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Characterization of individuals with osteoarthritis in the United States and their use of prescription and over-the-counter supplements

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ABSTRACT

Purpose: Osteoarthritis (OA) is a frequently occurring, chronic condition; however, few studies describe the clinical characteristics of individuals with OA and the treatments they use to manage their symptoms. We conducted a study to characterize the OA population in the US and describe the nonsurgical management used by this population based on consumer research data collected through an online survey.

Methods: Data from the 2017 US National Health and Wellness Survey (NHWS) for adults aged ≥35 years were used to evaluate the relationship between OA and certain study participant characteristics and to identify the most commonly used treatment options. NHWS data were collected through a survey of individuals drawn from the internet panel maintained by Lightspeed Research (Bridgewater, New Jersey) and its panel partners. Weighted estimates were generated using data from the 2016 Current Population Survey (Annual Demographics File) of the US Census Bureau. Comparisons between the general and OA populations were made based on body mass index (BMI), exercise frequency, and comorbid diagnoses of hypertension or diabetes. Among the OA population, the use of dietary supplements, prescription or over-the-counter (OTC) treatments with chondroitin with or without glucosamine (Ch ± Gl), prescription treatment by time since OA diagnosis, and utilization of a physical therapist were also recorded.

Results: The prevalence of OA in the overall population was 17.6 % and was higher for individuals with a BMI ≥ 25 (21.9 %), patients diagnosed with hypertension or diabetes (36.2 %), and those who did not exercise regularly (19.0 %). Adults without OA were more likely to exercise regularly (12 days per month or more) than adults diagnosed with OA. Ch ± Gl (6.0 %) was the most commonly used OTC dietary supplement in the OA population, followed by omega-3 fatty acids (2.8 %), vitamin D (1.9 %), calcium (1.1 %), and multivitamins (0.7 %). Individuals using Ch ± Gl were more likely to use OTC only products (75.4 % vs 37.3 %) or prescription medications, namely non-steroidal anti-inflammatory drugs (NSAIDs) and/or opioids, and OTC products (24.6 % vs 13.0 %) compared with individuals not using Ch ± Gl, while individuals not using Ch ± Gl were more likely to be untreated (30.3 % vs 0) or to use prescription medications only (19.4 % vs 0). Nearly 32 % of individuals with OA reported using prescription treatments, and the likelihood of using a prescription treatment increased with number of years since OA diagnosis (<3 years: 27.5 %; ≥21 years: 32.5 %). The pharmaceutical products used by this population primarily consisted of nonsteroidal anti-inflammatory drugs, acetaminophen and opioids. Approximately 13 % of patients with OA had visited a physical therapist in the past 6 months.

Conclusions: The prevalence of OA was higher in those with a high BMI, and comorbid diabetes or hypertension. Individuals with OA using Ch ± Gl primarily reported use of OTC products only or used them in combination with prescription products. The likelihood of using prescription products increased with the length of OA history. These data provide valuable new information about demographics, clinical characteristics, and commonly used prescription and OTC treatments and dietary supplements in the OA population.

1. Introduction

Osteoarthritis (OA) is a very prevalent, chronic condition associated with symptoms such as joint pain and stiffness that can impede functioning and negatively affect quality of life [1–4]. The prevalence of arthritis was estimated to affect 54.4 million (21.0 %) of US adults in 2013–2015, with OA as the most common form [5]. More recent estimates from 2015 suggest that the prevalence of arthritis has been substantially underestimated and affects nearly one-third of US adults between the ages of 18 and 64 years, or a total of 61.1 million adults [6]. Risk factors for developing OA include obesity, metabolic disease, sex and the female gender, genetics, nutrition, smoking, high and low bone density and muscle mass and function; however, the most notable factor is age, as age-related changes in joint tissue lead to the onset of OA [2,7, 8].

Treatment guidelines in the US recommend use of oral or topical analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) for the nonsurgical management of OA, as well as nonpharmacological interventions such as exercise and dietary weight management [9,10]. Although they are not included in current treatment guidelines, several natural products and dietary supplements have been shown to produce promising effect sizes but these require further confirmation in larger clinical trials [11]. Recently published systematic reviews suggest that some herbal supplements including curcumin from *Curcuma longa*, *Boswellia serrata* extract and pycnogenol appear to have large effects on symptoms and function but there is very limited evidence to support their use clinically and more well-designed and robust trials are needed for these as potential supplements [11–13]. Although widely used, there is conflicting evidence regarding the benefit of the use of vitamin D, glucosamine, and chondroitin due to small effect sizes [11,14,15]. Few studies have assessed the use of these natural products and dietary supplements for the management of OA, or described the demographic and clinical characteristics of individuals with OA as well as their physical activity levels [16–18].

