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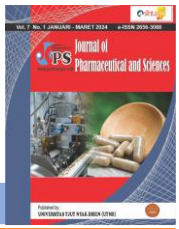

Complementary-Therapy Use, Neuropathic Screening Status, and Quality of Life in Patients with Hypertension or Diabetes: A Pre–Post Observational Study

Penggunaan Terapi Komplementer, Status Skrining Neuropatik, dan Kualitas Hidup pada Pasien Hipertensi atau Diabetes: Studi Observasional Pre–Post

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Abstract

Introduction: Peripheral neuropathy contributes to pain, functional impairment, and reduced quality of life in patients with diabetes mellitus and hypertension. This study evaluated changes in neuropathic screening status and quality of life during the use of complementary therapies alongside standard pharmacotherapy. **Methods:** This uncontrolled pre-post observational study included 147 patients at RSUD Nurdin Hamzah: 65 with hypertension and 82 with diabetes mellitus. Neuropathic characteristics and quality of life were assessed using the Douleur Neuropathique 4 (DN4) and WHOQOL-BREF, respectively. Paired DN4 observations were analyzed using the Wilcoxon signed-rank test, while associations with WHOQOL-BREF domains were analyzed using chi-square or likelihood-ratio tests. **Results:** After one month, DN4-positive screening decreased from 100% to 96.9% in the hypertension group and from 100% to 63.4% in the diabetes group. Paired DN4 observations differed significantly in both groups ($p<0.001$). No significant associations were found between complementary-therapy modalities and the physical, psychological, social, or environmental WHOQOL-BREF domains (all $p>0.05$). **Conclusion:** DN4 screening status improved during combined standard pharmacotherapy and self-selected complementary-therapy use, particularly among patients with diabetes, without a corresponding association with quality-of-life domains.

Keywords: Complementary therapy; Diabetes mellitus; Hypertension; Neuropathy; Quality of life; Observational study; Pre–post design.

Abstrak

Pendahuluan: Neuropati perifer berkontribusi terhadap nyeri, gangguan fungsi, dan penurunan kualitas hidup pada pasien diabetes melitus dan hipertensi. Penelitian ini mengevaluasi perubahan status skrining neuropatik dan kualitas hidup selama penggunaan terapi komplementer bersama farmakoterapi standar. **Metode:** Studi observasional pre-post tanpa kelompok kontrol ini melibatkan 147 pasien di RSUD Nurdin Hamzah, terdiri atas 65 pasien hipertensi dan 82 pasien diabetes melitus. Karakteristik neuropatik dan kualitas hidup dinilai menggunakan Douleur Neuropathique 4 (DN4) dan WHOQOL-BREF. Pengamatan DN4 berpasangan dianalisis dengan uji Wilcoxon signed-rank, sedangkan hubungan dengan domain WHOQOL-BREF dianalisis menggunakan uji chi-square atau likelihood ratio. **Hasil:** Setelah satu bulan, proporsi skrining DN4-positif menurun dari 100% menjadi 96,9% pada kelompok hipertensi dan dari 100% menjadi 63,4% pada kelompok diabetes. Pengamatan DN4 berpasangan berbeda bermakna pada kedua kelompok ($p<0,001$). Tidak ditemukan hubungan bermakna antara modalitas terapi komplementer dan domain fisik, psikologis, sosial, maupun lingkungan WHOQOL-BREF (seluruh $p>0,05$). **Kesimpulan:** Status skrining DN4 membaik selama penggunaan farmakoterapi standar bersama terapi komplementer pilihan sendiri, terutama pada pasien diabetes, tanpa hubungan yang sejalan dengan domain kualitas hidup.

Kata Kunci: Terapi komplementer; Diabetes melitus; Hipertensi; Neuropati; Kualitas hidup; Studi observasional; Desain pre–post.

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Introduction

Peripheral neuropathy is a clinically important complication of diabetes mellitus (DM) and is increasingly recognized as a major determinant of functional impairment, pain, and health-related quality of life (QoL). Diabetic peripheral neuropathy (DPN) is characterized by a heterogeneous spectrum of sensory, motor, and autonomic abnormalities, with distal symmetric polyneuropathy representing the most common clinical phenotype. Neuropathic manifestations may include burning pain, paresthesia, dysesthesia, numbness, impaired balance, and loss of protective sensation. Importantly, neuropathy may remain asymptomatic in a substantial proportion of patients, allowing progressive nerve dysfunction to develop before clinical recognition. The American Diabetes Association (ADA) therefore recommends systematic assessment of peripheral neuropathy in people with diabetes and emphasizes early recognition because neuropathy is associated with foot ulceration, impaired mobility, loss of independence, and deterioration in QoL[1], [2], [3].

