ORIGINAL RESEARCH

Frequency of nonaspirin NSAID-relevant coexisting medical conditions in the primary-care setting: a retrospective database review

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Background: Coexisting medical conditions and concomitant medications contribute to treatment challenges primary-care professionals (PCPs) face daily. The current study assessed the extent and distribution of nonaspirin NSAID-relevant coexisting medical conditions of interest (CMCOI) in patients visiting PCPs.

Methods: This retrospective database review analyzed data from three large health-care claim databases to identify the frequency of nonaspirin NSAID-relevant CMCOI among adults aged ≥18 years with a PCP visit in 2013. Claim databases employed were the Truven Health MarketScan® Commercial Claims and Encounters database, representative of the privately insured (PI) population; Truven Health MarketScan Multi-State Medicaid, representative of the Medicaid population (Medicaid); and Truven MarketScan Medicare Supplemental, representative of the Medicare population with employer-based supplemental Medicare insurance (Medicare-Supplement). Nonaspirin NSAID-relevant CMCOI, asthma, cardiovascular risk factors, gastrointestinal bleeding risk factors, and renal insufficiency were chosen based on US NSAID over-the-counter Drug Facts label warnings. Frequency of CMCOI was determined for those without and with a musculoskeletal diagnosis.

Results: In each database, ≥19% (19.0% PI, 29.9% Medicaid, 33.6% Medicare-Supplement) had a musculoskeletal diagnosis. A greater proportion of individuals with a musculoskeletal diagnosis had one or more CMCOI compared with those without a musculoskeletal diagnosis (61.3% vs 50.4% PI, 78.1% vs 66.8% Medicaid, 87.1% vs 82.3% Medicare-Supplement). The frequency of one or more CMCOI increased with age in each database. Across databases among CMCOI, cardiovascular risk factors were most common, followed by gastrointestinal bleeding risk factors, and proportions were higher among those with a musculoskeletal diagnosis.

Conclusion: These data confirm the high frequency of nonaspirin NSAID-relevant CMCOI among patients presenting to PCPs for musculoskeletal diagnosis, as well as among older patients. These analyses reinforce the critical role health-care professionals can play in identifying patients with nonaspirin NSAID-relevant CMCOI, providing those patients with ongoing guidance on appropriate choice and use of over-the-counter analgesics, and educating patients about the impact aging, health status, concomitant conditions, and medicines have on selection of all medicines, including analgesics.

Keywords: coexisting medical conditions, NSAIDs, musculoskeletal disease, health claim databases, OTC analgesics

Plain-language summary

Prescription or over-the-counter (OTC) pain relievers, such as NSAIDs, are often prescribed or recommended during patient visits. Using data from three large US health-care insurance-claim databases, we calculated the percentage of adults having a chronic medical condition

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(ie, asthma, heart conditions, gastrointestinal bleeding risk, or kidney disease) that could put them at risk of a side effect when taking an OTC NSAID. The data showed that at least 50% of patients had one or more of these underlying medical conditions and heart conditions were generally the most common. The percentage of patients with these underlying conditions increased with age and was higher among those with a musculoskeletal diagnosis. Women were as likely as men to have these conditions. When making recommendations, health-care professionals can reduce their patients' risk of experiencing reactions to drugs by reminding patients that instructions on OTC medicines (ie, Drug Facts label) are not suggestions, but rather are specific instructions to follow closely. As patients age and their medical conditions change, different warnings on Drug Facts labels may apply to them. They can contact their health-care professional with questions or visit the Get Relief Responsibly (www.getreliefresponsibly.com) or Alliance for Rational Use of NSAIDS (www.nsaidalliance.com) websites to find information and tools to choose, use, store, and dispose of nonprescription medicines safely.

Introduction

In the US, people visit their primary health-care professional (HCP) on average three times annually. While the most common reason for an HCP visit is preventive (19.1% of visits), the second-most common reason is musculoskeletal and connective tissue diseases (10.1%).[1] These patients are among those most likely to be prescribed or recommended to use analgesics.

