Integrative Medicine Patients Have High Stress, Pain, And Psychological Symptoms

By: Karen Caldwell, Ruth Q. Wolever, Nikita S. Goel, Rhonda S. Roberts, Benjamin Kligler, Jeffery A. Dusek, Adam Perlman, Rowena Dolor, and Donald I. Abrams

Abstract
Integrative medicine (IM) is a rapidly growing field whose providers report clinical success in treating significant stress, chronic pain, and depressive and anxiety symptoms. While IM therapies have demonstrated efficacy for numerous medical conditions, IM for psychological symptoms has been slower to gain recognition in the medical community. This large, cross-sectional study is the first of its kind to document the psychosocial profiles of 4182 patients at 9 IM clinics that form the BraveNet Practice-Based Research Network (PBRN). IM patients reported higher levels of perceived stress, pain, and depressive symptoms, and lower levels of quality of life compared with national norms. Per provider reports, 60% of patients had at least one of the following: stress (9.3%), fatigue (10.2%), anxiety (7.7%), depression (7.2%), and/or sleep disorders (4.8%). Pain, having both physiological and psychological components, was also included and is the most common condition treated at IM clinics. Those with high stress, psychological conditions, and pain were most frequently treated with acupuncture, IM physician consultation, exercise, chiropractic services, diet/nutrition counseling, and massage. With baseline information on clinical presentation and service utilization, future PBRN studies can examine promising interventions delivered at the clinic to treat stress and psychological conditions.
INTEGRATIVE MEDICINE PATIENTS HAVE HIGH STRESS, PAIN, AND PSYCHOLOGICAL SYMPTOMS

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Context: Integrative medicine (IM) is a rapidly growing field whose providers report clinical success in treating significant stress, chronic pain, and depressive and anxiety symptoms. While IM therapies have demonstrated efficacy for numerous medical conditions, IM for psychological symptoms has been slower to gain recognition in the medical community.

Objective and Design: This large, cross-sectional study is the first of its kind to document the psychosocial profiles of 4182 patients at 9 IM clinics that form the BraveNet Practice-Based Research Network (PBRN).

Results: IM patients reported higher levels of perceived stress, pain, and depressive symptoms, and lower levels of quality of life compared with national norms. Per provider reports, 60% of patients had at least one of the following: stress (9.3%), fatigue (10.2%), anxiety (7.7%), depression (7.2%), and/or sleep disorders (4.8%). Pain, having both physiological and psychological components, was also included and is the most common condition treated at IM clinics. Those with high stress, psychological conditions, and pain were most frequently treated with acupuncture, IM physician consultation, exercise, chiropractic services, diet/nutrition counseling, and massage.

Conclusion: With baseline information on clinical presentation and service utilization, future PBRN studies can examine promising interventions delivered at the clinic to treat stress and psychological conditions.

Key words: Integrative medicine, PBRN, stress, psychological disorders, pain

INTRODUCTION

While integrative medicine (IM) therapies have demonstrated efficacy for numerous physiological conditions,1,2 IM approaches for psychological conditions, including affective disorders, have not been as well accepted by the medical community.3,4 Despite IM provider reports of success treating psychological conditions5 and growth in high-quality research on IM for treating stress, other psychological conditions, and pain,6,7 there is yet to be substantial practice-based data available to guide clinicians in pairing psychological conditions, particularly affective disorders, with appropriate IM therapies.

IM is a rapidly growing field aimed at optimizing health and wellness while addressing core causes of illness through personalized care.8 Although IM combines evidence-based Western and non-Western therapies, IM is not simply a blend of complementary and alternative medicine (CAM) and conventional medicine; rather, it is a complex system of care that emphasizes prevention, wellness, and bio-psycho-socio-spiritual healing of the whole person to support the body’s innate healing abilities.9,10 As consumer interest grows in complementary therapies used in IM,11 so does the prevalence of IM clinics in academic medical centers and health systems. Despite this, research is limited on the practice-based applicability and effectiveness of IM, particularly regarding psychological symptoms.12 Psychological issues such as stress, depressive symptoms, fatigue, chronic pain, and disordered sleep affect multiple

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body systems, lifestyle choices, morbidity, and mortality.\textsuperscript{13–18} Because stress responses can impact multiple systems,\textsuperscript{9} it is not surprising that an estimated 60–90\% of physician visits are stress related.\textsuperscript{20,21} One particularly helpful aspect of IM treatment lies in its ability to positively impact multiple physiologic systems simultaneously. For example, the use of acupuncture and meditation to treat chronic stress simultaneously impacts a plethora of systems including the autonomic nervous system, musculoskeletal, cardiovascular, immune, and endocrine systems.