The pathophysiology of diabetic neuropathy is multifactorial and involves sustained metabolic and vascular disturbances rather than a single pathological mechanism. Chronic hyperglycemia promotes oxidative stress, mitochondrial dysfunction, advanced glycation end-product formation, polyol-pathway activation, and inflammatory signaling, while abnormalities in endothelial function and the microcirculation may compromise the nutritional supply of peripheral nerves. These processes interact to produce axonal injury, impaired nerve regeneration, and progressive sensory dysfunction. Hypertension may further amplify this pathological burden through chronic vascular stress and microvascular dysfunction. Consistent with this relationship, contemporary evidence identifies hypertension as an independent risk factor for DPN[4], with pooled data indicating a significant association between elevated blood pressure and neuropathy development [5], [6]. The coexistence of hypertension and diabetes is therefore clinically relevant because patients exposed to both metabolic and vascular risk may experience a greater cumulative burden of neurological complications.

Neuropathic symptoms are not confined to sensory discomfort but can substantially affect multiple dimensions of patients' daily lives. Painful DPN may interfere with sleep, mobility, physical activity, emotional well-being, and social functioning [7], [8], thereby extending its consequences beyond neurological impairment alone [9]. The clinical relevance of this multidimensional burden is particularly important because pharmacological control of the underlying metabolic disorder does not necessarily reverse established neuronal damage. Current diabetes guidelines emphasize that optimal glycemic management can prevent or delay neuropathy and may modestly slow progression in type 2 diabetes[10], while management of blood pressure, lipids, body weight[11], [12], [13], and other modifiable risk factors may further reduce neuropathy risk[14], [15]. Nevertheless, once painful neuropathy is established, symptom-directed treatment remains necessary. Recommended pharmacological options include gabapentinoids[16], [17], serotonin–norepinephrine reuptake inhibitors, tricyclic antidepressants[18], [19], and selected sodium-channel blockers, although treatment response, tolerability, comorbidity, polypharmacy, and patient preferences can influence therapeutic decisions [20].

These therapeutic challenges have increased interest in complementary approaches that can be integrated with, rather than necessarily replace, evidence-based conventional management. Complementary therapies encompass heterogeneous interventions, including structured physical activity, acupuncture, nutritional supplementation, and selected botanical or bioactive preparations. Their potential relevance to neuropathic symptoms has been proposed through several mechanisms, including modulation of inflammation and oxidative stress, improvement of metabolic control, enhancement of physical function, and

modulation of pain perception. However, the evidence is not uniform across modalities. For example, a recent systematic review and meta-analysis of randomized controlled trials reported that exercise therapy may improve neuropathic symptoms, clinical signs, and physical function in patients with diabetic neuropathy[21], [22], although the overall certainty of evidence was rated very low [23], [24]. Similarly, meta-analytic evidence suggests that acupuncture used in combination with conventional treatment may reduce pain in patients with painful DPN[25], [26], while the authors emphasized limitations in the existing evidence base and the need for higher-quality clinical trials [27], [28], [29].

Nutritional and bioactive interventions likewise warrant careful evaluation because their biological plausibility does not necessarily translate into clinically meaningful benefits. Vitamin D supplementation, for example, has been associated with improvements in neuropathic pain in previous clinical studies, although the available evidence remains limited by the small number of eligible trials [30], [31], [32]. Conversely, recent randomized evidence involving nanocurcumin found no significant improvement in pain severity[33], [34], neuropathy scores, or metabolic and cardiovascular outcomes compared with placebo after 16 weeks[35], illustrating the importance of distinguishing mechanistic plausibility from demonstrated clinical efficacy [36], [37]. Such findings highlight a central challenge in complementary pharmacotherapy research: the clinical value of an intervention should be evaluated not solely on its proposed antioxidant or anti-inflammatory mechanisms but on patient-centered outcomes, reproducibility, safety, and its incremental contribution to standard care.

