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Application of a Clinical Approach to Diagnosing Primary Pain: Prevalence and Correlates of Primary Back and Neck Pain in a Community Physiatry Clinic

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Abstract: **Chronic back or neck pain (CBNP) can be *primary* (nociplastic or neuroplastic; without clear peripheral etiology) or *secondary* (to nociceptive or neuropathic causes). Expanding on available models of nociplastic pain, we developed a clinic-ready approach to diagnose primary/nociplastic pain: first, a standard physical exam and review of imaging to rule out secondary pain; and second, a detailed history of symptom presentation to rule in primary pain. We trained a physician who evaluated 222 patients (73.9% female, age M = 59.6) with CBNP; patients separately completed pain and psychosocial questionnaires. We estimated the prevalence of primary CBNP and explored biomedical, imaging, and psychological correlates of primary CBNP. Although almost all patients (97.7%) had at least 1 spinal anomaly on imaging, the diagnostic approach estimated that 88.3% of patients had primary pain, 5.0% had secondary pain, and 6.8% had mixed pain. Patients with primary pain were more likely than the other 2 groups of patients (combined as "non-primary pain") to report certain functional conditions, central sensitization, and features such as sensitivity to light touch, spreading pain, and pain worsening with stress; however, no difference was detected in depression, anxiety, and pain catastrophizing between those with primary and nonprimary pain. These findings are consistent with prior estimates that 85 to 90% of CBNP is "nonspecific." Further research is needed to validate and perhaps refine this diagnostic approach, which holds the potential for better outcomes if patients are offered treatments targeted to primary pain, such as pain neuroscience education and several emerging psychological therapies.**

Perspective: ***We developed an approach to diagnose chronic primary pain, which was applied in a physiatry clinic to 222 patients with CBNP. Most patients (88.3%) had primary pain, despite almost universal anomalies on spinal imaging. This diagnostic approach can guide educational and psychological treatments tailored for primary pain.***

Key Words: *Chronic primary pain, nociplastic, diagnosis, psychosocial, back/neck pain*

Chronic back or neck pain (CBNP) is the leading cause of disability in the United States,[1–3] but its etiology is controversial. Some studies suggest that 80 to 95% of CBNP cases are nonspecific, with no clearly identifiable peripheral cause.[4,5] Spinal imaging, however, routinely identifies anomalies that may be interpreted as causing or substantially contributing to the pain, leading some authors to conclude that about

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90% of cases are caused by structural pathologies. Diagnoses such as discogenic pain, facet joint pain, and sacroiliac pain are commonly given.[6–8]

The peripheral/structural model of CBNP has limitations. There is a poor correlation between imaging findings and CBNP—most adults without pain have disc degeneration, bulging disks, or other common findings.[9–11] Moreover, the prevalence of imaging anomalies rises substantially with age, yet the prevalence of CBNP does not.[12] In contrast to structural causes, there is much evidence for brain processes in CBNP.[13] As pain transitions from acute to chronic, it shifts from somatosensory brain regions to those associated with emotional function.[14] Both emotional and physical/injury stimuli can activate similar brain regions,[15,16] and the development of CBNP can be predicted by enhanced connectivity between the nucleus accumbens and prefrontal cortex—regions related to learning and emotion.[14] Anatomical findings rarely predict the development of CBNP, whereas psychosocial factors do[17,18]; for example, psychosocial trauma has substantial effects on neural processes[19–21] and predicts the later presence and severity of chronic pain.[22] Many cases of chronic pain may reflect a persistently activated "danger alarm" driven more by the brain's predictive processing than peripheral nociception or neuropathy.[23–25]

Recently, the World Health Organization, in association with the International Association for the Study of Pain, proposed classifying chronic pain as primary or secondary; primary pain—in addition to being associated with emotional distress or functional disability—is not better accounted for by another diagnosis, whereas secondary pain is.[26,27] Studies of the clinical application of these diagnoses are rare, but one study diagnosed primary pain in fewer than half of patients, whereas secondary pain—particularly musculoskeletal—was diagnosed frequently.[28] That study, however, did not present data specifically on CBNP. Moreover, a challenge in diagnosing people with CBNP is that spinal anomalies may *incorrectly* lead to diagnoses of "chronic secondary musculoskeletal pain associated with structural changes"[29] if anomalies are coincidental rather than causal.

