



Quality of Bone Health Care in Patients with Cancer

Maria E. Suarez-Almazor, MD, PhD
Department of General Internal Medicine

THE UNIVERSITY OF TEXAS

MD Anderson
Cancer Center

Making Cancer History®

Acknowledgements

- Linda Elting, DrPH
- Ruili Luo, PhD
- Mamatha Siricilla, MD
- Prashanth Peddi, MD

- Jim Goodwin, MD, and CERCIT collaborators



Bone Health in Cancer Patients and Survivors

- Increasingly recognized as major determinant of outcomes
 - Quality of life
 - Survival (30% pts with hip fracture die within 1 yr)
- Cancer occurs more frequently later in life
- Therapies
 - Aromatase inhibitors (AI) – breast cancer
 - Androgen-deprivation therapy (ADT) – prostate cancer
 - Steroids – many malignancies ++ hematological
- Appropriate screening and therapy can mitigate bone loss

Bone Health in Cancer Patients and Survivors

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 - Androgen-deprivation therapy (ADT) – prostate cancer
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National Guidelines

- American Society of Clinical Oncology (ASCO)
- National Comprehensive Cancer Network (NCCN)
- European professional associations

Recommend measuring bone mineral density (BMD) with DXA prior to initiation of AI or ADT

DXA=dual-energy X-Ray absorptiometry



Cheap ~ \$200
Covered by Medicare
Quick
Inexpensive
Very little radiation
(less than coast-to-coast flight)

Objectives

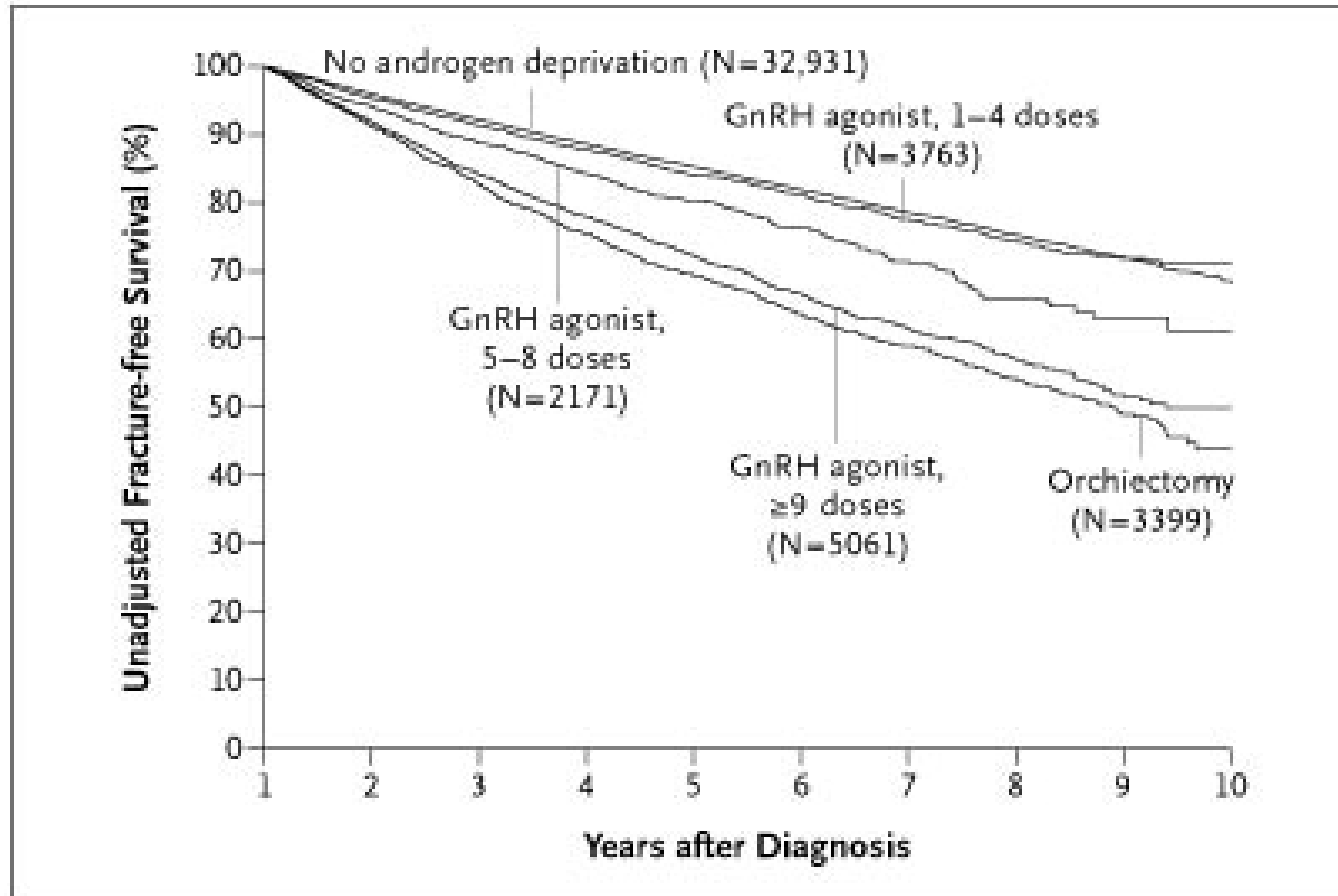
- TCR-linked Medicare databases
- To examine the utilization of bone mineral density (BMD) measurement with DXA and bone conserving agents (BCA)
 - Women with breast cancer initiating AI
 - Men with prostate cancer initiating parenteral ADT
 - Diagnosis
- Window of use of BMD within
 - 1 year prior to onset of therapy
 - 6 months after

