PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	An Observational Retrospective Study of the Association of Initial Health Care Provider for New-onset Low Back Pain with Early and Long-Term Opioid Use
AUTHORS	Kazis, Lewis; Ameli, Omid; Rothendler, James; Garrity, Brigid; Cabral, Howard; McDonough, Christine; Carey, Kathleen; Stein, Michael; Sanghavi, Darshak; Elton, David; Fritz, Julie; Saper, Robert

VERSION 1 – REVIEW

REVIEWER	Mary Jo Larson Brandeis University Heller School and Schneider Institutes, USA
REVIEW RETURNED	29-Jan-2019

GENERAL COMMENTS	This study examines private insurance claims and Medicare Advantage enrollees from a large private US health plan to associate opioid fills (immediate and long term) with an initial visit for low back pain (LBP). The key explanatory variables are the provider type for the initial visit and the state location. This manuscript presents new data and new analyses on a high priority topic of use of alternative services to opioids for patients with pain. Methodological concerns or questions. Concern about omitted variables. The authors may not be able to adjust for each of these variables, but it is plausible that the key independent variables are confounded by variables not discussed. At a minimum, more attention to these omissions should be considered in methods and limitations discussion. 1. Health plan coverage: given the focus on access to chiropractic, acupuncture, PT, did the study sample all have coverage for these modalities and if so was there variation in coinsurance level? Did utilization require referral? While claims are from one health plan, it is unclear that the benefit coverage was uniform for all sample members. 2. Pain severity. Patients with severe acute pain are likely to sort to different providers differently, and providers may base prescribing decision on patient self-report of severe or moderate pain (see Larson et al., 2018, J of Alternative and Complementary Medicine). 3. Other pain conditions. Why were other pain conditions limited to fibromyalgia and chronic pain codes (presumably ICD 338.29); does the Elixhauser adjust for other comorbid pain groups such as musculoskeletal, fractures, migraines, pelvic pain? 4. In a prior study, we noted that many patients had only a single visit for LBP, which was associated with opioid outcome and ultimately restricted analysis to longer episodes (again, Larson et al., 2018, JACM). Did you consider a covariate for single visit versus multiple as a covariate?

5. In general, looking at the magnitude of the odds ratios on Appendix Table 4 suggests possible omitted variables. The PT and chiropractic prior use measures have odds of 5.0 and 6.9 respectively. Given you ruled out prior LBP is it possible these visits were for other pain conditions? Should these measures be included as explanatory measures for the early and long-term opioid use models?

Other methods comments:

6. Please clarify statements about required window for inclusion that were confusing or conflicting. Lines 45-47, does 24 months prior to and after index date mean a total of 48 months? or 24 months in total with at least 12 months prior? Figure 1 states continued enrollment <24 mo before or after (not and). Presumably less than should be more than? Figure 1 "uses the phrase 4 years of continuous eligibility" which may be more clear than other statements.

7. Note the Figure 1 legend may need to be amended. "reducing the number of patients to 3,840,842" looks inaccurate if indeed these are the excluded group.

8. The very high rate of exclusion of new episodes of LBP (3.8 million relative to .4 million included) raises questions about generalizability. Please include discussion in the methods or limitation section. Given your analysis appears to be restricted to variables from 12 months before index and 12 months post index, what is the rationale for requiring 48 months of enrollment?

9. What is the rationale for examining initial visits to orthopedic surgeons, neurosurgeons, or physical medicine in main analyses? It is unclear how an index visit could be made to these specialists (which probably require a referral). Does this imply that certain initial visits where the referral was made were not classified as initial visits? Or were they preceded by a hospital stay not identified as LBP?

10. In order for readers to repeat the study (Review checklist item #4), readers would need to know more about variable definitions, including the diagnostic and procedure codes used to define LBP, spinal surgery, spinal injection, and classify opioids, etc. Citations were provided for the Elixhauser index and mental health comorbidities, but not other key measures. Consider more citations or an appendix with codes. Confirm (if true) that the opioid prescription may have been written by a different provider than the index provider.

11. Some patients may have had initial index visits with physician assistants or advanced practice nurses but these provider types were not mentioned. Were they excluded or classified as PCP (is so, please relabel physician as provider or clinician). Additionally, did you characterize provider based on specialty on the claim, clinic location, or some other variable? So, for example, was emergency medicine physician identified by location of visit as ED?

12. Regarding access to physical therapy in the U.S. state, what is the definition of limited, provisional, and unrestricted? How was the visit attributed to state, based on the residence of the patient or the location of the provider?

13. The statistical analysis plan is dense and a little confusing. The main analyses mentions geographic region but not the 3 level PT access variable, is that accurate (see Appendix table 4)? The section jumps back and forth between main analyses and supplemental alternative, and variable definition. Further, it appears the propensity models were for a limited sample (initial visits PT, chiro, or PCP), not the full sample e.g., Table 2 findings.

This is not clear in the analysis plan, and some tables lack n's. The Figure 1 identifies sensitivity analysis for 31,873; its unclear which models this applies to and there is not reference to propensity score sample.

Discussion:

14.   The discussion of factors that help explain the protective effect of conservative therapists appears incomplete. While later in limitations you discuss omitted variables, this paragraph also could consider other factors. For example, use of chiropractic, PT and acupuncture often requires more than one visit. This implies additional coinsurance payments (related to income), additional time off of work (related to education, preferences), and potentially seeking care before pain is severe (unmeasured).

15.   Under limitations, there is no measure of use of other prescribed medications (muscle relaxants) or over-the-counter medications that may have been used as alternatives to opioids. The role of pain severity, not observed, is understated in the limitations section.

Clarity. These comments are intended to identify areas where the manuscript would benefit from more clarity:

1.   Abstract: The description of setting includes inpatient claims but the flow diagrams appears to indicate these claims were excluded from study

2.   Article Summary: in the 4th bullet, the statement about "state access" is unclear as the term has not been introduced. Consider rewording.

3.   The term supplemental is used in the text, but the attachments are labeled Appendix.

4.   Methods: Consider moving the description of the race/ethnicity definition (pg 8, lines 10-14) to the earlier discussion of variable definitions; it's unclear why it is under analysis. Alternatively, given you do not discuss the impact of this variable consider removing this discussion.

5.   Results: It is not always clear which findings are from Table 2 and which are Appendix Table 4. Table 2 shows abbreviated findings and Table 4 has complete findings but the dependent variables and models are different. Perhaps subheadings would help the reader. It is also confusing to have main findings (e.g., impact of PT state access) only on a model in the Appendix (will these be readily available to the reader?) Perhaps Appendix Table 4 should be Table 2 and included in the main text.

6.   Appendix 5. The title of this table could be more clear. Were these variables included in the Main model but not shown on the table? Or are these alternative models?

Other.

1.   In the conflict of interest statement it would be appropriate to restate that some funding was from the American Physical Therapy Association and to explain the role of all funders in production of the manuscript. For example, was the study commissioned by the Association?

2.   Introduction: Consider clarifying the difference guidelines for acute versus chronic pain and the indication for opioids for moderate or severe pain.

