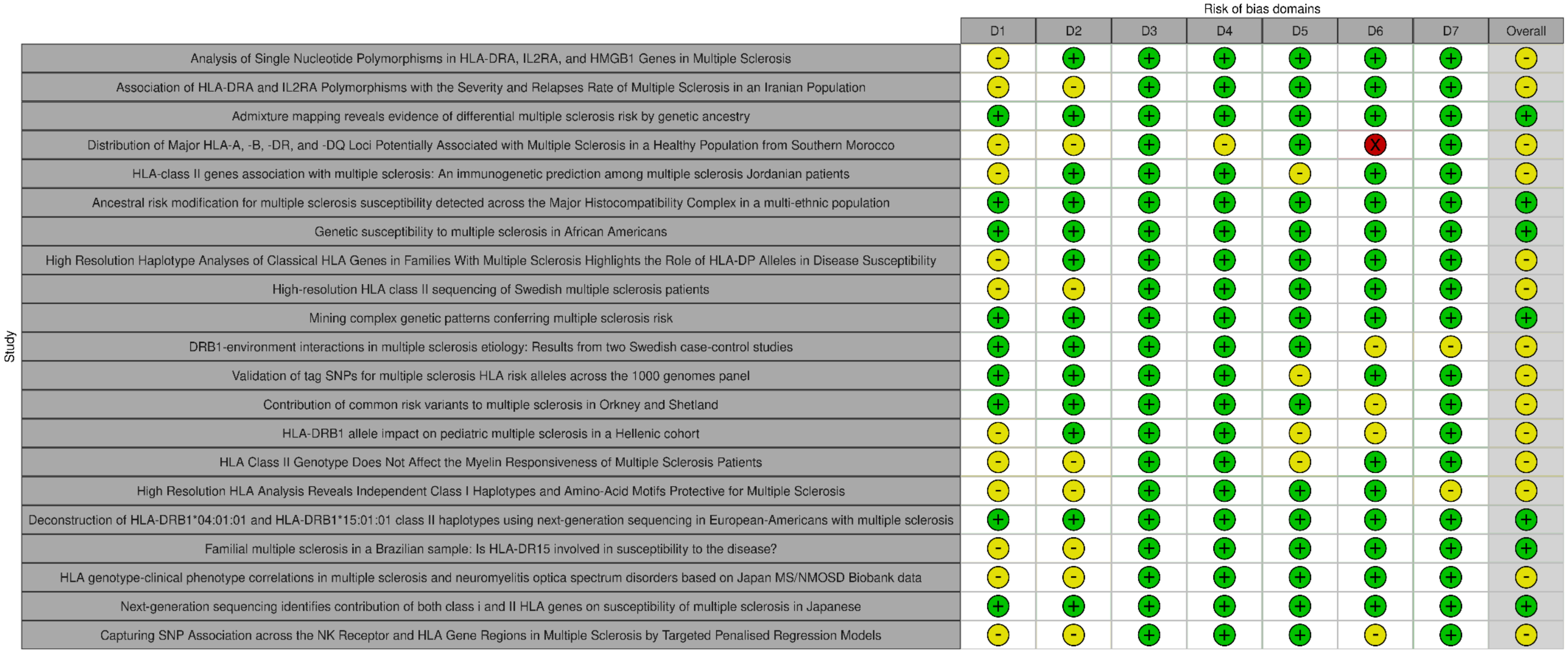
Figure S1. Summary chart of risk of bias.



