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Original Article

Opioid epidemic: does rheumatological practice favors risk for patients? National survey on rheumatologists' opioid prescriptions and compliance to guidelines for strong opioid prescription.

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Abstract

Objectives

Given the scope of rheumatology and its prevalence of pain it seems needed that a study should focus on prescription habits, in the midst of the international opioid epidemic and given the moderate efficacy of strong opioids in chronic musculoskeletal conditions. We compared rheumatologists' opioid prescribing patterns in non-cancer pain with recommended practice.

Methods

We performed a cross-sectional study of the French health insurance database, including all patients aged 16 years or over reimbursed for at least one strong opioid prescription from a rheumatologist in 2015. A nationwide survey of all registered rheumatologists in France was performed with a 47-item questionnaire in June 2015.

Results

Only 2.4% of the patients receiving a strong opioid in 2015 ($n=700,946$) had at least one prescription from a rheumatologist. Rheumatologists prescribed mostly morphine, and significantly less oxycodone and fentanyl ($p<0.00001$) than other specialists. Rheumatologists prescribed a mean of 35.8 mg morphine equivalent/day. A response rate of 33.7% was obtained to the questionnaire. Acute musculoskeletal pain was the principal condition for strong opioids prescription, with 94.5% re-evaluating opioid treatment within two weeks of initiation. For efficacy, 80% said that they stopped treatment if no benefit was observed after a test period (mean = 1.2 months). Rheumatologists with pain management training were significantly more likely to evaluate pain before prescribing strong opioids ($p=0.001$), evaluate efficacy within three months ($p=0.01$) and screen for risk factors for misuse at initiation ($p<0.0001$).

Conclusions

For non-cancer pain, rheumatologists generally prescribe opioids for short periods, at low doses, mostly according to national recommendations. Pain education strongly affected opioid prescription by rheumatologists.

Keywords: strong opioids, rheumatology, prescribing patterns, non-cancer pain

1. Introduction

Since the 1990s, strong and weak opioids have been prescribed for a widening array of conditions, including acute pain, chronic cancer and non-cancer pain. The first US recommendations were published 20 years ago, to promote correct opioid prescription practices for chronic non-cancer pain (CNCP) [1]. However, these first guidelines favored large opioid prescribing in chronic non-cancer pain and wrongfully said that risks such as addiction were low. In France, the first national recommendations were published in 1999, for chronic musculoskeletal non-cancer pain. They were updated in 2004 and 2010, and the latest recommendations were formulated in 2014-2015 and published in 2016 [2]. A part from these first misleading guidelines, multiple other factors such as prescribers unfamiliar with abuse risks, conflicts of interest of experts, dishonest marketing from the pharmaceutical companies ... led to an "endemic" increase in the number of opioid prescriptions worldwide [3]. Opioid prescriptions have doubled in the US over the last decade [4]. Europe is following a similar trend, but with a slight time lag relative to North America. Opioid sales have followed the same pattern in the UK as in the US [5]. This increase in opioid prescription has raised concerns about increases in prescription opioid-related deaths and opioid use disorder. Opioid overdose-related mortality in the US increased by 156% between 2010 and 2015 [6], and the latest figures show a 292% increase in the number of deaths attributable to opioids from 2001 to 2016 [7]. An estimated 1.68 million person-years of life were due to opioid-related mortality in 2016. Opioid mortality data for Europe are similar to those for North America, with for example an increase of 425% of opioid attributable deaths in 20 years in England and Wales and an increase of 146% between 2000 and 2015 in France [8, 9]. Morley et al. used the Global Drug Survey 2015 to investigate the misuse and abuse of opioid analgesics among participants (from various countries) with at least one delivered prescription of opioids in the preceding year. This survey of 5670 participants detected the misuse or abuse of codeine, hydrocodone, oxycodone, or tramadol in 8 to 22% of participants [10].

Pain is a central symptom in rheumatic disease, and international concerns about the epidemic of opioid misuse and deaths have complicated its management by rheumatologists [11]. The efficacy and safety of long-term opioid treatment for chronic non-cancer pain are debatable, particularly in rheumatology, with two studies showing an increased risk of infection and vertebral fracture in patients with rheumatoid arthritis treated with opioids [12, 13]. Therefore, strong opioids are not recommended as first line nor in second line treatment in chronic musculoskeletal pain [2]. We investigated the conformity of rheumatologists' prescribing habits with guidelines for strong opioid prescription for non-cancer pain, and assessed the need for training in pain management and strong opioid prescription.

