ARTHRITIS & RHEUMATISM
Vol. 52, No. 8, August 2005, pp 2485–2494
DOI 10.1002/art.21194

Longitudinal Patterns in the Prevention of Osteoporosis in Glucocorticoid-Treated Patients

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Objective. **To evaluate patient and physician factors associated with prevention of glucocorticoid-induced osteoporosis and to describe temporal trends in screening and prevention of glucocorticoid-induced osteoporosis.**

Methods. **Using databases from a national managed care organization, enrollees who had been prescribed glucocorticoids (taken for at least 60 days) during an 18-month period were identified. Administrative data from January 2001 through June 2003 and linked survey data from October 2003 were examined for measurement of bone mass, prescription of antiresorptive medication, and use of over-the-counter calcium and/or vitamin D treatment. Factors associated with screening and bone-protective therapies were identified using multivariable logistic regression, focusing on physician specialty and survey respondent ethnicity. Trends in glucocorticoid-induced osteoporosis prevention were assessed using administrative data from 2001–2003 versus 1995–1998.**

Results. **We identified 6,281 patients who were prescribed glucocorticoids in 2001–2003 (mean ± SD prescribed prednisone-equivalent dosage 16 ± 14 mg/day). Forty-two percent underwent bone mass measurement and/or were prescribed bone-protective medication; rates were lowest for men (25%). Compared with patients of internists, the odds of bone mass measurement were lowest among patients prescribed glucocorticoids by family physicians (odds ratio [OR] 0.56 [95% confidence interval] [95% CI] 0.30–1.04) and highest among patients prescribed glucocorticoids by rheumatologists (OR 1.48 [95% CI 1.06–2.08]). Patients prescribed glucocorticoids by gastroenterologists were less likely to be treated with antiresorptive agents (OR 0.49 [95% CI 0.28–0.86]). African American patients were less likely than white patients to be screened (OR 0.55 [95% CI 0.40–0.75]) or treated (OR 0.71 [95% CI 0.51–0.98]). The frequency of bone mass measurement among glucocorticoid-treated patients in 2001–2003 increased 3-fold compared with 1995–1998, and the use of prescription antiresorptive medication increased ~2-fold.**

Conclusion. **Despite significant temporal increases in the frequency of screening for and treatment of glucocorticoid-induced osteoporosis, absolute rates remain low, especially among men, African Americans, and patients of certain physician specialties.**

Glucocorticoids are prescribed widely in medical practice and are used by 0.5–2.5% of adults (1,2). Despite the acknowledged benefits of glucocorticoid treatment in controlling short-term inflammation, concerns about associated adverse events often limit its use. Among the most feared is glucocorticoid-induced osteoporosis. Rates of glucocorticoid-induced osteoporosis–associated fracture may approach 40% in selected populations (3,4), and this condition often results in

Supported by the Agency for Healthcare Research and Quality (grant HS-10389) and the NIH (grant P60-AR-48095 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases and grant T32-AR-47512-03).

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Dr. Saag has received consulting fees or honoraria of less than $10,000 from Procter & Gamble, Lilly, Novartis, and Pfizer and consulting fees and honoraria of more than $10,000 from Merck.

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Submitted for publication February 11, 2005; accepted in revised form April 20, 2005.

substantial morbidity and mortality (3,5–10). However, despite the high prevalence of these fractures, previous investigations have documented low utilization of over-the-counter (OTC) and prescription therapies for osteoporosis prevention and wide variations in practice patterns among physicians of various specialties (11–14). Most prior studies have lacked information on OTC calcium and vitamin D use, patient education, and patient ethnicity. Others have been limited by small sample sizes and have been cross-sectional in design.

Using managed care administrative data from 2001–2003 linked to a mailed survey of long-term glucocorticoid users, we determined rates and predictors of measurement of bone mass, prescription of bone-protective medications, and use of OTC supplements for glucocorticoid-induced osteoporosis. We also examined temporal trends in glucocorticoid-induced osteoporosis prevention strategies by comparing administrative data on receipt of bone mass measurement and use of bone-protective prescription medication from 2001–2003 with similar data from 1995–1998.

METHODS

Data sources. Long-term glucocorticoid users in 2001–2003 were identified from a national managed care organization (MCO) population covering 3 million lives in 36 states. The data source consisted of linked enrollment, outpatient encounter, pharmacy, and procedural billing databases on enrollees in the MCO's health maintenance organization (HMO), point-of-service (POS), and preferred provider organization (PPO) health plans. Diseases, medications, and procedures were coded using International Classification of Diseases, Ninth Revision codes, National Drug Codes, and Common Procedural Terminology codes, respectively. All individuals in the cohort had pharmacy benefits, with variable copayment amounts. A survey was mailed in 2003 to all qualifying glucocorticoid users identified during 2001–2003, and results were linked to their administrative data. The same administrative data source was used to identify long-term glucocorticoid users during 1995–1998, although no corresponding survey information was available.

