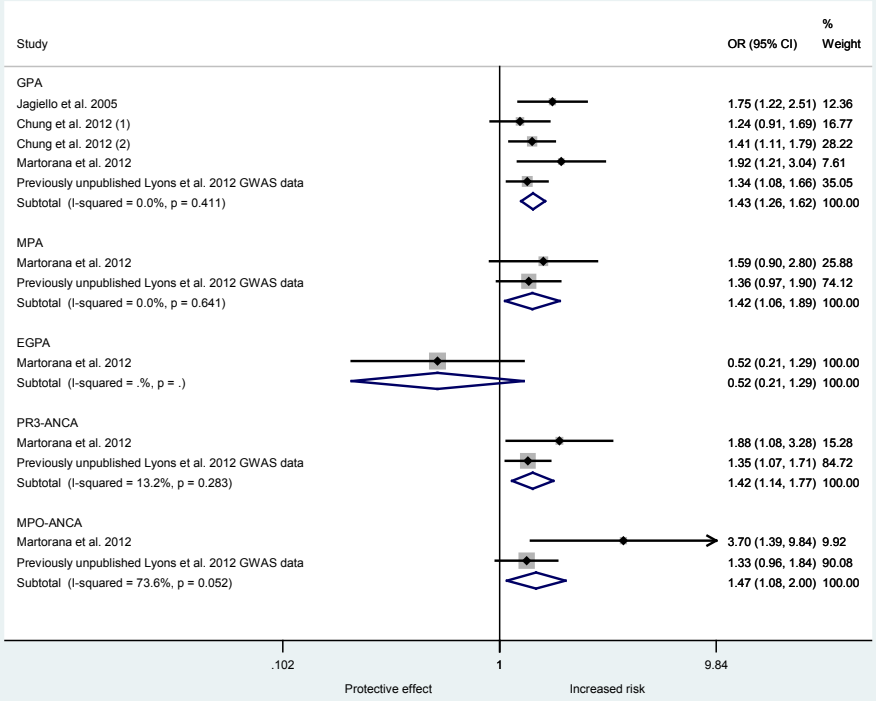


References: [44], [3], [45]



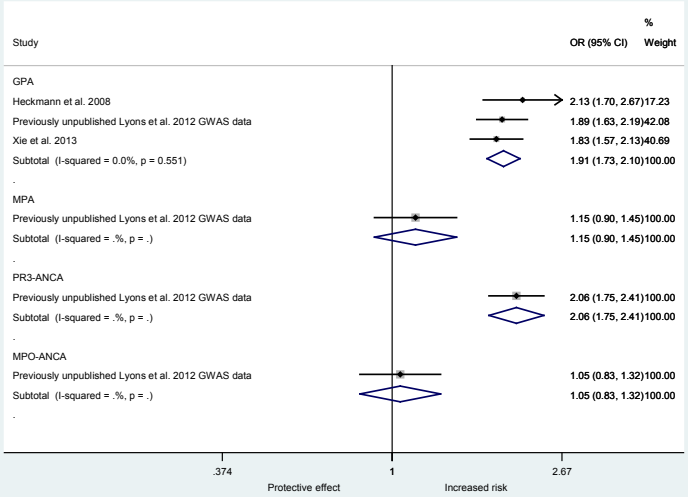
References: [15]**

Subgroup analysis PTPN22 rs2476601 (A)



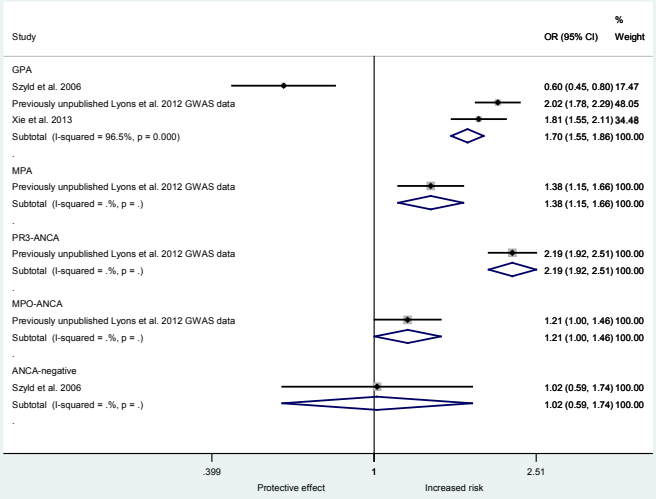
References: [50], [2]**, [51], [3]

Subgroup analysis RING1/RXRB rs213213 (A)

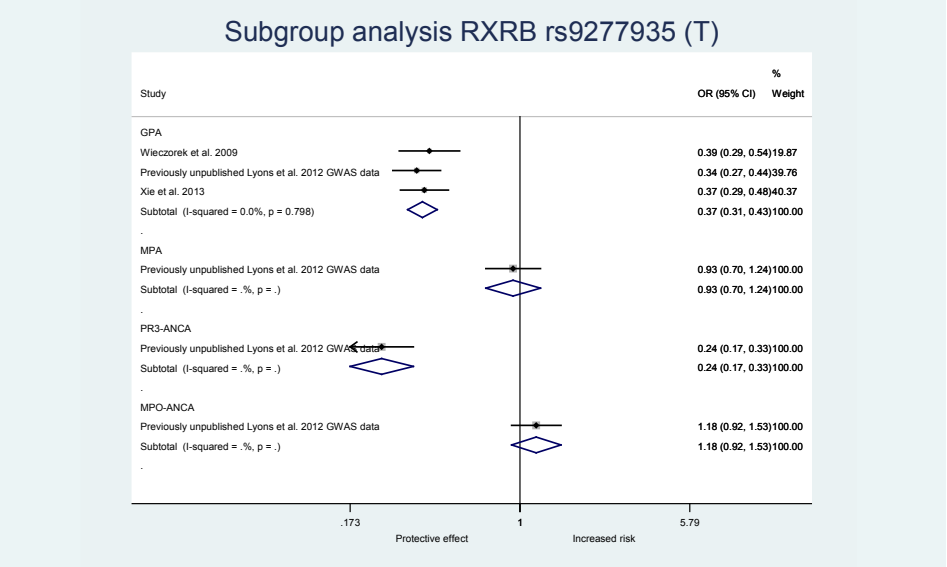


References: [24], [3], [25]

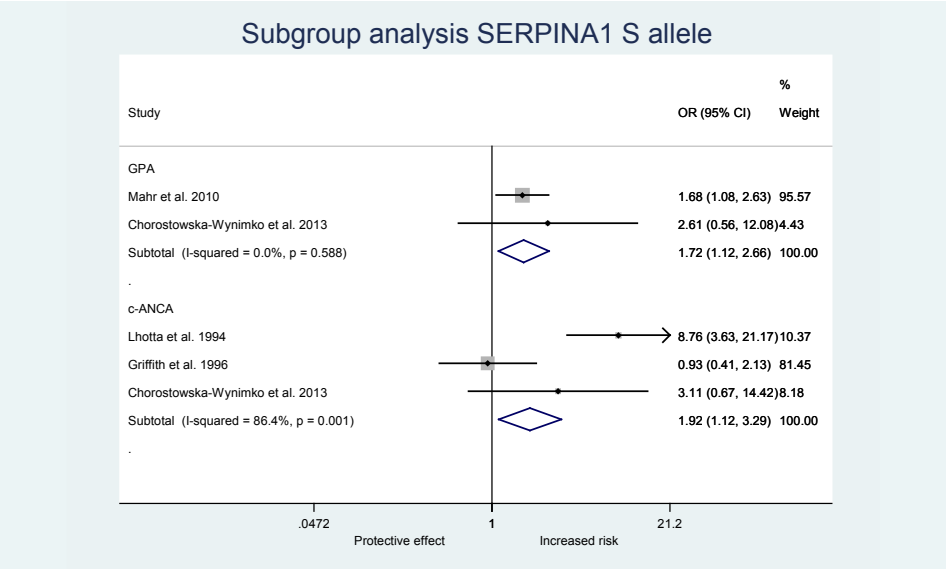
Subgroup analysis RXRB rs6531 (C)