Prostate Cancer

Fractures in Prostate Cancer

- 50,000 + patients
- 19.4% receiving ADT had fractures vs
- 12.6% not receiving ADT

Unadjusted Fracture-free Survival among Patients with Prostate Cancer, According to Androgen-Deprivation Therapy.



Shahinian VB et al. N Engl J Med 2005;352:154-164.



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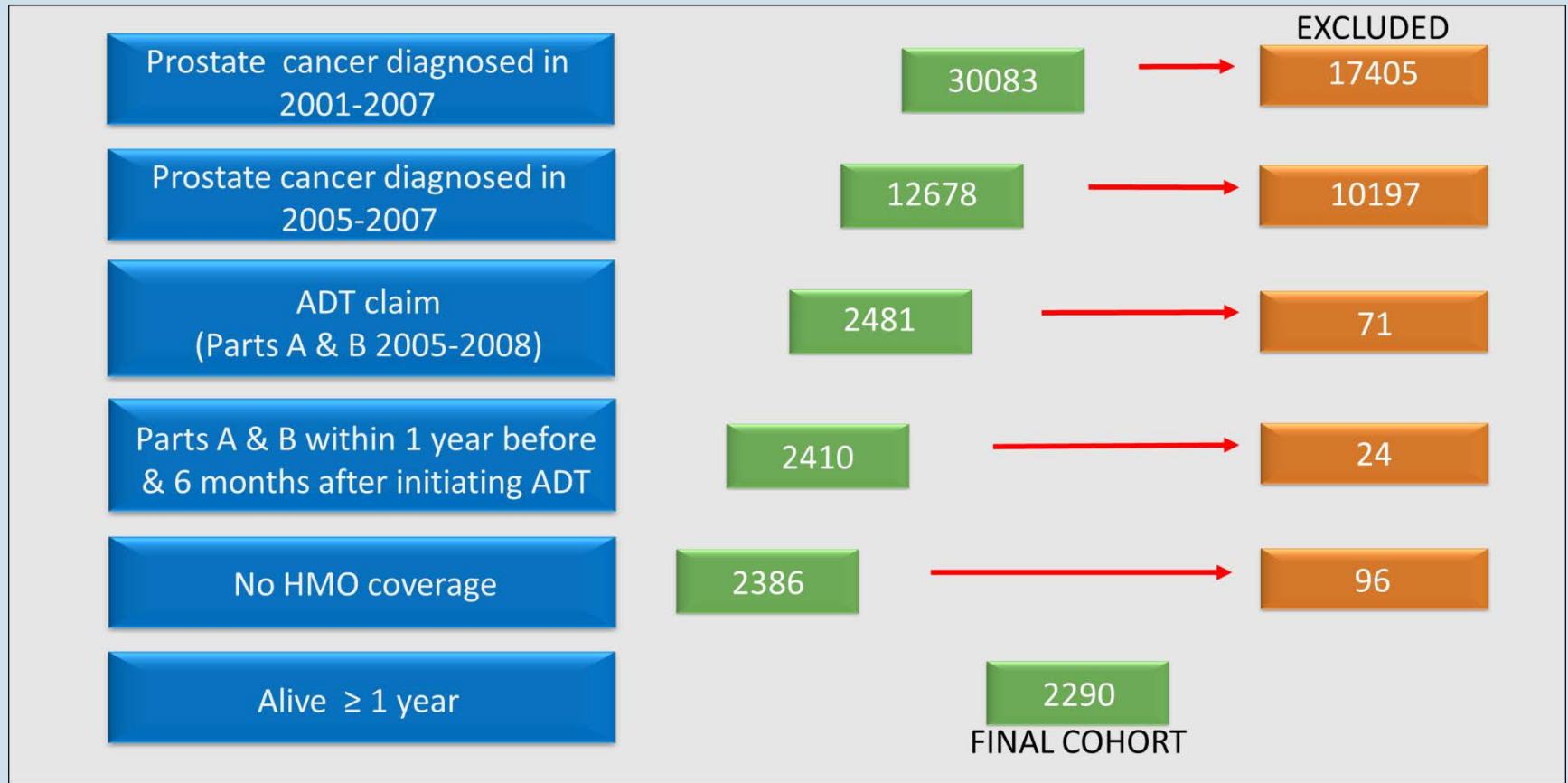
Methods - Inclusion Criteria

