Implementation of DEXA screening for prostate cancer patients on androgen deprivation therapy

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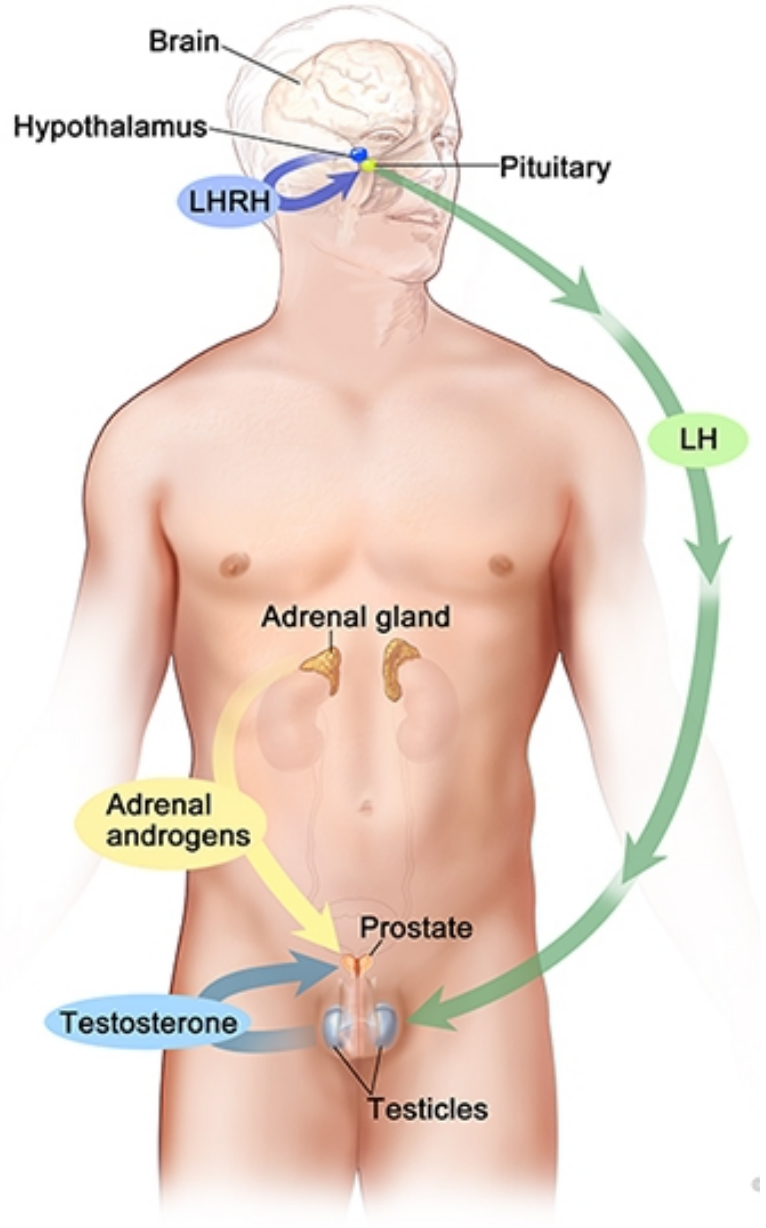
Background

- Prostate cancer development and progression is driven by androgens

- Androgen deprivation therapy (ADT) is the mainstay of treatment for men with advanced prostate cancer
  - Surgical castration (orchiectomy)
  - Chemical castration (LHRH agonists & antagonists)

- Adverse effects associated with ADT include
  - Hot flashes
  - Osteoporosis | fractures*
  - Weight gain | obesity
  - Insulin resistance | diabetes
  - Cardiovascular disease
  - Loss of libido



Background

- ADT is associated with 21%-54% relative increase in fracture risk
- Bone mineral density (BMD), a surrogate for fracture risk, declines steadily during ADT
- Multiple RCTs showed that bisphosphonates and denosumab increases BMD in prostate cancer patients treated with ADT
- Phase 3 placebo-controlled RCT of denosumab (N = 1468)
  - BMD: ↑ 5.6% vs. ↓ 1.0% (p<0.001)
  - Incidence of new vertebral fractures: 1.5% vs. 3.9% (RR = 0.38; p=0.006)

