Poorer Physical and Mental Health Status Are Associated with Subsequent Opioid Prescriptions: a U.S. National Study

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BACKGROUND: How physical and mental health status relate to receipt of opioid prescription remains unclear, creating uncertainty in minimizing opioid harms while avoiding pain under-treatment.

OBJECTIVE: To examine the associations of physical and mental health status with subsequent opioid prescriptions.

DESIGN: Observational study of 2005–2015 United States (U.S.) Medical Expenditure Panel Survey data.

PARTICIPANTS: Adult respondents ($N = 78,563$) participating for 2 years. The analyses focused on respondents reporting no opioid prescriptions in year 1 ($N = 65,249$).

MAIN MEASURES: In the primary analysis, a negative binomial regression yielding adjusted incidence rate ratios (IRRs), the dependent variable was the number of opioid prescriptions in year 2. In two secondary analyses, both logistic regressions yielding adjusted odds ratios (ORs), the dependent variables were receipt of any opioid prescription (versus none) and receipt of ≥ 6 opioid prescriptions (versus 0–5) in year 2. The key independent variables in all analyses were the SF-12 Physical and Mental Component Summary scores (PCS-12 and MCS-12, respectively; higher scores = better health status). All models adjusted for socio-demographics, health-related variables, and year.

KEY RESULTS: *Primary analysis.* With each 10-point decrement in year 1 PCS-12 or MCS-12 score, there were more opioid prescriptions received in year 2 (adjusted IRRs [95% CIs] 1.45 [1.39–1.52] and 1.22 [1.16–1.27], respectively). *Secondary analyses.* With each 10-point decrement in year 1 PCS-12 or MCS-12 score, there were higher odds in year 2 both of receiving any opioid prescription (adjusted ORs 1.23 [1.19–1.28] and 1.11 [1.08–1.15], respectively) and of receiving ≥ 6 opioid prescriptions (adjusted ORs 1.96 [1.75–2.17] and 1.37 [1.23–1.54], respectively).

CONCLUSIONS: In a nationally representative U.S. sample, both poorer physical and mental health status independently predicted receiving more opioid prescriptions received in a subsequent year, as well as receiving ≥ 6 prescriptions during the year. Our findings may contribute to a more nuanced picture of the drivers of opioid prescription.

KEY WORDS: analgesics; opioid; health status; pain; surveys and questionnaires; United States.

J Gen Intern Med 35(2):554–60

DOI: 10.1007/s11606-019-05401-z

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Increased clinician prescription of opioid medications in the United States (U.S.) has become a focus of concern triggering influential appeals for action to reverse the trend.^{1–4} Calls for clinicians to curtail opioid prescription have been driven by concerns regarding discretionary (e.g. excessive or inappropriate) prescription and its potential detrimental impacts on health.^{5,6} Emerging amidst these calls is the need to better identify the drivers of opioid prescription to help inform targeted interventions aimed at mitigating the problem.^{2,3,5}

Among an array of potential drivers, patient health status might be anticipated to influence subsequent opioid prescriptions. However, the nature of the relationship remains uncertain, since prior studies examining the association of health status with opioid prescription were cross-sectional in nature.^{7–9} The studies also had mixed findings, with some observing poorer health status among prescription in opioid recipients versus non-recipients^{7,8} and others observing better health status among those receiving opioids.⁹ The differences in findings among the studies likely relates in part to the widely varying patient samples examined, all relatively small and highly selected (patients with sickle cell disease;⁷ inflammatory bowel disease;⁸ or assorted chronic painful conditions receiving long-term opioid therapy).⁹

Of potential concern related to the health status-opioid prescription relationship was a U.S. national cross-sectional observational study that found 16% of individuals with mental health disorders received more than half of all opioids prescribed, adjusting for potential confounders.¹⁰ While causal mechanisms of this finding could not be examined due to the study design, several explanations that may relate to health status seem plausible and could co-exist. One explanation is that controlling pain may tend to be more difficult in the context of mental health disorders, due to impaired patient coping, heightened pain sensitivity, or other factors, leading clinicians to escalate treatment to opioids. Another potential explanation is that patients with mental health disorders may present their pain (and assess their health status) differently than others, in ways that trigger differential management by

