OSTEOPOROSIS MANAGEMENT AMONG CHRONIC GLUCOCORTICOID USERS: A SYSTEMATIC REVIEW

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ABSTRACT

Background
Clinical practice guidelines recommend that all patients starting chronic oral glucocorticoid (GC) therapy receive bone mineral density (BMD) testing and osteoporosis pharmacotherapy.

Objective
We completed a systematic review of observational studies to examine the proportion of patients on chronic oral GC therapy who receive osteoporosis management.

Methods
Two independent reviewers completed a systematic search of Ovid MEDLINE® and EMBASE® to identify all English language articles that examined the prevalence of osteoporosis management among chronic oral GC users. Clinical trials, abstracts, reviews, commentaries, and letters to the editor were excluded. Study methods and results (use of BMD testing and osteoporosis pharmacotherapy) were abstracted and summarized by year and region.

Results
We identified 29 eligible studies published between 1999 and October 2013: 17 were conducted in North America, 5 in Europe, and 7 in other regions. Heterogeneity between patient populations and methods used to define chronic GC use precluded the direct comparison of results between regions, or over time. Over 80% of studies identified that < 40% of chronic oral GC users received BMD testing or osteoporosis pharmacotherapy. When results of these studies were plotted by year, there was little evidence of improvement in osteoporosis management over time.

Conclusions
Despite consistent recommendations to target osteoporosis prevention at the onset of chronic oral GC therapy, osteoporosis is undermanaged among chronic oral GC users. Targeted interventions are needed to help reduce the burden of fracture-related morbidity associated with GC-induced osteoporosis.

Key Words: *Osteoporosis, glucocorticoids, practice patterns, systematic review*

Oral glucocorticoids (GC) are commonly prescribed to reduce pain and inflammation in patients with inflammatory arthritis, inflammatory bowel disease, and chronic lung disease.[1] The prevalence of oral GC use is approximately 1.2% among adults aged 20 years or more and it has been estimated that around 7.5% of adults aged 18 years or more have received at least one prescription for an oral GC.[2-4] Due to the severe pain and morbidity associated with chronic inflammatory conditions, the duration of GC therapy can persist for months to years in length.[4]

Chronic oral GC therapy is the leading cause of secondary osteoporosis, a condition labeled GC-induced osteoporosis.[5] Though there is no single definition of "chronic," it is

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commonly accepted that treatment lasting at least 3 months leads to deleterious effects on bone.[6] Oral GC therapy leads to a rapid reduction in bone formation through inhibition of osteoblast differentiation[7] and increased osteoclast activity.[8,9] This results in bone loss which manifests clinically as reduced bone mass and diminished microarchitectural integrity.[10] GC-induced bone loss occurs rapidly at a rate of 6% to 12% within the first year of therapy.[11] Fracture risk increases within 3 months of starting therapy with doses as low as 2.5 mg/day prednisone equivalent[12,13], and individuals on GC therapy are almost twice as likely to experience a bone fracture compared to non-GC users.[3]

Fortunately, treatment with osteoporosis medication has shown to improve bone mineral density (BMD) and reduce fracture risk in patients treated with oral GC therapy.[14] As a result, clinical practice guidelines recommend that BMD testing and osteoporosis pharmacotherapy be initiated in patients starting oral GC therapy for ≥ 3 months.[6,15] This recommendation is consistent across osteoporosis guidelines, though the duration (3 to 6 months) and dose (any to 15 mg/day) indicating osteoporosis management differ slightly.[15-22]

Since clinical practice guidelines frequently change to reflect the availability of new therapeutic options for osteoporosis, there is little known about how GC-induced osteoporosis management has changed over time, or if regional differences exist. An investigation of studies examining the proportion of chronic GC users that receive osteoporosis management may clarify current practice standards among this high-risk population, and help identify areas for improvement. Thus, we aimed to systematically examine the proportion of chronic oral GC users receiving osteoporosis management, by region and over time. A secondary objective was to identify patient and physician-level predictors of GC-induced osteoporosis management among identified studies.

