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Comparative effectiveness of usual care with or without chiropractic care in patients with recurrent musculoskeletal back and neck pain

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Abstract

Background: Chiropractic care is a popular alternative for back and neck pain, with efficacy comparable to usual care in randomized trials. However, the effectiveness of chiropractic care as delivered through conventional care settings remains largely unexplored.

Objective: To evaluate the comparative effectiveness of usual care with or without chiropractic care for patients with chronic recurrent musculoskeletal back and neck pain.

Study Design: Prospective cohort study using propensity score matched controls.

Participants: Using retrospective EHR data, we developed a propensity score model predicting likelihood of chiropractic referral. Eligible patients with back or neck pain were then contacted upon referral for chiropractic care and enrolled in a prospective study. For each referred patient, 2 propensity score matched non-referred patients were contacted and enrolled. We followed participants prospectively for 6 months.

Main measures: Main outcomes included pain severity, interference, and symptom bothersomeness. Secondary outcomes included expenditures for pain related health care.

Key results: Both groups' (N=70 referred, 139 non-referred) pain scores improved significantly over the first 3 months, with less change between months 3 and 6. No significant between-group difference was observed. (severity -.10 (95% CI -.30, .10), interference -.07 (-.31, .16), bothersomeness -.1 (-.39, .19)). After controlling for variances in baseline costs, total costs during the 6-month post enrollment follow-up were significantly higher on average in the non-referred versus referred group ($1,996 [SD=3,874] vs $1,086 [SD=1,212], p=.034). Adjusting for differences in age, gender, and Charlson comorbidity index attenuated this finding, which was no longer statistically significant (p=.072).

Conclusions: We found no statistically significant difference between the two groups in either patient reported or economic outcomes. As clinical outcomes were similar, and the provision of chiropractic care did not increase costs, making chiropractic services available provided an additional viable option for patients who prefer this type of care, at no additional expense.

Introduction

Chronic musculoskeletal pain remains a substantial clinical and public health challenge.[1,2] In 2008, the total financial cost of pain to society, including both health care costs and lost productivity, was estimated at $560 to $635 billion.[3] Spinal disorders are the 4th most common primary diagnosis for office visits in the United States,[4] and are reported by over a third of patients presenting with musculoskeletal complaints.[5] Conventional management commonly includes nonsteroidal anti-inflammatory drugs, skeletal muscle relaxants, and opioids, which are of modest benefit and are associated with serious toxicities.[6,7]

Chiropractic care is popular among patients,[8,9] with efficacy for treating back and neck pain comparable to usual care in experimental randomized controlled trial (RCT) settings.[10] [11,12] However, the effectiveness of chiropractic care as actually delivered in routine conventional and integrative medicine practice remains largely unexplored. Rigorous evaluation of such routine care is complicated by numerous methodological challenges. In comparative effectiveness research of this type, RCT study designs may be logistically difficult or even infeasible, where the requirements for informed consent, the mechanics of the randomization process, the protocols for blinding, and other experimental constraints often directly conflict with the flow of routine office care. Further, even if feasible, imposing these research constraints is likely to alter care as actually delivered in everyday clinical settings. Prospective cohort studies provide a compelling alternative, but introduce challenges in identifying an appropriate control group that minimizes confounding or bias.

Propensity scores represent one viable approach to controlling for confounding in observational studies. However, propensity scores are typically applied in retrospective analyses, and to our knowledge have not been previously used to recruit and match subjects on an ongoing basis in prospective cohort studies requiring the collection of patient-reported outcomes. [13] We sought to evaluate the

comparative effectiveness of usual care with or without chiropractic care as provided to patients in an established health maintenance organization (HMO), using novel and scientifically rigorous methods. Specifically, we used data from retrospective electronic health record (EHR) and administrative databases to develop a propensity score model describing the likelihood of a patient's being referred for chiropractic care,[13] and then implemented a prospective cohort study comparing patients with chronic musculoskeletal pain who were referred for chiropractic care with propensity score matched controls who were not.