Received March 12, 2019

Revised July 24, 2019

Accepted September 3, 2019

Published online October 21, 2019

clinicians. It may also be that at times, clinicians prescribe opioids in part to target the psychological distress (and poorer mental health status) that often co-occurs with physical pain.^{11, 12} Others have speculated on such mechanisms to help in explaining the rise in opioid prescription in the U.S. over recent decades, which has paralleled national increases in depression, other mental health diagnoses, and psychological distress and disability.^{13–21}

To our knowledge, no prior studies of representative U.S. samples have examined how physical and mental health status at a given time point may influence subsequent receipt of chronic opioid prescriptions. Nationally representative studies exploring this issue could offer guidance to clinicians, patients, and policymakers. Currently, these stakeholder groups have limited evidence to help in balancing fears of inappropriate opioid prescription and opioid-related harms against concerns regarding under-treatment of pain—a quality of care, ethical, and legal dilemma.^{22–29} We employed data from individuals enrolled for 2 years in the nationally representative 2005–2015 U.S. Medical Expenditure Panel Survey (MEPS) to examine the associations of physical and mental health status measured in participation year 1 with receipt of opioid prescriptions in participation year 2.

METHODS

The MEPS is a nationally representative survey of health care use and costs in the U.S. civilian and non-institutionalized population.³⁰ The survey is conducted by the Agency for Healthcare Research and Quality (AHRQ) as a subset of the National Health Interview Survey and employs an overlapping panel design. Data are collected for individuals over a 2-year period through baseline and follow-up interviews. The MEPS Household Component collects information including interview language, country of origin, socio-demographic information, health insurance coverage, and health status. Two additional MEPS components, both administered at each follow-up survey and based on respondent self-report, also were examined: the Prescribed Medicines file, which included information on opioid prescription, and the Medical Conditions file, with information reported at each follow-up survey. We utilized MEPS data from these three components for the years 2005–2015. Annual response rates declined from 61.3 to 47.7% during the study period.³¹

The analytic sample for this study included all participants aged 18 or older who provided baseline data and for whom opioid prescription and health status data were available for their 2-year study participation period. Ethical approval for the study was provided by the University of California Davis Institutional Review Board (exempted status).

Main Measures

The study measures of physical and mental health status were the 12-item Short-Form (SF-12) Health Survey Physical

Component Summary (PCS-12) and Mental Component Summary (MCS-12) scores, respectively, from MEPS participation year 1.³² Both scores range from 0 to 100, with higher scores indicating better health. Although not a pain measure per se, the PCS-12 includes an item assessing the degree of pain-related functional impairment during the preceding month. Further, generic health status measures including the SF-6D (a preference-based single-index measure which can be derived from SF-12 responses) have been sensitive to changes in opioid use in randomized trials of opioid dependence treatment.³³

The primary measure of opioid prescription use was the number of opioid prescriptions in participation year 2, a count variable from data in the MEPS Prescribed Medicines file. To further explore the nature of the health status-opioid prescription relationship, we examined the following measures (each again for year 2) in two separate secondary analyses: receipt of any opioid prescription (versus none) and receipt of ≥ 6 opioid prescriptions (versus 0–5). The ≥ 6 opioid prescriptions in year 2 category was chosen as a credible proxy for long-term opioid therapy, for which no unequivocal, broadly accepted definition exists. Support for the characterization of ≥ 6 prescriptions per year as indicating long-term use of opioids comes from the following findings. In the MEPS years we examined, 63% of those reporting ≥ 6 prescriptions in year 1 also reported ≥ 6 prescriptions in year 2, whereas only 33% of those reporting 1–5 prescriptions in year 1 reported any opioid prescriptions in year 2 (7% reported ≥ 6 prescriptions). Further, only 7% of those reporting no opioid prescriptions in year 1 reported ≥ 1 opioid prescriptions in year 2.

