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ORIGINAL ARTICLE

Population-Based Assessment of Adverse Events Associated With Long-Term Glucocorticoid Use

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Objective. **The frequency of many adverse events (AEs) associated with low-dose glucocorticoid use is unclear. We sought to determine the prevalence of glucocorticoid-associated AEs in a large US managed care population.**

Methods. **Using linked administrative and pharmacy claims, adults receiving ≥60 days of glucocorticoids were identified. These individuals were surveyed about glucocorticoid use and symptoms of 8 AEs commonly attributed to glucocorticoid use.**

Results. **Of the 6,517 eligible glucocorticoid users identified, 2,446 (38%) returned the mailed survey. Respondents were 29% men with a mean ± SD age of 53 ± 14 years; 79% were white and 13% were African American. Respondents had a mean ± SD of 7 ± 3 comorbid conditions and were prescribed a mean ± SD prednisone-equivalent dosage of 16 ± 14 mg/day. More than 90% of individuals reported at least 1 AE associated with glucocorticoid use; 55% reported that at least 1 AE was very bothersome. Weight gain was the most common self-reported AE (70% of the individuals), cataracts (15%) and fractures (12%) were among the most serious. After multivariable adjustment, all AEs demonstrated a strong dose-dependent association with cumulative glucocorticoid use. Among users of low-dose therapy (≤7.5 mg of prednisone per day), increasing duration of use was significantly associated with acne, skin bruising, weight gain, and cataracts.**

Conclusion. **The prevalence of 8 commonly attributed self-reported glucocorticoid-associated AEs was significantly associated with cumulative and average glucocorticoid dose in a dose-dependent fashion. Physicians should be vigilant for glucocorticoid-related AEs and should counsel patients about possible risks, even among low-dose long-term users.**

KEY WORDS. Glucocorticoids; Adverse events; Cataracts; Fractures.

INTRODUCTION

Glucocorticoids are estimated to be used long-term by 0.5–1% of the general population and up to 2.5% of older adults (1,2). Despite the established role of glucocorticoids in controlling short-term inflammation, and despite emerging evidence supporting a disease-modifying role in rheumatoid arthritis (3–6), concern for adverse events (AEs) associated with glucocorticoids often limits their use. For many individuals, potential AEs such as acne, weight gain, and sleep/mood disturbance may be mild. For others, perceived AEs such as cataracts or glucocorticoid-induced osteoporosis with subsequent fracture may be severe and result in substantial morbidity and mortality (7–15). Estimates regarding the prevalence and severity of many glucocorticoid-associated AEs are largely unknown, especially those less likely to require hospitalization or specific medications for prevention or treatment. Of note, the relationship between these common AEs and various glucocorticoid doses is also unclear, and the safety of long-term, low-dose prednisone (e.g., daily dosage ≤7.5 mg) remains controversial.

We hypothesized that the prevalence of AEs associated with even low-dose glucocorticoid use would be high and would be dose and duration dependent. We therefore conducted a population-based survey of glucocorticoid users to obtain prevalence estimates of glucocorticoid-associated AEs. We specifically focused on these endpoints

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among individuals who had prolonged use of an average daily dose of ≤7.5 mg of prednisone.

SUBJECTS AND METHODS

Data sources. Long-term glucocorticoid users were identified within a national managed care organization (MCO) population covering 3 million lives in 36 states. These users and some of their demographic and disease characteristics were identified from the linked claims and pharmacy databases of the MCO's health maintenance organization, point of service, and preferred provider organization health plans. Diseases, medications, and procedures were identified 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 copayments.

Cohort inclusion criteria. Individuals were characterized as long-term glucocorticoid users if they were ≥18 years of age and had filled ≥60 days of outpatient oral glucocorticoid prescriptions from July 1, 2001 to December 31, 2002. Each member was enrolled in the health plan at least 6 months prior to and following the first qualifying glucocorticoid prescription (the index date). A total of 6,517 health plan members met the inclusion criteria for long-term glucocorticoid use and were selected for further study.

Because of potential differences in the prevalence of both short- and long-term AEs associated with incident and prevalent glucocorticoid use, individuals were described as new or prevalent users. New users were defined as adults who had not received 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 might impact outcomes of interest. These 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.