- Men age ≥ 66 years diagnosed with prostate cancer between 2005 to 2007
- Received orchiectomy or initial parental ADT between 2005-2008
- Alive for at least 1 year after diagnosis
- Subgroup: Enrolled in Medicare Part D drug plans (2007 or 2008) (use of IV or oral bisphosphonates, calcitonin, and teriparatide)

Methods

- Window of use 1 year prior – to 6m months after ADT
- Multivariate logistic regression model
 - Likelihood of DXA use
 - Controlling for age, ethnicity, stage, size of area of residence and socioeconomic variables.
- Subgroup of patients enrolled in Medicare Part D were evaluated for use of BCA at time of ADT initiation.

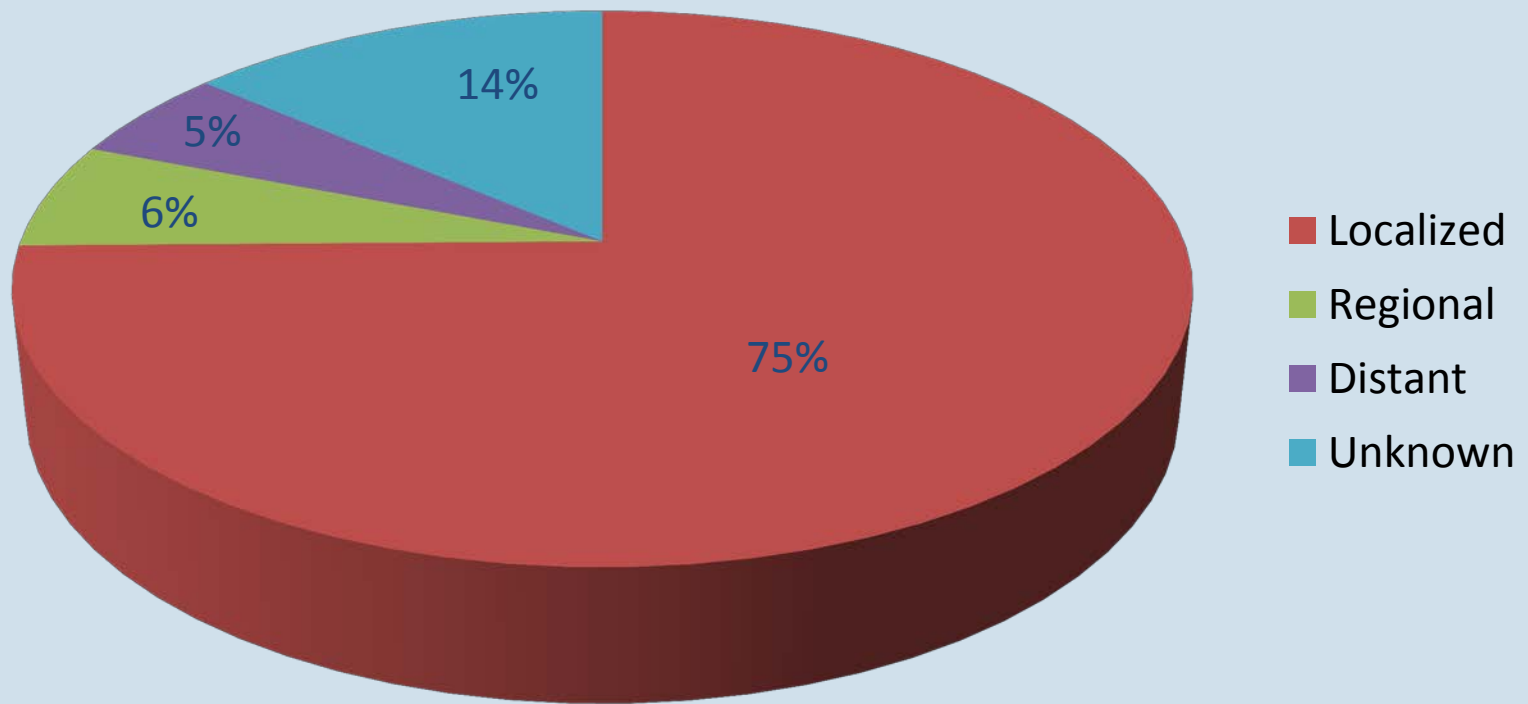
Cohort Selection



Prostate Cancer Cohort N=2290

Variable	Category	N= 2290
Age, yrs		75 yrs
Ethnicity	White	74%
	African-American	15%
	Hispanic	10%
	Other	1%
Androgen deprivation therapy	Orchiectomy	2%
	Leuprolide	80%
	Goserelin	8%