2. Methods

2.1 Population-based retrospective study of rheumatology patients reimbursed for strong opioids in 2015, according to the exhaustive data of the French health insurance database.

2.1.1 Data source

Data were extracted from the French health insurance database, SNIIR-AM (Système national d'information inter-régime de l'assurance maladie), which covers almost 65 million people. This database prospectively records all reimbursements of healthcare to the individuals covered by the national health insurance system in France. SNIIR-AM contains administrative, medical and pharmacy data. The administrative data include anonymous information about year of birth,

long-term diseases (LTD), and date of death for individuals. The pharmacy data exhaustively cover all claims for reimbursed drugs dispensed in retail pharmacies (including dates of prescription and dispensation, prescriber number and specialty, amounts supplied). Drugs are identified by their anatomical therapeutic chemical class (ATC) codes. Thirty major chronic diseases are designated long-term diseases (LTD) in the French healthcare system. The information recorded for LTDs includes the chronic disease code and associated International Classification of Disease (ICD)-10 code. The use of SNIIR-AM, a fully anonymized database, was approved by the French Data Protection Authority (CNIL, 1946535).

2.1.2 Participants

All male and female patients aged 16 years or over with at least one reimbursement of a strong opioid prescribed by a rheumatologist between January 1, 2015 and December 31, 2015 were included. Patients for whom a LTD of cancer was noted were excluded. All patients were identified by the ATC codes for the drugs dispensed. The strong opioids dispensed were morphine (ATC codes: N02AA01 and N02AA51), fentanyl (N02AB03), oxycodone (N02AA05 and N02AA55), buprenorphine (N02AE01) and hydromorphone (N02AA03).

2.1.3 Study data

Demographic data (year of birth, sex, date of death, LTD, and low-income status) were collected from this database. Data on dispensed drugs (analgesics and psychotropic drugs) were extracted from ATC class codes. Patients with mental health disorders were identified by ICD-10 codes of F00 to F99. A continuous sequence was defined as an interval of less than 45 days between consecutive dispensations (threshold based on the dispensation of drugs for a maximum of 4 weeks in France). For more specific detection of treatment interruptions, we added two weeks to the maximum duration of prescription. Patients with “shopping behavior” were defined as those with dispensations of strong opioid prescriptions overlapping by at least one day, from two different prescribers, at three or more pharmacies. Specialty of prescribers was available in the data set through the unique registration number of each french doctor.

2.2. Nationwide survey

We conducted a nationwide survey with a 47-item questionnaire. The questions were developed by the French Study Group on Rheumatic Pain (CEDR), focusing on opioid prescription and pain training. The questionnaire was mailed, with a response envelope in June 2015 with a 4 months delay for collecting the answers. The mailing list was constituted of all certified French rheumatologist, based on the National Medical Board data. A reminder was sent through email in September 2015. Answers were anonymous. Rheumatologists were

asked to provide demographic information, and information about their level of pain education, and whether they prescribed strong opioids (even if only rarely). If they replied that they “never” prescribed strong opioids, no further questions were asked. The later questions focused on prescribing habits. [Appendix A, Document S1; See the supplementary material associated with this article online]

2.3 Statistics

Data are expressed as frequencies and associated percentages for categorical data and as means $\pm$ standard deviation [min-max] or medians [interquartile range] for continuous data. We used χ^2 tests to compare responses between rheumatologists with and without training in pain management, for key issues relating to prescription guidelines. P values less than 0.05 were considered significant. All statistical analyses were performed with SAS for Windows version 9.3 (SAS Institute, North Carolina, USA).

2.4 Role of the funding source

This research was funded by the CEDR (Cercle d'Etude de la Douleur en Rhumatologie)”. The CEDR is the French Study Group on Rheumatic Pain, a non-profit organization. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

3. Results

3.1. National social security reimbursement data for 2015

In 2015, 700,946 patients in France received a strong opioid at least once out of which 533,299 patients without a cancer diagnosis (i.e. with no recording of cancer as a LTD in the SNIIR-AM database). Among them, 17,149 patients (4.5%) without a cancer diagnosis with at least one prescription by a rheumatologist were identified. Overall, 64.2% of these patients were women, and their mean age was 61.5 years [$\pm$ 15.8] (Table 1). The first prescriber for patients without a cancer diagnosis, was a general practitioner for 87.3%; an orthopedic surgeon for 2.5%; a rheumatologist for 1.8%; an anesthesiologist for 1%; a neurosurgeon for 0.5%; an internal medicine specialist for 0.4%; the rest being shared among various other specialties. Regarding previous treatment, 93% of the patients received acetaminophen, NSAID or weak opioids during the 3 months prior to strong opioid prescribing. For 11,860 (69.2%) of these 17,149 patients, only one prescription of strong opioid was delivered. Regarding long term opioid therapy, at 6 and 9 months of the first prescription, respectively 2.4% and 1.6% of patients are still receiving strong opioids. This data has to be

interpreted with great caution given that the study was transversal and not all patients had 12 months follow-up.

