RESEARCH

3-Year Results of a Member and Physician Intervention to Reduce Risk Associated With Glucocorticoid-Induced Osteoporosis in a Health Plan

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ABSTRACT

BACKGROUND: Accelerated bone loss is a well-known outcome of chronic treatment with glucocorticoids, making glucocorticoid-induced osteoporosis a significant cause of morbidity and a burden on health care resources. Recommendations for prevention and treatment of glucocorticoid-induced osteoporosis include therapy with a bisphosphonate or calcitonin for patients taking a prednisone equivalent of 5 mg per day or more for 3 months or more.

OBJECTIVE: To evaluate the effects of a targeted member and physician educational intervention on the use of anti-osteoporotic drug therapy in patients using chronic oral glucocorticoid therapy.

METHODS: Pharmacy claims were analyzed for a 4-month period in each of 3 years, for claims with dates of service from April 1 through July 30, 2003, May 1 through August 31, 2004, and February 4 through May 5, 2005, to identify all adult members of a health plan of approximately 1.3 million members who received an oral glucocorticoid (e.g., prednisone, dexamethasone) for at least 90 of 120 days (chronic use) and did not receive a medication for osteoporosis prevention (e.g., risedronate, ibandronate, etidronate, raloxifene, alendronate, calcitonin) during the same 120-day time period. The intervention involved direct-to-patient mailing of a cover letter and a 2-page educational brochure, and a physician mailing that included the same 2-page educational brochure, a 1-page table of recommended drug therapies for prevention of osteroporosis, and an invitation for physicians to request by fax-back a list of at-risk patients. Follow-up claims analyses were conducted for 120 days after each of the 3 intervention periods to determine the number and percentage of target patients who were initiated and maintained on a medication to prevent osteoporosis.

RESULTS: The prevalence of health plan members at risk of glucocorticoid-induced osteoporosis was 0.28% in 2003, 0.29% in 2004, 0.29% in 2005, and 0.29% during the 3 years combined. Approximately 47.5% of patients (n=5,140) during the 3-year period who received chronic glucocorticoids also received drug therapy for prevention or treatment of osteoporosis. Women made up 59.6% (6,450/10,822) of patients who received chronic glucocorticoid therapy during the 3 years; 50.9% (3,285/6,450) of the female patients, and 54.8% (2,397/4,372) of the male patients on chronic glucocorticoid therapy were at risk because of the absence of preventive therapy with an anti-osteoporosis medication. During the 3 years, 404 (7.1%) of the total 5,682 male and female patients at risk because of chronic glucocorticoid therapy and who were the subjects of the educational intervention were started on an osteoporosis medication following the mailings. Of these, 84.9% (343/404) continued on both the glucocorticoid therapy and an anti-osteoporosis medication in the subsequent 4-month follow-up period. During the 3 years, only 4.9% of targeted physicians (n=196), affecting 6.8% of at-risk patients (n=387), requested a list of their patients at risk via the fax-back opportunity.

CONCLUSION: A simple intervention program that screened at-risk patients and reached out to these patients and their physicians via a target-mailing intended to reduce the risk of glucorticoid-induced osteoporosis was associated with a modest increase in the proportion of at-risk patients receiving preventive drug therapy for osteoporosis.

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What is already known about this subject

- The use of oral glucocorticoids, such as prednisone, during a period as short as 90 days contributes to the reduction in bone mineral density and has been associated with increased risk of vertebral, hip, forearm, and non-vertebral fractures. The rate of increased risk varies with type of fracture and the dose and duration of therapy with glucocorticoids.

What this study adds

- During 3 years of observation, from 2003 through 2005, 0.29% of health plan members received 90 days or more (chronic) therapy with an oral glucocorticoid, and 47.5% of these patients also received an anti-osteoporosis drug.
- Slightly more than half of the patients who received 90 days or more of glucocorticoid therapy were at increased risk of fracture due to the absence of anti-osteoporosis therapy; 50.9% of female patients and 54.8% of male patients were at risk.
- Using a pre-post study design without a control group, a simple intervention program using direct-to-patient and physician mailings was associated with 6% to 9% (7.1% during 3 years) of targeted at-risk patients starting anti-osteoporosis drug therapy following the intervention.
- Only 4.9% of targeted physicians (accounting for 6.8% of at-risk patients) who received the mailing requested a list of their patients at risk for glucocorticoid-induced osteoporosis. The number of physicians contacted regarding patients at risk for glucocorticoid-induced osteoporosis decreased from 2,153 in 2003 to 1,202 in 2004 and 625 in 2005. However, the number of patients at risk for glucocorticoid-induced osteoporosis remained relatively constant: 1,782 (48.9%) in 2003, 2,191 (61.0%) in 2004, and 1,709 (47.6%) in 2005.