We hypothesized that subjects with musculoskeletal pain and OA, would be using both recommended and not recommended products for the treatment of pain. In addition, we hypothesized that individuals using supplements will differ in demographics from those not taking supplements. Therefore, we conducted a cross-sectional study to characterize the OA population in the United States and to describe the prescription and over-the-counter (OTC) treatments used by this population based on consumer research data collected through an online survey.

2. Methods

Data from the 2017 US National Health and Wellness Survey (NHWS) for adults ≥35 years of age were used to evaluate the relation between OA and a number of patient clinical characteristics and to identify the most frequently used treatment options. NHWS data were collected through a survey of individuals randomly drawn from the internet panel maintained by Lightspeed Research (Bridgewater, New Jersey) and its panel partners in 2017 for the study period of April 2017 through July 2017. The survey sample of adults was stratified according to gender, age, and race/ethnicity, and results were projected to reflect the total population using known population incidences for key subgroups. Weighted population estimates were created using the following weighting variables: gender, age, race/ethnicity, and education. The

population sizes for different gender, age, race/ethnicity, and education categories were drawn from the 2016 Current Population Survey (Annual Demographics File) of the US Census Bureau[1] .

Survey responses were analyzed using descriptive analyses and stratified by age group (35–44 years; 45–64 years; ≥65 years) and gender in order to discern key differences across these subgroups. The study outcomes included estimated prevalence of OA among the overall population and select subgroups based on the following criteria: normal body mass index (BMI) (≥19 and <25) versus high BMI (≥25), diagnoses of hypertension or diabetes, and level of physical activity (exercise ≥12 days per month vs <12 days per month).

Analyses were also conducted to descriptively compare individuals with and without OA with respect to BMI, physical activity level, and proportion who saw a physical therapist. For these analyses, regular exercise was defined as ≥12 days/month versus <12 days/month. Finally, to characterize treatment patterns in the OA population, we evaluated the utilization of prescription and OTC treatments, including dietary supplements, as reported by the surveyed OA population. Treatment patterns by time since diagnosis were also analyzed to provide insight into the treatment journey of OA patients.

3. Results

There was a total sample of 75,004 survey respondents representing a weighted base population of 245.7 million individuals. Of the total survey population, 62,107 respondents reported not experiencing arthritis (representing a weighted population of 200.7 million) and 8,147 respondents reported that they had been diagnosed with OA (weighted population of 43.3 million).

Based on the responses to the survey, the prevalence of OA was calculated to be 17.6 % in the general population. OA prevalence was higher in those with diabetes or hypertension, with a higher BMI (≥25), and among those who did not exercise regularly (Fig. 1).

3.1. Comparisons between OA and Non-OA populations

Compared with the non-OA population, there was a higher proportion of elevated BMI in the overall OA population and in men or women with OA (Fig. 2). Adults without OA were also more likely to exercise regularly than adults diagnosed with OA (Fig. 3). The mean number of days of exercise per month was higher in the general non-OA population (8.3 days) compared with the OA population (6.3 days overall; men: 6.7 days; women: 6.1 days). Among those diagnosed with OA, men aged ≥65 years reported exercising most frequently. There was a trend of increasing exercise frequency with increasing age, particularly between the age groups of 45–64 and ≥65 for men (25 % and 28 %, respectively) and between the age groups of 45–64 and ≥65 for women (22 % and 25 %, respectively). Overall, individuals with OA were also more likely to have visited a physical therapist in the past 6 months (12.6 %) compared with the non-OA population (3.5 %) (Table 1).

3.2. Use of prescription and OTC treatments among OA population

Approximately 32 % of individuals with OA reported using

prescription medications to treat their OA. There was a higher likelihood of using a prescription medication for patients who had been diagnosed with OA for longer periods (<3 years: 27.5 %; 3–5 years: 30.2 %; 6–10 years: 30.4 %; 11–20 years: 30.9 %; and ≥21 years: 32.5 %). Respondents with OA reported that tramadol (16.2 %), ibuprofen (15.6 %), meloxicam (15.5 %), gabapentin (12.3 %), and hydrocodone (11.4 %) were the most commonly used prescription treatments overall (Fig. 4). Other NSAIDs (e.g., naproxen, diclofenac) and other analgesics (e.g., acetaminophen) were also widely used in this population. Usage trends of individual medications shifted when considering the impact of length of time diagnosed, in particular in regard to use of meloxicam. For patients who had been with OA (<3 years), the most common prescription medication used was meloxicam (22.6 %), followed by ibuprofen (17.5 %), tramadol (13.4 %), hydrocodone (10.1 %) and gabapentin (7.1 %) whereas for patients diagnosed with OA 21 years or longer, the most common prescription medication was ibuprofen (17.0 %), followed by tramadol (15.7 %), meloxicam (13.1 %), gabapentin (11.6 %), and hydrocodone (11.5 %).

