Supplementary Table A. Assessment of heterogeneity and publication bias for trials included in traditional pair-wise meta-analyses

Treatment comparisons	I^2	P value of Cochrane Q-test	P value of Egger's test	P value of Begg's test
All-cause mortality				
ACEI vs Placebo	0.0%	0.80	0.83	0.22
ARB vs Placebo	0.0%	0.85	0.22	0.21
CCB vs Placebo	0.0%	0.49	0.96	0.60
ARB vs ACEI	0.0%	0.95	NA	0.32
ACEI+CCB vs ACEI	0.0%	0.84	NA	0.32
ACEI vs CCB	0.0%	0.81	0.90	1.00
ACEI+CCB vs CCB	0.0%	0.58	NA	0.32
ACEI vs Beta-blocker	0.0%	0.98	NA	0.32
End-stage renal disease				
ACEI vs Placebo	0.0%	0.62	0.72	0.50
ARB vs Placebo	0.0%	0.73	NA	0.32
ACEI vs CCB	0.0%	0.84	NA	0.32
ACEI vs Beta-blocker	0.0%	0.88	NA	0.32
Doubling of serum creatinine				
ACEI vs Placebo	24.7%	0.25	0.36	0.35
ARB vs Placebo	0.0%	0.40	0.65	0.60

Note. $P < 0.05$ indicates significant heterogeneity in Cochrane Q-test, publication bias in Egger's test, or publication bias in Begg's test. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; NA, not applicable due to scarce trial numbers.

Supplementary Table B. Quality assessment of risk of bias for trials included in network meta-analysis

Trial	Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Parving et al.[1,2]	1989	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Bauer et al.[3]	1992	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Björck et al.[4]	1992	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Chan et al.[5]	1992	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chase et al.[6]	1993	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk
Hallab et al.[7]	1993	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lewis et al.[8]	1993	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
O'Donnell et al.[9]	1993	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ravid et al.[10]	1993	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bakris et al.[11]	1994	Unclear risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Low risk
Capek et al.[12]	1994	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Elving et al.[13]	1994	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Sano et al.[14]	1994	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Laffel et al.[15]	1995	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bakris et al.[16]	1996	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Viberti et al.[17]	1996	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Nielsen et al.[18,19]	1997	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
ABCD.[20]	1998	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bakris et al.[21]	1998	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
Crepaldi et al.[22]	1998	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
FACET.[23]	1998	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk
Garg et al.[24]	1998	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Unclear risk
Nankervis et al.[25]	1998	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ravid et al.[26]	1998	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk
Cordonnier et al.[27]	1999	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Fogari et al.[28]	1999	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk
Mathiesen et al.[29,30]	1999	Unclear risk	Unclear risk	High risk	Low risk	Unclear risk	Low risk	Unclear risk
Muirhead et al.[31]	1999	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
ATLANTIS.[32]	2000	Unclear risk	Low risk	High risk	Low risk	Unclear risk	Low risk	Low risk
Lacourcière et al.[33]	2000	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Tarnow.[34]	2000	Unclear risk	Low risk	Unclear risk	Blinding of outcome	Low risk	Low risk	Low risk
Bojestig et al.[35]	2001	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Deerochanawong et al.[36]	2001	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Low risk	Low risk
ESPRIT.[37]	2001	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
IDNT.[38]	2001	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
IRMA-2.[39]	2001	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Jerums.[40]	2001	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kopf et al.[41]	2001	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kventy et al.[42]	2001	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
RENAAL.[43]	2001	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Fogari et al.[44]	2002	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
JAPAN-IDDM.[45]	2002	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
BENEDICT.[46]	2004	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
DETAIL.[47,48]	2004	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
DIABHYCAR.[49]	2004	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
NESTOR.[50]	2004	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ko et al.[51]	2005	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk

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Supplementary Table B. Continued.