Covariates

Socio-demographic covariates included age (in years), sex; self-reported race/ethnicity (White, Hispanic, Black, Other); US Census region (Northeast, Midwest, South, West); education level (less than high school, some high school, high school graduate, some college, college graduate); household income level as a percentage of the federal poverty level (FPL) (< 100%, 100–124%, 125–199%, 200–399%, or $\geq 400\%$); and health insurance status (uninsured, privately insured, or publicly insured). We further assessed morbidity using a count of eight self-reported chronic conditions (diabetes, hypertension, coronary heart disease, myocardial infarction, cerebrovascular disease, asthma, emphysema, and arthritis). Separately, persons reporting any visit with a diagnosis of any cancer (excluding non-melanoma skin cancer) were coded as having cancer.

Analyses

We analyzed data using Stata version 15.1 (StataCorp, College Station, TX). In our regression analyses, we utilized longitudinal strata and primary sampling unit identifiers, with survey weights to account for the complex survey design of successive waves of the MEPS. However, reported descriptive

statistics refer to the study sample and were not adjusted for survey design.

The primary analysis, a negative binomial regression yielding adjusted incidence rate ratios (IRRs) assessed the associations between year 1 physical (PCS-12) or mental (MCS-12) health status (the key independent variables, both continuous) and the number of opioid prescriptions in year 2 (the dependent variable, a count of prescriptions). Negative binomial regression was employed to account for overdispersion of the

distribution of opioid prescriptions.³⁴ Two separate secondary analyses, both logistic regressions yielding adjusted odds ratios (ORs), assessed the associations between year 1 PCS-12 or mental MCS-12 health status and year 2 receipt of the following: (1) any opioid prescription (versus none) and (2) ≥ 6 opioid prescriptions (versus 0–5). To explore potential non-linearity of the association between the SF-12 and subsequent opioid prescriptions, the analyses were repeated using the PCS-12 and MCS-12 as categorical variables (both < 40 ,

Table 1 Characteristics of the Study Sample in Year 1, by Year 2 Opioid Prescription Category^a

	No opioid prescriptions, N = 58,782	1–5 opioid prescriptions, N = 6083	≥ 6 opioid prescriptions, N = 384	p value	Total, N = 65,249
Age, mean (SD)	47.2 (17.7)	47.4 (17.3)	54.8 (14.7)	< 0.001	47.3 (17.7)
Female, no. (%)	32,511 (55.3)	3780 (62.1)	231 (60.2)	< 0.001	36,522 (56.0)
Race/ethnicity, no. (%)					
Non-Hispanic White	29,546 (50.3)	3433 (56.4)	198 (51.6)	< 0.001	33,177 (50.8)
Hispanic (any race)	13,772 (23.4)	1134 (18.6)	67 (17.4)		14,973 (22.9)
Non-Hispanic Black	10,272 (17.5)	1154 (19.0)	100 (26.0)		11,526 (17.7)
Other	5192 (8.8)	362 (6.0)	19 (4.9)		5573 (8.5)
Education level, no. (%)					
Less than high school	5087 (8.7)	460 (7.6)	48 (12.5)	< 0.001	5595 (8.6)
Some high school	7296 (12.4)	750 (12.3)	61 (15.9)		8107 (12.4)
High school graduate	17,289 (29.4)	1909 (31.4)	129 (33.6)		19,327 (29.6)
Some college	14,078 (23.9)	1640 (27.0)	99 (25.8)		15,817 (24.2)
College graduate	15,032 (25.6)	1324 (21.8)	47 (12.2)		16,403 (25.1)
Income as % FPL, no. (%)					
< 100	9469 (16.1)	1082 (17.8)	117 (30.5)	< 0.001	10,668 (16.3)
100 to < 125	3326 (5.7)	361 (5.9)	32 (8.3)		3719 (5.7)
125 to < 200	9282 (15.8)	914 (15.0)	68 (17.7)		10,264 (15.7)
200 to < 400	17,682 (30.1)	1807 (29.7)	88 (22.9)		19,577 (30.0)
≥ 400	19,023 (32.4)	1919 (31.5)	79 (20.6)		21,021 (32.2)
U.S. region, no. (%)					
Northeast	9658 (16.4)	836 (13.7)	46 (12.0)	< 0.001	10,540 (16.2)
Midwest	12,021 (20.5)	1450 (23.8)	75 (19.5)		13,546 (20.8)
South	21,515 (36.6)	2343 (38.5)	164 (42.7)		24,022 (36.8)
West	15,588 (26.5)	1454 (23.9)	99 (25.8)		17,141 (26.3)
Health insurance, no. (%)					
Any private	36,713 (62.5)	3846 (63.2)	163 (42.4)	< 0.001	40,722 (62.4)
Only public	12,341 (21.0)	1480 (24.3)	170 (44.3)		13,991 (21.4)
Uninsured	9728 (16.5)	757 (12.4)	51 (13.3)		10,536 (16.1)
Health status, mean (SD)					
PCS-12	49.6 (10.1)	47.2 (11.4)	36.5 (12.6)	< 0.001	49.3 (10.3)
MCS-12	50.6 (9.9)	49.3 (10.8)	44.5 (12.7)	< 0.001	50.5 (10.0)
Chronic conditions, median (IQR)	0.93 (1.18)	1.17 (1.28)	2.04 (1.55)	< 0.001	0.96 (1.20)
Current cancer, no. (%)	1997 (3.4)	315 (5.2)	28 (7.3)	< 0.001	2340 (3.6)
Opioid prescriptions, mean (SD)	0.00 (0.00)	1.49 (0.93)	9.46 (7.79)	< 0.001	0.19 (1.06)