Methods

Design

*T*he *Relief* project is a multi-phased study evaluating acupuncture and chiropractic care for patients with chronic musculoskeletal pain in an HMO setting. Full descriptions of our study design and propensity score methodology have been previously published.[13, 14] In brief, the project featured 2 prospective cohort studies evaluating the effectiveness of usual care with or without acupuncture, and usual care with or without chiropractic care. This paper presents data from the chiropractic study; results of the acupuncture study will be published separately.

Setting

The study was conducted at Kaiser Permanente Northwest (KPNW), an HMO serving approximately 550,000 members in the metropolitan Portland area. KPNW provides chiropractic care to patients through a contracted network of chiropractors at Complementary Health Plans (CHP). Most KPNW members are eligible for referral to a CHP chiropractor by a KPNW clinician for a limited number of visits. Over the period of this project, KPNW policy allowed patient referral for chiropractic care in the

setting of acute (3 months or less) non-radicular back or neck pain. Importantly, those with an acute exacerbation of a chronic back or neck pain syndrome were eligible for referral.

Participants

We developed a study-specific chronic pain registry employing a comprehensive *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* code list to identify patients whose pattern of clinical diagnoses in the EHR suggested chronic musculoskeletal pain.[14] (Online Appendix 1) The sample was operationally defined as including members at least 18 years old with ≥3 outpatient pain related encounters evident in the EHR, spanning at least 180 days but no more than 18 months.

During the course of the study (8/1/13-1/31/15), we used the EHR to electronically monitor the routine care delivered at KPNW to registry patients. We contacted and invited patients to enroll in the study immediately upon chiropractic referral. As this was an observational study, the decision to initiate chiropractic referral, or not, was made between physician and patient in the context of the delivery of routine care in the clinics. Exclusion criteria included a baseline score of < 4 on the (0-10) scale for pain bothersomeness, non-persistent pain, current or recent (last six months) chiropractic care, pregnancy, or plans to move out of area. Given both the study sample definition and the KPNW medical necessity criteria for chiropractic care, most eligible patients had chronic pain with acute exacerbations of back or neck pain. Patients were screened and provided written consent, and baseline measures were collected. For each referred patient enrolled, we targeted enrollment of two control patients with chronic musculoskeletal pain who had a recent (previous 10 day) office visit for back or neck pain but were not referred for chiropractic care. These patients were likewise identified through EHR monitoring, contacted, and invited to enroll. We matched patients in the control arm to referred patients based upon gender, pain bothersomeness (difference within ± 2 points), and propensity to be referred for

chiropractic care. The latter was based upon a propensity score model developed using retrospective EHR data from 2010, and then validated on 2011 data, before implementation for matching in the 2013 prospective cohort study. The rationale and methodology for development of the propensity score model was identical to that for the *Relief* acupuncture cohort, and is described elsewhere.[13] Baseline predictive factors ultimately included in the calculation of the propensity score were age; opioid and pain medication use; number of outpatient visits; physical therapy utilization; diagnoses of nonspecific chronic pain, sleep disorders, substance abuse, and anxiety; tobacco abuse; procedures for diagnosing and treating pain; ambulatory Charlson score; and months since cohort entry. (Online Appendix 2) Over the course of their study participation, both referred and non-referred patients continued to receive usual care as deemed appropriate by their primary care physicians.

The Institutional Review Board at Kaiser Permanente Northwest approved all study procedures.

Outcomes

We collected patient reported-measures at baseline, and at months 1, 3, and 6.

Main outcome measures: Two subscales (the 4-item pain severity and the 7-item pain interference subscales) from the short form of the **Brief Pain Inventory (BPI-SF)**[15-17]were used to assess pain and related disability. The BPI has sound psychometrics and has been widely adopted. We also included a measure of how bothered participants were by their pain. This instrument uses a 0 to 10 scale of "**symptom bothersomeness**," where 0 represents "not at all bothersome" and 10 is "extremely bothersome." This question has been frequently used in studies of back pain[18,19] and shown to have adequate construct validity.[20]

