Washington State Health Care Authority

Agency Medical Director Comments

Screening and Monitoring Tests for Osteopenia/Osteoporosis

Charissa Fotinos, MD, MSc
Deputy Chief Medical Officer
Washington State Health Care Authority
November 21, 2014

Agency Medical Directors' Concerns

- **Safety** = Low to Medium
- **Efficacy** = Medium
- **Cost** = Medium to High
  - Estimated annual cost: $680,000
  - Teriparatide (Forteo): 6th most written specialty drug; 26th in cost for PEBB

Background

- Defined by BMD (g/m^2) at hip or lumbar spine
- Adult hip or vertebral in absence of major trauma, (fall from height or MVA)
- Bone loss and fracture risk increase with age

Principles of Screening

- The condition being screened for carries a significant burden and/or is an important public health problem.
- A valid, reliable test exists to find disease while asymptomatic or in its early stages.
- There is an intervention/treatment that works.
- It is cost effective.
- The benefits outweigh the harm.

Adapted from Principles and Practice of Screening for Disease, World Health Organization

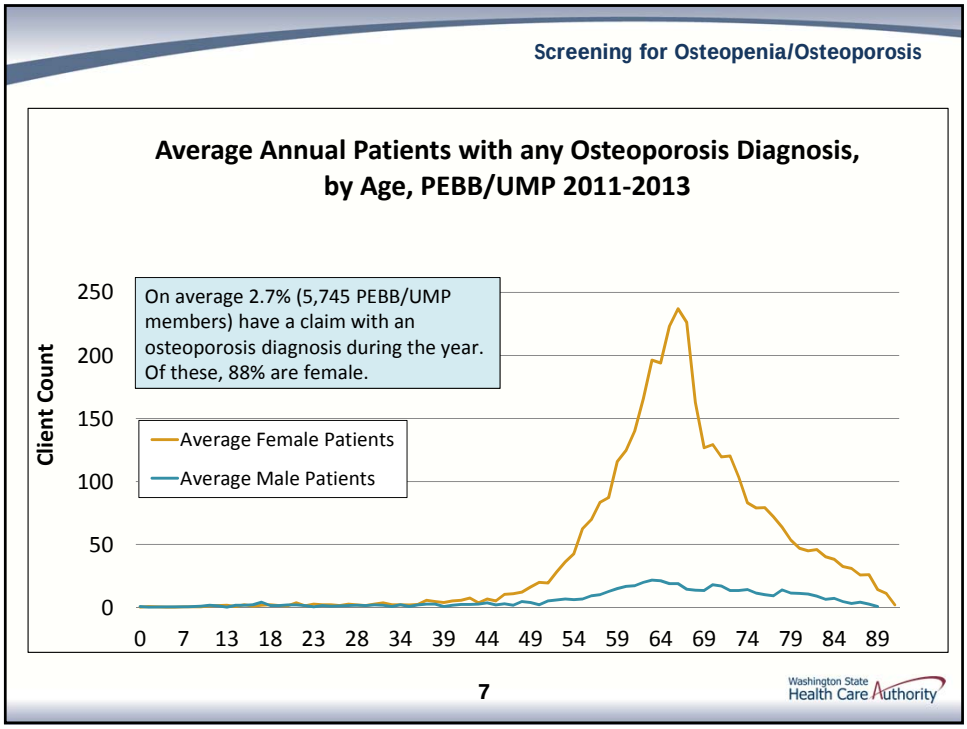
Key Questions

1. Is there direct evidence that screening for osteoporosis and low bone density improves health outcomes, clinical management decisions, or patient choice? (individuals & populations and do the outcomes vary by baseline characteristic?)
2. What is the minimum interval required to detect transition from normal or low BMD to osteoporosis or to assess treatment effect?
3. What is the number needed to screen (NNS) to prevent 1 fracture in subgroups defined by age, sex, and other risk factors?
4. Are bone density tests safe and what are the potential downstream adverse effects?
5. What are the costs and cost-effectiveness of osteoporosis screening and monitoring?

