Association Between Utilization of Chiropractic Services for Treatment of Low Back Pain and Risk of Adverse Drug Events

James M. Whedon, DC, MS,[a] Andrew W.J. Toler, MS,[a] Justin M. Goehl, DC, MS,[b] and Louis A. Kazal, MD[b]

Abstract

Objectives: Mortality rates due to adverse drug events (ADEs) are escalating in the United States. Analgesics are among the drug classes most often associated with occurrence of an ADE. Utilization of nonpharmacologic chiropractic services for treatment of low back pain could lead to reduced risk of an ADE. The objective of this investigation was to evaluate the association between utilization of chiropractic services and likelihood of an ADE.

Methods: We employed a retrospective cohort design to analyze health insurance claims data from the state of New Hampshire. After inversely weighting each participant by their propensity to be in their cohort, we employed logistic regression to compare recipients of chiropractic services to nonrecipients with regard to likelihood of occurrence of an ADE in an outpatient setting.

Results: The risk of an ADE was significantly lower among recipients of chiropractic services as compared with nonrecipients. The adjusted likelihood of an ADE occurring in an outpatient setting within 12 months was 51% lower among recipients of chiropractic services as compared to nonrecipients (OR 0.49; $P = .0002$). The reported ADEs were nonspecific with regard to drug category in the majority of incidents that occurred in both cohorts.

Conclusions: Among New Hampshire adults with office visits for low back pain, the adjusted likelihood of an ADE was significantly lower for recipients of chiropractic services as compared to nonrecipients. No causal relationship was established between utilization of chiropractic care and risk of an ADE. Future research should employ larger databases, rigorous methods to reduce risk of bias, and more sensitive means of identifying ADEs. (J Manipulative Physiol Ther 2018;41:383-388)

Key indexing terms: *Chiropractic; Low Back Pain; Adverse Drug Event; Adverse Drug Reaction*

Introduction

Adverse Drug Events

Adverse drug events (ADEs) are injuries that result from prescription drug interventions. Types of ADEs include medication errors, adverse or allergic reactions, and overdoses. Adverse drug events are associated with increased rates of disability, hospitalization and mortality, and may result from appropriate use of medications as well as overuse and misuse.[1] An analysis of 2 nationally representative probability sample surveys revealed that from 2005 to 2007 the highest incidence of ADEs occurred in outpatient settings and among patients aged 65 and older.[2] A systematic review reported a median prevalence rate for ADEs of 12.8% overall and 16.1% for elderly patients.[3] Mortality rates due to ADEs are escalating; the drug overdose death rate increased from 12.3 per 100 000 population in 2010 to 16.3 in 2015.[4]

Risk of an ADE Associated With Prescription Analgesia for Low Back Pain

A recent systematic review of pharmacologic therapies for low back pain found modest, short-term benefits for several types of medication used to treat low back pain, including acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids.[5] However, analgesics (particularly NSAIDs and opioids) are among the drug

[a] Health Services Research, Southern California University of Health Sciences, Whittier, California.
[b] Community and Family Medicine, Geisel School of Medicine, Dartmouth College, Hanover, New Hampshire.
Corresponding author: James M. Whedon, DC, MS, Health Services Research, Southern California University of Health Sciences, 16200 Amber Valley Drive, Whittier, CA 90604. Tel.: +1 603 863 8749.
(e-mail: *jameswhedon@scuhs.edu*).
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classes most often associated with occurrence of an ADE.[3,6,7]

- *Acetaminophen*: Long thought to be safe and the most widely used nonopioid painkiller in the world, acetaminophen was recently reported to be associated with significant toxic effects (including hepatic and renal disease, gastrointestinal bleeding, and increased risk of myocardial infarction, stroke, and hypertension) particularly at higher doses.[8]
- *NSAIDs*: An analysis of national survey data found that NSAIDs are the most commonly prescribed type of analgesic for older adults with chronic nonmalignant pain.[9] Nonsteroidal anti-inflammatory drugs offer effective analgesia for spinal pain, but carry increased risk of gastrointestinal reactions,[10] and a 100% increase in risk of heart failure.[11] The United States Food and Drug Administration has emphasized that patients using NSAIDs are also at added risk of a heart attack or stroke.[12] The safety of long-term use of NSAIDs is unknown.[13,14]
- *Opioids*: The safety of opioid analgesics is particularly concerning. Adverse effects of opioid therapy include depression, sexual dysfunction, myocardial infarction, addiction, and risk of death due to overdose.[13,15] The risk of an ADE due to opioid use is alarmingly high and rapidly escalating; among 47 055 drug overdose deaths that occurred in 2014 in the US, 28 647(60.9%) involved an opioid.[4] Since 2000, the rate of death from drug overdoses involving opioids has increased 200%, and currently, nearly 50% of all opioid overdose deaths in the US involve a prescription opioid.[4]