METHODS

This systematic review follows PRISMA guidelines for the reporting of systematic reviews.[23]

Search Strategy

Two reviewers (JMA, SY) independently completed a systematic search of the electronic database Ovid MEDLINE® from 1946 (database inception) to October 2013 to identify all English language articles that examined GC-induced osteoporosis management. Ovid EMBASE® was also searched through to October 2013. Search terms for "osteoporosis" and "glucocorticoids" were adapted from two separate Cochrane Collaboration reviews[24,25], and selected following consultation with a library scientist. A complete list of terms can be found in Appendix 1.

Identification of Relevant Articles

All observational studies that examined the proportion of chronic oral GC users receiving osteoporosis management (BMD testing *and* osteoporosis pharmacotherapy) were eligible. Studies that included users of inhaled or injectable GCs were included only if management outcomes were reported separately for oral GC users. Eligible osteoporosis pharmacotherapy included bisphosphonates, calcitonin, denosumab, hormone replacement therapy, raloxifene, teriparatide, and testosterone. Clinical trials, commentaries, letters to the editor, reviews, clinical practice guidelines, and abstracts were excluded. Articles that did not state the drug class of pharmacotherapy or that considered calcium/vitamin D as "pharmacotherapy" were excluded since all guidelines recommend drug therapy in addition to calcium/vitamin D to manage osteoporosis. In addition, articles that reported osteoporosis pharmacotherapy only or that did not report use of BMD testing and treatment separately were excluded since all guidelines recommend BMD testing at the onset of chronic oral GC therapy. Titles and abstracts were reviewed independently by two authors (JMA, SY) and inconsistencies settled through consultation with a third author (SMC).

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Data Abstraction

Study characteristics including data source, patient demographics, country, GC dose, GC indication, methods, and results were abstracted and summarized by one author (JMA) and verified by a second (SY). Patient characteristics and study methodology were compared between studies. The main osteoporosis clinical practice guidelines, referenced by each included study, were also summarized. Results of eligible studies were plotted by publication and "data year," based on the reported study period. For study periods spanning less than 3 years, data year was defined at the end of the study period. Data year for studies extending 3 or more years was defined as the middle year of the study. For example, studies using data collected from 2001 to 2002 and 2001 to 2003 were both assigned the data year 2002. For studies that reported several data points longitudinally, each reported year was plotted.

RESULTS

Of 3270 unique articles identified, 41 were retrieved for full text review based on title and abstract screening, Figure 1. After full text review, 18 additional articles were excluded: 3 focused on physician knowledge/prescribing habits[26-28], 3 reported no outcome[29-33], 8 reported osteoporosis pharmacotherapy only[34-44], 2 reported use of calcium/vitamin D only[45,46], and 2 included calcium/vitamin D as pharmacotherapy.[47,48] An additional 6 studies identified using EMBASE® were eligible.

In total, 29 papers published between 1999 and 2013 were eligible: 17 from North America[49-65], 5 from Europe[66-70], and 7 from other regions (Australia, 2; South Africa, 1; India, 3; Saudi Arabia, 1).[71-77] These studies referenced several osteoporosis guidelines to inform their methodology including 1996, 2001, and 2010 American College of Rheumatology[15-17], 1998 UK consensus group[18], 1998 and 2002 National Osteoporosis Society[19,20], 2003 American Gastroenterological Association[21], and 2000 South African Medical Association.[22] A summary of these guidelines is presented in Table 1.

A variety of data sources were used by these studies to examine GC-induced osteoporosis management, Table 2. Chart review was the most common source (n=13), followed by administrative databases (n=10) and telephone surveys (n=1). Five studies (17%) used a combination of different data sources. Furthermore, methods used to define chronic GC exposure and report osteoporosis management were not consistent with osteoporosis guidelines, and varied considerably across studies, Table 3. While 83% of studies assessed osteoporosis management in accordance with guideline recommendations, only 45% used guideline criteria to define chronic GC use. When defining osteoporosis pharmacotherapy, all studies included bisphosphonates, while fewer considered the use of hormone replacement therapy (62%), calcitonin (59%), testosterone (28%), raloxifene (24%), and teriparatide (7%). This made it difficult to compare results directly between studies.