Inclusion criteria for 2001–2003 cross-sectional analysis. Individuals were characterized as long-term glucocorticoid users if they were at least 18 years of age and had received outpatient oral glucocorticoid treatment on at least 60 days between July 1, 2001 and December 31, 2002 (the medication eligibility period). Each member was continuously enrolled in the health plan for at least 6 months prior to and following the date of his or her first qualifying glucocorticoid prescription (the index date) and throughout the study period. Individuals were linked to physicians using Drug Enforcement Agency (DEA) numbers listed on filled glucocorticoid prescriptions. If members received >60 days of glucocorticoid treatment from >1 provider, they were assigned to the most recent prescriber. We oversampled physicians in specialties in which glucocorticoids are commonly prescribed. A total of 6,281 health plan members met the inclusion criteria for long-term glucocorticoid use and were selected for further study.

Because of possible differences in screening and prevention patterns, we characterized subjects as new or prevalent glucocorticoid users. New users were defined as adults for whom there was no evidence of any glucocorticoid prescription in the 90 days prior to their index date; all others were considered prevalent users. Individuals were excluded from the study if they had diseases that were known or hypothesized a priori to significantly impact their perceived appropriateness for glucocorticoid-induced osteoporosis screening or use of medications for prevention. Such diagnoses included human immunodeficiency virus infection, alcoholism, dementia, lymphoma, leukemia, history of organ transplantation, Paget's disease of bone, and local or metastatic solid organ tumors.

Inclusion criteria for longitudinal analyses. We used administrative data to compare rates of bone mass measurement and prescription antiresorptive medication use in 2001–2003 versus 1995–1998. Because the American College of Rheumatology guidelines for glucocorticoid-induced osteoporosis management differed prior to 2001 (15) compared with current guidelines (16), we restricted our analysis to new glucocorticoid users who had received continuous therapy for ≥90 days (no more than a 5-day gap between prescriptions) to ensure that the inclusion and exclusion criteria for both cohorts in the longitudinal analyses were identical. Because no corresponding survey data for 1995–1998 were available, our longitudinal analyses were restricted to covariates and end points of interest that were included in the administrative data (i.e., bone mass measurement and prescription medication use). We previously reported the demographic characteristics of the 1995–1998 cohort (13).

Qualifying glucocorticoid medications. Qualifying glucocorticoids (from pharmacy data) included prednisone, prednisolone, dexamethasone, and other oral systemic glucocorticoids commonly used in practice in the US. Injectable, topical, and intraocular glucocorticoids were not included. The average daily prednisone equivalent dose for each subject was calculated by dividing the cumulative dose dispensed (number of pills × pill strength) by the number of fill days prescribed. Those with prescriptions for daily doses that appeared implausible (i.e., >100 mg/day of oral prednisone) were recoded using the members' average daily dose computed without these outlier prescriptions. Of the total of 60,465 glucocorticoid prescriptions written in 2001–2003, only 213 prescriptions among 134 members (0.35%) needed to be recoded in this manner.

Glucocorticoid survey administration. In the fall of 2003, a written survey was mailed to 6,281 members who met inclusion criteria for long-term glucocorticoid use in 2001–2003. A followup postcard and a second survey were mailed to nonresponders. In the survey, individuals were asked for demographic information and current use of OTC calcium and/or vitamin D supplements. Survey questions that were left blank or with multiple marks were treated as missing data and excluded from analysis.

Glucocorticoid-induced osteoporosis–related results of interest from claims data. Glucocorticoid-induced osteoporosis prevention–related end points of interest (bone mass

Table 1. Characteristics of patients in the 2001–2003 cohort of long-term glucocorticoid users (n = 6,281)*