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

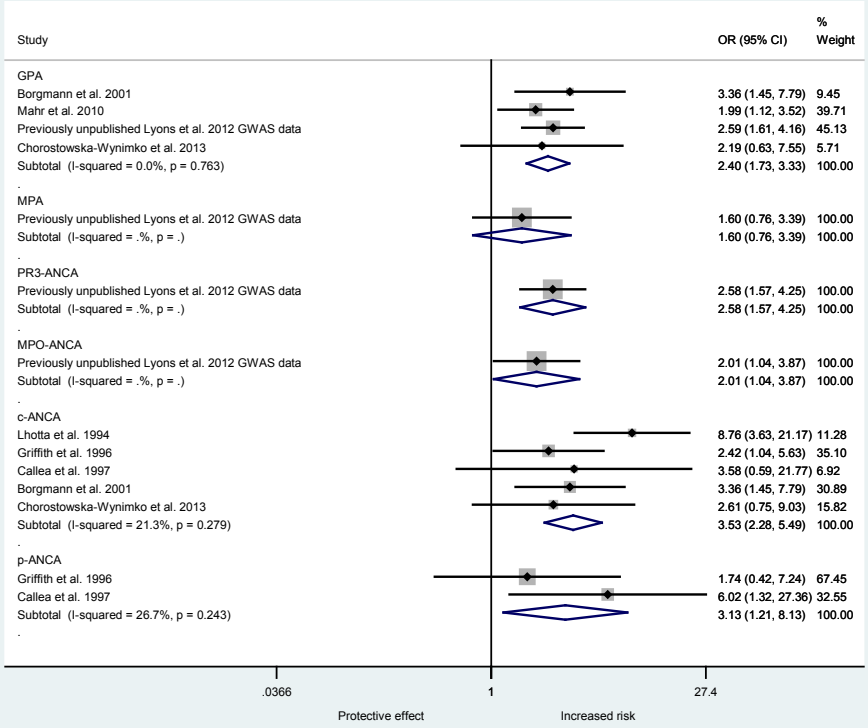


References: [53], [3], [25]

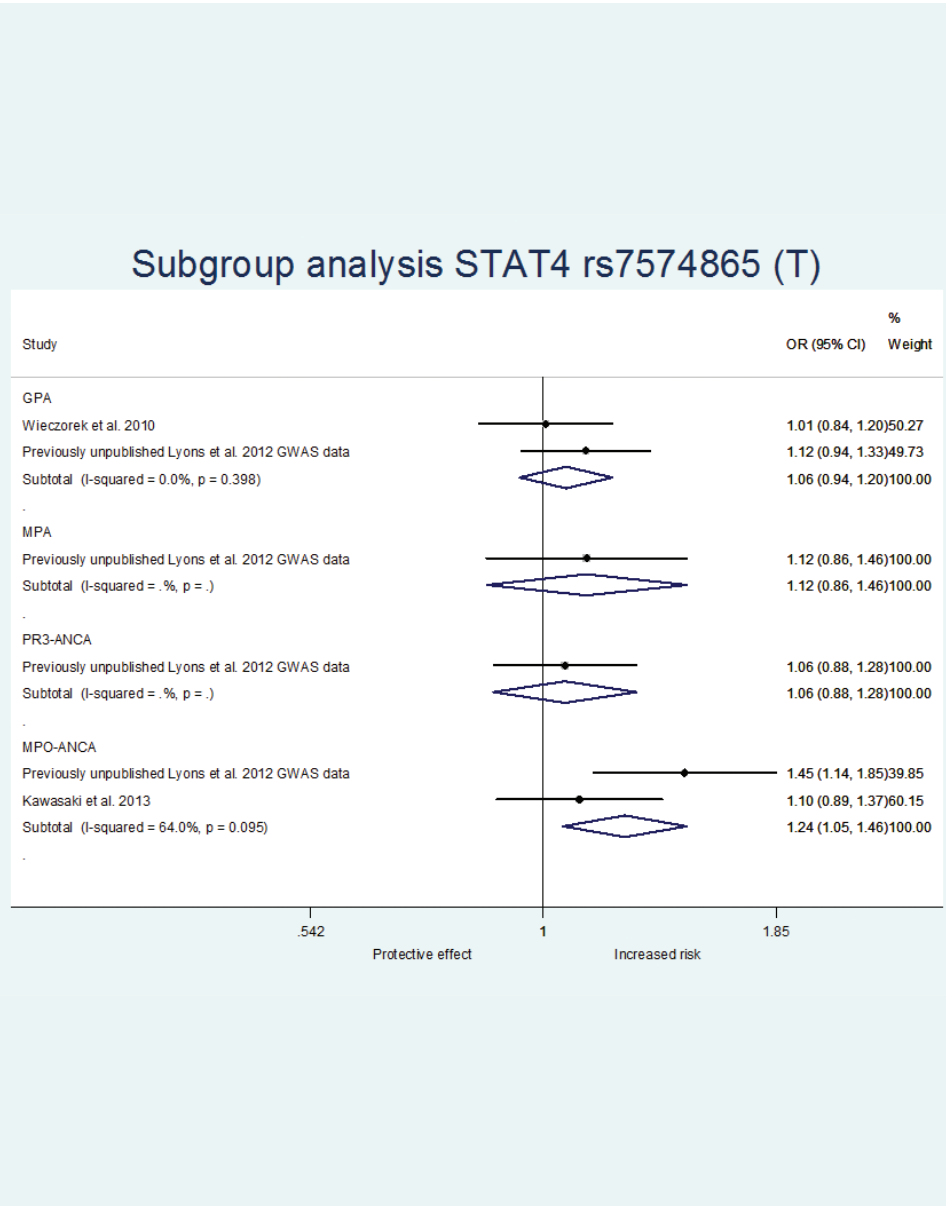


References: [54], [55], [56], [58]

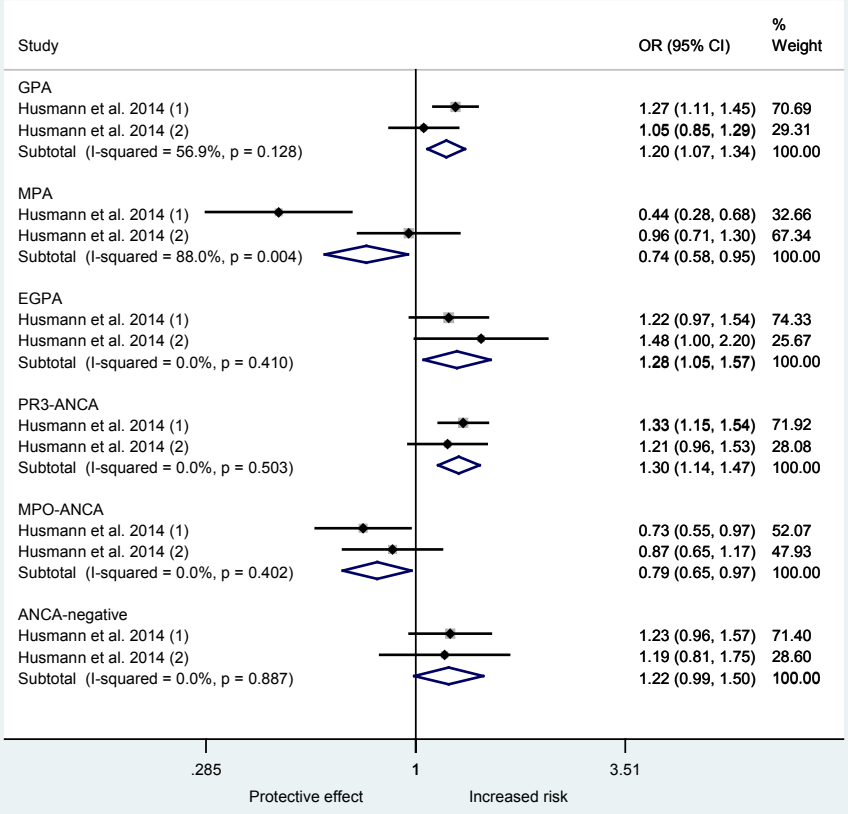
Subgroup analysis SERPINA1 Z allele



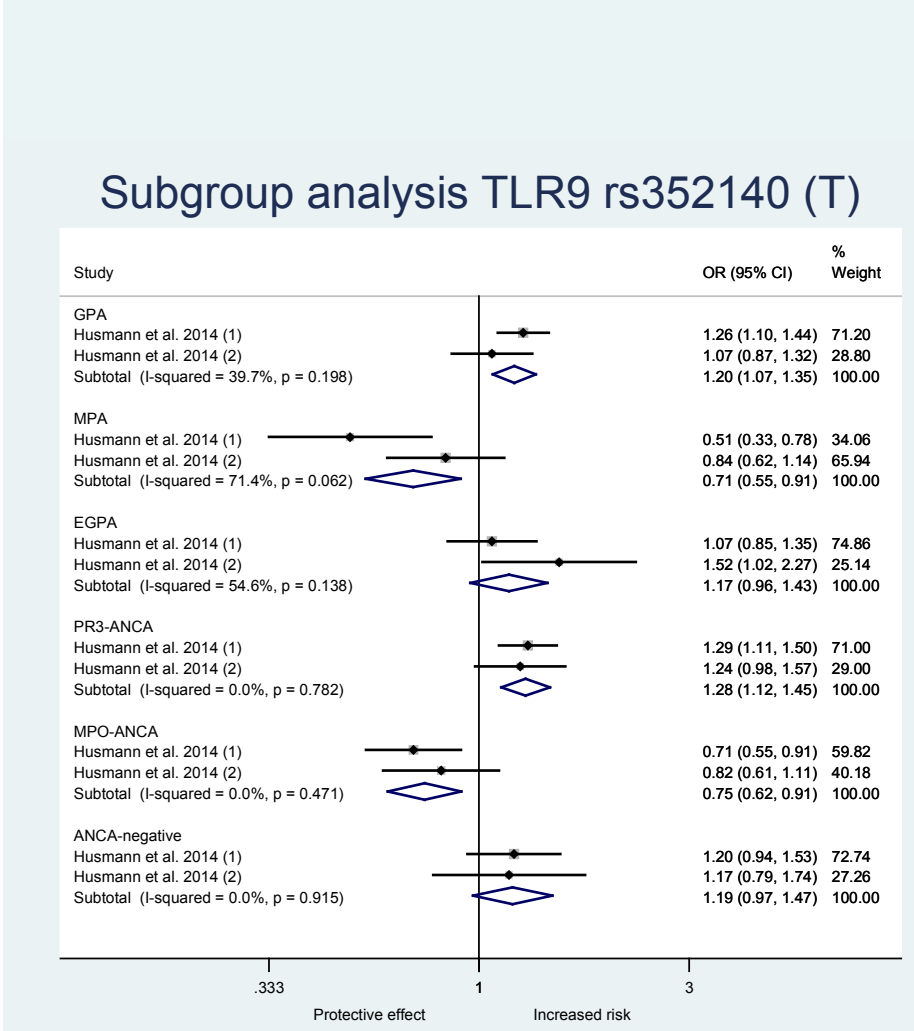
References: [54], [55], [59], [60], [56], [3], [58]



