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Panic attacks and psychiatric comorbidity in multiple sclerosis: reinterpreting a 2004–2006 Georgian case-control study in the context of contemporary evidence

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Abstract

Background Georgian evidence on psychiatric comorbidity in multiple sclerosis (MS) is sparse. A previously unpublished single-centre Batumi case-control dataset from 2004–2006 is reanalysed here and reinterpreted in the light of the 2026 clinical framework — current diagnostic criteria, disease-modifying therapies (DMTs), validated psychiatric instruments, and mechanistic neuroimaging — to establish a pre-DMT-era Georgian baseline against which contemporary MS care can be benchmarked.

Methods In this single-centre, hospital-based case-control study conducted between 2004 and 2006 at the High Technology Hospital Medical Centre (Batumi, Georgia), 30 adults with clinically confirmed MS (16 women, 14 men; age range 20–75 years; disease duration 1–5 years) were compared with 30 age- and sex-matched healthy controls. Anxiety was assessed using the Sheehan Patient-Rated Anxiety Scale. Frequency of panic attacks, impairment in daily functioning, social behaviour, capability changes, suicidal ideation, and somato-vegetative symptoms were recorded through structured clinical interview. Between-group comparisons used Fisher's exact test and chi-square tests; risk was expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

Results The overall distribution of panic-attack frequency differed significantly between groups ($\chi^2 = 8.83$; df = 2; p = 0.012). Any panic attacks (≥5 per month) were reported by 26/30 (86.7%) patients and 17/30 (56.7%) controls (OR 4.97; 95% CI 1.39–17.82; p = 0.020). Compared with controls, patients had significantly higher odds of impaired daily functioning (OR 7.56; 95% CI 2.41–23.75; p = 0.001), capability changes (OR 4.67; 95% CI 1.57–13.87; p = 0.009), and social-behaviour disturbance (OR 3.76; 95% CI 1.24–11.39; p = 0.033). Suicidal ideation was more frequent in the MS group (36.7% vs 13.3%; OR 3.76; 95% CI 1.04–13.65; p = 0.072).

Conclusions Georgian adults with MS in 2004–2006 showed strikingly elevated odds of panic attacks, functional impairment, and suicidal ideation compared with matched controls. The magnitude of this burden, reinterpreted against 2026 standards, plausibly reflects MS lived in the near-absence of modern care. These data establish a pre-DMT-era Georgian baseline and argue for urgent implementation of integrated psychiatric screening, expanded DMT access, and a contemporary multicentre Georgian MS registry.

Keywords multiple sclerosis; panic disorder; anxiety; psychiatric comorbidity; case-control studies; Georgia (Republic)

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1. Introduction

Between 2022 and 2025, consumer-facing generative artificial intelligence (AI) interfaces became a primary point of entry through which members of the public seek information about their health symptoms. Surveys across multiple jurisdictions during this period reported that between 30% and 50% of respondents had used ChatGPT, Gemini, Claude, or similar chatbot interfaces to ask about physical symptoms, and a substantial minority reported acting on the received information without subsequently consulting a clinician [1,2].

Three specific risks have been characterised in the emerging literature. First, hallucination — empirical audits of GPT-class models have found that 28–47% of citations generated in medical contexts are fabricated, misattributed, or combine real authors with fictional works [3,4]. Second, output instability — the same clinical query posed repeatedly can return materially different triage recommendations, because LLM outputs are sampled rather than deterministic [5]. Third, opacity — when a model states that a symptom pattern "is consistent with" a named condition, the underlying reasoning is not traceable to a specific clinical guideline, making independent review by a second clinician impossible [6,7].

For Georgian-speaking populations (approximately 3.7 million people), these risks are amplified. Commercial AI interfaces offer poor Georgian localisation; machine-translated outputs routinely drift from clinical standards of expression. Cardiovascular, respiratory, and metabolic diseases account for the majority of age-standardised mortality in Georgia, with cardiovascular disease alone representing approximately 67% of all-cause deaths per 2023 surveillance data from the National Center for Disease Control and Public Health of Georgia (NCDC) [8] — pathways where delayed or misdirected triage has disproportionate mortality consequences.

Prior to this work, no peer-reviewed, open-source, Georgian-language symptom triage tool had been published. Proprietary symptom-checker applications (Ada, Babylon, Isabel, K Health, Symptoma) either omit Georgian support entirely or provide machine-translated interfaces without clinical review. All operate on unaudited algorithms; systematic reviews of these systems have reported modest triage concordance with physician judgment (30–60%) and identified the absence of public evidence citation as a recurring methodological concern [9–11].

We designed SheniEkimi to address the intersection of these gaps: a Georgian-primary, bilingual, evidence-auditable, non-commercial symptom triage system anchored exclusively in named international guidelines and externally-validated clinical decision rules. This article reports the methodology, implementation, and public deployment of the system (plugin v3.1, April 2026) and positions the work against both commercial symptom-checkers and generative-AI chatbots as consumer medical-advice tools.

2. Methods

2.1 Design framework

We adopted a 16-body-system framework adapted from the World Health Organization Integrated Management of Adolescent and Adult Illness (IMAI) acute-care module [12], the WHO Integrated Management of Childhood Illness (IMCI) chart booklet [13], and the ICD-11 chapter structure [14]. System-level scenario allocation was weighted by disease burden from NCDC surveillance reports and by density of available externally-validated clinical decision rules per system.