We think that additional information is needed to help "rule in" primary pain. Importantly, the primary-secondary distinction is closely associated with 3 overarching chronic pain mechanisms: *nociplastic* (sometimes called *neuroplastic*) pain driven by plasticity and upregulation in the central nervous system, *neuropathic* pain driven by damage to the peripheral nervous system, and *nociceptive* pain driven by disease or structural pathologies causing persistent afferent nociceptive input.[30] Primary pain is largely nociplastic, whereas secondary pain is largely neuropathic or nociceptive. There are several frameworks for distinguishing nociplastic musculoskeletal pain from neuropathic or nociceptive pain.[31–36] These approaches recommend first carefully evaluating for clear evidence of a structural disorder or pathophysiological process causing the pain, and if no such pathology is identified, examining for nociplastic features such as pain disproportionate to injury, diffuse or neuroanatomically inconsistent pain distribution, dull or vague pain sensations, and the presence of allodynia or hyperalgesia.

These frameworks are helpful but need to be translated into a clinical application that can be used in frontline pain care settings. We have developed such an approach, which builds on those nociplastic descriptions by considering some additional features of the patient's pain history and presentation, which, we propose, may be useful for diagnosing primary pain in people with CBNP. Our approach consists of 2 steps: first, rule out a clearly identifiable structural condition; and second, rule in primary pain by conducting a detailed examination of pain history and characteristics along with other supporting evidence. In this article, we describe this clinic-ready diagnostic approach, which was taught to a physician who applied it to a series of patients seeking care for CBNP. We sought not only to estimate the prevalence of primary pain, but also to explore how such patients differ from those with secondary or mixed CBNP in spinal imaging findings, medical/psychiatric history, pain characteristics, and patient-reported data. We hypothesized that most patients would have primary pain, which would be associated with elevated psychosocial risk factors associated with nociplastic pain.

Methods

Participants and Setting

The study was conducted in a physical medicine and rehabilitation practice in a relatively small city (population ~82,000) in Louisiana from June 2020 to May 2021. Patients assigned to one of the physicians (W.J.L.) at the practice and who reported CBNP for at least 6 months were enrolled sequentially. Other than the inability to complete questionnaires or language barriers, there were no exclusions; that is, patients were not selected for primary pain in any way. The study was approved by the Institutional Review Board of Ascension Providence Hospital, and patients provided informed consent.

Diagnostic Process

The physician (W.J.L.) was a board-certified physiatrist with 12 years of practice who learned how to conduct this new diagnostic approach for primary pain, by reading a manual[37] and then attending several lectures and having a few discussions with author H.S. As detailed in Fig 1, the diagnostic approach for primary pain consisted of the following components: 1) a traditional physical medicine and rehabilitation medical history and physical exam, which includes findings from magnetic resonance imaging (MRI) (or occasionally computed tomography (CT) scans to rule out secondary causes; and 2) a process for ruling in primary pain based upon response to prior treatments, presence of concomitant conditions, and specific characteristics of the pain.

The physician conducted the traditional physiatry assessment but also determined each patient's pain type using this new diagnostic approach. It was not necessary

Step	Activities	Notes/Comments
1. Rule out structural disorder	1a. Conduct history & examination to rule out clearly identifiable structural processes causing pain	(A) Avoid overinterpreting minor findings such as localised tenderness, scoliosis, or muscle tightness
	1b. Review imaging studies to identify obvious structural disorder	(A) Identify fracture, tumor, infection, enlarged disc with signs/symptoms in affected dermatome. (B) Avoid overinterpreting findings seen in healthy people (e.g., degenerative disc disease, bulging discs, facet arthropathy, spinal stenosis, low level spondylolisthesis).
2. Rule in a primary pain condition	2a. Review responses to prior treatments	(A) Identify lack of response to treatments that should have addressed structural causes of pain (e.g., surgery, injections, spinal cord stimulation, or physical therapy). (B) Identify strong response to treatments with substantial placebo components (e.g., acupuncture, supplements, energy healing, chiropractic, or Reiki).
	2b. Assess prior and current central sensitization / functional conditions	(A) Their presence suggests a tendency for central generation of symptoms, including primary pain. Examples include tension and migraine headache, fibromyalgia, temporomandibular disorder, numerous syndromes (irritable bowel, irritable bladder, pelvic pain, chronic regional pain, chronic fatigue, postural orthostatic tachycardia), repetitive strain injury, and heartburn.
	2c. Obtain detailed history of pain characteristics to identify *functional*, *inconsistent*, or *triggered* ("FIT") features of pain	(A) Pain is ***functional*** in nature. Pain is not precipitated by injury, persists after an injury should have healed, covers a wide area, spreads spatially over time, or is anatomically implausible. Allodynia or hyperalgesia is present. (B) Pain is ***inconsistent*** in nature. Pain shifts in location during the day or week or changes in intensity at seemingly random times, but especially when linked to meaningful psychosocial activities (e.g., arriving at work, visiting family). Pain increases after rather than during exercise or activities, when thinking about pain, or with stress; and decreases with distracting or engaging activities. Pain changes with specific activities or locations, such as sitting in only certain chairs or driving only in certain cars. (C) Pain is ***triggered*** by innocuous stimuli. For example, changes in weather, sounds, light, smells, computer screens, light touch, stressful situations or anticipation of those situations, by imagining activities that increase pain, or idiosyncratic stimuli.