For 95.5% of patients, only one molecule was prescribed in 2015 (regardless of the number of prescriptions). Comorbid conditions were present in some of these patients: a known psychiatric condition in 2901 patients (16.9%), chronic alcoholism in 1.5% and opioid addiction in 0.4%. “Shopping behavior” was detected in 297 patients (1.7%), including only 75 patients (0.4%) with treatment initiated by a rheumatologist (Table 1). The strong opioid treatment was initiated by a rheumatologist in 9,816 patients (Figure 1). The molecule used at initiation was morphine in 58.4% of cases, oxycodone in 25.7% and fentanyl, buprenorphine or hydromorphone in 15.9%. Table 2 shows the molecules prescribed by rheumatologists and other specialists. Rheumatologists prescribed significantly less oxycodone and fentanyl ($p < 0.00001$) than other specialists for non-cancer pain (Table 2).

We stratified the analysis by the type of specialist initiating opioid treatment. For rheumatologists (9816 patients), initial opioid treatment was a single prescription for 5267 (53.7%) patients. For patients with two or more prescriptions, the mean number of dispensing events was 2.7 for patients managed exclusively by the rheumatologist, and 4.6 for patients managed jointly by the rheumatologist and other specialists. Mean daily morphine equivalent (MEQ) throughout patient follow-up was 35.8 milligrams (mg) per day for patients managed by the rheumatologist alone and 35.3 mg per day for those followed by a rheumatologist and another specialist, for treatments initiated by rheumatologists. The mean number of deliveries and mean daily MEQ were twice as high for opioid treatments initiated by other specialists than for those initiated by rheumatologists (Figure 1).

3.2. Nationwide survey

In total, 2490 questionnaires were sent, and 839 responses were obtained (response rate: 33.7%). The demographic data for respondents are presented in Table 3. In 2015, data of the national medical board indicate that in France, 54% of the rheumatologists were men, mean age was 52 years old and 47% had a private practice, 31.2% had a hospital practice. Overall, 65.4% of the responding rheumatologists reported having no pain management training, and 58 of the 839 respondents (6.9%) self-reported never prescribing opioids for non-cancer pain (Table 3). The use of a numerical rating scale (NRS) or a visual analog scale (VAS) to evaluate pain intensity before opioid treatment initiation was reported by 66.1% of rheumatologists. The principal condition for which rheumatologists considered prescribing strong opioids was acute musculoskeletal pain, such as acute radicular pain (93.1% of respondents), vertebral fracture (91.4%) and acute back pain (67.1%). Only 1% would consider prescribing strong opioids for fibromyalgia. Among prescribers, 464 (59.4%) answered they would try other analgesics before prescribing strong opioids. There was no statistical difference regarding previous prescription of other analgesics when comparing prescribers with or without pain management education or when comparing prescribers declaring they prescribe to 5 or more patients/month or less than 5 patients/months.

The first-line treatment was morphine or oxycodone for 613 prescribers (78.5%), fentanyl, hydromorphone or buprenorphine for 168 (21.5%). The declared mean starting daily dose was 45 mg morphine equivalent [± 17.6] and 66.3% ($n=518$) of respondents initiated treatment with titration. There was no statistical difference of mean starting daily dose when comparing prescribers with or without pain management education. Opioid treatment was reevaluated by 94.5% ($n=738$) within two weeks of initiation. For 80% ($n=625$), efficacy was assessed during a test period (mean duration 1.2 months), with treatment stopped in the absence of benefit. A ceiling dose of less than 150 mg morphine equivalent/day was reported by 37.6% ($n=294$) of respondents.

The risk of opioid misuse was assessed by 70.3% of respondents before treatment initiation. Prophylaxis treatments against the adverse effects of opioids were also prescribed: laxatives by 69.8% of rheumatologists and anti-vomiting treatments by 62.1%. (Answers to all other questions of the questionnaire are given as raw data in Appendix A, Document S2)

Prescribers with pain management education were more likely to evaluate pain before prescribing strong opioids ($p=0.001$), to initiate treatment with a titration phase ($p<0.0001$), to evaluate efficacy over a testing period of no more than three months ($p=0.01$), and to prescribe a laxative systematically with strong opioids ($p=0.004$). Finally, pain management education was significantly associated with screening for a risk of misuse at initiation ($p<0.0001$) (Figure 2).

