A Population-Based Study of the Effectiveness of Bisphosphonates at Reducing Hip Fractures among High Risk Women

APHA Conference
Washington, DC
November 2, 2011

Presenter Disclosures

Kathy Schneider, PhD

(1) The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose

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3

Background

- The Chronic Condition Data Warehouse (CCW) contains Medicare claims data for 1999+
- Medicare Part D event data are available for 2006 forward
- Linkage of these data files presents an opportunity to examine effectiveness of pharmacologic management of patients

4

Osteoporosis

- Is highly prevalent among older adults
  - Approximately 13-18% of women 50 years or older
  - Approximately 3-6% of men
  - Fee-for-service Medicare data from CCW indicate the point prevalence of treatment for osteoporosis was 12.6% in 2009

5

Fracture Risk

- Risk of fractures is high in the Medicare population
  - The lifetime risk of an osteoporotic fracture is 40-50% for women and 13-22% for men (Johnell & Kanis, 2005)
- Risk increases with age. The 10-year risk for low risk women:
  - At age 60 = 2.4%
  - At age 70 = 7.87%
  - At age 80 =18.0% (Kanis, 2002, p.1934)
- Fractures cause tremendous morbidity, cost, and can result in mortality
  - 25% of hip fracture patients who were 50 or older die within a year of the fracture(OTA, 1994)

6

Pharmacologic Options

- Pharmacologic therapies have been shown in trials to be effective in reducing risk of fractures
- Bisphosphonates can be used to inhibit bone resorption, thereby decreasing bone loss
- Many options – and dosage/regimen varies

7

Objectives

- Determine prevalence of bisphosphonate use among high risk women
- Identify whether use offered protection against fractures
- Demonstrate how the use of Medicare Part A and B claims data can support pharmacologic studies

8

Sample

- Selected a random 20% sample from the Medicare Denominator in 2006
- Limited population to women aged 65 or older
- Limited population to those with Medicare A/B coverage, without Medicare Advantage (i.e., fee-for-service), and Part D coverage – for 11+ months in 2006, and 1st month of 2007

9

Exclusions (applied using 2006 data)

- Women treated for Paget's disease
- Women with other 12 chronic conditions
  - Alzheimer's/dementia, CKD, COPD, Heart Failure, diabetes, Ischemic Heart Disease, Depression, Rheumatoid Arthritis or Osteoarthritis, Stroke, and 3 cancers: breast, colorectal, lung

10

Risk Strata

Stratified cohort into 3 risk-based strata:

1. History of hip fracture treatment
2. History of osteoporosis treatment
3. Controls – without any of the 12 chronic conditions, and without history of hip fracture or osteoporosis

11

Data Sources

- 2006-2009 CCW Medicare data
  - Part A Inpatient
  - Part A Outpatient
  - Part B Carrier
  - Part D prescription drug events
  - Beneficiary Annual Summary
  - Beneficiary Summary
- First DataBank® NDDP Plus database

12

Surveillance - Methods

- Obtained duration of continuous Medicare A/B fee-for-service (FFS) coverage, and Part D coverage (2007-2009)
- Duration of follow up
  - Censoring events = loss of FFS, disenrollment from Part D, or death

13

Prescription Drug Use - Methods

- Identified National Drug Codes (NDC) and Healthcare Common Procedure Coding System (HCPCS) codes for
  - Individual Bisphosphonates by strength – separate ones for Paget's disease vs. osteoporosis
  - Raloxifene
  - Calcitonin, Salmon
  - Estrogens
  - Progesterones
- Extracted PDEs and Part B line records with relevant NDCs and HCPCS, respectively

