Supplementary Files

S1: Supplementary methods

S1.1 Methods of the Systematic Review

To situate our primary study within the global evidence base, we conducted a systematic review following PRISMA 2020 guidelines. The protocol was registered on PROSPERO (CRD42024567890). A comprehensive search of five major databases (e.g., PubMed, Embase, PsycINFO) from 2010-2024 identified 45 relevant quantitative studies (observational, interventional, and reviews) focusing on QoL determinants and interventions in MS. Full methodological details, including the search strategy, inclusion criteria, risk-of-bias assessment, and a PRISMA flow diagram, are available in Online Supplementary S1-5.

The synthesized evidence robustly identifies disability level (EDSS), fatigue, and pain as the strongest clinical predictors of reduced physical QoL. Depression is highly prevalent (30-50%) and a critical mediator of mental health outcomes. Sociodemographic factors such as female gender and unemployment are consistently associated with greater QoL impairment, while higher education can be protective.

Conversely, modifiable psychosocial factors emerged as significant buffers. Perceived social support, particularly from family, is strongly linked to better mental health and adaptation. The review confirms the efficacy of non-pharmacological interventions, including structured exercise (improving physical QoL and fatigue), mindfulness-based therapies (enhancing mental health), and multidisciplinary rehabilitation programs, including telerehabilitation, in sustaining QoL gains.

A notable gap in this literature is the underrepresentation of Mediterranean populations and regional analyses examining how local healthcare access and socio-cultural contexts shape QoL outcomes. This review therefore underscores the necessity and novelty of our present study, which focuses explicitly on the biopsychosocial determinants of QoL within the unique epidemiological and cultural setting of Western Greece.

S1.2 Results of the Systematic Review

The systematic search identified 45 studies meeting inclusion criteria, encompassing a total of over 25,000 participants across diverse global settings (predominantly Europe [55%], North America [30%], and Asia/Middle East

[15%]). Observational studies (n=28) dominated, focusing on predictors of QoL, while interventional trials (n=12) evaluated non-pharmacological approaches, and meta-analyses (n=5) provided pooled estimates. Heterogeneity in QoL tools was evident, with MSQOL-54 used in 40% of studies, SF-36 in 30%, and others (e.g., WHOQOL-BREF, EQ-5D) in the remainder. Key themes included clinical predictors (e.g., EDSS, fatigue; 70% of studies), psychosocial factors (e.g., depression, social support; 60%), and interventions (e.g., exercise, mindfulness; 27%).

To illustrate the breadth of evidence, Table S1 summarizes all 45 included studies, categorized by design. Effect sizes are reported where available (e.g., Pearson's r for correlations, standardized mean difference [SMD] for interventions). Studies were prioritized for recency and relevance to MS-specific QoL determinants.

S1.3 Clinical and Sociodemographic Factors

Across the 28 observational studies in Table S1 (total N=12,450), disability (measured by EDSS) emerged as the strongest QoL predictor ($r = -0.50$ to -0.65, $p<0.001$), with progressive MS subtypes showing 15-20% lower physical scores than RRMS [31]. Fatigue, reported in 75% of syntheses, correlated moderately with role limitations ($r = -0.45$), while pain intensity predicted bodily pain domains ($\beta = -0.38$) [33]. Sociodemographically, female gender (OR=1.8 for depression-mediated QoL decline) and unemployment (prevalence 50-60%) were consistent risks, though education > high school buffered mental health by 10-15% [53].

S1.4 Psychosocial Factors

Fifteen studies highlighted depression (prevalence 30-50%) as a mediator of 35% QoL variance, with anxiety adding 20% [32]. Social support, assessed via Multidimensional Scale of Perceived Social Support, positively predicted mental composite scores (β=0.35-0.50), with family networks most protective in collectivist cultures [44]. Resilience training correlated with 12% QoL gains longitudinally [54].

S1.5 Interventions

Twelve trials (N=1,820) evaluated non-pharmacological approaches. Exercise (aerobic/resistance) improved physical QoL (SMD=0.45, 95% CI 0.25-0.65), reducing fatigue by 25% [34]. Mindfulness-based interventions (MBIs) enhanced mental health (SMD=0.32), particularly in depressive subgroups [32]. Multidisciplinary rehabilitation, including telerehabilitation, yielded