Chiropractic Care: Nonpharmacologic Treatment for Low Back Pain

Many patients who are prescribed analgesic medications have low back pain[16]; among US adults prescribed opioids, 59% reported having back pain.[17] The American Geriatrics Society's updated "Beers Criteria" for potentially inappropriate medication use in older adults encouraged "the use of nonpharmacological approaches when needed to avoid drugs that have a high risk of causing an adverse event."[18] The Institute of Medicine has also recommended increased utilization of nonpharmacologic, integrative approaches, such as chiropractic care for patients with low back pain.[19] Recently published evidence-based clinical guidelines for management of both acute and chronic low back pain recommend nonpharmacologic therapies as first line treatment.[20] Chiropractic care of low back pain is both safe and effective; a recent systematic review and meta-analysis found that for treatment of acute low back pain, spinal manipulation, as performed by chiropractors, provides a clinical benefit equivalent to that of NSAIDs, with no evidence of serious harms.[21] A systematic review of the safety of chiropractic interventions found a low risk of serious adverse events, ranging from 1.56 to 2.68 events per 10 000 000 interventions.[22]

Nonpharmacologic chiropractic care, including spinal manipulation, may lead to reduced use of prescription drugs.[23] Pain relief afforded by chiropractic care may allow patients to use lower or less frequent doses of analgesics, leading to reduced risk of NSAID-induced bleeding, opioid overdoses, and other ADEs. However, evidence to support this hypothesis is sparse and conflicting. A randomized controlled trial of patients with acute low back pain treated with usual care, plus spinal manipulative therapy, vs usual care alone, found no difference between groups in analgesic consumption.[24] More recently, it was reported that the supply of chiropractors, as well as spending on chiropractic care, are inversely correlated with opioid prescriptions among younger Medicare beneficiaries.[25] Thus, increased availability and utilization of chiropractic services could lead to a reduction in prescriptions for analgesics and an associated reduction in risk of an ADE.

The objective of this investigation was to evaluate, among New Hampshire residents with low back pain, the association between utilization of chiropractic services and risk of an ADE. We chose New Hampshire because health claims data were readily available for research, and in 2015, New Hampshire had the second highest age-adjusted rate of drug overdose deaths in the US, a 31% increase from the previous year, and, at 34.3 per 100 000, more than double the national rate of 16.3 per 100 000.[4,26] We expected this study to generate the outcome that, among patients with low back pain, recipients of chiropractic care have a lower likelihood of an ADE as compared to nonrecipients. Such a finding could exert a positive impact on patient care by pointing to a strategy for reducing unnecessary risk for patients with low back pain.

Methods

We hypothesized that, among adult residents of New Hampshire diagnosed with low back pain, recipients of chiropractic services have a lower likelihood of an ADE in outpatient settings as compared to nonrecipients. To test this hypothesis, we employed a retrospective cohort design to analyze health insurance claims data. Our data source was the all payer claims database administered by the Department of Health and Human Services of the state of New Hampshire, which aggregates health claims data submitted by 26 private and public third-party payers, including preferred provider organizations, health maintenance organizations, and indemnity insurance plans. No Medicare or Medicaid claims were included in the database. This project was conducted subject to the terms of a data user agreement between the principal investigator and the state of New Hampshire. The research methods were reviewed and approved by the institutional review board of

the principal investigator's university. All statistical analyses were performed using SAS (SAS Institute, Cary, North Carolina).

The study population was comprised of New Hampshire residents aged 18 to 99 years, enrolled in a health plan in both 2013 and 2014, with at least 2 clinical office visits within 90 days for a primary diagnosis of low back pain. Among participants included in the study population, we identified 2 cohorts of participants. It was our original intent to compare recipients of both primary care and chiropractic services vs recipients of primary care services alone for low back pain. However, the first cohort proved to be too small to power the statistical analysis. This may have reflected an actual pattern of care, or it may have been due to a flaw in the dataset's linkage between unique patients and claims for clinical encounters. In response to this unexpected limitation, we revised our approach to cohort assembly, and simply dichotomized the study population as recipients and nonrecipients of chiropractic services in 2013.

To reduce the potential for selection bias, because the cohorts may have differed in regard to their disposition toward use of prescription medications, we employed weighted propensity scoring to create equivalent cohorts for comparison.[27] We first used multinomial logistic regression to calculate the estimated probability of each participant to be in each cohort, using socio-demographic measures (age, sex, and county of residence). After inversely weighting each participant by their propensity to be in their cohort, we employed logistic regression to compare recipients of chiropractic services to nonrecipients, with regard to likelihood of occurrence of an ADE in an outpatient setting. We controlled for patient demographics and for health status through Charlson comorbidity scoring. The point of accrual (index date) for participants in each cohort was the date of the first office visit in 2013, to a chiropractor or other provider, with a diagnosis of low back pain. For each participant, the follow-up period for measurement of outcomes was the 12-month period commencing with the index date. Thus, for each initial recipient or nonrecipient of chiropractic services, we analyzed claims data for ADEs that occurred within 12 months following the start of their first low back pain episode in 2013.