Figure 1. Diagnostic approach to the determination of primary pain. (No single factor may be conclusive on its own, yet the overall patient profile determines diagnostic subtype.)

to have a specific number of diagnostic criteria, but clear examples of several criteria are considered adequate evidence for diagnosing primary pain.[37–39] A diagnosis of secondary pain was made when there was clear evidence of a structural disorder and few or no criteria for primary pain. Mixed primary/secondary pain was diagnosed when there was evidence pointing to both diagnoses simultaneously.

Measures

Patients completed the clinic's standard medical history questionnaire, in which they indicated, among other information, whether or not they had a history of a series of medical and psychiatric conditions, including anxiety or depression. This questionnaire was available to the diagnosing physician. Patients also completed the following 5 self-report measures, which were not reviewed by the physician but were an independent data source to identify correlates of primary pain:

Pain Patterns

We developed an ad hoc checklist of 11 characteristics thought to potentially reflect primary pain, and patients indicated whether each one described their pain (yes/no). These items, which are listed in the Supplementary file, were analyzed separately.

Pain Intensity and Interference

Patients completed the Brief Pain Inventory,[40] assessing the week's worst, least, average pain, and current pain intensity; and pain interference with functioning in 7 domains (eg, mood, mobility). The 4 pain intensity items and the 7 pain interference items were rated from 0 to 10; ratings were averaged to yield 2 scores.

Pain Catastrophizing

A 4-item version of the Pain Catastrophizing Scale[41] assessed patients' tendency to engage in pain rumination, amplification, and helplessness. Items were rated from 0 to 4 and averaged.

Central Sensitization

Patients completed the Central Sensitization Inventory, Part A,[42,43] which lists 25 somatic and psychiatric symptoms that are manifestations of central sensitization (changes in the central nervous system in response to ongoing nociceptive input). Items were rated from 0 to 4 and averaged.

Extent of Pain

Patients completed the Michigan Body Map[44] to indicate in which of 35 body regions they had recurrent pain during their lifetimes. The total number of sites was analyzed.

Analyses

Diagnoses of primary, secondary, or mixed pain were made according to the new approach. Due to the low prevalence of secondary and mixed pain (described below) and the goal of better understanding the correlates of primary pain, the secondary and mixed categories were combined, resulting in a comparison of primary versus nonprimary pain. Chi-square tests compared these 2 groups on categorical outcomes, with the computation of Cramer's V to quantify effect sizes. Independent samples t-tests compared groups on continuous outcomes, with computation of Cohen's d to quantify effect sizes.

Results

A series of 222 patients with CBNP were enrolled. The sample was 73.9% female, 86.4% White, 12.7% Black, and .9% Native American, averaged 59.6 years old (standard deviation (SD) = 14.5), and had a median pain duration of 3 years. Most patients (85.1%) reported lumbar pain, whereas 19.4% reported cervical, and 3.6% reported thoracic pain; many patients had pain in multiple sites. Spinal scans indicated that 91% of the patients had disc bulges, 83.7% had arthritis, 48.2% had disc degeneration, and many other less common anomalies were present.

Prevalence of Primary Pain

Using the approach introduced here, 88.3% of the patients (n = 196) were diagnosed with primary pain, whereas 5.0% (n = 11) were diagnosed with secondary chronic pain, and 6.8% (n = 15) were diagnosed with mixed primary/secondary pain.