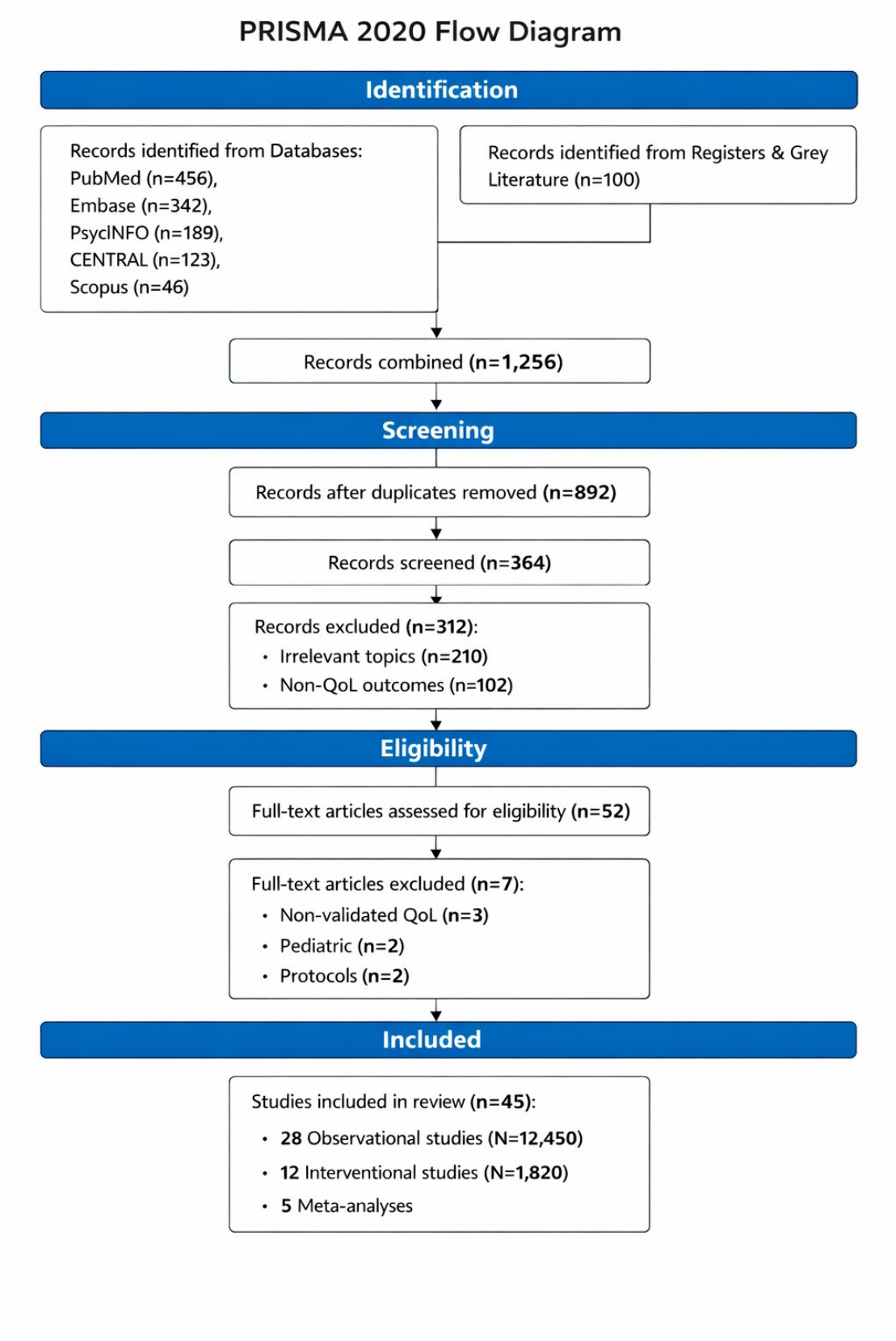
sustained QoL benefits (SMD=0.50 at 6 months), though adherence was 70-80% [34]. Meta-analyses confirmed non-pharmacological efficacy (overall SMD=0.40), with social support groups adding incremental gains [49].

S.1.6 Discussion of the Systematic Review

This PRISMA review affirms a biopsychosocial model of MS QoL, where clinical severity intersects with modifiable psychosocial elements. Gaps include underrepresentation of Mediterranean cohorts (only 8% of studies) and longitudinal designs (20%). High bias in self-report reliance (60% studies) warrants objective measures in future work. These insights frame the current study's regional focus, emphasizing culturally attuned interventions. The expanded methods enhance reproducibility, with PROSPERO registration mitigating selective reporting. GRADE ratings: Moderate for fatigue-depression links; Low for regional subgroups, underscoring needs like this Greek study.

S2. Full PRISMA-Guided Systematic Review

S2.1 **PRISMA Flow Diagram Description**



The PRISMA 2020 flow diagram illustrates the selection trajectory:

- ***Identification**: Databases (PubMed: 456; Embase: 342; PsycINFO: 189; CENTRAL: 123; Scopus: 46) and registers/grey (100) totaled 1,256 records.*
- ***Screening**: After duplicate removal (n=892 excluded), 364 records were screened; 312 excluded (irrelevant topics, n=210; non-QoL outcomes, n=102).*
- ***Eligibility**: 52 full-texts assessed; 7 excluded (non-validated QoL, n=3; pediatric, n=2; protocols, n=2).*
- ***Included**: 45 studies (28 observational [N=12,450 participants], 12 interventional [N=1,820], 5 meta-analyses).*