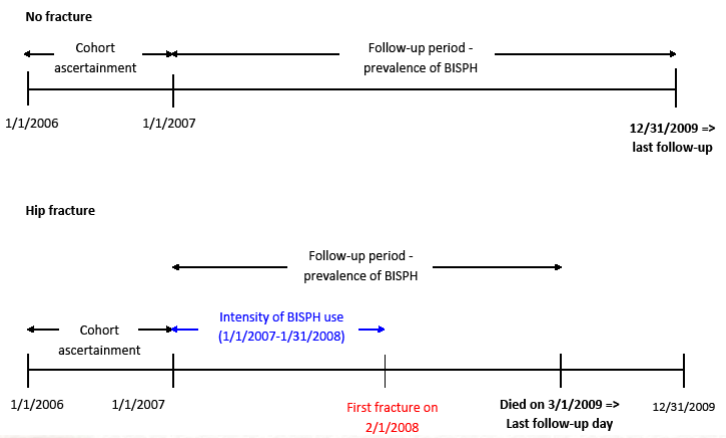
14

Outcomes - defined

Outcome	Claim Type	ICD-9 diagnosis code in any position on the claim
Hip/Pelvic Fracture	Part A - Hospital inpatient (IP) claim	* 733.98 * 808.0, 808.1, 808.2, 808.3, 808.41, 808.42, 808.43, 808.49, 808.51, 808.52, 808.53, 808.59, 808.8, 808.9 * 820.00, 820.01, 820.02, 820.03, 820.09, 820.10, 820.11, 820.12, 820.13, 820.19, 820.20, 820.21, 820.22, 820.30, 820.31, 820.32, 820.8, 820.9
Wrist Fracture	Part A IP, Hospital outpatient (HOP), or Part B carrier (Physician Evaluation and Management codes only)	* 733.12 * 813.40, 813.41, 813.42, 813.43, 813.44, 813.45, 813.46, 813.47 * 814.00, 814.10

15

Study Design



16

Study Exposures- 2 variables

1. Bisphosphonate prevalence – any time 2007-2009 (pre-fracture)

2. Intensity of bisphosphonate use
   - No use
   - Low
   - High

17

Study Exposures

- Intensity of bisphosphonate use
  - Calculated as a proportion of the sum of days supply of bisphosphonate from January 1, 2007 to
    - The last follow-up day for those without a fracture
    - The day prior to the first fracture in the follow-up period for those with a fracture
  - Assigned a standard days supply to injectable ibandronate and zoledronic acid
  - 80% of days or more = high-intensity

18

Demographic Characteristics

	Prior hip fx	%	Osteoporosis	%	Controls	%	All	%
n	**4,268**	**1.97**	**89,378**	**41.4**	**122,489**	**56.67**	**216,135**	**100**
Mean Age (in years)*	83.02		76.2		73.94		75.05	
Race Category*								
White	3,860	90.4	75,445	84.4	93,997	76.74	173,302	80.18
Black	124	2.91	3,388	3.79	12,519	10.22	16,031	7.42
Asian	95	2.23	4,087	4.57	3,993	3.26	8,175	3.78
Hispanic	135	3.16	4,873	5.45	8,038	6.56	13,046	6.04
Other	54	1.27	1,585	1.77	3,942	3.22	5,581	2.58
Original Reason for Entitlement								
Aged	3,956	92.7	84,791	94.9	115,189	94.04	203,936	94.36
Disabled	312	7.31	4587	5.13	7300	5.95	12199	5.64
Dual status in 2006 *								
None	2,759	64.6	68,675	76.8	83,080	67.83	154,514	71.49
Dual	1,509	35.36	20,703	23.16	39,409	32.18	61,621	28.51

19

Prescription Drug Use

Bisphosphonate use at any time during follow up period (disregarding fracture)

	n (%)
Any Bisphsphonate	59,333 (27.45)
Alendronate	41,621 (19.26)
Ibandronate	9,408 (4.35)
Risidronate	16,729 (7.74)
Zoledronic acid	2,361 (1.09)

20

Prescription Drug Use (cont.)

Intensity of bisphosphonate use (disregarding fracture)

	Prior hip fracture		Osteoporosis		Controls		Total	
	n	%	*n*	%	*n*	%	N	%
no use	2,657	62.25	45,704	51.14	108,441	88.53	156,802	72.55
low	1,019	23.88	27,314	30.56	11,359	9.27	39,692	18.36
high	592	13.87	16,360	18.3	2,689	2.2	1,9641	9.09

Level of bisphosphonate use varied significantly by study group (chi-square p <0.001)

The intensity of bisphosphonate use in the control group was lower than in either of the higher risk groups.

21

Prescription Drug Use (cont.)

Demographic differences in bisphosphonate use:

	No Bisphosphonate	%	Bisphosphonate	%	All	%
n	**156,802**	**72.6**	**59,333**	**27.5**	**216,135**	**100**
Mean Age	74.983		75.227		75	
Race Category*						
White	124,499	71.8	48,803	28.2	173,302	80.18
Black	14,018	87.4	2,013	12.6	16,031	7.42
Asian	4,587	56.1	3,588	43.9	8,175	3.78
Hispanic	9,479	72.7	3,567	27.3	13,046	6.04
Other	4,219	75.6	1,362	24.4	5,581	2.58
Original Reason for Entitlement *						
Aged	147,207	72.2	56,729	27.8	203,936	94.36
Disabled	9,595	78.7	2,604	21.4	12,199	5.64
Dual status in 2006						
None	109,448	70.8	45,066	29.2	154,514	71.49
Dual	47,354	76.85	14,267	23.15	61,621	28.51

22

Prescription Drug Use (cont.)