2.2 Inclusion and exclusion criteria

Candidate clinical scenarios were eligible for inclusion if they satisfied all four of the following criteria: (i) the presentation is assessable without physical examination or laboratory testing beyond patient-observable signs and self-measurable vital signs; (ii) an evidence-based triage threshold exists, sourced either from an international specialty-society guideline meeting AGREE II–informed quality criteria or from a validated peer-reviewed clinical decision rule with published derivation and at least one external validation study; (iii) the presentation can be mapped to an ICD-11 code at a chapter or block level of specificity; and (iv) the presentation is common in primary-care or general-population contexts, operationalised as occurring at an incidence greater than approximately 1 per 1,000 population per year in European or WHO-EURO epidemiological data.

Candidates were excluded under any of five conditions: (i) triage requires in-hospital diagnostics unavailable to the self-assessing user; (ii) presentation is restricted to post-surgical, transplant, or active-oncology populations requiring continuity with a named care team; (iii) presentation falls within palliative or end-of-life care domains where telemedicine triage is clinically inappropriate; (iv)

presentation is restricted to specialist-referred populations where self-triage risks inappropriate care delay; (v) available evidence is limited to expert opinion or single-centre case series lacking external validation.

2.3 Source hierarchy and guideline appraisal

Sources were selected according to a six-tier hierarchy prioritising international scope, methodological transparency, and peer-review status (Table 1). Where multiple high-quality sources addressed the same scenario, we selected the most recently updated guideline with explicit triage thresholds. Each selected source underwent AGREE II–informed assessment [15] across Domain 3 (rigour of development), Domain 4 (clarity of presentation), and Domain 5 (applicability to primary-care settings). Sources were rated strong, moderate, or insufficient; sources rated insufficient were rejected in favour of the next-highest-ranking alternative.

1. Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated, inflammatory demyelinating disease of the central nervous system. Clinical episodes are attributable to lesions disseminated in time and space and are followed by variable degrees of neurological recovery; over time, cumulative axonal injury leads to progressive disability [1–3]. Contemporary epidemiological estimates place the number of people living with MS worldwide at approximately 2.8 million (35.9 per 100 000 population), a figure that has risen in every world region since 2013 and reflects a combination of improved case ascertainment, evolving diagnostic criteria, and a genuine increase in incidence in several regions [4,5]. National-level data from high-latitude European settings, including Denmark, confirm a particularly marked rise in incidence among women and in late-onset disease over recent decades [6].

The diagnosis of MS is primarily clinical but is supported by magnetic resonance imaging, cerebrospinal fluid analysis, and evoked potentials; the 2017 revision of the McDonald criteria integrates these elements to enable earlier and more accurate diagnosis [7]. Disease course is described using the 2013 revised phenotypic framework, which distinguishes relapsing-remitting, primary progressive, and secondary progressive forms and adds modifiers for disease activity and progression [8]. Contemporary disease-modifying therapies (DMTs) — platform injectables, oral agents, and high-efficacy monoclonal antibodies — reduce relapse rate and slow disability progression but do not specifically target the psychiatric burden of the disease [9].

Beyond neurological impairment, MS is consistently associated with a high burden of psychiatric comorbidity. A systematic review of 118 studies estimated lifetime prevalence of any anxiety disorder in MS at approximately 36% and depression at approximately 24%, with bipolar disorder and schizophrenia also substantially increased [10]. Population-level Canadian data confirm that the incidence and prevalence of depression, anxiety, bipolar disorder, and schizophrenia are all significantly greater in MS than in age-, sex-, and geography-matched general-population controls [11]. Subsequent meta-analyses have reinforced these findings: pooled prevalence estimates of 30.5% for depression and 22.1% for anxiety using mixed instruments [12], a narrative systematic review of 131 studies identifying consistent associations between anxiety and disability, quality of life, and depression [13], a clinical-phenotype meta-analysis reporting depression prevalence of 27.0% and anxiety of 35.2% with higher rates in progressive forms [14], and a recent meta-analysis of 15 observational studies reporting pooled anxiety prevalence of approximately 35% with female sex, prior psychiatric history, comorbid depression, disease duration, absence of DMT, and higher Expanded Disability Status Scale scores as consistent risk factors [15].

Panic disorder has received comparatively less attention than depression in the MS literature, despite being both disabling and treatable. A Canadian structured-interview study using DSM-IV criteria found a lifetime prevalence of any anxiety disorder of 35.7% in MS, with panic disorder present in 10%, generalised anxiety in 18.6%, and obsessive-compulsive disorder in 8.6% [16]. Case series have also reported panic attacks as the presenting feature of MS in a subset of patients [17]. Biological plausibility is supported by MS-related demyelination in limbic and brainstem circuits involved in autonomic

and affective regulation, chronic neuroinflammatory cytokine release, hypothalamic-pituitary-adrenal axis dysregulation, and the psychological burden of a chronic, unpredictable neurological illness [18,19]. Functional and structural neuroimaging studies have further demonstrated specific network alterations underlying anxiety symptoms already in early MS [20], providing a mechanistic link between disease-related brain pathology and affective outcomes.