Respondents with OA also reported their use of OTC medications and dietary supplements. Of the overall OA population, 6.0 % reported use of chondroitin ± glucosamine (Ch ± Gl); for OA users of OTC medications or dietary supplement/natural products, Ch ± Gl was the most commonly used dietary supplement, followed by omega-3 fatty acids and vitamin D (Fig. 5). Use of omega-3 fatty acids was highest for the older OA population (≥65 years) with 3.4 % of both men and women reporting use of these supplements, while only 1.6 % of women aged 35–44 years reported using these supplements. Vitamin D use was highest for men and women aged 45–64 years (2.1 % and 2.4 %, respectively) and lowest for men and women aged 35–44 years (0 % and 0.8 %, respectively). The proportion of prescription or OTC analgesic medication use was compared in OA patients taking Ch ± Gl versus those who do not take these supplements. Among respondents who reported taking Ch ± Gl, nearly 25 % used prescription medications compared with 32 % of those who did not take Ch ± Gl (Fig. 6).

4. Discussion

The results of this study suggest that individuals with OA frequently have comorbidities, lower physical activity levels and higher BMIs than the general population. As shown by the current analysis, the prevalence
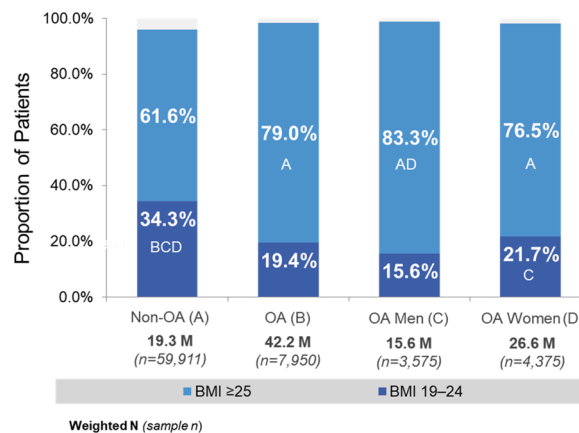
Fig. 2. BMI Among OA and Non-OA Populations[1].
[1]Percentages do not add up to 1.0 % because respondents with BMI < 19 were not included.
Letters indicate statistically significant difference at 95 % confidence level between subgroups; labeled beside group with higher value.
BMI, body mass index; M, million; OA, osteoarthritis.

of OA was higher in individuals with a high BMI or comorbid medical condition, including diabetes or hypertension, and those less likely to exercise on a regular basis. The prevalence estimate of 17.6 % from this study is consistent with US prevalence estimates reported by other studies, which range from 7.2 % for hip OA to 19.2 % for knee OA [2]. The higher rates of OA observed in this study for those with a higher BMI are consistent with the generally accepted association between excess body weight and development and progression of OA [13].

Despite recommendations for those with OA to get regular exercise as part of the management for OA [10], the level of regular exercise (≥12 days per month) reported in this study was lower for those with OA (25 %) compared with the non-OA population (32 %). However, exercise frequency in patients with OA may be complicated by the potential for the symptoms of OA to decrease exercise, which may explain the results observed here. National activity level estimates calculated from the US National Health Interview Survey (NHIS) based on exercise guidelines showed that levels of activity in people with OA are low, which is consistent with the present study. In 2015, 36.2 % of adults
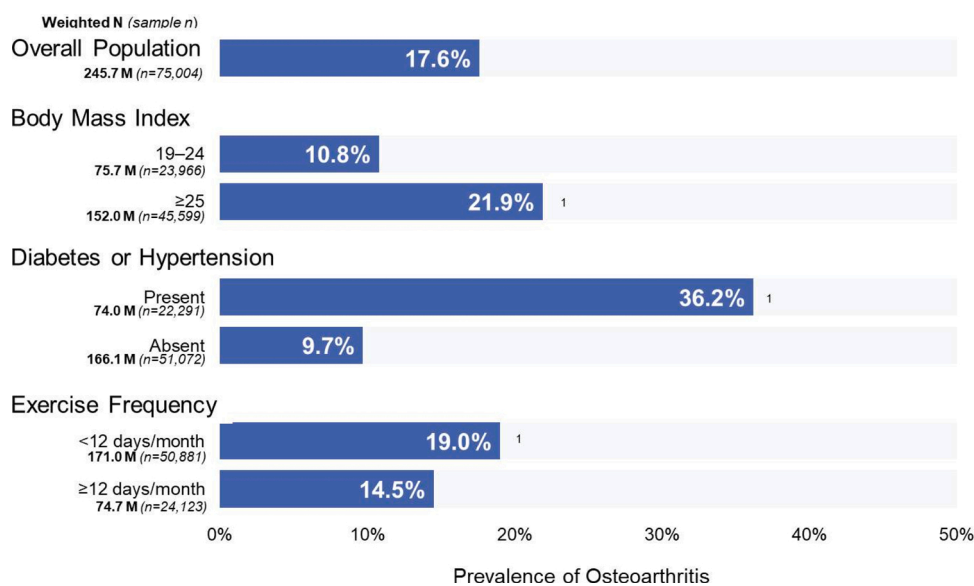
Fig. 1. Prevalence of Osteoarthritis Overall and by Subgroups.
[1]Statistically significant difference at 95 % confidence level between subgroups.
M, million.