Trial	Year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Rizzoni et al.[52]	2005	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Schram et al.[53]	2005	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
ABCD-2V.[54]	2006	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Katayama et al.[55]	2006	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Tong et al.[56]	2006	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
ADVANCE.[57][58]	2007	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
DIRECT-Prevent 1.[59]	2008	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
DIRECT-Protect 1.[59]	2008	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
DIRECT-Protect 2.[60]	2008	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
GUARD.[61]	2008	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Perrin et al.[62]	2008	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Kohlmann et al.[63]	2009	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mehdi et al.[64]	2009	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
MITEC.[65]	2009	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
RASS.[66]	2009	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
ROADMAP.[67]	2011	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Supplementary Table C. Results of traditional pair-wise and Bayesian network meta-analyses

	Outcomes	β-blocker OR	(95% CI)	Placebo OR	(95% CI)	Diuretic OR	(95% CI)	CCB OR	(95% CI)	ACEI OR	(95% CI)	ARB OR	(95% CI)	ACEI+diuretic OR	(95% CI)	ARB+diuretic OR	(95% CI)	ACEI+CCB OR	(95% CI)	ARB+CCB OR	(95% CI)	ACEI+ARB OR	(95% CI)
β-blocker	All-cause deaths							0.18	(0.02 – 1.78)	**0.17**	**(0.04 – 0.87)**												
	ESRD									0.88	(0.17 – 4.68)												
	DSC							0.28	(0.05 – 1.68)	0.13	(0.01 – 1.26)												
Placebo	All-cause deaths	**0.14**	**(0.02 – 0.73)**					0.86	(0.63 – 1.18)	1.03	(0.88 – 1.21)	1.05	(0.89 – 1.24)	**0.86**	**(0.75 – 0.98)**			0.40	(0.08 – 2.06)				
	ESRD	1.14	(0.16 – 9.95)					1.04	(0.77 – 1.41)	0.69	(0.43 – 1.10)	**0.73**	**(0.60 – 0.89)**	1.19	(0.67 – 2.13)								
	DSC	0.21	(0.03 – 1.30)					1.09	(0.84 – 1.43)	**0.60**	**(0.39 – 0.91)**	**0.75**	**(0.63 – 0.89)**	1.23	(0.83 – 1.82)								
Diuretic	All-cause deaths	0.30	(0.01 – 11.21)	2.19	(0.17 – 55.7)					0.49	(0.04 – 5.47)	NA											
CCB	All-cause deaths	**0.14**	**(0.02 – 0.73)**	1.02	(0.74 – 1.46)	0.46	(0.02 – 5.83)			0.81	(0.48 – 1.37)	1.03	(0.74 – 1.43)					0.67	(0.18 – 2.43)				