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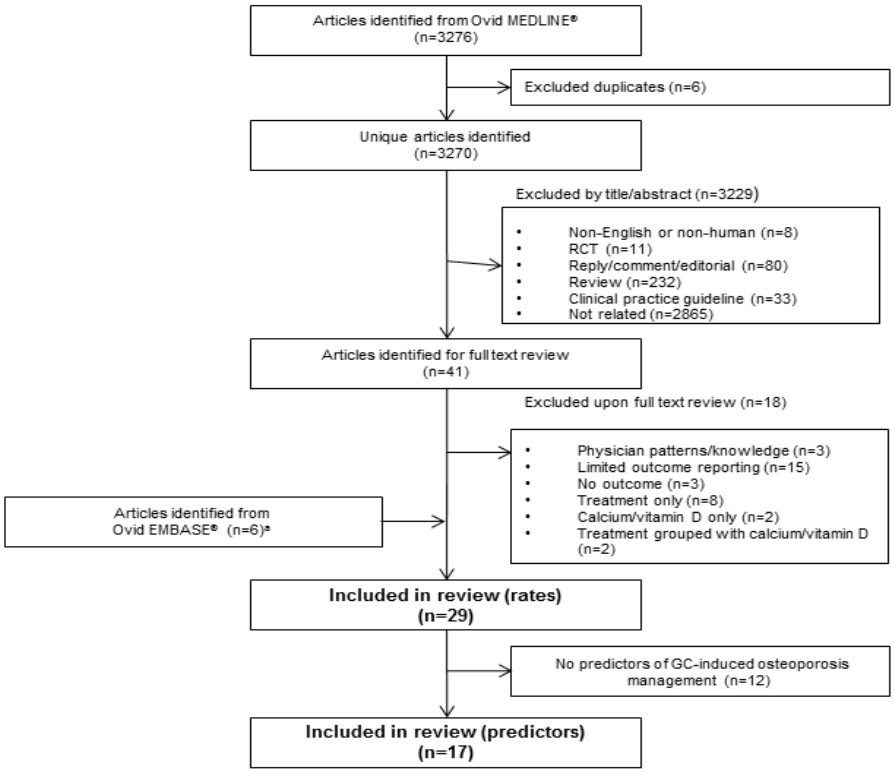
FIG. 1 Flow diagram of systematic search results



[a]Electronic search of Ovid EMBASE® (completed July 2014 in response to reviewer comments) yielded 6077 articles published between 1964 and October 2013. After thorough review, 6 additional articles were included in our systematic review.

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TABLE 1 International guidelines for glucocorticoid-induced osteoporosis management

	American College of Rheumatology (USA)			American GI Association (USA)	UK Consensus Group (UK)	National Osteoporosis Society (UK)		South Africa
Variable	**1996**	**2001**	**2010**	**2003**	**1998**	**1998**	**2002**	**2000**
Treatment Indications								
Prevalent Fracture	Yes	Yes	FRAX	Yes	Yes	Yes	Yes	Yes
GC Dose (mg/day)[a]	NR	5.0	7.5	7.5	15.0	7.5	NR	7.5
GC Duration	≥ 6 months	≥ 3 months	≥ 3 months	> 3 months	≥ 6 months	≥ 6 months	≥ 3 months	≥ 3 months
Screening (BMD Testing)								
BMD Testing	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Repeat Frequency	0.5 – 1 year	6 months	1 year	1 – 2 years	1 – 3 years	1 – 3 years	1 – 3 years	1 – 2 years
Treatment Options								
Calcium (mg/day)[b]	1500	NR[c]	1200	1000 – 1500	NR[c]	NR[c]	NR[c]	1000
Vitamin D (IU/day)[b]	800	800	800	800	NR[c]	NR[c]	NR[c]	400
Pharmacotherapy								
Bisphosphonate								x
Alendronate		x	x	x			x	
Etidronate	x				x	x	x	
Pamidronate	x			x			x	
Risedronate		x	x	x			x	
Zoledronic Acid			x					
Calcitonin	x	x			x		x	
HRT or T	x	x			x	x	x	
Raloxifene								
Teriparatide			x					

BMD – bone mineral density, FRAX – WHO fracture risk assessment tool, GC – glucocorticoid, GI – gastroenterological, HRT – hormone replacement therapy, T – testosterone, NR – not reported