Table 2. Proportions of Patients with Bone-Related Toxic Effects before and after the Diagnosis of Prostate Cancer, According to the Presence or Absence of Androgen-Deprivation Therapy.*

Toxic Effect	12 Mo before Diagnosis	P Value	12 to 60 Mo after Diagnosis	P Value
	%		%	
Osteoporosis		0.19		<0.001
Androgen-deprivation therapy	0.59		6.92	
No androgen-deprivation therapy	0.46		3.69	
Any fracture		0.01		<0.001
Androgen-deprivation therapy	3.41		19.37	
No androgen-deprivation therapy	2.80		12.63	
Fracture resulting in hospitalization		0.49		<0.001
Androgen-deprivation therapy	0.26		5.19	
No androgen-deprivation therapy	0.21		2.37	
Fracture site				
Skull		0.70		0.006
Androgen-deprivation therapy	0.18		1.23	
No androgen-deprivation therapy	0.20		0.86	
Spine		0.44		<0.001
Androgen-deprivation therapy	0.36		3.20	
No androgen-deprivation therapy	0.30		1.64	
Rib		0.02		<0.001
Androgen-deprivation therapy	0.63		3.77	
No androgen-deprivation therapy	0.40		2.44	
Pelvis		0.53		0.002
Androgen-deprivation therapy	0.06		1.07	
No androgen-deprivation therapy	0.08		0.68	
Upper arm		0.62		<0.001
Androgen-deprivation therapy	0.30		2.21	
No androgen-deprivation therapy	0.26		1.19	
Lower arm		0.89		<0.001
Androgen-deprivation therapy	0.21		2.08	
No androgen-deprivation therapy	0.22		1.04	
Hand		0.79		<0.001
Androgen-deprivation therapy	0.57		3.16	
No androgen-deprivation therapy	0.54		1.99	
Femoral neck (hip)		0.02		<0.001
Androgen-deprivation therapy	0.44		4.06	
No androgen-deprivation therapy	0.26		2.06	
Other parts of femur		0.47		<0.001
Androgen-deprivation therapy	0.06		1.17	
No androgen-deprivation therapy	0.09		0.64	
Lower leg		0.36		<0.001
Androgen-deprivation therapy	0.36		2.24	
No androgen-deprivation therapy	0.29		1.56	
Foot		0.28		<0.001
Androgen-deprivation therapy	0.44		2.17	
No androgen-deprivation therapy	0.34		1.48	