Age, mean ± SD years	50 ± 14
Female	4,153 (66)
Duration of enrollment in the health plan prior to the study period, mean ± SD months	27 ± 13
Prednisone equivalent dosage, mean ± SD mg/day†	16 ± 14
Cumulative prednisone equivalent dose, mean ± SD gm†	3.5 ± 3.1
Duration of prednisone use, mean ± SD months†	9 ± 6
New glucocorticoid user (≥90 days without prior prescription)	4,058 (65)
No. of comorbid conditions, mean ± SD	6 ± 3
Comorbid conditions	
Diabetes	954 (15)
Hypertension	2,618 (42)
Chronic renal failure	525 (8)
Congestive heart failure	477 (8)
Diagnoses associated with glucocorticoid use	
Rheumatoid arthritis	2,363 (38)
Chronic obstructive pulmonary disease	707 (11)
Systemic lupus erythematosus	800 (13)
Asthma/reactive airway disease	783 (12)
Inflammatory bowel disease	535 (9)
Health plan type	
Health maintenance organization	4,048 (64)
Point-of-service	788 (13)
Preferred provider organization	1,446 (23)
Ethnicity‡	
White	1,741 (78)
African American	301 (13)
Hispanic	107 (5)
Asian	63 (3)
American Indian	24 (1)
Multiracial	12 (1)
High school education or less‡	889 (39)
Married‡	1,548 (67)
Employed‡	1,207 (55)
Annual income <$20,000‡	273 (13)

* Except where indicated otherwise, values are the number (%) and information is based on administrative and pharmacy claims data.
† During study period of 2 years.
‡ Information derived from survey (does not total the 2,363 individuals who returned the survey, because of missing data).

measurement and prescription medications) were examined using MCO claims and pharmacy databases from January 2001 through June 2003 and from January 1995 through March 1998. Rates of screening and treatment were grouped into demographic categories of scientific interest (men, women <50 years of age, and women ≥50 years of age) and also by the specialty of the physician prescribing glucocorticoids. To allow comparable longitudinal analysis, the physician specialty mix for the 2001–2003 cohort was adjusted to the physician specialty mix for the 1995–1998 cohort using direct standardization. This was accomplished by computing stratum-specific performance rates by physician specialty in 2001–2003 for each end point and applying them to the 1995–1998 physician case mix.

Statistical analysis. Categorical variables were compared using the chi-square test of independence, and continuous variables were compared by 2-tailed *t*-test. Using administrative data in conjunction with survey data, multivariable logistic regression was performed to identify factors significantly associated with bone mass measurement, glucocorticoid-induced osteoporosis prevention–specific prescription medications, and OTC calcium and vitamin D supplement use. Individuals with chronic renal failure (n = 188) were excluded from these analyses since their end-stage renal disease was expected to be a determinant of calcium/vitamin D use and would limit their eligibility for some glucocorticoid-induced osteoporosis–preventive therapies such as oral bisphosphonates. Variables of biologic or clinical importance were included in all regression models. Because of known interactions between age and sex on the end points of interest, these variables were categorized by group (men <50 years of age, men 50–70 years of age, men >70 years of age, women <50 years of age, women 50–70 years of age, and women >70 years of age) and forced into all models. For all other variables, a univariate *P* value of <0.25 was required for the variable to be entered into the model, and a *P* value of <0.05 was required for a variable to

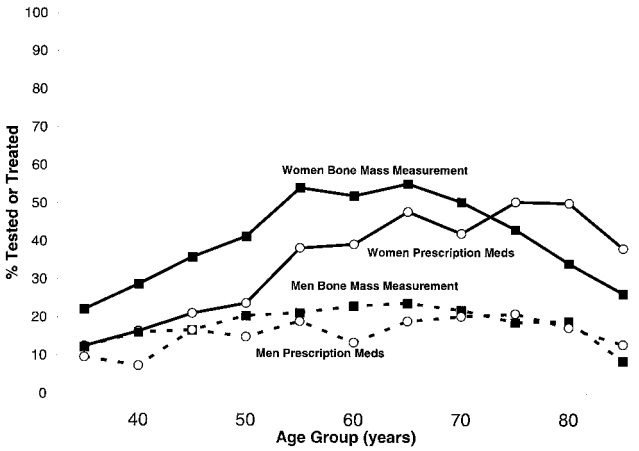

Figure 1. Screening by bone mass measurement and prescription of non-estrogen therapies (oral bisphosphonates, raloxifene, calcitonin) for the prevention of glucocorticoid-induced osteoporosis in 2001–2003 in 6,281 patients, by age and sex.

remain in the model. To assess for differing levels of improvement over time between physician specialties, an interaction term between specialty and time was used. Model building was conducted as described by Hosmer and Lemeshow (17). For highly collinear covariates (e.g., average daily prednisone dose and cumulative prednisone dose), the one(s) with the strongest association were included in the final models. Goodness-of-fit and model calibration for logistic regression were assessed using the Hosmer-Lemeshow goodness-of-fit and c statistics, respectively (17,18). To account for patient clustering by the treating physician, we used generalized estimating equations (GEE), although almost half of the treating physicians had only 1 patient in the cohort. Results obtained using GEE were similar to those obtained using logistic regression; therefore, only the results of the logistic regression models are presented. All analyses were performed using SAS software (SAS Institute, Cary, NC).