Secondary outcome measures, clinical / patient-reported: Quality of sleep was measured using the 5-item **Insomnia Severity Index (ISI**)[21-23] We used the Personal Health Questionnaire **(PHQ-8**)[24] to evaluate depression severity. The PHQ-8 is established as a valid severity measure for depressive disorders in large clinical studies.[24-26] We used the 7-item Generalized Anxiety Disorder Scale **(GAD-7**)[27] to screen for anxiety disorders. Health-Related Quality of Life (QOL) was assessed using the five level **EuroQol** instrument **(EQ-5D**).[28]

Secondary outcome measures, health care costs: We monitored the cost of pain-related outpatient visits (including both conventional and chiropractic care), inpatient hospitalizations, and drugs dispensed for the 6 months prior to and following study entry. We estimated health plan costs (in 2014 U.S. dollars) by applying internal unit costs (developed and tested in previous studies)[29-31] to patient-level utilization measures, with the final cost variable acting as a proxy for HMO resource cost.

Adverse events: On each of the assessment surveys, we asked participants to report any adverse events associated with pain treatments.

Data sources

We collected patient-reported outcomes and adverse events over the phone or online.[32] (Online Appendix 3)

We used EHR data to determine pain-related and comorbid diagnoses, estimate pain-related health care costs, and to calculate Charlson comorbidity index scores.[33] We obtained patient data for the 180 days before and after patient enrollment. The data included ICD-9-CM diagnostic codes and Current Procedural Terminology (CPT) codes for procedures and filled prescription data associated with chronic pain.

Finally, we mailed a questionnaire to chiropractors who cared for study participants to collect information on the treatments they provided (session frequency, reason for referral, and use of specific treatment approaches including: joint manipulative procedures, soft tissue manipulative procedures, physical modalities, prescriptions/devices, rehabilitative exercises, and self-care /lifestyle recommendations).

Sample size

Sample size calculations demonstrated that 100 study participants per group would yield statistical power of approximately 0.90 to detect standardized effect sizes of 0.50 or greater.[14] Using an alpha of .025, and given the number of participants actually enrolled, we have statistical power of 0.72 and 0.61 to detect standardized effect sizes of 0.50 or greater for BPI pain interference and severity, respectively. Using a 0.05 alpha, the power calculations are .81 for pain interference, and 0.71 for pain severity, respectively.

Statistical analysis

Patient-reported outcomes.

For pain scores, our primary analytic model was a piecewise continuous, segmented regression model that allowed us to estimate shorter-term (first 3 months, which, given the benefit structure, was the expected maximum duration of chiropractic treatment) and longer-term (second 3 months) changes in pain scores. The model was fit using the **mixed** procedure in Stata (version 13.1) in order to account for clustering of observations within patients and propensity score deciles, and adjusted for age, gender, and baseline Charlson comorbidity index (dichotomized as 0, Charlson=0 and 1, Charlson=1+). We included this parsimonious set of additional control variables because they were considered the factors most likely to confound the relationship between chiropractic referrals and patient outcomes. Similar

models were used to analyze the secondary clinical outcomes. We also conducted analyses using only the baseline and six-month data to assess the net impact of the chiropractic referrals six months after enrollment. Here, we used simple linear regression models to predict six month outcomes as a function of referral status, again adjusting for baseline level of the outcome measure and age, gender and baseline Charlson comorbidity index. Finally, we performed sensitivity analyses which retained only referred patients who actually received chiropractic care, and non-referred patients who actually did not receive such care.

Costs.

We modeled health care costs using generalized linear models with gamma specification and log link to accommodate the distributional properties of cost data and to avoid interpretation issues associated with back-transformation from transformation models. Model-based cost estimates were presented for the "typical" study participant where relevant,[34] and models were adjusted for age, gender, baseline Charlson comorbidity index, and baseline costs.

Missing data

Each analysis was performed on participants with available data. Multilevel estimation procedures allowed all participants to contribute to estimates if they had at least one observation for primary and secondary outcomes. Models estimating the net impact of the chiropractic referrals six months after enrollment required completion of the 6-month follow-up assessment. Costs analyses extracted data from the EHR and thus required continuous health plan enrollment during the 6-month follow-up. Results using multiple imputation with chained equations yielded similar results.