The clinical implications of psychiatric comorbidity in MS extend beyond symptom burden. Suicide-related outcomes in MS are approximately double those of the general population, with depression severity, disability, social isolation, and earlier disease course the most consistent determinants [21–23]. Psychiatric comorbidity has been linked to accelerated disability progression [24], a higher rate of clinical relapse in individuals with three or more comorbid conditions [25], and increased diagnostic delays and mortality in MS overall [26]. Despite this, both pharmacological and psychological treatments for depression and anxiety in MS are under-studied [27], and formal American Academy of Neurology guidelines on the assessment and management of psychiatric disorders in MS note that most recommendations rest on evidence of only modest strength [28].

The present manuscript revisits a Georgian case-control dataset collected prospectively at a single Batumi centre between 2004 and 2006 — data that have not previously appeared in the indexed literature. In the two decades since these data were generated, the MS clinical framework has been fundamentally reshaped: the McDonald diagnostic criteria have undergone successive revisions culminating in the 2017 update [7]; the Lublin phenotypic classification has been refined with activity and progression modifiers [8]; high-efficacy disease-modifying therapies and robust network-meta-analytic evidence have redefined the achievable disease course [9]; contemporary meta-analyses [10–15], mechanistic neuroimaging of anxiety-related network alterations [20], and formal American Academy of Neurology guidance on psychiatric assessment and management in MS [28] have collectively clarified both the psychiatric burden and the response pathway. At the same time, Georgian MS research capacity remains limited; to our knowledge, the dataset analysed here is still the principal published Georgian case-control evidence on panic and anxiety in MS. Reinterpreting this pre-disease-modifying-therapy-era cohort against the 2026 evidence base therefore serves two distinct scientific purposes: (i) it situates historical Georgian findings within the now-consolidated international understanding of psychiatric comorbidity in MS; and (ii) it provides a documented baseline against which contemporary Georgian MS care — and the multicentre research that should accompany it — can be objectively measured.

The aims of this reanalysis are threefold: (i) to quantify the frequency of panic attacks and associated psychiatric features in a historical Georgian MS cohort relative to matched healthy controls; (ii) to reinterpret these findings against the 2026 clinical evidence base, including current diagnostic criteria, disease-modifying therapies, validated psychiatric screening instruments, and mechanistic neuroimaging; and (iii) to use the resulting then-vs-now comparison to identify priority interventions for the contemporary Georgian MS care system.

2. Methods

2.1 Study design and setting

This was a single-centre, hospital-based, case-control study conducted at the High Technology Hospital Medical Centre in Batumi, Georgia. Patient recruitment, structured clinical assessment, and control-group matching were carried out prospectively between 2004 and 2006 under a protocol approved at the time by the local institutional ethics committee. The present manuscript is a retrospective reanalysis of these previously unpublished data, reinterpreted in the light of the 2026 MS clinical and evidence context. All statistical analyses reported here were performed de novo on the pseudonymised dataset in 2026 using contemporary methods. The study is reported in accordance with the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) statement [29].

2.2 Ethics and consent

The study protocol was reviewed and approved by the Institutional Ethics Committee of the High Technology Hospital Medical Centre prior to enrolment. All participants provided written informed consent after receiving a full explanation of study procedures and the voluntary nature of participation. The study was conducted in accordance with the principles of the Declaration of Helsinki as in force at the time of the study [30]. Data were pseudonymised at the point of collection and analysed under coded identifiers.

2.3 Participants

A total of 60 adults were enrolled: 30 patients with clinically confirmed MS and 30 age- and sex-matched healthy controls. Inclusion criteria for patients were (i)

a confirmed clinical diagnosis of MS established in the chronic phase according to the diagnostic criteria in force at the time of enrolment; (ii) age between 20 and 75 years; (iii) disease duration between 1 and 5 years; and (iv) ability to provide written informed consent. Controls were unrelated volunteers with no personal or family history of MS or other demyelinating disease, recruited from the same geographical catchment. Exclusion criteria for both groups were diagnosed hyperthyroidism, epilepsy, cardiac arrhythmia, and regular use of analgesic medication, each of which could confound anxiety-related symptomatology. Patients and controls were frequency-matched on age (within 5 years) and sex.

2.4 Clinical assessment

All participants underwent a structured clinical interview covering the frequency and severity of panic attacks, suicidal thoughts, difficulties in work and personal life, and the level of social functioning. Panic attacks were classified by reported frequency as frequent (15–20 episodes per month), infrequent (5–10 per month), or none or rare (fewer than 5 per month). Anxiety severity was quantified using the Sheehan Patient-Rated Anxiety Scale [31], a widely used instrument in which each item is scored from 0 ("not at all") to 4 ("extremely") and summed to provide a total score; scores above 30 are considered indicative of abnormal anxiety and scores above 80 indicate severe anxiety, with a typical mean score of approximately 57 ± 20 in patients with panic disorder [31]. Somato-vegetative symptoms (headache, dizziness, palpitations, weakness), sleep disturbance, asthenia, and suicidal ideation were recorded as present or absent during the preceding month.