[a]Glucocorticoid doses given as prednisone equivalent

[b]Recommended minimum intake refers to the total intake (diet and supplementation)

[c]Recommended, yet dose is not stated in the guideline

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TABLE 2 Characteristics of studies identified through systematic search (n=29)

Author (year)	Country	Data Source	Main Guideline(s) Referenced	Patients, N (% female)	Mean age, years	GC Indication, included (main)	Mean GC dose[a], mg/day	Pharmacotherapy Identified[b]
North America (n=17)								
Buckley (1999)	USA	Telephone survey	1996 ACR	147 (58)	51.0	Any (rheumatic)	10.0	bisphosphonate, calcitonin, HRT
Elliot (2000)	USA	Administrative database & chart review	1996 ACR	72 (0)	57.0	Any (transplant)	12.5	bisphosphonate, calcitonin, testosterone
Osiri (2000)	USA	Chart review	1996 ACR	365 (59)	52.5	Any (rheumatic)	11.4	bisphosphonate, calcitonin, HRT, testosterone
Ettinger (2001)	USA	Administrative database	1996 ACR 1998 UK	8,807 (60)	NR	Any (respiratory)	NR	bisphosphonate, calcitonin
Mudano (2001)	USA	Administrative database	1996 ACR	6,821 (62)	51.9	Any (rheumatic)	13.6	bisphosphonate, calcitonin, HRT, testosterone

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Author (year)	Country	Data Source	Main Guideline(s) Referenced	Patients, N (% female)	Mean age, years	GC Indication, included (main)	Mean GC dose[a], mg/day	Pharmacotherapy Identified[b]
Yood (2001)	USA	Administrative database & chart review	1996 ACR	224 (57)	70.0	Any (respiratory)	8.9	bisphosphonate, calcitonin, HRT
Solomon (2002)	USA	Chart review	2001 ACR	236 (80)	60.3	Rheumatic	8.8	bisphosphonate, calcitonin, HRT, raloxifene
Curtis (2005)	USA	Administrative database & mailed survey	1996 ACR 2001 ACR	6,281 (66)	50.0	Any, excluding transplantation (rheumatic)	16.0	bisphosphonate, calcitonin, HRT, raloxifene, testosterone
Feldstein (2005)	USA	Administrative database	2001 ACR	3,031 (60)	61.4	Any (respiratory)	20.0	bisphosphonate, calcitonin, raloxifene, HRT
Che (2006)	USA	Administrative database	2001 ACR	13,862 (58)	NR	Any	NR	bisphosphonate, calcitonin, raloxifene
Cruse (2006)	USA	Chart review	2001 ACR	370 (0)	64.0	Any (rheumatic)	NR	bisphosphonate, calcitonin, testosterone
Liu (2006)	USA	Chart review	2001 ACR	35 (60)	54.0	Dermatologic	53.0[c]	bisphosphonate

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Author (year)	Country	Data Source	Main Guideline(s) Referenced	Patients, N (% female)	Mean age, years	GC Indication, included (main)	Mean GC dose[a], mg/day	Pharmacotherapy Identified[b]
Saag (2006)	USA	Administrative database	2001 ACR	3,125 (59-63)[d]	NR	Any (respiratory)	11.0	bisphosphonate, calcitonin, raloxifene, HRT
Guzman-Clark (2007)	USA	Chart review	2001 ACR	100 (6)	73.0	Any (respiratory)	7.5 (median)	bisphosphonate
Ledwich (2009)	USA	Chart review	2001 ACR	73 (82)	60.9	Rheumatic	NR	bisphosphonate, HRT
Majumdar (2012)	Canada	Administrative database	none	15,825[e] (58)	60.0	Any	NR	bisphosphonate, calcitonin, raloxifene, teriparatide
Thanou (2013)	USA	Administrative database & chart review	2003 AGA	63 (3)	55.0	Inflammatory bowel disease	15.0 (median)	bisphosphonate
Europe (n=5)								
Erb (2002)	UK	Chart review	1998 NOS	235 (71)	NR	Rheumatic	NR	Bisphosphonate, calcitonin, HRT, raloxifene, testosterone