Results

Participants

Among potential referred participants, 264 completed screening, 94 screened eligible, and 70 consented and were enrolled. (Figure 1) The most common reason for screening ineligibility was undocumented chiropractic care within the preceding 6 months (N=127). Among potential controls, 717 completed screening, 422 screened eligible, and 139 consented and were enrolled. The most common reasons for screening ineligibility were similarly undocumented chiropractic care within the preceding 6 months (N=162) and low baseline pain scores (N=151).

Baseline Patient Characteristics

Participants were predominantly Caucasian (90.7%) and female (66.0%), with a mean age of 48.0 years (Table 1). Nearly all had back and/or neck pain. Despite propensity score matching, patients referred for chiropractic care were less likely than non-referred patients to be involved with litigation, to have depressive symptoms, or to have received physical therapy, spinal injections, or pain clinic specialty care. At 6 months, 89% of referred patients, and 86% of controls provided follow-up data.

Chiropractic Services

Among referred patients, the mean number of visits with the chiropractor, based upon EHR data, was 4.0 (sd 4.4; median=3, IQR=0-7).

Based upon both EHR data and participant self-report, 73% percent of those referred for chiropractic care actually received such care, while in the non-referred group, 16% sought and received chiropractic care on their own.

Forty chiropractors returned questionnaire responses describing the care for 43 referred patients. Regarding spinal care, 80% of responses reported providing thrust adjustment, 51% segmental mobilization, 31% instrument adjustment, and 21% traction / distraction. For soft tissue manipulative procedures, 52% of responses reported using massage, 42% muscle stretching, 39% point-pressure

techniques, and 13% Graston Technique (a method using metal instruments to rub patient muscles). Regarding physical modalities, 60% reported electrical stimulation, 60% hot / cold packs, and 24% ultrasound. For home care, 81% of the responses recommended stretching, 41% core stabilization, 33% resistance strengthening, 11% McKenzie exercises, and 11% proprioceptive drills. Regarding lifestyle recommendations, 61% provided exercise handouts, 33% advised stress reduction, 24% coached regarding injury prevention, and 12% provided dietary and nutritional counselling.

Main results

Patient reported outcomes

For bothersomeness, pain severity, and pain interference, both groups improved significantly over the first 3 months, with much less change between months 3 and 6. None of these changes differed significantly between the referred and non-referred groups in either adjusted (Table 2), unadjusted, or sensitivity analyses. Table 3 presents mean pain scores at the six-month visit. Although these tended to be lower for the referred than for the non-referred groups, again none of the differences were statistically significant.

We likewise found no significant difference between groups for any secondary clinical outcome measure. (Table 2) Similarly, there was no significant difference between groups for any of these outcome measures in terms of the percentage of patients showing clinically significant improvement at 6 months.

Economic outcomes

As shown in Table 4, total costs during the 6-month post enrollment follow-up were significantly higher on average in the non-referred versus referred group ($1,996 [SD=3,874] vs $1,086 [SD=1, 212], p=.034) after controlling for differences in baseline costs. Sensitivity analyses demonstrated similar results

during the 6-month follow-up with non-referred patients having higher costs than referred patients ($2,272 [SD=4,545] vs $819 [SD=882], p= .020). However, adjusting for differences in age, gender, and Charlson comorbidity index attenuated these differences, which were no longer statistically significant.

Adverse *events*

A total of 20 participants reported an adverse event: 14, or 10%, of the participants from the non-referred group, and six, or 8.5%, of those referred for chiropractic care. Among non-referred patients, four (3%) reported an adverse event attributable to medications, four (3%) to physical activity, one (<1%) to acupuncture treatments, and five (4%) to other factors. Among those referred for chiropractic care, three (4%) reported an adverse event attributable to physical activity, and three (4%) potentially to chiropractic care. Of these, one participant noted at 6-month follow-up that although neck pain improved with chiropractic care, hip pain worsened. A second participant indicated worsening pain at 3-month follow-up, but expressed uncertainty as to whether this was attributable to chiropractic treatments, or to their discontinuation. A third participant specified chiropractic care as a cause of worsening symptoms at one month follow-up, without further details.