In 2015, the National Ambulatory Medical Care Survey found that patients had one or more chronic conditions at 61.0% of office visits: 24.6% of the visits related to one chronic condition, 14.6% to two, and 21.8% to more than three.[1] The National Health Interview Survey, which provides patient-reported health information, identified arthritis (21.6%), chronic joint symptoms (28.3%), diabetes (8.8%), gastrointestinal ulcers (5.7%), and kidney disease (1.9%) as among the most common chronic diseases with which Americans report being diagnosed.[2] Considering these data, it is not surprising that patients in the US discussed medication(s) with their HCP at 76% of all office visits. Analgesics, including narcotics, non-narcotics, and NSAIDs, were the most commonly discussed medications, accounting for 11.0% of all drug mentions.[1]

Research, evidence-based guidelines, and recommendations from professional societies and regulatory bodies identify that when recommending a treatment plan, which may include either prescription or over-the-counter (OTC) analgesics, HCPs should consider patient risks, ie, the patient's age, concomitant medications, and coexisting medical conditions, such as asthma, cardiovascular disorders, gastrointestinal bleeding, renal insufficiency, and liver disease.[3–6] Drug Facts labels for OTC NSAIDs contain clear

warnings describing who should not use the medication and who should seek doctor or pharmacist advice before using the product. Notably, in April 2009 the FDA published updated organ-specific warnings, including stomach-bleeding warnings, for OTC NSAID labels in the Federal Register to be implemented within 12 months.[7] Again, in 2016 OTC NSAID new-drug-application holders received FDA correspondence directing them to update nonaspirin OTC NSAID labels to include warnings that alerted patients with cardiovascular conditions to speak with their doctor before using. These label changes were approved for implementation in 2017. When recommending an analgesic, HCPs can take the opportunity to review an OTC Drug Facts label with patients and explain why specific medicines and not other medicines are recommended based on the patient's medical history and current medications. HCPs should educate patients that medicines are prescribed or recommended based on the patient's current health status and that previous prescriptions or recommendations may no longer be appropriate, due to changes in the patient's age, medications, or medical conditions.

Information from health-care claim databases that are representative of the majority of Americans can provide insights into the nature of the population receiving NSAIDS and thereby provide important reminders to clinicians to consider comorbidities when prescribing. Therefore, three health-claim databases were analyzed to perform a descriptive analysis of the extent and distribution of nonaspirin NSAID-relevant coexisting medical conditions in patients with and without a musculoskeletal disorder who had visited a primary-care professional (PCP).

Methods

A retrospective database review was performed.

Data sources

Three large health-care claim databases were the sources of patient-level information: the Truven Health MarketScan® Commercial Claims and Encounters database, representative of the PI population; Truven Health MarketScan Multi-State Medicaid (Medicaid), representative of the Medicaid population; and Truven MarketScan Medicare Supplemental (Medicare-Supplement), representative of the Medicare population with employer-based supplemental Medicare insurance.

All three databases capture diagnoses and procedures submitted for office visits and hospitalizations and prescription-drug dispensing in retail and mail-order pharmacies. Patient-level information in all MarketScan database records is deidentified and fully compliant with US patient-confidentiality requirements, including the Health Insurance

Portability and Accountability Act (HIPAA) of 1996. Further, Truven databases are certified to satisfy conditions described in sections 164.514 (a)–(b)1ii of the HIPAA privacy rule regarding determination and documentation of statistically deidentified data. A description of the data available in each of the three databases can be found in the Supplementary material.

Selection and definition of relevant coexisting medical conditions

Nonaspirin NSAID-relevant coexisting medical conditions of interest (CMCOI) were selected based on review of US OTC NSAID labels and consideration of which NSAID-relevant coexisting medical condition(s) are most frequently encountered in typical PCP populations based on other literature.[1,2,8] Based on these considerations, asthma, cardiovascular risk, gastrointestinal bleeding risk, and renal impairment (including renal failure, hereafter referred to as renal impairment) were chosen for analysis. Hepatic cirrhosis was not chosen as a CMCOI, due to its lower frequency in the primary-care setting compared to the selected CMCOI.[8] Throughout this report, CMCOI relate to the four specific conditions evaluated, and do not indicate the absence or presence of other medical conditions.

Medical concepts associated with the CMCOI were defined by the authors. Specifically, one or more standard Systematized Nomenclature of Medicine (SNOMED) concepts (Observational Medical Outcomes Partnership Vocabulary version 5.0, April 3, 2015) were used for each of the four CMCOI, and all terms from the lists were reviewed to exclude terms not consistent with the concept of interest. For example, for gastrointestinal bleeding risk factors, all descendant terms (using the SNOMED hierarchy) of the SNOMED concepts for gastrointestinal hemorrhage and gastrointestinal ulcer were used. In addition, gastrointestinal bleeding risk factors also included all drugs linked to the RxNorm concepts for anticoagulants and corticosteroids (Table 1). All diagnosis and drug-code lists used in this study are available from the authors.

The New England Institutional Review Board (NEIRB, 12–284) determined that studies conducted in these databases did not meet the definition of human-subject research. Therefore, board review and approval of the protocol was not required.