REVIEWER	Erin Krebs
	Minneapolis VA Health Care System and University of Minnesota, Minneapolis, MN, USA
REVIEW RETURNED	16-Feb-2019

GENERAL COMMENTS	Major comments:
	1. Overall, the clarity and organization of the manuscript needs improvement. Incomplete and inconsistent descriptions made it difficult for me to understand the analysis approach and results (see specific comments below).
	2. The issue of differential access to PT as first-line providers is interesting and—in my opinion—underdeveloped in the manuscript (especially as is described as "extremely important" in the discussion, page 11). Please add state PT access (i.e., limited, provisional, and unrestricted) to table 1 to show rates of initial provider use by state access type. At a minimum, I would like to see the relationship of state access with initial provider mentioned in results text. It would be interesting to see whether state-based policies on PT access modify associations between initial provider and opioid use outcome.
	3. The discussion would benefit from editing to improve organization and concision. It could also be improved by focusing more on how study results contribute to, support, extend, or differ from results of prior studies and less on study design differences.
	Additional comments in rough chronological order:
	4. Page 4, paragraph 2: The studies on use of nondrug therapies and opioids used data prior to the CDC and ACP guidelines, so it doesn't make sense to characterize the practice patterns they describe as occurring "despite these recommendations."
	5. Page 5, first sentence in methods section: "Medical provider" could be interpreted as referring to physicians and not inclusive of all clinicians examined in this study (e.g., acupuncturists are not typically referred to as "medical providers"). "Health care provider" is a potentially broader term.
	6. Page 5, last sentence of first methods paragraph: "Comprehensive full insurance coverage for physician, hospital, and prescription drug services" doesn't provide relevant background for this study. What does "comprehensive" mean? Please briefly describe plan coverage of PT, acupuncture, chiropractic, and physician office services—are they all covered similarly? Do copays or other out of pocket expenses differ by clinician type?
	7. Page 6, patient characteristics section: The specific "other comorbidities" and mental health conditions should be specified in the methods text (or in the appendix if word count does not allow). Please clarify how the Elixhauser index was used—I am confused about this based on differing descriptions in the methods (page 6 and page 7) and Figure 2 legend. Please clarify how geography was coded ("state of residence" on page 6 vs. "geographic region" on page 7) All patient variables should be described together in this section (currently, race/ethnicity is described on page 8). Also, did the study use sex or gender identity and how was this variable determined?
	8. Page 7: Please briefly describe the 3 levels of access (i.e., what defines limited, provisional, and unrestricted).
	9. Page 7: Define the term "conservative therapists" at first use.

10.   Results: Table 2 suggests a potentially interesting discrepancy between early use and late use associations with physician specialists vs. PCPs, but this is not mentioned elsewhere. I would like to see text related to this in the results section (and discussion, if appropriate).

11.   Page 11, first full paragraph, first sentence: I suggest changing "protective effect" to "apparent protective effect" given the observational nature of this study. Also, please include other possibilities, such as confounding by patient preference for conservative care, here (not just in limitations).

12.   Page 11, first full paragraph, last sentence: The authors suggest conservative therapists could prevent need for MD visits. Can this be shown with the study dataset?

13.   Page 13, last sentence: Change "observational quasi-experimental" to "observational retrospective."

14.   Page 14: Did the funders (UnitedHealth, APTA, OptumLabs) have any role in the research (e.g., design, interpretation of results, decision to publish)?

15.   Table 1: Why are some numbers preceded by ">"?

16.   Table 2: Clarify variables in the models. The legend description seems to differ from methods text.

17.   Figure 1: Please clarify terminology and ensure descriptions of eligibility criteria match across methods text, legend, and figure. For example, the legend states the first step was excluding patients with "insufficient clean period (opioid use within the last 1 year)," which is not consistent with the text in the figure box or methods.

18.   Why does Figure 2 have fewer provider types than Table 2? Why are radiologists included in appendix tables but nowhere else?

19.   Appendix tables: These are not intuitive and require explanation in footnotes.

REVIEWER	Ying Chen Keele University, UK
REVIEW RETURNED	28-Mar-2019

| GENERAL COMMENTS | For statistical review only:

The study design was clear and the statistical methods used were generally appropriate according to the design. However, there was a potential indication bias in the study as patients may go the different services influenced by their condition e.g. severity of pain. No measurement was presented in this paper with regard to this.

I also found in table 1 there are some cells with "%" but some not, and the quality of figures 1 and 2 is quite bad --- almost unreadable. In the next version of paper the authors need to improve these to a higher standard. |

REVIEWER	Danielle Robinson
	CSM, NDORMs
	University of Oxford,
	UK
REVIEW RETURNED	16-Apr-2019

GENERAL COMMENTS	Thank you for inviting me to review this paper titled "Non-pharmacologic Therapies for New-onset Low Back Pain: Predictors of Early and Long-Term Opioid Use in the United States". This is an interesting paper comparing the initial provider of treatment for lower back pain with regards to both the early use of opioids and long-term opioids. However, there are areas for improvement in this paper and some of the numbers do not add up hence I would suggest major revisions. Also I feel there are a lot of unmeasured biases in this study, however for the dataset used it would be impossible to address them all and the limitations generally highlights these.
	In the title:
	- This title suggests it produces predictors for opioid use in lower back pain. I would not agree with this statement as its more compares different initial treatment providers. The title may need changing to reflect this.
	In the abstract:
	- Numbers needed to treat can be calculated from odds ratios and should be calculated and included for the primary outcomes of this study
	In the article summary:
	- The bullet points appear very long and should be shortened
	In the method section:
	- You mention "If a patient saw both a physician and a conservative therapist on the index date, the initial provider was assumed to be the physician". This may introduce bias as patients who see both may have more severe pain. What proportion of patients saw both physician and conservative therapist? Were these patients more likely to use opioids than physician treated alone? If so could a sensitivity analysis excluding these patients be undertaken?
	- There appear to be more covariates included in the propensity score than in the multivariable model. Why was this? To be comparable between models the same covariates should be included.
	- In the propensity score matching, what calliper width was used?
	- Please clarify the direction of the 2:1 PS matching e.g. 2 PCP to 1 chiropractor
	In the results section:
	- The short term use of early opioids were highlighted for physical therapy and acupuncture in the text, however this is also reduced for nearly all initial providers, the exception being emergency care. Please add the odds ratios to the text for these other providers.
	- Please make sure all appendixes are referred to in the text as appendix instead of supplementary table.
	In the discussion section:
	- You state that the propensity score matching may mitigate some concern regarding consumer choice. I would not agree with this statement since whilst it controls for age, gender and geographical location, no information about socio-economic status, health seeking behaviour or pain levels was included hence there

	is likely unmeasured confounding in this study. I would consider rewording the limitation to highlight whether this information is not available in claims databases.
	In Table 1:
	- Full sample N (%) the values in the conservative and physician therapies add up to 196461 patients and 90.1%. Please check the numbers in this table are correct. If these were missing please add a note at the bottom of the table.
	- Table 1 would benefit from numbers of patients with each of fibromyalgia, chronic pain, fatigue and the psychiatric conditions mentioned in page 12.
	In Figure 2:
	- The scale of the x-axis should be log.
	In appendix 4:
	- Gender is significant in PT but no *
	- This table needs tidying for clarity particularly different groupings between race and region
	In appendix 5
	- I didn't understand why the total column is included.
	In references:
	- References for propensity score matching should be included

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Mary Jo Larson

Institution and Country: Brandeis University Heller School and Schneider Institutes, USA

Please state any competing interests or state 'None declared': None declared.

Please leave your comments for the authors below See attached file for explanation of #4, #12, #14 (BMJopen.2019.docx) that can be addressed by author revisions. As a convenience to the authors, I attached an article (that I authored) that I reference in my comments (Larson et al_2018_J Alternative and Complementary Med.pdf). Please note the authors should not feel compelled to include this as a citation unless it is appropriate.

Thank you for providing the Larson et al (2018) reference which we have cited in the text with some additional explanation below.