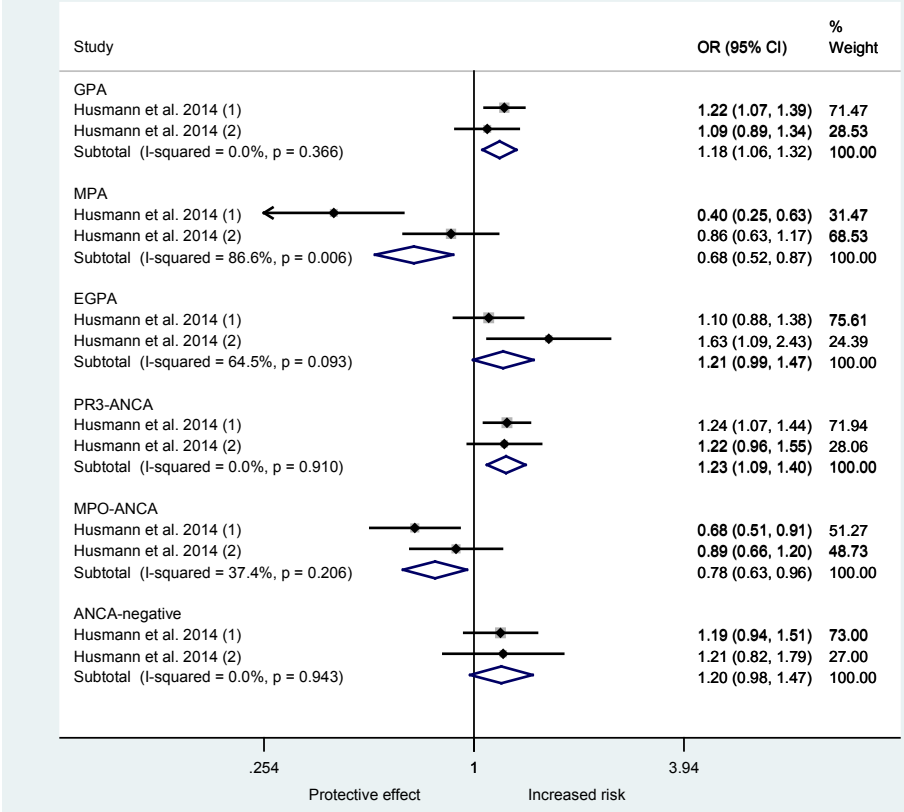
References: [44], [45]