Other osteoporosis drugs used

	n (%)
Other osteoporosis drugs	42,842 (19.82)
Estrogen	29,623 (13.71)
Progesterone	1,409 (0.65)
Raloxifene	10,281 (4.76)
Teriparatide	1,202 (0.56)
Calcitonin	4,232 (1.96)

Only 6.2% of women used both a bisphosphonate and another osteoporosis drug.

These other drugs are controlled in the multivariable analyses.

23

Results: Risk of Hip Fractures

Group	No bisphosphonate			Any bisphosphonate use			Total hip fractures	
	n	Fractures	%	*n*	Fractures	%	Fractures	%
Prior hip fracture	2,689	240	8.93	1,579	129	8.17	369	8.65
Osteoporosis	45,946	1,345	2.93	43,432	1,000	2.3	2,345	2.62
Controls	108,672	1,819	1.67	13,817	131	0.95	1,950	1.59
TOTAL	157,307	3,404	2.16	58,828	1,260	2.14	4,664	2.16

There are significant differences in fracture rates by risk strata (chi-sq $p<0.001$)

Bisphosphonate users in the osteoporosis and control groups were significantly less likely than non-users to have a subsequent hip fracture (chi-sq $p<0.001$)

There are no overall hip fracture differences between bisphosphonate users and non-users (chi-sq $p=0.75$)

24

Results: Risk of Wrist Fractures

Group	No bisphosphonate			Any bisphosphonate use			Total wrist fractures	
	n	Fractures	%	*n*	Fractures	%	Fractures	%
Prior hip fracture	2,682	91	3.39	1,586	63	3.97	154	3.61
Osteoporosis	45,922	1,079	2.35	43,456	925	2.13	2,004	2.24
Controls	108,636	1,617	1.49	13,853	185	1.34	1,802	1.47
TOTAL	157,240	2,787	1.77	58,895	1,173	1.99	3,960	1.83

There are significant differences in fracture rates between bisphosphonate users and non-users for the osteoporosis stratum (chi-sq p=0.026)

There are overall wrist fracture differences between bisphosphonate users and non-users, however the drugs don't appear to be protective (chi-sq p<0.001)

25

Results: Fracture Risk (either hip or wrist) and Bisphosphonate Use

Group	No bisphosphonate			Any bisphosphonate use			Total fractures	
	n	Fractures	%	*n*	Fractures	%	Fractures	%
Prior hip fracture	2,710	310	11.44	1,558	179	11.49	489	11.46
Osteoporosis	46,141	2,323	5.03	43,237	1,844	4.26	4,167	4.66
Controls	108,857	3,333	3.06	13,632	307	2.25	3,640	2.97
TOTAL	157,708	5,966	3.78	58,427	2,330	3.99	8,296	3.84

There are significant differences in fracture rates for the osteoporosis and control groups (chi-sq p<0.001)

There are overall fracture differences between bisphosphonate users and non-users (chi-sq p=0.028)

26

Multivariable Modeling

- Univariate models resulted in conflicting information regarding effectiveness of bisphosphonates
- Ran logistic regression models for all 3 outcomes: hip, wrist, or either type of fracture
- Included demographic variables (age, race, sex, original reason for entitlement, dual status), study group, and drug exposure, controlling for use of other osteoporosis drugs

27

Results: Multivariable Modeling – Hip Fracture

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
aged Age 71-75 vs Age 66-70	1.816	1.596	2.067
aged Age 76-80 vs Age 66-70	3.771	3.345	4.251
aged Age 81-85 vs Age 66-70	7.303	6.497	8.209
aged Age 86-115 vs Age 66-70	13.993	12.48	15.689
RACE Asian vs White	0.456	0.371	0.56
RACE Black vs White	0.366	0.31	0.433
RACE Hispanic vs White	0.544	0.463	0.639
RACE Other vs White	0.897	0.716	1.124
OREC2006 1 vs 0	1.577	1.385	1.795
duals2006 dual vs none	1.214	1.13	1.305
ot_drug 1 vs 0	1.103	1.022	1.191
BISPH prevalence 1 vs 0	**0.864**	**0.804**	**0.928**
GROUP hip fx vs controls	2.274	2.013	2.569
GROUP osteoporosis vs controls	1.344	1.256	1.439