	ESRD	1.161	(0.15 – 10.51)	1.01	(0.54 – 1.90)					0.77	(0.16 – 3.68)	0.74	(0.54 – 1.01)										
	DSC	0.25	(0.04 – 1.50)	1.18	(0.57 – 2.54)					0.47	(0.04 – 5.71)	**0.60**	**(0.45 – 0.80)**										
ACEI	All-cause deaths	**0.14**	**(0.02 – 0.71)**	0.99	(0.73 – 1.26)	0.44	(0.02 – 5.37)	0.96	(0.64 – 1.35)					1.07	(0.37 – 3.13)	NA		0.56	(0.16 – 1.95)			3.24	(0.13 – 83.1)
	ESRD	0.82	(0.12 – 6.43)	0.71	(0.39 – 1.28)			0.70	(0.33 – 1.55)					NA									
	DSC	**0.12**	**(0.02 – 0.74)**	**0.58**	**(0.32 – 0.90)**			0.50	(0.18 – 1.06)														
ARB	All-cause deaths	**0.15**	**(0.03 – 0.79)**	1.08	(0.87 – 1.39)	0.49	(0.02 – 6.26)	1.06	(0.73 – 1.51)	1.10	(0.80 – 1.61)											NA	
	ESRD	0.84	(0.11 – 7.61)	0.73	(0.43 – 1.25)			0.72	(0.37 – 1.42)	1.04	(0.48 – 2.16)												
	DSC	0.16	(0.02 – 1.04)	0.76	(0.47 – 1.32)			0.65	(0.30 – 1.40)	1.30	(0.71 – 3.04)												
ACEI+diuretic	All-cause deaths	**0.12**	**(0.02 – 0.66)**	0.86	(0.59 – 1.26)	0.39	(0.02 – 5.03)	0.85	(0.50 – 1.35)	0.87	(0.57 – 1.43)	0.80	(0.50 – 1.21)					0.50	(0.05 – 5.53)			3.24	(0.13 – 83.1)
	ESRD	1.38	(0.16 – 14.20)	1.20	(0.50 – 2.93)			1.19	(0.40 – 3.51)	1.70	(0.58 – 4.84)	1.64	(0.59 – 4.60)										
	DSC	0.25	(0.03 – 1.92)	1.22	(0.49 – 3.03)			1.03	(0.31 – 3.27)	2.09	(0.82 – 6.48)	1.60	(0.55 – 4.38)										
ARB+diuretic	All-cause deaths	7.25×10^4	(2.04×10^{28} – 5.41×10^6)	7.06×10^5	(2.07×10^{27} – 4.38×10^7)	3.25×10^5	(1.03×10^{27} – 2.43×10^7)	6.89×10^5	(1.88×10^{27} – 4.08×10^7)	7.20×10^5	(2.27×10^{27} – 4.60×10^7)	6.58×10^5	(1.84×10^{27} – 3.96×10^7)	8.25×10^5	(2.53×10^{27} – 4.69×10^7)					NA			
ACEI+CCB	All-cause deaths	**0.07**	**(0.01 – 0.56)**	0.51	(0.15 – 1.35)	0.21	(0.01 – 3.68)	0.50	(0.14 – 1.30)	0.52	(0.14 – 1.36)	0.47	(0.13 – 1.26)	0.59	(0.16 – 1.62)	64.1	(1.23×10^{14} – 2.39×10^{26})						
ARB+CCB	All-cause deaths	6.04×10^{15}	(4.64×10^{52} – 5.93×10^6)	4.42×10^{14}	(2.81×10^{51} – 4.25×10^5)	2.58×10^{14}	(7.65×10^{52} – 2.11×10^6)	4.55×10^{14}	(2.81×10^{51} – 3.85×10^5)	4.42×10^{14}	(3.10×10^{51} – 4.65×10^5)	4.04×10^{14}	(2.54×10^{51} – 3.92×10^5)	5.19×10^{14}	(3.10×10^{51} – 4.99×10^5)	8.70×10^5	(6.48×10^{45} – 8.30×10^6)	1.04×10^{15}	(6.90×10^{51} – 7.29×10^5)		
ACEI+ARB	All-cause deaths	2.23×10^4	(21.3 – 1.27×10^9)	2.10×10^5	(90.7 – 7.26×10^8)	7.80×10^4	(34.7 – 2.28×10^9)	2.16×10^5	(85.6 – 9.68×10^8)	2.18×10^5	(93.0 – 7.26×10^8)	1.90×10^5	(83.2 – 6.57×10^8)	2.44×10^7	(107 – 8.44×10^8)	3.90×10^5	(6.01×10^2 – 1.09×10^8)	3.29×10^5	(118 – 1.42×10^7)	1.43×10^8	(3.38×10^6 – 2.74×10^8)