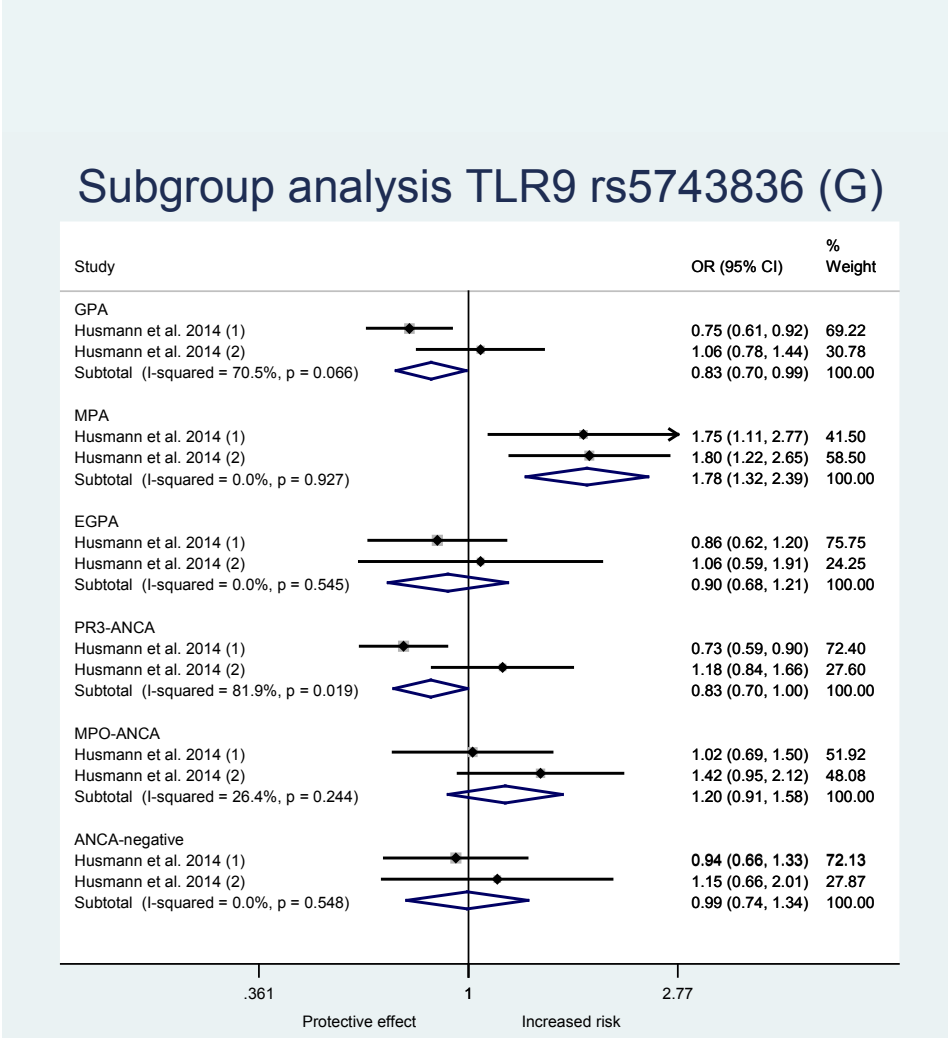
References: [40]**



References: [40]**



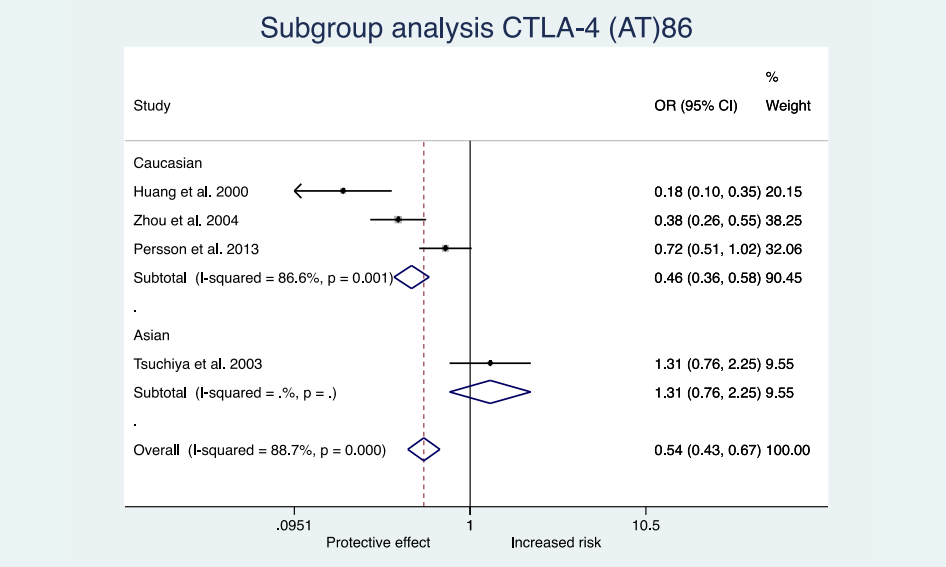
References: [40]**



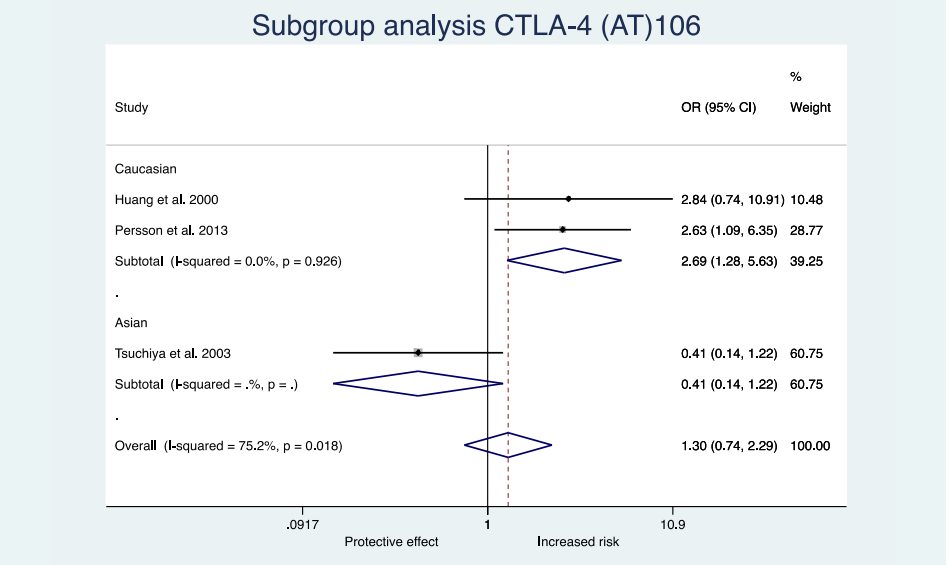
References: [40]**

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

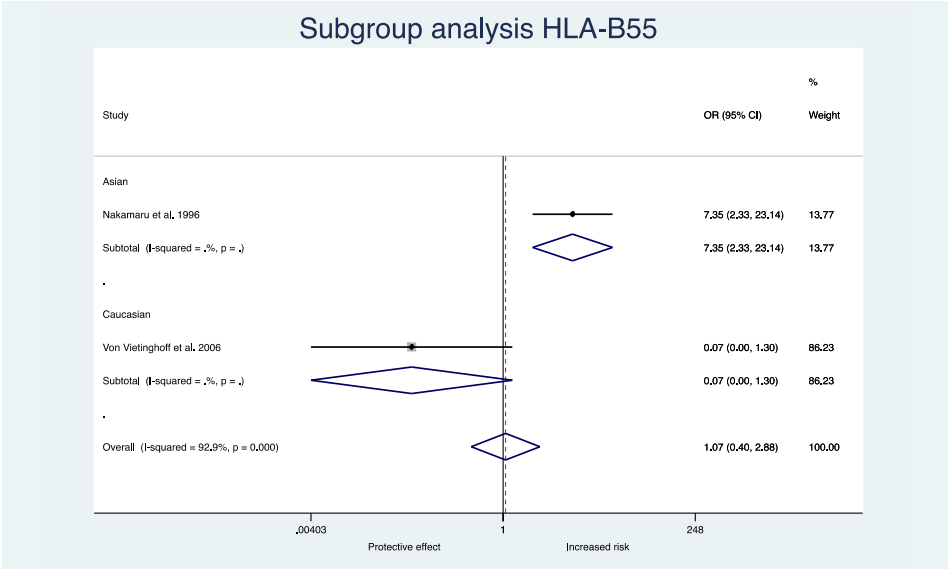
Supplementary figure 3. Forest plots by ethnic subgroups



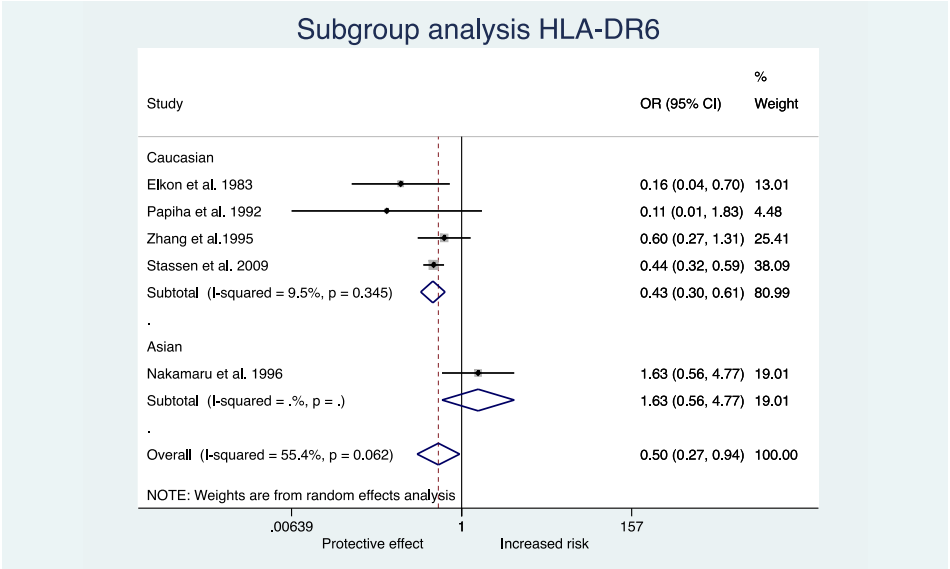
References: [4], [5], [6], [7]



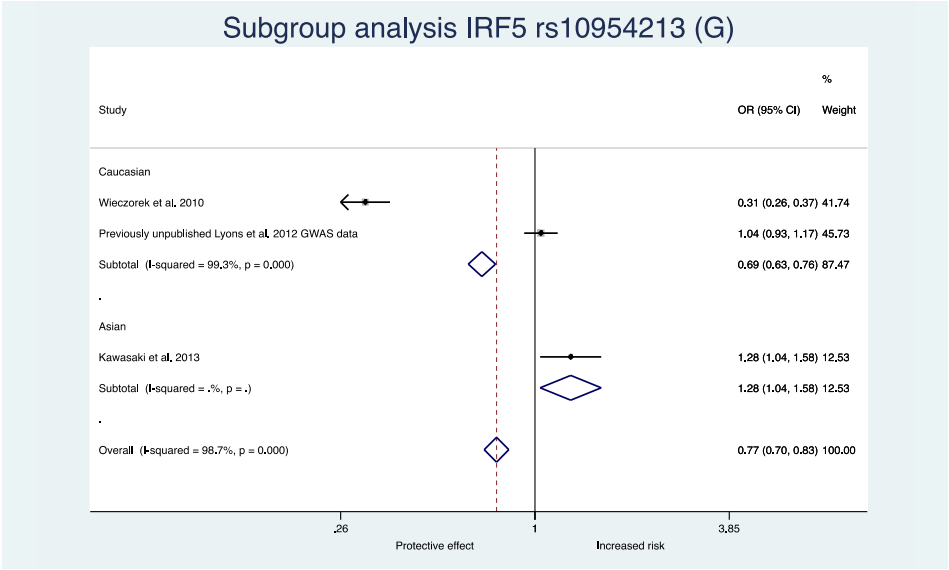
References: [4], [5], [7]



References: [20], [18]