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Author (year)	Country	Data Source	Main Guideline(s) Referenced	Patients, N (% female)	Mean age, years	GC Indication, included (main)	Mean GC dose[a], mg/day	Pharmacotherapy Identified[b]
Gudbjornsson (2002)	Iceland	Chart review & mailed survey	1996 ACR 1998 UK	191 (55)	66.0	Any (rheumatic)	6.0	bisphosphonate, calcitonin, HRT, testosterone
Walker-Bone (2004)	UK	Chart review	1998 UK	175 (76)	Male: 64.2 Female: 66.9	Rheumatic	Male: 7,816.5 Female: 9,465 (median cumulative)	bisphosphonate, HRT
Wall (2008)	UK	Chart review	2002 UK	104 (74)	61.8	Rheumatic	8.6	bisphosphonate, HRT, teriparatide
Haroon (2011)	Ireland	Chart review	2002 NOS	81 (64[g])	62.0	Rheumatic	NR	bisphosphonate
Other (n=7)								
Hougardy (2000)	Australia	Chart review	1998 NOS	212 (58)[f]	69 (median)	Any (respiratory)	10.0 (median)	bisphosphonate, HRT
Rothberg (2000)	South Africa	Administrative database	2000 SAMA	1,614 (54)	Male: 51.0 Female: 53.0	Any (respiratory)	NR	bisphosphonate, HRT
Smith (2001)	Australia	Chart review	1996 ACR	189 (38)	75.2	Any (respiratory)	NR	bisphosphonate, HRT

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Author (year)	Country	Data Source	Main Guideline(s) Referenced	Patients, N (% female)	Mean age, years	GC Indication, included (main)	Mean GC dose[a], mg/day	Pharmacotherapy Identified[b]
Gera (2009)	India	Chart review	2002 NOS	105 (64)	42.0	Any (rheumatic)	NR	bisphosphonate, calcitonin, HRT, testosterone
Sadat-Ali (2009)	Saudi Arabia	Administrative database	2001 ACR	165 (39)	Male: 37.0 Female: 40.8	Any (rheumatic)	Male: 15.9 Female: 21.5	bisphosphonate, calcitonin, HRT
Srinivasulu (2010)	India	Administrative database	2001 ACR	151 (58)	52.5	Any (rheumatic)	NR	bisphosphonate
Kohli (2013)	India	Administrative database	2010 ACR	203 (60)	50.5	Any (rheumatic)	NR	bisphosphonate

ACR – American College of Rheumatology, AGA – American Gastroenterological Association, GC – glucocorticoid, HRT – hormone replacement therapy, NOS – National Osteoporosis Society, NR – not reported, SAMA – South American Medical Association.
[a] All doses reported in mg prednisone equivalent
[b] All studies also reported the proportion of patients who received a BMD test
[c] Highest daily dose on file
[d] 1996-1997 (62%), 1998-1999 (63%), 2000-2001 (59%)
[e] Unique patients identified from 17,736 new long-term systemic GC initiations
[f] Total GC users (inhaled + oral); approximately 53.3% were on oral GC therapy only, and 74.1% on combined oral + inhaled GC therapy
[g] % female only reported for 2009 cohort (n=34)

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TABLE 3 Summary of study methods (n=29)

		Total (n=29)		North America (n=17)		Europe (n=5)		Other (n=7)	
		N	%	N	%	N	%	N	%
Chronic Glucocorticoid Exposure Definition[a]									
Duration	**Dose**								
1 month	10 mg/day	1	3.4	1	5.9	0	0	0	0
2 months	Not specified	1	3.4	1	5.9	0	0	0	0
3 months	5 mg/day	4	13.8	3	17.6	0	0	1	14.3
	7.5 mg/day	4	13.8	1	5.9	0	0	3	42.9
	Not specified	6	20.7	2	11.8	3	60.0	1	14.3
6 months	5 mg/day	1	3.4	1	5.9	0	0	0	0
	7.5 mg/day	6	20.7	2	11.8	2	40.0	2	28.6
Any	2 g	2	6.9	2	11.8	0	0	0	0
	5 mg/day	1	3.4	1	5.9	0	0	0	0
Any[b]	Any	2	6.9	2	11.8	0	0	0	0
1 prescription/quarter		1	3.4	1	5.9	0	0	0	0
Outcome Reporting (Pharmacotherapy)									
Drugs included									
Bisphosphonate		29	100.0	17	100.0	5	100.0	7	100.0
Calcitonin		17	58.6	13	76.5	2	40.0	2	28.6
HRT		18	62.1	10	58.9	4	80.0	4	57.1
Raloxifene		7	24.1	6	35.3	1	20.0	0	0
Teriparatide		2	6.9	1	5.9	1	20.0	0	0
Testosterone		8	27.6	5	29.4	2	40.0	1	14.3
Drug reporting									
Any pharmacotherapy		8	27.6	7	41.2	1	20.0	0	0
Stratify by drug		7	24.1	3	17.6	1	20.0	3	42.9
Both		14	48.3	7	41.2	3	60.0	4	57.1