Study	Risk of bias domains							
	D1	D2	D3	D4	D5	D6	D7	Overall
Analysis of Single Nucleotide Polymorphisms in HLA-DRA, IL2RA, and HMGB1 Genes in Multiple Sclerosis	-	+	+	+	+	+	+	-
Association of HLA-DRA and IL2RA Polymorphisms with the Severity and Relapses Rate of Multiple Sclerosis in an Iranian Population	-	-	+	+	+	+	+	-
Admixture mapping reveals evidence of differential multiple sclerosis risk by genetic ancestry	+	+	+	+	+	+	+	+
Distribution of Major HLA-A, -B, -DR, and -DQ Loci Potentially Associated with Multiple Sclerosis in a Healthy Population from Southern Morocco	-	-	+	-	+	X	+	-
HLA-class II genes association with multiple sclerosis: An immunogenetic prediction among multiple sclerosis Jordanian patients	-	+	+	+	-	+	+	-
Ancestral risk modification for multiple sclerosis susceptibility detected across the Major Histocompatibility Complex in a multi-ethnic population	+	+	+	+	+	+	+	+
Genetic susceptibility to multiple sclerosis in African Americans	+	+	+	+	+	+	+	+
High Resolution Haplotype Analyses of Classical HLA Genes in Families With Multiple Sclerosis Highlights the Role of HLA-DP Alleles in Disease Susceptibility	-	+	+	+	+	+	+	-
High-resolution HLA class II sequencing of Swedish multiple sclerosis patients	-	-	+	+	+	+	+	-
Mining complex genetic patterns conferring multiple sclerosis risk	+	+	+	+	+	+	+	+
DRB1-environment interactions in multiple sclerosis etiology: Results from two Swedish case-control studies	+	+	+	+	+	-	-	-
Validation of tag SNPs for multiple sclerosis HLA risk alleles across the 1000 genomes panel	+	+	+	+	-	+	+	-
Contribution of common risk variants to multiple sclerosis in Orkney and Shetland	+	+	+	+	+	-	+	-
HLA-DRB1 allele impact on pediatric multiple sclerosis in a Hellenic cohort	-	+	+	+	-	-	+	-
HLA Class II Genotype Does Not Affect the Myelin Responsiveness of Multiple Sclerosis Patients	-	-	+	+	-	+	+	-
High Resolution HLA Analysis Reveals Independent Class I Haplotypes and Amino-Acid Motifs Protective for Multiple Sclerosis	-	-	+	+	+	+	-	-
Deconstruction of HLA-DRB1*04:01:01 and HLA-DRB1*15:01:01 class II haplotypes using next-generation sequencing in European-Americans with multiple sclerosis	+	+	+	+	+	+	+	+
Familial multiple sclerosis in a Brazilian sample: Is HLA-DR15 involved in susceptibility to the disease?	-	-	+	+	+	+	+	+
HLA genotype-clinical phenotype correlations in multiple sclerosis and neuromyelitis optica spectrum disorders based on Japan MS/NMOSD Biobank data	-	-	+	+	+	+	+	-
Next-generation sequencing identifies contribution of both class i and II HLA genes on susceptibility of multiple sclerosis in Japanese	+	+	+	+	+	+	+	+
Capturing SNP Association across the NK Receptor and HLA Gene Regions in Multiple Sclerosis by Targeted Penalised Regression Models	-	-	+	+	+	-	+	-

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
X Serious
\- Moderate
\+ Low

Table S1. Genetic markers and typing methods in the included studies.

Reference	Author/Year	Typing method	Loci/genes analyzed (haplotype/SNP)	Reported genetic marker (haplotype/SNP)
[27]	Asouri *et al.*/2020	PCR amplification and NGS	HLA-DRA; IL2RA	rs12722489
[28]	Chi *et al.*/2019	Illumina Immunochip and HLA imputation	HLA class I/II (A, B, C, DRB1, DQB1, DPB1); ~200 non-HLA MS risk SNPs	DRB1*15:01; HLA-B*07:02; HLA-A*03:01
[29]	Fguirouche *et al.*/2025	CDC; PCR-SSP and PCR-SSO	HLA-A, HLA-B, HLA-DRB1, HLA-DQB1	DRB1*03, DRB1*13, DRB1*15
[30]	Khdair *et al.*/2025	PCR-SSP	HLA-DRB1 and HLA-DQB1	DRB1*03:01, DRB1*04:01 DRB1*04:03, DQB1*06:03 DRB1*04:03~DQB1*03:02; DRB1*13:01~DQB1*06:03
[31]	Beecham *et al.*/2022	Illumina MS Chip; HLA-TAPAS imputation and Sanger-typed HLA	HLA-A, B, C, DRB1, DQB1, DPB1, ~10 000 SNPs across chr6:29–34 Mb	HLA-DQB1*06:02; HLA-DRB1*15:01; HLA-A*02:01; HLA-B*53:01; MICB; OR5V1; HCG24; HLA-F-AS1.
[32]	Goodin *et al.*/2021	Illumina MS Chip and HLA imputation	HLA-A, C, B, DRB1, DQB1 and 11 SNPs defining conserved extended haplotypes (CEHs)	A*03:01~C*07:02~B*07:02~DRB1*15:01~DQB1*06:02~a1; HLA-DRB1*15:03~DQB1*06:02~a36
[33]	Osoegawa *et al.*/2021	NGS	HLA-A, C, B, DRB3/4/5, DRB1, DQA1, DQB1, DPA1, DPB1	DRB5*01:01~DRB1*15:01; DPB1*104:01; DQB1*03:01, DQB1*03:03; A*02:01~C*03:04~B*40:01; B*27:05, B*38:01, B*44:02; DPB1*09:01
[34]	Akel *et al.*/2022	NGS	HLA-DRB3, DRB4, DRB5, DRB1, DQA1, DQB1, DPA1, DPB1	DRB5*01:01:01~DRB1*15:01:01~DQA1*01:02:01~DQB1*06:02:01; DRB3*02:02:01~DRB1*03:01:01~DQA1*05:01:01~DQB1*02:01:01; DRB4*01:03:01~DRB1*04:02:01~DQA1*03:01:01~DQB1*03:02:01; DRB4*01:03:01~DRB1*04:03:01~DQA1*03:01:01~DQB1*03:02:01; DRB5*02:02~DRB1*16:01:01~DQA1*01:02:02~DQB1*05:02:01;