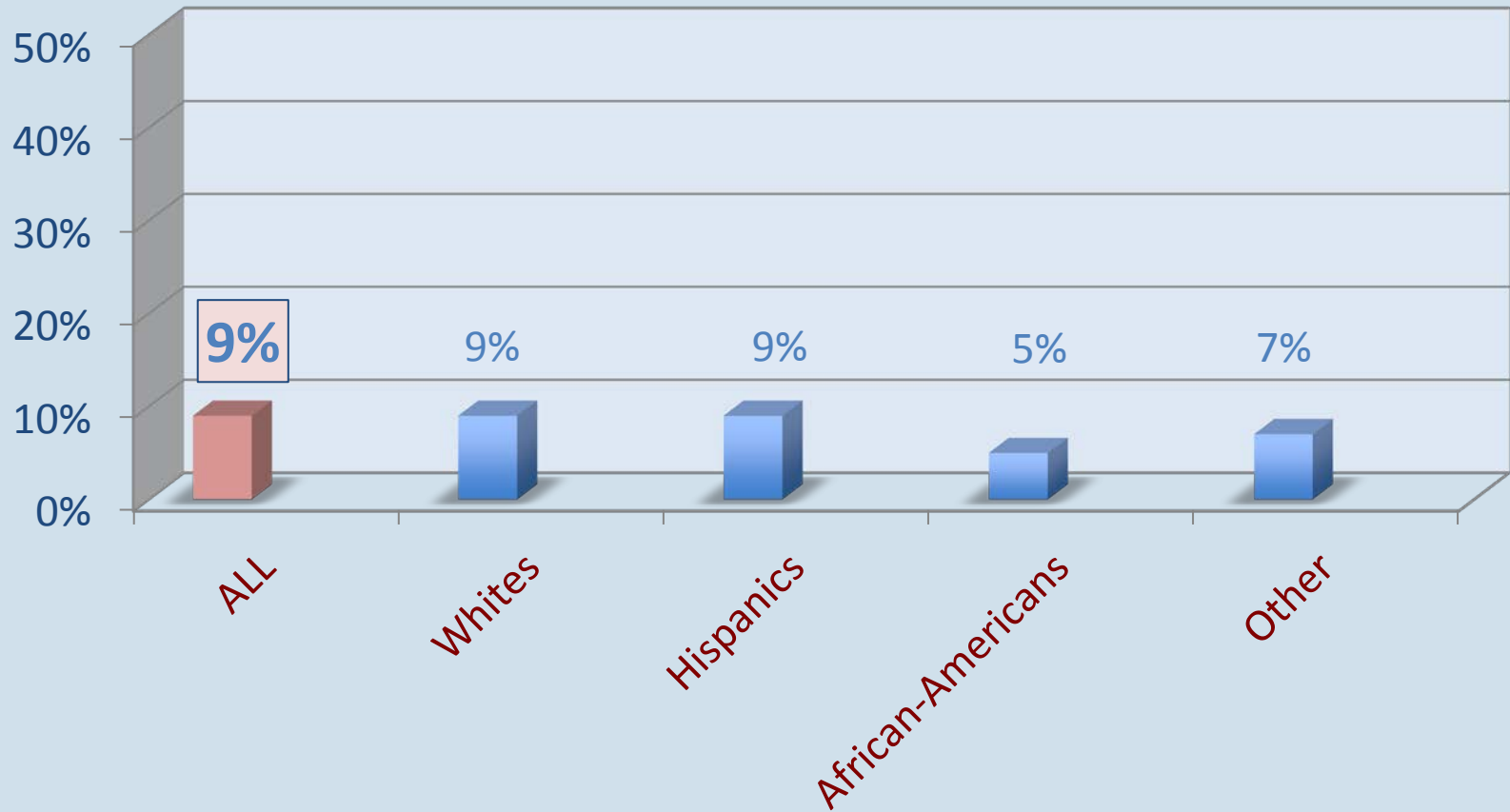
Prostate Cohort Stage



Use of ADT

		All (N=2290) (% over total)	DXA (n=197) (% with DXA per row category)	P value (DXA vs no DXA)
Age group, years	66 - 74	1153 (50.4%)	81 (7.0%)	0.007*
	≥75+	1137 (49.6%)	116 (10.2%)	
Type of ADT	Parenteral ADT	2262 (98.8%)	197 (8.7%)	0.10
	Orchiectomy	28 (1.2%)	0 (0%)	
Type of parenteral ADT	Abarelix	2 (0.1%)	0 (0%)	>0.20
	Goserelin	190 (8.3%)	14 (7.4%)	
	Histrelin	68 (3.0%)	5 (7.4%)	
	Leuprolide	1842 (80.4%)	163 (8.8%)	
	Triptorelin	160 (7.0%)	15 (9.4%)	

DXA Use



$p > 0.20$

Multivariate logistic regression model for use of DXA

Independent variables§		OR (95% CI)	P value
Age, years			
(66 – 74)	≥75	1.5 (1.1 -2.1)	0.007*
Race			
(Non-Hispanic White)	Hispanic	0.87 (0.53-1.4)	>0.20
	African-American	0.58 (0.30-1.1)	0.10
	Other	0.77 (0.18-3.4)	>0.20
Stage			
(Localized)	Regional	1.2 (0.6-2.1)	>0.20
	Distant	0.7 (0.3-1.6)	>0.20