Sample selection and study-population characteristics

Patients aged ≥18 years in 2013 with a visit to a PCP in the same year were included in the study. Only patients

Table 1 Medical concept(s) used to identify patients with NSAID-relevant coexisting medical conditions of interest

Medical condition	Medical concepts
Asthma	Asthma
Cardiovascular risks	Acute myocardial infarction, cerebrovascular disease, disorder of coronary artery, heart failure, hypertensive disorder
Gastrointestinal bleeding risks	Gastrointestinal hemorrhage, gastrointestinal ulcer, anticoagulant, alcohol dependence
Renal impairment	Renal impairment

with ≥1 year of enrollment prior to their first PCP visit in 2013 were included, so that medical history was available to review. For this analysis, PCP specialties were defined as family practice, geriatric medicine, or internal medicine.

Patients' electronic claim records were examined to identify the presence or absence of a musculoskeletal diagnosis and the index date. To identify the musculoskeletal diagnosis population within each database, the first visit with a musculoskeletal complaint in the primary-care outpatient setting in 2013 was considered the index date. Among those without a musculoskeletal complaint within the year, the first visit in the primary-care outpatient setting was the index date. Once each study population had been identified, each patient's electronic claim records were examined for evidence of a CMCOI in the 365 days prior to and including the index date. Patients were then grouped together based on their age, sex, and number and type of CMCOI or lack thereof.

Statistical analyses

All patient characteristics are described using means and SD for continuous variables and frequencies and percentages for categorical variables.

Results

Individuals within the PI database ranged between ages of 18 and 74 years; those between 65 and 74 years likely represent individuals who maintain private insurance while they are enrolled in Medicare. The Medicaid database includes individuals aged from 18 to >85 years. The Medicare-Supplement database includes only individuals with both a Medicare-Supplemental health-care plan and Medicare benefits. Table 2 identifies characteristics of individuals enrolled in each database. Although a few individuals aged 18–64 years were identified in the Medicare-Supplement database, only individuals aged >65 years were included in all subsequent analyses.

Overall patient characteristics by database

Mean ages among patients in the overall population and in the musculoskeletal diagnosis population in the PI and Medicaid populations were similar. In both the PI and Medicaid population databases, the percentage of individuals with a musculoskeletal diagnosis increased with increasing age up to age 65 years. In the Medicaid population, the percentage of individuals with a musculoskeletal diagnosis decreased with age >65 years (Table 2).

Prevalence of one or more CMCOI by database

Half (50.4%) the patients in the PI database had one or more CMCOI. In both the Medicaid (66.8%) and Medicare-Supplement (82.3%) populations, a greater proportion of patients had one or more CMCOI (Table 2). The Medicare-Supplement population had the highest proportion of patients with one (45.9%), two (28.8%), three (7.1%), or four (0.6%) CMCOI. In comparison, the PI database had the lowest proportion of patients with one (37.6%), two (11.3%), three

(1.5%), or four (0.1%) CMCOI. While 61.3% of patients with a musculoskeletal diagnosis in the PI population had been diagnosed with one or more CMCOI, 78.1% of patients in the Medicaid and 87.1% in the Medicare-Supplement populations with a musculoskeletal diagnosis had been diagnosed with one or more of these conditions (Table 2, Figure 1).

The proportion of patients with a musculoskeletal diagnosis and one or more CMCOI increased with increasing age within each database. Furthermore, the percentage of individuals within each age-group with one or more CMCOI was higher among those with a musculoskeletal diagnosis compared to the overall population (Figure 2).

Prevalence of specific CMCOI by database

Cardiovascular risk factors were generally the most commonly identified CMCOI across the three databases (Figure 3). Cardiovascular risk factors were lower among females than males within each database (PI, 26.2% and 34.2%, respectively; Medicaid, 50.0% and 55.5%, respectively; Medicare-Supplement, 70.3% and 74.1%, respectively).

Table 2 Demographic characteristics of individuals in the Privately Insured, Medicaid, and Medicare-Supplement databases by total population within database and by musculoskeletal diagnosis