NOTE. Traditional pair-wise meta-analysis values are above the diagonal whereas Bayesian network meta-analysis values are below the diagonal. For values above the diagonal, values less than 1 reflect a decreased risk by the row-defining treatment. For values below the diagonal, values less than 1 reflect a decreased risk by the column-defining treatment. Numbers in bold denote a statistically significant difference. The result of a single trial is provided when traditional meta-analysis in a specific comparison is not feasible.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CI, confidence interval in direct comparison, credible interval in Bayesian network meta-analysis; DSC, doubling of serum creatinine; ESRD, end-stage renal disease; NA, not applicable in direct comparison due to zero events in both treatment arms; OR, odds ratio.

Supplementary Table D. Assessment of inconsistency between direct and indirect evidence

Treatment comparisons	*P* value of node-splitting method
All-cause mortality	
ACEI+CCB vs Placebo	0.71
ACEI+CCB vs CCB	0.81
ACEI+CCB vs ACEI	0.53
ACEI+CCB vs ACEI+diuretic	0.74
ACEI+diuretic vs Placebo	0.69
ACEI+diuretic vs ACEI	0.48
ARB vs Placebo	0.59
ARB vs Diuretic	0.69
ARB vs CCB	0.52
ARB vs ACEI	0.82
ACEI vs Placebo	0.49
ACEI vs CCB	0.37
CCB vs Beta-blocker	0.60
CCB vs Placebo	0.15
End-stage renal disease	
ARB vs Placebo	0.65
ARB vs CCB	0.91
ARB vs ACEI	0.52
ACEI vs Placebo	0.87
ACEI vs CCB	0.87
CCB vs Placebo	0.82
Doubling of serum creatinine	
ARB vs CCB	0.61
ACEI vs Placebo	0.77
ACEI vs CCB	0.98
CCB vs Placebo	0.64

Note. $P < 0.05$ indicates significant inconsistency in the treatment comparison. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

Supplementary Table E. Results of network meta-analysis for treatments compared with the placebo in sensitivity analyses

Treatment	Base case OR 95% Crl	Omit Katayama[55] OR 95% Crl	Omit Kohlmann[63] OR 95% Crl	Omit Mehdi[64] OR 95% Crl	Omit Katayama, Kohlmann, Mehdi OR 95% Crl	Omit DIABHYCAR[49] OR 95% Crl	Omit ROADMAP[67] OR 95% Crl	Omit ADVANCE[57 58] OR 95% Crl	Omit ACEI+CCB OR 95% Crl	Omit ACEI+diuretic OR 95% Crl
ACEI+CCB	0.51 (0.15-1.35)	0.51 (0.16-1.35)	0.52 (0.14-1.45)	0.51 (0.17-1.35)	0.51 (0.16-1.33)	0.48 (0.16-1.28)	0.51 (0.16-1.24)	0.51 (0.16-1.53)		0.58 (0.15-1.49)