	Unknown	0.8 (0.5-1.2)	>0.20
Type of ADT			
(Triptorelin)	Leuprolide	1.0 (0.57-1.8)	>0.20
	Goserelin	0.76 (0.35-1.6)	>0.20
	Histrelin	0.77 (0.26-2.2)	>0.20
Area of residence			
(Big metropolitan)	Metropolitan	1.3 (0.92-1.9)	0.14
	Urban	0.67 (0.33-1.3)	>0.20
	Small urban	0.40 (0.19-0.82)	0.012*
	Rural	1.5 (0.54-4.2)	>0.20
Enrolled in state buy-in (No)	Yes	0.92 (0.54-1.6)	>0.20
% with high school †			
(Q1: 2.84% - 19.63%)	Q2: 19.64% - 26.53%	1.0 (0.66-1.5)	>0.20
	Q3: 26.54% - 32.65%	0.74 (0.46-1.2)	>0.20
	Q4: 32.66%+	0.70 (0.41-1.2)	0.18
Median annual income † (Q1: \$8,063 - \$30,133)			
	Q2: \$30,134 - \$37,924	0.80 (0.50-1.3)	>0.20
	Q3: \$37,925 - \$51,611	0.92 (0.58-1.5)	>0.20

Use of BCA agents

- Medicare Part D
- N=1060
- 5.6% received BCA within 6 months after starting DXA
- Overall 12.6% either underwent DXA or received BCA

Multivariate logistic regression model for use of BCA/DXA (subgroup enrolled in Part D) N = 1059