4. Discussion

Both sources of data regarding opioid prescription showed that the prescription of these drugs by rheumatologists was reasonable. Moreover, rheumatologists clearly prescribed strong opioids predominantly for acute pain. However we would like to stress here the lack of evidence for the use of strong opioid in such acute pain context. Indeed, most patients with treatment initiated by a rheumatologist received only one prescription, and even when the prescription was renewed, the daily morphine equivalent dose was low. Pain is a prevalent symptom in rheumatological conditions and weak and strong opioids are widely prescribed for various musculoskeletal conditions despite strong evidence for such use. Prevalence of opioids use in various countries varies depending on type of opioid analyzed (strong, weak, both) and musculoskeletal condition. Moreover, countries with the highest prevalence of use are those reporting an “opioid epidemic”. In Germany, in a cohort of 3140 patients with rheumatoid arthritis (RA), 6% of patients without or with mild pain and 32.6% of those with severe pain received opioids [14]. In the United States, Curtis et al. found that 41% of patients in a cohort of more than 240,000 RA patients were on regular opioid treatment and 19% were treated intermittently [15]. In a cohort of 706 patients with spondyloarthritis (SpA) in the United States, 21.7% had intermittent opioid use and 9.5% used opioids regularly [16]. A large national evaluation of trends in back pain treatment over 12 years in the US showed an increase in opioid use from 19.3% to 29.1% [17]. Based on a large administrative claims database, DeMik et al. calculated that about 11.5% of patients with osteoarthritis would be prescribed an opioid in any given year [18]. However, the effectiveness of opioids against chronic non-cancer pain remains a matter of debate. Most literature reviews for various musculoskeletal conditions have drawn moderate conclusions regarding the benefit of opioids for chronic pain. A Cochrane review in 2014 reported small benefits against pain, of dubious clinical relevance, accompanied by a significant risk of adverse effects in patients with osteoarthritis [19]. Smith et al., in another systematic review,

concluded that NSAIDs and opioids yielded similar levels of pain relief in osteoarthritis patients [20]. In chronic low back pain, multiple reviews and meta-analyses have concluded that opioids have short-term benefits, with a moderate effect on pain and a small effect on function, but the benefits and safety of long-term treatment have yet to be demonstrated [21, 22]. There is only one Cochrane review available for chronic inflammatory rheumatism, from 2011. It found that weak opioids may be effective against pain in RA patients, but there is too little evidence to draw conclusions about long-term opioid therapy or the benefits of strong opioids [23]. There has been no demonstration of efficacy for opioids in fibromyalgia. In two large cohorts no improvement in pain, function, or quality of life was shown [24, 25]. Both sources of opioid prescription data in this study showed that French rheumatologists prescribed such analgesic treatments reasonably. Moreover, they prescribed strong opioids principally for acute pain, and rheumatologists' prescriptions accounted for less than 3% of French patients receiving opioid treatment in a year. Yet this has to be balanced by the fact that rheumatologists account for less than 3% of the total population of French medical doctors. Most treatments initiated by rheumatologists were limited to a single prescription, and even when renewed, the daily morphine equivalent dose was low (<40 mg/day).

In this context of complex benefit-risk balance with a moderate expected benefit but a risk of abuse or misuse with sometimes deadly consequences, national and international [2, 26-28] recommendations for the prescription of opioids for non-cancer pain recommend the introduction of strong opioids only after the failure of recommended first-line treatments at the maximum tolerated effective dose. Comprehensive patient care should include at least a psychological evaluation for patients with comorbid depression or anxiety, and in cases of social, professional and rehabilitative management for osteoarthritis pain and chronic low back pain. Strong opioids should not be used in nociceptive pain, such as fibromyalgia. The recommendations advise caution above a defined daily morphine equivalent dose, ranging from 50 mg/day to 200 mg/day, depending on the recommendations considered. All the recommendations agree that regular reassessment is necessary and that strong opioid treatment should be discontinued if no improvement is observed after three months of treatment. This nationwide survey demonstrates that most prescribers know the recommendations for opioid prescription for non-cancer pain. French rheumatologists appear to have a better knowledge of opioid prescription recommendations than the physicians evaluated in other studies assessing their adherence to opioid risk reduction strategies and prescription recommendations, such as that by Tournebise et al. who identified substantial gaps in practice and knowledge in a systematic review performed in 2016 [29]. In the review by Tournebise, pain intensity was assessed on a scale by only 8% to 56% of prescribers, whereas our survey indicates that more than 65% of rheumatologists assess pain intensity [29]. This literature review also reported a mean of 56% of prescribers in other studies screening for misuse risk factors before prescription. In a recent survey of family doctors in Quebec, Roy et al. reported that 44.5% never and 35.7% only sometimes assessed the risk of dependence, whereas 70.3% of the French rheumatologists declared screening for such risk factors [29, 30]. However, only a few rheumatologists seemed to know the suggested maximum daily dose not to be exceeded in non-cancer patients, whereas Tournebise reported that 89% of physicians observed this recommendation [29]. Overall, 80% of the respondents in our study reported using a test period (mean of 1.2 months) to assess efficacy, after which treatment was stopped if no benefit was observed, in accordance with recommendations. Both the survey and national database data showed that only a small proportion of rheumatologists initiated opioid treatment with a molecule not recommended in guidelines, such as fentanyl or molecules not authorized for the treatment of non-cancer pain in France, such as buprenorphine or hydromorphone. Tournebise et al. reported that 33% and 43% of prescribers, in two different