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue resulting in bone fragility and an increased susceptibility to fractures, especially of the hip, spine, and wrist. Osteoporosis is a major public health issue that affects an estimated 10 million Americans.[1] It has a large economic impact in the United States because of the loss of productivity and independence following fractures. The estimated national direct expenditure for osteoporotic fractures is $18 billion per year in 2002 dollars, and costs are rising due to the aging population in the United States.[2]

Osteoporosis may be primary (postmenopausal or age-related) or secondary to an identifiable cause, such as a drug, a disease, or a condition.[2] Osteoporosis affects women disproportionately, with a 4-to-1 female-to-male ratio,[1] and most commonly affects those aged >50 years.[3] Efforts at preventing osteoporosis have been directed primarily at minimizing accelerated bone loss during menopause and the early postmenopausal period in women, leaving other patient populations potentially overlooked. The common causes of secondary osteoporosis, which can occur in patients of all age groups, include hypogonadism (men), hyperparathyroidism, thyrotoxicosis, malnutrition, malabsorption, chronic immobilization, rheumatoid arthritis, alcoholism, vitamin D deficiency, and chronic glucocorticoid therapy.[2] The most frequent cause of drug-induced osteoporosis is chronic glucocorticoid therapy.[4-7] Glucocorticoids alter bone metabolism such that bone formation is reduced and resorption is increased, leading to rapid bone loss after initiation of therapy.[8]

Decreases in bone mineral density have been demonstrated after as little as 90 days of treatment with glucocorticoids and with a daily dose of as little as 5 mg of prednisolone or its equivalent.[9] In a large cohort study of 244,235 patients receiving oral glucocorticoids, the rate of vertebral fracture in glucocorticoid users (0.3%, n=1,033) was higher than that in 244,235 control patients who did not receive oral glucocorticoids (0.1%, n=465, relative risk [RR]=2.60, 95% confidence interval [CI], 2.31-2.92).[10] In addition, the risk of fractures is dose related; patients taking higher daily doses of oral glucocorticoids (i.e., at least 7.5 mg per day of prednisolone or equivalent) had significantly increased risk of non-vertebral fractures compared with low-dose (i.e., <2.5 mg per day of prednisolone or equivalent): absolute rate 2.6 fractures per 100 person-years for the high-dose group versus 1.6 fractures per 100 person-years in the low-dose group, RR=1.44, 95% CI, 1.34-1.54), hip fractures (RR=2.21, 95% CI, 1.85-2.64), and vertebral fractures (RR=2.83, 95% CI, 2.35-2.40).[7]

Table 1 lists risk factors for glucocorticoid-induced osteoporotic fractures. The American College of Rheumatology (ACR) Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis in 2001 published recommendations for prevention and treatment of this disease.[11] The recommendations of this committee, last updated in 2001, include lifestyle changes (e.g., weight-bearing exercise, smoking cessation, and reduction of alcohol consumption), supplementation with calcium and vitamin D, and therapy with bisphosphonates (Table 2). Hypogonadal patients receiving long-term glucocorticoids should receive hormone replacement therapy or testosterone. Treatment with a bisphosphonate is recommended for all men and postmenopausal women who receive long-term glucocorticoid treatment with 5 mg or more per day of prednisone or its equivalent, as well as for men and postmenopausal women receiving long-term glucocorticoids in whom the bone mineral density T-score at either the lumbar spine or hip is below normal.[11] Furthermore, the committee recommends that therapy to prevent or treat bone loss should be continued as long as the patient continues to receive glucocorticoids.

Despite the availability of effective therapies for glucocorticoid-induced osteoporosis prevention and treatment, and ACR's recommendations for prevention and treatment of glucocorticoid-induced osteoporosis, studies have shown that many patients receiving glucocorticoid therapy do not receive prophylaxis. In a study of 295 men receiving glucocorticoids for more than 3 months, bone mineral density testing was performed for less than half of the patients (44.1%) and less than one fourth (23.5%) were taking bisphosphonate therapy.[12] A study of 224 patients within a managed care population found that 37.9% of members receiving long-term glucocorticoid therapy had no documented intervention aimed at osteoporosis prevention, with men less likely than women to receive such an intervention (56.2% of men and 21.8% of women had no documented intervention).[13] In a retrospective cohort study of 3,031 patients (60.3% women) within a large managed care population (450,000 members) identified as receiving a glucocorticoid and at risk for osteoporosis, bone mineral density testing was performed in 9.6% of the

TABLE 1 Risk Factors for Fracture in Patients Taking Steroids[a]

Age
Previous osteoporotic fracture
Family history of osteoporosis
Hypogonadism
Smoking
Low body weight
Poor health and/or frailty
Inadequate calcium intake
Inadequate vitamin D intake
Inadequate exercise
Alcohol intake (>2 drinks per day)
Dose and duration of glucocorticoids

[a] *Derived from Bijlsma JW. Prevention of glucocorticoid-induced osteoporosis. Ann Rheum Dis. 1997;56:507-09,16; and Aagaard EM, Lin P, Modin GW, Lane NE. Prevention of glucocorticoid-induced osteoporosis: physician practice at an urban county hospital. Am J Med. 1999;107:456-60.*[17]

patients (13.0% of women and 4.9% of men), and antiresorptive medications other than hormone replacement therapy were dispensed to 14.5% (18.3% of women and 8.9% of men).[14]