RESULTS

Characteristics of the 2001–2003 cohort. The characteristics of the 6,281 managed care enrollees identified using pharmacy data who met the definition of long-term glucocorticoid use in 2001–2003 are described in Table 1. Subjects had an average of 6 comorbid diagnoses, and a majority were new rather than prevalent glucocorticoid users. Thirty-eight percent (n = 2,363) returned the survey, and >91% confirmed that they had actually taken glucocorticoids. Compared with survey responders, the survey nonresponders were significantly younger (mean 48 versus 53 years) and included a higher percentage of men (36% versus 30%). Their duration of enrollment in the health plan prior to the study, mean daily prednisone dose, and average number of comorbid conditions were similar to the findings in survey responders (data not shown).

Glucocorticoid-induced osteoporosis screening and preventive treatment in 2001–2003. Figure 1 presents the cross-sectional trends in bone mass measurement and nonhormone therapies for glucocorticoid-induced osteoporosis in the subjects, by sex-specific 5-year age category. Among women, bone mass measurement increased up to age 55, plateaued, and then declined. Prescription of non-estrogen medications for glucocorticoid-induced osteoporosis among women increased linearly up to age 80. In contrast, both bone mass measurement and bone-specific medication use among men were relatively flat across age categories. Rates of bone-specific prescription therapy were ≤50% for women in all age groups and ≤20% for men in all age groups.

Using a combined end point of bone mass measurement or any non-estrogen medication for glucocorticoid-induced osteoporosis, we found that 42% of the cohort was screened or treated (data not shown). Rates were highest for women ≥50 years of age (65%) compared with women <50 years of age (38%) and men (25%). Among the individuals with claims for bone mass measurement, 93% had central dual x-ray absorptiometry (DXA) alone and 3% had bone mass measurement using both central DXA and another technology such as heel ultrasound or peripheral DXA. Apparent rates of bone mineral density testing were ~4% lower among enrollees in HMO health plans compared with those in POS or PPO health plans, although this finding might have been due to small variations in data capture between health plan types. Use of bone-protective prescription medications did not vary by health plan type.

Rates of bone mass measurement, use of antiresorptive therapies for glucocorticoid-induced osteoporosis, and self-reported calcium and/or vitamin D supplement use were categorized by physician specialty, as shown in Table 2. The highest rate of bone mass measurement was in patients who were prescribed glucocorticoids by a rheumatologist and was almost double the rate among family/general practice patients. Similar variations between physician specialties were observed for use of bone-specific medications such as bisphosphonates and use of OTC calcium and vitamin D. Among survey respondents, ~25% of those receiving prescription medications and 30% of the group overall reported no use of calcium supplements.

Table 2. Number (%) of patients receiving bone mass measurement and prophylactic therapies for glucocorticoid-induced osteoporosis in 2001–2003, by specialty of the patient's glucocorticoid-prescribing physician

Physician specialty	Bone mass measurement*	Any prescription medication*†	Estrogen (n = 4,153 women)‡	Oral bisphosphonates*	Calcitonin	Raloxifene (n = 4,153 women)§	Calcium and/or vitamin D*¶	Calcium and vitamin D*¶
Internal medicine (293 physicians, 601 patients)	176 (29)	234 (39)	93 (25)	129 (21)	25 (4)	18 (5)	161 (75)	107 (50)
Rheumatology (667 physicians, 3,449 patients)	1,361 (39)	1,388 (40)	587 (23)	877 (25)	124 (4)	88 (3)	865 (71)	665 (55)
Family practice (131 physicians, 249 patients)	53 (21)	97 (39)	42 (27)	41 (16)	12 (5)	3 (2)	55 (56)	34 (35)
Gastroenterology (309 physicians, 509 patients)	135 (27)	111 (22)	35 (13)	72 (14)	7 (1)	2 (1)	92 (57)	65 (40)
Pulmonology (226 physicians, 446 patients)	133 (30)	167 (37)	50 (19)	117 (26)	17 (4)	9 (3)	82 (50)	59 (36)
Other specialty (470 physicians, 1,027 patients)	244 (24)	343 (33)	108 (20)	142 (14)	28 (3)	18 (2)	170 (85)	110 (55)
Total (2,096 physicians, 6,281 patients)	2,102 (33)	2,340 (37)	915 (22)	1,378 (22)	219 (3)	138 (3)	1,425 (69)	1,040 (51)

* $P < 0.0001$ for the distribution among specialties.
† Estrogen, testosterone, oral bisphosphonates, calcitonin, and raloxifene.
‡ $P < 0.001$ for the distribution among specialties.
§ $P < 0.05$ for the distribution among specialties.
¶ Self-reported use of over-the-counter treatments. Totals in this column include only survey respondents (n = 2,059), as opposed to the other columns, which reflect results from the entire cohort (n = 6,281) or the female members of the entire cohort, obtained using pharmacy claims.