^aAll participants reported no opioid prescriptions in year 1; percentages refer to the sample and are not adjusted for survey characteristics. FPL, federal poverty level; IQR, interquartile range; MCS-12, SF-12 Mental Component Summary; PCS-12, SF-12 Physical Component Summary; SD, standard deviation; U.S., United States.

40 ≤ 50, 50 ≤ 60, and ≥ 60). The use of the < 40 and ≥ 60 categories reflected the relatively small numbers of respondents at the low and high ends of the score ranges.

The models examining the association of the PCS-12 score with subsequent opioid prescriptions adjusted for MCS-12 score; similarly, the models examining the association of the MCS-12 score with opioid prescriptions adjusted for PCS-12 score. All models also included the year 1 values for several other covariates. Socio-demographic characteristics included were age, gender, race/ethnicity category, U.S. Census region, education level, household income level as a percentage of the FPL, and health insurance status. Health-related adjustor variables included the count of eight chronic health conditions, and current cancer diagnosis. All analyses also adjusted for MEPS panel year to account for potential secular temporal trends.

The differences in the number of opioid prescriptions received per one unit change in the PCS-12 or MCS-12 score are small. Thus, we report the differences in the number of opioid prescriptions received per 10-point increment or decrement in PCS-12 or MCS-12 score, corresponding to approximately one standard deviation in each measure. The 10-point increments also exceed the previously reported minimal clinically important differences (MCIDs) for these measures (and for the identically scaled SF-36 measure from which the SF-12 items derive) of 3–6 points.^{35–37}

RESULTS

The analytic sample included 65,249 adult MEPS participants between the years 2005 and 2015 who reported (1) no opioid prescriptions in participation year 1 and who also had (2) no missing physical and mental health status data in year 1 and (3) no missing opioid prescription data in year 2. The year 1 characteristics of the sample by opioid prescription status in year 2 and overall are shown in Table 1. A total of 58,782 participants (90%) reported receiving no opioid prescriptions in year 2, and most of those reporting opioid prescriptions had 1–5 prescriptions. Among the three opioid prescription categories, those who received no opioids had the most favorable physical and mental health status, followed by those who received 1–5 prescriptions and then those who received ≥ 6 opioid prescriptions. As compared with those in the other opioid prescription categories, higher proportions of those receiving ≥ 6 prescriptions were older, female, non-Hispanic Black, less educated, poorer, lived in the South or West, had only public health insurance, and had a current cancer diagnosis (Table 1).