Independent variables §		OR (95% CI)	P value
Age, years			
(66 – 74)	≥75	1.4 (0.91-2.0)	0.13
Ethnicity			
(Non-Hispanic white)	Hispanic	0.96 (0.53-1.7)	>0.20
	African-American	1.0 (0.52-2.0)	>0.20
	Other	0.73 (0.16-3.3)	>0.20
Stage			
(Localized)	Regional	1.5 (0.65-3.6)	>0.20
	Distant	7.6 (4.1-14.0)	<.0001*
	Unknown	1.4 (0.82-2.4)	>0.20
Type of ADT			
(Parenteral ADT)	Orchiectomy	0.12 (0.02-1.00)	0.05*
Area of residence			
(Big metropolitan)	Metropolitan	1.3 (0.81-2.2)	>0.20
	Urban	0.92 (0.41-2.1)	>0.20
	Small urban	1.1 (0.56-2.2)	>0.20
	Rural	4.6 (1.6-13.6)	0.01*
Enrolled in state buy-in (No)	Yes	0.98 (0.58-1.6)	>0.20
% with high school †			
(Q1: 3.87%-19.75%)	Q2: 19.76% - 26.88%	1.3 (0.75-2.2)	>0.20
	Q3: 26.89% - 32.89%	0.41 (0.21-0.81)	0.01*
	Q4: ≥32.90%	0.73 (0.38-1.44)	>0.20
Median annual income †			
(Q1: \$8,063 - \$27,937)	Q2: \$27,938 - \$35,426	1.5 (0.84-2.7)	0.16
	Q3: \$35,427 - \$49,512	1.5 (0.80-2.8)	>0.20

Conclusions

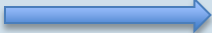
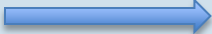
- Fewer than 1 in 10 men with prostate cancer undergo DXA when initiating ADT therapy
- Only ~ 5% received BCA
- Non-significant differences in utilization according to ethnicity (African-American less likely to undergo DXA)

Breast Cancer

Estrogen and Bone

- Estrogen deficiency is the major determinant of bone loss after menopause
- Estrogen inhibits osteoclastogenesis
 - Cytokines
 - Growth factors
 - Direct effect on cell receptors
- Estrogen deficiency results in increased bone resorption

Aromatase Inhibitors (AI)

- Adjuvant endocrine therapy for post-menopausal women with estrogen receptor + breast cancer
- AIs inhibit conversion of androgens to estrogens through binding to aromatase
- Estrogen deficiency
- Steroidal inhibitors  IRREVERSIBLE BINDING
EXAMESTANE ≈ andostrenedione analogue
- Nonsteroidal inhibitors  REVERSIBLE BINDING
LETROZOLE
ANASTROZOLE

Effects of Aromatase Inhibitors on Bone

	Aromatase Inhibitors	Tamoxifen
Bone Mineral Density (BMD)	↓ 6-7%	↑ 1-2%
Biochemical Markers	Increased bone turnover	Constant or decreased bone turnover
Clinical Fractures Rate	9 to 11%	6 to 8%