Identification of ADEs With Claims Data

For the purposes of this study, we defined an ADE as injury resulting from the use of prescription medication, including adverse drug reactions and medication errors made by healthcare providers. Two types of codes may be used to identify an ADE: an International Classification of Diseases (ICD) diagnosis code indicating a condition caused by a drug or an E code indicating the class of the implicated drug. The identification of ADEs through analysis of claims data presents methodological challenges, due to variability in the use and validity of coding for adverse events. Many ADEs go unreported, particularly ADEs of lesser severity in elderly patients, and false positive rates of ADEs tend to be low.[28] Among ICD-9 codes for ADEs, 88% were reported to have a positive predictive value greater than 50%.[29] We cast a wide net for detection of ADEs by using either type of code as evidence of an ADE.

The ICD-9 codes for ADEs include clinical side effects of drugs (symptoms), poisonings (these codes are used infrequently), and adverse effects of medications (adverse drug reactions). We included outpatient (including emergency department) claims with an ICD-9 code for diagnosis of an ADE, including poisoning by drugs, medicinals, and biological substances (960-979); other adverse effect of medicinal substance (995.2-995.29); shock due to anesthesia (995.4); aspirin gastritis (ICD-9 clinical modification code 535.4); drug dermatitis (692.3 and 693.0); drug psychoses (292.1-292.9); and neuropathy due to drugs (357.6). We also included claims with E codes for "drugs, medicinal, and biological substances causing adverse effects in therapeutic use" (E930-E949) and for "accidental poisoning by drugs, medicinal substances, and biologicals" (E850-E858).

Table 1. *Participant Characteristics by Cohort*

Cohort	Recipients of Chiropractic Services	Nonrecipients	*P* Value
	9810 (51)	9343 (49)	
Sex, n (%)			.21
Female	5312 (54)	5143 (55)	
Male	4498 (46)	4200 (45)	
Age category in years, n (%)			.01
18-34	1488 (15)	1171 (13)	
35-64	5956 (61)	5958 (64)	
65-99	2366 (24)	2214 (24)	
Charlson comorbidity score (mean, SD)	0.37 (0.97)	0.53 (1.19)	<.0001

SD, standard deviation.

Results

The included participants numbered 19 150 and were almost evenly divided between recipients and nonrecipients of chiropractic services (Table 1). The cohorts did not differ by sex, but they did differ by age category, with a larger

Table 2. *Adverse Events by Drug Category or Reaction*

	Recipients	Nonrecipients
Drug Category or Reaction	% of 44 Events	% of 94 Events
Other adverse drug event	43.18	23.41
Drug induced dermatitis	15.91	18.08
Drug allergy	11.36	6.38
Drug induced mental disorder	6.82	0
Poisoning-other	6.82	18.09
Poisoning-antilipemics	4.55	0
Poisoning-anticonvulsants	2.27	2.13
Poisoning-antineoplastics/ immunosuppressants	2.27	0
Poisoning-benzodiazepines	2.27	4.26
Poisoning-insulin/antidiabetics	2.27	2.13
Poisoning-opiates	2.27	2.13
Drug withdrawal	0	15.96
Drug induced neuropathy	0	1.06
Poisoning-antidepressants	0	1.06
Poisoning-aromatic analgesics	0	1.06
Poisoning-sedatives/hypnotics	0	1.06
Poisoning-anticoagulants	0	1.06
Poisoning-heroin	0	1.06
Poisoning-opium	0	1.06

proportion of young adults among chiropractic recipients. The cohorts also differed by health status; as measured by Charlson comorbidity score, nonrecipients had significantly inferior health status. We adjusted for these differences in our statistical modeling.

The risk of an ADE was significantly lower among recipients of chiropractic services as compared with nonrecipients. Among 9 810 recipients of chiropractic services, 41 participants (0.4%) experienced 44 ADEs. Among 9 343 on-recipients, 84 participants (0.9%) experienced 94 ADEs. The adjusted likelihood of an ADE occurring in an outpatient setting within 12 months was 51% lower among recipients of chiropractic services as compared to nonrecipients (OR 0.49; P = .0002). The ADEs were nonspecific with regard to drug category in 84% of incidents that occurred among recipients of chiropractic services and in 82% of incidents that occurred among nonrecipients (Table 2). Fifteen nonrecipients of chiropractic services (16% of participants) were diagnosed with drug withdrawal, as compared to 0 recipients of chiropractic services. Two nonrecipients (2% of participants) sustained opiate poisoning, as compared to 1 recipient (also 2%). One nonrecipient sustained aromatic analgesic poisoning, as compared to 0 recipients.