28

Results: Multivariable Modeling - Wrist Fracture

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
aged Age 71-75 vs Age 66-70	1.186	1.081	1.301
aged Age 76-80 vs Age 66-70	1.353	1.229	1.489
aged Age 81-85 vs Age 66-70	1.75	1.582	1.936
aged Age 86-115 vs Age 66-70	1.899	1.702	2.119
RACE Asian vs White	0.56	0.453	0.692
RACE Black vs White	0.314	0.256	0.386
RACE Hispanic vs White	0.714	0.61	0.835
RACE Other vs White	0.887	0.713	1.103
OREC2006 1 vs 0	1.135	0.983	1.31
duals2006 dual vs none	1.033	0.951	1.122
ot_drug 1 vs 0	0.932	0.86	1.011
BISPH prevalence 1 vs 0	**0.938**	**0.87**	**1.011**
GROUP hip fx vs controls	1.827	1.536	2.173
GROUP osteoporosis vs controls	1.41	1.312	1.515

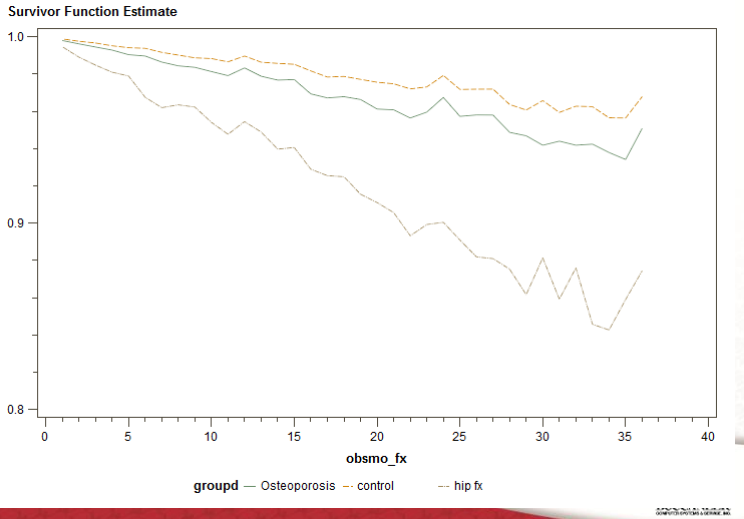
29

Results: Multivariable Modeling - either Hip or Wrist Fracture

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
aged Age 71-75 vs Age 66-70	1.381	1.28	1.49
aged Age 76-80 vs Age 66-70	2.044	1.897	2.202
aged Age 81-85 vs Age 66-70	3.341	3.101	3.6
aged Age 86-115 vs Age 66-70	5.365	4.982	5.778
RACE Asian vs White	0.492	0.423	0.572
RACE Black vs White	0.345	0.303	0.394
RACE Hispanic vs White	0.611	0.545	0.686
RACE Other vs White	0.864	0.735	1.017
OREC2006 1 vs 0	1.33	1.205	1.469
duals2006 dual vs none	1.145	1.082	1.21
ot_drug 1 vs 0	1.009	0.953	1.069
bisph prevalence 1 vs 0	**0.907**	**0.859**	**0.956**
GROUP hip fx vs controls	2.121	1.91	2.356
GROUP osteoporosis vs controls	1.369	1.301	1.44