2.5 Statistical analysis

All analyses were performed using R version 4.3 with RStudio (Posit, Boston, MA, USA). Categorical variables were compared between patients and controls using the chi-square test on 2 × 3 contingency tables for panic-attack frequency, and with Fisher's exact test on 2 × 2 tables for dichotomous outcomes. Risk was expressed as odds ratios (ORs) with 95% confidence intervals (CIs) computed by the Wald method on the natural logarithm of the OR. Continuous variables (age) were compared with the Student t test. A two-sided p-value < 0.05 defined statistical significance. No adjustment for multiple testing was applied; given the sample size, results are presented as exploratory and hypothesis-generating.

3. Results

3.1 Demographic characteristics

Sixty participants were analysed: 30 patients with MS (16 women, 14 men; age range 20–75 years; disease duration 1–5 years) and 30 age- and sex-matched healthy controls (15 women, 15 men; age range 20–65 years). The groups were comparable in sex distribution (female 53.3% vs 50.0%; p = 1.00). Demographic characteristics are summarised in Table 1.

Table 1. Demographic characteristics of patients with multiple sclerosis and healthy controls.

Characteristic	MS patients (n = 30)	Controls (n = 30)	p-value
Age range, years	20–75	20–65	— [a]
Sex, female, n (%)	16 (53.3)	15 (50.0)	1.00 [b]
Sex, male, n (%)	14 (46.7)	15 (50.0)	—
Disease duration, years	1–5 (chronic)	n/a	—

[a] Groups were frequency-matched on age within 5-year strata; exact individual ages were not recorded in the original dataset. [b] Fisher's exact test on the 2 × 2 sex table.

3.2 Panic-attack frequency

The overall distribution of panic-attack frequency differed significantly between patients and controls (Pearson $\chi^2 = 8.83$; df = 2; p = 0.012) (Table 2, Figure 1). Frequent panic attacks (15–20 episodes per month) were reported by 22/30 (73.3%) patients and 11/30 (36.7%) controls; infrequent attacks (5–10 per month) were reported by 4/30 (13.3%) patients and 6/30 (20.0%) controls. Only 4/30 (13.3%) patients reported no or rare panic attacks in the preceding month, compared with 13/30 (43.3%) controls. Considered as a single binary outcome, any panic attack (≥5 per month) was reported by 26/30 (86.7%) MS patients and 17/30 (56.7%) controls, corresponding to an almost fivefold increase in odds among MS patients (OR 4.97; 95% CI 1.39–17.82; p = 0.020).

Table 2. Frequency of panic attacks over the preceding month in patients with multiple sclerosis and healthy controls.

Panic-attack frequency	MS patients (n = 30)	Controls (n = 30)	p-value [a]
Frequent (15–20/month), n (%)	22 (73.3)	11 (36.7)	
Infrequent (5–10/month), n (%)	4 (13.3)	6 (20.0)	0.012
None or rare (<5/month), n (%)	4 (13.3)	13 (43.3)	

[a] Pearson chi-square test on the 2 × 3 contingency table; $\chi^2 = 8.83$, df = 2.

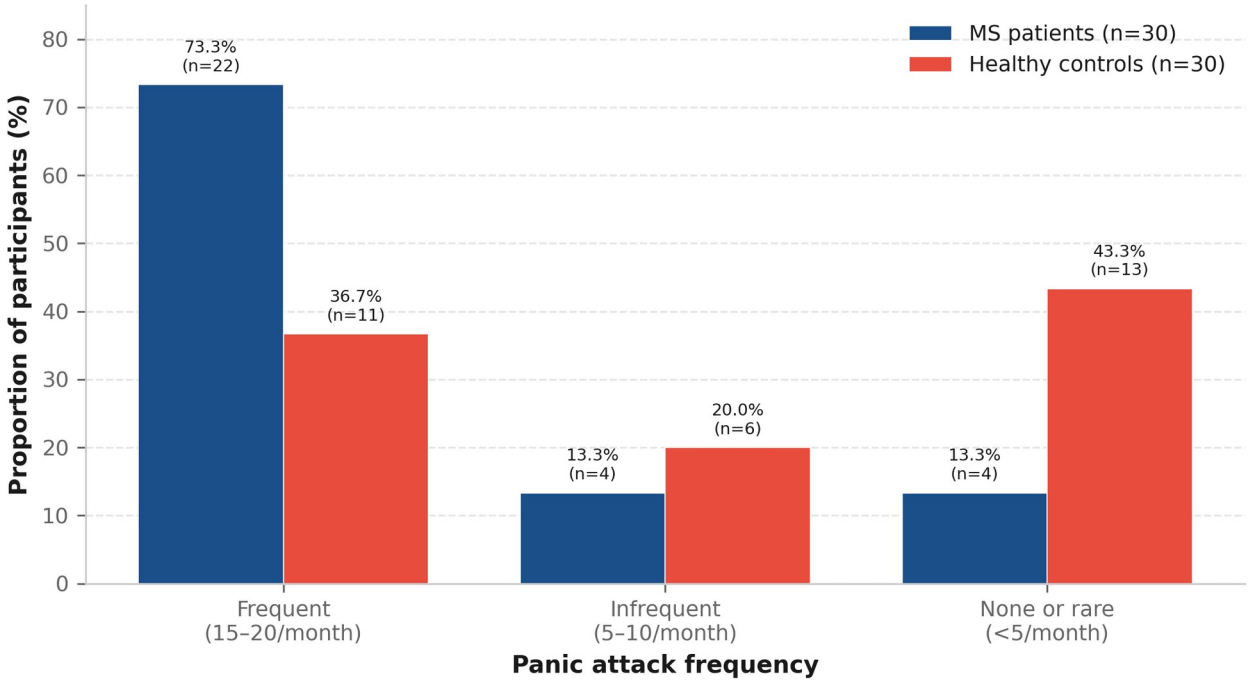

Figure 1. Frequency of panic attacks over the preceding month in patients with multiple sclerosis (blue) and healthy controls (red). Categories reflect the number of self-reported panic episodes during the prior 30 days. Percentages are calculated from the column totals; raw counts are shown in parentheses.