with arthritis were physically active according to activity guidelines, 17.9 % were meeting muscle strengthening guidelines, and 13.7 % met both guidelines [18]. Although the overall exercise levels were similarly low between these studies, the NHIS data showed a trend of decreasing activity with increasing age [18]. In contrast, we observed that activity levels increased from the age groups of 45–64 years to ≥65 years for both men and women. Variation in activity definitions may explain some of these differences. Murphy et al. [18] defined active as engaging in moderate to vigorous exercise and in our study, we asked respondents how often they had exercised vigorously. In contrast, data from the Osteoarthritis Initiative (OAI) and National Health and Nutrition Examination Survey (NHANES) showed similar levels of physical activity between the OA and general populations, although this study differed also from the present study in that it focused on moderate-to-vigorous physical activity and was conducted in people with symptomatic knee OA [19].

In our study, we observed fairly low numbers of patients with OA who utilized physical therapy, with only 11%–13% of the population more than 45 years of age reporting a visit in the past 6 months. This low proportion may be in part because the question specifically focused on the past 6 months. In the PRIMO (Patient and PRovider Interventions for Managing OA in Primary Care) study, higher utilization was reported by patients with hip (34.0 %) and knee OA (39.1 %) when asked if they had ever seen a physical therapist [16]. The PRIMO study identified variations in the use of physical therapy between clinics; knee OA patients at rural clinics were less likely to receive physical therapy. It is possible that the low rates of physical therapy observed in our study reflect a greater proportion of respondents from underserved areas; additional studies would be needed to investigate this finding further.

In this study, the likelihood of using prescription products increased with the length of OA history. Individuals with OA using Ch ± Gl were more likely to report using OTC products only or to use them combined with prescription products, while those not using Ch ± Gl most commonly used OTC products only or were untreated. Notably though, the Ch ± Gl data were collected from the OTC variables in the NHWS, which may have increased the proportion of patients who used OTC products. Although the literature is limited, a few other studies have examined the utilization of medications and supplements among the OA population. Another study of the OAI data examined utilization of prescription and OTC analgesics and natural products for symptomatic knee OA and reported prescription analgesic use at 30.1 %, which is similar to

our study's finding of 31.9 % [20]. Likewise, Kingsbury et al. [20] reported that patients were commonly combining analgesics with use of natural products such as Ch ± Gl. However, reported use of prescription NSAIDs and opioids in the OAI study was lower (8.2 % and 3.3 %, respectively), while reported use of Ch ± Gl was higher (40.7 %), compared with the current study [20].

A cross-sectional study of patients with knee and hip OA identified from a US urban hospital-based outpatient clinic evaluated prescription and OTC medication use as well as use of dietary supplements [21]. In that study, the most commonly used medications or supplements were NSAIDs, and naproxen (29.6 %) and ibuprofen (24.1 %) were the most frequently used medications in the class. Similar to the present study, dietary supplements were used less frequently than prescription and OTC medications, with only 6.8 % of respondents reporting their use. The study also reported on the combination of OTC and prescription medications. Nearly 20 % of patients used both prescription and OTC medications and supplements, a finding slightly higher than the 13.7 % of study participants observed in the present study. A much higher proportion used prescription medications only (49.4 %) [21] compared with only 18.2 % of the current study population.