Table 3. Factors associated with receipt of bone mass measurement and non-estrogen prescription and self-reported over-the-counter therapies for glucocorticoid-induced osteoporosis prevention in 2001–2003*

Characteristic	Bone mass measurement		Prescription medication†		Calcium and/or vitamin D‡	
	OR	95% CI	OR	95% CI	OR	95% CI
Physician specialty (referent: internal medicine)						
Gastroenterology	0.98	0.60–1.61	0.49	0.28–0.86	0.87	0.55–1.38
Family/general practice	0.56	0.30–1.04	0.75	0.41–1.36	0.66	0.39–1.12
Pulmonology	0.69	0.42–1.12	1.04	0.64–1.69	0.62	0.39–0.96
Rheumatology	1.48	1.06–2.08	1.26	0.89–1.79	1.25	0.90–1.73
Other	0.76	0.47–1.22	0.71	0.43–1.18	0.91	0.60–1.40
Sex and age (referent: men <50 years)						
Men 50–70 years	0.95	0.58–1.57	1.23	0.73–2.06	1.21	0.82–1.78
Men >70 years	0.61	0.28–1.35	0.88	0.41–1.91	1.76	1.00–3.09
Women <50 years	2.28	1.47–3.56	1.35	0.84–2.19	2.52	1.76–3.62
Women 50–70 years	4.40	2.81–6.91	3.69	2.29–5.95	5.57	3.84–8.11
Women >70 years	2.28	1.32–3.95	4.31	2.45–7.59	6.38	3.86–10.74
Previous fracture	NS		1.83	1.00–3.38	NS	
New glucocorticoid user (nonuse in past 90 days)	0.65	0.53–0.80	0.74	0.60–0.92	0.75	0.61–0.91
No. of comorbid diseases	1.09	1.05–1.13	1.09	1.05–1.13	NS	
Cumulative glucocorticoid dose (per 300-mg increment)	1.02	1.01–1.03	1.04	1.03–1.05	1.02	1.00–1.03
Ethnicity (referent: white)						
African American	0.55	0.40–0.75	0.71	0.51–0.98	0.55	0.41–0.73
Other (Asian, American Indian, Hispanic, multiracial)	0.56	0.38–0.82	0.68	0.45–1.03	1.26	0.88–1.80
No. of visits to glucocorticoid prescriber	1.03	1.02–1.04	NS		NS	
C statistic	0.75		0.73		0.70	
Hosmer-Lemeshow goodness-of-fit statistic	0.51		0.31		0.64	

* Values are from the 2,059 patients who reported that they had taken glucocorticoids, excluding those with end-stage renal disease (n = 188) and those who did not report ethnicity or reported multiple ethnicities (n = 127). OR = odds ratio; 95% CI = 95% confidence interval; NS = not significant.
† Oral bisphosphonates, calcitonin, and raloxifene.
‡ Self-reported use of over-the-counter products.

Table 3 describes the independent factors that, after adjustment for physician case mix using multivariable logistic regression, were associated with receipt of bone mass measurement, non-estrogen prescription glucocorticoid-induced osteoporosis–preventive medications, and OTC use of calcium and/or vitamin D. Compared with patients of internists, patients of family physicians were somewhat less likely to undergo bone mass measurement, and those of rheumatologists were significantly more likely to do so. Gastroenterology patients were significantly less likely to receive therapy with osteoporosis-specific prescription medications (i.e., bisphosphonates, calcitonin, and raloxifene) compared with internal medicine patients. Patients prescribed glucocorticoids by pulmonologists were significantly less likely to take calcium and/or vitamin D supplements than patients prescribed glucocorticoids by internists. African American patients and patients of other nonwhite ethnicities were less likely to be screened with bone mass measurement or prescribed medications for glucocorticoid-induced osteoporosis. African Americans also were less likely to report use of calcium and vitamin D supplements. Goodness-of-fit statistics for all multivariable models were nonsignificant, consistent with reasonable fit.