Glucocorticoid medications. Qualifying glucocorticoids identified using pharmacy data included prednisone, prednisolone, dexamethasone, and other oral systemic glucocorticoids commonly used in practice in the United States. Injectable, topical, and intraocular glucocorticoids were not included. Each prescription was converted to a daily measure of a prednisone-equivalent dose (in milligrams). The number of days the individual received oral glucocorticoids within the 18-month medication eligibility window was examined to calculate the average and cumulative glucocorticoid exposure. Prescriptions for implausible daily doses (i.e., >100 mg/day of oral prednisone) were recoded using the patient's average daily dose computed without these outlier prescriptions. Of the 60,465 total glucocorticoid prescriptions, only 213 (0.35%) prescriptions among 134 subjects needed to be recoded in this fashion.

Glucocorticoid survey administration. A 4-page, 69-question survey was mailed to 6,517 members who met the inclusion criteria for long-term glucocorticoid use. A followup postcard and a second survey were mailed to nonresponders within 60 days of the first mailing. In the survey, we asked individuals to confirm that they had actually taken oral glucocorticoids and whether they had experienced ≥1 of 8 specific AEs commonly attributed to glucocorticoid use (sleep disturbance, acne, skin bruising/thinning, weight gain, mood problems, diabetes or high blood sugar, cataracts, and fractures) while taking oral glucocorticoids. Respondents were asked to classify symptoms as not, a little, or very bothersome. Individuals were not requested to speculate on a causal relationship between glucocorticoid use and the symptoms listed, but were only asked, "Have you ever had . . . while taking steroids?" Subjects were also asked whether their physician had discussed possible AEs of glucocorticoid use with them prior to use. Questions left blank or with multiple responses were treated as missing data and were excluded from analysis.

Statistical analyses. Descriptive statistics characterized basic demographics of survey responders and nonresponders. Categorical variables were compared using the chi-square test of independence, and continuous variables were compared using the 2-tailed *t*-test. Despite MCO pharmacy data documenting filled prescriptions for at least 60 days of glucocorticoids for each subject, only those who confirmed that they had actually taken the glucocorticoids were analyzed. To facilitate comparison of AEs related to glucocorticoid dose, cumulative dose (over 24 months) was categorized into quartiles (<1.7 gm, 1.7–2.8 gm, 2.8–4.7 gm, and >4.7 gm of prednisone) and average daily dose was categorized into groups of clinical relevance (0–7.5 mg, 7.6–20 mg, and >20 mg of prednisone per day).

Multivariable stepwise logistic regression was performed to identify significant associations between cumulative glucocorticoid dose and AEs. Cumulative glucocorticoid dose was included in all models, and age and sex were also included in the fracture models. To test hypotheses related to the safety of increasing duration of use among recipients of ≤7.5 mg/day of prednisone, total duration of use was forced into each model. For all other variables, a univariate P value < 0.25 was required for entry into the model and a P value < 0.05 was required to remain in the model. Model building was conducted according to Hosmer and Lemeshow (16), and model discrimination was assessed using the c statistic (17). To assess trends across glucocorticoid dose groups, we modeled increasing dose category as a continuous variable and used a Wald statistic to assess significance. All analyses were performed using SAS software (SAS Institute, Cary, NC).

RESULTS

A total of 2,446 (38%) managed care enrollees that met the definition for long-term glucocorticoid use returned the

Table 1. Characteristics of long-term glucocorticoid (GC) users responding to survey (n = 2,167)*

Demographics	Value
Age, mean ± SD years	53 ± 14
Female sex	1,538 (71)
Length of enrollment in the health plan, mean ± SD months	27 ± 13
Ethnicity†	
White	1,628 (79)
African American	266 (13)
Other (e.g., Asian, Hispanic)	160 (8)
High school education or less†	792 (38)
Married†	1,414 (67)
Employed†	1,127 (56)
Annual household income <$20,000†	236 (12)
GC use	
Average prednisone equivalent dose, mean ± SD mg/day	16 ± 14
Highest dose prednisone received, mean ± SD mg/day	28 ± 30
Cumulative prednisone equivalent dose, mean ± SD gm	3.6 ± 3.1
Duration of prednisone use, mean ± SD days‡	284 ± 177
New GC user (≥90 days without prior GC prescription)	1,329 (61)
Medical comorbidities	
Number of comorbid conditions, mean ± SD	7 ± 3
Medical diagnoses from claims data	
Diabetes	342 (16)
Hypertension	962 (44)
Chronic renal failure	171 (8)
Congestive heart failure	170 (8)
Diagnoses associated with GC use	
Rheumatoid arthritis	892 (41)
Chronic obstructive pulmonary disease	290 (13)
Systemic lupus erythematosus	264 (12)
Asthma/reactive airway disease	266 (12)
Inflammatory bowel disease	167 (8)