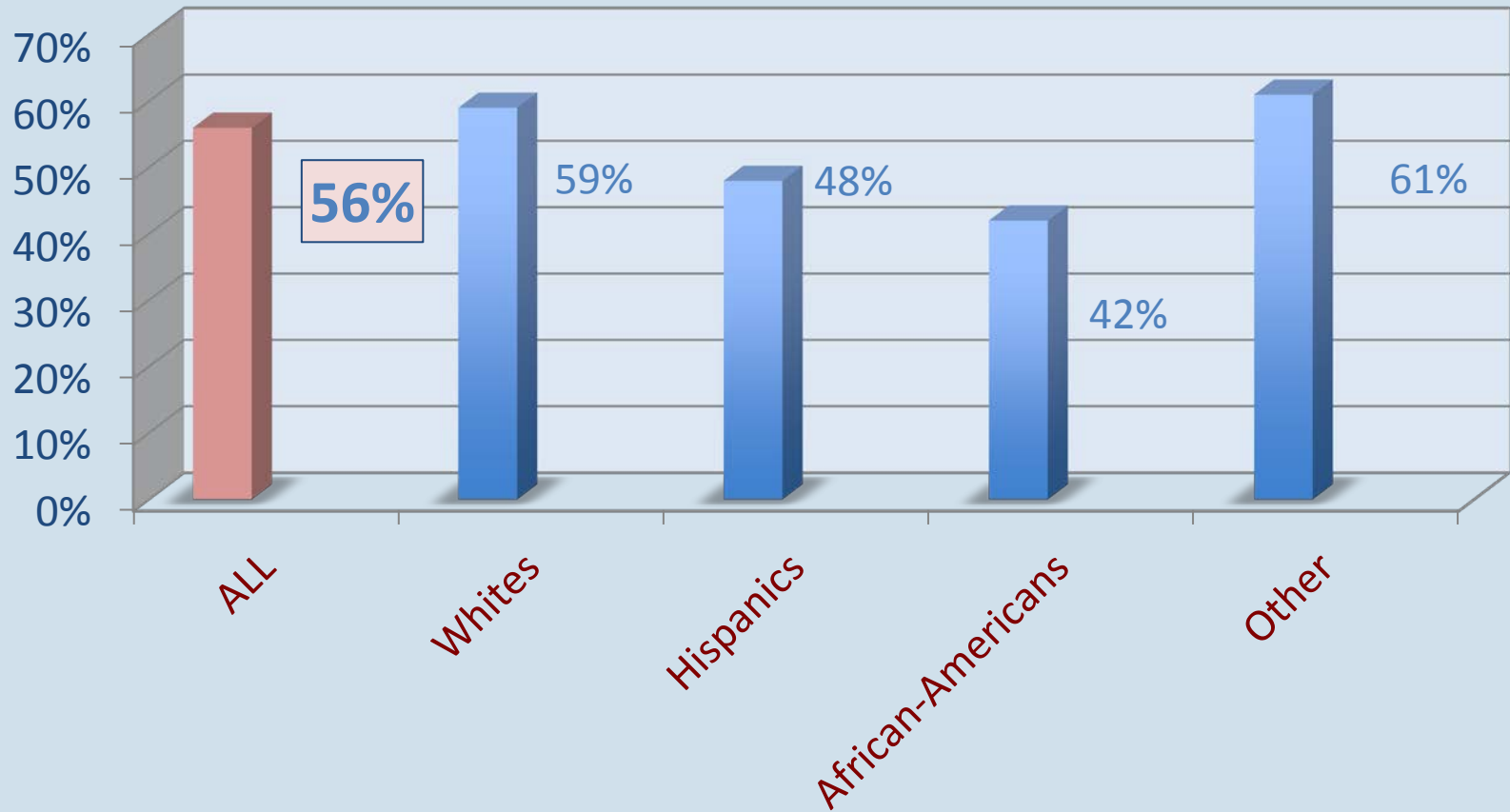
Methods - Inclusion Criteria

- Women age ≥ 66 years diagnosed with breast cancer between 2005 to 2010
- Received aromatase inhibitors (AI) between 2005-2010
- Alive for at least 1 year after diagnosis
- Enrolled in Medicare Part D drug plans
- Excluded distant disease

Methods

- Window of use 1 year prior – to 6m months after ADT
- Multivariate logistic regression model
 - Likelihood of DXA use
 - Controlling for age, ethnicity, stage, size of area of residence and socioeconomic variables.
- Subgroup of patients enrolled in Medicare Part D were evaluated for use of BCA at time of ADT initiation.

Breast Cohort - DXA Use (N = 3587)



P=0.001

Breast Cancer Cohort - Use of DXA (N = 3587)

		All (N=3587) (% over total)	DXA (n=1999) (% with DXA per row category)	P value
Age group, years	66 - 74	1912(53.3%)	1112(58.2%)	0.001*
	75+	1675(46.7%)	887(53.0%)	
Ethnicity	Non-Hispanic White	2669(74.4%)	1568(58.7%)	0.001*
	Hispanic	578(16.1%)	278(48.1%)	
	Black	283(7.9%)	118(41.7%)	
	Other	57(1.6%)	35(61.4%)	
Stage	In situ	137(3.8%)	71(51.8%)	0.002*
	Localized	2224(62.0%)	1290(58.0%)	
	Regional	1078(30.1%)	569(52.8%)	
	Unknown	148(4.1%)	69(46.6%)	
Type of AI	Anastrozole	2420(67.5%)	1345(55.6%)	0.72
	Exemestane	144(4.0%)	85(59.0%)	
	Letrozole	1023(28.5%)	569(55.6%)	

