IGOA-23-23278

Multiple Sclerosis and Health Outcomes: A Comprehensive Analysis Based On Observational Meta-Analyses

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Received: 05-Apr-2023, Manuscript No. IGOA-23-23278; **Editor assigned:** 07-Apr-2023, PreQC No. IGOA-23-23278 (PQ); **Reviewed:** 21-Apr-2023, QC No. IGOA-23-23278; **Revised:** 23-Apr-2024, Manuscript No. IGOA-23-23278 (R); **Published:** 30-Apr-2024, DOI: 10.35248/IGOA.23.9.228
Citation: Shen L, Long F, Zhong L, Chen S, Li L, Tang S (2024) Multiple Sclerosis and Health Outcomes: A Comprehensive Analysis Based On Observational Meta-Analyses. Immunogenet Open Access. 9:228.

SUPPLEMENTARY FILE

Supplementary Table 1: Characteristics of the unique meta-analyses investigating the associations between MS and multiple health outcomes.

Health outcomes	Author, year	No. of studies	No.of cases /total	Cohort/Case-control/Cross-sectional	Type of metric	Effect size		Heterogeneity		Small-study effect
						95% CI	P Value	I^2	P Value	
Digestive diseases (N=3)										
Inflammatory bowel disease	Wang, et al.	10	3075/597098	0/10/0	RR	1.53(1.38, 1.70)	<0.00001	26%	0.2	0.337
Ulcerative colitis	Kosmidou, et al.	6	2388/673462	0/6/0	RR	1.55(1.38, 1.74)	<0.00001	0	0.43	0.348
Crohn's disease	Kosmidou, et al.	6	2028/621549	0/6/0	RR	1.52(1.34, 1.73)	<0.00001	0	0.82	0.928
Cardiovascular diseases (N=7)										
Preeclampsia	Arafa, et al.	9	17713/28	9/0/0	OR	0.99(0.89,	0.82	0	0.67	0.357

			875341			1.09)	7		2	
Ischemic heart disease	Rapp, et al.	6	>78300/595131	6/0/0	HR	1.04(0.78, 1.38)	0.649	86%	<0.01	0.774
Myocardial infarction	Rapp, et al.	6	49206/430576	6/0/0	HR	1.57(1.21, 2.03)	0	86%	<0.01	0.447
Heart failure	Rapp, et al.	5	38856/345668	5/0/0	HR	1.68(1.32, 2.15)	0	49%	0.1	0.837
Atrial fibrillation	Rapp, et al.	3	26384/209246	3/0/0	HR	0.66(0.58, 0.75)	0	0	0.84	0.568
Bradycardia	Rapp, et al.	3	>16703/188111	3/0/0	HR	1.45(0.42, 4.99)	0.159	50%	0.14	0.749
Ischemic stroke	Hong, et al.	2	49/86240	2/0/0	RR	6.09(3.44, 10.77)	<0.00001	35%	0.21	NA
Infectious diseases (N=8)										
Human herpes virus 6	Pormohammad, , et al.	17	2693/5022	0/17/0	OR	2.23(1.49. 3.33)	0.06	0	<0.001	0.58
Herpes simplex virus type 1-IgG	Xu, et al.	5	818/1922	0/5/0	OR	1.17(0.74, 1.85)	0.512	59.30%	0.043	0.411
Herpes simplex virus type 2-IgG	Xu, et al.	5	1382/7318	0/5/0	OR	1.76(1.41, 2.21)	0	20.10%	0.282	0.527
Herpes simplex virus type 1-DNA	Xu, et al.	2	138/197	0/2/0	OR	0.96(0.31, 2.95)	0.938	0	0.348	NA
Herpes simplex virus type 2-DNA	Xu, et al.	2	138/197	0/2/0	OR	0.51(0.02, 11.42)	0.668	63.80%	0.097	NA
Varicella-zoster virus	Rice, et al.	8	2266/4084	0/8/0	OR	1.44(0.50, 4.12)	0.497	87.40%	0	0.27
Cytomegal	Thakol	15	3591	0/15/0	OR	1.19(	0.	32.7	0	0.45