Burden

- 9% of adults over 50 yrs have osteoporosis and about 48% have osteopenia
- 2.5 million office visits annually (~0.5%)
- 432,000 hospital admissions (~1.9%)
- 180,000 nursing home admissions
- Hip fracture associated with increased mortality at 1 year: (Estimates 8 - 36%)
- *Partnership for Prevention* ranks osteoporosis 21st out of 25 (clinical preventive burden & cost-effectiveness)

NHANES Osteoporosis 2005-2008, cdc.gov


Screening for Osteopenia/Osteoporosis
Average Annual Patients with any Osteoporosis Diagnosis, by Age, PEBB/UMP 2011-2013
On average 2.7% (5,745 PEBB/UMP members) have a claim with an osteoporosis diagnosis during the year. Of these, 88% are female.
Client Count
250
200
150
100
50
0
Average Female Patients
Average Male Patients
0 7 13 18 23 28 34 39 44 49 54 59 64 69 74 79 84 89
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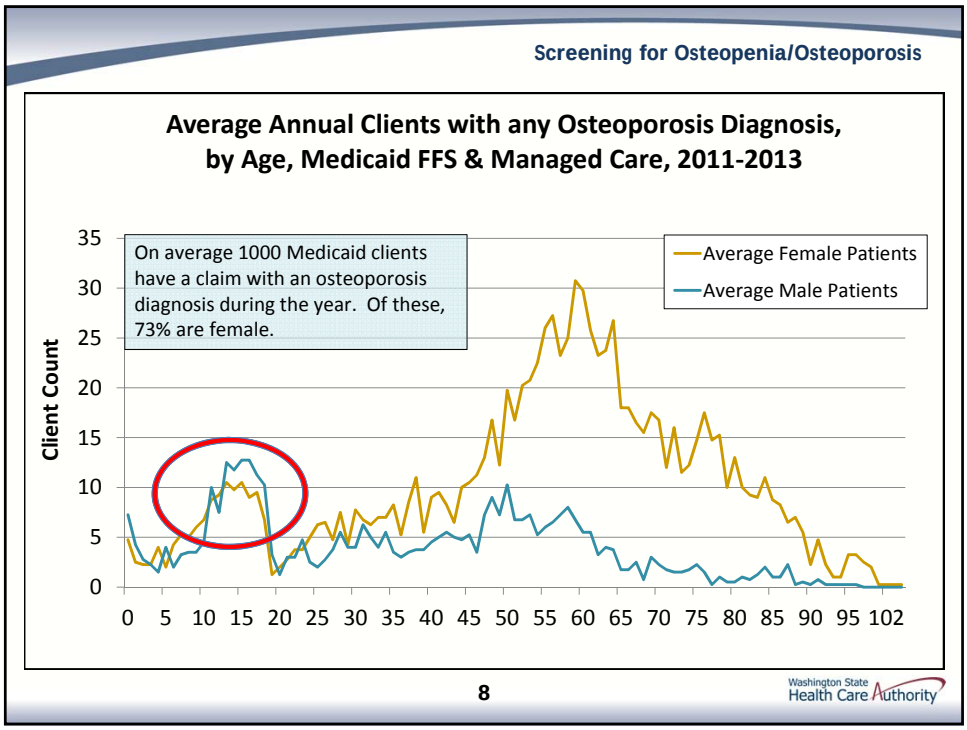
Screening for Osteopenia/Osteoporosis
Average Annual Clients with any Osteoporosis Diagnosis, by Age, Medicaid FFS & Managed Care, 2011-2013
On average 1000 Medicaid clients have a claim with an osteoporosis diagnosis during the year. Of these, 73% are female.
Client Count
35
30
25
20
15
10
5
0
Average Female Patients
Average Male Patients
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 102
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Screening for Osteopenia/Osteoporosis

Testing

- Multiple validated instruments exist, both with and without direct measurements of bone mineral density to predict fracture risk.
- The Standard of Care is to measure bone density with dual X-ray densitometry DXA
  - In addition to the actual measurement in g/m^2, 2 scores are generally reported : T- Score BMD compared to a young adult and Z-Score compared to an aged matched reference population
- Technologies other than DXA exist but they are not in routine clinical use in part because the standards are built around DXA:
  - Quantitative Computed tomography, QCT, Quantitative ultrasound Densitometry, QUS, bone turnover markers