The OAI database has also been used to examine the utilization of complementary and alternative medicine (CAM), including use of supplements, for the treatment of radiographic-confirmed OA of the knee [22]. Of the study participants reporting CAM use, nearly 70 % used a
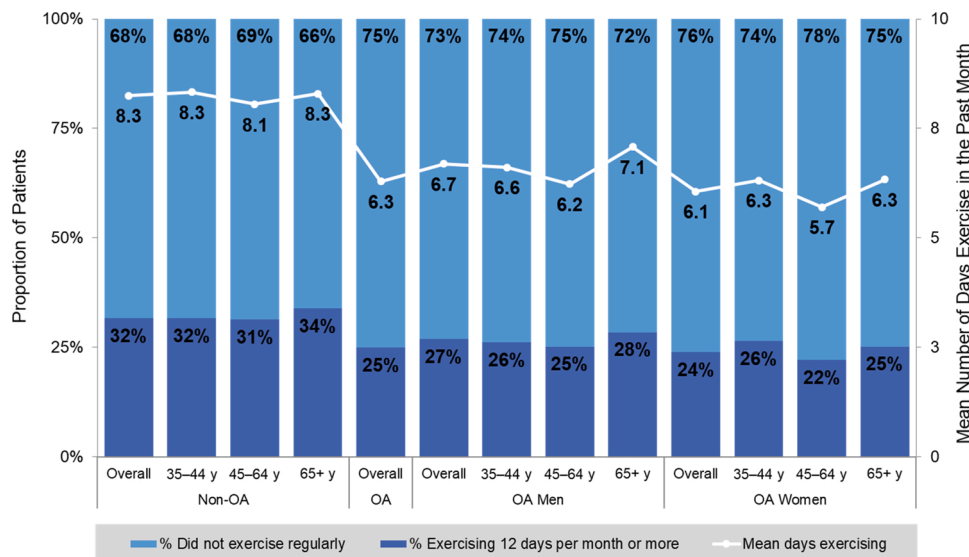
Table 1

Use of Physical Therapy Over the Past 6 Months Among OA and Non-OA Populations.

	Non-OA Population	OA Population				
		Overall	Men 45–64 y	Men ≥65 y	Women 45–64 y	Women ≥65 y
Weighted N	200.7 M	43.3 M	6.6 M	7.0 M	11.6 M	13.9 M
Sample n	62,107	8147	1,403	2,009	2,307	1,717
Visited a PT in past 6 months (%)	3.5	12.6	12.3	11.3	13.1	12.2

M, million; OA, osteoarthritis; PT, physical therapist; y, years of age.

Fig. 3. Exercise Frequency Among OA and Non-OA Populations.
Weighted N (sample n): Non-OA: 200.7 M (n = 62,107); OA: 43.3 M (n = 8,147); OA Men: 15.7 M (n = 3,591); OA Women: 27.6 M (n = 4,556).
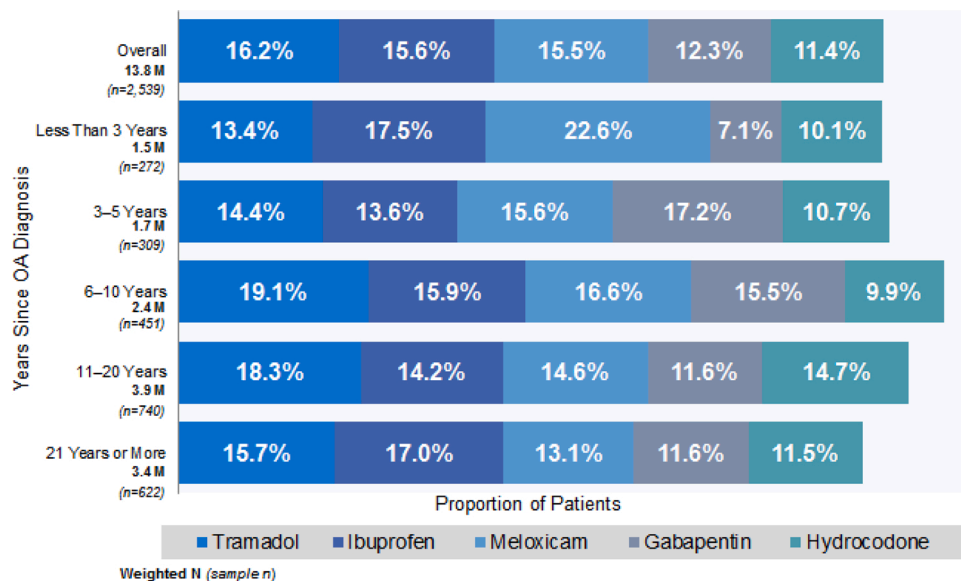M, million; OA, osteoarthritis; y, years of age.