Patients with PCP visits in 2013[a]	Total population[b]			Musculoskeletal diagnosis[c]		
	Privately Insured[d]	Medicaid[e]	Medicare-Supplement[f]	Privately Insured[d]	Medicaid[e]	Medicare-Supplement[f]
n	2,967,442	584,787	377,079	565,071	174,841	126,595
% Total population	100.0	100.0	100.0	100.0	100.0	100.0
Age, mean (SD), years	45.3 (13.0)	49.4 (20.0)	76.3 (7.7)	48.2 (12.3)	53.8 (18.6)	76.8 (7.8)
% >60 years old	14.9	31.6	99.6	19.7	37.1	99.6
Age group, years, %						
18–44	43.1	42.8	0.0	32.8	31.5	0.0
45–64	55.3	33.3	1.2	65.5	40.8	1.4
65–84	1.6	18.6	82.0	1.7	21.2	80.2
85+	0.0	5.3	16.7	0.0	6.5	18.4
Sex, %						
Female	57.3	68.7	56.0	58.3	71.0	62.0
Coexisting medical condition(s), %						
One or more	50.4	66.8	82.3	61.3	78.1	87.1
Asthma	5.8	12.5	5.9	7.3	16.1	7.6
Cardiovascular	29.7	51.7	72.0	34.3	61.8	74.6
Gastrointestinal	28.0	26.7	37.4	42.1	38.8	50.4
Renal	1.4	9.3	11.7	2.0	10.8	13.6

Notes: Values are n (percentage) unless otherwise indicated. Comorbidities were measured in the 365 days prior to and including the index date. Demographics were measured as of the index date. [a]A patient could have more than one comorbidity. The code occurred up to 365 days prior to the index date through and including the index date. [b]Total population: individuals who had a visit with the PCP in 2013. [c]Musculoskeletal diagnosis: individuals whose medical claim record reflected a musculoskeletal diagnosis code on the index date and at least one time in the preceding 365 days. [d]Privately Insured: Truven Health MarketScan® Commercial Claims and Encounters database. [e]Medicaid: Truven Health MarketScan Multi-State Medicaid. [f]Medicare Supplement: Truven MarketScan Medicare-Supplemental.
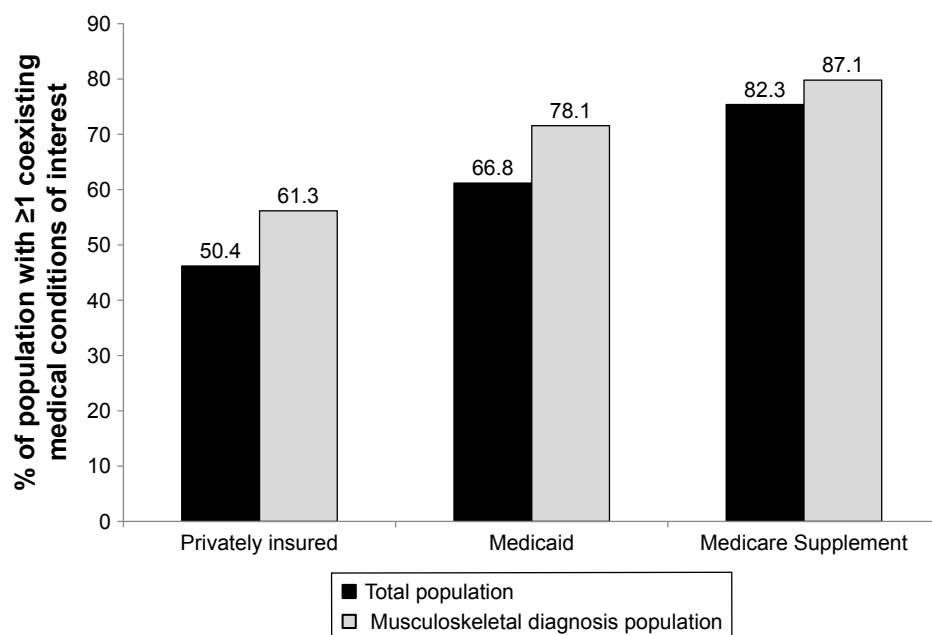**Abbreviation:** PCP, primary-care professional.

Figure 1 Percentage of total population and MSD population in each database with one or more coexisting medical conditions of interest.
Notes: Privately Insured: Truven Health MarketScan® Commercial Claims and Encounters database. Medicaid: Truven Health MarketScan Multi-State Medicaid. Medicare Supplement: Truven MarketScan Medicare-Supplemental.
Abbreviation: MSD, musculoskeletal diagnosis.