3.3 Functional and psychiatric outcomes

Compared with controls, MS patients had significantly higher odds of impairment across all functional domains assessed (Table 3, Figure 2). Impaired daily functioning was the strongest and most consistent finding, reported by 22/30 (73.3%) MS patients versus 8/30 (26.7%) controls (OR 7.56; 95% CI 2.41–23.75; p = 0.001). Capability changes — including reduced work or study capacity — were reported by 21/30 (70.0%) patients and 10/30 (33.3%) controls (OR 4.67; 95% CI 1.57–13.87; p = 0.009). Social-behaviour disturbance was also significantly more frequent in MS (16/30 [53.3%] versus 7/30 [23.3%]; OR 3.76; 95% CI 1.24–11.39; p = 0.033).

Suicidal ideation during the preceding month was reported by 11/30 (36.7%) MS patients and 4/30 (13.3%) controls (OR 3.76; 95% CI 1.04–13.65; p = 0.072). This threefold difference did not reach conventional statistical significance in the Fisher's exact test at the study sample size but is clinically meaningful, consistent with published MS literature [21–23], and warrants confirmation in larger cohorts. Somato-vegetative symptoms (headache, dizziness, palpitations, weakness) were more common in MS patients (66.7%) than controls (46.7%), with an odds ratio of 2.29 (95% CI 0.80–6.50; p = 0.192) that did not reach statistical significance. Sleep disturbance and asthenia were reported by 17/30 (56.7%) MS patients each; corresponding control-group prevalence was not systematically recorded in the original protocol (Figure 3).

Table 3. Psychiatric and functional outcomes in patients with multiple sclerosis compared with healthy controls.

Outcome	MS patients, n (%)	Controls, n (%)	OR (95% CI)	p-value [a]
Any panic attacks (≥5/month)	26 (86.7)	17 (56.7)	4.97 (1.39–17.82)	0.020

Impaired daily functioning	22 (73.3)	8 (26.7)	7.56 (2.41–23.75)	0.001
Capability changes	21 (70.0)	10 (33.3)	4.67 (1.57–13.87)	0.009
Social-behaviour disturbance	16 (53.3)	7 (23.3)	3.76 (1.24–11.39)	0.033
Suicidal ideation	11 (36.7)	4 (13.3)	3.76 (1.04–13.65)	0.072
Somato-vegetative symptoms	20 (66.7)	14 (46.7)	2.29 (0.80–6.50)	0.192
Sleep disturbance	17 (56.7)	not assessed [b]	—	—
Asthenia	17 (56.7)	not assessed [b]	—	—

[a] Fisher's exact test on the 2 × 2 contingency table; odds ratios and 95% CIs calculated by the Wald method. [b] Control-group prevalence for sleep disturbance and asthenia was not systematically recorded in the original study protocol.