Practice-based research networks (PBRNs) have emerged as an effective means to connect researchers and clinicians in the clinical setting to systematically collect data about typical practices and clinical effectiveness.\textsuperscript{22–24} BraveNet, the first IM PBRN, has conducted two studies to better understand patients seeking and receiving IM. In one study,\textsuperscript{25} mean PBRN, has conducted two studies to better understand participants and procedures.

Participants and Procedures
A total of 4182 patients were recruited from nine IM clinics that comprise the BraveNet PBRN (Table S1). Eligible participants were \( \geq 18 \) years old, English- or Spanish-literate, able and willing to provide informed consent, and receiving treatment by an IM clinician. Participants completed a uniform set of questionnaires, within two weeks of their IM clinic visit. A corresponding form was completed by the clinician (or research staff using the medical record) to indicate provider assessment of conditions that were addressed and IM services that were provided. Site-research personnel entered de-identified data into a central database through a secure website. All procedures for each study center and the coordinating center received full approval by the appropriate institutional review boards (IRBs).\textsuperscript{9}

Measures
Participants were provided a case report form, which included basic demographic information and three well-validated psychological questionnaires. Perception of stress level was determined via the four-item Perceived Stress Scale (PSS-4).\textsuperscript{28} PSS-4 scores range from 0 to 16, with a national average of 4.4 [standard deviation (SD) = 2.9] for individuals aged 45–54 years.\textsuperscript{27} Mood was assessed via the 10-item Center for Epidemiologic Studies Depression Scale (CESD),\textsuperscript{29} for which scores range from 0 to 30.\textsuperscript{29} Quality of life was assessed using the 12-Item Short Form Health Survey (SF-12) to obtain both physical and mental function estimates.\textsuperscript{30} US physical-health norms have a mean of 50 (SD = 9.6), and mental-health norms have a mean of 50 (SD = 9.5).\textsuperscript{31} Participants indicated their experience over the past month from 0 to 10 for pain (average and worst), fatigue, and restfulness of sleep using numerical rating scales (NRSs). Finally, clinicians indicated health conditions addressed during the visit and services received onsite (31 categories of services were listed in the survey). Descriptive labels of services were agreed upon by BraveNet investigators, drawing from Eisenberg et al\textsuperscript{11,32} and National Health Interview Survey CAM definitions.\textsuperscript{33,34}

Statistical Analyses
All descriptive statistics were calculated using SAS version 9.4 and JMP Pro version 11.0 (SAS Institute, Inc., Cary, NC). Categorical variables were summarized using frequencies and percentages. Means and SDs were reported for continuous variables. Univariate analyses were utilized to detect outliers, which were subsequently submitted as queries to sites to ensure clean data. Age values were calculated from birthdate to visit date, and those below 18 years that could not be validated by the sites were excluded from subsequent descriptive analyses.

RESULTS
Demographics and Patient Status
Of 4182 participants, the majority were non-Hispanic white (84.5\%) women (73.4\%), with a mean age of 51.6 (SD = 15.1) years (Table 1). Patients were mostly self-referred (70\%); 88.3\% had health insurance, although the range of patients planning to submit for insurance reimbursement varied widely according to site (7–95\%).

Perceived Stress, Symptoms of Depression, and Quality of Life per Patient Report
Average PSS-4 scores were 5.9 (SD = 3.29), a half-SD above the national mean (Table 2). In fact, 64\% scored above the national mean for individuals with similar socioeconomic status, and 20\% of the sample was more than two SDs above. Average CESD scores were 8.9 (SD = 6.15), one point below the cutoff suggestive of likely clinical depression.\textsuperscript{29} More importantly, 39\% scored \( \geq 10 \), suggesting likely clinical depression. The average SF-12 mental-health score was 44.1 (SD = 11.19), a little more than a half-SD below the national norm (mean = 50, SD = 9.5). The average SF-12 physical-health score was 43.1 (SD = 10.09), three-fourths of an SD below the national norm (mean = 50, SD = 9.6).