Similar percentages of individuals in the PI (28.0%) and Medicaid (26.7%) databases had gastrointestinal bleeding risk factors, and more individuals in the Medicare-Supplement database (37.4%) had such risk factors (Figure 3). Similar percentages of women and men in each database were diagnosed with a gastrointestinal bleeding risk factor. Asthma was diagnosed twice as frequently in the Medicaid (12.5%) as the PI (5.8%) and Medicare-Supplement (5.9%) databases (Figure 3).
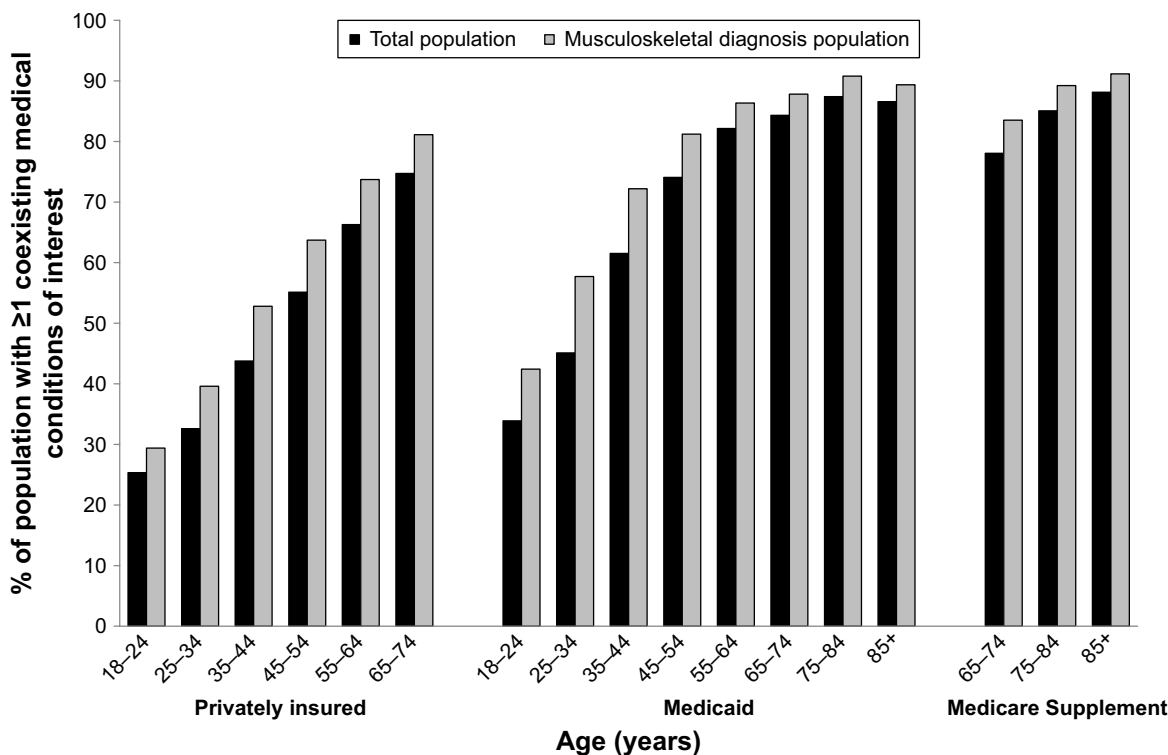

Figure 2 Percentage of population with one or more coexisting medical condition of interest by age-group, total, and MSD populations.
Notes: Privately Insured: Truven Health MarketScan® Commercial Claims and Encounters database. Medicaid: Truven Health MarketScan Multi-State Medicaid. Medicare Supplement: Truven MarketScan Medicare-Supplemental.
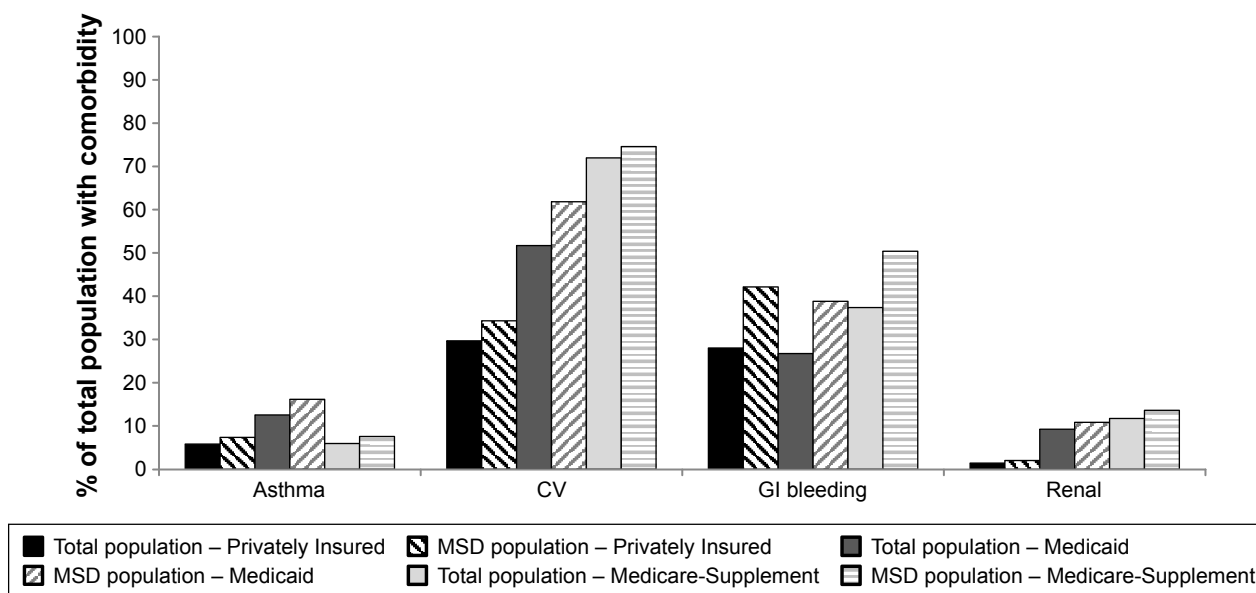**Abbreviation:** MSD, musculoskeletal diagnosis.