Comparison of glucocorticoid-induced osteoporosis screening and preventive treatment in 1995–1998 versus 2001–2003. Figures 2A–C show the changes in prescription of bone mass measurement and use of prescription bone-protective medications and bisphosphonates between the 1995–1998 period and the 2001–2003 period among new users receiving continuous glucocorticoid therapy for ≥90 days. Men experienced the greatest relative change between these 2 time periods, and women age ≥50 years experienced the greatest absolute change. However, even though women age ≥50 years had the highest absolute rates of bone mass measurement and treatment compared with men and younger women, fewer than half underwent bone mass measurement, and fewer than one-third were prescribed a bisphosphonate in 2001–2003. Longitudinal improvement in rates of prescription of these measures from the

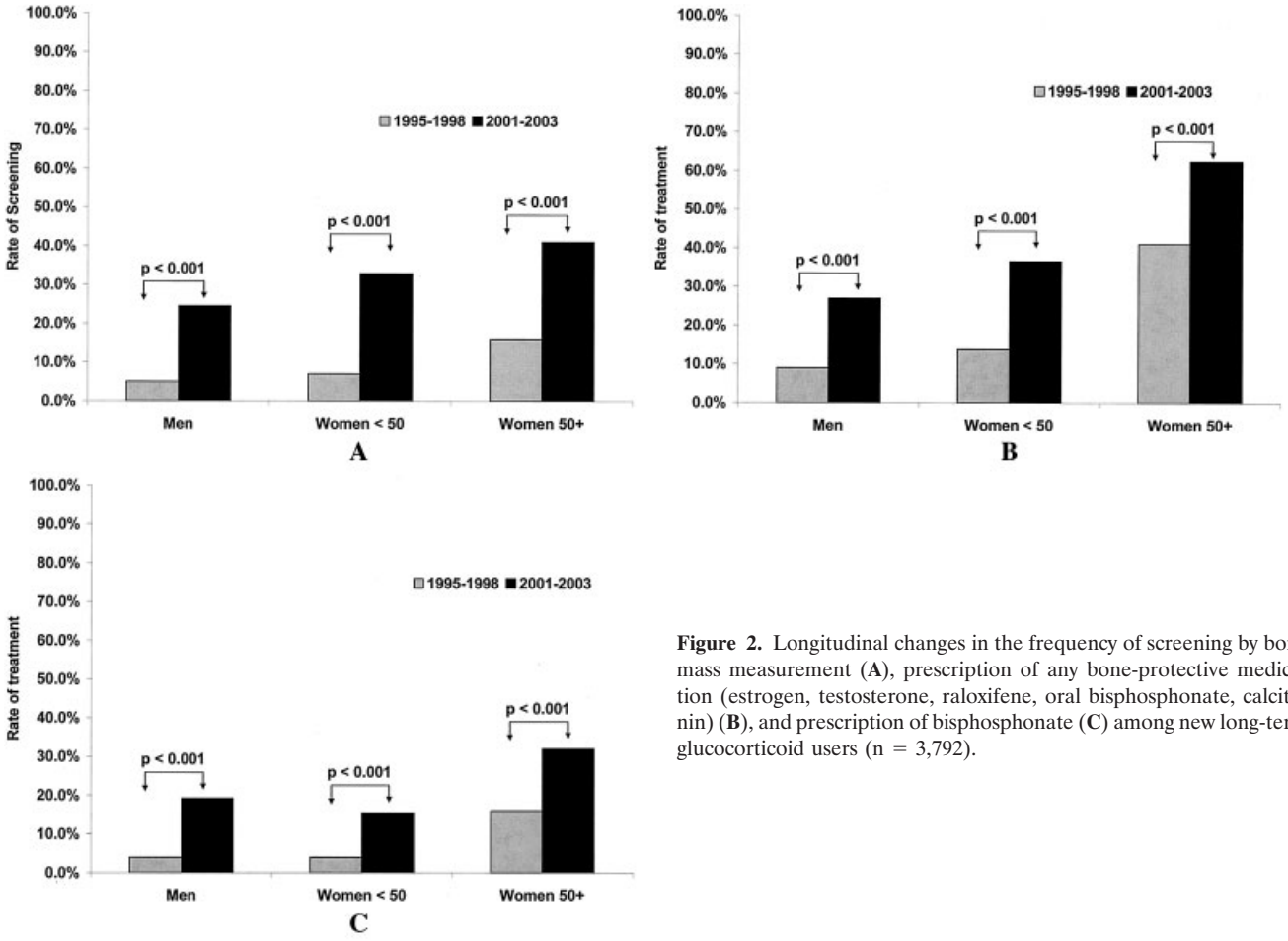

Figure 2. Longitudinal changes in the frequency of screening by bone mass measurement (**A**), prescription of any bone-protective medication (estrogen, testosterone, raloxifene, oral bisphosphonate, calcitonin) (**B**), and prescription of bisphosphonate (**C**) among new long-term glucocorticoid users (n = 3,792).

1995–1998 period to the 2001–2003 period did not differ significantly according to the specialty of the patient's physician (data not shown).