* N = 2,167 subjects after excluding individuals who did not confirm that they had actually taken glucocorticoids. Values are the number (percentage) unless otherwise indicated.
† Total <2,167 because of missing survey data.
‡ During study period of 2 years.

survey. Their characteristics are described in Table 1. Individuals were middle aged, predominantly women, and received prescriptions for an average of 16 mg/day of prednisone. A majority were new users rather than prevalent glucocorticoid users. Persons with rheumatoid arthritis were prescribed a mean ± SD dosage of 12 ± 8 mg/day of prednisone, in contrast to persons with inflammatory bowel disease who received a mean ± SD prednisone dosage of 31 ± 16 mg/day (data not shown). The mean daily prednisone doses for the other diseases, including systemic lupus erythematosus, chronic obstructive pulmonary disease, and asthma, fell between these 2 extremes. Hypertension and rheumatoid arthritis were among the most common comorbid diagnoses. More than 91% of respondents indicated that they had ever taken glucocorticoids, 7% said that they had never taken them, and 2% did not answer (data not shown). Sixty-five percent of the ever users reported current use at the time they completed the survey. Among those who reported ever using glucocorticoids, a majority (68%) reported discussing potential glucocorticoid-related AEs with their doctor prior to use.

Compared with survey responders, the 4,071 survey nonresponders were younger (mean age 48 versus 53 years) and were more likely to be male (36% versus 30%). Nonresponders' duration of enrollment in the health plan, mean prednisone dose, and average number of comorbid conditions were similar to survey responders (data not shown).

Relationship between glucocorticoid dose and AEs. The prevalence and self-reported severity of AEs experienced, stratified by quartile of cumulative glucocorticoid use, are shown in Figure 1. The AE with the greatest self-reported prevalence was weight gain, which was experienced by almost 80% of subjects in the highest quartile of glucocorticoid use. Skin bruising/thinning and sleep disturbance were the next most commonly reported AEs. Cataracts (15% overall) and fractures (12% overall) were reported less frequently. Only 10% of subjects reported that they had not experienced any of the AEs concurrent with glucocorticoid use. We examined claims data for fractures separately during the 30-month observation period. Ten percent of the cohort had ≥1 medical service claims for a fracture during the 2.5-year period of observation.

The adjusted relative risks of AEs associated with cumulative glucocorticoid dose are described in Table 2. A strong dose-response relationship was observed between increasing quartiles of glucocorticoid use and all of the AEs examined. To assess the validity of our self-reported

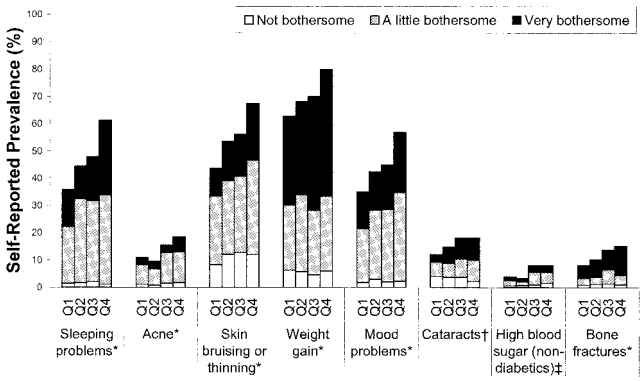

Figure 1. Prevalence of adverse events associated with long-term glucocorticoid use stratified by cumulative glucocorticoid dosage (n = 2,167 subjects after excluding individuals who did not confirm that they had actually taken glucocorticoids). Quartiles of cumulative prednisone-equivalent glucocorticoid dosage: Q1 = <1.7 gm (e.g., 10 mg/day of prednisone for 6 months); Q2 = 1.7–2.8 gm (e.g., 10 mg/day of prednisone for 9 months); Q3 = 2.9–4.7 gm (e.g., 10 mg/day of prednisone for 12 months); Q4 = >4.7 gm (e.g., 10 mg/day of prednisone for 18 months). * $P < 0.0001$ (Cochran-Armitage trend test). † $P < 0.01$ (Cochran-Armitage trend test). ‡ $P < 0.001$ (Cochran-Armitage trend test).