studies, would not prescribe fentanyl patches for opioid-naïve patients. Our national reimbursement data analysis indicated that fentanyl was prescribed to opioid-naïve patients in less than 16% of initial prescriptions [29]. Fentanyl is not indicated for the treatment of pain in opioid-naïve patients [31], and should be considered a second-line therapy [32].

Worldwide, pain management education is currently considered inadequate [33, 34], as demonstrated by the results of the survey of Roy et al., which revealed that family doctors in Quebec were critical of their university education relating to opioid analgesic prescribing practices for chronic non-cancer pain; 70% reported that it was “not very” or “not at all” adequate [30]. French rheumatologists with only basic pain management training (French medical student have a 20 hours of pain education in their core curriculum before specialization) adhered well to guidelines. Extra training in pain management had a marked impact in our study, resulting in significantly stronger adherence to current guidelines. Only a few studies have investigated the impact of educational strategies on patient care and their results are inconsistent. Liebschutz et al. tested a multicomponent intervention to increase the use of guideline-concordant strategies [35]. At 12 months of follow-up, the intervention resulted in significant differences in favor of the intervention group for all outcomes except early refills. Alford et al. showed that a 3 hours program of training in safe and appropriate opioid prescribing improved knowledge [36]. This improvement was maintained two months after the program. Holliday et al. assessed the benefits of a brief training workshop on opioid prescribing [37]. This training significantly reduced “hypothetical” opioid prescribing, but had no significant effect on the overall prescription of opioids by registrars. The long history of recommendations and guidelines formulated by rheumatologists in France may account for the good knowledge of the recommendations among rheumatologists, regardless of their level of pain management education.

Our study has several limitations. The main limitation relating to the survey is the desirability bias, making it impossible to rule out the possibility that the respondents gave what they considered to be the “right” answer rather than their truth. The French health insurance database lacks several important items of information, such as pain diagnosis and the prescribed daily dose for patients receiving only one prescription. This lack of dose in the database might explain partly the little mean dose prescribe since it was calculated on the total dose delivered and the time between two deliveries for each patient. It is also difficult to assess misuse from the national database data, but the rheumatologists reported screening for risks of abuse and misuse in the national survey. Finally with around 2500 rheumatologists and around 17150 patients with a prescription from a rheumatologist, one could argue each rheumatologist prescribe very few opioid, this has to be put into the perspective of a database study that lacks some prescription, in particular prescription issued during a hospitalization with only the hospital registration number on the prescription and not the specialists.

Prescribers act right at the start of the process and therefore have a major role in combating deaths from prescription opioid misuse. The French example shows how, when compared to other countries where such compliance to guidelines were researched, through long-standing recommendations developed by rheumatologists, the majority of the national community of rheumatologists prescribe in alignment with the recommendations.

Appendix A. Supplementary data

Supplementary data (Documents S1-S2) associated with this article can be found in the online version at ...