Figure 3 Percentage of total population and MSD population in each database with specific coexisting medical condition of interest.
Notes: Privately Insured: Truven Health MarketScan® Commercial Claims and Encounters database. Medicaid: Truven Health MarketScan Multi-State Medicaid. Medicare Supplement: Truven MarketScan Medicare-Supplemental.
Abbreviations: CV, cardiovascular; GI, gastrointestinal; MSD, musculoskeletal diagnosis.

Overall, the prevalence of renal disease was low in all three databases relative to cardiovascular and gastrointestinal bleeding risk factors (Figure 2). Similar percentages of women and men were diagnosed with renal disease within each database. In each database, a higher percentage of individuals with a musculoskeletal diagnosis had a CMCOI compared to the total study population (Figure 3).

Discussion

Evaluation of individuals in the PI, Medicaid, and Medicare-Supplement claim databases showed that ≥50% with a PCP visit had one or more of the selected NSAID-relevant CMCOI (ie, asthma, cardiovascular risk factors, gastrointestinal bleeding risk factors, or renal impairment). We found that this percentage increased with age and that the percentage was universally higher among individuals who had a musculoskeletal diagnosis. The analysis also showed that women were as likely as men to have a nonaspirin, NSAID-relevant CMCOI. These health-related conditions need to be considered when consumers choose or HCPs recommend an OTC analgesic to adults of all ages.

Estimates of relative risk of NSAID-related asthma, cardiovascular risk, gastrointestinal bleeding, and renal impairment events varied depending on dose, duration, and source of exposure information (eg, survey of frequency of use, electronic medical records of dispensing), study design (eg, observational, randomized clinical), indication, and comparator (eg, no use, placebo, aspirin/acetaminophen). Following are some examples of cited relative risks. Data from meta-analyses and systematic reviews identified that NSAID-related increases in relative risks for cardiovascular disease ranged from 1.22 to 2.26[9–12] and for gastrointestinal bleeding ranged from 1.09 to 18.45 compared to placebo or no use or remote use of NSAIDs.[11,13] Considering these relative risks along with the frequency of patient visits to an HCP for musculoskeletal and connective tissue diseases, as well as the frequency of one or more CMCOI among individuals in each database evaluated in this study, the potential magnitude of patients exposed to these NSAID-related risks is substantial.

Given the high proportion of patients diagnosed with one or more nonaspirin NSAID-relevant CMCOI and the high frequency of discussions about medicines that occur during a visit with an HCP,[1] it is vital that patients inform their HCPs and that HCPs inquire about any changes in health status, as well as all medicines, OTC and prescription drugs, and supplements patients are taking. Research has addressed patient beliefs, perceptions, and behaviors related to OTC and prescription medicines.[14–16] Counseling and education provided by community pharmacists improved patients' knowledge about nonaspirin NSAID-related safety issues.[17] These favorable outcomes support the notion that primary HCPs can effectively educate patients about information available on OTC Drug Facts labels (eg, dosing, risks, warnings) and how that information supports why a specific analgesic is recommended, while a different analgesic is not. Moreover, HCPs should educate patients to understand that they should not assume that choice or dose of analgesics previously recommended to them is still acceptable. This is

especially important, since individuals may not realize that an OTC pain reliever they have used in the past may no longer be the most appropriate choice for them, based on their changing age, coexisting medical conditions, and current medications. Of specific concern are patients with asthma and cardiovascular, gastrointestinal, and renal disorders, and older adults with several chronic conditions, since they are more likely than those without these disorders to experience adverse events while taking nonaspirin NSAIDs.[6,18–21]