ovirus	wiboon, et al.		/7832			0.78, 1.81)	42	0%		
Chlamydia pneumoniae infection	Bagos, et al.	26	1332/2796	0/26/0	OR	5.15(1.07.24.64)	0.04	85.60%	0	0.139
Health outcomes	Author year	No. of studies	No.of cases/total	Cohort/Case-control/Cross-sectional	Type of metric	Effect size		Heterogeneity		Small-study effect
						95% CI	P Value	I^2	P Value	
Systemic lupus erythematosus	Dobson, et al.	5	21938/66431	02-03-2000	OR	2.80(0.76, 10.25)	0.12	88%	<0.00001	NA
Diabetes	Dobson, et al.	11	>40000/2000000	04-06-2001	OR	1.49(1.15, 1.94)	0.002	74%	<0.0001	0.003
Type 1 diabetes	Dobson, et al.	7	8206/48519	02-01-2004	OR	2.02(1.22, 3.40)	0.006	91%	<0.00001	0.16
Hypothyroidism	Dobson, et al.	14	>50000/2000000	07-06-2004	OR	1.66(1.35, 2.05)	<0.00001	27%	0.16	0.76
Cognitive affective disorders (N=18)										
Facial emotion recognition	Lin, et al.	24	879/1684	0/24/0	g	-0.62(-0.86,-0.43)	<0.01	88.60%	0	0.536
Empathy	Lin, et al.	27	1275/2385	0/27/0	g	-0.67(-0.84,-0.50)	<0.01	74.10%	0	0.099
Theory of mind（ToM）	Lin, et al.	34	1295/2503	0/34/0	g	-0.74(-0.88,-0.61)	<0.01	70.80%	0	0.303
Cognitive ToM	Lin, et al.	22	805/1515	0/22/0	g	-0.72(-0.92,-0.51)	<0.01	82.30%	0	0.062
Cognitive empathy/a	Lin, et al.	25	972/1929	0/25/0	g	-0.79(-	<0.0	68.90%	0	0.244

ffective ToM						0.96,-0.62)	01			
Affective empathy	Lin,, et al.	3	106/212	0/3/0	g	-0.19(-0.63, 0.26)	0.405	0	0.936	0.005
Working memory	Johnen, et al.	32	3057/NA	0/32/0	g	-0.33(-0.47,-0.19)	<0.001	NA	0	0.79
Processing speed	Johnen, et al.	27	1836/NA	0/27/0	g	-0.56(-0.72,-0.41)	<0.001	NA	0	0.56
Verbal learning	Johnen, et al.	10	556/NA	0/10/0	g	-0.65(-0.91,-0.38)	<0.001	NA	0	0.55
Immediate verbal memory	Johnen, et al.	20	1415/NA	0/20/0	g	-0.51(-0.74,-0.28)	<0.001	NA	0	0.69
Delayed verbal memory	Johnen, et al.	20	1415/NA	0/20/0	g	-0.53(-0.69,-0.38)	<0.001	NA	0	0.01
Visual memory	Johnen, et al.	14	1074/NA	0/14/0	g	-0.42(-0.60,-0.25)	<0.001	NA	0	0.17
Cognitive fluency	Johnen, et al.	16	1205/NA	0/16/0	g	-0.32(-0.50,-0.13)	<0.001	NA	0	0.48
Higher executive functions	Johnen, et al.	12	710/NA	0/12/0	g	-0.28(-0.44,-0.11)	<0.001	NA	0	0.99
Visuospatial function	Johnen, et al.	6	336/NA	0/6/0	g	-0.43(-0.74,-0.11)	0.008	NA	0	0.21
Manual dexterity	Johnen, et al.	14	1258/NA	0/14/0	g	-0.73(-0.94,-0.52)	<0.001	NA	0	0.53
Anxiety &	Johnen,	26	1910	0/26/0	g	-	0.	0	0.	0.37