DISCUSSION

In the present study, we observed that rates of prescription of therapy for prevention or treatment of glucocorticoid-induced osteoporosis increased significantly over time, although they remained <50%, even among individuals treated by specialists. Fewer than half of the long-term glucocorticoid users we studied underwent any form of bone mass measurement. Approximately one-third of the cohort was not taking OTC calcium supplements, and one-fourth of the individuals taking prescription antiresorptive medications were not taking calcium or vitamin D. In light of the wide availability of effective therapies to prevent and treat glucocorticoid-induced osteoporosis, some believe the incidence of fractures should be significantly attenuated (19). However, our results suggest that insufficient glucocorticoid-induced osteoporosis screening and preventive treatment remains a barrier to this potentially achievable goal.

In a previous investigation, we examined 2,378 managed care enrollees who had received glucocorticoid therapy for ≥90 days and found that only 21% received any form of prescription therapy for prevention of glucocorticoid-induced osteoporosis, and the majority of these prescriptions were for estrogen (13). Fewer than 10% of the overall group received any form of bone mass measurement. Our longitudinal results comparing 1995–1998 with 2001–2003 show that rates of bone mass measurement and use of bone-specific medication such as bisphosphonates doubled or tripled among patients

treated by generalists and specialists alike. However, similar to findings in our prior study and other US and international studies (11,12,20–24), we found low utilization rates and significant practice pattern variation between physician specialties in screening and preventive therapies for glucocorticoid-induced osteoporosis. We also found significant variation between prescribing physician specialties in the proportion of their patients taking OTC calcium or vitamin D supplements.

Although postmenopausal women are generally at highest absolute risk of fracture, large epidemiologic studies have shown that men and premenopausal women have an increased relative risk of fracture compared with non–glucocorticoid users (25). However, both men and women younger than age 50 years were significantly less likely to receive any form of screening or preventive measures (including calcium or vitamin D) for glucocorticoid-induced osteoporosis than were women age 50 years or older in our study. Our data also are consistent with previous reports that individuals of nonwhite ethnicity are less likely to receive preventive therapies for glucocorticoid-induced osteoporosis (14). Although US and international groups recommend prescription of bisphosphonates or other antiresorptive agents for patients *beginning* glucocorticoid therapy regimens of ≥3 months (16) in recognition of the early bone loss often observed when glucocorticoids are first prescribed (26,27), we found that new users were significantly less likely to receive preventive medications or take OTC calcium and/or vitamin D.

The optimal rate of screening and preventive treatment for glucocorticoid-induced osteoporosis cannot be definitively determined using our methodology, since evidence-based guidelines may not be entirely relevant to the care of an individual patient (28,29). A limitation inherent to claims-based data is that these sources may underreport care that is delivered or care that the physician offers but the patient declines. Thus, a benchmark should reasonably be set at <100%. However, rates in our cohort were <50% even using our conservative definitions of screening and treatment, i.e., 1 bone mass measurement or 1 bone-protective medication prescription over 2.5 years. To put this in a more general perspective, in the US, adherence to many of the benchmarks established by the National Committee on Quality Assurance for chronic disease management routinely exceeds 80% (30).

One potential controversy surrounds the appropriate frequency of bone mass measurement in long-term glucocorticoid users, and some guidelines suggest that bone mass measurement every 6–12 months is reasonable (16). Bone mineral density screening has been associated with a significantly decreased risk of future hip fracture (31), although the mechanism by which this association may be causal remains unclear. Given the uncertainties regarding the optimal timing for bone mass measurement in long-term glucocorticoid users, we allowed bone mass measurement within 30 months of glucocorticoid prescription to represent a reasonable quality standard. Even if the argument is made that bone mass measurement is unnecessary in long-term glucocorticoid users and that empiric treatment is warranted, our data do not provide much evidence that this actually occurred in a majority of individuals in our large, population-based sample. However, we did note that among women age ≥50 years, bone mass measurement declined in older age groups (age ≥70 years) even though rates of prescription of treatment continued to increase. We speculate that this may reflect an attempt to risk-stratify 55–65-year-old women using bone mass measurement and provide empiric treatment to older women based on their age-related fracture risk. We did observe that increasing cumulative glucocorticoid dose was a significant predictor of both testing and preventive treatment for glucocorticoid-induced osteoporosis in our multivariable models.