Table 2. Relationship between cumulative prednisone-equivalent dose and self-reported adverse events*

Characteristics/quartile†	Adjusted OR	95% CI
Sleep disturbance (n = 2,146)‡		
Q1	1.0	–
Q2	1.57	1.22–2.02
Q3	1.68	1.31–2.16
Q4	2.77	2.14–3.59
Acne (n = 2,040)§		
Q1	1.0	–
Q2	1.05	0.69–1.60
Q3	1.50	1.02–2.20
Q4	1.63	1.12–2.37
Skin bruising or thinning (n = 2,144)¶		
Q1	1.0	–
Q2	1.51	1.18–1.94
Q3	1.65	1.28–2.12
Q4	3.04	2.33–3.95
Weight gain (n = 2,040)#		
Q1	1.0	–
Q2	1.42	1.08–1.85
Q3	1.79	1.36–2.37
Q4	2.20	1.65–2.95
Mood problems (n = 2,025)**		
Q1	1.0	–
Q2	1.65	1.27–2.16
Q3	1.55	1.19–2.02
Q4	2.39	1.83–3.12
High blood sugar (among nondiabetics; n = 1,719)††		
Q1	1.0	–
Q2	0.67	0.33–1.34
Q3	1.68	0.95–2.99
Q4	1.82	1.04–3.19
Cataracts (n = 1,869)‡‡		
Q1	1.0	–
Q2	1.19	0.80–1.78
Q3	1.51	1.03–2.23
Q4	1.83	1.25–2.69
Fracture (n = 1,899)§§		
Q1	1.0	–
Q2	1.32	0.83–2.08
Q3	1.73	1.11–2.69
Q4	1.97	1.27–3.05

* Total sample size for each model shown in parentheses less than entire cohort (n = 2,167) due to missing survey responses. OR = odds ratio; 95% CI = 95% confidence interval.
† Quartiles of cumulative glucocorticoid dosage (prednisone equivalents): Q1 = <1.7 gm (e.g., 10 mg/day of prednisone for 6 months); Q2 = 1.7–2.8 gm (e.g., 10 mg/day of prednisone for 9 months); Q3 = 2.9–4.7 gm (e.g., 10 mg/day of prednisone for 12 months); Q4 = >4.7 gm (e.g., 10 mg/day of prednisone for 18 months).
‡ Adjusted for age, sex, and number of comorbid diseases; c statistic = 0.66.
§ Adjusted for age, sex, and ethnicity; c statistic = 0.76.
¶ Adjusted for age, sex, new user, and number of comorbid diseases; c statistic = 0.67.
# Adjusted for age, sex, new user, ethnicity, and number of comorbid diseases; c statistic = 0.70.
** Adjusted for age, sex, ethnicity, and number of comorbid diseases; c statistic = 0.69.
†† Adjusted for ethnicity and number of comorbid diseases; c statistic = 0.68.
‡‡ Adjusted for age, ethnicity, number of comorbid diseases, and income; c statistic = 0.72.
§§ Adjusted for age, sex, income, and number of comorbid diseases; c statistic = 0.65.

fracture models, we separately modeled fractures using medical claims data. Even after multivariable adjustment, a positive and significant association with increasing cumulative glucocorticoid dose was observed (data not shown).

Among users of >7.5 mg/day of prednisone, glucocorticoid dose and duration of use were strongly associated with all AEs (data not shown). The adjusted odds ratios of increasing duration of glucocorticoid use among individuals prescribed ≤7.5 mg/day of prednisone are presented in Table 3. Acne, skin bruising, weight gain, and cataracts were significantly associated with longer durations of low-dose glucocorticoid use. In contrast, increasing daily dose (within the 0–7.5 mg/day range) was more strongly associated with sleep disturbance and fractures than was increased duration of use. The Spearman correlation coefficient between cumulative glucocorticoid dose and average daily dose was 0.55.

DISCUSSION

We found a high prevalence of self-reported AEs associated with glucocorticoid use among individuals treated long-term for a variety of conditions. Almost all respondents reported at least 1 AE that was temporally associated with concurrent glucocorticoid use, and more than half reported that at least 1 AE was very bothersome. Serious AEs potentially attributable to glucocorticoid exposure were also common, with 15% of the cohort self reporting cataracts and 12% self reporting ≥1 fractures. Increasing cumulative glucocorticoid dose had a strong positive association with serious AEs typically attributed to glucocorticoid use, even after multivariable adjustment for demographic and disease comorbidities that were also associated with these outcomes.