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Prostate Cancer

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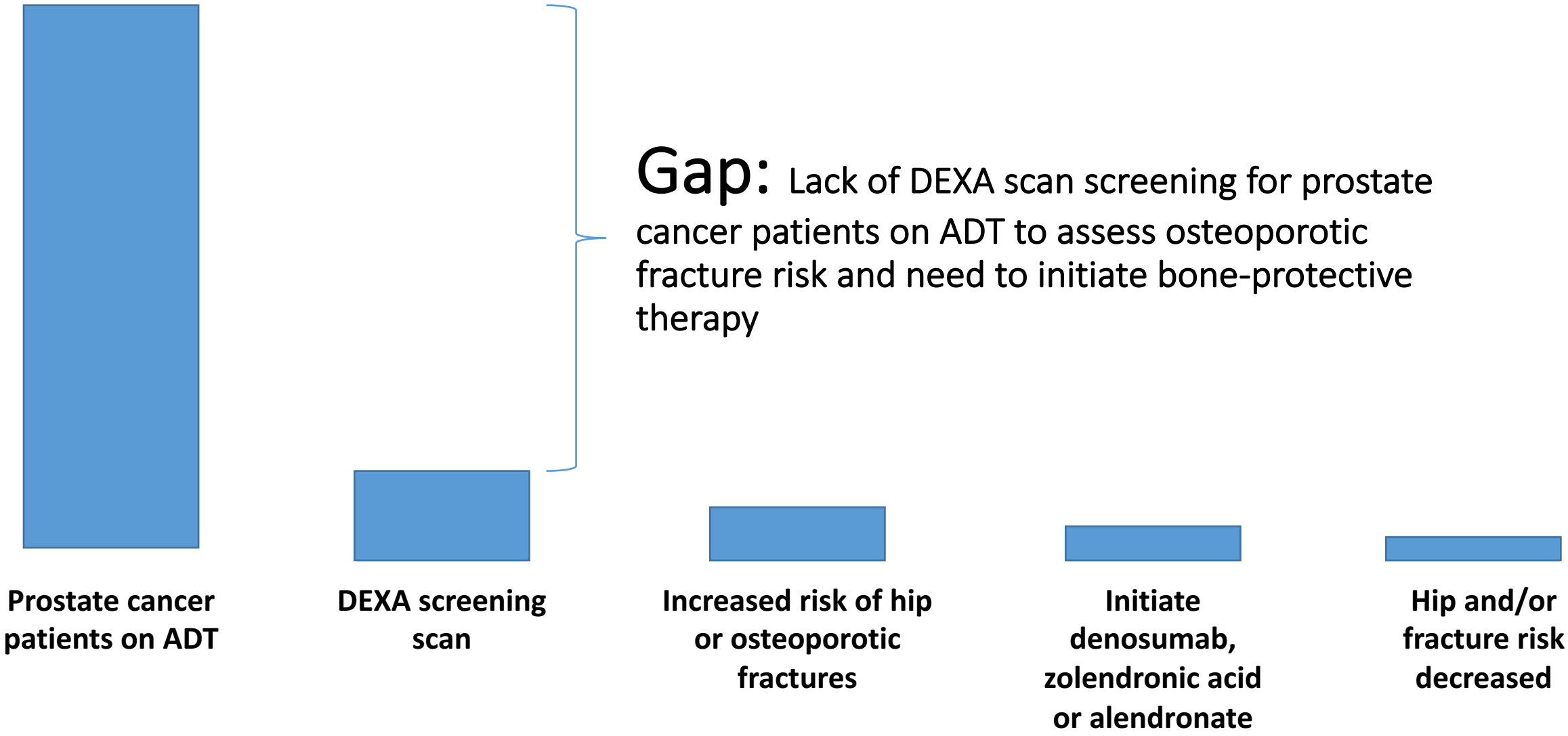
Discussion

PRINCIPLES OF ANDROGEN DEPRIVATION THERAPY

Monitor/Surveillance

- ADT has a variety of adverse effects including hot flashes, loss of libido and erectile dysfunction, shrinkage of penis and testicles, loss of muscle mass and strength, fatigue, depression, hair loss, osteoporosis, greater incidence of clinical fractures, obesity, insulin resistance, alterations in lipids, and greater risk for diabetes and cardiovascular disease. Patients and their medical providers should be advised about these risks prior to treatment.
- Screening and treatment for osteoporosis are advised according to guidelines for the general population from the National Osteoporosis Foundation (www.nof.org). The National Osteoporosis Foundation guidelines include recommendations for: 1) supplemental calcium (1200 mg daily) and vitamin D3 (800–1000 IU daily) for all men >50 y of age; and 2) additional treatment for men when the 10-y probability of hip fracture is ≥3% or the 10-y probability of a major osteoporosis-related fracture is ≥20%. Fracture risk can be assessed using FRAX®, the algorithm recently released by WHO. ADT should be considered "secondary osteoporosis" when using the FRAX® algorithm. Treatment options to increase bone density, a surrogate for fracture risk in men without metastases, include denosumab (60 mg SQ every 6 mo), zoledronic acid (5 mg IV annually), and alendronate (70 mg PO weekly).
- A baseline DEXA scan should be obtained before starting therapy in men at increased risk for fracture based on FRAX® screening. A follow-up DEXA scan after 1 year of therapy is recommended by the International Society for Clinical Densitometry, although there is no consensus on the optimal approach to monitoring the effectiveness of drug therapy. Use of biochemical markers of bone turnover to monitor response to therapy is not recommended.
- The serum level of 25-hydroxy vitamin D and average daily dietary intake of vitamin D will assist the nutritionist in making a patient-specific recommendation for vitamin D supplementation. There are currently no guidelines on how often to monitor vitamin D levels. However, for those who require monitoring with DEXA scans, it makes sense to check the serum vitamin D level at the same time.
- Denosumab (60 mg SQ every 6 mo), zoledronic acid (5 mg IV annually), and alendronate (70 mg PO weekly) increase bone mineral density, a surrogate for fracture risk, during ADT for prostate cancer. Treatment with either denosumab, zoledronic acid, or alendronate sodium is recommended when the absolute fracture risk warrants drug therapy.
- Screening for and intervention to prevent/treat diabetes and cardiovascular disease are recommended in men receiving ADT. These medical conditions are common in older men and it remains uncertain whether strategies for screening, prevention, and treatment of diabetes and cardiovascular disease in men receiving ADT should differ from the general population.