Data from a survey completed more than a decade ago by 194 U.S. physicians (including 30 family practitioners, 52 internists, 25 gastroenterologists, 18 nephrologists, 33 rheumatologists, 16 neurologists, and 20 pulmonologists), a 49% response rate, revealed that while 80% of the physicians were aware that postmenopausal women have an increased risk of fracture during glucocorticoid therapy, only 10% considered it an important risk for males and 25% for premenopausal women.[15] In addition, differences were noted in physicians' knowledge and attitudes toward glucocorticoid-induced osteoporosis by specialty. Physicians with the greatest experience in prescribing glucocorticoids (e.g., rheumatologists and pulmonologists) were the most likely to report that they would prescribe preventive treatments for osteoporosis.[15] As this retrospective survey suggests, barriers to effective prophylaxis and treatment of glucocorticoid-induced osteoporosis may include lack of recognition by physicians of the frequency of glucocorticoid-induced osteoporotic fractures in men and premenopausal women or a lack of awareness of the existence and effectiveness of prophylactic therapy.[13,14,16,17]

We implemented an intervention program with the goal of increasing awareness of the risk of glucocorticoid-induced osteoporosis and the importance of its prevention in this health plan with approximately 1.3 million members in 2003 and 1.2 million members in 2005. The objectives of the program were to: (1) identify members receiving glucocorticoids and at risk for glucocorticoid-induced osteoporosis; (2) create awareness among members and physicians about the risk of glucocorticoid-induced osteoporosis; and (3) educate members and physicians about the options for preventing and treating this drug-induced disease, with the goal of increasing the use of preventative medications in patients who are receiving chronic glucocorticoid therapy.

TABLE 2 *Recommendations for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis: 2001 Update*[a]

Patients beginning therapy with glucocorticoid (prednisone equivalent of 5 mg or more per day) with plans for treatment duration of 3 months or longer:

1. Modify lifestyle risk factors for osteoporosis:
   a. Smoking cessation or avoidance
   b. Reduction of alcohol consumption if excessive
2. Receive instructions in weight-bearing physical exercise
3. Initiate calcium supplementation
4. Initiate vitamin D supplementation (plain or activated form)
5. Prescribe bisphosphonate (use with caution in premenopausal women)

Patients receiving long-term glucocorticoid therapy (prednisone equivalent of 5 mg or more per day):

1. Modify lifestyle risk factors for osteoporosis:
   a. Smoking cessation or avoidance
   b. Reduction of alcohol consumption if excessive
2. Receive instructions in weight-bearing physical exercise
3. Initiate calcium supplementation
4. Initiate vitamin D supplementation (plain or activated form)
5. Prescribe treatment to replace gonadal sex hormones if deficient or otherwise clinically indicated
6. Measure bone mineral density (BMD) at lumbar spine and/or hip. If BMD is not normal (i.e., T-score below -1), then:
   a. Prescribe bisphosphonate (use with caution in premenopausal women)
   b. Consider calcitonin as second-line agent if patient has contraindication to or does not tolerate bisphosphonate therapy
7. If BMD is normal, follow up and repeat BMD measurement either annually or biannually

[a] *Reference: American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Arthritis Rheum. 2001;44:1496-503.*[11] *Available at: www.rheumatology.org/publications/guidelines/osteo/prev_tx_gluco_osteoporosis.asp?aud=mem. Accessed February 21, 2008.*

Methods

Members of Excellus BlueCross BlueShield at risk for glucocorticoid-induced osteoporosis were identified through a pharmacy claims analysis. The analysis consisted of a 120-day measurement period of pharmacy claims for all adult patients (aged ≥21 years) within the plan and identified patients who were receiving an oral prednisone equivalent of ≥5 mg per day for at least 90 of 120 days without a prescription medication for prevention or treatment of osteoporosis, which was defined as 1 or more pharmacy claims for bisphosphonate (e.g., risedronate, ibandronate, etidronate, or alendronate), raloxifene, teriparatide, or calcitonin, during the same 120-day time frame. Pharmacy claims fitting the criteria were identified using the Generic Product Identifier (GPI) numbers listed in Table 3. Claims that included 1 of the products listed were reviewed by a clinical pharmacist to determine if they matched the criteria.

Between September 2003 and May 2005 (Table 4), interventions with both members and their physicians were conducted 3 times. Each intervention consisted of identifying patients at risk, mailing the intervention packet, and evaluating pharmacy claim records for a 4-month period immediately following each of the mailings (Table 4). Each patient could receive subsequent mailings if there was no (a) physician or patient response or (b) addition of osteoporosis-prevention treatment per our evaluation of pharmacy claims data.