Depression	et al.		/NA			0.09(-0.26,-0.07)	26		525	
Fatigue	Johnen, et al.	17	1088/NA	0/17/0	g	-0.14(-0.35,-0.07)	0.18	NA	0	0.14
Serum marker disorders (N=14)										
Malondialdehyde	Zhang, et al.	9	508/963	0/9/0	g	2.25(1.08, 3.42)	0	97.79%	0	0.369
Lipid hydroperoxide	Zhang, et al.	3	594/1506	0/3/0	g	0.38(0.07, 0.70)	0.018	86.08%	0.001	0.742
Albumin	Zhang, et al.	7	554/1237	0/7/0	g	−1.04 (−1.68,−0.39)	0.002	95.35%	0	0.137
Advanced oxidation protein product	Zhang, et al.	3	501/1217	0/3/0	g	−0.07 (−0.39,0.24)	0.64	85.69%	0.001	0.525
Total oxidative status	Zhang, et al. 2020	3	100/197	0/3/0	g	0.62(−0.16,1.39)	0.119	86.13%	0.001	0.24
Copper	Zhang, et al.	3	113/212	0/3/0	g	−5.11 (−11.29,1.06)	0.104	98.71%	0	0.238
Cholesterol	Zhang, et al.	9	371/907	0/9/0	g	0.36(−0.09,0.81)	0.119	89.13%	0	0.427
Superoxide dismutase	Zhang, et al.	6	154/318	0/6/0	g	−1.42 (−3.33,0.50)	0.146	97.58%	0	0.71
Total antioxidant status	Zhang, et al.	5	260/454	0/5/0	g	−0.28 (−1.70,1.14)	0.697	97.20%	0	0.629
Glutathione	Zhang, et al.	6	285/554	0/6/0	g	−0.71 (−1.67,0.26)	0.152	95.87%	0	0.76
Uric acid	Zhang, et al.	13	1072/1965	0/13/0	g	−0.13 (−0.40,0.1	0.367	86.48%	0	0.474

						5)				
Homocysteine	Li, et al.	17	1419/2624	0/17/0	SMD	0.64(0.33, 0.95)	<0.0001	92%	<0.00001	0.001
Vitamin B12	Li, et al.	16	1245/2351	0/16/0	SMD	-0.08(-0.35, 0.20)	0.58	89%	<0.00001	0.318
Folate levels	Li, et al.	13	1132/2161	0/13/0	SMD	0.07(-0.14, 0.28)	0.52	81%	<0.00001	0.262
Other outcomes (N=12)										
Psoriasis	Chi, et al.	11	43643/114101 7	02-05-2004	OR	1.51(1.21, 1.88)	0	68.10%	0.001	0.67
Vitiligo	Shen, et al.	5	12829/44060	0/5/0	OR	1.33(0.80, 2.20)	0.27	44%	0.13	0.816
Restless legs syndrome	Ning, et al.	13	559/NA	0/13/0	OR	3.96(3.29, 4.77)	<0.001	23%	0.211	0.71
Female sexual dysfunction	Zhao, et al.	5	644/1042	0/3/2	RR	1.87(1.25, 2.78)	0.002	89%	<0.001	0.027
Suicide	Shen, et al.	16	260752/NA	16/0/0	RR	1.71(1.37, 2.15)	0	87.10%	<0.001	>0.05
Cancer	Ghajarzadeh, et al.	5	59607/465615	0/5/0	RR	0.83(0.73, 0.96)	<0.001	90%	<0.001	0.211
Primary headaches	Wang, et al.	16	3560/NA	0/7/9	OR	0.55(0.51, 0.59)	<0.001	82%	0	0.44
Traumatic injury	Warren, et al.	13	455/3420	0/13/0	OR	1.41(1.03, 1.93)	0.03	43%	0.06	0.286
Reactive imbalance	Mohamed Suhaimy, et al.	9	216/342	0/9/0	SMD	0.78(0.44, 1.11)	<0.00001	47%	0.06	0.617
Center of mass (CoM)	Mohamed Suhaim	4	157/NA	0/4/0	SMD	0.41(0.05, 0.77)	0.02	9%	0.35	0.36

displacement	y, et al.									
Onset latency response times	Mohamed Suhaimy, et al.	9	342/NA	0/9/0	SMD	31.45 (19.91,42.98)	<0.00001	75%	<0.001	NA
Step length	Mohamed Suhaimy, et al.	2	98/NA	0/2/0	SMD	-8.34(-18.50,1.83)	0.11	81%	0.02	0.195