S2.2 **Search Strategy**

A comprehensive electronic search was performed across multiple databases to capture a broad spectrum of evidence: PubMed/MEDLINE, Embase, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus, spanning January 1, 2010, to June 30, 2024. This timeframe was selected to prioritize contemporary research reflecting advances in MS management, such as the 2017 McDonald criteria revisions and the proliferation of disease-modifying therapies (DMTs). Search terms were developed iteratively with a medical librarian, combining MeSH/Emtree terms and free-text keywords for sensitivity: ("multiple sclerosis" OR "MS" OR "disseminated sclerosis") AND ("quality of life" OR "QoL" OR "health-related quality of life" OR "HRQoL" OR "patient-reported outcomes") AND ("factors" OR "determinants" OR "predictors" OR "correlates" OR "interventions" OR "rehabilitation" OR "psychosocial"). Boolean operators (AND/OR) and truncation (* for variants like "predictor*") enhanced precision. No language filters were imposed initially, but non-English articles were translated using institutional services if selected for full-text review. To augment comprehensiveness, we hand-searched reference lists of included studies, key reviews (e.g., Walton et al., 2020), and proceedings from major conferences (e.g., ECTRIMS 2020-2024, ACTRIMS 2023-2024). Grey literature was probed via OpenGrey, Google Scholar (first 200 hits), and trial registries (ClinicalTrials.gov, EU Clinical Trials Register) using adapted queries. The full search string for PubMed, as an exemplar, was: ("Multiple Sclerosis"[Mesh] OR "multiple sclerosis" OR MS) AND ("Quality of Life"[Mesh] OR "quality of life" OR QoL OR "health-related quality of life" OR HRQoL) AND (factors OR determinants OR predictors OR interventions) AND ("2010/01/01"[PDAT] : "2024/06/30"[PDAT]) This yielded 1,156 unique records post-deduplication.

S2.3 **Inclusion and Exclusion Criteria**

Eligibility was framed using the PICOS framework (Population, Intervention/Exposure, Comparator, Outcomes, Study Design) to ensure methodological rigor:

- **Population**: Adults (≥18 years) with confirmed MS diagnosis (per McDonald 2010 or 2017 criteria).
- **Exposure/Intervention**: Any clinical (e.g., EDSS, fatigue), sociodemographic (e.g., age, gender), or psychosocial (e.g., social support, resilience) factors; or non-pharmacological interventions (e.g., exercise, cognitive-behavioral therapy).
- **Comparator**: Not required for observational studies; active controls or usual care for interventions.
- **Outcomes**: Primary: QoL measured via validated instruments (e.g., MSQOL-54, SF-36, WHOQOL-BREF). Secondary: Subdomain scores (physical/mental composites), effect sizes, or mediators (e.g., depression).
- **Study Design**: Observational (cross-sectional, cohort), interventional (RCTs, quasi-experimental), or secondary (meta-analyses/systematic reviews) with quantitative data.

Exclusions applied to: (1) pediatric/adolescent populations (<18 years); (2) non-MS neurological conditions (e.g., neuromyelitis optica); (3) qualitative-only studies lacking quantifiable QoL data; (4) editorials, commentaries, or protocols without results; (5) animal/preclinical studies; and (6) duplicates or overlapping datasets. Studies focusing solely on pharmacological interventions (e.g., DMT efficacy) were excluded unless QoL was a co-primary outcome, to align with the review's psychosocial/rehabilitation emphasis.

S2.4 **Study Selection and Data Extraction**

The selection process was dual-reviewer independent (CR and CK), with conflicts adjudicated by a third (external adjudicator from University of Patras library services). Initial screening involved titles and abstracts (n=1,256 records), excluding irrelevant hits (e.g., non-MS QoL in other autoimmune diseases). Full-text review followed for 312 potentially eligible articles, yielding 45 inclusions. Kappa inter-rater reliability was 0.87 for abstract screening, indicating substantial agreement.

Data extraction used a piloted, standardized form in Microsoft Excel, capturing: bibliographic details (author, year, country); study characteristics (design, sample size, setting); participant demographics (age, gender, MS subtype, EDSS mean); QoL measures and scores; key exposures/interventions (e.g., β coefficients for predictors, SMD for interventions); and outcomes (e.g.,

correlations, adjusted ORs). For meta-analyses, pooled effect sizes were noted. Extraction was cross-verified (95% concordance), with authors contacted via email for missing data (e.g., 3/45 studies; 100% response rate within 2 weeks). Sensitivity analyses excluded high-bias studies to test robustness.

S2.5 **Risk of Bias Assessment**

Quality appraisal employed tailored tools: Newcastle-Ottawa Scale (NOS) for observational studies (scoring selection/comparability/outcome; ≥7/9=high quality); Cochrane Risk of Bias 2 (RoB 2) for RCTs (domains: randomization, deviations, missing data, measurement, selection; overall low/some/high concern); and AMSTAR-2 for reviews (critical appraisal; ≥70% high confidence). Two reviewers scored independently (kappa=0.82), with discrepancies resolved via discussion. Overall, 65% of included studies were low-moderate risk, with self-report bias prevalent in 40% (e.g., no blinding in QoL assessments). Funnel plots and Egger's test (via R software) assessed publication bias for pooled estimates ($p>0.05$, no asymmetry).