HRT – Hormone Replacement Therapy
[a]Glucocorticoid doses given as prednisone equivalent
[b]Results stratified by dose

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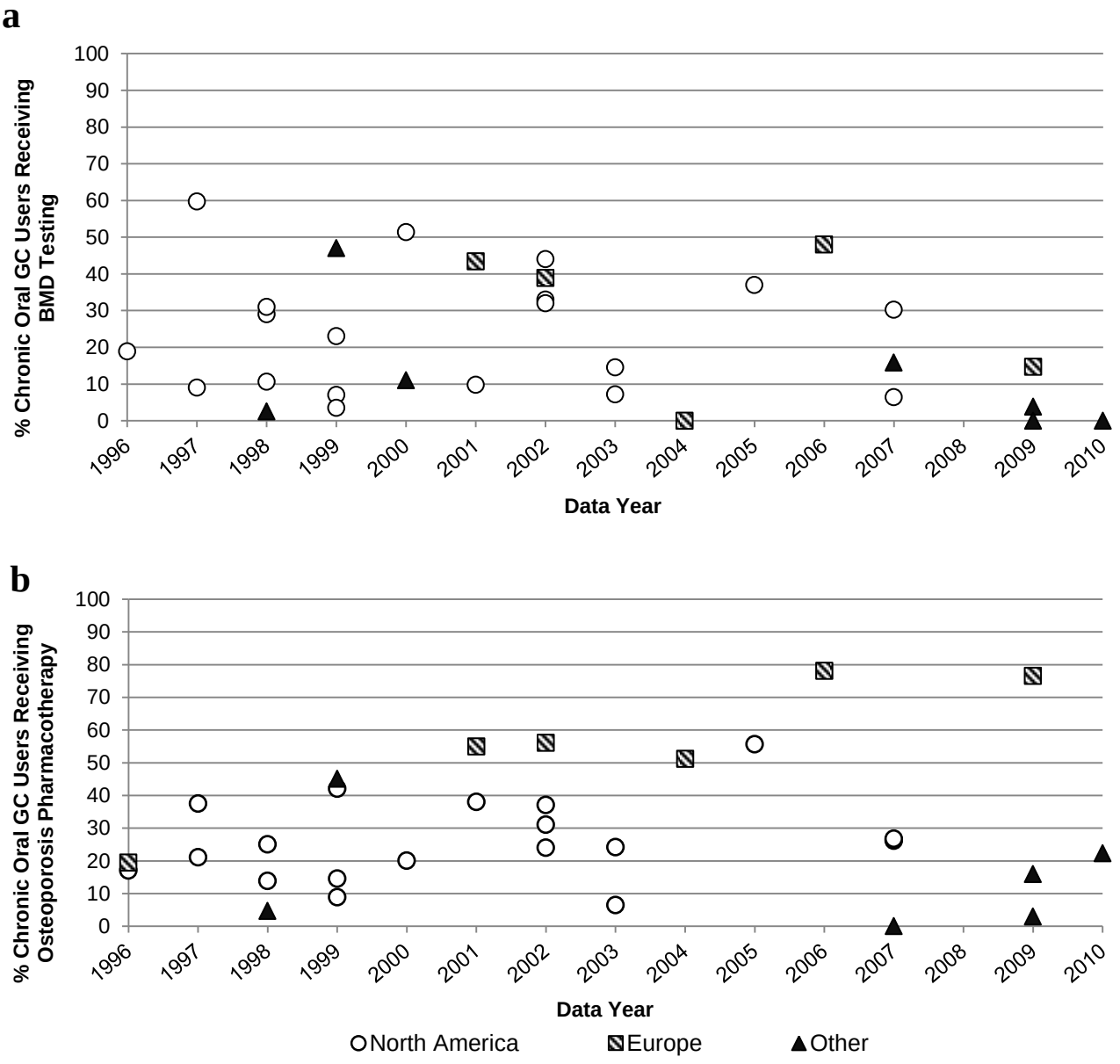
FIG. 2 Reported GC-induced osteoporosis management rates among chronic oral GC users, by region over time, (a) BMD testing (n=28), one study[67] reported no dual x-ray absorptiometry (DXA) machines at the time of study and is not reported here; (b) osteoporosis pharmacotherapy (n=27), two studies[51,71] did not report total pharmacotherapy and are not reported here. Year was identified by period of time examined in each study and thus does not match publication year.