Such patient-management challenges as these are addressed by guidelines published by professional societies and regulatory agencies, both of which recommend that HCPs prescribe or recommend the lowest dose of NSAID for the shortest duration to reduce the risk of complications.[3,6,18,19,22–31] Moreover, information available on the FDA website that is directed to HCPs reminds HCPs of the increased risks of serious cardiovascular events (10%–50%) associated with NSAID use, regardless of an individual's history of or risk factors for cardiovascular disease.[32]

While HCPs are able to prescribe higher dosages of NSAIDs for defined durations while patients are under their care, HCPs should instruct their patients always to read OTC-product Drug Facts labels and follow dosage directions for both single dose and maximum daily dose when self-medicating with OTC NSAIDs. Health authorities and companies are continuously monitoring a medicine's safety profile and updating Drug Facts labels and patient-information leaflets accordingly. For example, updated warnings that strengthen and expand existing warnings relating to the risk of heart attack and stroke associated with NSAIDs were implemented in 2017 for all nonaspirin OTC NSAIDs. These include the addition of a heart attack and stroke warning, a warning to ask a doctor before use if you have had a stroke, and an updated direction to stop use and ask a doctor if you have symptoms of heart problems or stroke. HCPs should educate their patients to understand that OTC Drug Facts labels are not guidelines that are open to personal judgment, but rather specific and important instructions about dosing, duration of use, risks, and warnings meant to direct their safe and effective use of the product. Furthermore, HCPs should alert patients to Drug Facts label information, which instructs when they should contact their HCP (eg, before using if they have specific disorders, including ulcers, bleeding problems, high blood pressure, heart or kidney disease, or are 60 years of age or older)[33] and reinforce to their patients the importance of consulting with an HCP whenever they have additional questions. Communication and engagement with older patients with multiple chronic conditions or with their caregivers is vital while assessing treatment options,

considering the increased likelihood of complexity related to balancing risks associated with treatment of chronic conditions with patients' preferences and priorities later in life.[18]

The current study confirms data collected by the National Ambulatory Medical Care Survey: the percentage of individuals reporting a diagnosis of any of the coexisting medical conditions increased with age and the percentage of individuals reporting musculoskeletal complaints increased with age until 65 years and then effectively stabilized. Furthermore, the current study defines the high frequency of nonaspirin NSAID-relevant CMCOI among patients with a musculoskeletal diagnosis as >60%.

In recognition of the fact that data used in the current analyses were extracted from health-care claim databases, some factors should be considered. The pool of patients in each database population was identified by a health-care claim for a visit to their primary HCP within the specified time frame. For the overall population, these visits may have been well-patient visits or visits due to a symptom including a musculoskeletal complaint or other reasons. Chronicity (ie, duration) was not determined or categorized for further analysis. Moreover, it was not possible to distinguish between acute and chronic status for any of the diagnoses (eg, musculoskeletal or cardiovascular disease). Records of filled prescriptions for medications to individuals were identifiable within each database; however, actual use of any medication by an individual could not be confirmed in the databases. It is important to note that the Medicare-Supplement population, which is covered by employer-sponsored private insurance, is likely to be healthier than the nonworking Medicare population.

Another potential limitation of this study was that patients with a diagnosis of a CMCOI and with frequent HCP follow-up visits may be more likely to be diagnosed with a musculoskeletal diagnosis during follow-up visits, simply because they have more opportunities to report musculoskeletal complaints. These individuals may naturally have more conditions diagnosed because they are already seeing an HCP for another condition. Nonetheless, the focus of the current study was to capture the clinical setting of an outpatient general practice (ie, family, internal medicine, or geriatric medicine practice) and specific disease or event risks the HCP might identify in a patient with or without a musculoskeletal diagnosis. It is important to recognize that within this setting, diagnoses and treatment recommendations could be based on any information available at the time, including the patient's medical record. Because we were interested in capturing risk information accessible to clinicians, our diagnoses were based on what appeared in the data, ie, the patient's medical

record. The diagnosis codes for the selected coexisting conditions of interest and musculoskeletal disorders were based on a disease vocabulary that is created and maintained with clinical input through the Unified Medical Language System. Moreover, musculoskeletal diagnoses were required to be made in an outpatient general practice setting.

A protocol with defined risks and systematic methods for analysis was specified before the health-care claim databases were explored. That analysis plan included the decision not to conduct statistical analyses, since statistical analyses of such large databases could identify small mathematical differences that would qualify as statistically significant without necessarily being clinically relevant. It should be noted that the use of health-care claim databases served as a strength of the study. Each health-care claim database was representative of its respective population and provided a cross-sectional view of the US primary HCP population. Interestingly, findings were fairly consistent across databases and so likely represent primary HCP populations on a national basis.