Patient interventions included a direct-to-member mailing of a 1-page cover letter and a 2-page educational brochure that described the risk for glucocorticoid-induced osteoporosis and encouraged a conversation with the member's physician. The 2-page brochure defined osteoporosis, identified risk factors, and

TABLE 3 GPI Numbers Used to Identify Pharmacy Claims Fitting the Program Criteria

GPI	Product Name
22100010002010	Celestone oral solution 0.6 mg/5 ml
22100012007020	Entocort EC oral capsule extended release 24 hour 3 mg
22100015100310	Cortisone acetate oral tablet 25 mg
22100020000315	Dexamethasone oral tablet 0.5 mg
22100020000320	Dexamethasone oral tablet 0.75 mg
22100020000325	Dexamethasone oral tablet 1 mg
22100020000330	Dexamethasone oral tablet 1.5 mg
22100020000335	Dexamethasone oral tablet 2 mg
22100020000340	Dexamethasone oral tablet 4 mg
22100020000345	Dexamethasone oral tablet 6 mg
22100020001005	Dexamethasone oral elixir 0.5 mg/5 ml
22100020001320	Dexamethasone intensol oral concentrate 1 mg/ml
22100020002005	Dexamethasone oral solution 0.5 mg/5 ml
22100020006420	DexPak 13 day oral tablet 1.5 mg
22100025000303	Hydrocortisone oral tablet 5 mg
22100025000305	Hydrocortisone oral tablet 10 mg
22100025000310	Hydrocortisone oral tablet 20 mg
22100030000305	Medrol oral tablet 2 mg
22100030000310	Methylprednisolone oral tablet 4 mg
22100030000315	Methylprednisolone oral tablet 8 mg
22100030000320	Medrol oral tablet 16 mg
22100030000330	Medrol oral tablet 32 mg
22100030006405	Methylprednisolone (pak) oral tablet 4 mg
22100040000305	Prednisolone oral tablet 5 mg
22100040001203	Prednisolone oral syrup 5 mg/5 ml
22100040001205	Prednisolone oral syrup 15 mg/5 ml
22100040002900	Prednisolone anhydrous powder
22100040102900	Prednisolone acetate powder
22100040200910	Prednisolone sodium phosphate oral liquid 6.7 mg/5 ml
22100040202020	Orapred oral solution 15 mg/5 ml
22100040207215	Orapred ODT oral tablet dispersible 10 mg
22100040207220	Orapred ODT oral tablet dispersible 15 mg
22100040207240	Orapred ODT oral tablet dispersible 30 mg
22100045000305	Prednisone oral tablet 1 mg
22100045000310	Prednisone oral tablet 2.5 mg
22100045000315	Prednisone oral tablet 5 mg
22100045000320	Prednisone oral tablet 10 mg
22100045000325	Prednisone oral tablet 20 mg
22100045000335	Prednisone oral tablet 50 mg
22100045001310	Prednisone intensol oral concentrate 5 mg/ml
22100045002005	Prednisone oral solution 5 mg/5 ml
22100045006405	Prednisone (pak) oral tablet 5 mg
22100045006410	Sterapred DS oral tablet 10 mg
22200030100305	Fludrocortisone acetate oral tablet 0.1 mg
30042010100305	Fosamax oral tablet 5 mg (alendronate)
30042010100310	Fosamax oral tablet 10 mg (alendronate)
30042010100335	Fosamax oral tablet 35 mg (alendronate)
30042010100340	Fosamax oral tablet 40 mg (alendronate)
30042010100370	Fosamax oral tablet 70 mg (alendronate)
30042010102020	Fosamax oral solution 70 mg/75 ml (alendronate)
30042010200370	Fosamax plus D oral tablet 70-2800 mg-unit (alendronate)
30042010200380	Fosamax plus D oral tablet 70-5600 mg-unit (alendronate)
30042040100305	Didronel oral tablet 200 mg (etidronate)
30042040100310	Etidronate disodium oral tablet 400 mg
30042048100320	Boniva oral tablet 2.5 mg (ibandronate)
30042048100360	Boniva oral tablet 150 mg (ibandronate)
30042048106420	Boniva intravenous kit 3 mg/3 ml (ibandronate)
30042065100305	Actonel oral tablet 5 mg (risendronate)
30042065100320	Actonel oral tablet 30 mg (risendronate)
30042065100330	Actonel oral tablet 35 mg (risendronate)
30042065100360	Actonel oral tablet 75 mg (risendronate)
30042065110320	Actonel with calcium oral tablet 35-1250 mg (risendronate)
30043020002080	Miacalcin nasal solution 200 unit/ACT (calcitonin)
30043020002080	Fortical nasal solution 200 unit/ACT (calcitonin)
30044070002020	Forteo subcutaneous solution 750 mcg/3 ml (teriparatide)
30053060100320	Evista oral tablet 60 mg (raloxifene)

GPI=Medi-Span Generic Product Identifier.

promoted lifestyle changes to minimize the risk of osteoporosis. It also instructed members not to discontinue their steroids without first discussing discontinuation with their physician.

The physician intervention included (a) a 1-page letter describing the program, (b) the same 2-page brochure about osteoporosis and its prevention and treatment that was sent to patients, and (c) a 1-page table listing options for drug treatments for osteoporosis, including bisphosphonates, raloxifene, intranasal calcitonin, and teriparatide (parathyroid hormone); the table included the notation that "combination hormone replacement therapy is no longer recommended as monotherapy for osteoporosis" based on the results of the Womens Health Initiative.