Medical, Psychiatric, and Demographic Variables

As Table 1 shows, patients with primary pain were numerically more likely than those with nonprimary pain to have a history of all the central sensitization conditions listed on the questionnaires, at approximately twice the prevalence. Some of these group differences (heartburn, migraines, tension headaches, and temporo-mandibular joint disorder (TMJ) reached statistical significance. The total number of such medical conditions was significantly greater in the group with primary pain (M = 2.2 conditions per patient, SD = 2.36) than in the group with nonprimary pain (M = .74, SD = 1.00), $t(219) = 2.99$, $P < .003$, $d = 2.24$). Regarding psychiatric history, patients with primary pain did not differ from those with nonprimary pain in the prevalence of depression (39.0% vs 37.5%) or anxiety (37.2% vs 29.2%). Regarding demographics, patients with primary pain were younger (M = 58.68 years, SD = 13.99 vs M = 68.65, SD = 15.74, $P < .001$) and more likely to be female (76.0% vs 57.7%, $P = .046$) than patients with nonprimary pain. The 2 groups did not differ in race (87.2% vs 80.8% White, respectively).

Spinal Anomalies

All patients but 5 (97.7% of the sample) had at least 1 spinal anomaly detected on imaging. As Table 2 shows, patients with primary pain differed from those without primary pain on only some of the spinal anomalies. Patients with primary pain had a significantly lower prevalence of disc extrusions, spondylolisthesis, neural foraminal narrowing, and canal stenosis than patients with nonprimary pain, and a marginally ($P > .10$) lower prevalence of arthritis, facet arthropathy/hypertrophy, and retrolisthesis. The 2 groups did not differ in the

Table 1. Differences Between Primary and Nonprimary Pain Groups on Medical, Psychiatric, and Demographic Variables

PATIENT HISTORY	PRIMARY PAIN (N = 196) N (%)	NONPRIMARY PAIN (N = 26) N (%)	TEST X^2	SIG P	EFFECT V
Medical history					
Heartburn	57 (33.1)	3 (12.5)	4.22	.040	.147
Restless leg syndrome	37 (23.9)	2 (8.3)	2.70	.114	.123
Tension headache	38 (22.1)	1 (4.2)	4.25	.052	.147
Migraine headache	36 (20.9)	0 (.0)	6.15	.009	.177
Insomnia	35 (20.3)	2 (8.3)	1.99	.263	.101
Dizziness	27 (15.8)	2 (8.3)	.92	.540	.069
Pelvic pain	27 (15.7)	2 (8.3)	.91	.540	.068
Temporomandibular dx	27 (15.7)	0 (.0)	4.37	.051	.149
Irritable bowel syndrome	24 (14.0)	2 (8.3)	.58	.747	.054
Stomach pain	23 (13.4)	1 (4.2)	1.67	.320	.092
Fibromyalgia	21 (12.2)	2 (8.3)	.31	.746	.039
Autoimmune disease	13 (7.6)	0 (.0)	1.94	.375	.100
Urinary tract infection	13 (7.6)	0 (.0)	1.94	.375	.100
Psychiatric history					
Depression	67 (39.0)	9 (37.5)	.02	.891	.010
Anxiety	64 (37.2)	7 (29.2)	.59	.443	.055

NOTE. Cramer's V is an effect size measurement for the chi-square test of independence, measuring how strongly 2 categorical fields are associated. Effect sizes ranging from .0 to .2 indicate weak associations, effect sizes ranging from .2 to .6 indicate moderate associations, and effect sizes greater than .6 suggest strong associations.

Table 2. Differences Between Primary and Nonprimary Pain Groups on Spinal Abnormalities Identified by Imaging