Despite growing interest in integrative management of diabetic neuropathy, an important evidence gap remains concerning the real-world use of multiple complementary therapies among patients with coexisting hypertension and diabetes. Much of the existing literature evaluates individual interventions under controlled experimental conditions, whereas routine clinical practice may involve heterogeneous combinations of exercise, traditional or herbal preparations, nutritional supplements, and other complementary practices alongside conventional medications. Moreover, studies frequently prioritize pain intensity or physiological outcomes, while comparatively less attention is given to the simultaneous relationship between neuropathic symptom burden and multidimensional QoL. This distinction is clinically important because an intervention that produces a modest change in symptom intensity may nevertheless have meaningful implications for physical, psychological, social, or environmental well-being.

Accordingly, this study described changes in DN4 screening status over one month and explored associations between self-selected complementary-therapy categories and WHOQOL-BREF domains among patients receiving standard care at RSUD Nurdin Hamzah. Because exposure was neither assigned nor randomized and no standard-care-only comparator was enrolled, the study was designed to generate associations and hypotheses, not causal estimates of efficacy.

Methods

Materials and Apparatus

Data-collection instruments comprised a demographic and treatment questionnaire, the Douleur Neuropathique 4 (DN4) screening tool, and the Indonesian WHOQOL-BREF. DN4 was used to identify features compatible with neuropathic pain; it was not treated as a validated treatment-response scale. Consequently, changes in DN4 score/rank and conversion across the screening threshold were interpreted as exploratory. The analysis focused on DN4 screening classifications and signed ranks; continuous summary measures and additional pain-severity instruments were not included. WHOQOL-BREF covers physical, psychological, social-relationship, and environmental domains; Indonesian population data support moderate-to-good test–retest reliability across these domains [54].

Study Design and Patient Recruitment

This uncontrolled pre–post observational study was conducted at RSUD Nurdin Hamzah and included 147 participants: 65 patients with hypertension and 82 with diabetes mellitus who had neuropathic symptoms. All participants continued prescribed standard pharmacotherapy and independently selected one or more complementary modalities during routine care; exposure was not assigned, randomized, standardized, or controlled by the investigators, and no standard-care-only group was enrolled. Therefore, observed changes may reflect complementary-therapy exposure, conventional treatment, medication adherence, regression to

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the mean, natural history or symptom fluctuation, and placebo/contextual effects. Ethical approval was granted by the Health Research Ethics Committee of Poltekkes Kemenkes Jambi (No. LB.02.06/2/2222/2026).

Procedure and Statistical Analysis

Baseline DN4 screening and WHOQOL-BREF assessments were obtained before the one-month observation period. Participants continued standard medical therapy alongside self-selected exercise, herbal preparations, supplements, or acupuncture. Available records identified modality names but did not consistently capture dose, preparation, frequency, intensity, supervision, manufacturer/source, adherence, changes in pharmacotherapy adherence, or systematic adverse-event monitoring. These unmeasured features prevent exposure standardization and modality-specific safety or effectiveness conclusions. Table 4 summarizes what was and was not documented; future protocols should use diaries, pill counts or electronic monitoring, standardized product records, and prospective adverse-event surveillance.

Data were analyzed using SPSS. The Wilcoxon signed-rank test explored paired differences in DN4 observations. Because DN4 is a diagnostic screening instrument rather than a validated responsiveness measure, the analysis was considered exploratory. Chi-square or likelihood-ratio tests explored associations between broad modality categories and WHOQOL-BREF classifications. Sparse cells, heterogeneous exposures, self-selection, and the lack of an unexposed comparator limit statistical power and interpretability. Two-sided $p<0.05$ denoted statistical significance; p values reported by software as 0.000 are presented as $p<0.001$.

Results and Discussion

Demographic Profiles and Clinical Characteristics

The clinical profiles of hypertensive (n = 65) and DM (n = 82) patients are presented in Table 1. The majority of hypertensive patients were aged 46–55 years (43.1%), female (52.3%), had a disease duration ≥ 5 years (55.4%), and exhibited uncontrolled blood pressure (75.4%). For DM patients, most were aged 46–55 years (46.3%), male (52.4%), had disease duration < 5 years (69.5%), and presented with elevated blood glucose levels ≥ 200 mg/dL (79.3%).

Table 1. Baseline Characteristics of Neuropathy Patients at RSUD Nurdin Hamzah.