This study examines private insurance claims and Medicare Advantage enrollees from a large private US health plan to associate opioid fills (immediate and long term) with an initial visit for low back pain (LBP). The key explanatory variables are the provider type for the initial visit and the state location. This manuscript presents new data and new analyses on a high priority topic of use of alternative services to opioids for patients with pain.
Methodological concerns or questions.
Concern about omitted variables. The authors may not be able to adjust for each of these variables, but it is plausible that the key independent variables are confounded by variables not discussed. At a minimum, more attention to these omissions should be considered in methods and limitations discussion.
1.   Health plan coverage: given the focus on access to chiropractic, acupuncture, PT, did the study sample all have coverage for these modalities and if so was there variation in coinsurance

level? Did utilization require referral? While claims are from one health plan, it is unclear that the benefit coverage was uniform for all sample members.

While all patients in the study were covered by the same health care insurer, there were different health care "plans" in which patients were enrolled for both the commercial and Medicare Advantage sector. There were many individual plans that could differ in a number of ways. The plans could differ by factors such as deductibles, coinsurance and copayments. While virtually all of the plans covered services provided by physical therapists and chiropractors, only some of them covered services provided by acupuncturists. These different plan characteristics can affect the likelihood of seeing a particular provider, but that analysis is beyond the scope of this paper. In this paper, we were mainly interested in how the choice of a particular initial health care provider was associated with opioid use. We have removed references to specific plans to make this clearer.

"We used de-identified administrative claims data from the OptumLabs Data Warehouse (OLDW), which includes medical and pharmacy claims, laboratory results, and enrollment records for commercial and Medicare Advantage (MA) enrollees. The database contains longitudinal health information on enrollees and patients, representing a diverse mixture of ages, ethnicities and geographical regions across the United States."

2.   Pain severity. Patients with severe acute pain are likely to sort to different providers differently, and providers may base prescribing decision on patient self-report of severe or moderate pain (see Larson et al., 2018, J of Alternative and Complementary Medicine).

We appreciate your inclusion of the publication "Associations of Early Treatments for Low-Back Pain with Military Readiness Outcomes". Our cohort and analyses differ from that study in a number of respects, one of which is that we investigated the initial type of provider rather than the type of treatment received in the first 30 days. (For example, a patient seen initially by an M.D. and then exclusively by a PT is categorized as M.D. first.) However, your study does indicate that opioids are prescribed more commonly in those with more severe pain which would be a potential confounding issue in our population if those with more severe pain had been more likely to seek an M.D. rather than conservative therapist as initial provider. As this study was based on a claims database, we did not have access to pain severity or duration. Notably, our study was not done in a military population and may differ significantly from Larson et al. 2018 because of this. Other researchers have reported similar levels of pain between those seeing MDs and conservative therapists for treatment of LBP, as referenced in the manuscript. However, for our particular cohort, the absence of information on pain severity was certainly a limitation of our study, and we have added further text in the Discussion regarding this issue.

"The observational nature of the study and the use of claims data limited our ability to eliminate the influence of unmeasured confounders. In particular, confounding by indication may bias our results. Patients who seek early treatment with non-pharmacologic practitioners may be more likely to have mild back pain that does not require more aggressive treatment such as opioids, compared to individuals with more severe back pain who may be more likely to see practitioners able to prescribe opioids."

3.   Other pain conditions. Why were other pain conditions limited to fibromyalgia and chronic pain codes (presumably ICD 338.29); does the Elixhauser adjust for other comorbid pain groups such as musculoskeletal, fractures, migraines, pelvic pain?

The specifications of the fibromyalgia/chronic pain/fatigue category was obtained from the CMS Chronic Conditions Data Warehouse (as referenced in the revised manuscript) and consisted of the following ICD-9 codes: 338.2, 338.21, 338.22, 338.23, 338.29, 338.3, 338.4, 780.7, 780.71, 729.1,

729.2. While this list does not include migraines or pelvic pain, it does include other sources of chronic pain.

4.   In a prior study, we noted that many patients had only a single visit for LBP, which was associated with opioid outcome and ultimately restricted analysis to longer episodes (again, Larson et al., 2018, JACM). Did you consider a covariate for single visit versus multiple as a covariate?

In comparison to those who saw a conservative therapist first, patients who saw an MD first were substantially more likely to have only a single visit. This is not unexpected, as conservative therapists tend to have programs of care that often include multiple visits.. For this reason, we did not think that using single vs. multiple visits would be useful as a covariate.

5.   In general, looking at the magnitude of the odds ratios on Appendix Table 4 suggests possible omitted variables. The PT and chiropractic prior use measures have odds of 5.0 and 6.9 respectively. Given you ruled out prior LBP is it possible these visits were for other pain conditions? Should these measures be included as explanatory measures for the early and long-term opioid use models?
The outcome measures for Appendix Table 4 (now Appendix Table 6) are odds ratios of first visit with a PT or chiropractor in comparison to PCP. With regard to visits to PTs, chiropractors or acupuncturists in the 24 months prior to the index LBP event, such visit in the 1-12 months prior to the event were for diagnoses other than LBP while visits in the 13-24 month period could be for any reason. We have clarified this in the revised manuscript. We do not feel it would be appropriate for these measures to be included as explanatory measures for the early and long-term opioid use models because prior visits to PT and chiropractors are likely to be collinear with the index visit.
Other methods comments:
6.   Please clarify statements about required window for inclusion that were confusing or conflicting. Lines 45-47, does 24 months prior to and after index date mean a total of 48 months? or 24 months in total with at least 12 months prior? Figure 1 states continued enrollment <24 mo before or after (not and). Presumably less than should be more than? Figure 1 "uses the phrase 4 years of continuous eligibility" which may be more clear than other statements.

A total of 48 months of continuous enrollment with available medical and pharmacy claims data was required, including 24 months prior to the index event as well as 24 months afterward. We have clarified this in the third paragraph of the methods in the text and in Figure 1.

"Patients needed to be continuously enrolled for at least 24 months both before and following the index date (total 48 months) with both medical and pharmacy claims data available during that period."

7.   Note the Figure 1 legend may need to be amended. "reducing the number of patients to 3,840,842" looks inaccurate if indeed these are the excluded group.

Inaccuracies in the Figure 1 legend have been corrected in the revised version.

Figure 1 Legend: Initially, 8,797,787 patients with low back pain (LBP) were identified. Patients with an insufficient clean period (LBP within the last 1 year), patients with a diagnosis of LBP that was not in the first position of their diagnosis, and LBP in only inpatient settings were excluded, reducing the number of patients to 4,263,713. Patients were excluded if they were not continuously enrolled in their insurance for 24 months before and after the initial LBP visit and if they were <18 years old, reducing the number of patients to 422,871. Patients with exclusionary conditions, LBP that was not limited to the low back, patients with back procedures in the 12 months prior to the index LBP visit, and patients with any opioid use in the 12 months before the index visit were excluded, leaving 216,504 patients in our sample.

8.   The very high rate of exclusion of new episodes of LBP (3.8 million relative to .4 million included) raises questions about generalizability. Please include discussion in the methods or limitation section. Given your analysis appears to be restricted to variables from 12 months before index and 12 months post index, what is the rationale for requiring 48 months of enrollment?

Generalizability is addressed in the limitation section of the paper, We have added the following: "There are several limitations to this study. Analysis was conducted using claims data, limiting our generalizability beyond commercial and Medicare Advantage enrolled patients. However, the sample is national in scope and provides a range of sociodemographic and clinical characteristics."

We also have emphasized internal validity as our research question was focused on the outcomes of new onset acute musculoskeletal LBP episodes in patients without recent exposure to opioids and treated by physical therapists, chiropractors, or acupuncturists. Given the heterogeneity of claims data in a commercial insured population, we constructed our inclusion and exclusion criteria with the specific purpose of maximizing the likelihood that our analytic sample comprised our target population.