Logistic regression models for odds of DXA claim

Independent variables§		Bivariate OR (95% CI)	Multivariate OR (95% CI)
Age, years (66 - 74)			
	75+	0.81(0.71-0.92)*	0.80(0.70-0.92)*
Ethnicity (Non-Hispanic White)			
	Hispanic	0.65(0.54-0.78)*	1.0(0.83-1.3)
	Black	0.50(0.39-0.64)*	0.70(0.53-0.92)*
	Other	1.12(0.65-1.9)	1.3 (0.72-2.2)
Stage (In Situ)			
	Localized	1.28(0.91-1.8)	1.2(0.87-1.8)
	Regional	1.04(0.73-1.5)	1.1(0.75-1.5)
	Unknown	0.81(0.51-1.3)	0.81(0.51-1.3)
Type of AI (Exemestane)			
	Anastrozole	0.87(0.62-1.2)	0.91(0.64-1.3)
	Letrozole	0.87(0.61-1.2)	0.92(0.64-1.3)
Area of residence (Large metropolitan)			
	Metropolitan	0.74(0.62-0.88)*	0.86(0.70-1.0)
	Urban	0.62(0.47-0.83)*	0.72(0.53-0.97)*
	Small urban	0.81(0.64-1.0)	0.96(0.74-1.2)
	Rural	0.85(0.50-1.4)	1.0(0.60-1.8)
	Unknown	0.95(0.79-1.1)	1.0(0.84-1.2)
State buy-in enrollment (No)			
	Yes	0.52(0.45-0.61)*	0.61(0.51-0.73)*
Median annual income † (Q1:\$8063 - \$30019)			
	Q2:\$30020 - \$37479	1.5(1.2-1.8)*	1.3(1.1-1.6)*
	Q3:\$37480- \$50974	1.6(1.4-2.0)*	1.3(1.1-1.6)*
	Q4:\$50975 - \$64479	1.5(1.3-1.8)*	1.5(1.3-1.8)*

Use of BCA agents

- 29.2% received BCA during the window of observation
- Overall 60.3% either underwent DXA or received BCA

Logistic regression model – Use of DXA or BCA

Independent variables§		Bivariate OR (95% CI)	Multivariate OR (95% CI)
Age, years (66 - 74)	75+	0.81(0.71-0.92) *	0.80(0.70-0.92) *
Ethnicity (Non-Hispanic White)	Hispanic	0.75(0.63-0.90)*	1.2(0.96-1.5)
	Black	0.49(0.38-0.63)*	0.69(0.52-0.90) *
	Other	1.0(0.59-1.8)	1.2(0.66-2.0)
Stage (In Situ)	Localized	1.3(0.91-1.8)	1.3(0.89-1.8)
	Regional	1.0(0.73-1.5)	1.1(0.76-1.6)
	Unknown	0.92(0.57-1.5)	0.93(0.58-1.5)
Type of AI (Exemestane)	Anastrozole	0.88(0.62-1.2)	0.91(0.64-1.3)
	Letrozole	0.89(0.62-1.3)	0.93(0.65-1.3)
Area of residence (Large metropolitan)	Metropolitan	0.77(0.64-0.92)*	0.87(0.71-1.1)
	Urban	0.75(0.57-1.0)	0.87(0.64-1.2)
	Small urban	0.79(0.63-0.99)*	0.95(0.73-1.2)
	Rural	0.89(0.52-1.5)	1.1(0.64-2.0)
	Unknown	0.96(0.79-1.2)	1.0(0.84-1.2)
State buy-in enrollment (No)	Yes	0.55(0.48-0.65)*	0.62(0.51-0.74) *
Median annual income † (Q1:\$8063 - \$30019)	Q2:\$30020 - \$37479	1.4(1.2-1.7)*	1.3(1.0-1.6)*

Conclusions

- Less than 60% of Texas Medicare breast cancer patients initiating AI had a DXA
- ~ 60% had DXA or BCA
- Disparities
 - Ethnic: lower utilization in African Americans
 - Socioeconomic

Limitations

- Important clinical variables not available
- Our data cannot differentiate between:
 - Physician recommendations
 - Patient adherence
- Early discontinuation of hormonal therapy not adjusted for
- Some physicians may not request DXA if patient receiving therapy (e.g. Bisphosphonates)

Future Directions

- Challenging to publish descriptive data alone
- Expand to include SEER-Medicare
- Examine outcomes of guidelines
 - Confounding by indication
 - Lack of clinical data on BMD