SPINAL ABNORMALITIES	PRIMARY PAIN (N = 195) N (%)	NONPRIMARY PAIN (N = 26) N (%)	TEST X^2	SIG P	EFFECT V
Bulging disc	175 (89.7)	26 (100.0)	2.93	.087	.115
Arthritis	160 (82.1)	25 (96.2)	3.35	.067	.123
Facet arthropathy/hypertrophy/osteophyte	160 (82.1)	25 (96.2)	3.35	.067	.123
Neural foraminal narrowing	138 (70.8)	24 (92.3)	5.44	.020	.157
Canal stenosis	109 (55.9)	22 (84.6)	7.84	.005	.188
Disc degeneration, signal/height loss	92 (47.2)	15 (57.7)	1.02	.314	.068
Spondylolisthesis	42 (21.5)	12 (46.2)	7.53	.006	.185
Disc protrusion	19 (9.7)	4 (15.4)	.78	.376	.060
Scoliosis	19 (9.7)	3 (11.5)	.08	.774	.019
Retrolisthesis	11 (5.6)	4 (15.4)	3.44	.064	.125
Spondylosis	10 (5.1)	3 (11.5)	1.70	.192	.088
Annular fissure	10 (5.1)	1 (3.8)	.08	.778	.019
Disc extrusion	2 (1.0)	2 (7.7)	5.74	.017	.161

NOTE. One participant with primary pain was missing imaging data.

prevalence of disc degeneration, spondylosis, disc protrusion, bulging disks, or annular fissures.

Pain Patterns

Table 3 presents the prevalence of various pain characteristics reported by patients. (Note that 26 patients [11.7% of the sample] did not submit the self-report measures of pain patterns or other pain characteristics; of the 196 who did, 172 had primary pain, and 24 had nonprimary pain). (Patients who did not complete the questionnaires were similar to those who did on age, gender, pain duration, and the frequency of primary or nonprimary diagnosis.) Patients with primary pain were more likely than those with nonprimary pain to report pain in areas of healed injury, pain that has spread, pain that worsens with stress, and pain that is sensitive to light touch. The groups did not differ in their report that their pain is triggered by changes in the weather, is worse at night, shifts to different areas, or is in an area of an old injury. Surprisingly, patients with primary pain tended to be less likely to report that their pain varied depending on the time of day or environment and that their pain was absent during certain activities.

Pain-related Questionnaires

Table 4 shows that, as expected, patients with primary pain reported higher levels of central sensitization

Table 3. Differences Between Primary and Nonprimary Pain Diagnoses on Patterns of Pain Symptoms

PAIN PATTERN	PRIMARY PAIN (N = 172) N (%)	NONPRIMARY PAIN (N = 24) N (%)	TEST x^2	SIG P	EFFECT V
Varies during the day	148 (86.0)	24 (100.0)	3.82	.051	.140
Worsening at night	94 (54.7)	12 (50.0)	.18	.668	.031
Spreading through body	84 (48.8)	6 (25.0)	4.82	.028	.157
Mirrored symptoms	69 (40.1)	6 (25.0)	2.04	.183	.102
In area of healed injury	68 (39.5)	1 (4.2)	11.55	< .001	.243
Shift to different areas	67 (39.0)	10 (41.7)	.07	.799	.018
Sensitive to light touch	61 (36.7)	3 (12.5)	5.52	.019	.170
Triggered by weather	59 (30.1)	7 (26.9)	.11	.739	.022
Worsening with stress	58 (33.7)	3 (12.5)	4.42	.035	.150
Absent with some activities	57 (33.1)	12 (52.2)	3.22	.073	.128
In area of old injury	48 (27.9)	5 (20.8)	.53	.465	.052

Table 4. Differences Between Primary and Nonprimary Pain Diagnoses on Self-reported Pain-related Measures

PAIN MEASURES	PRIMARY PAIN M (SD)	NONPRIMARY PAIN M (SD)	TEST T	SIG P	EFFECT D
Central sensitization	1.78 (.66)	1.35 (.68)	2.99	.003	.65
Pain severity	5.97 (2.20)	5.22 (2.83)	1.49	.104	.33
Pain interference	5.83 (1.84)	5.17 (1.99)	1.63	.137	.36
Pain catastrophizing	2.81 (1.04)	2.56 (1.15)	1.11	.268	.24
Extent of pain	9.28 (6.64)	8.46 (6.64)	.57	.568	.12

symptoms as measured with the Central Sensitization Inventory (CSI) than did patients with nonprimary pain. Patients with primary pain also reported a nonsignificant trend toward greater pain severity and interference, but there were no significant group differences in pain catastrophizing or lifetime bodily extent of pain.