While the 12 months prior to the index date was used to exclude patients based on LBP (and certain other) diagnoses as well as opioid use, the full 24 months prior to the index date was used to collect comorbidities. In addition, months 13-24 prior to the index date was used to collect data on opioid use as well as visits with conservative therapists that were used in some analyses. For long-term opioid analyses in this report, we required at least 14 months of data following the index date (i.e. opioid use starting within 60 days of the index date and then meeting certain additional criteria within the next year). However, certain other longer-term (i.e. up to 24 months post-index date) analyses on health care utilization were included as part of the larger project that were not included in this manuscript. We have included a discussion in the limitation section on the issue of enrollment.

Other text added to methods: "Given the heterogeneity of claims data in a commercial insured population, we constructed our inclusion and exclusion criteria with the specific purpose of maximizing the likelihood that our analytic sample comprised our target population."

9.   What is the rationale for examining initial visits to orthopedic surgeons, neurosurgeons, or physical medicine in main analyses? It is unclear how an index visit could be made to these specialists (which probably require a referral). Does this imply that certain initial visits where the referral was made were not classified as initial visits? Or were they preceded by a hospital stay not identified as LBP?

In some types of health plans, a referral to a specialist is not required so that index visits for new-onset LBP to such providers would be a reasonable observation. For example, many patients are permitted to access orthopedic surgeons and neurosurgeons directly without a referral. While it is possible that patients were referred to such providers, that seems unlikely in our final sample as we excluded those with any LBP diagnosis (outpatient or inpatient) in the 12 months prior to the "index" visit and those making such a referral would likely have listed some type of LBP diagnosis.

10.   In order for readers to repeat the study (Review checklist item #4), readers would need to know more about variable definitions, including the diagnostic and procedure codes used to define LBP, spinal surgery, spinal injection, and classify opioids, etc. Citations were provided for the Elixhauser index and mental health comorbidities, but not other key measures. Consider more citations or an appendix with codes. Confirm (if true) that the opioid prescription may have been written by a different provider than the index provider.

We have included as this reviewer suggests in the appendix various diagnostic and procedure codes, as well as types of opioids included in the analyses. This is a new appendix in the revised manuscript. Opioid prescriptions may have been written by a different provider than the index provider (which would be the case for virtually all instances in which the initial provider was a conservative therapist and not a clinician able to prescribe opioids).

11. Some patients may have had initial index visits with physician assistants or advanced practice nurses but these provider types were not mentioned. Were they excluded or classified as PCP (is so, please relabel physician as provider or clinician). Additionally, did you characterize provider based on specialty on the claim, clinic location, or some other variable? So, for example, was emergency medicine physician identified by location of visit as ED?

Patients who had initial visits with physician assistants or nurse practitioners were included as part of a non-MD others category. We have added this to the text and to the Table 1 and Table 2 footnotes. We found that place of service/location was not reliable particularly for ED physicians so we chose to classify provider based on specialty, which is on the basis of contracts between provider and health plan.This has been added to the text:

"Based on the index claim date of patients with an eligible LBP diagnosis, initial providers were characterized as physical therapist, chiropractor, acupuncturist, primary care physician, orthopedic surgeon, emergency medicine physician, neurosurgeon, radiologists, other non-physicians (physician assistant or nurse practitioners), or physical medicine and rehabilitation physician according to provider specialty and procedure codes."

12. Regarding access to physical therapy in the U.S. state, what is the definition of limited, provisional, and unrestricted? How was the visit attributed to state, based on the residence of the patient or the location of the provider?

The definitions for limited, provisional and unrestricted access were those of the American Physical Therapy Association, as described in reference #19. The residence of the subscriber to the plan, which in most cases would also be the residence of a family member in the plan, was used to assign a state access category.

13. The statistical analysis plan is dense and a little confusing. The main analyses mentions geographic region but not the 3 level PT access variable, is that accurate (see Appendix table 4)? The section jumps back and forth between main analyses and supplemental alternative, and variable definition. Further, it appears the propensity models were for a limited sample (initial visits PT, chiro, or PCP), not the full sample e.g., Table 2 findings. This is not clear in the analysis plan, and some tables lack n's. The Figure 1 identifies sensitivity analysis for 31,873; its unclear which models this applies to and there is not reference to propensity score sample.
Thank you for this point. We have revised the methods section and the statistical analysis plan accordingly. There were two separate propensity models: PT/PCP and chiropractor/PCP. Both PT state access and geographical region were included in the first step of the regression model which estimates propensity scores. For the chiropractor/PCP propensity model, only region was included, as physical therapists were not part of this analysis and therefore PT state access is not relevant for prediction of chiropractic care. Propensity models do include only a small subset of the same due to propensity matching. The PT sample is small which reduces the number of matched individuals from other groups. We have added two references for propensity score matching. We have added n's to tables to make them more clear and have edited figure1 to remove the sensitivity analysis as we did not include that in this manuscript.

Discussion:

14.	The discussion of factors that help explain the protective effect of conservative therapists appears incomplete. While later in limitations you discuss omitted variables, this paragraph also could consider other factors. For example, use of chiropractic, PT and acupuncture often requires more than one visit. This implies additional coinsurance payments (related to income), additional time off of work (related to education, preferences), and potentially seeking care before pain is severe (unmeasured).

We have added more on potential selection bias to the discussion, prior to the limitations section. While we agree that selection bias may affect which provider a patient chooses and even a patient's desire to be prescribed opioid use, conservative therapy plans are frequently bundled and prior studies have shown that they may not increase costs. In particular, studies have shown that early and initial chiropractic treatment are associated with lower costs than initial PCP visits for musculoskeletal pain. We have added the following to the text to explain this point.

"Several factors may help explain the protective effect of conservative therapists. Since non-physicians are unable to prescribe opioids, patients seeking conservative therapy do not receive opioid prescriptions at the index visit, and subsequent visits to an MD would be required to obtain such prescriptions. There may be selection bias among patients choosing to seek initial treatment from conservative therapists, and such biases could be related to educational level or preferences which may also result in decreased desire for those patients to use opioids. Additionally, the conservative therapy provided may result in decreased pain and improved back-related function so that patients do not need or seek opioid medications. A growing body of evidence suggest that spinal manipulation, massage, acupuncture, and superficial heat are effective for reducing acute low back pain intensity and improving function.23 The conservative therapists studied in this analysis can incorporate one or more of these approaches: physical therapist (manipulation, massage, heat), chiropractor (manipulation, massage, heat), and acupuncturist (acupuncture, massage).23 Therefore and importantly, use of conservative therapists may prevent the need for use of opioids or MD visits by providing evidence-based interventions."