Pain, Sleep Quality, and Fatigue per Patient Report
Worst pain over the past month was rated at 5.2 (SD = 3.11) (0 = no pain, 10 = worst-imaginable pain), and average pain

\textsuperscript{9} Full approval for the study was received by Allina Health IRB; Beth Israel Medical Center Human Subjects Protection Office IRB; Duke University Health Systems IRB; The Scripps Clinic IRB; Thomas Jefferson University, Division of Human Subjects Protection; University of California Los Angeles IRB; University of California San Francisco Committee on Human Research; and University of Maryland IRB. The BraveNet Network Coordinating and Statistical Center first received IRB approval through Duke University Health System (Protocol #18346) in 2008 and has maintained this approval through the present.
Table 1. Demographics (n = 4182)

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<thead>
<tr>
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<tbody>
<tr>
<td>Female (%)</td>
<td>73.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>84.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic (%)</td>
<td>8.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>51.6 (15.1)</td>
<td>72.7</td>
<td></td>
</tr>
<tr>
<td>Income &gt; $100,000 (%)</td>
<td></td>
<td>42.3</td>
<td></td>
</tr>
<tr>
<td>College or graduate degrees (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>53.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>22.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>13.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have insurance (%)</td>
<td>88.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plan to use insurance</td>
<td></td>
<td>57.8</td>
<td></td>
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</tbody>
</table>

was rated at 3.5 (SD = 2.54). How rested participants felt within the first hour upon waking over the past month was rated at 5.8 (SD = 2.54) (0 = not at all, 10 = very rested). Overall fatigue experienced throughout the day in the past month was indicated as 5.0 (SD = 2.38) (0 = none, 10 = worst). The two latter scales were positively skewed, with 58% and 57% of the sample reporting scores above the group mean.

Psychological Issues per Provider Report

Common psychological conditions (not mutually exclusive) addressed during visits included pain (43%, combining all pain-related conditions), fatigue (10%), stress (9%), anxiety (8%), depression (7%), and sleep difficulty (5%) (Table 3). Of 4182 patients, providers identified 2526 (60%) as having at least one of the following: chronic or acute pain, fatigue, stress, anxiety, depression, or a sleep disorder. Of these 2526 patients, the percentages with psychological issues and/or pain were understandably higher than those in the entire patient cohort, although they reflected the same pattern: pain (56%, combining all pain-related conditions), fatigue (12%), stress (11%), anxiety (9%), depression (7%), and sleep difficulty (5%). Differences between the overall and psychological cohorts are shown in Table 2.

Services Received

Percentages of the psychological cohort receiving or participating in each therapeutic modality are listed in Table 4:

Table 2. Comparison of Means of Psychosocial and Non-Psychosocial Cohort via Wilcoxon Signed-Rank Test

<table>
<thead>
<tr>
<th>Score</th>
<th>Overall (n = 4182)</th>
<th>Psychosocial Cohort (n = 2526)</th>
<th>Non-Psychosocial Cohort (n = 1656)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>CESD</td>
<td>8.93</td>
<td>6.15</td>
<td>9.65</td>
<td>6.25</td>
</tr>
<tr>
<td>PSS-4</td>
<td>5.93</td>
<td>3.29</td>
<td>6.28</td>
<td>3.26</td>
</tr>
<tr>
<td>SF-12 mental</td>
<td>44.09</td>
<td>11.19</td>
<td>43.21</td>
<td>11.32</td>
</tr>
<tr>
<td>SF-12 physical</td>
<td>43.12</td>
<td>10.09</td>
<td>41.28</td>
<td>10.16</td>
</tr>
<tr>
<td>Worst pain</td>
<td>5.21</td>
<td>3.11</td>
<td>5.89</td>
<td>2.92</td>
</tr>
<tr>
<td>Average pain</td>
<td>3.52</td>
<td>2.54</td>
<td>4.01</td>
<td>2.48</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.99</td>
<td>2.38</td>
<td>5.27</td>
<td>2.34</td>
</tr>
<tr>
<td>Quality-of-sleep</td>
<td>5.84</td>
<td>2.54</td>
<td>5.58</td>
<td>2.56</td>
</tr>
</tbody>
</table>

acupuncture, 29.3%; IM physician consultations, 24.3%; diet/nutritional counseling, 19.6%; exercise consults, 7.5%; and chiropractic care, 6.7%.

Relationship between psychological conditions and services received. To display which services were used to treat which psychological issues, Figure 1 shows the cross-reference between (1) psychological conditions addressed at the IM visit for at least 2% of the psychological cohort of n = 2526, and (2) the specific IM services received by at least 2% of the cohort. The x-axis includes a “bar” per psychological condition where the width of the bar indicates the proportions of services utilized by the cohort with the specified condition addressed at their IM visit. Conditions are listed from left to right on the x-axis in order of proportion. For example, chronic pain was the most-frequent condition addressed and therefore is represented by the widest “bar.” In contrast, sleep disorders were the least frequent (5.0%). The y-axis represents a breakdown of the types of services received per condition report. The indicator bar to the far left of the plot provides color-coding for each service as well as the overall proportion of each service provided. For instance, acupuncture is color-coded as magenta and constituted the largest portion of the services provided across all conditions (24.0%). In contrast, energy therapy is color-coded as green and was the least-received service (2.2%). Within each condition “bar” is shown the proportion of services received by patients utilizing a specific modality. So among services provided for chronic pain, for example, nearly 40% were acupuncture, approximately 12% were IM consults, and so forth. Interestingly, among all conditions involving pain, acupuncture was the most frequently received service, whereas stress and fatigue were treated with greater proportions of IM consultation and acupuncture.