TABLE 4 Timeline of Interventions—2003-2005

Year of Intervention	Identification Period Begins	Identification Period Ends	Mailings Sent	Follow-up Period Begins	Follow-up Period Ends
2003	April 1, 2003	July 30, 2003	Sept. 1, 2003	Oct. 1, 2003	March 1, 2004
2004	May 1, 2004	Aug. 31, 2004	Oct. 5, 2004	Nov. 1, 2004	Feb. 28, 2005
2005	Feb. 4, 2005	May 5, 2005	June 16, 2005	July 1, 2005	Oct. 31, 2005

TABLE 5 Patients Receiving Chronic Oral Glucocorticoids at the Time of Each Sample Analysis

	2003	2004	2005	3-Year Total
Total health plan membership	1,323,086	1,220,847	1,227,571	3,771,504
Prevalence % (n) of patients taking chronic oral glucocorticoid	0.28% (3,643)	0.29% (3,590)	0.29% (3,589)	0.29% (10,822)
% (n) male % (n) female	40.5% (1,476) 59.5% (2,167)	40.3% (1,448) 59.7% (2,142)	40.3% (1,448) 59.7% (2,141)	40.4% (4,372) 59.6% (6,450)
% (n) patients on chronic oral glucocorticoid + anti-osteoporosis drug	51.1% (1,861)	39.0% (1,399)	52.4% (1,880)	47.5% (5,140)
% (n) male % (n) female	36.8% (684) 63.2% (1,177)	31.4% (439) 68.6% (960)	33.2% (625) 66.8% (1,255)	34.0% (1,748) 66.0% (3,392)
Intervention group: % (n) patients on chronic oral glucocorticoid without anti-osteoporosis medication	48.9% (1,782)	61.0% (2,191)	47.6% (1,709)	52.5% (5,682)
% (n) male % (n) female	44.4% (792) 55.6% (990)	46.1% (1,009) 53.9% (1,182)	48.2% (823) 51.8% (886)	46.2% (2,624) 53.8% (3,058)
% (n) male patients at risk[a]	53.6% (792/1,476)	69.7% (1,009/1,448)	56.8% (823/1,448)	54.8% (2,397/4,372)
% (n) female patients at risk[a]	45.7% (990/2,167)	55.2% (1,182/2,142)	41.4% (886/2,141)	50.9% (3,285/6,450)

[a] *At-risk patients received chronic glucocorticoid therapy.*

Chronic glucocorticoid therapy was defined as at least 90-days supply.

The 1-page physician letter included a fax-back box by which the physician could request a list of the patients "for whom I have prescribed steroids."

The physician letters were sent by first-class mail without return-receipt notification. However, there were very few physician mailings returned with incorrect addresses, and these few mailings were resent after the address corrections. Physicians who requested the fax-back information about individual patients were sent the following data for each member at risk (i.e., taking more than 90 days of a steroid without an accompanying medication for osteoporosis prevention): patient name, date of birth, date of last fill of glucocorticoid prescription, and strength of glucocorticoid prescribed. (The quantity dispensed was not included in the list.)

Physician specialty was identified by the health plan claims system that matched the physician's name with the medical specialty. The medical specialty of 47.9% of the prescribers could not be determined from claims data, and these unknown specialty physicians were included in the "other specialties" category. In the analysis, patients who initiated a bisphosphonate during the 4-to-6-week time lag between the end of the patient identification time period and the intervention start date were not documented.

Results

Table 5 shows the number of at-risk patients at the time of each analysis during the 3-year period. Less than 1% (n = 10,822) of our members were receiving chronic oral glucocorticoids, but 52.5% of these patients were not receiving drug therapy for prevention or treatment of osteoporosis. On average, women made up 59.6% of patients receiving chronic glucocorticoid therapy during the 3-year study period and 53.8% of patients defined as being at risk for glucocorticoid-induced osteoporosis (i.e., not receiving preventative medication). About half of the female patients (50.9%, 3,285/6,450) and male patients (54.8%, 2,397/4,372) were at increased risk of fracture due to receipt of 90 days or more of glucocorticoid therapy without anti-osteoporosis drug therapy.

Table 6 shows a breakdown of patients who were receiving chronic glucocorticoids with or without osteoporosis prevention

TABLE 6 Breakdown of Patients Treated With Glucocorticoids by Physician Specialty During the Identification Periods