Fig. 4. Use of Prescription Medication by Length of Time Diagnosed.
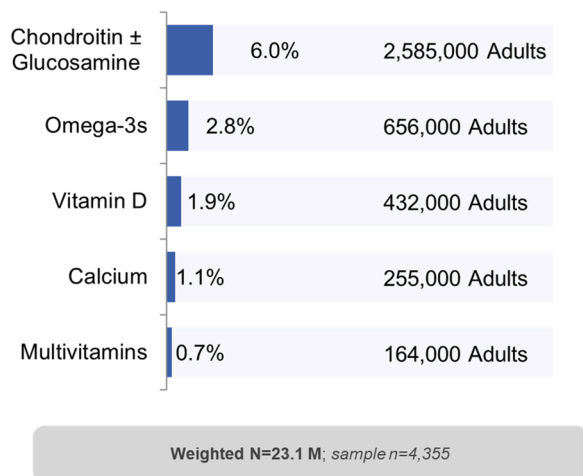M, million, OA, osteoarthritis.

Fig. 5. Use of OTC Medications/Dietary Supplements Among OA Population[1].
[1]Diagnosed with OA using OTC medications or herbal products.
M, million; OA, osteoarthritis.

Fig. 6. Use of Prescription and OTC Pain Medications Among OA Population Taking Ch ± Gl.
[1]OTC/herbal products.
M, million; OA, osteoarthritis; OTC, over-the-counter; Rx, prescription medication.

supplement, most commonly glucosamine (59 %), chondroitin (54 %), vitamins/minerals (13 %), and methylsulfonylmethane (12 %). As with the present study, Ch ± Gl and vitamins were among the most commonly used supplements, although the OAI study questionnaire did not include a question on omega-3 use [22].

The findings of our study point to several potential opportunities to improve nonsurgical management of OA. We observed lower levels of regular exercise in the OA population compared with the non-OA population. Yet, one of the core recommendations of the Osteoarthritis Research Society International (OARSI) guidelines for the nonsurgical management of OA is participation in a structured land-based exercise program that includes strengthening, cardiovascular, or balance training/neuromuscular components [10]. Stepped-care strategies (SCSs) for the management of hip and knee OA are one approach to bridge the gap between guideline recommendations and real-world implementation. SCSs have resulted in increased adoption of recommendations around education, lifestyle advice, acetaminophen use, and exercise therapy, with exercise therapy increasing from ≈40 % to 63 % after 2 years in one SCS program [23]. We also observed a higher
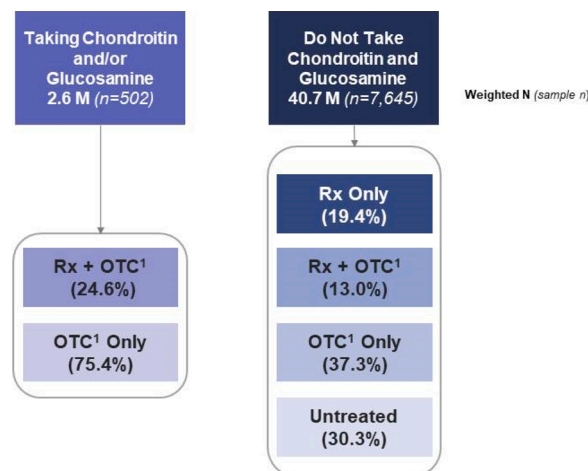
prevalence of OA among respondents with a higher BMI in our study. Dietary weight management is another core recommendation of the OARSI guidelines [10], and weight loss through dietary modification has been shown to reduce pain and increase functioning [13]. Although guidelines do not currently include natural products and dietary supplements, these products may potentially benefit patients with OA [11–13] and our study demonstrated that patients with OA are using supplements to manage their symptoms.

There are several important limitations that should be noted. First, identification of the OA population was based on a survey questionnaire and did not include questions about symptoms nor was OA verified by radiographic screening. Second, although this study was based on a survey of a very large population, findings may not be generalizable to the overall population, since respondents were drawn from an internet survey panel which may introduce selection bias. Third, although data were stratified by age and gender in this study, results are unadjusted and do not account for possible interactions between participant

characteristics and other potential confounders such as comorbidities. In addition, these are cross-sectional analyses, which limits our ability to determine any directionality such as whether joint pain reduced exercise or if reduced exercise resulted in joint pain when OA developed [24,25]. Longitudinal data will be needed to address this issue. The analysis also did not adjust for symptoms of OA including pain, functional status, and disease severity; it is possible that these factors influence patients' management of their OA, and particularly their ability to maintain a regular exercise program. Finally, respondents were asked to recall and self-report data on their use of supplements, medications, and exercise frequency, and the collection of healthcare data from patients may be subject to recall bias [26]; prescription medications were also not verified by prescription claims data and may be subject to misclassification bias as well. Additionally, the usage rates of individual OTC medications, which may have provided some additional insights into the pharmaceutical products used by the OA population, were not individually determined for the specific treatments.