No serious study-related adverse events were reported.

Discussion:

In this prospective cohort study, patients referred for chiropractic care showed statistically significant improvement comparable to propensity score matched non-referred patients for clinical pain-related outcomes. After adjusting for differences in baseline costs, total pain related health care expenditures during the 6-month post-enrollment follow-up were significantly higher on average in the non-referred versus referred group. Although this result persisted in a sensitivity analysis, and is consistent with previously published retrospective analyses,[35] it did not maintain statistical significance after

adjustment for differences in age, gender, and Charlson comorbidity index. As clinical outcomes were generally similar, however, and the provision of chiropractic care clearly did not increase costs, chiropractic care may have to some degree substituted for conventional care, rather than just adding to it. Chiropractic care thus provided an additional clinically viable option for patients who prefer this type of care, at no additional expense.

There were no serious adverse events associated with chiropractic care. Chiropractors reported considerable heterogeneity in the types of modalities offered to patients, and chiropractic care commonly included a substantial component of self-care instruction.

Strengths of this study include the prospective cohort design, incorporating patient reported outcomes and employing a novel approach to matching referred patients with controls at baseline using propensity score modeling. The study setting provided a unique opportunity to describe and evaluate chiropractic benefits as actually provided in a conventional HMO setting.

Study limitations include a relatively small sample size, as we did not achieve our targeted enrollment. This was largely due to many patients having recently used chiropractic care undetected by the EHR, thus rendering them ineligible for the study. Excluding such individuals from the study may have removed those most likely to use chiropractic care routinely from consideration, thereby limiting generalizability of our findings. Further, our analyses do not distinguish between those with neck pain and back pain, which may likewise limit generalizability. In addition, not everyone who was referred actually sought chiropractic care, while some participants in the non-referred group did receive such care. This would generally blunt real differences that might exist, likely biasing our results toward the null.

Even so, the study provides important insight. We found that referred and non-referred participants had comparable clinical outcomes, and that chiropractic referral neither added to healthcare costs nor

introduced significant safety concerns. Data suggest that although two thirds of primary care physicians have recommended chiropractic care to their patients,[36] lack of communication remains a major barrier to care coordination.[37,38] Better integration of chiropractors into conventional care spine management algorithms could represent a sensible approach to enhancing patient-centered care for patients with chronic musculoskeletal pain. Finally, the project establishes the feasibility of a methodologic alternative for prospectively evaluating the comparative effectiveness of clinical interventions in routine settings for chronic musculoskeletal pain.

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Conflicts of Interest: Dr. Deyo reports royalties from UpToDate for authoring topics on low back pain, an endowment from Kaiser Permanente to Oregon Health and Science University, and a financial gift from NuVasive as part of a lifetime achievement award from the International Society for Study of the Lumbar Spine. For the remaining authors, no conflicts of interest were declared.