Physician Speciality—% Patients (n)	2003 N = 3,643	2004 N = 3,590	2005 N = 3,589	3-Year Total N = 10,822
Primary care				
with osteoporosis treatment	39.1% (479)	39.6% (481)	67.5% (780)	48.4% (1,740)
without osteoporosis treatment	60.9% (745)	60.4% (735)	32.5% (375)	51.6% (1,855)
Allergy				
with osteoporosis treatment	49.2% (31)	57.1% (32)	76.5% (62)	62.5% (125)
without osteoporosis treatment	50.8% (32)	42.9% (24)	23.5% (19)	37.5% (75)
Endocrinology				
with osteoporosis treatment	27.5% (28)	24.4% (20)	67.9% (53)	38.5% (101)
without osteoporosis treatment	72.5% (74)	75.6% (62)	32.1% (25)	61.5% (161)
Gastroenterology				
with osteoporosis treatment	23.6% (17)	33.0% (34)	61.3% (57)	40.3% (108)
without osteoporosis treatment	76.4% (55)	67.0% (69)	38.7% (36)	59.7% (160)
Pulmonary				
with osteoporosis treatment	39.8% (33)	43.6% (34)	73.3% (55)	51.7% (122)
without osteoporosis treatment	60.2% (50)	56.4% (44)	26.7% (20)	48.3% (114)
Rheumatology				
with osteoporosis treatment	44.8% (187)	40.0% (128)	70.1% (237)	51.3% (552)
without osteoporosis treatment	55.2% (230)	60.0% (192)	29.9% (101)	48.7% (523)
Other specialities or specialty unknown				
with osteoporosis treatment	64.6% (1,086)	38.6% (670)	36.0% (636)	46.1% (2,392)
without osteoporosis treatment	35.4% (596)	61.4% (1,065)	64.0% (1,133)	53.9% (2,794)
Total				
Patients on glucocorticoids (n)	3,643	3,590	3,589	10,822
with osteoporosis treatment	51.1% (1,861)	39.0% (1,399)	52.4% (1,880)	47.5% (5,140)
without osteoporosis treatment	48.9% (1,782)	61.0% (2,191)	47.6% (1,709)	52.5% (5,682)

by physician specialty. The "other specialties" group includes physicians for whom the specialty could not be determined (e.g., hospital outpatient physicians, hospital clinic physicians). The other specialties group accounted for the largest number of patients receiving steroids (47.9%, n = 5,186) of which 53.9% (n = 2,794) were at risk for glucocorticoid-induced osteoporosis because they were not receiving preventative medications. The primary care specialty group had the second largest number of patients receiving steroids (33.2%, n = 3,595) of which 51.6% (n = 1,855) were at risk for glucocorticoid-induced osteoporosis for not receiving preventative medications. These 2 specialties groups account for 81.1% of the patients at risk for glucocorticoid-induced osteoporosis.

The specialty with the largest increase in percentage of patients treated for glucocorticoid-induced osteoporosis across the 3 years of the intervention was endocrinologists, a group for whom 27.5% of at-risk patients were treated with an osteoporosis medication at the time of the first analysis in 2003 versus 67.9% at the time of the final analysis in 2005 (40% increase). However, endocrinologists were associated with only 2.4% of all patients in this health plan who received long-term glucocorticoid therapy during 3 years.

Increases in anti-osteoporosis drug use from 2003 to 2005 were noted for glucocorticoid-treated patients of primary care physicians (from 39.1% to 67.6%), allergists (from 49.2% to 76.5%), gastroenterologists (from 23.6% to 61.3%), pulmonologists (from 39.8% to 73.3%), and rheumatologists (from 44.8% to 70.1%). The other specialties group was unique in that a marked decrease in the use of anti-osteoporosis medication was noted, 64.6% of patients in 2003 to 36.0% of patients in 2005.

Anecdotal feedback from physicians regarding the program was consistently positive, and 196 physicians (4.9%), accounting for 387 patients (6.8%) at risk for glucocorticoid-induced osteoporosis, requested a list of their patients at risk via the fax-back opportunity.

Table 7 shows the changes in the use of preventative medication for osteoporosis following the interventions. Of the at-risk members who were subjects of the educational intervention during the 3 years, 404 (7.1%) were started on an osteoporosis medication following the mailings. Of these, 84.9% of patients (n = 343) continued on both glucocorticoid therapy and an anti-osteoporosis medication for the 4-month follow-up period. Of the patients who started on preventative therapy after the intervention, 72.8% were women, and 96.3% of the women were aged ≥ 40 years.

Discussion

Glucocorticoid-induced osteoporosis was targeted for this intervention because it represents a disease that is underdiagnosed and undertreated, and we suspected that there were a significant number of at-risk patients within our health plan. Our intervention was designed to identify the at-risk patients and provide educational materials to increase awareness among members and physicians about the risk of glucocorticoid-induced osteoporosis and the importance of its prevention. An objective of our program was to promote dialogue between members and their clinicians

regarding options for preventing or treating glucocorticoid-induced osteoporosis. While we expected to see an increase in percentage of patients receiving medication to prevent glucocorticoid-induced osteoporosis, this is only 1 possible outcome of the member-physician discussion.