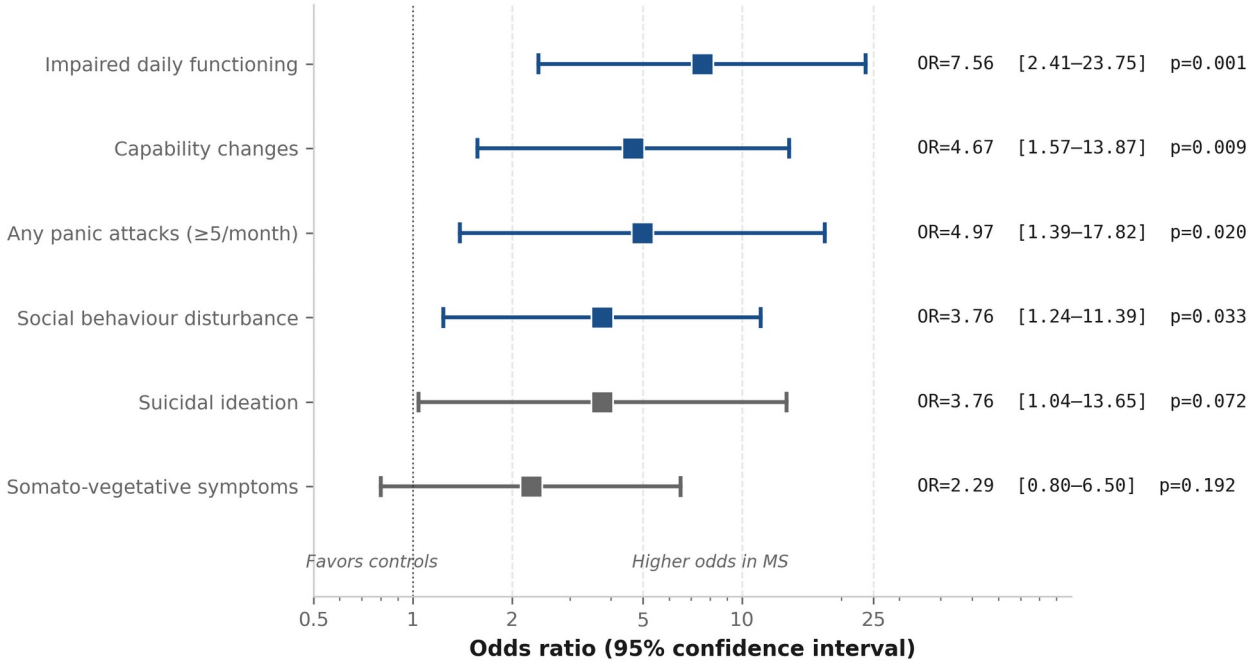

Figure 2. Forest plot of odds ratios (OR) with 95% confidence intervals (CI) for psychiatric and functional outcomes in multiple sclerosis patients compared with matched healthy controls.

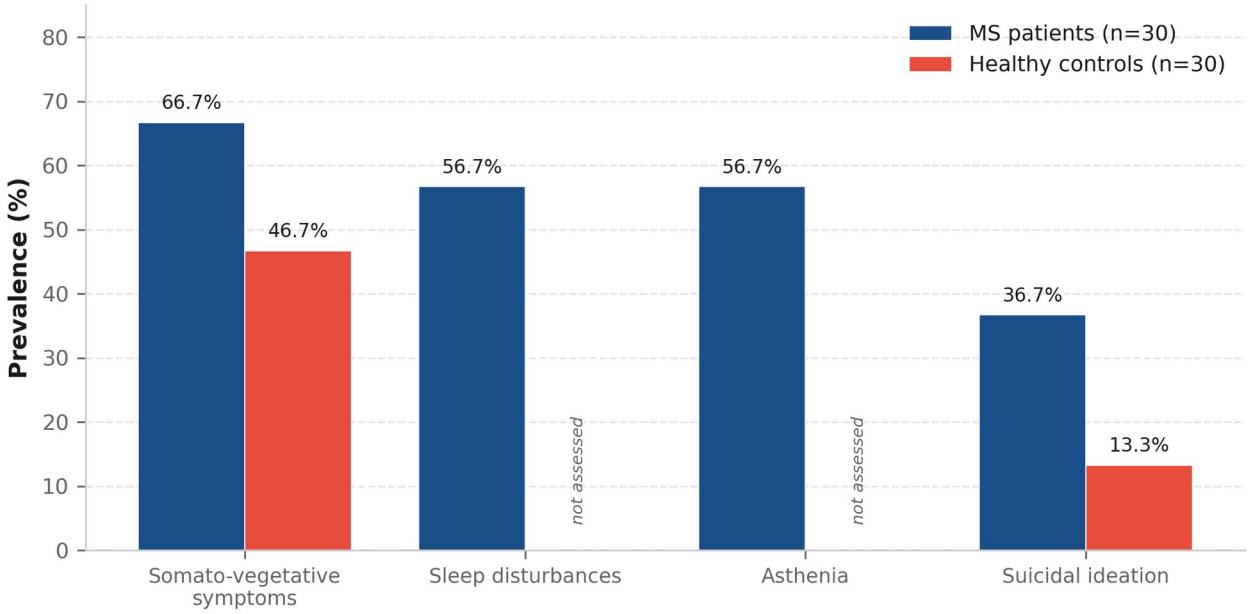

Figure 3. Prevalence of additional symptoms in MS patients (blue) and healthy controls (red). Sleep disturbance and asthenia were recorded only in the MS group (greyed bars denote outcomes not assessed in controls).

4. Discussion

In this case-control study of 60 Georgian adults, we observed that patients with multiple sclerosis had substantially higher odds of panic attacks and functional impairment than matched healthy controls. The strongest association was with impaired daily functioning (more than sevenfold higher odds), followed by panic attacks and capability changes (approximately fivefold and nearly fivefold, respectively). Suicidal ideation showed a threefold increase that, while not reaching conventional statistical significance at this sample size, is consistent with the broader MS literature.

4.1 Comparison with the international literature on anxiety and depression in MS

Our findings are consistent with the contemporary international evidence base on psychiatric comorbidity in MS. The systematic review by Marrie and colleagues pooled 118 studies and reported lifetime prevalence of any anxiety disorder of 35.7% in MS, with panic disorder 10%, generalised anxiety disorder 18.6%, and obsessive-compulsive disorder 8.6% [10,16]. Population-level Canadian data using administrative records show that the incidence and prevalence of depression, anxiety, bipolar disorder, and schizophrenia are all significantly greater in MS than in the matched general population, and that the excess begins before and persists after MS diagnosis [11]. Meta-analyses converge on pooled estimates of approximately 30% for depression and 22–35% for anxiety [12–15].