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407

408

Table 1. Baseline Characteristics of Chiropractic Sample			
Characteristic / Health Services	**Referred for Chiropractic (n=70)**	**Not Referred for Chiropractic (n=139)**	**p-value‡**
Demographics			
Age, mean, SD	47.2 ± 13.6	48.4 ± 11.4	.506
% Female	64.3%	66.9%	.706
Race/Ethnicity			
White	89.6%	91.3%	.683
% Latino	2.9%	10.1%	.073
Education - some college or more	85.3%	76.7%	.156
Married / living with a partner	69.1%	76.6%	.258
Household income			.337
<$25,000	10.6%	10.2%	
≥$100,000	15.2%	24.2%	
Involved with litigation	1.5%	16.4%	**.002**
Pain Characteristics			
Time since first experienced persistent pain			.626
< 1 year	22.0%	18.7%	
1-5 years	36.8%	32.4%	
5-10 years	16.2%	23.7%	
> 10 years	25.0%	25.2%	
Time since first saw health professional for pain			.840
< 1 year	42.7%	37.4%	
1-5 years	27.9%	27.3%	
5-10 years	11.8%	15.1%	
> 10 years	17.7%	20.1%	
Baseline pain level			
Bothersomeness, mean, SD	6.6 ± 1.9	6.4 ± 2.0	.687
Pain severity (BPI-SF subscale) Mean, SD	5.3 ± 1.6	5.3 ± 1.5	.962
Pain interference (BPI-SF subscale) mean, SD	5.2 ± 2.1	5.3 ± 2.1	.669
Other Reported Symptoms			
Sleep disturbance (ISI - % w/score > 14)	28.6%	35.7%	.299
Depression symptoms (PHQ - % w/score > 10)	28.6%	40.4%	.094
Anxiety symptoms (GAD - % w/score > 10)	19.1%	27.7%	.179
Self-reported Use of Pain-related Health Care Services			
Physical therapy services in past 6 months	13.0%	19.7%	**.009**
Steroid/trigger point injections in past 6 months	4.4%	14.4%	**.030**
Acupuncture ever received	33.3%	40.3%	.331
Chiropractic Care ever received	56.5%	53.2%	.654
Use of Pain-related Health Care Services (from EHR)			
Physical therapy services in past 6 months	8.6%	9.4%	.853

Steroid/trigger point injections in past 6 months	2.9%	8.6%	.115
Pain clinic services in past 6 months	1.4%	15.8%	**.002**
Pain-related Imaging in past 6 months	15.7%	25.2%	.119
Pain-related Surgery in past 6 months	0%	0%	NA
Pharmacotherapy (data from EMR)			
Receipt of Long Term Opioid Treatment	11.4%	18.7%	.179
EMR Record of Opioid Therapy Plan	10.0%	18.7%	.103
Opioid Morphine Equivalent Dose (MED) (SD) (mg / day of morphine, or equivalent)	0.04 ± 0.16	0.14 ± 0.58	.142
% ≥ 120 MED	4.3%	6.5%	.521
Antidepressant receipt	32.9%	51.1%	**.012**
Medical and Psychiatric Comorbidities (from EHR)			
Diabetes	14.3%	10.1%	.367
Cardiovascular Disorders	40.0%	34.5%	.438
Respiratory Disorders	20.0%	10.8%	.069
Two or more of above chronic medical conditions	12.9%	10.8%	.658
Psychiatric Disorders	34.3%	44.6%	.153
Types of Non-Malignant Chronic Pain (NCP) (from EHR)			
Back pain	75.7%	79.1%	.573
Neck pain	57.1%	46.8%	.157
Back and neck pain	100.0%	97.8%	.216
Joint pain (including osteoarthritis)	70.0%	68.4%	.807
Fibromyalgia and other myofascial pain	15.7%	14.4%	.799
Headaches	14.3%	16.6%	.672
Neuropathy	5.7%	2.2%	.178
Nonspecific and other Pain	18.6%	25.2%	.284
Two of above NCP types	82.9%	80.6%	.690

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Table 2. Change in pain scores and other outcomes from piecewise regression model[1]

Outcome	Change from enrollment to 3 months				Change from 3 months to 6 months			
			Between group difference				Between group difference	
	Referred	Not referred	Mean (CI)	p-value	Referred	Not referred	Mean (CI)	p-value
Bother	-.50[4]	-.40[4]	-.10 (-.39, .19)	.499	-.04	-.02	-.02 (-.29, .26)	.91
Pain severity	-.35[4]	-.25[4]	-.10 (-.30, .10)	.336	.02	-.05	.07 (-.12, .27)	.46
Pain interference	-.38[4]	-.30[4]	-.07 (-.31, .16)	.534	.02	-.06	.07 (-.16, .30)	.54
Sleep	-.12	-.20	.08 (-.36, .51)	.315	.03	-.11	.14 (-.27, .55)	.50
PHQ	-.25	.02	-.27 (-.68, .15)	.209	-.08	-.21	.13 (-.30, .56)	.42
GAD	-.06	.19	-.25 (-.68, .18)	.258	.30	-.32[4]	.62 (.18, 1.05)	.006*
EQ-5D	.007	.004	.004 (-.01, .02)	.601	.001	.003	-.002(-.02, .01)	.77

[1] all results are adusted for age, gender, and Charlson comorbidity index

[2] p≤.05 for test that short term (or long term) slope is different from zero

[3] p≤.01 for test that short term (or long term) slope is different from zero

[4] p≤.001 for test that short term (or long term) slope is different from zero

*The trend favored the referred group from enrollment to 3 months, then the non-referred group from 3 months to 6 months, with no significant overall difference at 6 months

For EQ-5D (quality of life), higher scores are better. For the other measures, higher scores are worse.