SEER data (28,960 men diagnosed with prostate cancer between 2001-2007 who received ≥ 1 year of ADT), and multiple single center institution retrospective studies showed that only **8.7%-10.2%** of prostate cancer patients receiving long-term ADT underwent DEXA scan screening for BMD assessment


Gap: Lack of DEXA scan screening for prostate cancer patients on ADT to assess osteoporotic fracture risk and need to initiate bone-protective therapy
Prostate cancer patients on ADT
DEXA screening scan
Increased risk of hip or osteoporotic fractures
Initiate denosumab, zolendronic acid or alendronate
Hip and/or fracture risk decreased

Gap Analysis: COM-B

Capability	**Physical**	Providers can physically order DEXA scans and assess fractures risks, and make decisions on bone protective agents accordingly
	Psychological	Oncologists may not remember to order DEXA scans in the mist of a busy clinic
Motivation	**Reflective**	Most oncologists would agree that it is their job and role to address bone health in prostate cancer patients receiving ADT, but often let the issue “slip” as they **prioritize treating the cancer relative to trying to prevent something that might not happen**
	Automatic	Bone health screening should not illicit a strong emotional response
Opportunity	**Physical**	Because prostate cancer patients on ADT typically follow up with oncologists regularly for PSA monitoring, Lupron injections (typically given every 3 months), and management decisions, there are ample opportunities to address bone health issues
	Social	**The engagement of oncologists to follow the DEXA screening guidelines by opinion leaders and stakeholders should help to provide more incentives for guidelines to be followed**

Intervention: A workgroup that motivates and incentivizes prioritization of bone health in prostate cancer patients receiving ADT

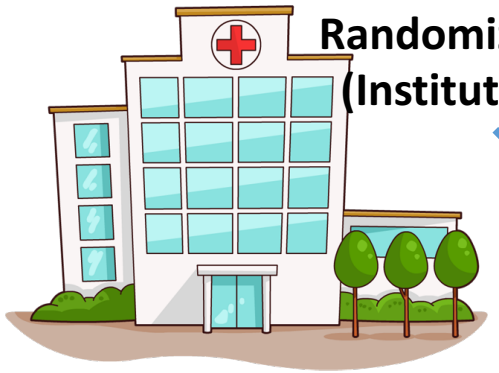
- GU med onc leadership
- GU oncology lead RN
- Practice assistant
- Patient representative
- Data gatherer & analyst

- Meetings quarterly
- Goals set quarterly
- Potential for lunch party quarterly

- Increase rate of DEXA screening
- Decrease rate of preventable skeletal complications from ADT

- Education
- Regular meetings to assess rate of appropriate DEXA screening
- Set screening goals
- Reward all staff when goals are met (free taco bar lunch!)

- 1 hr session each quarter in context of a pre-existing weekly GU med onc half-day meeting (Wednesdays)



1:1 cluster Randomization (Institutions)

Pre-intervention DEXA screening rate and fracture rate

2-yr

Workgroup (standardized)

2-yr

Post-intervention DEXA screening rate and fracture rate

2-yr

Pre-intervention DEXA screening rate and fracture rate

2-yr

No Workgroup

(Usual care)

2-yr

Post-intervention DEXA screening rate and fracture rate

2-yr

Primary objective: Change in rate of DEXA screening before, during, and after intervention

Secondary objective: Change in rate of osteoporosis-related fracture before, during, and after intervention

Thanks!