Abbreviation: CI: Confidence Interval; HR: Hazard Risk; RR: Relative Risk; OR: Odd Ratio; SMD: Standardized Mean Difference; g: hedges' g; PPMS: Progressive Primary Multiple Sclerosis; RRMS: Relapsing-Remitting Multiple Sclerosis; BMD: Bone Mineral Density; ToM: Theory of Mind.

Supplementary Table 2: Assessments of AMSTAR2 scores.

Reference	**AMSTAR 2 checklist**																**Overall assessment quality**
	NO.1	**NO.2**	**NO.3**	**NO.4**	**NO.5**	**NO.6**	**NO.7**	**NO.8**	**NO.9**	**NO.10**	**NO.11**	**NO.12**	**NO.13**	**NO.14**	**NO.15**	**NO.16**	
Wang, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Kosmidou, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Arafa, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Rapp, et al.	Y	Y	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Hong, et al.	Y	N	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	N	Y	Critically low
Pormohammad, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Xu, et al.	Y	N	Y	PY	N	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Rice, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Thakolwiboon, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Bagos, et al.	Y	N	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Monteiro, et al.	Y	N	Y	PY	Y	N	PY	PY	Y	N	Y	Y	Y	Y	N	Y	Critically low
Dong, et al.	Y	N	Y	PY	N	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low

Huang, et al.	Y	N	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Dobson, et al.	Y	N	Y	PY	N	N	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Lin, et al. 2021	Y	Y	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Lin, et al.	Y	Y	Y	PY	Y	Y	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Johnen, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Zhang, et al.	Y	N	Y	PY	N	N	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Li, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Chi, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Shen, et al.	Y	Y	Y	PY	Y	N	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Ning, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Zhao, et al.	Y	Y	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Shen, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Ghajarzadeh, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	N	Y	Critically low
Wang, et al.	Y	N	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Warren, et al.	Y	N	Y	Y	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	Y	Low
Mohamed Suhaimy, et al.	Y	Y	Y	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	N	Y	Critically low

AMSTAR 2 checklist (items in italic are considered critical):

1, PICO description; 2, protocol registered before the commencement of the review; 3, study design included in the review; 4, adequacy of the literature search; 5, two authors study selection; 6, two authors study extraction; 7, list for excluding individual studies; 8, included studies descripted in detail; 9, risk of bias for the single studies that included in the review; 10, source of funding of primary studies; 11, appropriateness of meta-analytical methods; 12, impact of risk of bias of single studies on the results of the meta-analysis; 13, consideration of risk of bias when interpreting the results of the review; 14 explanation and discussion of the heterogeneity observed; 15, assessment of presence and likely impact of publication bias; 16, funding sources and conflict of interest declared.

Abbreviations: Y, yes; PY, partial yes; N, no.

Footnotes:

High: 0-1 non-critical weakness. The systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest. Moderate: >1 non-critical weakness. The systematic review has more than one weakness, but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.

Low: 1 critical flaw with or without non-critical weaknesses. The review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.

Critically low: >1 critical flaw with or without non-critical weaknesses. The review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

No2, 4, 7, 9, 11, 13, 15 are the critical items.

Supplementary Table 3: The strength of epidemiologic evidence of 84 unique health outcomes.