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Prevalence of GC-Induced Osteoporosis Management

In the articles reviewed, the proportion of patients reported to have received BMD testing ranged from 0% to 60%, and pharmacotherapy ranged from 0% to 78%, Figure 2. Over 80% of studies identified that < 40% of chronic oral GC users received BMD testing or osteoporosis treatment.

Only three studies examined trends over time.[54,56,57] Ettinger *et al.* (2001) identified an increased prevalence of osteoporosis medication prescribing to a high of 9% over an 18-month time period from January 1999 to June 2000 in California, USA.[54] However, this increase was attributed to selecting only patients without prior exposure to osteoporosis medication. Saag *et al.* (2006) similarly described an increase in GC-induced osteoporosis management among older women (aged ≥ 65) in the United States from 1996 to 2001. BMD testing increased from 10% to 19% and osteoporosis treatment increased from 24% to 44%. However, little improvement (< 6%) was noted among men and younger women.[56] More recently, Majumdar *et al*. (2012) reported an increase in BMD testing or osteoporosis treatment in Manitoba, Canada from 17% to 27% between 1998 and 2008, yet note that the trend appeared to plateau in 2002.[57]

Predictors of GC-Induced Osteoporosis Management

Seventeen studies (59%) identified predictors of GC-induced osteoporosis management, 9 as a primary study objective. Patient sex (88%), patient age (71%), and provider specialty (65%) were the most frequently examined predictors of GC-induced osteoporosis management. Thirteen of the fifteen studies (87%) examining sex identified female sex to be significantly associated with osteoporosis management[50-60,71,72], and seven of twelve studies (58%) that investigated age identified older age as a statistically significant predictor.[50,52-57] Ten of eleven studies (91%) that examined provider specialty reported that rheumatologists provided osteoporosis management more frequently than general practitioners and other specialists.[50-54,56-58,61,74] Other statistically significant predictors of GC-induced osteoporosis management included: prior fracture[50,52,54,56,71], prior BMD test[54,71,74], race,[50-52,65] post-menopausal status[50,51,59], greater number of comorbidities,[52,59] new GC use[52], higher cumulative GC dose[52], longer duration of GC use[50,65,71], and greater number of healthcare visits.[53] Socio-demographic (residence, income, insurance, education)[51,53,57], behavioural (GC knowledge, tobacco use)[51,59], and provider-related (demographic, training)[59] factors were also examined by some studies; yet, none of these were statistically significant predictors of GC-induced osteoporosis management.

DISCUSSION

Chronic oral GC therapy is the leading cause of secondary osteoporosis,[5] and osteoporotic fracture is associated with significant morbidity and mortality.[78-81] As a result, many organizations have published guidelines outlining the risk of chronic oral GC therapy and consistently recommend BMD testing and osteoporosis pharmacotherapy to minimize bone loss and reduce fracture risk. Despite these recommendations, our systematic review identified low levels of GC-induced osteoporosis management. Furthermore, articles identified in this systematic review provide little evidence that GC-induced osteoporosis management is improving over time, particularly in recent years.