Long-term observational studies of patients receiving commonly prescribed doses of glucocorticoids have reported high rates of glucocorticoid-associated AEs. A study of 120 patients with giant cell arteritis (mean age at diagnosis 75 years) followed for a median of 10 years found that 86% of patients experienced ≥1 AEs (18); 58% of the patients experienced ≥2 serious AEs, the most common of which were cataracts (41%) and fractures (38%). In a similarly designed study of 232 patients with polymyalgia rheumatica (19) (mean age at diagnosis 73 years) followed for an average of 8 years, 65% of individuals treated with glucocorticoids experienced at least 1 AE, the most common of which were vertebral fracture (18%) and cataracts (36%). Cumulative glucocorticoid dose had a strong association with AEs, particularly after the dosage reached 1.8 gm, which was the approximate cutpoint between the first and second quartiles in our analyses. Our results are similar to these studies because 90% of our subjects reported at least 1 AE while receiving glucocorticoids. Rates of self-reported fracture (12%) and cataract (15%) in our study were high, although lower than these 2 reports, likely reflecting a younger population, diverse indications for glucocorticoid treatment, and lower cumulative glucocorticoid exposure.

More recent interest has focused on the clinical efficacy and potential disease-modifying properties of long-term

Table 3. Relationship between glucocorticoid dose and duration and adverse events among low-dose (prednisone ≤7.5 mg/day) glucocorticoid users (n = 670)*

Characteristics	90-day increase in duration of use	95% CI	Average daily dose (per 1-mg/day increase within 0–7.5 mg/day range)	95% CI
Sleep disturbance†	NS	NS	1.14	1.02–1.28
Acne‡	1.17	1.04–1.32	NS	NS
Skin bruising or thinning§	1.17	1.08–1.26	NS	NS
Weight gain¶	1.09	1.01–1.18	NS	NS
Mood problems#	NS	NS	NS	NS
High blood sugar (among nondiabetics)**	NS	NS	NS	NS
Cataracts††	1.17	1.06–1.29	NS	NS
Fracture‡‡	NS	NS	1.26	1.04–1.53

* 95% CI = 95% confidence interval; NS = not significant.
† Adjusted for age, sex, and number of comorbid diseases; c statistic = 0.63.
‡ Adjusted for age and sex; c statistic = 0.77.
§ Adjusted for age and sex; c statistic = 0.65.
¶ Adjusted for age and sex; c statistic = 0.68.
# Adjusted for age, ethnicity, and heart failure; c statistic = 0.69.
** Adjusted for ethnicity; c statistic = 0.64.
†† Adjusted for age and number of comorbid diseases; c statistic = 0.71.
‡‡ Adjusted for age, sex, income, and number of comorbid diseases; c statistic = 0.65.

low-dose prednisone (≤7.5 mg/day), particularly for patients with arthritis. In small clinical trials of patients with rheumatoid arthritis randomized to low glucocorticoid doses (prednisolone 7.5–10 mg daily), vertebral fractures, weight gain, and hyperglycemia were observed among the glucocorticoid-treated patients, although incidence rates of these AEs were low (3,4). These and other trials with aggressive glucocorticoid tapering regimens (5) have demonstrated that low-dose or rapidly tapered glucocorticoids may result in minimal short-term glucocorticoid-associated toxicity. The strengths of these randomized, prospective, placebo-controlled trials are their blinded outcomes assessment; lack of confounding by disease severity; and prohibition of even short-term, high-dose glucocorticoid exposure. Factors that may limit their generalizability include selection of individuals with few comorbid illnesses and insufficient duration of followup to detect many of the AEs that develop and/or progress over time.

In contrast to these clinical trial findings, an observational study with a longer followup period compared patients with rheumatoid arthritis treated with a mean of 7 mg/day of near-continuous prednisone therapy for 4.9 years with similar patients with rheumatoid arthritis not treated with glucocorticoids (12). In the glucocorticoid-treated group, 82% experienced at least 1 AE compared with 24% in the control group. Fractures (19%) and cataracts (15%) were the most common serious AEs. We also found several AEs that were significantly associated with longer durations and small increments in glucocorticoid dose, even among ≤7.5 mg/day prednisone users (Table 3), and we demonstrated a dose-dependent increase in fracture risk in this group that is concordant with other studies of low-dose glucocorticoid users (10,20). Moreover, although the 892 individuals with rheumatoid arthritis in our study received the lowest mean daily dosage of prednisone (12 mg/day) compared with those with other diseases that we examined, only 40% received a mean of ≤7.5 mg/day over 24 months. These data suggest that long-term use of low-dose prednisone in a large, diverse managed care population is typically administered only to a minority of individuals with rheumatoid arthritis.