Health outcomes	Author, year	Precision of the estimate		Consistency of results	No evidence of small-study effects (P>0.1)	Grade
		>1000 disease cases	P<0.001	I2<50% and Cochran Q test P>0.10		
Digestive diseases (N=3)						
Inflammatory bowel disease	Wang, et al.	Yes	Yes	Yes	Yes	High
Ulcerative colitis	Kosmidou et al.	Yes	Yes	Yes	Yes	High
Crohn's disease	Kosmidou et al.	Yes	Yes	Yes	Yes	High
Cardiovascular diseases (N=7)						
Preeclampsia	Arafa, et al.	Yes	No	Yes	Yes	NA
Ischemic heart disease	Rapp, et al.	Yes	No	No	Yes	NA
Myocardial infarction	Rapp, et al.	Yes	Yes	No	Yes	Moderate
Heart failure	Rapp, et al.	Yes	Yes	No	Yes	Moderate
Atrial fibrillation	Rapp, et al.	Yes	Yes	Yes	Yes	High
Bradycardia	Rapp, et al.	Yes	No	No	Yes	NA
Ischemic stroke	Hong, et al.	No	Yes	Yes	No	Weak
Infectious diseases (N=8)						

Human herpes virus 6	Pormohammad et al.	Yes	No	No	Yes	NA
Herpes simplex virus type 1-IgG	Xu, et al.	No	No	No	Yes	NA
Herpes simplex virus type 2-IgG	Xu, et al.	Yes	Yes	Yes	Yes	High
Herpes simplex virus type 1-DNA	Xu, et al.	No	No	Yes	No	NA
Herpes simplex virus type 2-DNA	Xu, et al.	No	No	No	No	NA
Varicella-zoster virus	Rice, et al.	Yes	No	No	Yes	NA
Cytomegalovirus	Thakolwiboon, et al.	Yes	No	No	Yes	NA
Chlamydia pneumoniae infection	Bagos, et al.	Yes	No	No	Yes	Weak
Allergic diseases (N=4)						
Allergic disease	Monteiro, et al.	Yes	No	No	Yes	NA
Asthma	Monteiro, et al.	Yes	No	No	Yes	NA
Allergic rhinitis	Monteiro, et al.	Yes	No	No	Yes	NA
Eczema	Monteiro, et al.	Yes	No	Yes	Yes	NA
Skeletal system disorders (N=13)						
Fracture	Dong, et al.	No	Yes	No	Yes	Weak
Tibia fracture	Dong, et al.	No	Yes	No	No	Weak
Femur fracture	Dong, et al.	No	Yes	No	No	Weak
Hip fracture	Dong, et al.	No	Yes	Yes	No	Weak
Pelvis fracture	Dong, et al.	No	Yes	Yes	No	Weak
Vertebrae fracture	Dong, et al.	No	No	Yes	No	Weak
Ribs fracture	Dong, et al.	No	No	No	No	NA

Radius/ulna fracture	Dong, et al.	No	No	No	No	NA
Humerus fracture	Dong, et al.	No	No	No	No	Weak
Osteoporosis	Huang, et al.	Yes	Yes	No	No	Weak
Lumbar spine BMD	Huang, et al.	No	Yes	No	No	Weak
Femur neck BMD	Huang, et al.	No	Yes	No	Yes	Weak
Hip BMD	Huang, et al.	No	Yes	No	Yes	Weak
Immune and metabolic diseases (N=5)						
Rheumatoid arthritis	Dobson, et al.	Yes	No	Yes	Yes	NA
Systemic lupus erythematosus	Dobson, et al.	Yes	No	No	No	NA
Diabetes	Dobson, et al.	Yes	No	No	No	Weak
Type 1 diabetes	Dobson, et al.	Yes	No	No	Yes	Weak
Hypothyroidism	Dobson, et al.	Yes	Yes	Yes	Yes	High
Cognitive affective disorders (N=18)						
Facial emotion recognition	Lin, et al.	No	Yes	No	Yes	Weak
Empathy	Lin, et al.	Yes	Yes	No	No	Weak
Theory of mind（ToM）	Lin, et al.	Yes	Yes	No	Yes	Moderate
Cognitive ToM	Lin, et al.	No	Yes	No	No	Weak
Cognitive empathy/affective ToM	Lin, et al.	No	Yes	No	Yes	Weak
Affective empathy	Lin, et al.	No	No	Yes	No	NA
Working memory	Johnen, et al.	Yes	Yes	No	Yes	Moderate
Processing speed	Johnen, et al.	Yes	Yes	No	Yes	Moderate
Verbal learning	Johnen, et al.	No	Yes	No	Yes	Weak
Immediate verbal memory	Johnen, et al.	Yes	Yes	No	Yes	Moderate
Delayed	Johnen,	Yes	Ye	No	No	Weak