Author Contributions: Conceptualization, APT., RMJ., PVS., FL., SPo., NA. and SP.; methodology, APT. NA. and SP.; validation, NA. and SP. ; formal analysis, MR., EC. and IN.; investigation, APT. and CC.; data curation, APT. and CC; writing—original draft preparation, APT.; writing—review and editing, APT., CC., EC., IN., RMJ., PVS., FL., SPo., NA. and SP.; supervision, SP. and NA.; project administration, APT.,

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References

1. American Academy of Pain Medicine and American Pain Society. The Use of Opioids for the Treatment of Chronic Pain: A Consensus Statement. Glenview, Ill: American Academy of Pain Medicine and American Pain Society; 1997.
2. Moisset X, Trouvin AP, Tran VT, Authier N, Vergne-Salle P, Piano V, et al. Use of strong opioids in chronic non-cancer pain in adults. Evidence-based recommendations from the French Society for the Study and Treatment of Pain. *Presse Med* 2016;45:447-62. doi: 10.1016/j.lpm.2016.02.014
3. deShazo RD, Johnson M, Eriator I, Rodenmeyer K. Backstories on the US Opioid Epidemic. Good Intentions Gone Bad, an Industry Gone Rogue, and Watch Dogs Gone to Sleep. *Am J Med* 2018;131: 595-601
4. Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, et al. Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med* 2015;372:1573-4. doi: 10.1056/NEJMsa1406143.
5. Weisberg D, Becker W, Fiellin D, Stannard C. Prescription opioid misuse in the United States and the United Kingdom: Cautionary lessons. *Int J Drug Policy* 2014;26:1124-30. doi: 10.1016/j.drugpo.2014.07.009. Epub 2014 Jul 30.
6. National Institutes of Health, National Institute of Drug Abuse. Overdose death rates. <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>. Updated January 2017.
7. Gomes T, Tadrous M, Mamdani MM, Paterson JM, Juurlink DN. The burden of opioid-related mortality in the United States. *JAMA Network Open* 2018;1(2):e180217. doi: 10.1001/jamanetworkopen.2018.0217.
8. Giraudon I, Lowitz K, Dargan PI, Wood DM, Dart RC. Prescription opioid abuse in the UK. *Br J Clin Pharmacol* 2013;76:823-4. doi: 10.1111/bcp.12133
9. Chenaf C, Kaboré JL, Delorme J, Pereira B, Mulliez A, Zenut M, et al. Prescription opioid analgesic use in France: trends and impact on morbidity-mortality. *Eur J Pain*. 2018 Jul 27. doi: 10.1002/ejp.1291.
10. Morley KI, Ferris JA, Winstock AR, Lynskey MT. Polysubstance use and misuse or abuse of prescription opioid analgesics: a multi-level analysis of international data. *Pain* 2017;158:1138-1144. doi: 10.1097/j.pain.0000000000000892.
11. Borenstein DG, Hassett AL, Pisetsky D. Pain management in rheumatology research, training, and practice. *Clin Exp Rheumatol* 2017;35 Suppl 107(5):2-7.
12. Wiese AD, Griffin MR, Stein CM, Mitchel EF Jr, Grijalva CG. Opioid analgesics and the risk of serious infections among patients with rheumatoid arthritis: A self-controlled case series study. *Arthritis Rheumatol* 2016;68:323-31. doi: 10.1002/art.39462.
13. Acurcio FA, Moura CS, Bernatsky S, Bessette L, Rahme E. Opioid use and risk of nonvertebral fractures in adults with rheumatoid arthritis: A nested case-control study using administrative databases. *Arthritis Rheumatol* 2016;68:83-91. doi: 10.1002/art.39422.
14. Jobski K, Luque Ramos A, Albrecht K, Hoffmann F. Pain, depressive symptoms and medication in German patients with rheumatoid arthritis-results from the linking patient-reported outcomes with claims data for health services research in rheumatology (PROCLAIR) study. *Pharmacoepidemiol Drug Saf* 2017;26:766-774. doi: 10.1002/pds.4202.
15. Curtis JR, Xie F, Smith C, Saag KG, Chen L, Beukelman T, et al. Changing trends in opioid use among patients with rheumatoid arthritis in the United States. *Arthritis Rheumatol* 2017;69:1733-1740. doi: 10.1002/art.40152.
16. Dau JD, Lee M, Ward MM, Gensler LS, Brown MA, Leach TJ, et al. Opioid analgesic use in patients with ankylosing spondylitis: an analysis of the prospective study of outcomes in an ankylosing spondylitis cohort. *J Rheumatol* 2018;45:188-194. doi: 10.3899/jrheum.170630.
17. Mafi JN, McCarthy EP, Davis RB, Landon BE. Worsening trends in the management and treatment of back pain. *JAMA Intern Med* 2013;173:1573-1581. doi: 10.1001/jamainternmed.2013.8992.
18. DeMik DE, Bedard NA, Dowdle SB, Burnett RA, McHugh MA, Callaghan JJ. Are we still prescribing opioids for osteoarthritis? *J Arthroplasty* 2017;32:3578-3582.e1. doi: 10.1016/j.arth.2017.07.030.