In light of increasing data documenting an elevated risk of fracture when glucocorticoids are used long-term even at low doses (7) and evidence supporting the efficacy of therapies to attenuate this risk, it is somewhat surprising that many patients are not screened or treated for glucocorticoid-induced osteoporosis. Based on our data, we identified a variety of factors associated with lack of screening and prevention. Individuals receiving long-term glucocorticoid treatment in our study population had a high burden of comorbidity (average of 6 major diseases), and high or low burdens of disease comorbidity may alter physicians' provision of glucocorticoid-induced osteoporosis–related care. Although our data showed that an increasing number of comorbid diseases was positively associated with osteoporosis care, other studies have indicated that individuals with high comorbidity burdens were less likely to be screened or treated for osteoporosis (32,33). Differences in the methods used to code comorbidity (e.g., using a disease count threshold instead of a continuous count) may account for this apparent discordance.

For men and premenopausal women, uncertainties regarding absolute risk for fracture, the applicability of clinical trials of glucocorticoid-induced osteoporosis in which bone mineral density rather than fracture is the

end point, and the cost-effectiveness of preventive therapy for glucocorticoid-induced osteoporosis in lower-risk patients (34) may contribute to the low rate of diagnostic and therapeutic intervention. Some glucocorticoid-induced osteoporosis guidelines recommend caution in the use of bisphosphonates in premenopausal women at risk for pregnancy (16). However, to date, no drugs other than bisphosphonates have documented efficacy in terms of fracture risk reduction in glucocorticoid-treated patients. Although there is increasing evidence in support of the contention that glucocorticoids lower the fracture threshold (35) and are an independent risk factor for fracture even after controlling for bone mineral density (36,37), these data may not be widely known, especially among physicians without a particular interest in metabolic bone diseases. Our observation that patients of rheumatologists and internists had higher rates of bone mass measurement and osteoporosis-related treatment than patients of physicians in most other specialties supports this contention.

Our study has several strengths. The large, population-based claims data source permitted us to examine and adjust for a variety of comorbid illnesses. Pharmacy data, rather than self-report, were used to determine glucocorticoid use patterns and reduce potential recall bias. Our study design captured the diverse diseases treated with glucocorticoids and included patients who had intermittent use of glucocorticoids, allowing better generalizability than other studies that focus on populations treated with glucocorticoids for only 1 condition or with only continuous oral therapy. Using a linked survey, we were able to include factors, such as ethnicity, which often cannot be assessed in observational studies that utilize only administrative data or even medical chart review. We also were able to examine use of OTC calcium and vitamin D supplements. Unlike previous studies, our time period of interest postdated major improvements in reimbursement for bone mass measurement and the introduction (in the late 1990s) of several bone-protective medications.

Despite these strengths, some limitations of our study deserve mention. Although less than half of the cohort underwent bone mass measurement, we did not have access to the results of this test in those who were screened. Bone mass measurement results would be expected to influence physicians' decisions to prescribe or withhold therapy for glucocorticoid-induced osteoporosis. Our use of a combined end point (receipt of bone mass measurement *or* prescription of a bone-protective medication) may partially mitigate this concern. However, despite our examination of the 6 months before the index date for bone mass measurement and inclusion of a predominantly new glucocorticoid user population, it is possible that bone mass measurement may have been performed prior to that time and followup testing deemed unnecessary by managing physicians. We were unaware of the indication for treatment with hormone replacement therapy, which is a less specific approach to prevention of glucocorticoid-induced osteoporosis compared with the other medications we studied. Thus, our inclusion of hormone replacement yields an even more conservative estimate of the degree of undertreatment for prevention of glucocorticoid-induced osteoporosis. Although all enrollees had pharmacy benefits through the MCO, the amount of their copayment requirement was unknown to us and may have modestly influenced filling of prescriptions. We recorded provider specialty based on the DEA number linked to the glucocorticoid prescriptions, but physician specialty may be misclassified if another specialist was responsible for the majority of the patient's followup care. Notwithstanding, we contend that all physicians prescribing glucocorticoids should assume at least some responsibility for the management of the potential side effects of these agents. Finally, although our cohort was drawn from a large, diverse managed care setting, our results may not be generalizable to US residents not enrolled in managed care plans or to persons living in other countries.

In summary, although glucocorticoid-induced osteoporosis is potentially preventable, physicians continue to utilize screening technologies and prescribe medications that mitigate the risk of fracture at relatively low rates. Although we found an increase in the use of bone-protective agents over time, overall bone mass measurement and rates of prescription of prophylaxis for glucocorticoid-induced osteoporosis remain low in comparison with management of other common disorders, even among specialists. Improving care for long-term glucocorticoid users remains a high priority. Further characterization of general and specialty-specific barriers to improved preventive care for glucocorticoid-induced osteoporosis and targeted intervention efforts aimed at improving adherence to evidence-based practice management guidelines are necessary activities to improve health care for this all-too-common complication.

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