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



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

References

1. Wieczorek S, Hoffjan S, Chan A, *et al.* Novel association of the CD226 (DNAM-1) Gly-307Ser polymorphism in Wegener's granulomatosis and confirmation for multiple sclerosis in German patients. *Genes Immun* 2009;10:591-5.
2. Chung SA, Xie G, Roshandel D, *et al.* Meta-analysis of genetic polymorphisms in granulomatosis with polyangiitis (Wegener's) reveals shared susceptibility loci with rheumatoid arthritis. *Arthritis Rheum* 2012;64:3463-71.
3. Lyons PA, Rayner TF, Trivedi S, *et al.* Genetically distinct subsets within ANCA-associated vasculitis. *N Engl J Med* 2012;367:214-23.
4. Huang D, Giscombe R, Zhou Y, *et al.* Polymorphisms in CTLA-4 but not tumor necrosis factor-alpha or interleukin 1beta genes are associated with Wegener's granulomatosis. *J Rheumatol* 2000;27:397-401.
5. Tsuchiya N, Kobayashi S, Kawasaki A, *et al.* Genetic background of Japanese patients with antineutrophil cytoplasmic antibody-associated vasculitis: association of HLA-DRB1*0901 with microscopic polyangiitis. *J Rheumatol* 2003;30:1534-40.
6. Zhou Y, Huang D, Paris PL, *et al.* An analysis of CTLA-4 and proinflammatory cytokine genes in Wegener's granulomatosis. *Arthritis Rheum* 2004;50:2645-50.
7. Persson U, Gullstrand B, Pettersson A, *et al.* A candidate gene approach to ANCA-associated vasculitis reveals links to the C3 and CTLA-4 genes but not to the IL1-Ra and Fcgamma-RIIa genes. *Kidney Blood Press Res* 2013;37:641-8.
8. Slot MC, Sokolowska MG, Savelkouls KG, *et al.* Immunoregulatory gene polymorphisms are associated with ANCA-related vasculitis. *Clin Immunol* 2008;128:39-45.
9. Kamesh L, Heward JM, Williams JM, *et al.* CT60 and +49 polymorphisms of CTLA 4 are associated with ANCA-positive small vessel vasculitis. *Rheumatology (Oxford)* 2009;48:1502-5.
10. Kelley JM, Monach PA, Ji C, *et al.* IgA and IgG antineutrophil cytoplasmic antibody engagement of Fc receptor genetic variants influences granulomatosis with polyangiitis. *Proc Natl Acad Sci U S A* 2011;108:20736-41.
11. Edberg JC, Wainstein E, Wu J, *et al.* Analysis of FcgammaRII gene polymorphisms in Wegener's granulomatosis. *Exp Clin Immunogenet* 1997;14:183-95.
12. Dijstelbloem HM, Scheepers RH, Oost WW, *et al.* Fcgamma receptor polymorphisms in Wegener's granulomatosis: risk factors for disease relapse. *Arthritis Rheum* 1999;42:1823-7.
13. Tse WY, Abadeh S, McTiernan A, *et al.* No association between neutrophil FcgammaRIIa allelic polymorphism and anti-neutrophil cytoplasmic antibody (ANCA)-positive systemic vasculitis. *Clin Exp Immunol* 1999;117:198-205.
14. Tse WY, Abadeh S, Jefferis R, *et al.* Neutrophil FcgammaRIIIb allelic polymorphism in anti-neutrophil cytoplasmic antibody (ANCA)-positive systemic vasculitis. *Clin Exp Immunol* 2000;119:574-7.
15. Wieczorek S, Holle JU, Bremer JP, *et al.* Contrasting association of a non-synonymous leptin receptor gene polymorphism with Wegener's granulomatosis and Churg-Strauss syndrome. *Rheumatology (Oxford)* 2010;49:907-14.
16. Strimlan CV, Taswell HF, Kueppers F, *et al.* HLA-A antigens of patients with Wegener's granulomatosis. *Tissue Antigens* 1978;11:129-31.
17. Murty GE, Mains BT, Middleton D, *et al.* HLA antigen frequencies and Wegener's

granulomatosis. *Clin Otolaryngol Allied Sci* 1991;16:448-51.

18. von Vietinghoff S, Busjahn A, Schonemann C, *et al.* Major histocompatibility complex HLA region largely explains the genetic variance exercised on neutrophil membrane proteinase 3 expression. *J Am Soc Nephrol* 2006;17:3185-91.
19. Stassen PM, Cohen-Tervaert JW, Lems SP, *et al.* HLA-DR4, DR13(6) and the ancestral haplotype A1B8DR3 are associated with ANCA-associated vasculitis and Wegener's granulomatosis. *Rheumatology (Oxford)* 2009;48:622-5.
20. Nakamaru Y, Maguchi S, Takizawa M, *et al.* The association between human leukocyte antigens (HLA) and cytoplasmic-antineutrophil cytoplasmic antibody (cANCA)-positive Wegener's granulomatosis in a Japanese population. *Rhinology* 1996;34:163-5.
21. Katz P, Alling DW, Haynes BF, *et al.* Association of Wegener's granulomatosis with HLA-B8. *Clin Immunol Immunopathol* 1979;14:268-70.
22. Papasteriades C, Hatziyannakos D, Siakotos M, *et al.* HLA antigens in microscopic polyarteritis (MP) with renal involvement. *Dis Markers* 1997;13:117-22.
23. Elkon KB, Sutherland DC, Rees AJ, *et al.* HLA antigen frequencies in systemic vasculitis: increase in HLA-DR2 in Wegener's granulomatosis. *Arthritis Rheum* 1983;26:102-5.
24. Heckmann M, Holle JU, Arning L, *et al.* The Wegener's granulomatosis quantitative trait locus on chromosome 6p21.3 as characterised by tagSNP genotyping. *Ann Rheum Dis* 2008;67:972-9.
25. Xie G, Roshandel D, Sherva R, *et al.* Association of granulomatosis with polyangiitis (Wegener's) with HLA-DPB1*04 and SEMA6A gene variants: evidence from genome-wide analysis. *Arthritis Rheum* 2013;65:2457-68.
26. Zhang L, Jayne DR, Zhao MH, *et al.* Distribution of MHC class II alleles in primary systemic vasculitis. *Kidney Int* 1995;47:294-8.
27. Jagiello P, Gencik M, Arning L, *et al.* New genomic region for Wegener's granulomatosis as revealed by an extended association screen with 202 apoptosis-related genes. *Hum Genet* 2004;114:468-77.
28. Tsuchiya N, Kobayashi S, Hashimoto H, *et al.* Association of HLA-DRB1*0901-DQB1*0303 haplotype with microscopic polyangiitis in Japanese. *Genes Immun* 2006;7:81-4.
29. Wieczorek S, Hellmich B, Gross WL, *et al.* Associations of Churg-Strauss syndrome with the HLA-DRB1 locus, and relationship to the genetics of antineutrophil cytoplasmic antibody-associated vasculitides: comment on the article by Vaglio et al. *Arthritis Rheum* 2008;58:329-30.
30. Arning L, Holle JU, Harper L, *et al.* Are there specific genetic risk factors for the different forms of ANCA-associated vasculitis? *Ann Rheum Dis* 2011;70:707-8.
31. Spriewald BM, Witzke O, Wassmuth R, *et al.* Distinct tumour necrosis factor alpha, interferon gamma, interleukin 10, and cytotoxic T cell antigen 4 gene polymorphisms in disease occurrence and end stage renal disease in Wegener's granulomatosis. *Ann Rheum Dis* 2005;64:457-61.
32. Papiha SS, Murty GE, Ad'Hia A, *et al.* Association of Wegener's granulomatosis with HLA antigens and other genetic markers. *Ann Rheum Dis* 1992;51:246-8.
33. Cao Y, Schmitz JL, Yang J, *et al.* DRB1*15 allele is a risk factor for PR3-ANCA disease in African Americans. *J Am Soc Nephrol* 2011;22:1161-7.
34. Luo H, Chen M, Yang R, *et al.* The association of HLA-DRB1 alleles with antineutrophil cytoplasmic antibody-associated systemic vasculitis in Chinese patients. *Hum Immunol* 2011;72:422-5.

35. Vaglio A, Martorana D, Maggiore U, *et al.* HLA-DRB4 as a genetic risk factor for Churg-Strauss syndrome. *Arthritis Rheum* 2007;56:3159-66.
36. Fujii A, Tomizawa K, Arimura Y, *et al.* Epitope analysis of myeloperoxidase (MPO) specific anti-neutrophil cytoplasmic autoantibodies (ANCA) in MPO-ANCA-associated glomerulonephritis. *Clin Nephrol* 2000;53:242-52.
37. Tsuchiya N. Genetics of ANCA-associated vasculitis in Japan: a role for HLA-DRB1*09:01 haplotype. *Clin Exp Nephrol* 2013;17:628-30.
38. Spencer SJ, Burns A, Gaskin G, *et al.* HLA class II specificities in vasculitis with antibodies to neutrophil cytoplasmic antigens. *Kidney Int* 1992;41:1059-63.
39. Borgmann S, Endisch G, Hacker UT, *et al.* Proinflammatory genotype of interleukin-1 and interleukin-1 receptor antagonist is associated with ESRD in proteinase 3-ANCA vasculitis patients. *Am J Kidney Dis* 2003;41:933-42.
40. Husmann CA, Holle JU, Moosig F, *et al.* Genetics of toll like receptor 9 in ANCA associated vasculitides. *Ann Rheum Dis* 2014;73:890-6.
41. Wieczorek S, Hellmich B, Arning L, *et al.* Functionally relevant variations of the interleukin-10 gene associated with antineutrophil cytoplasmic antibody-negative Churg-Strauss syndrome, but not with Wegener's granulomatosis. *Arthritis Rheum* 2008;58:1839-48.
42. Murakozy G, Gaede KI, Ruprecht B, *et al.* Gene polymorphisms of immunoregulatory cytokines and angiotensin-converting enzyme in Wegener's granulomatosis. *J Mol Med (Berl)* 2001;79:665-70.
43. Bartfai Z, Gaede KI, Russell KA, *et al.* Different gender-associated genotype risks of Wegener's granulomatosis and microscopic polyangiitis. *Clin Immunol* 2003;109:330-7.
44. Wieczorek S, Holle JU, Muller S, *et al.* A functionally relevant IRF5 haplotype is associated with reduced risk to Wegener's granulomatosis. *J Mol Med (Berl)* 2010;88:413-21.
45. Kawasaki A, Inoue N, Ajimi C, *et al.* Association of IRF5 polymorphism with MPO-ANCA-positive vasculitis in a Japanese population. *Genes Immun* 2013;14:527-9.
46. Reynolds WF, Stegeman CA, Tervaert JW. -463 G/A myeloperoxidase promoter polymorphism is associated with clinical manifestations and the course of disease in MPO-ANCA-associated vasculitis. *Clin Immunol* 2002;103:154-60.
47. Fiebeler A, Borgmann S, Woywodt A, *et al.* No association of G-463A myeloperoxidase gene polymorphism with MPO-ANCA-associated vasculitis. *Nephrol Dial Transplant* 2004;19:969-71.
48. Rajp A, Adu D, Savage CO. Meta-analysis of myeloperoxidase G-463/A polymorphism in anti-neutrophil cytoplasmic autoantibody-positive vasculitis. *Clin Exp Immunol* 2007;149:251-6.
49. Sakthivel P, Giscombe R, Ramanujam R, *et al.* Polymorphisms in PDCD1 gene are not associated with Wegener's granulomatosis. *Rheumatol Int* 2009;29:1247-50.
50. Jagiello P, Aries P, Arning L, *et al.* The PTPN22 620W allele is a risk factor for Wegener's granulomatosis. *Arthritis Rheum* 2005;52:4039-43.
51. Martorana D, Maritati F, Malerba G, *et al.* PTPN22 R620W polymorphism in the ANCA-associated vasculitides. *Rheumatology (Oxford)* 2012;51:805-12.
52. Szyld P, Jagiello P, Csernok E, *et al.* On the Wegener granulomatosis associated region on chromosome 6p21.3. *BMC Med Genet* 2006;7:21.
53. Wieczorek S, Knaup S, Gross WL, *et al.* Genetic variability of RXRB, PPARA, and PPARG in Wegener's granulomatosis. *PPAR Res* 2009;2009:786781.
54. Lhotta K, Vogel W, Meisl T, *et al.* Alpha