19. da Costa BR, Nüesch E, Kasteler R, Husni E, Welch V, Rutjes AW, et al. Oral or transdermal opioids for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev* 2014;(9):CD003115. doi: 10.1002/14651858.CD003115.pub4.
20. Smith SR, Deshpande BR, Collins JE, Katz JN, Losina E. Comparative pain reduction of oral non-steroidal anti-inflammatory drugs and opioids for knee osteoarthritis: systematic analytic review. *Osteoarthritis Cartilage* 2016;24:962-72. doi: 10.1016/j.joca.2016.01.135.
21. Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared with placebo or other treatments for chronic low back pain: an update of the Cochrane Review. *Spine (Phila Pa 1976)* 2014;39:556-63. doi: 10.1097/BRS.0000000000000249.
22. Koes BW, Backes D, Bindels PJE. Pharmacotherapy for chronic non-specific low back pain: current and future options. *Expert Opin Pharmacother* 2018;19:537-545. doi: 10.1080/14656566.2018.
23. Whittle SL, Richards BL, Husni E, Buchbinder R. Opioid therapy for treating rheumatoid arthritis pain. *Cochrane Database Syst Rev* 2011;(11):CD003113. doi: 10.1002/14651858.CD003113.pub3.
24. Peng X, Robinson RL, Mease P, Kroenke K, Williams DA, Chen Y, et al. Long-term evaluation of opioid treatment in fibromyalgia. *Clin J Pain* 2015;31:7-13. doi: 10.1097/AJP.0000000000000079.
25. Fitzcharles MA, Faregh N, Ste-Marie PA, Shir Y. Opioid use in fibromyalgia is associated with negative health related measures in a prospective cohort study. *Pain Res Treat* 2013;2013:898493. doi: 10.1155/2013/898493.
26. Dowell D, Haegerich TM, Chou R. CDC Guideline for prescribing opioids for chronic pain--United States, 2016. *JAMA* 2016;315:1624-45. doi: 10.15585/mmwr.rr6501e1.
27. O'Brien T, Christrup LL, Drewes AM, Fallon MT, Kress HG, McQuay HJ, et al. European Pain Federation position paper on appropriate opioid use in chronic pain management. *Eur J Pain* 2017;21:3-19. doi: 10.1002/ejp.970.
28. Häuser W, Schug S, Furlan AD. The opioid epidemic and national guidelines for opioid therapy for chronic noncancer pain: a perspective from different continents. *Pain Rep* 2017;2:e599. doi: 10.1097/PR9.0000000000000599.
29. Tournebise J, Gibaja V, Muszczak A, Kahn JP. Are physicians safely prescribing opioids for chronic noncancer pain? A systematic review of current evidence. *Pain Pract* 2016;16:370-83. doi: 10.1111/papr.12289.
30. Roy É, Côté RJ, Hamel D, Dubé PA, Langlois É, Labesse ME, et al. Opioid prescribing practices and training needs of Québec family physicians for chronic noncancer pain. *Pain Res Manag* 2017;2017:1365910. doi: 10.1155/2017/1365910.
31. Hooten WM, Timming R, Belgrade M, et al. Institute for Clinical Systems Improvement. Assessment and Management of Chronic Pain. Updated November 2013:43-44
32. Manchikanti L, Kaye AM, Knezevic NN, McAnally H, Slavin K, Trescot AM, et al. Responsible, safe, and effective prescription of opioids for chronic non-cancer pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines. *Pain Physician* 2017;20(25):S3-S92.
33. Webster F, Bremner S, Oosenbrug E, Durant S, McCartney CJ, Katz J. From opiophobia to overprescribing: a critical scoping review of medical education training for chronic pain. *Pain Med* 2017;18:1467-1475. doi: 10.1093/pm/pnw352.
34. Briggs EV, Battelli D, Gordon D, Kopf A, Ribeiro S, Puig MM, et al. Current pain education within undergraduate medical studies across Europe: Advancing the Provision of Pain Education and Learning (APPEAL) study. *BMJ Open* 2015;5:e006984. doi: 10.1136/bmjopen-2014-006984.
35. Liebschutz JM, Xuan Z, Shanahan CW, LaRochelle M, Keosaian J, Beers D, et al. Improving adherence to long-term opioid therapy guidelines to reduce opioid misuse in primary care: A cluster-randomized clinical trial. *JAMA Intern Med* 2017;177:1265-1272. doi: 10.1001/jamainternmed.2017.2468.
36. Alford DP, Zisblatt L, Ng P, Hayes SM, Peloquin S, Hardesty I, et al. SCOPE of Pain: An evaluation of an opioid risk evaluation and mitigation strategy continuing education program. *Pain Med* 2016;17:52-63.
37. Holliday SM, Hayes C, Dunlop AJ, Morgan S, Tapley A, Henderson KM, et al. Does brief chronic pain management education change opioid prescribing rates? A pragmatic trial in Australian early-career general practitioners. *Pain* 2017;158:278-288. doi: 10.1097/j.pain.0000000000000755.