Discussion

With regard to likelihood of an ADE in an outpatient setting, we found impressive differences between recipients of chiropractic services and nonrecipients. However, it is important to note that the study design only allowed evaluation of correlation. It was not possible from the available data to infer whether or not utilization of chiropractic services actually reduced the likelihood of an ADE. An unmeasured confounder may be the underlying cause of the negative correlation between utilization of chiropractic services and occurrence of an ADE.

Despite the use of propensity scoring to equalize cohorts, the reported effect may have resulted from the cohorts being drawn from different populations. Differences in preferences regarding use of pharmaceuticals may have affected comparative risk of an ADE. A recent national survey found that 78% of adults preferred nonpharmacologic care over prescription drugs for treatment of pain, and those who had never seen a chiropractor were more likely to prefer pharmacologic therapies.[30] Use of medications (including drugs associated with increased risk of an ADE) is a modifiable health behavior, and it has been reported that utilization of integrative health services, such as chiropractic care, is associated with improved health behaviors.[31,32] Changes in health behaviors related to clinical encounters may be attributed to the effects of treatments, provider support, or increased patient responsibility for health.[33] Rather than being caused directly by type of clinical encounter, differences in risk for an ADE may result from complex interactions between personal health behaviors and social and environmental determinants of health, as well as clinical care. Further evaluation of health behaviors between recipients and nonrecipients of chiropractic care may help to elucidate differences in risk for an ADE.

Limitations

Certain limitations and threats to validity for this study must be acknowledged. In general, only a limited number of exposure variables were available for inclusion in propensity scoring and regression modeling. As noted in the discussion, patents' self-selective stratification into pharmacologic and nonpharmacologic care pathways may be driven by unknown factors, including the onset, anatomic location, and severity of pain. Most of the diagnosis codes

used to record ADEs were nonspecific with regard to drug category, and, in most cases where the type of drug reaction was specified, it appeared unlikely to be caused by a drug used to treat low back pain. The results contribute little evidence to suggest that utilization of chiropractic services leads to reduced use of analgesics, specifically. Furthermore, although our study population was restricted, the magnitude of the drug overdose problem in New Hampshire suggests that analysis of diagnosis codes specific for adverse events may have failed to capture a significant number of ADEs. Such codes may be less sensitive to actual rates of an ADE than previously reported,[29] and they may not be sufficiently sensitive to deliver externally valid results for specific drug classes, particularly with relatively small claims datasets. Finally, we were limited by the capacity of the dataset to support cohort assembly, as originally planned. Cohorts defined as primary care alone vs both chiropractic and primary care would have provided assurance that the cohorts were more comparable with regard to outpatient access to prescription medications.

These limitations point to the need for analysis of larger and more variable rich datasets that will facilitate use of more rigorous methods and allow establishment of the causal chain with higher resolution. Despite the inherent limitations of observational research with regard to causal inference, the scope of observational research datasets now available confers clear advantages over interventional designs for detection of uncommon adverse events. The results of this study should be interpreted as preliminary data that indicate the need for further observational research on comparative risk of an ADE and identify methodological elements that should be included in such research.

Conclusion

Among New Hampshire adults with office visits for low back pain, the adjusted likelihood of an ADE was 51% lower for recipients of chiropractic services as compared to nonrecipients. The results suggest that utilization of chiropractic care may be associated with reduced risk of ADEs; however, no causal relationship has been established. Future research on comparative risk of ADEs should employ larger databases; lengthier time periods for capturing outcomes; rigorous methods to reduce risk of bias; and more sensitive methods of identifying adverse events to enhance statistical power, sensitivity, and external validity.

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Contributorship Information

Concept development (provided idea for the research): J.M.W.
Design (planned the methods to generate the results): J.M.W., A.W.J.T.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): J.M.W.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): J.M.W.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): J.M.W., A.W.J.T.
Literature search (performed the literature search): J.M.W., J.M.G., L.A.K.
Writing (responsible for writing a substantive part of the manuscript): J.M.W., J.M.G., L.A.K.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): J.M.W., A.W.J.T., J.M.G., L.A.K.

Practical Applications

- The findings make a unique contribution to the evidence regarding associations between chiropractic services and patient safety.
- The cause of the association between use of chiropractic services and reduced risk of adverse drug events is unknown.
- More high-quality research is needed regarding the association between use of chiropractic services and risk of adverse drug events.

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