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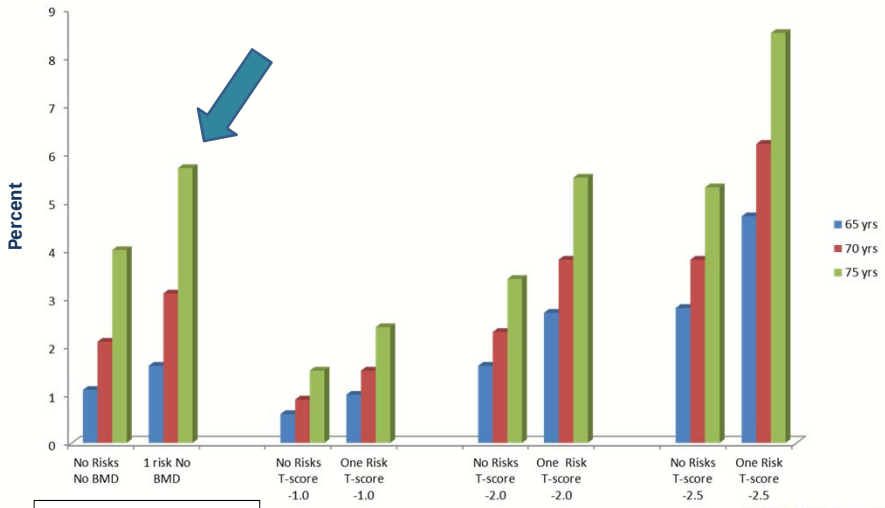
Screening for Osteopenia/Osteoporosis