5. Conclusion

This study provides information on the health characteristics and patterns of prescription and OTC medication use among the US OA population. The prevalence of OA is high, particularly for individuals with a high BMI or comorbid diseases, including diabetes or hypertension, and those less likely to exercise on a regular basis. Individuals with OA using Ch ± Gl were more likely to report use of OTC products only or to use them combined with prescription products, and the likelihood of using prescription products increased with the duration of OA. We observed that many patients with OA may not be following OARSI recommendations for nonsurgical management of OA which highlights that there are many opportunities to improve the nonsurgical management of OA.

Contributors

Nancy E. Lane contributed to study design and data interpretation.
Jasmina Ivanova contributed to collection and assembly of data, and data analysis and interpretation.
Birol Emir contributed to collection and assembly of data, and data analysis and interpretation.
Ali Mobasheri contributed to data interpretation.
Morten Georg Jensen contributed to study design, and data analysis and interpretation.
All authors contributed to the preparation of the paper and saw and approved the final version.

Conflict of interest

Nancy E. Lane has no conflict of interest to disclose.
Jasmina Ivanova and Birol Emir are employed by Pfizer, Inc.
Morten Georg Jensen is employed by Pfizer Consumer Healthcare.
Ali Mobasheri is President of OARSI.

Funding

Ethics

This study used pre-existing data from the 2017 US National Health and Wellness Survey (NHWS) and was therefore except from institutional ethical review.

Data sharing and collaboration

There are no linked research data sets for this paper. This study used pre-existing data from the 2017 US National Health and Wellness Survey (NHWS) and did not include any anonymized data files.

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

References

[1] T. Neogi, The epidemiology and impact of pain in osteoarthritis, Osteoarthr. Cartil. 21 (9) (2013) 1145–1153, https://doi.org/10.1016/j.joca.2013.03.018.

[2] A. Litwic, M.H. Edwards, E.M. Dennison, C. Cooper, Epidemiology and burden of osteoarthritis, Br. Med. Bull. 105 (2013) 185–199, https://doi.org/10.1093/bmb/lds038.

[3] D.J. Hunter, J.J. McDougall, F.J. Keefe, The symptoms of osteoarthritis and the genesis of pain, Rheum. Dis. Clin. North Am. 34 (3) (2008) 623–643, https://doi.org/10.1016/j.rdc.2008.05.004.

[4] F. Xie, B. Kovic, X. Jin, X. He, M. Wang, C. Silvestre, Economic and humanistic burden of osteoarthritis: a systematic review of large sample studies, Pharmacoeconomics. 34 (11) (2016) 1087–1100, https://doi.org/10.1007/s40273-016-0424-x.

[5] K.E. Barbour, C.G. Helmick, M. Boring, T.J. Brady, Vital signs: prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation - United States, 2013-2015, MMWR Morb. Mortal. Wkly. Rep. 66 (9) (2017) 246–253, https://doi.org/10.15585/mmwr.mm6609e1.

[6] S.R. Jafarzadeh, D.T. Felson, Updated estimates suggest a much higher prevalence of arthritis in United States adults than previous ones, . 70 (2) (2018) 185–192, https://doi.org/10.1002/art.40355.

[7] R.F. Loeser, J.A. Collins, B.O. Diekman, Ageing and the pathogenesis of osteoarthritis, Nat. Rev. Rheumatol. 12 (7) (2016) 412–420, https://doi.org/10.1038/nrrheum.2016.65.

[8] Y. Li, X. Wei, J. Zhou, L. Wei, The age-related changes in cartilage and osteoarthritis, Biomed Res. Int. 2013 (2013), 916530, https://doi.org/10.1155/2013/916530.

[9] S.L. Kolasinski, T. Neogi, M.C. Hochberg, C. Oatis, G. Guyatt, J. Block, et al., 2019 American College of Rheumatology/Arthritis foundation guideline for the management of osteoarthritis of the hand, hip, and knee, Arthritis Rheumatol. 72 (2) (2020) 220–233.

[10] R.R. Bannuru, M.C. Osani, E.E. Vaysbrot, N.K. Arden, K. Bennell, S.M.A. Bierma-Zeinstra, et al., OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis, Osteoarthr. Cartil. (2019), https://doi.org/10.1016/j.joca.2019.06.011.

[11] Y. Henrotin, A. Mobasheri, Natural products for promoting joint health and managing osteoarthritis, Curr. Rheumatol. Rep. 20 (11) (2018) 72, https://doi.org/10.1007/s11926-018-0782-9.