ACEI+diuretic	0.86 (0.59-1.26)	0.86 (0.59-1.26)	0.86 (0.59-1.26)	0.86 (0.60-1.25)	0.86 (0.59-1.26)	0.86 (0.58-1.28)	0.86 (0.62-1.22)	1.34 (0.09-81.86)	0.85 (0.58-1.24)	
ACEI	0.99 (0.73-1.26)	0.98 (0.72-1.26)	0.98 (0.73-1.26)	0.98 (0.74-1.25)	0.98 (0.72-1.25)	0.84 (0.57-1.33)	0.98 (0.74-1.23)	0.99 (0.73-1.27)	0.98 (0.74-1.25)	0.98 (0.73-1.24)
CCB	1.02 (0.74-1.46)	1.01 (0.74-1.48)	1.03 (0.74-1.46)	1.02 (0.74-1.46)	1.02 (0.74-1.46)	0.98 (0.69-1.46)	1.01 (0.72-1.41)	1.02 (0.74-1.46)	1.03 (0.74-1.44)	1.03 (0.74-1.44)
ARB	1.08 (0.87-1.39)	1.08 (0.87-1.40)	1.08 (0.87-1.38)	1.08 (0.87-1.39)	1.08 (0.87-1.40)	1.06 (0.86-1.38)	1.03 (0.82-1.31)	1.08 (0.87-1.39)	1.08 (0.87-1.38)	1.08 (0.87-1.38)
Diuretic	2.19 (0.17-55.70)	2.94 (0.25-104.79)	2.73 (0.24-76.55)	2.33 (0.22-202.35)	3.00 (0.23-62.24)	2.12 (0.16-34.88)	2.67 (0.14-114.78)	2.25 (0.17-99.68)	2.29 (0.16-49.95)	2.08 (0.14-46.43)
β-blocker	**7.13 (1.37-41.39)**	**6.24 (1.52-40.37)**	**6.25 (1.39-34.09)**	**6.55 (1.18-39.41)**	**6.53 (1.66-42.48)**	**6.53 (1.29-35.59)**	**6.97 (1.62-44.70)**	**6.56 (1.54-31.25)**	**5.76 (1.75-41.85)**	**6.83 (1.63-47.09)**
ARB+CCB*	4.42×10^{-14} $(2.81 \times 10^{-51} - 4.25 \times 10^{5})$		9.30×10^{4} $(1.21 \times 10^{-42} - 5.96 \times 10^{29})$	3.87×10^{-5} $(1.87 \times 10^{-21} - 1.31 \times 10^{12})$		2.24 $(3.83 \times 10^{-20} - 1.60 \times 10^{28})$	3.80×10^{10} $(1.88 \times 10^{-8} - 3.92 \times 10^{32})$	9.61×10^{-4} $(1.69 \times 10^{-22} - 2.00 \times 10^{25})$	1.59×10^{-5} $(1.01 \times 10^{-26} - 5.45 \times 10^{13})$	0.11 $(1.33 \times 10^{-30} - 2.28 \times 10^{10})$
ARB+diuretic*	7.06×10^{-3} $(2.07 \times 10^{-27} - 4.38 \times 10^{17})$	3.04×10^{-5} $(2.86 \times 10^{-58} - 5.05 \times 10^{31})$		2.23×10^{-13} $(1.27 \times 10^{-33} - 2.72)$		4.54×10^{-32} $(1.07 \times 10^{-64} - 3.03 \times 10^{8})$	3.15×10^{-10} $(5.68 \times 10^{-53} - 6.11 \times 10^{31})$	20.84 $(5.92 \times 10^{-15} - 9.24 \times 10^{18})$		8.23×10^{-7} $(1.40 \times 10^{-36} - 7.79 \times 10^{18})$
ACEI+ARB*	2.10×10^{15} $(90.74 - 7.26 \times 10^{26})$	3.01×10^{19} $(23.43 - 2.96 \times 10^{44})$	2.34×10^{19} $(2.37 \times 10^{3} - 5.04 \times 10^{32})$			3.89×10^{28} $(1.63 \times 10^{13} - 3.81 \times 10^{63})$	1.19×10^{18} $(3.43 - 1.30 \times 10^{35})$	2.83×10^{15} $(3.99 - 1.44 \times 10^{25})$	1.41×10^{21} $(23.90 - 5.84 \times 10^{52})$	1.32×10^{19} $(295.60 - 3.46 \times 10^{42})$