15.	Under limitations, there is no measure of use of other prescribed medications (muscle relaxants) or over-the-counter medications that may have been used as alternatives to opioids. The role of pain severity, not observed, is understated in the limitations section.
We have added additional text to the limitations section to highlight the role of pain severity.
"There are several limitations to this study. Analysis was conducted using claims data, limiting our generalizability beyond commercial and Medicare Advantage enrolled patients. However, the sample is national in scope and provides a range of sociodemographic and clinical characteristics. The observational nature of the study and the use of claims data limited our ability to eliminate the influence of unmeasured confounders. In particular, confounding by indication may bias our results. Patients who seek early treatment with non-pharmacologic practitioners may be more likely to have mild back pain that does not require more aggressive treatment such as opioids, compared to individuals with more severe back pain who may be more likely to see practitioners able to prescribe opioids. Studies have suggested that those with more severe LBP are more likely to receive opioids,36 and if patients with less severe pain were more likely to choose conservative therapists rather than physicians, this could contribute to overestimation of the protective effect of conservative therapy on opioid use. Several prior studies have shown comparable baseline pain scores for those who choose conservative therapists compared to those who choose to see physicians initially, however it is important to note that these studies had different patient populations than this study as they were conducted either only in one state or in countries other than the United States.36-40"

Clarity. These comments are intended to identify areas where the manuscript would benefit from more clarity:

1.   Abstract: The description of setting includes inpatient claims but the flow diagrams appears to indicate these claims were excluded from study

Only outpatient claims were used to identify the index episode of new onset LBP.   The flow diagram indicates "inpatient" as an exclusion if an inpatient diagnosis of LBP was the only instance in which it occurred. Inpatient claims were used for collecting comorbidities and for various outcome measures. Additionally, an inpatient diagnosis for LBP (and certain other diagnoses as listed in Methods) could exclude a subject if it occurred in the 12 months prior to an outpatient diagnosis of LBP.

2.   The term supplemental is used in the text, but the attachments are labeled Appendix.

We have modified the revised manuscript to consistently use the term Appendix.

3.   Methods: Consider moving the description of the race/ethnicity definition (pg 8, lines 1014) to the earlier discussion of variable definitions; it's unclear why it is under analysis.
Alternatively, given you do not discuss the impact of this variable consider removing this discussion.

The description of race/ethnicity was moved to the section on patient characteristics in the methods section of the paper.

4.   Results: It is not always clear which findings are from Table 2 and which are Appendix Table 4. Table 2 shows abbreviated findings and Table 4 has complete findings but the dependent variables and models are different. Perhaps subheadings would help the reader. It is also confusing to have main findings (e.g., impact of PT state access) only on a model in the Appendix (will these be readily available to the reader?) Perhaps Appendix Table 4 should be Table 2 and included in the main text.

The Table 2 outcome is opioid use, while the appendix Table 4 (now appendix table 6) outcome is odds of seeing PT or chiropractor vs seeing a PCP. We have added an expanded Table 2 to include all opioid outcomes, including those previously noted in appendix Table 5. We have added separate sections to the methods and results sections that better describe Appendix 4 (now Appendix 6). Please note that the previous appendix 4 is now appendix 6 as we have reordered some of the text to make the manuscript more clear.

5.   Appendix 5. The title of this table could be more clear. Were these variables included in the Main model but not shown on the table? Or are these alternative models?
The same covariates and outcomes are measured in table 2 and appendix 5. Therefore, we have merged appendix table 5 with Table 2 to make it clearer that these are the same models with the opioid use as the outcome.
Other.
1.   In the conflict of interest statement it would be appropriate to restate that some funding was from the American Physical Therapy Association and to explain the role of all funders in production of the manuscript. For example, was the study commissioned by the Association?

This research was supported by UnitedHealthcare and the American Physical Therapy Association. Neither institution had editorial control or influence for the final content of this paper.

2.   Introduction: Consider clarifying the difference guidelines for acute versus chronic pain and the indication for opioids for moderate or severe pain.

The ACP and CDC guidelines are consistent in recommending that non-pharmacological approaches as first-line, and non-opioid medications first when medications are considered, and this is the main point that we meant to cover in the introduction. As Dr. Larson points out, there are many important

complexities to treating patients with pain, as evidenced by the extensive set of special considerations provided in the guidelines, and the limitations in categorizing patients as acute or chronic, and radicular and non-radicular. A detailed description of these issues and the related differences between treatment considerations for acute and chronic conditions is beyond the scope of this study.

Reviewer: 2
Reviewer Name: Erin Krebs

Institution and Country: Minneapolis VA Health Care System and University of Minnesota, Minneapolis, MN, USA

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below Major comments:
1.   Overall, the clarity and organization of the manuscript needs improvement. Incomplete and inconsistent descriptions made it difficult for me to understand the analysis approach and results (see specific comments below).

We have revised the organization of the manuscript and have included more headings in the methods and results section to make the manuscript more clear. We have also provided a clearer description of the analysis approach and results that were also in response to reviewer #1 comments.

2.   The issue of differential access to PT as first-line providers is interesting and—in my opinion—underdeveloped in the manuscript (especially as is described as "extremely important" in the discussion, page 11). Please add state PT access (i.e., limited, provisional, and unrestricted) to table 1 to show rates of initial provider use by state access type. At a minimum, I would like to see the relationship of state access with initial provider mentioned in results text. It would be interesting to see whether state-based policies on PT access modify associations between initial provider and opioid use outcome.

We agree that this would provide a more thorough exploration of the importance of the variable of direct access to PT and have added text to the manuscript to show rates of initial provider use by state access type. Evaluating whether state access to PT modify associations between initial provider and opioid use was achieved in the propensity match analyses, as state access was included in the propensity match. PT state access did not change the odds ratios significantly in the propensity analysis. We have added to the text of the manuscript in the first paragraph of the results section.

"The choice of initial provider varied by state PT access category. For example, in limited access states, 55.2% of initial providers were PCP, 0.9% were PTs, and 25.7% were chiropractors. In provisional access states, the rates were 51.7% for PCPs, 1.6% for PTs, and 23.2% for chiropractors, and in unrestricted access states, the rates were 55.8% for PCPs, 2.6% for PTs, and 22.6% for chiropractors."

3.   The discussion would benefit from editing to improve organization and concision. It could also be improved by focusing more on how study results contribute to, support, extend, or differ from results of prior studies and less on study design differences.

Thank you for this suggestion. We have edited the discussion section to improve organization and concision. We also have edited the text discussing other papers.

Additional comments in rough chronological order:

4.   Page 4, paragraph 2: The studies on use of nondrug therapies and opioids used data prior to the CDC and ACP guidelines, so it doesn't make sense to characterize the practice patterns they describe as occurring "despite these recommendations."

We have edited the text in the introduction to reflect this.

"Prior to the release of these recommendations, non-pharmacologic therapies like chiropractic care, PT, and acupuncture were rarely used for treatment of acute pain, and physicians frequently prescribe opioids for acute onset LBP.8-11"

5.   Page 5, first sentence in methods section: "Medical provider" could be interpreted as referring to physicians and not inclusive of all clinicians examined in this study (e.g., acupuncturists are not typically referred to as "medical providers"). "Health care provider" is a potentially broader term.
        We have edited the text to say "health care provider."

"We conducted a retrospective study of patients seen by a health care provider for new-onset, LBP management and who were opioid-naïve at the time of the initial visit (Boston Medical Center IRB approval number: H-36499)".

6.   Page 5, last sentence of first methods paragraph: "Comprehensive full insurance coverage for physician, hospital, and prescription drug services" doesn't provide relevant background for this study. What does "comprehensive" mean? Please briefly describe plan coverage of PT, acupuncture, chiropractic, and physician office services—are they all covered similarly? Do copays or other out of pocket expenses differ by clinician type?

Comprehensive health insurance simply refers to health plans that cover the vast majority of medical services. In general, chiropractic care and PT are universally covered, while there is variable acupuncture coverage. Copays and deductibles are variable and are outside the scope of this study. We have edited this sentence in the methods section to better explain what is meant by comprehensive health insurance.

"The various health plans individuals were enrolled in all provide comprehensive insurance coverage for physician, hospital, and prescription drug services."

7.   Page 6, patient characteristics section: The specific "other comorbidities" and mental health conditions should be specified in the methods text (or in the appendix if word count does not allow). Please clarify how the Elixhauser index was used—I am confused about this based on differing descriptions in the methods (page 6 and page 7) and Figure 2 legend. Please clarify how geography was coded ("state of residence" on page 6 vs. "geographic region" on page 7) All patient variables should be described together in this section (currently, race/ethnicity is described on page 8). Also, did the study use sex or gender identity and how was this variable determined?