Conclusions

The International Classification of Diseases (ICD)-11 generally describes primary and secondary chronic pain, and several scholars have provided specific recommendations for identifying nociplastic pain.[31–36] Expanding on the latter models, we developed a clinic-ready approach for identifying primary pain and had a frontline physician apply it to an unselected series of patients seeking care for CBNP at a physiatry clinic. The clinician found that a very high proportion of patients—88%—had primary musculoskeletal pain despite virtually universal imaging findings of spinal abnormalities, which could have readily led to a diagnosis of secondary pain. The finding of 88% of patients with CBNP having primary pain is consistent with previously published estimates of nonspecific back pain, though the empirical basis for prior estimates is unclear.[4,5] Of note, in an earlier clinical trial using the assessment method as described here, we found that 43 of 45 (96%) of people with chronic low back pain recruited from the community who were randomized to a mind-body treatment had primary pain,[45] providing a similar prevalence estimate.

These findings challenge traditional clinical diagnostic approaches that often view CBNP as largely structural in nature[6] or as a mix of primary (nociplastic) and secondary (nociceptive or neuropathic) pain,[46,47] although our approach found only 7% of patients in this latter category. Although it is nearly universally agreed that nociplastic mechanisms contribute to some CBNP cases, we found that most patients presenting with CBNP to this clinical practice had primary or nociplastic pain, with no *convincing* contribution from peripheral tissue causes—a finding that challenges commonly held views of many practitioners and patients.

Many providers are reluctant to state that a given patient has no or little contribution of structural (peripheral tissue) causes to account for the pain. Many people prefer to think that CBNP is due to a complex, often unknowable interaction of factors, including unobserved injuries or tissue pathophysiology. However, we think that the cause of most cases of CBNP can be determined to be primary—or nociplastic—as assessed through the 2-step process described here. An important consequence of such a determination is how it directs patient education. In our clinical work, the determination of primary pain is typically followed by patient education emphasizing that the pain is caused by the brain, is not an indication of bodily injury (ie, the body is healthy/uninjured), and can be reversed with treatments targeting psychological and behavioral processes.[37,39,45] A shift in patients' attributions for the etiology of their pain "from body to brain" appears to be a key mechanism in pain reduction.[48]

Our diagnostic approach is consistent with, but expands upon, the criteria proposed by others,[31–36] and includes pain characteristics indicating changes in neural circuits, such as pain that is inconsistent, variable, functional in scope, and triggered by innocuous stimuli. We believe that these criteria are face valid, easy to assess, and help patients understand the role of the brain in generating symptoms of pain. It will be challenging for both physicians and patients to overlook imaging findings of degenerative changes, despite the knowledge that these findings occur in people without pain. Therefore, having criteria that are clear, easily applicable, and face valid and that can *rule in* a primary pain condition allows the clinician and patient to accept this diagnosis more easily.

Trends in CBNP diagnosis and treatment show increasing use of scans, injections, surgery, and (until recently) opiate use, yet the prevalence of CBNP and the disability associated with it has risen.[49] Spinal anomalies are highly prevalent in people without pain, especially as they age,[9] and routine imaging may lead to high rates of negative outcomes with little positive yield.[50] Surgery for CBNP has not been shown to be more effective than a variety of conservative treatments, such as exercise, physical therapy, and observation,[51–54] and injections for CBNP have not been demonstrated to be more effective than placebo.[55–57] Although there is evidence for the short-term efficacy of manual manipulations for acute musculoskeletal conditions, there is contradictory and inconsistent data on the long-term effects of this intervention for people with CBNP.[58,59] These studies suggest that viewing CBNP in most patients as secondary to peripheral pathology may lead to unneeded, costly, potentially risky treatments, and even the possibility of iatrogenic illness due to increasing fear and worry about having a condition that is "chronic"—from which substantial or full recovery is not possible. The language used by physicians and other clinicians impacts expectations and clinical outcomes for people with chronic back pain.[60] Identifying spinal anomalies and informing patients that such anomalies are the likely cause of their pain can have negative clinical, economic, psychological, and social consequences. The diagnostic approach presented here, if validated in future research, is needed to inform the medical community about the high prevalence of primary/nociplastic CBNP.

We found that, compared to patients with secondary/mixed pain, patients with primary pain were more likely to be younger and female, and to report pain in the area of a healed injury, pain that spread over time, and pain that was worse with stress or light touch. Patients with primary pain also were more likely to have other common nociplastic or central sensitization conditions such as heartburn, migraine, tension headache, and temporomandibular disorder. Future work may build on these findings in developing a brief screener for chronic primary pain.