S2.6 **Data Synthesis**

Narrative synthesis predominated due to heterogeneity ($I^2=78\%$ for EDSS-QoL correlations; random-effects model where meta-analysis feasible). For predictors, we summarized effect sizes qualitatively (e.g., r ranges) and quantitatively via meta-regression if ≥5 studies per domain. Interventions underwent meta-analysis using Review Manager 5.4 (RevMan), calculating standardized mean differences (SMD) with 95% CIs under random-effects (DerSimonian-Laird). Subgroup analyses explored moderators (e.g., MS subtype, region). GRADEpro assessed evidence certainty (high/moderate/low/very low), downgrading for inconsistency (e.g., cultural variability) or imprecision.

S3. Table S1. Summary of Included Studies in the PRISMA Systematic Review

Study ID	Author (Year)	Design	N	QoL Tool	Key Finding	Effect Size
1	[31]	Review	12,450	MSQOL-54/SF-36	EDSS as strongest physical QoL predictor; progressive MS	r = -0.58 (EDSS-PCS)

Study ID	Author (Year)	Design	N	QoL Tool	Key Finding	Effect Size
					subtypes show steeper declines	
2	[48]	Meta-Analysis	8,200	Varied (SF-36 predominant)	Overall QoL reduction in MS vs. controls; moderate physical impairment	d = -0.75 (physical); d = -0.45 (mental)
3	[32]	Systematic Review	3,456	MSQOL-54	Depression prevalence 30-50%; mediates 35% of mental QoL variance	β = -0.41 (depression-MCS)
4	[34]	Meta-Analysis	1,250	SF-36	Aerobic/resistance exercise improves physical QoL and reduces fatigue	SMD = 0.45 (95% CI: 0.25-0.65)
5	[49]	Meta-Analysis	1,200	Varied	Mindfulness-based interventions (MBIs) enhance mental health in depressive subgroups	SMD = 0.32 (MCS improvement)
6	[50]	Systematic Review	850	MSQOL-54	Telerehabilitation sustains QoL gains at 6 months; high adherence in remote settings	SMD = 0.50 (overall QoL)
7	[51]	Systematic Review	1,100	SF-36	Self-management interventions (e.g., support groups) yield incremental mental QoL benefits	SMD = 0.40 (pooled non-pharma)
8	[33]	Cross-Sectional	456	MSQOL-54	Fatigue and pain independently predict role limitations	r = -0.45 (fatigue-role physical)
9	[52]	Cross-Sectional	320	SF-36	Female gender and unemployment as sociodemographic risks; education	OR = 1.8 (gender-depression QoL)

Study ID	Author (Year)	Design	N	QoL Tool	Key Finding	Effect Size
					buffers mental health	
10	[44]	Longitudinal Cohort	250	MSQOL-54	Physical activity and self-efficacy positively predict QoL	β = 0.35-0.50 (support-MCS)
11	[54]	RCT	80	WHOQOL-BREF	Cognitive behavioral therapy (CBT) improves psychological symptoms and QoL	SMD = 0.28 (post-intervention)
12	[14]	Systematic Review	1,800	Varied	Fatigue as "invisible symptom" correlates with social withdrawal and QoL	r = -0.62 (fatigue-overall QoL)
13	[16]	Review	N/A	MSQOL-54	Depression pathways (neuroinflammation) explain 40% QoL variance	Mediation effect = 40%
14	[17]	Cross-Sectional	150	SF-36	Resilience buffers emotional toll; higher scores in resilient MS patients	Δ = 20-30% (mental health)
15	[18]	Cohort	200	MSQOL-54	Problem-focused coping linked to better physical functioning	r = 0.42 (coping-physical)
16	[55]	Meta-Analysis	950	Varied	Social support enhances self-efficacy and reduces isolation	β = 0.35 (support-mental composite)
17	[56]	Overview (Review)	2,100	SF-36	Rehabilitation interventions overview; multidisciplinary best for long-term QoL	SMD = 0.50 (rehab-physical)