On average, 52.5% of patients receiving a glucocorticoid were not receiving medication to prevent glucocorticoid-induced osteoporosis. Women represented 53.8% (3,058/5,682) of the at-risk patient group (i.e., long-term glucocorticoid therapy without osteoporosis prevention drug therapy), which is high compared with the rates found in previous research (24.2%,[12] 42.1%,[14] and 30.4%[17]). The intervention was associated with a 9.6% increase (294/3,058) in the number of women who received osteoporosis-preventive drug therapy. We wonder why so many women are at risk and not being managed with medications to prevent glucocorticoid-induced osteoporosis. Nearly all the women (96.3%) who started preventative medications following the intervention were aged ≥40 years. One possibility is that a large percentage of those who are not being treated are premenopausal and treatment is inappropriate, but our data does not provide this level of detail. We included premenopausal women in our intervention because the goal was for the physicians and patients to discuss their care and determine the most appropriate course. Of the 5,682 patients who were at risk for glucocorticoid-induced osteoporosis during the 3-year intervention, 2.7% (11) of the women who started preventative therapy were clearly premenopausal women, which is less than 1% of the at-risk population. We considered this to be reasonable and consistent with our goal that physicians and patients would make individualized decisions. However, including premenopausal women in the intervention without breaking them into specific age bands limited the utility of the data.

Even though raloxifene and teriparatide are not included in the ACR recommendations, we included them in our educational materials. Teriparatide (Forteo) is an agent that contains recombinant human parathyroid hormone (PTH 1-34), and it was approved by the U.S. Food and Drug Administration (FDA) in November 2002. Although the ACR recommendations were published in July 2001, the anabolic agent PTH 1-34 (i.e., teriparatide) was considered, and the recommendations state that there were not enough data in glucocorticoid-treated patients to draw conclusions. Our health plan added teriparatide to the formulary in 2006 as a tier-3 drug that could be used as part of step therapy; teriparatide was included in the educational materials for completeness.

Raloxifene is a selective estrogen receptor modulator approved by the FDA in December 1997 for the treatment and prevention of postmenopausal osteoporosis.[23] At the time the ACR recommendations were published, there were no data describing the efficacy of raloxifene in glucocorticoid-induced osteoporosis. However, we considered it a viable option in postmenopausal women receiving glucocorticoids who are unable or unwilling to take other available therapies (e.g., antiresorptive medications). Raloxifene was added to our formulary prior to beginning the intervention in 2003 as a tier-2 copayment (preferred) drug.

TABLE 7 Changes in the Use of Preventative Medication for Osteoporosis Following Intervention

	2003	2004	2005	3 Years
No. of patients in intervention group (N)	1,782	2,191	1,709	5,682
% (n) patients starting anti-osteoporosis medication	7.4% (131)	5.6% (122)	8.8% (151)	7.1% (404)
% (n) female (aged 0-39 years)	5.3% (7)	0.8% (1)	2.0% (3)	2.7% (11)
% (n) female (aged 40-59 years)	24.4% (32)	23.0 % (28)	17.2% (26)	21.3% (86)
% (n) female (aged ≥60 years)	48.1% (63)	49.2% (60)	49.0% (74)	48.8% (197)
% (n) male	22.1% (29)	27.0% (33)	31.8% (48)	27.2% (110)
% (n) patients continuing on glucocorticoid and anti-osteoporosis medication 4 months later	70.2% (92)	93.4% (114)	90.7% (137)	84.9% (343)

The proportion of patients at risk from osteoporosis in our intervention falls in the approximate midpoint of the data range reported in the literature.[12,14,17,18] In our patient population during 3 years, 50.9% of women (3,285/6,450) and 54.8% of men (2,397/4,372) on chronic glucocorticoid therapy were at risk for glucocorticoid-induced osteoporosis because of the absence of medication to prevent osteoporosis. Others have reported percentages between 24% and 89% for women and between 56% and 95% for men.[12,13,14,18] The percentage of patients within the health plan receiving glucocorticoids during the 3 years (0.29%) is similar to 0.3% reported elsewhere.[18] Overall, 7.1% of the patients at risk for glucocorticoid-induced osteoporosis started preventative therapy, of which 72.8% were women, and 8.9% of the women at risk and targeted by our intervention (n=294) started preventative therapy for osteoporosis. Without a control group, we cannot conclude with certainty that our intervention is responsible for the very modest changes. It's likely that other educational efforts and marketing by the pharmaceutical industry contributed as well.

Kaufman et al. in *JMCP* (2005) described a 4-year physician intervention program in a health plan of about the same enrollment as our health plan.[19] The goal of their intervention was to minimize the use of medications contraindicated in older adults, and the objective was to change the prescribing habits of physicians within the health plan. Their intervention involved direct mail to physicians of elderly patients who were prescribed inappropriate medications, publishing educational pieces in the health plan newsletter, and making follow-up phone calls to a subset of high-volume prescribers of the target drugs defined as

TABLE 8 *Physician Requests for Fax-Back Lists of Patients*

	2003	2004	2005	3-Year Total
No. of (n) physicians contacted	2,153	1,202	625	3,980
% (n) physicians requesting fax-back list of patients	2.8% (61)	7.5% (90)	7.2% (45)	4.9% (196)
Patients (n) at risk for glucocorticoid-induced osteoporosis and not on preventative medication	1,782	2,191	1,709	5,682
% (n) patients associated with physicians who requested fax-back lists	6.3% (113)	8.7% (191)	4.9% (83)	6.8% (387)

contraindicated in older adults. As in our study, Kaufman et al. conducted a descriptive analysis without a control group and reported a relative 58% reduction in use of medications defined as contraindicated in older adults, from 5.3% of medications in the last calendar quarter of 1999 to 2.2% in the last quarter of 2003. Their seemingly greater success in affecting physician prescribing may be related, in part, to the higher-intensity intervention that involved telephone contact of high-volume prescribers.