1-antitrypsin phenotypes in patients with anti-neutrophil cytoplasmic antibody-positive vasculitis. *Clin Sci (Lond)* 1994;87:693-5.

55. Griffith ME, Lovegrove JU, Gaskin G, *et al.* C-antineutrophil cytoplasmic antibody positivity in vasculitis patients is associated with the Z allele of alpha-1-antitrypsin, and P-antineutrophil cytoplasmic antibody positivity with the S allele. *Nephrol Dial Transplant* 1996;11:438-43.
56. Mahr AD, Edberg JC, Stone JH, *et al.* Alpha(1)-antitrypsin deficiency-related alleles Z and S and the risk of Wegener's granulomatosis. *Arthritis Rheum* 2010;62:3760-7.
57. Morris H, Morgan MD, Wood AM, *et al.* ANCA-associated vasculitis is linked to carriage of the Z allele of alpha(1) antitrypsin and its polymers. *Ann Rheum Dis* 2011;70:1851-6.
58. Chorostowska-Wynimko J, Gawryluk D, Struniawski R, *et al.* Incidence of alpha-1 antitrypsin Z and S alleles in patients with granulomatosis with polyangiitis - pilot study. *PneumonolAlergolPol* 2013;81:319-22.
59. Callea F, Gregorini G, Sinico A, *et al.* alpha 1-Antitrypsin (AAT) deficiency and ANCA-positive systemic vasculitis: genetic and clinical implications. *Eur J Clin Invest* 1997;27:696-702.
60. Borgmann S, Endisch G, Urban S, *et al.* A linkage disequilibrium between genes at the serine protease inhibitor gene cluster on chromosome 14q32.1 is associated with Wegener's granulomatosis. *Clin Immunol* 2001;98:244-8.
61. Mascher B, Schmitt W, Csernok E, *et al.* Polymorphisms in the tumor necrosis factor genes in Wegener's granulomatosis. *Exp Clin Immunogenet* 1997;14:226-33.

II. Supplementary data Chapter III

Renal function and ear, nose, throat involvement in ANCA associated vasculitis: prospective data from the European Vasculitis Society clinical trials

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Supplementary table 1. ENT manifestations

ENT symptom	Patients
Nasal obstruction	76 (43)
Bloody nasal discharge	70 (40)
Nasal crusting	60 (34)
Sinus involvement	45 (25)
Hearing loss	46 (26)
Hoarseness/stridor	12 (7)
Otorhinolaryngologist's opinion	
Granulomatous sinusitis	28 (16)
Conductive hearing loss	20 (11)
Sensorineural hearing loss	9 (5)
Significant subglottic inflammation	4 (2)

All data are presented as n (%). ENT symptoms scored using the Birmingham Vasculitis Activity Score are shown. Data were available for 177 of the 185 patients with ENT involvement. Percentages are expressed relative to the number of patients with ENT involvement. All items below 'otorhinolaryngologist's opinion' were only scored by the otorhinolaryngologist. ENT, ear-, nose-, and throat**.**

Supplementary table 2. Associations between ENT symptoms and ANCA-subtype in patients with ENT involvement

ENT symptom	PR3-ANCA patients (n=116)	MPO-ANCA patients (n=46)	P Value
Nasal obstruction	57 (49)	14 (30)	0.03
Bloody nasal discharge	45 (39)	19 (41)	0.77
Nasal crusting	43 (37)	13 (28)	0.29
Sinus involvement	30 (26)	13 (28)	0.76
Hearing loss	34 (29)	7 (15)	0.06
Hoarseness/stridor	7 (6)	5 (11)	0.30
Otorhinolaryngologist's opinion			
Granulomatous sinusitis	25 (22)	2 (4)	0.008
Conductive hearing loss	16 (14)	3 (7)	0.20
Sensorineural hearing loss	5 (4)	2 (4)	0.99
Significant subglottic inflammation	2 (2)	2 (4)	0.33

Data are presented as n (%). The distribution of ANCA-subtype in patients with ENT involvement is shown. Data regarding the specific ENT symptoms were available for 177 of the 185 patients with ENT involvement. All 8 patients with missing ENT symptoms data were PR3-ANCA positive. All items listed under 'otorhinolaryngologist's opinion' were scored by the otorhinolaryngologist alone. ENT, ear-, nose-, and throat; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; MPO-ANCA, anti-myeloperoxidase anti-neutrophil cytoplasm antibody.

Supplementary table 3. Associations between ENT symptoms and baseline eGFR

ENT symptom	eGFR in symptom+ patients (mL/min/1.73 m^2)	eGFR in symptom- patients (mL/min/1.73 m^2)	95% CI	P Value
Nasal obstruction	43.09	26.59	9.91 – 23.10	<0.001
Bloody nasal discharge	37.81	28.05	2.82 – 16.71	0.006
Nasal crusting	43.25	27.36	8.60 – 23.19	<0.001
Sinus involvement	36.38	28.93	-0.95 – 15.84	0.08
Hearing loss	36.78	28.86	-0.40 – 16.23	0.06
Hoarseness/stridor	28.70	29.82	-16.72 – 14.47	0.89
Otorhinolaryngologist's opinion				
Granulomatous sinusitis	41.56	28.88	2.32 – 23.03	0.02
Conductive hearing loss	44.89	29.98	3.80 – 28.02	0.01
Sensorineural hearing loss	26.88	29.86	-20.91 – 14.96	0.74
Significant subglottic inflammation	45.53	29.63	-10.78 – 42.60	0.24

ENT symptoms were scored using the Birmingham Vasculitis Activity Score. Data regarding the specific ENT symptoms were available for 177 of the 185 patients with ENT involvement. All items listed under 'otorhinolaryngologist's opinion' were scored by the otorhinolaryngologist alone. ENT, ear-, nose-, and throat; eGFR, estimated glomerular filtration rate.

Supplementary table 4. Correlations of clinical and histological parameters with baseline and 5-year follow-up eGFR

	Baseline eGFR		5-year follow-up eGFR	
	r	p Value	r	P Value
ENT involvement	0,274	< 0.001	0,224	0.005
Age	-0,379	< 0.001	-0,395	< 0.001
PR3-ANCA	0,240	< 0.001	0,097	<0.24
Tubulitis	-0,445	< 0.001	-0,266	0.12
Interstitial infiltrate	-0,477	< 0.001	-0,396	< 0.001
IFTA	-0,436	< 0.001	-0,477	< 0.001
AAGN classification	-0,424	< 0.001	-0,511	< 0.001

ENT, ear-, nose-, and throat; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; IFTA, interstitial fibrosis and tubular atrophy; AAGN, anti-neutrophil cytoplasm antibody associated glomerulonephritis; eGFR, estimated glomerular filtration rate.