[12] S. Thomas, H. Browne, A. Mobasheri, M.P. Rayman, What is the evidence for a role for diet and nutrition in osteoarthritis? Rheumatology. 57 (suppl 4) (2018) iv61–iv74.

[13] K.J. Melanson, Diet, nutrition and osteoarthritis, Am. J. Lifestyle Med. 1 (4) (2007) 260–263, https://doi.org/10.1177/1559827607302033.

[14] X. Liu, G.C. Machado, J.P. Eyles, V. Ravi, D.J. Hunter, Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis, Br. J. Sports Med. 52 (3) (2018) 167–175, https://doi.org/10.1136/bjsports-2016-097333.

[15] W. Zhang, W.B. Robertson, J. Zhao, W. Chen, J. Xu, Emerging trend in the pharmacotherapy of osteoarthritis, Front Endocrinol (Lausanne). 10 (2019) 431, https://doi.org/10.3389/fendo.2019.00431.

[16] Kd Allen, Hb Bosworth, R. Chatterjee, Cj Coffman, L. Corsino, As Jeffreys, et al., Clinic variation in recruitment metrics, patient characteristics and treatment use in a randomized clinical trial of osteoarthritis management, BMC Musculoskelet. Disord. 15 (2014) 413, https://doi.org/10.1186/1471-2474-15-413.

[17] K.E. Barbour, S. Moss, J.B. Croft, C.G. Helmick, K.A. Theis, T.J. Brady, et al., Geographic variations in arthritis prevalence, health-related characteristics, and management - United States, 2015, Surveill. Summ. 67 (4) (2018) 1–28, https://doi.org/10.15585/mmwr.ss6704a1.

[18] L.B. Murphy, J.M. Hootman, M.A. Boring, S.A. Carlson, J. Qin, K.E. Barbour, et al., Leisure time physical activity among U.S. Adults with arthritis, 2008-2015, Am. J. Prev. Med. 53 (3) (2017) 345–354, https://doi.org/10.1016/j.amepre.2017.03.017.

[19] L.M. Thoma, D. Dunlop, J. Song, J. Lee, C. Tudor-Locke, E.J. Aguiar, et al., Are older adults with symptomatic knee osteoarthritis less active than the general population? Analysis from the Osteoarthritis Initiative and the National Health and

Nutrition Examination Survey, Arthritis Care Res (Hoboken). 70 (10) (2018) 1448–1454, https://doi.org/10.1002/acr.23511.

[20] S.R. Kingsbury, E.M. Hensor, C.A. Walsh, M.C. Hochberg, P.G. Conaghan, How do people with knee osteoarthritis use osteoarthritis pain medications and does this change over time? Data from the Osteoarthritis Initiative, Arthritis Res. Ther. 15 (5) (2013) R106, https://doi.org/10.1186/ar4286.

[21] J.B. Driban, S.A. Boehret, E. Balasubramanian, N.M. Cattano, J. Glutting, M. R. Sitler, Medication and supplement use for managing joint symptoms among patients with knee and hip osteoarthritis: a cross-sectional study, BMC Musculoskelet. Disord. 13 (2012) 47, https://doi.org/10.1186/1471-2474-13-47.

[22] K.L. Lapane, M.R. Sands, S. Yang, T.E. McAlindon, C.B. Eaton, Use of complementary and alternative medicine among patients with radiographic-confirmed knee osteoarthritis, Osteoarthr. Cartil. 20 (1) (2012) 22–28, https://doi.org/10.1016/j.joca.2011.10.005.

[23] A.J. Smink, J. Dekker, T.P. Vliet Vlieland, B.A. Swierstra, J.H. Kortland, J. W. Bijlsma, et al., Health care use of patients with osteoarthritis of the hip or knee after implementation of a stepped-care strategy: an observational study, Arthritis Care Res (Hoboken). 66 (6) (2014) 817–827, https://doi.org/10.1002/acr.22222.

[24] V. Silverwood, M. Blagojevic-Bucknall, C. Jinks, J.L. Jordan, J. Protheroe, K. P. Jordan, Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis, Osteoarthr. Cartil. 23 (4) (2015) 507–515, https://doi.org/10.1016/j.joca.2014.11.019.

[25] D.M. Urquhart, C. Soufan, A.J. Teichtahl, A.E. Wluka, F. Hanna, F.M. Cicuttini, Factors that may mediate the relationship between physical activity and the risk for developing knee osteoarthritis, Arthritis Res. Ther. 10 (1) (2008) 203, https://doi.org/10.1186/ar2343.

[26] N.K. Brusco, J.J. Watts, Empirical evidence of recall bias for primary health care visits, BMC Health Serv. Res. 15 (2015) 381, https://doi.org/10.1186/s12913-015-1039-1.