The specific "other comorbidities" and "mental health conditions" are listed in Table 2. The OptumLabs Data Warehouse has state of residence for the enrollee on the health care plan. The Elixhauser index was used as follows and added to the text in the methods section under patient characteristics. Region is an aggregation of states of residence. We mapped states to their geographical region or to their PT state access category. We have moved all information on patient variables to the "Patient characteristics" section of the methods section. Sex/gender is determined based on enrollment records.

"Physical comorbidities were assessed using a modification of the Elixhauser index15 in which mental health conditions were excluded. Other comorbidities, listed in Table 2, included 8 mental health conditions and a condition comprising chronic pain, fibromyalgia and fatigue."

8.   Page 7: Please briefly describe the 3 levels of access (i.e., what defines limited, provisional, and unrestricted).

    We have added a description of the 3 levels of access in the methods section.

Patient access to PT in every state was classified as either 'limited', 'provisional', or 'unrestricted', based on the three levels of patient access outlined by the American Physical Therapy Association.19 To access a PT for their initial LBP visit in limited access states, patients must have had a prior relevant medical diagnosis, a recent diagnosis from a physician or other specified clinician, and/or a prior physician referral to a PT. States with provisional access permitted patients to see physical therapists with some provisions that vary by state. Restrictions in provisional access states include time and/or visit limits and physician referrals for specific interventions. Patients in unrestricted states do not face these restrictions when seeking initial care from a PT.

9.   Page 7: Define the term "conservative therapists" at first use.

We have included this definition in the text (Introduction, paragraph 3).

"Comparisons of the treatment patterns of primary care physicians (PCPs) and conservative therapists (defined as chiropractors, PTs, acupuncturists) suggest that the use of conservative therapies for LBP may decrease the likelihood of opioid use.9"

10.   Results: Table 2 suggests a potentially interesting discrepancy between early use and late use associations with physician specialists vs. PCPs, but this is not mentioned elsewhere. I would like to see text related to this in the results section (and discussion, if appropriate).

We agree that this is an interesting point and have included odds ratios in the second paragraph of the results section, as well as mentioning this discrepancy in the fourth paragraph of the discussion.

"Compared to PCPs, orthopedic surgeons, neurosurgeons and rehab physicians as initial providers decreased patients' odds of early opioid use (0.63, 95% CI: (0.60,0.67); 0.58, 95% CI: (0.47,0.71); 0.54, 95% CI: (0.49,0.59), respectively), while patients seeing emergency physicians initially had significantly increased odds of early opioid use (2.66, 95% CI: (2.54,2.78)). However, compared to PCP as first provider, odds for long-term opioid use were no longer significantly different for orthopedic surgeons, neurosurgeons, and emergency physicians (1.10, 95% CI: (0.92,1.30); 1.50, 95% CI: (0.88,2.58); 0.92, 95% CI: (0.77,1.10), respectively), but were significantly increased for rehab physicians (1.78, 95% CI: (1.40,2.26)). (Table 2)."

"The discrepancy between early and long-term use among PCPs and physicians specialists is also interesting. While patients who initially see orthopedic surgeons, neurosurgeons, rehabilitation physicians, and other physicians have significantly lower odds of early opioid use compared to PCPs, patients who initially see these physicians have similar or increased odds of long-term opioid use compared to PCPs. While we do not have access to pain severity, we hypothesize that physician specialists are trying to avoid prescribing opioids at the index visit, but if patients come back due to persistent pain, physicians will then prescribe opioids."

11.   Page 11, first full paragraph, first sentence: I suggest changing "protective effect" to "apparent protective effect" given the observational nature of this study. Also, please include other possibilities, such as confounding by patient preference for conservative care, here (not just in limitations).

We have made these changes to the text (page 10, paragraph 2).

"Several factors may help explain the apparent protective effect of conservative therapists."

12.   Page 11, first full paragraph, last sentence: The authors suggest conservative therapists could prevent need for MD visits. Can this be shown with the study dataset?

We have changed the text to make it clear that we are suggesting that conservative therapists could prevent opioid prescriptions associated with MD visits, as opioid use is the outcome of interest for this paper.

"Therefore and importantly, early engagement of conservative therapists may decrease initial opioid prescriptions in association with MD visits by providing the opportunity to incorporate evidence-based non-pharmacological interventions."

13.   Page 13, last sentence: Change "observational quasi-experimental" to "observational retrospective."

We have changed this on page 13 and in the title of the paper.

"Therefore, while the associations between initial health care providers for LBP and subsequent opioid therapy found in our analyses have potentially important implications, one cannot infer causality due to the observational retrospective nature of the study".

14.   Page 14: Did the funders (UnitedHealth, APTA, OptumLabs) have any role in the research (e.g., design, interpretation of results, decision to publish)?

This research was supported by UnitedHealthcare and the American Physical Therapy Association. Neither institution had editorial control or influence of the content of this paper. We have added this text to the acknowledgements.

15.   Table 1: Why are some numbers preceded by ">"?

Outcomes with a sample size <11 are not shown due to small sample size. There were a small number of individuals with unknown gender and insurance type, and if we provided exact n's, readers may be able to infer the unknown n's which would be problematic since we cannot disclose n<11 for reasons of confidentiality of the data. For example, in Table 1 under Male PT, >1493 means that there was an unknown gender row or column with n<11. Therefore, the number of male PT first individuals is between 1,493 and 1,504. We have updated the footnote of Table 1 to explain this.

16.   Table 2: Clarify variables in the models. The legend description seems to differ from methods text.

We have updated Table 2 and the associated footnote.

Table 2 Legend: The following variables were all included in the regression: Age, gender, race/ethnicity, insurance, Elixhauser, which includeds physical comorbidities and mental health

comorbidities. Primary care physician is the reference group (N=114,782); adjusted for race/ethnicity, gender, region, and insurance type. PT: physical therapy; PCP: primary care physician; DC: chiropractor; Ortho: orthopedic surgeon; Emerg Med: emergency medicine physician; Neurosgn: neurosurgeon; MD other: other physician; Rehab: rehab physician.*p<0.01. Two additional initial providers – other non-MD (eg. Physician assistants, advance practice nurses) and radiologist - were included in the analyses but not reported in this table.

17.   Figure 1: Please clarify terminology and ensure descriptions of eligibility criteria match across methods text, legend, and figure. For example, the legend states the first step was excluding patients with "insufficient clean period (opioid use within the last 1 year)," which is not consistent with the text in the figure box or methods.

        Thank you for catching this. We have updated Figure 1 and have edited the legend.

18.   Why does Figure 2 have fewer provider types than Table 2? Why are radiologists included in appendix tables but nowhere else?

        We have removed Figure 2.

19.   Appendix tables: These are not intuitive and require explanation in footnotes.

We have provided more detail in the footnotes given for the appendix tables.

Reviewer: 3
Reviewer Name: Ying Chen

Institution and Country: Keele University, UK

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below For statistical review only:

1.   The study design was clear and the statistical methods used were generally appropriate according to the design. However, there was a potential indication bias in the study as patients may go the different services influenced by their condition e.g. severity of pain. No measurement was presented in this paper with regard to this.

Thank you for your comments. We have added additional text to the limitations section to make it clear that patients may seek care from certain providers based on the severity of their pain which we were unable to measure.