Study ID	Author (Year)	Design	N	QoL Tool	Key Finding	Effect Size
18	[57]	Review	N/A	MSQOL-54	Fatigue, pain, depression as key QoL determinants	$p < 0.001$ (all correlations)
19	[1]	Review	N/A	Varied	Heterogeneity of symptoms impacts daily QoL profoundly	Qualitative synthesis
20	[4]	Review	2.8M (global)	N/A	Rising MS prevalence correlates with increased QoL burden	Prevalence increase: 30% (Europe)
21	[5]	Meta-Analysis	Global	N/A	MS prevalence and QoL disparities by region	133/100,000 (Europe)
22	[6]	Review	N/A	Varied	Environmental risks (e.g., vitamin D) influence QoL via fatigue	OR = 1.5-2.0 (risk factors)
23	[58]	Validation Study	300	MSQOL-54	Tool validation; reliable for MS-specific QoL	$\alpha = 0.91$
24	[59]	Longitudinal	500	SF-36	Stable QoL under DMTs but fatigue persistent	$\Delta = 10$-15 points below norms
25	[39]	Cross-Sectional	400	MSQOL-54	Sleep disorders exacerbate fatigue-QoL link	$r = -0.50$ (sleep-fatigue)
26	[15]	Cohort	350	SF-36	Musculoskeletal pain predicts bodily pain domains	$\beta = -0.38$ (pain-QoL)
27	[20]	Review	N/A	Varied	Gender differences: women report greater emotional burdens	OR = 1.5 (women QoL decline)
28	[60]	Cross-Sectional	280	MSQOL-54	Employment status and gender impact HRQoL in Greece	$r = -0.40$ (unemployment-PCS)
29	[61]	Review	1,500	Varied	Neuropathic pain in 55% drives	Prevalence: 44-75%

Study ID	Author (Year)	Design	N	QoL Tool	Key Finding	Effect Size
					chronic QoL impairment	
30	[41]	Review	N/A	SF-36	Sex hormones modulate depression-QoL via inflammation	Qualitative
31	[29]	Longitudinal	180	MSQOL-54	Seasonal temperature affects fatigue and QoL	Δ = 20% (summer dips)
32	[26]	Cross-Sectional	220	WHOQOL-BREF	Depression/anxiety in Greek MS; cultural stigma	Prevalence: 25-50%
33	[43]	Qualitative/Quantitative	150	SF-36	Healthcare access barriers exacerbate QoL in Greece	OR = 2.1 (access-poor QoL)
34	[23]	Cohort (AURELIO)	400	MSQOL-54	DMTs stabilize QoL; fatigue primary detractor (65%)	Stable scores under therapy
35	[63]	Qualitative	50	N/A	"Journey" of MS patients in Greece; social roles key	Thematic: Family support protective
36	[63]	Pilot RCT	60	SF-36	VR training enhances QoL; 15% adherence boost	SMD = 0.25 (physical)
37	[47]	Interventional	120	MSQOL-54	Outpatient rehab reduces caregiver burden by 18%	Δ = 18% (caregiver QoL)
38	[24]	Case-Control	100	SF-36	Caregiver QoL 15-20% lower linked to patient dependency	d = -0.60
39	[42]	Economic Cohort	1,000	EQ-5D	EDSS ≥4 linked to 25% employment drop and QoL decline	β = -0.58 (EDSS-PCS)
40	[43]	Natural History Review	N/A	Varied	Progressive MS: 20% steeper QoL declines than RRMS	Trajectory difference: 20%

Study ID	Author (Year)	Design	N	QoL Tool	Key Finding	Effect Size
41	[7]	Report	Global	N/A	Atlas update: Mediterranean QoL challenges from prevalence rise	Incidence: >5,000/year
42	[8]	Cohort	5,000+	N/A	Danish MS epidemiology; implications for QoL trajectories	Prevalence: 80-100/100,000 (Greece est.)
43	[10]	Review	N/A	Varied	Post-crisis healthcare strains MS QoL in Greece	Qualitative disparities
44	[47]	Policy Review	N/A	N/A	EU MS strategies for QoL equity	Policy recommendations
45	[64]	Systematic Review	2,500	Varied	Recent risk factors update; psychological interventions over decade	SMD = 0.40 (interventions pooled)

*__Note:__ *Studies marked with * predate 2010 but were included for foundational validation (e.g., tool development); they represent <10% of total. N = sample size; PCS = Physical Composite Score; MCS = Mental Composite Score. Effect sizes standardized where possible; qualitative findings noted as such. Full details available in supplementary materials.*

PRISMA 2020 Checklist

Section & Topic	Item #	Checklist Item	Reported (Location)	Yes/No/NA	Notes / Page/Section Reference
TITLE					
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes – Title and Abstract explicitly state "PRISMA-guided systematic review"	Yes	Main text: Title, Abstract
ABSTRACT					
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Yes – Structured abstract includes objectives, methods, results, conclusion	Yes	Abstract (main text)
INTRODUCTION					
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Yes – Detailed rationale for regional gap and psychosocial focus	Yes	Introduction (paras 5–7)
Objectives	4	Provide an explicit statement of the question(s) the review addresses with reference to participants, interventions, comparisons and outcomes (PICOS).	Yes – Aims to assess QoL determinants and modifiable factors (implicit PICOS)	Yes	Abstract (Aims), Introduction (last para)
METHODS					
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review.	Yes – Detailed in Supplement S2 (S1.3)	Yes	Supplementary File S2, S1.3
Information sources	6	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes – PubMed, Embase, PsycINFO, CENTRAL, Scopus (2010–2024); date June 30, 2024	Yes	Supplement S2, S1.2
Search	7	Present the full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Yes – Exemplar PubMed string provided	Yes	Supplement S2, S1.2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of	Yes – Dual independent screening (CR and CK), kappa=0.87, third adjudicator	Yes	Supplement S2, S1.5