Table 3. Percentage of all IM Patients (n = 4182) Presenting With Psychological Conditions as Reported by Practitioners

<table>
<thead>
<tr>
<th>Psychological Condition</th>
<th>Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pain conditions</td>
<td>42.8</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>10.2</td>
<td></td>
</tr>
<tr>
<td>Stress</td>
<td>9.3</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>7.2</td>
<td></td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>5.2</td>
<td></td>
</tr>
</tbody>
</table>

was rated at 3.5 (SD = 2.54). How rested participants felt within the first hour upon waking over the past month was rated at 5.8 (SD = 2.54) (0 = not at all, 10 = very rested). Overall fatigue experienced throughout the day in the past month was indicated as 5.0 (SD = 2.38) (0 = none, 10 = worst). The two latter scales were positively skewed, with 58% and 57% of the sample reporting scores above the group mean.
diet/nutritional counseling. Patients with anxiety, depression, and/or sleep disorders were treated with IM consultation and relatively similar levels of acupuncture and diet/nutritional counseling.

DISCUSSION

There were two major findings. First, an astounding 60% of IM patients were treated for high stress, a psychological condition, or pain. Patient-reported outcomes supported this finding, documenting higher levels of perceived stress and depressive symptoms and lower quality of life relative to national norms. They also showed more pain, poorer sleep quality, and greater fatigue than comparison groups from the literature. Second, this systematic data collection allows us to characterize the IM treatments most frequently offered for patients with stress and other psychological issues.

Stress, Depression, and Quality of Life

Despite geographical differences, remarkable similarities were seen across sites in psychological patient-reported outcomes of the entire IM cohort. Perceived stress was consistently high in our population (mean = 5.9, SD = 3.29) compared with national norms. This was true for all patients together and for each of the nine sites. BraveNet patients noted stress levels almost an SD above national normal. Moreover, 20% reported stress levels that exceeded two SDs above the normative mean. In other words, 20% of IM patients were as stressed as the top 2.3% of the regular population. In addition, IM patients reported greater levels of stress compared with other medical populations. Since women typically report higher levels of stress than men, the higher percentage of women in our sample might contribute to this presentation. However, this is clearly not the whole explanation; three national surveys using the PSS-10 consistently found that stress decreased with increasing age, education, and income, and was lower for whites. With this highly educated, fairly affluent, mostly white sample, lower stress levels would have been expected.

For depressive symptoms, the IM patients as a group did not meet the established criterion of 9.0 for symptoms of...
moderate clinical depression.²⁹ More importantly, though, 39% scored in the range indicative of likely moderate depression, which is quite high compared with the 12.2% prevalence of depression in other studies of medical outpatients.³⁹ IM patient scores were generally comparable to those of different groups of chronic medical patients.⁴⁰–⁴³ IM patient scores on the CESD were higher than those of patients in hemodialysis,⁴⁴ those with limb loss,⁴⁵ and those of elderly individuals.⁴⁶–⁴⁹

For quality of life, our population exhibited mental and physical scores half to three-fourths of an SD below the national mean, but scores were consistent with reports of other IM patient groups. This is similar to subsets of IM patients with asthma⁵⁰ and in general patients seeking IM.⁵¹,⁵²

### Pain, Sleep Quality, and Fatigue

While there are no normative samples available for 0–10 NRSs to compare reports on pain, sleep quality, and fatigue, BraveNet outcomes can be compared with NRS reports from previous studies. Our patients reported an average of 5.2 (SD = 3.11) for worst pain and 3.5 (SD = 2.54) for average pain. Higher ratings have been seen in other groups seeking IM for pain. For example, a study of 251 patients with low back pain reported an 8.5 rating of worst pain and a 5.4 rating of average pain—those seeking CAM interventions for herpes zoster and post-herpetic neuralgia reported average pain levels of 7.5–7.8.⁵⁴ The lower pain profiles in our sample likely relate to inclusion of patients seeking IM for prevention, overall wellness, and chronic health conditions not associated with pain. We know that chronic-pain patients seeking IM in these same clinics have averaged 4.7 on the same scale prior to treatment.⁵⁵

For sleep quality, there is a single study available to compare with our sample. Chinese patients, older than 90 years and without dementia, averaged 5.2 on a similar scale (SD = 2.55). The mean age of our sample was significantly younger, and sleep quality averaged 5.8 (SD = 2.54).