"There are several limitations to this study. Analysis was conducted using claims data, limiting our generalizability beyond commercial and Medicare Advantage enrolled patients. However, the sample is national in scope and provides a range of sociodemographic and clinical characteristics. The observational nature of the study and the use of claims data limited our ability to eliminate the influence of unmeasured confounders. In particular, confounding by indication may bias our results. Patients who seek early treatment with non-pharmacologic practitioners may be more likely to have mild back pain that does not require more aggressive treatment such as opioids, compared to individuals with more severe back pain who may be more likely to see practitioners able to prescribe opioids. Studies have suggested that those with more severe LBP are more likely to receive opioids,36 and if patients with less severe pain were more likely to choose conservative therapists

rather than physicians, this could contribute to overestimation of the protective effect of conservative therapy on opioid use. Several prior studies have shown comparable baseline pain scores for those who choose conservative therapists compared to those who choose to see physicians initially, however it is important to note that these studies had different patient populations than this study as they were conducted either only in one state or in countries other than the United States.36-40 Other unmeasured confounders may include patient preferences and behavioral characteristics. For example, those who chose conservative therapists as initial providers for LBP may have preferences to avoidpharmacological and/or opioid therapy. Therefore, while the associations between initial health care providers for LBP and subsequent opioid therapy found in our analyses have potentially important implications, one cannot infer causality due to the observational retrospective nature of the study."

2.   I also found in table 1 there are some cells with "%" but some not, and the quality of figures 1 and 2 is quite bad --- almost unreadable. In the next version of paper the authors need to improve these to a higher standard.
Thank you for noticing this. We have removed the duplicate "%" from Table 1 and have uploaded higher resolution figures in this revision.

Reviewer: 4
Reviewer Name: Danielle Robinson

Institution and Country: CSM, NDORMs, University of Oxford, UK

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below Please see attached file (review.docx).

Thank you for inviting me to review this paper titled "Non-pharmacologic Therapies for New-onset Low Back Pain: Predictors of Early and Long-Term Opioid Use in the United States". This is an interesting paper comparing the initial provider of treatment for lower back pain with regards to both the early use of opioids and long-term opioids. However, there are areas for improvement in this paper and some of the numbers do not add up hence I would suggest major revisions. Also I feel there are a lot of unmeasured biases in this study, however for the dataset used it would be impossible to address them all and the limitations generally highlights these.

In the title:
-       This title suggests it produces predictors for opioid use in lower back pain. I would not agree with this statement as its more compares different initial treatment providers. The title may need changing to reflect this.
The title has been changed to reflect this.

New Title: An Observational Retrospective Study of the Association of Initial Health Care Provider for New-onset Low Back Pain with Early and Long-Term Opioid Use

In the abstract:
-       Numbers needed to treat can be calculated from odds ratios and should be calculated and included for the primary outcomes of this study
As with similar literature that focuses on back pain, other musculoskeletal conditions and opioid use, we choose to present odds ratios for the primary outcomes of this study. We think that including the number needed to treat overcomplicates the issue and also note that the number needed to treat

(NNT) is typically only used in the context of a randomized trial where adjustment for confounding is not needed. Additionally, we would only be able to calculate the NNT for initial provider type, as it is unclear how we would calculate it for other predictors.

In the article summary:
-        The bullet points appear very long and should be shortened
We have shortened the bullet points.
In the method section:
-        You mention "If a patient saw both a physician and a conservative therapist on the index date, the initial provider was assumed to be the physician". This may introduce bias as patients who see both may have more severe pain. What proportion of patients saw both physician and conservative therapist? Were these patients more likely to use opioids than physician treated alone? If so could a sensitivity analysis excluding these patients be undertaken?

A relatively small fraction of individuals (n=262) in the final analytic sample had both MD and PT visits on the index date. Given this number, it would be unlikely that this small sample would greatly affect the results. We have added this to the text of the Patient Characteristics section of the methods. Furthermore, a sensitivity analysis would be difficult given the small sample size.

"If a patient saw both a physician and a conservative therapist on the index date, the initial provider was assumed to be the physician, although this was notably a small number of individuals (n=262)."

-        There appear to be more covariates included in the propensity score than in the multivariable model. Why was this? To be comparable between models the same covariates should be included.

Given that there is no single standard for comparing models, we opted to use as many variables as we could in the propensity analysis to achieve better balance and provide better matching. This approach is frequently used when comparing models.

-        In the propensity score matching, what calliper width was used?

We have added this as the last sentence in the propensity paragraph in the methods. "The caliper for propensity matching was set to 0.001 for both PT and chiropractor models."

-        Please clarify the direction of the 2:1 PS matching e.g. 2 PCP to 1 chiropractor
For each propensity analysis, there were 2 PCP (2 PCP: 1 PT and 2 PCP:1 chiropractor). We have added this to the statistical analysis section of the Methods.

"As a supplemental alternative to adjusting for baseline confounding through regression adjustment, we invoked two-to-one propensity score matching (2 PCP: 1 physical therpist or 2 PCP: 1 chiropractor) without replacement to achieve baseline covariate balance among patients who initially saw chiropractor first, saw a physical therapist first or who saw PCP first.20,21"

In the results section:
-        The short term use of early opioids were highlighted for physical therapy and acupuncture in the text, however this is also reduced for nearly all initial providers, the exception being emergency care. Please add the odds ratios to the text for these other providers.

We have added these additional odds ratios to the text in the second paragraph of the Results section.

"Compared to seeing a PCP as initial provider, patients who first saw conservative therapists (chiropractor, acupuncturists and PTs) all had significantly decreased odds of both early and long-term opioid use. For early opioid use, patients initially visiting chiropractors had 90% decreased odds [95% CI: (0.09,0.10)] those visiting an acupuncturists had 91% decreased odds [95% CI: (0.07,0.12)] and those visiting PTs had 85% decreased odds [95% CI: (0.13,0.17)]. Chiropractors, acupuncturists and PTs all had major decreased odds of long term opioid use compared to those who initially saw PCPs (0.22, 95% CI: (0.18,0.26); 0.07, 95% CI: (0.01,0.48); 0.27, 95% CI: (0.15,0.48) respectively). Compared to PCPs, orthopedic surgeons, neurosurgeons and rehab physicians as initial providers decreased patients' odds of early opioid use (0.63, 95% CI: (0.60,0.67); 0.58, 95% CI: (0.47,0.71); 0.54, 95% CI: (0.49,0.59), respectively), while patients seeing emergency physicians initially had significantly increased odds of early opioid use (2.66, 95% CI: (2.54,2.78)). However, compared to PCP as first provider, odds for long-term opioid use were no longer significantly different for orthopedic surgeons, neurosurgeons, and emergency physicians (1.10, 95% CI: (0.92,1.30); 1.50, 95% CI: (0.88,2.58); 0.92, 95% CI: (0.77,1.10), respectively), but were significantly increased for rehab physicians (1.78, 95% CI: (1.40,2.26)). The estimates reported using bootstrapping indicated little or no differences with the actual results (Appendix Tables 3 and 4)."