Our patient-level prevalence of any panic attacks (86.7%) is substantially higher than the panic-disorder prevalence reported in these reviews, most plausibly because our dichotomous outcome captured self-reported panic episodes rather than structured DSM-based diagnosis of panic disorder; a single month's frequency also differs from the lifetime recall used in most published estimates. Despite this methodological difference, the direction and magnitude of the between-group contrast are consistent with the international consensus that anxiety-spectrum symptoms are markedly elevated in MS.

Biological mechanisms underlying this association include MS-related demyelination in limbic and brainstem circuits involved in autonomic and affective regulation, chronic neuroinflammatory cytokine release, hypothalamic-pituitary-adrenal axis dysregulation, and the psychological burden of a chronic, unpredictable neurological condition [18,19]. A recent German cohort study used resting-state functional MRI to demonstrate that network alterations in specific anxiety-related brain pathways are already detectable in early MS [20], establishing a neurobiological substrate for the clinical observations reported here and elsewhere.

4.2 Suicidal ideation in MS

The threefold higher prevalence of suicidal ideation in MS patients compared with controls is clinically important even though it did not reach statistical significance at our sample size. Feinstein's structured-interview study of 140 MS patients found that 28.6% had experienced lifetime suicidal ideation,

with depression severity, social isolation, and younger age as predictors [21]. A subsequent systematic review confirmed that suicidal behaviour in MS is approximately double the general-population rate, with depression, disability, and social isolation as the strongest predictors [22]. A population-level Canadian study of 1 322 MS patients confirmed that prevalence of suicidal ideation is significantly associated with depression severity, hopelessness, and social support [23]. The consistency of our findings with this literature reinforces the need for systematic suicide-risk screening in Georgian MS care.

4.3 Psychiatric comorbidity and MS disease course

Beyond symptom burden, psychiatric comorbidity in MS has measurable consequences for neurological outcomes. A large Canadian administrative-database cohort study demonstrated that presence of a psychiatric comorbidity (depression, anxiety, or bipolar disorder) was independently associated with faster disability progression on the EDSS [24]. A related study from the same group found that individuals with MS and three or more comorbid conditions had significantly higher relapse rates than those with fewer comorbidities [25]. Additionally, psychiatric comorbidity has been shown to delay MS diagnosis and to increase overall mortality in a large Danish national registry study [26]. These data underscore that untreated psychiatric burden in MS is not merely an issue of patient wellbeing but a determinant of neurological prognosis.

4.4 Treatment and service-delivery implications

Despite the magnitude of the psychiatric burden in MS, evidence for specific interventions in this population remains limited. The systematic review by Fiest and colleagues identified modest evidence for both pharmacological and psychological treatments for depression in MS, but found insufficient data to make definitive recommendations for anxiety disorders specifically [27]. The American Academy of Neurology evidence-based guideline on psychiatric assessment in MS recommends screening for depression and anxiety at every clinical encounter, but acknowledges that the supporting evidence is predominantly based on clinical consensus rather than randomised controlled trials [28].

4.5 The 2004–2006 cohort through a 2026 lens: what would change today

Interpreting the present findings requires explicit acknowledgement of how much the MS clinical context has changed since the data were collected. Table 4 summarises the most consequential shifts between the 2004–2006 diagnostic, therapeutic, and psychiatric-assessment environment within which this cohort was recruited and the 2026 international standards against which a contemporary Georgian MS study would be judged.

Psychiatric assessment has undergone equally substantial transformation. At the time of the present study, anxiety was quantified using the Sheehan Patient-Rated Anxiety Scale [31], an instrument designed to measure symptom severity rather than to generate DSM-compliant categorical diagnoses. A contemporary replication would employ a structured clinical interview (the Mini International Neuropsychiatric Interview, MINI) for categorical diagnosis, the Hospital Anxiety and Depression Scale (HADS) for dimensional screening, and validated suicide-risk instruments (PHQ-9 item 9 and the Columbia-Suicide Severity Rating Scale) alongside DSM-5 diagnostic criteria.

Table 4. Comparison of the 2004–2006 clinical context within which the present cohort was recruited and the 2026 international standards against which a contemporary Georgian MS study would be judged.

Clinical domain	2004–2006 context (study cohort)	2026 standard
MS diagnostic criteria	Clinical + structural MRI; pre-McDonald 2005 framework	2017 McDonald criteria integrating CSF and MRI [7]
Disease phenotyping	1996 Lublin clinical phenotypes (no activity modifiers)	2013 revised phenotypes with activity/progression modifiers [8]
Disease-modifying therapy	No routine Georgian access; platform injectables only	High-efficacy monoclonals and oral agents; network meta-analytic evidence [9]
Anxiety assessment	Sheehan Patient-Rated Anxiety Scale only [31]	Structured clinical interview (MINI); HADS; DSM-5 criteria
Depression screening	Ad hoc; not systematic	Validated instruments (PHQ-9, BDI) with AAN guideline [28]

Suicide-risk screening	Ad hoc clinical interview	Routine validated screening (PHQ-9 item 9, C-SSRS) [22,23]
Disability measurement	Not routinely recorded	EDSS at every visit; MSFC; patient-reported outcomes
Mechanistic neuroimaging	Structural MRI for diagnosis only	Functional connectivity; network analysis of anxiety pathways [20]
Service delivery	Hospital-based neurology; no mental-health integration	Multidisciplinary MS care with embedded psychiatric/psychological services [28]

The plausible interpretation is therefore that a substantial fraction of the burden quantified here reflects MS lived in the near-absence of modern care: no high-efficacy DMT, no systematic psychiatric screening, no formal referral pathway to mental-health services, no EDSS-guided disability stratification. The magnitude of the observed associations should not be generalised uncritically to MS populations with contemporary treatment access; rather, they define a pre-DMT-era Georgian baseline that can inform the design and expected effect sizes of future studies.