Variable	Category	Hypertension (n=65)	%	Diabetes Mellitus (n=82)	%
Age	17–25 years	6	9.2	0	0
	26–35 years	3	4.6	1	1.2
	36–45 years	13	20.0	24	29.3
	46–55 years	28	43.1	38	46.3
	56–65 years	13	20.0	17	20.7
	> 65 years	2	3.1	2	2.5
Gender	Male	31	47.7	43	52.4
	Female	34	52.3	39	47.6
Duration of Disease	< 5 years	29	44.6	57	69.5
	≥ 5 years	36	55.4	25	30.5
Blood Pressure / Glucose	Normal / < 200 mg/dL	16	24.6	17	20.7
	Abnormal / ≥ 200 mg/dL	49	75.4	65	79.3

Pharmacotherapy and Complementary Therapy Patterns

Table 2. Modalities of Complementary Therapy Utilized by Patients

Complementary Modality	Hypertension (n=65)	%	Diabetes Mellitus (n=82)	%
Exercise / Physical Activity	50	76.9	13	15.9
Bay leaf (Syzygium polyanthum)	9	13.8	0	0
Sambiloto (Andrographis paniculata)	2	3.1	0	0
Acupuncture	1	1.5	0	0
Garlic / Noni / Ginger	3	4.5	13	15.9
Cinnamon / Omega-3 / Vitamin D / Curcumin	0	0	56	68.2

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Amlodipine monotherapy (67.7%) was the predominant antihypertensive regimen, followed by combination regimens such as amlodipine + candesartan (18.5%). In DM patients, metformin + glimepiride combination (26.8%) and metformin monotherapy (25.6%) were most common.

Physical exercise (76.9%) was the main complementary choice for hypertensive patients, whereas natural products/supplements (curcumin, omega-3, cinnamon, vitamin D) accounted for 84.1% of modalities used by DM patients.

Table 3. Characteristics and documentation of complementary modalities used by participants.

Category	Modalities recorded	Dose/preparation	Frequency/duration/adherence	Safety monitoring
Exercise	Physical activity	Not recorded	Not recorded; one-month observation	Not systematically recorded
Herbal preparations	Bay leaf, sambiloto, garlic, noni, ginger, cinnamon	Plant part, preparation, dose, and source not recorded	Not recorded	Not systematically recorded
Supplements	Omega-3, vitamin D, curcumin	Product, dose, and manufacturer not recorded	Not recorded	Not systematically recorded
Acupuncture	Acupuncture	Points and practitioner qualifications not recorded	Sessions and duration not recorded	Not systematically recorded

Effect of Complementary Therapy on Neuropathic Symptoms

At baseline, all participants screened DN4-positive. After one month of standard pharmacotherapy accompanied by self-selected complementary modalities, 63 of 65 patients with hypertension (96.9%) and 52 of 82 patients with diabetes (63.4%) remained DN4-positive. Thus, 2 hypertensive participants (3.1%) and 30 diabetic participants (36.6%) crossed below the screening threshold. These threshold changes are exploratory and should not be interpreted as remission or a validated treatment response.

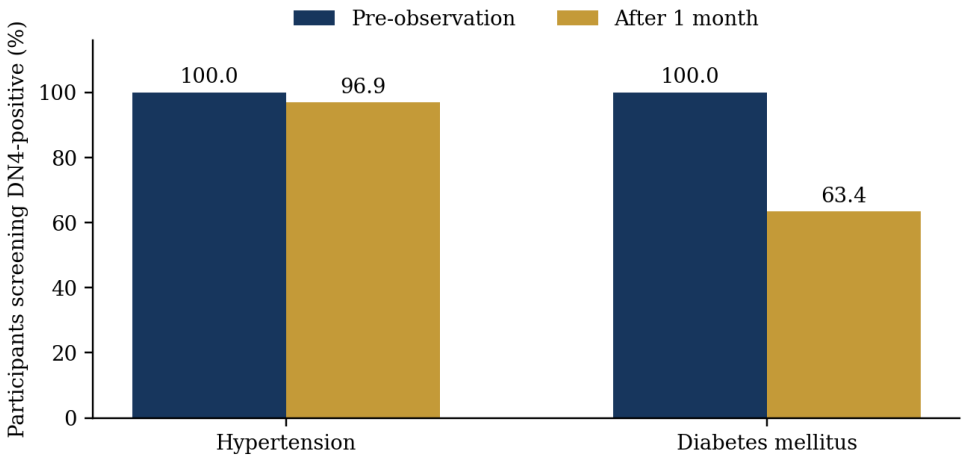

Figure 1. Proportion of participants screening DN4-positive before and after the one-month observation period. The figure is descriptive and does not establish a treatment effect.