				DRBXnull~DRB1*01:02:01~DQA1*01:01:02~DQB1*05:01:01.
[35]	Briggs and Sept/2021	Genome-wide SNP genotyping with imputation and association rule mining (ARM)	HLA-DRB1, HLA-A and 194 non-MHC MS risk SNPs	HLA-DRB1*15:01~SLC30A7-rs56678847~AC093277.1-rs6880809; HLA-DRB1*15:01~ADCY3-rs11125803~rs13327021; HLA-DRB1*15:01~rs13327021~rs735542; HLA-DRB1*15:01~SLC30A7-rs56678847~ZFP36L1-rs12434551.
[36]	Hedström *et al.*/2021	Illumina MS replication chip and HLA imputation	HLA-DRB1, HLA-A	HLA-DRB1*15:01; HLA-A*02:01
[40]	Boullerne *et al.*/2024	Genome-wide SNP tagging validation	HLA-DRB1, HLA-DQB1, HLA-A	HLA-DRB1*15:01; HLA-DQB1*06:02; HLA-A*02:01
[37]	Barnes *et al.*/2021	Genome-wide SNP PRS analysis	127 MS risk SNPs	rs9271069 (DRB1*15:01 tag)
[38]	Gontika *et al.*/2020	PCR-SSO	HLA-DRB1	HLA-DRB1*03; HLA-DRB1*15; HLA-DRB1*11; HLA-DRB1*03
[39]	Derdelinckx *et al.*/2020	NGS	HLA-DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1, DPB1	HLA-DRB1*15:01; HLA-DQA1*01:02; HLA-DQB1*06:02
[41]	Mack *et al.*/2019	NGS	HLA-A, C, B, DRB1, DRB3/4/5, DQA1, DQB1, DPB1	DRB1*15:01~DQB1*06:02; DRB1*03:01~DQB1*02:01; A*02:01; C*03:04~B*40:01; A*02:01~C*03:04~B*40:01
[42]	Creary *et al.*/2019	NGS	HLA-DQB1, DQA1, DRB1, DRB4, DRB5	DQB1*06:02~DQA1*01:02~DRB1*15:01~DRB5*01:01; DQB1*03:01~DQA1*03:03~DRB1*04:01~DRB4*01:03; DQB1*03:02~DQA1*03:01~DRB1*04:01~DRB4*01:03.
[43]	da Silva Bernardes *et al.*/2019	PCR-SSP	HLA-DRB1, DQA1, DQB1	DRB1*15:01~DQA1*01:02~DQB1*06:02; DQB1*06:02; DQA1*01:02; DRB1*15:01
[44]	Asouri *et al.*/2020	Sanger sequencing	HLA-DRA, IL2RA, HMGB1	HLA-DRA rs4935356, rs3177928, rs7197; IL2RA rs12722489, rs12722490
[45]	Watanabe *et al.*/2021	Luminex method	HLA-DRB1, HLA-DPB1	DRB1*04:05; DRB1*15:01; DPB1*03:01; DRB1*01:01; DRB1*09:01; DRB1*13:02; DPB1*04:01

[46]	Ogawa *et al.*/2019	NGS	HLA-A, B, C; DRA, DRB1, DQA1, DQB1, DPA1, DPB1, E, F, G, DOA, DOB, DMA, DMB	DRB1*15:01; DRB1*04:05; B*39:01; B*15:01
[47]	Burnard *et al.*/2022	Genome-wide SNP arrays	HLA, NKC, LRC TAP1/2, TNXB, LTA, GPX6, KLR/CLEC, RPS9	rs9271366; rs2844482; rs3819721; rs2284178; rs2394160; rs9277554

ARM: Association Rule Mining; CDC: Complement-Dependent Cytotoxicity; HLA: Human Leukocyte Antigen; HLA-TAPAS: HLA Typing and Association Pipeline Suite; MS: Multiple Sclerosis; NGS: Next-Generation Sequencing; PCR: Polymerase Chain Reaction; PCR-SSO: PCR with Sequence-Specific Oligonucleotide Probes; PCR-SSP: PCR with Sequence-Specific Primers; PRS: Polygenic Risk Score; SNP: Single-Nucleotide Polymorphism.