4.6 Georgian health-systems perspective

The observation that a 2004–2006 Batumi cohort still represents the principal indexed Georgian evidence on psychiatric comorbidity in MS is itself informative. It reflects a broader pattern: Georgian MS care has historically been concentrated in a small number of referral centres, with uneven access to DMTs and limited systematic psychiatric assessment.

Embedding brief psychiatric screening into every MS clinic visit is internationally established best practice [28] and, given the magnitude of the burden quantified here, is likely to deliver substantial patient-level benefit at modest marginal cost to the Georgian health system. Pragmatic first steps include mandatory PHQ-9 and GAD-7 administration at every MS outpatient encounter, a defined referral pathway to clinical psychology or psychiatry for positive screens, and a national MS registry enabling longitudinal tracking of both neurological and psychiatric outcomes.

4.7 Strengths and limitations

Strengths of this study include the use of a matched case-control design within a single Georgian centre, structured clinical interview with a validated anxiety scale, a direct comparison with healthy controls drawn from the same geographical catchment, and — in the present reanalysis — explicit reinterpretation against the contemporary international evidence base.

Limitations are substantial and should be acknowledged transparently. First, the sample size (n = 60) limits statistical power and precludes multivariable adjustment. Second, panic attacks were classified by self-reported frequency rather than structured DSM criteria, preventing direct comparison with published panic-disorder prevalence estimates. Third, the study did not record EDSS scores, limiting the ability to stratify by disability level. Fourth, control-group assessments were incomplete for sleep disturbance and asthenia, precluding between-group comparison for these outcomes. Fifth, recruitment from a single Batumi hospital may not represent the broader Georgian MS population. Sixth, the absence of contemporary DMT exposure in this cohort limits direct extrapolation to MS populations with modern treatment access.

4.8 Implications and future directions

The immediate clinical implication of this reanalysis is that systematic psychiatric screening should be considered a minimum deliverable of Georgian MS care, irrespective of resource constraints. The immediate research implication is that a contemporary, multicentre, adequately powered Georgian MS registry study — incorporating validated psychiatric instruments (MINI, HADS, PHQ-9, GAD-7, C-SSRS), EDSS-stratified disability assessment, and DMT exposure data — is both scientifically necessary and methodologically feasible.

5. Conclusions

In this reanalysis of a previously unpublished Georgian case-control dataset, patients with multiple sclerosis assessed in 2004–2006 showed strikingly elevated odds of panic attacks (OR 4.97), impaired daily functioning (OR 7.56), and suicidal ideation (OR 3.76) compared with age- and sex-matched healthy controls. Reinterpretation against the 2026 clinical framework reveals that these findings were generated in a pre-DMT, pre-structured-screening, pre-multidisciplinary-care environment that differs fundamentally from the current international standard. The data therefore define a documented pre-DMT-

era Georgian baseline and provide a quantitative mandate for embedding integrated psychiatric screening into every Georgian MS clinic encounter, expanding DMT access, and establishing a contemporary multicentre Georgian MS research programme.

Abbreviations

AAN — American Academy of Neurology
BDI — Beck Depression Inventory
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CI — Confidence interval
CSF — Cerebrospinal fluid
C-SSRS — Columbia-Suicide Severity Rating Scale
DMT — Disease-modifying therapy
DOI — Digital Object Identifier
DSM-5 — Diagnostic and Statistical Manual of Mental Disorders, 5th edition
EDSS — Expanded Disability Status Scale
GAD-7 — Generalized Anxiety Disorder 7-item scale
GMJ — Georgian Medical Journal
HADS — Hospital Anxiety and Depression Scale
MINI — Mini International Neuropsychiatric Interview
MRI — Magnetic resonance imaging
MS — Multiple sclerosis
MSFC — Multiple Sclerosis Functional Composite
OR — Odds ratio
ORCID — Open Researcher and Contributor ID
PHIG — Public Health Institute of Georgia
PHQ-9 — Patient Health Questionnaire-9
STROBE — Strengthening the Reporting of Observational Studies in Epidemiology

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Authors' contributions

MK: Methodology; formal analysis; writing — review and editing. SV: Conceptualisation; investigation; methodology; data curation; writing — original draft. KS: Investigation; resources; writing — review and editing. KG: Investigation; data curation; writing — review and editing. KV: Investigation; writing — review and editing. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate The study was approved by the Institutional Ethics Committee of the High Technology Hospital Medical Centre, Batumi, Georgia, prior to enrolment. All participants provided written informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki as in force at the time of the study [30].

Consent for publication Not applicable; no individually identifiable information is reported in this manuscript.

Conflict of interest disclosures The authors declare that they have no competing interests.

Data sharing The anonymised datasets generated and analysed during this study are available from the corresponding author on reasonable request, subject to ethics approval and institutional data-sharing agreements.

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