Table **4.** Pre- and Post-Intervention Neuropathy Status (DN4) and Wilcoxon Analysis.

Patient Category	DN4 Pretest Positive (%)	DN4 Posttest Positive (%)	Negative Rank	Positive Rank	Ties	p-value
Hypertension	65 (100%)	63 (96.9%)	16	0	49	0.000
Diabetes Mellitus	82 (100%)	52 (63.4%)	58	14	10	0.000

Paired DN4 observations differed between assessments in both groups (Wilcoxon $p<0.001$). This finding indicates within-person change during the observation period, not an independent effect of

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complementary therapy. Continuous DN4 distributions were unavailable, and rank counts included both decreases and increases, particularly in the diabetes group. Accordingly, the result may also reflect concurrent pharmacotherapy, adherence changes, regression to the mean, natural fluctuation, or contextual effects.

Quality of Life and Bivariate Analysis

Quality of life evaluation via WHOQOL demonstrated that hypertensive patients generally maintained good QoL scores across physical (58.5%), psychological (70.8%), social (63.1%), and environmental (76.9%) domains. Conversely, DM patients reported higher proportions of poor QoL in psychological (62.2%), social (73.2%), and environmental (68.3%) domains.

Table 5. Bivariate Analysis (Chi-Square / Likelihood Ratio) Between Complementary Therapy and WHOQOL Domains.

QoL Domain	Hypertension Group (p-value)	Diabetes Mellitus Group (p-value)
Physical Domain	0.486	0.747
Psychological Domain	0.278	0.561
Social Relationships Domain	0.057	0.513
Environmental Domain	0.827	0.827

No statistically significant association was detected between broad complementary-modality categories and WHOQOL-BREF classifications (all $p>0.05$). These null results should be interpreted with extreme caution: every participant used at least one complementary modality, categories were heterogeneous, and several cells were sparse. The analysis therefore does not demonstrate absence of an effect on QoL and cannot substitute for within-person QoL change scores or comparison with a standard-care-only group.

Discussion

This uncontrolled pre–post observational study found changes in DN4 screening observations over one month while all participants received standard pharmacotherapy and self-selected complementary modalities. The Wilcoxon findings ($p<0.001$) describe paired change only. They do not show that complementary therapies caused improvement. Although more participants with diabetes crossed below the DN4 screening threshold than participants with hypertension (36.6% vs 3.1%), DN4 threshold conversion is not a validated endpoint for therapeutic response. The result should therefore be considered hypothesis-generating and may reflect multiple measured and unmeasured influences.

The modalities were clinically heterogeneous. Exercise predominated in the hypertension group, whereas cinnamon, omega-3, vitamin D, curcumin, and other products predominated in diabetes. Bay leaf (Syzygium polyanthum), sambiloto (Andrographis paniculata), noni (Morinda citrifolia), garlic, and ginger have traditional or preclinical rationales related to metabolic, inflammatory, or oxidative pathways, but direct clinical evidence for neuropathic pain is limited or absent for several of these botanicals. Mechanistic plausibility must not be interpreted as clinical efficacy. Because species authentication, plant part, preparation, dose, product quality, and adherence were not recorded, this study cannot identify which modality—or combination—was associated with the observed change.

The larger proportion of participants crossing below the DN4 screening threshold in the diabetes group coincided with a markedly different exposure pattern, not with a randomized comparison of modalities. Patients with diabetes more often used nutraceutical or botanical products, whereas exercise predominated among patients with hypertension. Consequently, the between-group contrast may reflect differences in baseline neuropathic phenotype, metabolic control, disease duration, conventional treatment, adherence, or other confounding factors rather than greater effectiveness of one complementary approach. The finding is therefore useful for generating modality-specific hypotheses, but it should not be interpreted as comparative-effectiveness evidence.