- Please make sure all appendixes are referred to in the text as appendix instead of supplementary table.
We have made this edit throughout the text.
In the discussion section:
- You state that the propensity score matching may mitigate some concern regarding consumer choice. I would not agree with this statement since whilst it controls for age, gender and geographical location, no information about socio-economic status, health seeking behaviour or pain levels was included hence there is likely unmeasured confounding in this study. I would consider rewording the limitation to highlight whether this information is not available in claims databases.
We agree that there is definitely unmeasured confounding due to the claims nature of this study. However, propensity studies are frequently used to control for measurable factors which does mitigate some, but not all, of the unmeasured confounding.
We have reworded the limitations to highlight that pain severity is not included in the claims database we used.
"There are several limitations to this study. Analysis was conducted using claims data, limiting our generalizability beyond commercial and Medicare Advantage enrolled patients. However, the sample is national in scope and provides a range of sociodemographic and clinical characteristics. The observational nature of the study and the use of claims data limited our ability to eliminate the influence of unmeasured confounders. In particular, confounding by indication may bias our results. Patients who seek early treatment with non-pharmacologic practitioners may be more likely to have mild back pain that does not require more aggressive treatment such as opioids, compared to individuals with more severe back pain who may be more likely to see practitioners able to prescribe opioids. Studies have suggested that those with more severe LBP are more likely to receive opioids,36 and if patients with less severe pain were more likely to choose conservative therapists rather than physicians, this could contribute to overestimation of the protective effect of conservative therapy on opioid use. Several prior studies have shown comparable baseline pain scores for those who choose conservative therapists compared to those who choose to see physicians initially, however it is important to note that these studies had different patient populations than this study as they were conducted either only in one state or in countries other than the United States.36-40 Other unmeasured confounders may include patient preferences and behavioral characteristics. For example, those who chose conservative therapists as initial providers for LBP may have preferences to avoidpharmacological and/or opioid therapy. Therefore, while the associations between initial health care providers for LBP and subsequent opioid therapy found in our analyses have potentially important implications, one cannot infer causality due to the observational retrospective nature of the study."

In Table 1:

- Full sample N (%) the values in the conservative and physician therapies add up to 196461 patients and 90.1%. Please check the numbers in this table are correct. If these were missing please add a note at the bottom of the table. Table 1 would benefit from numbers of patients with each of fibromyalgia, chronic pain, fatigue and the psychiatric conditions mentioned in page 12.

We have added a footnote to Table 1 explaining this discrepancy. Two additional initial types of providers – other non-MD (eg. Physician assistants, advance practice nurses) and radiologist - were examined but not reported in this table due to small sample size.

Two additional initial providers – other non-MD (eg. Physician assistants, advance practice nurses) and radiologist - were examined but not reported in this table due to small sample size. We have added all opioid outcomes to Table 1 and have updated the footnote to include this information.
In Figure 2:
- The scale of the x-axis should be log.
We have removed Figure 2 from the paper.
In appendix 4:
- Gender is significant in PT but no *

Thank you for noticing this. We have added this. Please note that the previous appendix 4 is now appendix 6 due to re-ordering of the text.

- This table needs tidying for clarity particularly different groupings between race and region
We have added information about the analyses in appendix 6 (previously appendix 4) to the methods and results sections.
In appendix 5
- I didn't understand why the total column is included.
We have moved the overall N and deleted the word 'total' to make Appendix 5 more clear.
In references:
- References for propensity score matching should be included
This is an excellent point. We have added the below references for propensity score matching.

20. Stuart, E. A., King, G., Imai, K., & Ho, D. E. (2011). MatchIt: nonparametric preprocessing for parametric causal inference. Journal of Statistical Software, 42(8).
21. Dehejia, R. H., & Wahba, S. (2002). Propensity score-matching methods for nonexperimental causal studies. Review of Economics and statistics, 84(1), 151-161.

VERSION 2 – REVIEW

REVIEWER	Erin Krebs Minneapolis VA Health Care System and University of Minnesota, Minneapolis, MN, USA
REVIEW RETURNED	20-Jun-2019

GENERAL COMMENTS	My concerns have been addressed by the authors in the revised manuscript, which is much improved overall. I have a few minor remaining comments: 1. Thank you for clarifying in the response letter that "Sex/gender is determined based on enrollment records." This information should also be included in the manuscript under patient characteristics (page 8). Also, please revise terminology to use "sex," "gender," or "sex/gender" as appropriate, rather than using both "sex" and "gender" as though they are synonyms to describe the same variable. (I suggest https://orwh.od.nih.gov/sex-gender as a potentially useful resource). 2. Page 11, first paragraph of results: A new sentence describes receipt of "fast-acting opioids" and "prescription NSAIDs." These results are interesting, but the variables should be described in methods so readers know what is being reported. "Fast-acting" suggests rapid speed of onset; I wonder if the authors mean short-acting or immediate-release opioids, which are typically distinguished from long-acting opioids by duration. Were long-acting opioids also prescribed? Also, does "prescription NSAIDs" mean any NSAID that was prescribed or does it specifically refer to NSAIDs that are only available by prescription? Were other analgesics medications (e.g., acetaminophen) assessed? 3. For clarity, I recommend using consistent terminology regarding the main dependent variables (i.e., always "early and long-term opioid use" and not sometimes "short and long-term opioid use.")

REVIEWER	Danielle Robinson CSM, NDORMs, University of Oxford, UK
REVIEW RETURNED	24-Jun-2019

GENERAL COMMENTS	The authors have sufficiently addressed all the queries I raised in my first review of this paper. Some very minor comments which should be addressed at the draft stage include: Appendix 6: Opioid use 13-24 months back, PT is significant but is missing a *, please check for further missing *s

Reviewer: 2
Reviewer Name
Erin Krebs

Institution and Country
Minneapolis VA Health Care System and University of Minnesota, Minneapolis, MN, USA

Please state any competing interests or state 'None declared':
None declared

Please leave your comments for the authors below
My concerns have been addressed by the authors in the revised manuscript, which is much improved overall. I have a few minor remaining comments:

1.   Thank you for clarifying in the response letter that "Sex/gender is determined based on enrollment records." This information should also be included in the manuscript under patient characteristics (page 8). Also, please revise terminology to use "sex," "gender," or "sex/gender" as appropriate, rather than using both "sex" and "gender" as though they are synonyms to describe the same variable. (I suggest https://orwh.od.nih.gov/sex-gender as a potentially useful resource).

> We have changed all references from sex to "sex/gender" and have inserted the sentence below into the patient characteristics section of the methods on page 7 of the manuscript.

> "Sex/gender is determined based on enrollment records."

2.   Page 11, first paragraph of results: A new sentence describes receipt of "fast-acting opioids" and "prescription NSAIDs." These results are interesting, but the variables should be described in methods so readers know what is being reported. "Fast-acting" suggests rapid speed of onset; I wonder if the authors mean short-acting or immediate-release opioids, which are typically distinguished from long-acting opioids by duration. Were long-acting opioids also prescribed? Also, does "prescription NSAIDs" mean any NSAID that was prescribed or does it specifically refer to NSAIDs that are only available by prescription? Were other analgesics medications (e.g., acetaminophen) assessed?

> We have changed "fast-acting opioids" to "short-acting opioids." Long-acting opioids were prescribed to <0.1% of patients in the first 3 days so chose not to include it in the text given the very small percentage. We have also edited the text in the first paragraph of the results section to clarify that we only evaluated prescriptions for NSAIDs, as non-prescription NSAIDs cannot be measured in a claims based study. No other analgesic medications were assessed for the reasons listed in the text.

> "18% of patients received short-acting opioids (e.g., oxycodone, hydrocodone, codeine). 17.4% received prescriptions for NSAIDs."

3.   For clarity, I recommend using consistent terminology regarding the main dependent variables (i.e., always "early and long-term opioid use" and not sometimes "short and long-term opioid use.")

> We have edited the text to use early and long-term opioid use throughout.

Reviewer: 4

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Please state any competing interests or state 'None declared':
None declared

Please leave your comments for the authors below
The authors have sufficiently addressed all the queries I raised in my first review of this paper.

Some very minor comments which should be addressed at the draft stage include:
Appendix 6: Opioid use 13-24 months back, PT is significant but is missing a *, please check for further missing *s.

Thank you for noticing this. We have made this edit to appendix table 4.