Table 2 shows the findings of the primary and secondary adjusted analyses. In the *primary analysis*, with 10-point decrements in year 1 PCS-12 or MCS-12, there were more adjusted opioid prescriptions received in year 2. In the *secondary analyses*, with 10-point decrements in year 1 PCS-12 or MCS-12, there were higher odds in year 2 both of receiving

any opioid prescription and of receiving ≥ 6 opioid prescriptions (Table 2). As depicted in Figure 1, in both the primary and secondary analyses, the PCS-12 and MCS-12 were related linearly to the dependent variable.

DISCUSSION

In a study of a nationally representative sample of adults who received no opioid prescriptions during their first of two MEPS participation years, we found that 10-point decrements in both the year 1 PCS-12 and MCS-12 scores predicted receiving more opioid prescriptions in year 2. These findings were mirrored in two secondary analyses in which the dependent variables were categorical: receipt of any opioid prescriptions (versus none) and receipt of ≥ 6 opioid prescriptions (versus 0–5), respectively. In all three analyses, the relationships of the PCS-12 and MCS-12 scores with the dependent variable were essentially linear (Fig. 1). These findings suggest that in the general U.S. population, both poor physical and mental health status are key independent drivers of opioid prescription, with lower scores (i.e., worse physical and mental health status) being associated with receipt of more prescriptions.

Our study was not designed to address the mechanisms of the observed findings. However, the PCS-12 is focused on physical symptoms and functioning and includes one item specifically addressing pain-related interference with home and work activities. Thus, it seems unsurprising that PCS-12 scores would be predictive of subsequent opioid prescriptions, particularly given the emphasis in recent pain management guidelines on targeting functional goals as the key treatment outcome rather than focusing primarily on pain severity (e.g., pain scale scores).⁵

Table 2 Adjusted Associations of Physical and Mental Health Status in Year 1 with Opioid Prescriptions in Year 2 (N = 65,249)^a

Number of opioid prescriptions	Adjusted IRR (95% CI) ^b	p value
PCS-12	1.45 (1.39–1.52)	< 0.001
MCS-12	1.22 (1.16–1.27)	< 0.001
Any opioid prescription (versus none)	Adjusted OR (95% CI) ^b	p value
PCS-12	1.23 (1.19–1.28)	< 0.001
MCS-12	1.11 (1.08–1.15)	< 0.001
≥ 6 opioid prescriptions (versus 0–5)	Adjusted OR (95% CI) ^b	p value
PCS-12	1.96 (1.75–2.17)	< 0.001
MCS-12	1.37 (1.23–1.54)	< 0.001

^aAnalyses adjusted for age, sex, race/ethnicity category, education level, income level as a percentage of FPL, U.S. region, health insurance, MEPS panel, a count of chronic health conditions, and presence of cancer, as well as survey characteristics. The PCS-12 analyses also adjusted for MCS-12 score; the MCS-12 analyses also adjusted for PCS-12 score

^bPer 10-point decrement in PCS-12 or MCS-12 score

CI confidence interval, FPL Federal Poverty Level, IRR incidence rate ratio, OR odds ratio, MCS-12 SF-12 Mental Component Summary, MEPS Medical Expenditures Panel Survey, PCS-12 SF-12 Physical Component Summary, U.S. United States

Figure 1 Adjusted associations of year 1 SF-12 Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) scores (in 10-point increments or decrements) with year 2: number of opioid prescriptions (top row); receipt of any opioid prescription (versus none) (middle row); and receipt of ≥ 6 opioid prescriptions (versus 0–5) (bottom row). Analyses adjusted for age, sex, race/ethnicity category, education level, and income level as a percentage of federal poverty level, United States region, health insurance, Medical Expenditure Panel Survey panel, a count of chronic health conditions, and presence of cancer, as well as survey characteristics. The PCS-12 analyses also adjusted for MCS-12 score; the MCS-12 analyses also adjusted for PCS-12 score.