Exercise may support metabolic control, balance, physical capacity, and vascular or neuromuscular function. Recent syntheses suggest short-term benefits for neuropathic symptoms, signs, and physical function, although certainty and protocol consistency remain limited [22–24]. An Elsevier-published systematic review and meta-analysis of 13 randomized trials in diabetic peripheral neuropathy also reported reductions in HbA1c and fasting and postprandial glucose after exercise training, providing a plausible metabolic pathway through which structured exercise could support neuropathy management [59]. However, the present study did not document exercise type, intensity, frequency, duration, supervision, or adherence.

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It is therefore not possible to estimate a dose–response association, distinguish metabolic from symptomatic effects, or compare exercise with herbal, supplement, or acupuncture categories.

Acupuncture was reported by only a small subgroup and therefore cannot be evaluated independently in this dataset. Recent meta-analysis has suggested possible improvements in symptoms and nerve-conduction measures when acupuncture is used alone or alongside conventional treatment [58]. Nevertheless, an evidence-mapping overview of 18 meta-analyses involving 23,240 patients found that most reviews and outcome estimates were of low or critically low methodological or evidence quality [60]. Thus, the external literature supports continued investigation but does not justify attributing the present DN4 changes to acupuncture, particularly because treatment protocol, number of sessions, acupoints, practitioner qualifications, and adherence were not recorded.

Safety interpretation is equally constrained. Garlic and ginger may increase bleeding risk when combined with antiplatelet or anticoagulant therapy; curcumin and omega-3 products warrant similar caution in susceptible patients; and cinnamon or glucose-lowering botanicals may add to the effects of antidiabetic medicines. Garlic may also add to blood-pressure lowering. The magnitude and clinical relevance of many herb–drug interactions remain product- and dose-dependent, but medication reconciliation and active surveillance are prudent [55–57]. Because the study did not include systematic adverse-event monitoring, safety conclusions cannot be drawn. Regional familiarity may help explain use of Indonesian botanicals, but it does not resolve uncertainties about standardization, efficacy, or interaction risk.

No association was detected between modality category and any WHOQOL-BREF domain. This differs from the paired DN4 finding but is not evidence that complementary modalities have no relationship with QoL. Neuropathic pain can influence sleep, mobility, mood, anxiety, self-care, and social functioning, yet WHOQOL-BREF also captures broader physical, psychological, social, and environmental circumstances [8]. These domains may change more slowly than screening symptoms and may be shaped by disease burden, treatment complexity, socioeconomic conditions, family support, and mental health. A one-month observation period and categorical cross-sectional analysis may therefore miss clinically relevant within-person change. Indonesian normative research supports the instrument's domain reliability [54], but validation in the specific RSUD Nurdin Hamzah metabolic-disease population was not documented. Future studies should analyze paired continuous domain scores and prespecify a clinically meaningful QoL change in addition to neuropathic symptom outcomes.

The principal limitations are the absence of randomization and a standard-care-only comparator; self-selection and heterogeneity of modalities; sparse category-specific samples; a one-month follow-up; use of DN4 as an exploratory screening indicator rather than a validated response measure; lack of continuous DN4 and paired WHOQOL domain summaries; and no standardized records of dose, preparation, adherence, conventional-medication changes, or adverse events. These limitations make causal attribution and modality-specific comparisons impossible. Future studies should evaluate each modality separately using standardized protocols, validated pain and function outcomes, paired QoL scores, objective adherence measures, systematic interaction/adverse-event surveillance, and an adequately powered randomized or carefully controlled design.

Clinically, complementary modalities should be considered, if used, only as monitored adjuncts to evidence-based management. Glycemic, blood-pressure, lipid, and weight management remain central, and established pharmacological options should be individualized. The present results provide a real-world description of self-selected practices and exploratory symptom-screening change; they do not establish efficacy, comparative effectiveness, or safety of any modality.

Conclusions

In this uncontrolled pre–post observational study, DN4 screening observations changed over one month among patients receiving standard pharmacotherapy and self-selected complementary modalities (Wilcoxon $p<0.001$ in both diagnostic groups). No association was detected between broad modality categories and WHOQOL-BREF classifications, but the null findings are inconclusive because all participants were exposed and categories were heterogeneous. The results cannot be causally attributed to complementary therapy and should be interpreted as hypothesis-generating. Controlled, modality-specific studies using standardized exposures, validated treatment-response outcomes, adherence assessment, and systematic safety monitoring are required.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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