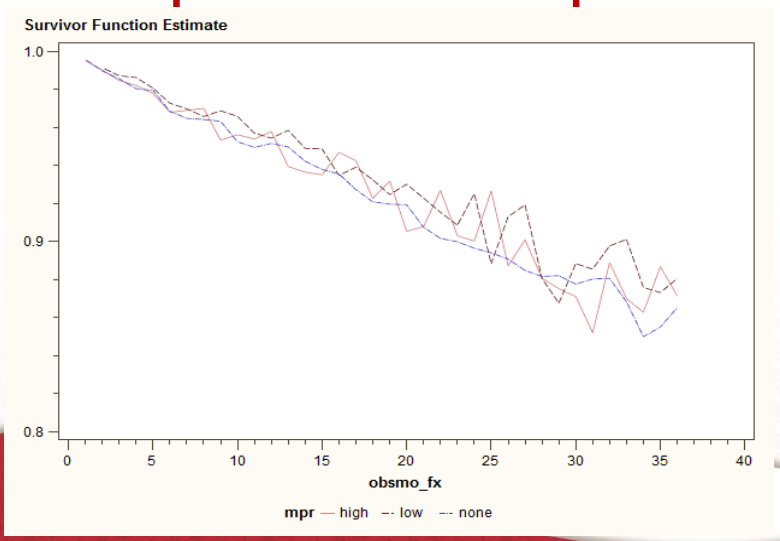
30

Time to Either Type of Fracture - by Risk Strata



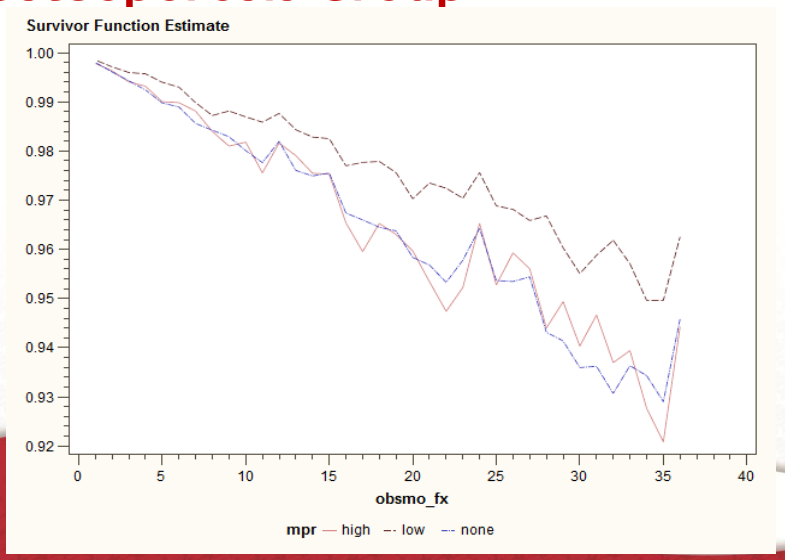
31

Time to Either Type of Fracture - Prior Hip Fracture Group



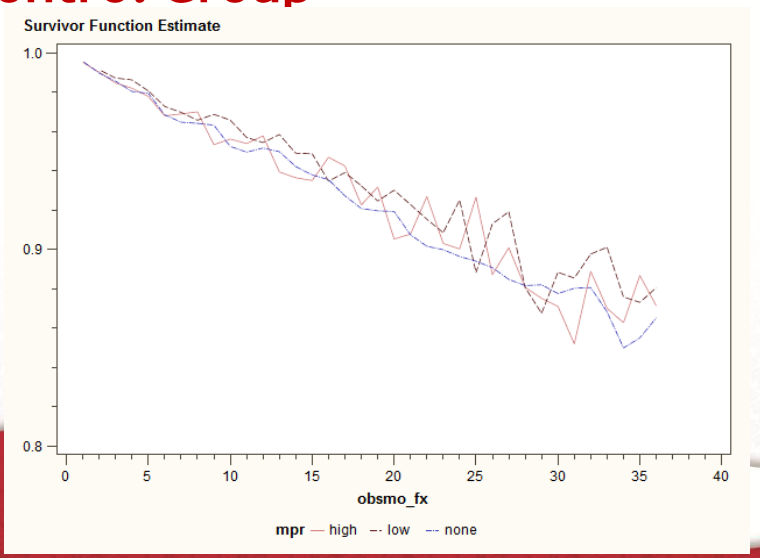
32

Time to Either Type of Fracture- Osteoporosis Group



33

Time to Either Type of Fracture - Control Group



34

Results: Time to Fracture

- More intense bisphosphonate use did not appear to delay time to fractures
  - Low-intensity users from the osteoporosis and control groups had lower risk of fracture than the high-intensity users

35

Limitations

- Did not directly assess risk of fractures due to no BMD measure
- Could not measure other risk factors: smoking, nutrition, BMI, physical activity
- Small population subsets with high drug use intensity – may limit conclusions
- Some potential misclassification for "intensity" measure - did not limit Part D surveillance days due to person being hospitalized in follow-up period

36

Conclusions

- Much underuse of bisphosphonates
  - Both in terms of prevalent use and intensity of use
- Bisphosphonates appear to be effective in reducing risk of either type of fractures (hip or wrist)
  - Little difference is seen in the prior hip fracture group for reducing risk of another hip fracture
- Only the low-intensity bisphosphonate use appeared to delay fractures

37

Conclusions (cont.)

- Using Medicare A/B in addition to Part D is helpful for pharmacologic studies

38