For fatigue, BraveNet patients reported levels averaging 5.0 (SD = 2.38), indicating less fatigue than those with chronic fatigue syndrome (mean = 6.8, SD = 1.6)⁵⁶, but greater fatigue than seen in cancer patients (mean range from 2.5 to 4.7).⁵⁷–⁶⁰

While this is the first large-scale report of the psychological profile of IM patients across multiple clinics, our findings are consistent with reports from individual IM clinics. In a recent review of 29 clinics, 75% reported clinical success with chronic pain, 55% with depression/anxiety, 52% with stress, and 48% with fatigue/sleep disorders. These were among the top conditions for which IM clinicians reported greatest clinical success.⁷

### Relevance to Clinical Care

High rates of pain, fatigue, depression, and stress-related disorders, and significant accompanying morbidity make development of successful treatment approaches a high priority. Chronic pain impacts more American adults than those who are affected by heart disease, cancer, and diabetes combined at a cost between $560 billion and $635 billion annually.⁶¹ Similarly, major depressive disorder affects 10–20% of the US population and is the leading cause of disability and significant healthcare costs.⁶²,⁶³ The prevalence of clinically significant fatigue ranges from 5% to 20% in the general population, depending on the threshold for severity and persistence with survey reports.⁶⁴

In addition, substantial concern exists regarding conventional treatments. Medications used to treat chronic pain have adverse side effects and/or high addictive potential, and patients frequently develop tolerance. Likewise, anxiolytics and hypnotics are often prescribed for hyperarousal after significant stressors and are potentially addictive.¹⁹ First-line treatments for depression typically consist of cognitive-behavioral therapy or serotonin reuptake inhibitors; the latter can have gastrointestinal and sexual dysfunction side effects.⁶⁵ Furthermore, 37% of patients with depression do not receive treatment; of those who do, 60% aged <64 years discontinue treatment in the first 6 months.⁶⁶ Recurrence rates range from 40% to 85%.⁵⁷,⁶⁸ Similarly, treatment of fatigue has challenges because it is a nonspecific symptom, and the mechanisms underlying it are poorly understood. One longitudinal study of primary-care patients reporting fatigue found that half did not receive any diagnosis that could explain fatigue.⁶⁹ Lack of explanation and understanding of mechanism leads to difficulty in choosing an appropriate conventional therapy for the provider.

Given the challenges of conventional treatments for psychological and pain conditions, it is understandable that individuals seek IM. Moreover, evidence demonstrating IM’s effectiveness continues to accumulate. Acupuncture and mind–body treatments like meditation now have demonstrated efficacy and effectiveness for many psychological issues, including stress, depression, low quality of life, and pain (acupuncture⁷⁰–⁷³ and meditation⁷⁴–⁷⁵). Moreover, the importance of lifestyle change is burgeoning.⁷⁶–⁸⁰

### Treatment Received

While IM emphasizes individually tailored treatments, modalities tend to be similar across sites for specific psychological issues (Figure 1). In contrast to earlier reports,² our participants most often received combinations of acupuncture, IM consult, diet/nutrition counseling, exercise consultation, and chiropractic services.

### Limitations and Next Steps

First, given the sample heterogeneity, assessment of psychological features may be diluted. Additionally, comparisons with other populations must be made conservatively. Prospective, longitudinal, and comparative-effectiveness trials are needed to better understand the effectiveness of IM approaches. Nevertheless, systematic data-collection procedures within this PBRN represent a significant step toward the ability to characterize how psychological profiles of IM patients change over time.

### CONCLUSION

IM focuses on a holistic approach to optimizing health by blending evidence-based Eastern and Western practices into patient-centered care. While patient interest and use has
increased, the literature on clinical practice of IM has been limited. This is the first large-scale study describing psychological profiles and therapies received across a national network of IM clinics. Despite subtle demographic differences across our clinics, patients seeking IM care demonstrated remarkably similar psychological characteristics, including high stress levels, elevated pain, significant fatigue, moderate depressive symptoms, reduced quality of life, and poor sleep quality. The most common therapies received were acupuncture, IM consultation, diet/nutrition counseling, exercise consultation, and chiropractic care. These findings set the stage for future PBRN studies to examine promising interventions for stress and other psychological conditions in IM patients.

APPENDIX A SUPPLEMENTARY MATERIAL
Supplementary data associated with this article can be found in the online version at 2015.04.003.

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