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Table 3. Pain and other outcome scores at 6-month visit

Outcome	Referred	Not referred	Between group difference Mean (95% CI)	p-value
Bother	4.76	5.00	-.33 (-1.09 – 0.41)	.39
Pain severity	4.06	4.10	-.10 (-0.63 – 0.43)	.71
Pain interference	3.91	4.06	-.21 (-0.88 – 0.46)	.54
Sleep	11.11	11.35	.46 (-0.77 – 1.69)	.47
PHQ	6.92	8.34	-.65 (-2.02 – 0.76)	.37
GAD	6.34	6.54	.64 (-0.69 – 1.92)	.34
EQ-5D	.754	.706	.02 (-0.014 – 0.052)	.25

all results are adjusted for age, gender, and Charlson comorbidity index

413 For EQ-5D (quality of life), higher scores are better. For the other measures, higher scores are worse.

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417 **Table 4(A).** Average Health Care Expenditures (U.S. Dollars) Related to Pain during 6 months following
418 Qualifying Visit
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Expenditure Category	R Mean (SD) *(N=68)*	NR Mean (SD) *(N=139)*	*Coef. Estimate* (SE)[1]	*p*-value[1]	*Coef. Estimate*[2]	*p*-value[2]
Outpatient*	1,026 (1,192)	1,445 (1,866)	-0.18 (0.21)	.404	-0.19 (0.20)	.344
Pharmaceutical	60 (155)	174 (1,265)	0.10 (0.45)	.819	0.64 (0.55)	.246
Total Pain-Related Expenditures	1,086 (1,212)	1,996 (3,874)	-0.41 (0.20)	.034	-0.37 (0.21)	.072
Total Pain-Related Expenditures *less* inpatient	1,086 (1,212)	1,619 (2,242)	-0.17 (0.21)	.423	-0.17 (0.19)	.382

420 [1]Generalized linear models with Gamma specification and log link, robust standard errors, unadjusted beyond matched-design and baseline
421 expenditures (12 months prior to study entry; within category)
422 [2]Additional control variables include gender; age; Charlson Risk Score, dichotomized to 0=0 and 1=1+.
423 [*]Limited to mental health and pain-related encounters.
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Table 4(B). Average Health Care Expenditures (U.S. Dollars) Related to Pain during 6 months following Qualifying Visit,
Sensitivity Analyses

Expenditure Category	R Mean (SD) *(N=43)*	NR Mean (SD) *(N=91)*	*Coef. Estimate* (SE)[1]	*p*-value[1]	*Coef. Estimate*[2]	*p*-value[2]
Outpatient*	756 (839)	1,460 (1,804)	-0.38 (0.29)	.191	-0.35 (0.30)	.234
Pharmaceutical	63 (159)	234 (1,561)	2.78 (0.82)	.001	3.13 (1.00)	.002
Total Pain-Related Expenditures	819 (882)	2,272 (4,545)	-0.66 (0.28)	.020	-0.49 (0.30)	.109
Total Pain-Related Expenditures *less* inpatient	1,086 (1,212)	1,619 (2,242)	-0.32 (0.28)	.267	-0.27 (0.29)	.343

[1]Generalized linear models with Gamma specification and log link, robust standard errors, unadjusted beyond matched-design and baseline expenditures (12 months prior to study entry; within category)
[2]Additional control variables include gender; age; Charlson Risk Score, dichotomized to 0=0 and 1=1+.
*Limited to mental health and pain-related encounters.

Figure 1. Participant Flow