Less clear are the reasons for the association of MCS-12 scores with subsequent opioid prescriptions, present despite adjusting for PCS-12 scores. In lieu of a definite explanation, there are several plausible hypotheses as noted previously. Patients with poorer mental health status may have heightened sensitivity to pain or more trouble coping with pain and may also convey and describe pain in more compelling ways than others, including through non-verbal cues.¹⁴ Additionally, it is possible that clinicians may at times prescribe opioids partly with the goal of alleviating psychological distress, often concurrent with pain.^{15–21} Collectively, these potential explanations for the association of mental health status with subsequent opioid prescriptions represent hypotheses to be

examined empirically. Each hypothesis has somewhat different implications for efforts to improve opioid prescription safety and promote deprescribing. For example, if our hypotheses regarding the mechanisms of the association of MCS-12 scores with receipt of opioid prescriptions are confirmed, it might be beneficial to make clinicians aware of the mechanisms and to provide training in safer and more effective approaches to responding to patients' psychological distress. Thus, studies examining the hypotheses in broadly representative samples could provide much-needed guidance to clinicians, patients, and policymakers seeking to reduce discretionary opioid prescription while also avoiding under-treatment of pain.^{22–29}

Strengths of our study included the use of a nationally representative sample, and the observational cohort (rather than cross-sectional) design. As noted previously, the existing literature has often conflated opioid abuse and misuse with *all* use of opioids, including as-prescribed. Further, the studies were purely cross-sectional, precluding causal or even temporal inferences, and employed relatively small and non-representative (highly selected) samples. Though we are unable to assess longer-term associations between health status and opioid prescriptions, the examination of relationships over the short (2 years) MEPS participation period was also a strength in that it allowed us to examine a more direct link between the exposure and the outcome, with less opportunity for exogenous confounding than in longer-term studies.

Our study also had some limitations. Non-response to the MEPS may have introduced bias, as the degrees to which receipt of opioid prescriptions or health status may differ among responders and non-responders is unknown. Additionally, opioid prescriptions were self-reported by MEPS participants. To the extent that under- or over-reporting of opioid prescriptions may have occurred, this could bias the findings, particularly if misreporting varied systematically with physical or mental health status, though with uncertain net impact. We did not have information regarding specific mental health diagnoses contributing to the association between MCS-12 scores and subsequent opioid prescriptions. Nonetheless, the MCS-12 measure has been shown to be sensitive in capturing the functional impact of prevalent mental health conditions such as depression.^{38, 39} We also lacked information regarding the doses (e.g., morphine-equivalent units) of, indications for, and potential non-medical uses of prescribed opioids. Additionally, we lacked information regarding the timing and sequencing of opioid prescriptions, so it was not possible to discern whether multiple opioid prescriptions in a given MEPS participation year were continuous or separated by off periods. Nonetheless, examining how physical and mental health status in participation year 1 are associated with the number (duration) of opioid prescriptions received in participation year 2, independent of dosage and sequence information, is still worthwhile given studies suggesting more detrimental health effects for longer versus shorter exposure over a given time period.^{9, 40, 41}

In conclusion, in the primary study analysis, we found that 10-point decrements in physical and mental health status in MEPS participation year 1 were associated with receiving more opioid prescriptions in year 2, an essentially linear relationship. These findings were closely mirrored in two secondary analyses with categorical dependent variables: receipt of any opioid prescription (versus none) and receipt of ≥ 6 opioid prescriptions (versus 0–5) in year 2. That physical health status would predict subsequent opioid prescriptions is unsurprising. The finding for mental health status is less intuitive and suggests the possibility of opioid prescription targeted to psychological distress concurrent with physical pain. Further studies to elucidate the mechanisms underlying

the association of mental health status with opioid prescription would be useful, to guide targeted opioid deprescribing efforts that balance avoiding opioid harms with concerns about under-treatment of pain.

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Compliance with ethical standards:

Ethical approval for the study was provided by the University of California Davis Institutional Review Board (exempted status).

Conflict of interest: The authors have no conflicts of interest to disclose.

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