Supplementary table 5. Three multivariable regression models investigating the association between ENT involvement and baseline eGFR

Model 1	**β (95% CI)**	**P Value**
ENT involvement	10.40 (5.24 – 15.55)	< 0.001
Age	-0.65 (-0.82 – -0.47)	< 0.001
PR3-ANCA	6.21 (1.03 – 11.38)	0.02

Model 2	**β (95% CI)**	**P Value**
ENT involvement	10.32 (4.05 – 16.59)	0.001
Age	-0.46 (-0.68 – -0.24)	< 0.001
PR3-ANCA	-1.43 (-7.73 – 4.88)	0.66
Tubulitis	-13.93 (-20.87 – -6.99)	< 0.001
Interstitial infiltrate	-8.56 (-12.64 – -4.47)	< 0.001
IFTA	-10.54 (-15.61 – -5.47)	< 0.001

Model 3	**β (95% CI)**	**P Value**
ENT involvement	9.14 (2.30 – 15.98)	0.009
Age	-0.60 (-0.83 – -0.36)	< 0.001
PR3-ANCA	-1.26 (-8.28 – 5.75)	0.71
Tubulitis	-17.82 (-25.78 – -9.86)	< 0.001
Interstitial infiltrate	-6.86 (-11.20 – -2.52)	0.002
IFTA	-8.72 (-14.67 – -2.77)	0.004
AAGN classification	-6.20 (-9.84 – -2.57)	0.001

Since renal biopsies were not available for all patients, including the histopathological parameters limited the number of patients included in the analysis. To be able to include all patients we therefore created three models. The first model included only clinical parameters (n=412). In the second model, we added tubulointerstitial parameters (n=195). The third model, we added the histopathological classification (n=149). In all models, age is included per year unit. ENT involvement was significantly associated with higher baseline eGFR. 95% CI, 95% confidence interval; ENT, ear-, nose-, and throat; eGFR, estimated glomerular filtration rate; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; IFTA, interstitial fibrosis and tubular atrophy; AAGN, anti-neutrophil cytoplasm antibody associated glomerulonephritis.

Supplementary table 6. Multivariable regression analyses investigating the relationship between ENT involvement and eGFR in GPA patients

	β (95% CI)	**P Value**
ENT involvement	12.44 (0.08 – 24.80)	0.04
Age	-1.26 (-8.28 – 5.75)	0.02
PR3-ANCA	-5.17 (-17.02 – 6.68)	0.39
Tubulitis	-9.47 (-23.10 – 4.15)	0.17
Interstitial infiltrate	-16.29 (-24.93 – -7.64)	< 0.001
IFTA	-9.35 (-18.46 – -0.24)	0.01
AAGN classification	-9.79 (-15.58 – -4.00)	0.001

ENT involvement is associated with higher baseline eGFR in GPA patients. Age is included per year unit in the model. 95% CI, 95% confidence interval; ENT, ear-, nose-, and throat; eGFR, estimated glomerular filtration rate; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; IFTA, interstitial fibrosis and tubular atrophy; AAGN, anti-neutrophil cytoplasm antibody associated glomerulonephritis.

Supplementary table 7. Multivariable regression analyses investigating the relationship between ENT involvement and 5-year follow-up eGFR

	Model investigating 5-year follow-up eGFR		**Model investigating 5-year follow-up eGFR in PR3-ANCA positive patients**	
	β (95% CI)	P Value	β (95% CI)	P Value
ENT involvement	2.12 (-4.90 – 9.14)	0.55	8.10 (-1.73 – 17.93)	0.10
Age	-0.27 (-0.52 – -0.03)	0.03	-0.03 (-0.37 – 0.30)	0.84
PR3-ANCA	-6.28 (-13.33 – 0.77)	0.08	N/A	N/A
Baseline eGFR	0.33 (0.17 – 0.48)	< 0.001	0.43 (0.24 – 0.61)	< 0.001
Tubulitis	4.25 (-4.43 – 12.92)	0.33	-1.92 (-13.49 – 9.64)	0.74
Interstitial infiltrate	-2.42 (-8.13 – 3.29)	0.40	-0.86 (-9.05 – 7.32)	0.83
IFTA	-1.65 (-8.23 – 4.92)	0.62	-2.73 (-11.14 – 5.69)	0.52
AAGN classification	-5.44 (-9.71 – -1.17)	0.01	N/A	N/A

ENT involvement is no longer associated with 5-year follow-up eGFR when baseline eGFR is included in the model. Both models are adjusted for within-trial therapy. Age is included per year unit in both models. 95% CI, 95% confidence interval; ENT, ear-, nose-, and throat; eGFR, estimated glomerular filtration rate; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; IFTA, interstitial fibrosis and tubular atrophy; AAGN, anti-neutrophil cytoplasm antibody associated glomerulonephritis; N/A, not applicable.

Supplementary table 8. Three multivariable regression models investigating the association between baseline eGFR and other early disease manifestations

	Cutaneous model		Arthralgia/arthritis model		Lung model	
Model 1	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**
Cutaneous involvement	5.61 (-0.27 – 11.49)	0.06	N/A	N/A	N/A	N/A
Arthralgia/arthritis	N/A	N/A	3.40 (-1.67 – 8.48)	0.19	N/A	N/A
Lung involvement	N/A	N/A	N/A	N/A	-2.63 (-7.56 – 2.30)	0.30
Age	-0.66 (-0.84 – -0.48)	< 0.001	-0.63 (-0.81 – -0.45)	< 0.001	-0.69 (-0.87 – -0.51)	< 0.001
PR3-ANCA	8.78 (3.74 – 13.82)	0.001	8.73 (3.65 – 13.80)	0.001	9.58 (4.56 – 14.60)	< 0.001
Model 2	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**
Cutaneous involvement	-0.76 (-8.47 – 6.95)	0.85	N/A	N/A	N/A	N/A
Arthralgia/arthritis	N/A	N/A	-1.74 (-7.94 – 4.46)	0.58	N/A	N/A
Lung involvement	N/A	N/A	N/A	N/A	-5.46 (-11.46 – 0.53)	0.07
Age	-0.48 (-0.71 – -0.25)	< 0.001	-0.40 (-0.63 – -0.16)	0.001	-0.48 (-0.71 – -0.25)	< 0.001
PR3-ANCA	1.45 (-4.81 – 7.70)	0.65	0.67 (-5.65 – 6.99)	0.83	2.57 (-3.74 – 8.89)	0.42
Tubulitis	-13.12 (-20.27 – -5.97)	< 0.001	-11.02 (-18.30 – -3.74)	0.003	-13.20 (-20.25 – -6.14)	< 0.001
Interstitial infiltrate	-8.86 (-13.06 – -4.66)	< 0.001	-9.21 (-13.46 – -4.95)	< 0.001	-8.75 (-12.91 – -4.59)	< 0.001
IFTA	-11.97 (-17.11 – -6.84)	< 0.001	-11.89 (-17.16 – -6.62)	< 0.001	-12.07 (-17.16 – -6.98)	< 0.001
Model 3	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**
Cutaneous involvement	-2.98 (-11.58 – 5.62)	0.49	N/A	N/A	N/A	N/A
Arthralgia/arthritis	N/A	N/A	-4.85 (-11.40 – 1.71)	0.15	N/A	N/A
Lung involvement	N/A	N/A	N/A	N/A	-4.74 (-11.19 – 1.70)	0.15
Age	-0.63 (-0.87 – -0.38)	<0.001	-0.54 (-0.78 – -0.29)	<0.001	-0.61 (-0.85 – -0.37)	<0.001
PR3-ANCA	1.29 (-5.62 – 8.21)	0.71	0.41 (-6.52 – 7.33)	0.91	1.86 (-5.06 – 8.78)	0.60

Supplementary table 8. Three multivariable regression models investigating the association between baseline eGFR and other early disease manifestations (Continued)

	Cutaneous model		Arthralgia/arthritis model		Lung model	
Model 3	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**	**β (95% CI)**	**P Value**
Tubulitis	-16.54 (-24.62 – -8.47)	<0.001	-14.71 (-22.91 – -6.50)	0.01	-16.83 (-24.87 – -8.79)	<0.001
Interstitial infiltrate	-7.48 (-11.96 – -3.00)	0.001	-7.38 (-11.83 – -2.93)	0.001	-7.12 (-11.53 – -2.71)	0.002
IFTA	-9.57 (-15.62 – -3.51)	0.002	-9.92 (-16.01 – -3.83)	0.002	-9.97 (-15.97 – -3.97)	0.001
AAGN classification	-6.82 (-10.61 – -3.03)	0.001	-6.98 (-10.79 – -3.17)	<0.001	-6.79 (-10.49 – -3.09)	<0.001

Since renal biopsies were not available for all patients, including the histopathological parameters limited the number of patients included in the analysis. To be able to include all patients we therefore created three models. The first model included only clinical parameters (n=412). In the second model, we added tubulointerstitial parameters (n=195). The third model, we added the histopathological classification (n=149). In all models, age is included per year unit. 95% CI, 95% confidence interval; eGFR, estimated glomerular filtration rate; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; IFTA, interstitial fibrosis and tubular atrophy; AAGN, anti-neutrophil cytoplasm antibody associated glomerulonephritis.