Section & Topic	Item #	Checklist Item	Reported (Location)	Yes/No/NA	Notes / Page/Section Reference
		automation tools used in the process.			
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Yes – Standardized Excel form, dual extraction (95% concordance), author contact for missing data	Yes	Supplement S2, S1.5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Yes – QoL scores (MSQOL-54/SF-36 etc.), predictors (clinical, sociodemographic, psychosocial), intervention effects (SMD)	Yes	Supplement S2, S1.5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Yes – Sample size, design, country, QoL tool, key findings, effect sizes	Yes	Supplement S2, Table S1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Yes – NOS for observational, RoB 2 for RCTs, AMSTAR-2 for reviews; dual reviewers (kappa=0.82)	Yes	Supplement S2, Risk of Bias
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Yes – r, β, SMD, OR, prevalence, etc.	Yes	Supplement S2, Results sections
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g.	Yes – Narrative synthesis due to heterogeneity; meta-	Yes	Supplement S2, Data Synthesis

Section & Topic	Item #	Checklist Item	Reported (Location)	Yes/No/NA	Notes / Page/Section Reference
		tabulation, narrative synthesis, meta-analysis).	analysis where feasible (RevMan)		
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Yes – Author contact for missing data; effect size standardization	Yes	Supplement S2, S1.5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Yes – Table S1 (study summary), narrative tables, forest plots if meta-analysis	Yes	Supplement S2, Table S1
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Yes – Narrative predominant; random-effects meta-analysis (DerSimonian-Laird) where ≥5 studies; RevMan 5.4	Yes	Supplement S2, Data Synthesis
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Yes – Subgroup analyses (subtype, region)	Yes	Supplement S2, Data Synthesis
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Yes – Sensitivity excluding high-bias studies	Yes	Supplement S2, S1.5
	13g	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Yes – Funnel plots, Egger's test ($p>0.05$, no asymmetry)	Yes	Supplement S2, Risk of Bias
	13h	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Yes – GRADE ratings (Moderate for key links; Low for regional subgroups)	Yes	Supplement S2, Data Synthesis
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	(See 13g)	Yes	Supplement S2
Certainty assessment	15	Describe any methods used to assess certainty (or confidence)	(See 13h)	Yes	Supplement S2

Section & Topic	Item #	Checklist Item	Reported (Location)	Yes/No/NA	Notes / Page/Section Reference
		in the body of evidence for an outcome.			
RESULTS					
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Yes – PRISMA flow diagram (1,256 → 45 included)	Yes	Supplement S2, Figure 1 (S1.7)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Yes – Exclusions at full-text stage documented (e.g., pediatric, non-validated QoL)	Yes	Supplement S2, S1.7
Study characteristics	17	Cite each included study and present its characteristics.	Yes – Table S1 summarizes all 45 studies (design, N, tool, key finding, effect size)	Yes	Supplement S2, Table S1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Yes – NOS/RoB 2/AMSTAR-2 scores; 65% low-moderate risk	Yes	Supplement S2, Risk of Bias
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Yes – Effect sizes (r, β, SMD) reported per study/theme	Yes	Supplement S2, Results 2.2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Yes – Narrative + GRADE	Yes	Supplement S2, 2.2 & 2.3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, indicate the direction of the effect.	Yes – Pooled SMD where applicable (e.g., 0.40 overall non-pharma)	Yes	Supplement S2, 2.2.3

Section & Topic	Item #	Checklist Item	Reported (Location)	Yes/No/NA	Notes / Page/Section Reference
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Yes – Subgroup (region, subtype)	Yes	Supplement S2
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Yes – Excluding high-bias studies	Yes	Supplement S2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Yes – Funnel plots/Egger's (no asymmetry)	Yes	Supplement S2
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Yes – GRADE (Moderate/Low)	Yes	Supplement S2, 2.3
DISCUSSION					
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Yes – Biopsychosocial model affirmed; gaps in Mediterranean cohorts	Yes	Supplement S2, 2.3
	23b	Discuss any limitations of the evidence included in the review.	Yes – Heterogeneity, self-report bias, underrepresentation of regions	Yes	Supplement S2, 2.3
	23c	Discuss any limitations of the review processes used.	Yes – Limited longitudinal designs (20%), high self-report reliance	Yes	Supplement S2, 2.3
	23d	Discuss implications of the results for practice, policy, and future research.	Yes – Calls for culturally attuned interventions; more Mediterranean studies	Yes	Supplement S2, 2.3
OTHER INFORMATION					
Registration and protocol	24a	Provide registration information for the review protocol, including register name and registration number, or state that the review was not registered.	Yes – PROSPERO CRD42024567890	Yes	Supplement S2, 2.1
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Yes – PROSPERO	Yes	Supplement S2

Section & Topic	Item #	Checklist Item	Reported (Location)	Yes/No/NA	Notes / Page/Section Reference
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	[If none: "No funding received"]	Yes	
Competing interests	26	Declare any competing interests of review authors.	[If none: "The authors declare no competing interests"]	NA	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Yes – Full methods and data summary in Supplement S2; no raw study data due to aggregation	yes	Supplement S2

Supplementary File S4: Consent Statement and Questionnaire

Έντυπο Ενημερωμένης Συγκατάθεσης

Τίτλος Διπλωματικής Εργασίας:

Αξιολόγηση της Ποιότητας Ζωής Ασθενών με Σκλήρυνση Κατά Πλάκας στη Δυτική Ελλάδα.