The overall physician response rate was 4.9% of physicians who received our mailing and requested patient information via the fax-back program (Table 8). In 2003, we contacted 2,153 physicians and 2.8% requested additional information (n=61); in 2005, we contacted less than one third as many physicians (n=625) and 7.2% responded (n=45). The number of patients at risk for glucocorticoid-induced osteoporosis remained relatively constant during the 3 years, while the number of physicians contacted by this intervention including fax-back opportunity dropped by 71% (2,153 in 2003 to 625 in 2005).

The percentage of patients at risk for glucocorticoid-induced osteoporosis who were taking a preventative medication dropped from 51.1% in 2003 to 39.0% in 2004, and then returned close to the baseline in 2005 (52.4%). Our analysis did not identify a reason for this apparent dip in 2004. In looking at trends among the physician medical specialties, there appeared to be an increase during the 3 years in the proportion of patients at risk for glucocorticoid-induced osteoporosis who received preventative medications except for the largest category of prescribers, the "other specialties," including unknown medical specialty. This group is also significant because it was responsible for prescribing glucocorticoids for nearly half (47.9%) of the patients at risk for glucocorticoid-induced osteoporosis during the 3-year study period.

Limitations

The foremost limitation of the present study is the absence of a control group, so we cannot be certain how many of the 404 patients who started on medication for prevention of osteoporosis during the 3 years was the result of the intervention or coincidental events. Second, we only measured 1 possible outcome of our intervention—the addition of preventative medications (i.e., bisphosphonates, calcitonin, teriparatide, or raloxifene); we did not assess other behavioral changes, such as smoking cessation, increase in weight-bearing exercise, reduction in alcohol use, or the initiation of supplementation with calcium and vitamin D that may have been related to our education-intervention.

Third, we did not measure discontinuation of glucocorticoid therapy beyond 120 days, previous failure on bisphosphonates, or the conduct of bone mineral density tests. Fourth, we could not identify patients who might have received their medications via another source, such as physician samples, or who obtained medications outside the health plan. Fifth, our intervention did not account for those patients who started therapy after the end of the identification period but prior to the receipt of the intervention-mailing, which may have contributed to underestimation of the effect of our intervention.

Sixth, we did not measure patient adherence or persistence with osteoporosis drug therapy other than the assessment of the proportion of patients remaining on preventative medication after 4 months of follow-up. For those who were started on bisphosphonates, it is likely that some were unable to tolerate the medication. Adherence to medications for the prevention of osteoporosis is often poor. Ettinger et al. found that 34.9% of women initiated on alendronate had discontinued therapy at 6 months, and the most common reason for discontinuation, gastrointestinal problems, were reported by 51.9% of the women who had stopped taking the drug.[20] Others have reported rates of discontinuation of bisphosphonates in the range of 60.5% to 75% at 12 months of follow-up.[21,22] During our intervention, 83.4% of those who began preventative therapy continued it for at least 4 months, but we did not identify the reasons for discontinuation of treatment.

Seventh, it is not possible from this intervention to determine what proportion of patients on chronic glucocorticoid therapy remained at risk over time. For example, a patient who received as little as 90 days of glucocorticoid therapy could have been identified as at risk because of the absence of drug therapy for prevention of osteoporosis. In other words, we do not know

the true denominator for the patients at elevated risk. We also do not know the true numerator for patients for whom physicians and patients initiated behavioral changes or drug therapy (e.g., via physician samples) to prevent glucocorticoid-induced osteoporosis.

Eighth, despite the recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis from the ACR (2001), there is no evidence that bisphosphonates or other anti-osteoporosis drug therapy actually reduce the risk of meaningful glucocorticoid-induced fractures. Therefore, the increase in use of drug therapy to prevent osteoporosis from 47.5% of patients on chronic glucocortioid therapy to 51.2% after the intervention in this health plan may represent a reasonable expectation of success in attaining optimal drug therapy to prevent osteoporosis.

Conclusion

Our mail-based intervention program received a response rate greater than expected with a typical direct-mail marketing campaign but significantly less than that reported by others who have conducted similar intervention programs with physicians. Our efforts were designed to educate and increase the use of drug therapy to prevent osteoporosis in patients on chronic glucocorticoids, defined as at least 90 days of dispensed drug therapy. Our intervention was associated with the initiation of medications, as measured in pharmacy claims data, to prevent osteoporosis in a small percentage of target patients (7.1% over 3 years), but because there was no control group, the proportion of new starts on anti-osteoporosis medications attributable to the intervention cannot be ascertained. This intervention program documented that slightly more than half of the patients on chronic glucocorticoid therapy were at risk of osteoporosis because of the absence of concomitant therapy with an anti-osteoporosis medication.

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