Supplementary table 9. Multivariable regression analyses investigating the relationships between 5-year follow-up eGFR and other early disease manifestations

	Cutaneous model		Arthralgia/arthritis model		Lung model	
	β (95% CI)	P Value	β (95% CI)	P Value	β (95% CI)	P Value
Cutaneous involvement	0.78 (-8.80 – 10.35)	0.87	N/A	N/A	N/A	N/A
Arthralgia/arthritis	N/A	N/A	0.00 (-8.62 – 8.62)	0.99	N/A	N/A
Lung involvement	N/A	N/A	N/A	N/A	6.99 (-1.19 – 15.17)	0.09
Age	-0.37 (-0.67 – -0.07)	0.02	-0.32 (-0.63 – -0.01)	0.04	-0.32 (-0.61 – -0.03)	0.03
PR3-ANCA	-4.19 (-12.48 – 4.09)	0.32	-5.39 (-13.67 – 2.89)	0.20	-5.66 (-13.97 – 2.65)	0.18
Tubulitis	-3.68 (-12.87 – 5.50)	0.43	-0.96 (-10.45 – 8.53)	0.84	-2.70 (-11.76 – 6.36)	0.56
Interstitial infiltrate	-4.84 (-11.66 – 1.99)	0.16	-6.89 (-13.77 – -0.02)	0.05	-4.74 (-11.42 – 1.94)	0.16
IFTA	-10.07 (-16.84 – -3.29)	0.004	-10.74 (-17.91 – -3.57)	0.004	-10.12 (-16.75 – -3.48)	0.003

To investigate whether our associations are specific to ENT involvement, analyses between eGFR at 5-year follow-up and other early disease manifestations were performed. There are no associations between eGFR at 5-year follow-up and cutaneous involvement, arthralgia/arthritis, or lung involvement. All models are adjusted for within-trial therapy. In all models, age is included per year unit. 95% CI, 95% confidence interval; eGFR, estimated glomerular filtration rate; PR3-ANCA, anti-proteinase 3 anti-neutrophil cytoplasm antibody; IFTA, interstitial fibrosis and tubular atrophy; AAGN, anti-neutrophil cytoplasm antibody associated glomerulonephritis; N/A, not applicable

III. Supplementary data Chapter VI

Effect of rituximab on malignancy risk in patients with ANCA-associated vasculitis

Table S1. Subgroup analysis *312*

Table S2. Cyclophosphamide and rituximab treatment in the subgroups *313*

Table S3. SIR according to cumulative cyclophosphamide and rituximab dose *314*

Table S4. Treatment dose of each patient with a malignancy *314*

Supplementary table 1. Subgroup analysis

	N patients	N observed malignancies	SIR (95% CI)*	SIR p value*	RR (95% CI)*	RR p value*
Gender						
Male	149	20	1.58 (0.96–2.44)	0.07	1 (reference)	
Female	174	25	2.25 (1.45–3.32)	<0.001	1.43 (0.76–2.71)	0.30
Age at diagnosis						
≥59 years	159	29	1.60 (1.07–2.29)	0.02	1 (reference)	
<59 years	164	16	2.84 (1.62–4.61)	<0.001	1.78 (0.90–3.38)	0.10
Clinical diagnosis						
Microscopic polyangiitis	160	23	1.59 (1.01–2.38)	0.05	1 (reference)	
Granulomatosis with polyangiitis	109	14	2.20 (1.20–3.68)	0.01	1.39 (0.66–2.81)	0.43
Eosinophilic granulomatosis with polyangiitis	54	8	2.75 (1.19–5.41)	0.02	1.73 (0.67–4.02)	0.27
ANCA serotype†						
MPO-ANCA	110	15	1.56 (0.87–2.58)	0.13	1 (reference)	
PR3-ANCA	152	24	2.18 (1.40–3.25)	<0.001	1.40 (0.70–2.87)	0.39
Renal transplantation						
No	311	41	1.79 (1.29–2.43)	<0.001	1 (reference)	
Yes	12	4	4.31 (1.17–11.04)	0.03	2.40 (0.62–6.62)	0.20
Follow-up						
0–5 years	156	16	2.38 (1.36–3.86)	<0.001	1 (reference)	
5–10 years	135	23	1.81 (1.15–2.72)	0.01	0.76 (0.39–1.54)	0.50
>10 years	32	6	1.38 (0.51 – 3.00)	0.55	0.58 (0.19–1.56)	0.35

* The standard incidence ratio (SIR) is the ratio of observed to expected malignancies and represents the malignancy risk compared to the general population, and the relative risk (RR) represents the malignancy risk compared to the reference group. Calculated by exact Poisson regression analysis.

† Unknown for 61 patients.

MPO-ANCA, myeloperoxidase ANCA; PR3-ANCA, proteinase 3 ANCA.

Supplementary table 2. Cyclophosphamide and rituximab treatment in the subgroups

	N patients treated with cyclophosphamide	Duration of cyclophosphamide treatment, months (SD)	Mean cumulative cyclophosphamide dose, g (SD)	N patients treated with rituximab	Duration of rituximab treatment, months (SD)	Mean cumulative rituximab dose, g (SD)
Gender						
Male	107	5.5 (5.5)	9.9 (6.5)	68	22.1 (14.9)	5.8 (3.4)
Female	116	6.4 (14.4)	8.4 (10.8)	85	20.9 (14.4)	5.9 (3.4)
Age at diagnosis						
≥59 years	114	6.5 (13.8)	6.8 (3.9)	63	20.2 (14.2)	5.2 (2.9)
<59 years	109	5.1 (4.2)	11.5 (11.8)	90	22.5 (14.9)	6.3 (3.6)
Clinical diagnosis						
Microscopic polyangiitis	116	6.3 (12.6)	8.1 (10.5)	65	18.7 (13.3)	5.2 (2.6)
Granulomatosis with polyangiitis	88	5.4 (4.4)	10.7 (7.3)	66	27.7 (15.0)	6.7 (4.0)
Eosinophilic granulomatosis with polyangiitis	19	4.5 (2.8)	7.8 (4.2)	22	22.6 (15.7)	5.3 (2.9)
ANCA serotype*						
MPO-ANCA	72	7.4 (16.1)	7.2 (4.7)	43	20.7 (16.9)	5.1 (2.9)
PR3-ANCA	121	5.0 (4.2)	9.2 (6.5)	82	20.9 (13.0)	6.1 (3.3)
Renal transplantation						
No	213	5.2 (4.9)	9.1 (9.0)	149	21.6 (14.4)	5.9 (3.4)
Yes	10	15.6 (37.3)	8.5 (8.6)	4	16.7 (19.4)	4.5 (2.4)
Follow-up						
0–5 years	102	4.7 (3.5)	7.0 (4.6)	52	17.5 (10.9)	4.6 (2.8)
5–10 years	101	7.2 (15.5)	10.8 (11.9)	82	23.5 (15.2)	6.3 (3.6)
>10 years	20	5.4 (5.1)	10.9 (6.8)	19	24.6 (19.6)	7.4 (3.1)

* Unknown for 61 patients.

MPO-ANCA, myeloperoxidase ANCA; PR3-ANCA, proteinase 3 ANCA.

Supplementary table 3. SIR for non-melanoma skin cancer according to cumulative cyclophosphamide and rituximab dose*

Cumulative dose (g)	N patients	N observed non-melanoma skin cancer	SIR (95% CI)†	SIR p value†
Cyclophosphamide				
0	89	3	2.17 (0.45– 6.34)	0.16
0.1–20	207	18	4.89 (2.90 – 7.72)	<0.001
20–108	16	3	11.72 (2.42 – 34.25)	0.002
Rituximab				
0	167	23	8.47 (5.37 – 12.71)	<0.001
0.1–6	70	1	0.83 (0.02 – 4.64)	0.66
6–18	83	0	0 (0 – 2.47)	0.23

* SIR, standardised incidence ratio; the SIR is the ratio of the observed to expected malignancies adjusted for sex, age (per 5-year age group), and calendar time period (per 1-year calendar time period).
† Calculated by exact Poisson regression analysis.

Supplementary table 4. Cumulative cyclophosphamide and rituximab dose of each patient with a malignancy

Malignancy or malignancy site	N observed malignancies	Cumulative cyclophosphamide dose (g)*	Cumulative rituximab dose (g)*	Time to malignancy (years)†
Lung	4	36.0; 21.1; 4.9; 0.0	0.0; 7.0; 0.0; 5.0	3.7; 4.8; 0.5; 8.5
Breast	3	18.0; 6.0; 3.4	0; 4.0; 8.0	0.9; 1.1; 4.0
Colon or rectum	3	13.8; 9.5; 4.0	0.0; 0.0; 0.0	2.4; 4.5; 4.0
Prostate	2	10.0; 0.0	0.0; 0.0	7.4; 1.2
Bladder	1	0.0	1.0	2.4
Pancreas	1	0.0	0.0	1.4
Testis	1	7.0	5.0	4.6
Ovary	1	3.0	6.6	2.4
Melanoma	1	3.3	0.0	1.8
Tongue	1	0.0	0.0	4.5
Central nervous system	1	2.0	5.6	3.2
Kidney	1	7.0	4.0	2.4

* The cumulative doses of each patient with a malignancy is given. Patients with a cumulative dose of 0.0 did not receive the treatment. When more cases of the malignancy were observed, the first reported cumulative cyclophosphamide dose corresponds to the first reported cumulative rituximab dose, and to the first reported time to malignancy.
† This is the time between the date of diagnosis of ANCA-associated vasculitis and the date of diagnosis of the malignancy.