Three studies described an increase in GC-induced osteoporosis management since the late 1990s',[54,56,57], yet, report that the proportion of chronic GC users who received BMD testing or osteoporosis treatment remains suboptimal (< 30%) in later years. There is also some evidence to suggest that GC-induced osteoporosis management is more common in Europe compared to North America and other regions. All studies completed in Europe after 2002 report rates > 50% for osteoporosis pharmacotherapy. However, these were based entirely in rheumatology clinics where GC-induced osteoporosis management has been observed more commonly than at the general population level.[50-54,56-58,61,74] This disparity may indicate a possible disconnect between osteoporosis guidelines and clinical practice.

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While 83% of studies assessed osteoporosis management according to guideline recommendations, only 45% used guideline criteria to identify their chronic GC user population. This produced heterogeneity in methods used to define chronic GC use and osteoporosis management that preclude the direct comparison of results between studies. Studies also described highly diverse patient populations that varied substantially in age, sex, and comorbidity, making it difficult to compare the consistency of predictor variables between studies.

Though the majority of studies identify female sex as a predictor of GC-induced osteoporosis management, both studies that exclusively examined men reported treatment prevalence estimates (31% Cruse *et al.* and 38% Elliot *et al.*)[49,61] consistent with other studies that included both men and women. In addition, there was no apparent relationship between average patient age (range 37 to 75 years) and rates of osteoporosis management. Several studies noted that patients between the age of 50 and 70 were more likely to receive a BMD test compared to patients under the age of 50, while patients over the age of 70 were more likely to be treated for osteoporosis compared to younger patients.[52,56,57] This finding may represent an important shift in a physician's priorities from testing to treatment in older patients where age-related bone loss may be more apparent.

Recent reports of adverse events,[82,83] particularly with bisphosphonates, may contribute to the challenge in managing osteoporosis. In addition, patients requiring chronic oral GC therapy often have disease indicating GC therapy as well as several additional chronic comorbidities. Thus, in the context of chronic oral GC therapy, osteoporosis management may be more difficult to coordinate due to the number of physicians involved in caring for patients with multiple chronic comorbidities. This combination of factors has been noted in similar clinical areas including post-hip fracture osteoporosis management.[84]

Future work aimed at improving our understanding of patients treated with chronic oral GC therapy may help identify barriers to treatment and provide insight into why GC-induced osteoporosis management is suboptimal. In turn, this may help researchers develop targeted interventions to improve GC-induced osteoporosis management.

There are several limitations that must be noted for our study. First, we acknowledge that some observational studies relating to GC-induced osteoporosis management may have been missed. To mitigate this risk, we used a comprehensive search strategy derived from previous Cochrane systematic reviews, used two search databases, and had two independent reviewers thoroughly conduct the search. Second, due to the heterogeneity between studies and patients, we are unable to comment on overall trends identified and determine the relative importance of predictor variables such as age, sex, and physician specialty for GC-induced osteoporosis management. Nonetheless, all studies consistently report suboptimal management of GC-induced osteoporosis.

CONCLUSION

Despite consistent guideline recommendations to target osteoporosis prevention at the onset of chronic oral GC therapy, results from our systematic review identify that the proportion of chronic GC users receiving osteoporosis management is low, with little evidence of improvement over time, particularly in recent years. Although it is unclear if this represents true mismanagement, it does indicate a missed opportunity for fracture prevention among chronically ill patients requiring long-term GC therapy. Future research should focus on improving our understanding of these patients to identify clinical barriers to treatment.

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APPENDIX 1

Search
1. *Osteoporosis/
2. osteoporos#s.tw.
3. bone loss$.tw.
4. Bone Density/
5. (bone adj2 (density or fragil$)).tw.
6. bone mass.tw.
7. bmd.tw.
8. exp Fractures, Bone/
9. fracture$.tw.
10. Postmenopause/
11. (post menopaus$ or postmenopaus$ or post- menopaus$).tw.
12. or/1-11
13. prednisone.tw,sh,rn.
14. glucocorticoid.rn,tw,sh.
15. corticosteroid$.tw
16. glucocorticoids/
17. or/13-16
18. 12 and 17
19. limit 18 to (English language and humans)
20. limit 19 to clinical trial, all
21. 19 not 20

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