verbal memory	et al.		s			
Visual memory	Johnen, et al.	Yes	Yes	No	Yes	Moderate
Cognitive fluency	Johnen, et al.	Yes	Yes	No	Yes	Moderate
Higher executive functions	Johnen, et al.	No	Yes	No	Yes	Weak
Visuospatial function	Johnen, et al.	No	No	No	Yes	Weak
Manual dexterity	Johnen, et al	Yes	Yes	No	Yes	Moderate
Anxiety & Depression	Johnen, et al.	Yes	No	Yes	Yes	NA
Fatigue	Johnen, et al.	Yes	No	No	Yes	NA
Serum marker disorders (N=14)						
Malondialdehyde	Zhang, et al.	No	Yes	No	Yes	Weak
Lipid hydroperoxide	Zhang, et al.	No	No	No	Yes	Weak
Albumin	Zhang, et al.	No	No	No	Yes	Weak
Advanced oxidation protein product	Zhang, et al.	No	No	No	Yes	NA
Total oxidative status	Zhang, et al.	No	No	No	Yes	NA
Copper	Zhang, et al.	No	No	No	Yes	NA
Cholesterol	Zhang, et al.	No	No	No	Yes	NA
Superoxide dismutase	Zhang, et al.	No	No	No	Yes	NA
Total antioxidant status	Zhang, et al.	No	No	No	Yes	NA
Glutathione	Zhang, et al.	No	No	No	Yes	NA
Uric acid	Zhang, et al.	Yes	No	No	Yes	NA
Homocysteine	Li, et al.	Yes	Yes	No	No	Weak
Vitamin B12	Li, et al.	Yes	No	No	Yes	NA
Folate levels	Li, et al.	Yes	No	No	Yes	NA

Other outcomes (N=13)						
Psoriasis	Chi, et al.	Yes	Yes	No	Yes	Moderate
Vitiligo	Shen, et al.	Yes	No	Yes	Yes	NA
Restless legs syndrome	Ning, et al.	No	Yes	Yes	Yes	Weak
Female sexual dysfunction	Zhao, et al.	No	No	No	No	Weak
Suicide	Shen, et al.	Yes	Yes	No	No	Weak
Cancer	Ghajarzadeh, et al.	Yes	Yes	No	Yes	Moderate
Primary headaches	Wang, et al.	Yes	Yes	No	Yes	Moderate
Traumatic injury	Warren, et al.	No	No	No	Yes	Weak
Reactive imbalance	Mohamed Suhaimy, et al.	No	Yes	No	Yes	Weak
Center of mass (CoM) displacement	Mohamed Suhaimy, et al.	No	No	Yes	Yes	Weak
Onset latency response times	Mohamed Suhaimy, et al.	No	Yes	No	No	Weak
Step length	Mohamed Suhaimy, et al.	No	No	No	Yes	NA

Abbreviation: PPMS: Progressive Primary Multiple Sclerosis; RRMS: relapsing-Remitting Multiple Sclerosis; BMD: Bone Mineral Density; ToM: Theory of Mind.

Note: The strength of epidemiologic evidence was rated as follows:

High, if all criteria were satisfied: precision of the estimate ($P<0.001$ and >1000 disease cases), consistency of results ($I2<50\%$ and Cochran Q test $P>0.10$), and no evidence of small-study effects ($P>0.10$).

Moderate, if a maximum of 1 criterion was not satisfied and a $P<0.001$ was found.

Weak, in other cases ($P<0.05$).

NA, P values are greater than 0.05, so the epidemiologic quality of these meta cannot be rated.