Table 1: Demographic and opioid delivery data for the 17,149 patients

	N=17149
Women, No. (%)	11059 (64.5)
Age (years), mean $\pm$ SD [min;max]	60.7 $\pm$ 15.9 [16 ; 105]
Initiation by a rheumatologist, No. (%)	9816 (57.2)
Number of different rheumatologists/patient, mean $\pm$ SD [min;max]	1.02 $\pm$ 0.15 [1 ; 4]
Number of deliveries of strong opioid / patient, mean $\pm$ SD [min;max]	1.81 $\pm$ 2.05 [1 ; 42]
n=1 delivery, No. (%)	11860 (69.2)
n=2, No. (%)	2867 (16.7)
n=3, No. (%)	970 (5.7)
n>3, No. (%)	1452 (8.5)
Doctor shopping, No. (%)	297 (1.73)
Doctor shopping with strong opioids initiated by the rheumatologist, No (%)	75 (0.4)
Number of different strong opioid molecules / patient, mean $\pm$ SD [min;max]	1.05 $\pm$ 0.22 [1 ; 3]
Only one molecule, No. (%)	16379 (95.5)
Number of different pharmacies/patient, mean $\pm$ SD [min;max]	1.08 $\pm$ 0.32 [1 ; 6]
Only one pharmacy, No. (%)	15913 (92.8)
Consultation at pain medicine department, No. (%)	82 (0.48)
Psychiatric comorbidity, No. (%)	2901 (16.9)
Alcohol dependence, No. (%)	258 (1.5)
Opioid addiction, No. (%)	71 (0.4)
Drug substitution treatment, No. (%)	25 (0.15)

SD: standard deviation

Table 2: Strong opioid prescription by rheumatologists or other specialists

Molecule No. (%)	N=31652 prescriptions by rheumatologists	N=47668 prescriptions by other prescribers
Morphine only	16040 (50.7)	19094 (40.1)
Oxycodone only	8272 (26.1)	15318 (32.1)
Fentanyl only	6136 (19.4)	10937 (22.9)
Hydromorphone only	174 (0.55)	196 (0.41)
Buprenorphine only	234 (0.74)	99 (0.21)
Fentanyl and morphine	532 (1.68)	1082 (2.27)
Fentanyl and oxycodone	169 (0.53)	706 (1.48)
Morphine and oxycodone	70 (0.22)	161 (0.34)
Morphine and hydromorphone	15 (0.05)	24 (0.05)
Oxycodone and hydromorphone	10 (0.03)	46 (0.1)
Fentanyl and buprenorphine	3 (0.01)	5 (0.01)
Fentanyl and hydromorphone	1 (0.001)	8 (0.01)

Table 3: Demographic data for the national survey of rheumatologists

	No. = 839
Age (years), mean ($\pm$ SD)	50.4 ($\pm$ 11.7)
Men, No. (%)	413 (49.2)
Type of practice	
Hospital practice, No. (%)	285 (34)
Private practice, No. (%)	353 (42)
Both, No. (%)	201 (24)
Pain management education	
Pain specialist, No. (%)	40 (4.8)
1 year extracurricular on general pain management, No. (%)	39 (4.6)
Pain-focused continuing medical education conference for non-pain specialists No. (%)	211(25.1)
None, No. (%)	549 (65.4)
Prescription of strong opioids	
Never, ever, No. (%)	58 (6.9)
< 3 patients per month, No. (%)	371 (44.2)
3 to 5 patients per month, No. (%)	176 (21)
5 to 10 patients per month, No. (%)	113 (13.5)
> 10 patients per month, No. (%)	121 (14.4)

Figures

Figure 1: Flow chart of the patients by prescriber at treatment initiation. MEQ: morphine equivalent; Mean age $\pm$ standard deviation; Mean delivery $\pm$ standard deviation; Mean daily MEQ $\pm$ standard deviation

Figure 2: Proportions of French rheumatologists prescribing strong opioids with respect to the latest recommendations. * $p < 0.05$