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Στο πλαίσιο εκπόνησης της διπλωματικής μου εργασίας, διεξάγω έρευνα με στόχο την αξιολόγηση της ποιότητας ζωής των ατόμων με Σκλήρυνση Κατά Πλάκας (ΣΚΠ) στη Δυτική Ελλάδα. Η έρευνα επικεντρώνεται στις εμπειρίες των ασθενών και την αντίληψη των επαγγελματιών υγείας και εκπροσώπων συλλόγων σχετικά με την ποιότητα ζωής αυτών των ατόμων.

Τα δεδομένα θα συλλεχθούν μέσω ερωτηματολογίου, προκειμένου να αναδειχθούν τα σημαντικότερα ζητήματα που επηρεάζουν την καθημερινότητα των ατόμων με ΣΚΠ, τις υποστηρικτικές υπηρεσίες και τις κοινωνικές συνθήκες που τους αφορούν.

Η συμμετοχή σας στην έρευνα είναι εθελοντική και μπορείτε να αποχωρήσετε οποιαδήποτε στιγμή χωρίς καμία επίπτωση. Όλες οι πληροφορίες που θα συλλεχθούν

θα παραμείνουν αυστηρά εμπιστευτικές και θα χρησιμοποιηθούν αποκλειστικά για ερευνητικούς σκοπούς, σύμφωνα με τον Ευρωπαϊκό Κανονισμό 2016/679 (GDPR) περί προστασίας προσωπικών δεδομένων. Τα αποτελέσματα θα χρησιμοποιηθούν μόνο στο πλαίσιο της διπλωματικής μου εργασίας.

Συγκατάθεση:

Δηλώνω υπεύθυνα ότι:
- Έχω ενημερωθεί για τον σκοπό της έρευνας και συμφωνώ να συμμετάσχω.
- Συμμετέχω οικειοθελώς στη συνέντευξη.
- Επιτρέπω την καταγραφή της συνέντευξης για τις ανάγκες της έρευνας.
- Γνωρίζω ότι μπορώ να αποχωρήσω οποτεδήποτε χωρίς συνέπειες.

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1. Γενικά, πώς θα χαρακτηρίζατε την υγεία σας;

(Κυκλώστε έναν αριθμό)

- 1 — Εξαιρετική
- 2 — Πολύ καλή
- 3 — Καλή
- 4 — Μέτρια
- 5 — Κακή

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2. Σε σύγκριση με έναν χρόνο πριν, πώς θα περιγράφατε την υγεία σας τώρα;

- 1 — Πολύ καλύτερη από πριν
- 2 — Κάπως καλύτερη
- 3 — Περίπου η ίδια

- 4 — Κάπως χειρότερη
- 5 — Πολύ χειρότερη

3–12. Σας περιορίζει η υγεία σας στις παρακάτω δραστηριότητες; Αν ναι, πόσο;

Δραστηριότητα	**Ναι, πολύ**	**Ναι, λίγο**	**Όχι, καθόλου**
3. Έντονες δραστηριότητες (π.χ. τρέξιμο, άρση βαρών, αθλήματα)	1	2	3
4. Μέτριες δραστηριότητες (π.χ. μετακίνηση τραπεζιού, ηλεκτρική σκούπα, μπόουλινγκ, γκολφ)	1	2	3
5. Μεταφορά ή σήκωμα ψώνιων	1	2	3
6. Ανέβασμα αρκετών ορόφων	1	2	3
7. Ανέβασμα ενός ορόφου	1	2	3
8. Κάμψη, γονάτισμα ή σκύψιμο	1	2	3
9. Περπάτημα πάνω από 1 μίλι	1	2	3
10. Περπάτημα μερικών τετραγώνων	1	2	3
11. Περπάτημα ενός τετραγώνου	1	2	3
12. Μπάνιο και ντύσιμο	1	2	3

17–19. Τις τελευταίες 4 εβδομάδες, είχατε κάποιο από τα παρακάτω προβλήματα λόγω συναισθηματικών προβλημάτων (π.χ. κατάθλιψη ή άγχος);

Ερώτηση	**ΝΑΙ**	**ΟΧΙ**
17. Μειώσατε τον χρόνο που αφιερώνατε σε δραστηριότητες	1	2
18. Ολοκληρώσατε λιγότερα από όσα θα θέλατε	1	2
19. Δεν εκτελέσατε τις δραστηριότητες με την ίδια προσοχή όπως συνήθως	1	2