Our study has several strengths. The large, population-based design coupled with the claims data and pharmacy linkage permitted us to analytically account for a variety of comorbid illnesses that were ascertained using both self-reported and administrative sources. Pharmacy data, rather than self report, were used to determine glucocorticoid use patterns and thus reduce potential recall bias. We were able to capture self-reported AEs that are often not assessed in observational studies that utilize only administrative data or even medical chart review. Our study captured the diverse diseases treated with glucocorticoids and included use of intermittent glucocorticoid prescriptions, allowing better generalizability than other studies that have focused on populations treated with glucocorticoids for only 1 condition or with only continuous therapy. Finally, we were able to examine demographic covariates such as ethnicity and education that are rarely available in medical record or claims-based data sources.

One limitation of our work is that AEs were self reported, and confirmation by a physician was not available. Although self report may be the only reasonable source of information for certain subjective AEs such as mood and sleep disturbance, acne, and skin changes associated with glucocorticoid use, it may not be optimal for other outcomes such as fracture. However, the positive predictive value of self-reported fracture has been reported to be >80% at any fracture site and often in excess of 95% for osteoporotic fracture sites (21–24). Because of uncertainty as to whether a medical claim for fracture represented a new (incident) fracture or followup for a prevalent fracture, we censored fracture data after a single event and therefore likely underestimated fracture incidence among individuals who experienced >1 new fracture. Vertebral

fractures may be asymptomatic and may not be identified in as many as two-thirds of patients (25,26), which provides an additional reason for our fracture estimates to be conservative. We were able to compare our results based on self-reported outcomes with fracture outcomes from administrative data and achieved similar results. Compared with fractures, less research has been conducted to validate self report of cataracts, but the positive predictive value of self-reported cataracts has been estimated to be ~83% (95% confidence interval 79–88%) (27).

Another limitation of our work is that the self-reported outcome data are cross-sectional, and determining the temporal sequence of AEs to implicate a causal relationship with glucocorticoid exposure is problematic. For this reason, we intentionally excluded persons with medically recognized diabetes from our high blood sugar analysis (16% of the cohort). This conservative strategy underestimates the proportion of those who developed incident diabetes as a consequence of glucocorticoid therapy. Despite the similarity of survey respondents and nonrespondents in the distribution of comorbid conditions and mean daily prednisone dose (ascertained using administrative data), possible response bias may have influenced our findings if individuals that experienced glucocorticoid-associated AEs were more likely to respond to the survey. Additionally, glucocorticoids have been associated with a variety of other AEs (e.g., infection, hypertension) that we did not assess.

Finally, we were not able to compare our prevalence of self-reported AEs with that of a control group with similar diseases of equal severity that did not receive glucocorticoids. Confounding by disease severity is a concern in observational studies where "sicker" patients have increased exposure to a drug of interest (28). We adjusted for general comorbidity using the number of unique diseases for which the individual received medical care in the prior 30 months. However, because of the diverse nature of the diseases for which individuals were prescribed glucocorticoids, we were not able to adjust for all factors indicative of more severe disease (e.g., rheumatoid nodules and erosions for patients with rheumatoid arthritis); therefore, residual confounding by disease indication or severity is possible. However, we demonstrated a strong dose-response relationship between rates and severity of AEs and increasing doses of cumulative and daily oral glucocorticoids, even after adjusting for a variety of demographic factors and comorbidities.

The prevalence of overall and very bothersome AEs associated with long-term glucocorticoid use was high, even among users of lower doses, and this observation may be underappreciated by clinicians. Because patients may be concerned about the potential AEs of glucocorticoids prior to use (29), physicians need to be well apprised of their risks. A majority of individuals in our cohort reported discussing potential glucocorticoid-associated AEs with their physician prior to initiating therapy. This observation highlights the opportunity for physicians to discuss with patients the possible AEs of glucocorticoids in the context of their expected benefits.

Although the best way to reduce glucocorticoid-associated AEs is to limit exposure and dose, for some individuals the expected benefits will outweigh the possible risks. For example, among patients with early rheumatoid arthritis, combination therapy that includes glucocorticoids may have a sustained, disease-modifying effect (30). However, minimizing potentially avoidable AEs such as glucocorticoid-induced osteoporosis, for which there are efficacious but underutilized therapies (31–34), must be a shared responsibility among physicians and patients. Despite advances in chronic disease management, it is unlikely that the long-term use of glucocorticoids will disappear any time soon. As such, heightened attention to common glucocorticoid-associated AEs that bother patients, even among users of lower doses, is warranted.

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