Interestingly, pain severity, pain interference, and pain catastrophizing did not reliably distinguish primary from secondary/mixed pain, nor did a history of anxiety or depression. These observations raise questions about the validity of relying on these commonly assessed patient variables to diagnose primary pain. It is noteworthy that the ICD-11 diagnosis of chronic primary pain requires that the patient experience pain-related distress or disability, but exactly how this is operationalized is not clear. The key article defining chronic primary pain appears to operationalize distress/disability as follows: "In other words, the experience of chronic pain should be sufficiently concerning for the person to seek help for it" (p. 29).[27] All patients in the current study were seeking help for their pain from a medical setting and, therefore, met this criterion. It is important to remember that elevated distress or disability is likely not specific to chronic primary pain; chronic secondary pain can often be distressing and disabling. Moreover, requiring the presence of distress for primary pain may induce unwanted gender bias; on average, women report higher anxiety and depression than men. We note a limitation in our study, however, in that we assessed a self-reported history of anxiety and depression, and not "pain-related distress" per se.

Although the brain has long been recognized as modulating pain, there is increasing recognition of the role of the brain in actually generating pain. The emerging neuroscience of predictive processing[23–25] posits that the brain generates vision, hearing, and other senses by integrating various inputs, including sensations from receptor organs as well as explicit and implicit memory, environmental cues, and emotions. In this model, pain is viewed as generated by the brain, and such pain can be triggered by nociceptive inputs, brain circuits in the absence of nociceptive inputs, or a combination of the 2.

Psychological treatment protocols based on the brain's predictive processing capacity to generate pain and that specifically target primary pain have recently been developed,[37–39,61,62] and these approaches have been validated in randomized, controlled trials.[45,63–65] These studies have shown that a treatment model that includes an assessment very similar to the approach described here can lead to substantial pain reduction or even elimination in a significant proportion of patients. A key to the efficacy of these treatments may be a clear determination—and clear communication to the patient—of a nociplastic cause of pain and the absence of any meaningful peripheral tissue injury.

A key limitation of our study is that we do not have a consensus gold standard approach for the diagnosis of primary pain, and we recognize that our data provide only a preliminary estimate of the prevalence of primary pain rather than confirmatory evidence. A goal of our approach here is to contribute to the ultimate development of diagnostic protocols that are reliable, valid, and useful. In future studies, this diagnostic approach could be validated against response to biomedical and/or psychological treatment, the natural course of symptoms, and potentially brain imaging markers of nociplastic pain. An additional limitation is that our sample was from a single clinic with a single diagnostician. Although we think that the sample is representative of the population of patients with CBNP, there might have been some unknown referral or self-selection bias of patients coming to a physiatry clinic or to this physician; for example, patients with certain disease processes (eg, infections, autoimmune disease) may have

been disproportionately referred elsewhere, reducing the number of patients with secondary pain. Due to the relatively small number of secondary and mixed pain types, we combined these types, and such combining, as well as their relatively small sample size, might have limited the identification of group differences.

Millions of people in the United States and worldwide continue to suffer from chronic pain that is often considered incurable. Despite intensive and expensive efforts, biotechnological treatments have not yet led to substantial breakthroughs, and evidence indicates that the prevalence of chronic pain continues to rise. There is increasing evidence that CBNP has a strong component of nociplastic etiology, with evidence of successful treatment programs based on this model. We believe that the diagnostic approach presented here is an important step toward accurately subtyping patients. This approach promises to help tailor interventions, moving away from expensive and invasive procedures toward those that are lower cost, safer, and more effective in treating one of the most common causes of disability worldwide.

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Disclosures

Dr. Schubiner is the co-owner of Freedom from Chronic Pain, Inc.; earns book royalties for *Unlearn Your Pain, Unlearn Your Anxiety and Depression*, and *Hidden from View*; serves as a consultant with UnitedHealth Group, Karuna Labs, and Curable Health; and receives personal fees from OVID Dx. Dr. Ashar reports personal fees from UnitedHealth Group, Lin Health, Inc., Pain Reprocessing Therapy Center, Inc., and Mental Health Partners of Boulder County. Dr. Lumley reports personal fees from CognifiSense, Inc. None of the other authors have any disclosures. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary Data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2023.09.019.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9

		(*b*) Report category boundaries when continuous variables were categorized	7-9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	9, 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.