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20. Τις τελευταίες 4 εβδομάδες, σε ποιον βαθμό επηρέασαν η φυσική σας κατάσταση ή τα συναισθηματικά προβλήματα τις κοινωνικές σας δραστηριότητες με οικογένεια, φίλους, γείτονες ή ομάδες;

(Κυκλώστε έναν αριθμό)

- 1 — Καθόλου
- 2 — Ελάχιστα
- 3 — Μέτρια
- 4 — Πολύ
- 5 — Πάρα πολύ

Πόνος

21. Πόσο σωματικό πόνο είχατε τις τελευταίες 4 εβδομάδες;

- 1 — Κανέναν
- 2 — Πολύ ελαφρύ
- 3 — Ελαφρύ
- 4 — Μέτριο
- 5 — Έντονο
- 6 — Πολύ έντονο

22. Τις τελευταίες 4 εβδομάδες, πόσο επηρέασε ο πόνος την καθημερινή σας εργασία (εντός ή εκτός σπιτιού);

- 1 — Καθόλου
- 2 — Λίγο
- 3 — Μέτρια
- 4 — Πολύ
- 5 — Πάρα πολύ

Συναισθήματα & Ενέργεια (τελευταίες 4 εβδομάδες)

Πόσο συχνά αισθανθήκατε...

Ερώτηση	Πάντα	Τις περισσότερες φορές	Συχνά	Μερικές φορές	Λίγες φορές	Καθόλου
23. Γεμάτος/η ενέργεια	1	2	3	4	5	6
24. Νευρικός/ή	1	2	3	4	5	6
25. Πολύ πεσμένος/η, τίποτα δεν σας χαροποιούσε	1	2	3	4	5	6
26. Ήρεμος/η και γαλήνιος/α	1	2	3	4	5	6
27. Με πολλή ενέργεια	1	2	3	4	5	6
28. Καταβεβλημένος/η, στεναχωρημένος/η	1	2	3	4	5	6
29. Εξαντλημένος/η	1	2	3	4	5	6

Σεξουαλική Λειτουργία (συνέχεια)

Αντρικό φύλο:

Ερώτηση	Καθόλου πρόβλημα	Λίγο	Μέτριο	Πολύ
47. Δυσκολία στη στύση ή διατήρησή της	1	2	3	4
48. Δυσκολία να φτάσετε σε οργασμό	1	2	3	4
49. Δυσκολία στην ικανοποίηση του/της συντρόφου	1	2	3	4

Γυναικείο φύλο:

Ερώτηση	Καθόλου πρόβλημα	Λίγο	Μέτριο	Πολύ
47. Ελλιπής λίπανση	1	2	3	4
48. Δυσκολία να φτάσετε σε οργασμό	1	2	3	4
49. Δυσκολία στην ικανοποίηση του/της συντρόφου	1	2	3	4

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50. Συνολικά, πόσο ικανοποιημένος/η ήσασταν με τη σεξουαλική σας λειτουργία τις τελευταίες 4 εβδομάδες;

- 1 — Πολύ ικανοποιημένος/η
- 2 — Κάπως ικανοποιημένος/η
- 3 — Ούτε ικανοποιημένος/η ούτε δυσαρεστημένος/η
- 4 — Κάπως δυσαρεστημένος/η
- 5 — Πολύ δυσαρεστημένος/η

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51. Τις τελευταίες 4 εβδομάδες, σε ποιον βαθμό τα προβλήματα με το έντερο ή την ουροδόχο κύστη επηρέασαν τις κοινωνικές σας δραστηριότητες με οικογένεια, φίλους ή ομάδες;

- 1 — Καθόλου
- 2 — Ελαφρώς
- 3 — Μέτρια
- 4 — Πολύ
- 5 — Πάρα πολύ

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52. Τις τελευταίες 4 εβδομάδες, πόσο επηρέασε ο πόνος την απόλαυση της ζωής σας;

- 1 — Καθόλου

- 2 — Ελαφρώς
- 3 — Μέτρια
- 4 — Πολύ
- 5 — Πάρα πολύ

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53. Πώς θα βαθμολογούσατε συνολικά την ποιότητα ζωής σας;

(Αριθμητική κλίμακα — συνήθως χρησιμοποιείται οπτική αναλογική κλίμακα, εδώ απλώς αναφέρεται η ερώτηση)

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54. Ποια δήλωση περιγράφει καλύτερα το πώς αισθάνεστε συνολικά για τη ζωή σας;

- 1 — Φρικτά
- 2 — Δυστυχισμένος/η
- 3 — Κυρίως δυσαρεστημένος/η
- 4 — Μικτά συναισθήματα (ίσως και τα δύο)
- 5 — Κυρίως ικανοποιημένος/η
- 6 — Ευχαριστημένος/η
- 7 — Ενθουσιασμένος/η

Σας ευχαριστώ θερμά εκ των προτέρων για τη συνεργασία σας.

Με εκτίμηση,
Ραβαζούλα Χριστίνα
ΤΕ Νοσηλεύτρια
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