Conclusion

These data show the prevalence of individuals who have CMCOI and the elevated prevalence of coexisting medical conditions among those presenting with a musculoskeletal disorder, as well as among older patients. The analyses reinforce the critical role HCPs can play in identifying patients with nonaspirin NSAID-relevant CMCOI, providing those patients with ongoing guidance on appropriate choice and use of OTC analgesics, and educating patients about the impact that aging, health status, concomitant conditions, and medicines has on selection of all medicines, including analgesics. Non-NSAID OTC analgesics and nonpharmacological treatment modalities may provide important alternatives for such patients.

Abbreviations

CMCOI, coexisting medical conditions of interest; FDA, US Food and Drug Administration; HCP, health-care professional; HIPAA, Health Insurance Portability and Accountability Act; IRB, institutional review board; MSD, musculoskeletal diagnosis; NDA, new drug application; NEIRB, New England Institutional Review Board; OTC, over the counter; PCP, primary-care professional; PI, Privately Insured; SNOMED, Systematized Nomenclature of Medicine.

Data sharing statement

All diagnosis and drug-code lists used in this study are available from the authors on reasonable request.

Author contributions

LB, AEM, CB, and RW were responsible for the protocol/study design, data review and analysis, critical review and revision of manuscript, final approval of the version to be published, agreement to be accountable for all aspects of the work, and questions being appropriately investigated and resolved; KEB was responsibile for drafting the manuscript, data review and analysis, critical review and revision of the manuscript, final approval of the version to be published, agreement to be accountable for all aspects of the work and questions being appropriately investigated and resolved.

Disclosure

LB and AEM are employees of Johnson & Johnson Consumer Inc, McNeil Consumer Healthcare Division. RW and CB are employees of Janssen Research and Development. KEB is a consultant to Johnson & Johnson Consumer Inc, McNeil Consumer Healthcare Division. The authors report no other conflicts of interest in this work.

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Supplementary material

The Truven Health MarketScan® Commercial Claims and Encounters database (privately insured; [PI]) database is representative of a PI population of >121 million Americans from ~350 companies/employers in a wide range of industries and occupations in the US. The Truven Health MarketScan Multi-State Medicaid (Medicaid) database contains data on >17 million Medicaid enrollees from 12 contributing states. This database contains a blinded subset of Medicaid data derived from the pooled health-care experience of ~6 million Medicaid enrollees that is made available to private companies. This database represents ~12 million Medicaid beneficiaries each year. The Truven MarketScan Medicare Supplement (Medicare-Supplement) database is representative of Medicare-eligible active and retired employees and their Medicare-eligible dependents who are enrolled in employer-sponsored supplemental plans (predominantly fee-for-service plans). Medicare-Supplement represents >9 million PI Americans and a wide range of industries and occupations in the US. Only plans where both the Medicare-paid amounts and the employer-paid amounts were available and evident on the claims were selected for this database.

Each database includes inpatient and outpatient services, pharmacy claims, and health-plan enrollment data for all beneficiaries for services provided. Medical claim-capture information on inpatient and outpatient care includes date, type, and place of service, provider type, and payment information. ICD9-CM diagnosis codes, ICD9-CM procedure codes, and Current Procedural Terminology codes are provided for each medical claim. Pharmacy claim files capture the National Drug Code (NDC), dispensing date, quantity of drug, number of days supplied, and payment information.

Enrollment/eligibility records contain enrollment information and demographics (ie, year of birth, sex). For the Medicare-Supplement database, only individuals with both an employer-sponsored plan and Medicare benefits are included, indicating a high-cost health-care benefits plan and higher socioeconomic status. To allow for ease of use, data from these sources were converted to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM), version 5 (OMOP CDM) (Observational Health Sciences and Informatics Example ETLs) before any analyses were performed. The conversion of the databases to the OMOP CDM included the mapping of ICD-9-CM and NDC codes to Systematized Nomenclature of Medicine (SNOMED) and RxNorm standard concepts, respectively. To construct diagnosis definitions in the databases, one or more standard SNOMED concepts (OMOP Vocabulary version 5.0, April 3, 2015) was used for each of the four conditions/risk groups of interest, and all terms from the lists were reviewed to exclude terms that were not consistent with the concept of interest. For example, for gastrointestinal bleeding risk, all descendant terms (using the SNOMED hierarchy) of the SNOMED concepts for gastrointestinal hemorrhage and gastrointestinal ulcer were used. In addition, gastrointestinal bleeding risk also includes all drugs linked to the RxNorm concepts for anticoagulants and corticosteroids. For cardiovascular risk, all descendant terms of the SNOMED concepts for cerebrovascular disease, heart failure, disorder of coronary artery, acute myocardial infarction, and hypertensive disorder were used.