NOTE. See panel for full trial names. Numbers in bold denote a statistically significant difference. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CrI, credible interval; OR, odds ratio.

*Extremely wide CrI owing to small patient numbers and rare death events among treatment arm.
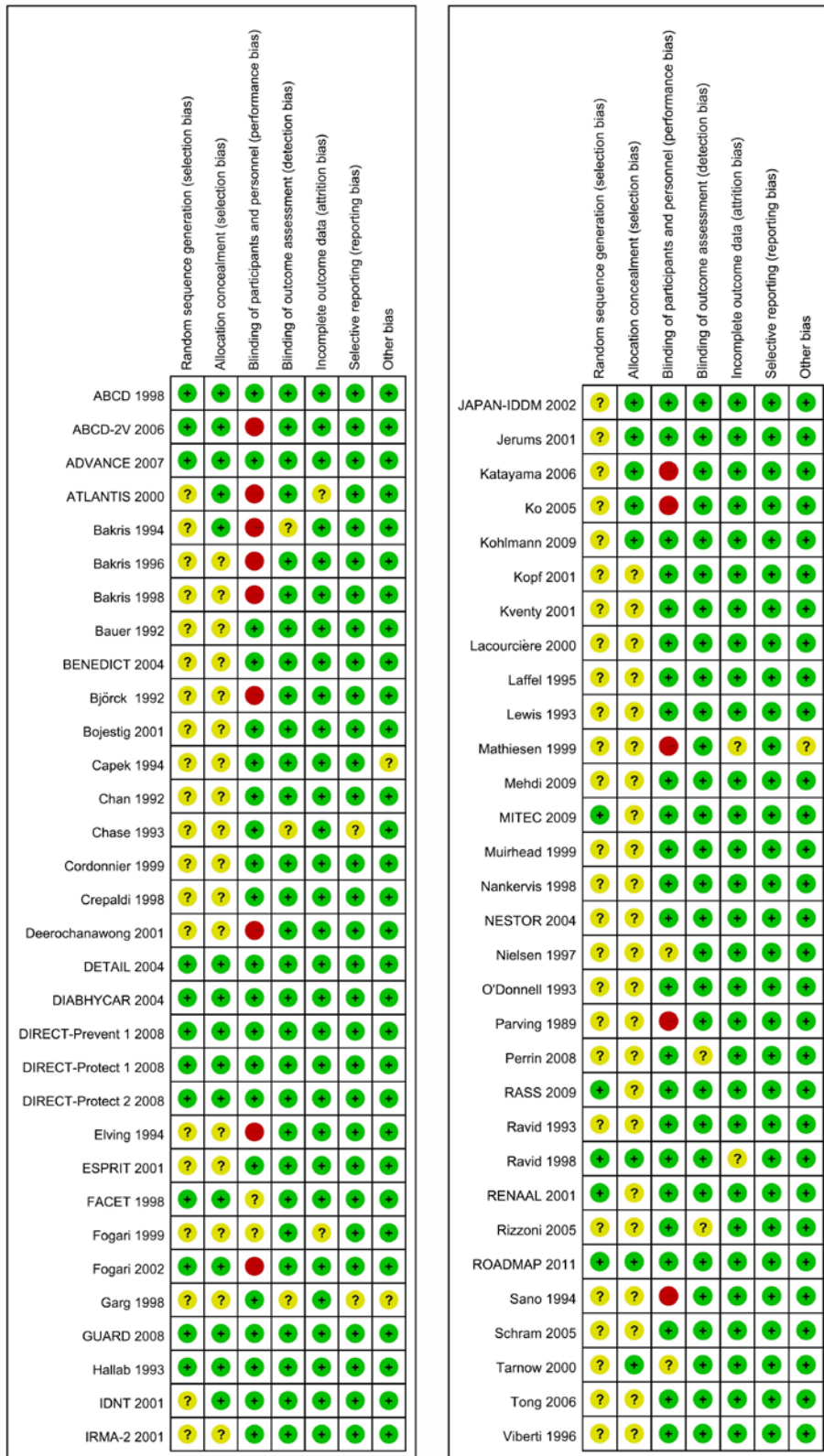
Supplementary Figure A. Summary for risk of bias of included clinical trials. The green symbols represent low risk of bias, the yellow symbols represent unclear risk of bias, and the red symbols represent high risk of bias. The figure was generated using Review Manager Version 5.1.
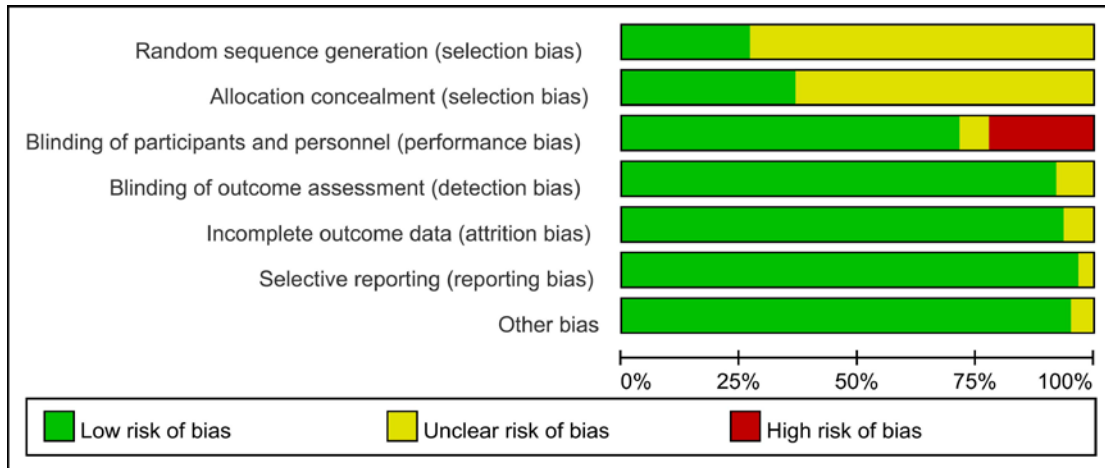
Supplementary Figure B. Risk of bias graph of included clinical trials. Each methodological quality item is presented as percentages across all included studies. The figure was generated using Review Manager Version 5.1.

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