10-year Risk Hip Fracture, Caucasian Women



shef.ac.uk/FRAX/tool

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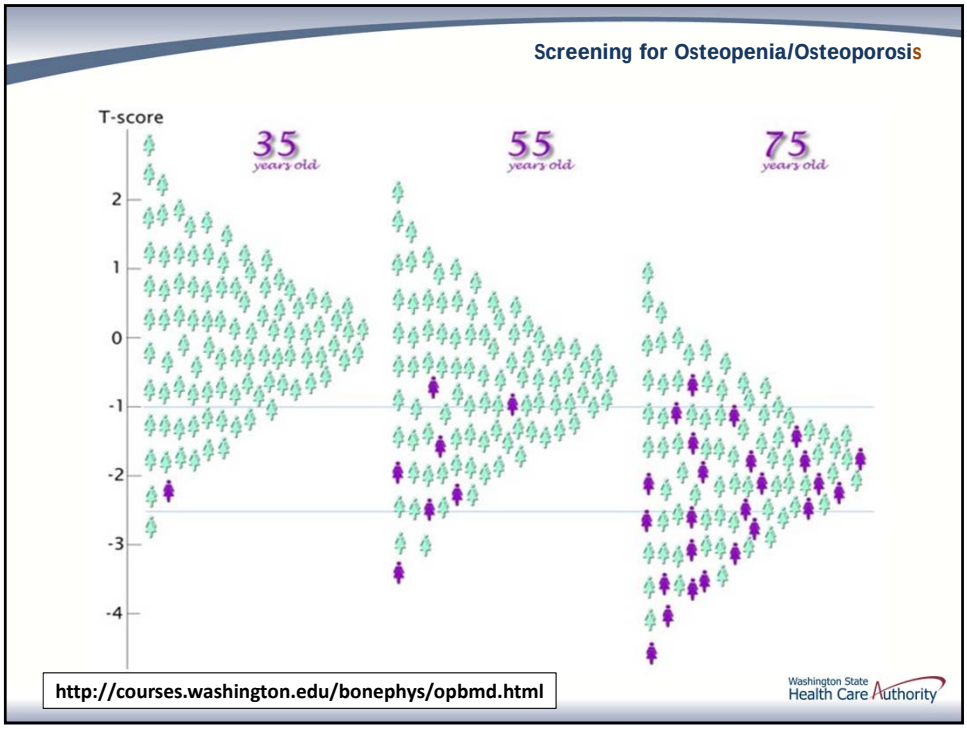
Screening for Osteopenia/Osteoporosis
T-score
35 years old
55 years old
75 years old
2
1
0
-1
-2
-3
-4
http://courses.washington.edu/bonephys/opbmd.html
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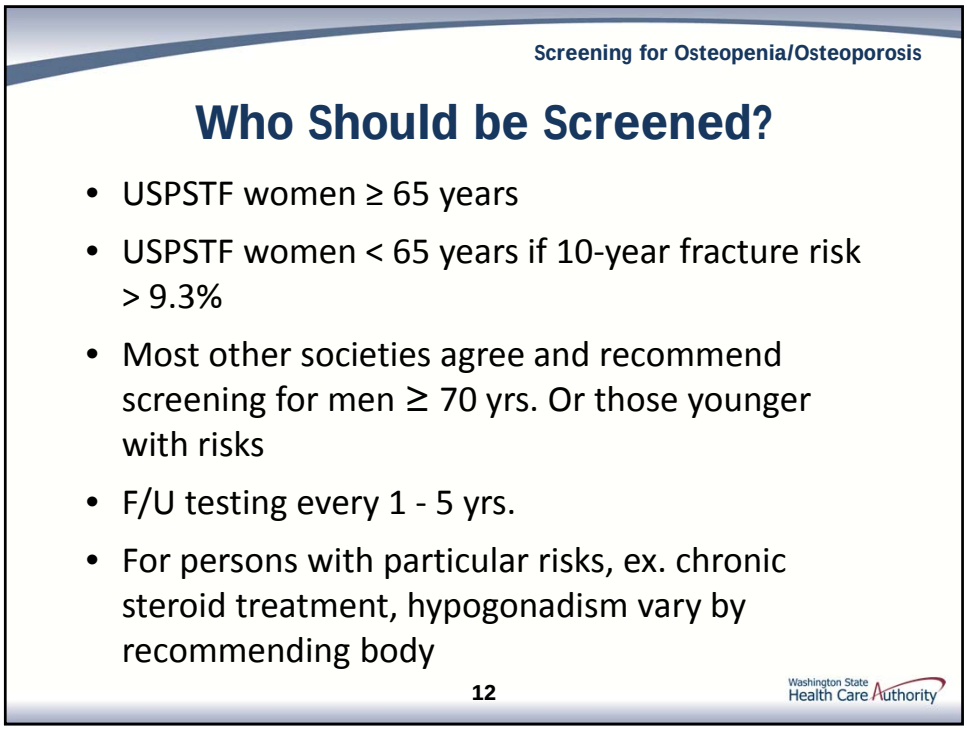
Screening for Osteopenia/Osteoporosis
Who Should be Screened?
• USPSTF women ≥ 65 years
• USPSTF women < 65 years if 10-year fracture risk > 9.3%
• Most other societies agree and recommend screening for men ≥ 70 yrs. Or those younger with risks
• F/U testing every 1 - 5 yrs.
• For persons with particular risks, ex. chronic steroid treatment, hypogonadism vary by recommending body
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Harms of Testing

- **Variability of the test 'precision'**
  - 'Least significant change' value for each machine and operator and site
- **Radiation exposure is minimal**
  - Dose about equivalent to daily dose of background radiation (10µSV) X-ray (60µSV)

Treatment

- Effective for osteoporosis in women ≥65yrs:
  - NNT 60 - 89 to prevent 1 vertebral; and
  - NNT 50 - 67 to prevent 1 hip fracture in women over 1 - 3 years
  - *(In people having an MI and given ASA, the NNT to prevent a cardiac-related death in 5 weeks: 40, given thrombolysis within 5 hours: 100)*
  - Unclear effects of treatment for osteopenia, prevention for patients with secondary risks, data for men is sparse
- Risks of medications:
  - Hot flashes, thrombosis, GI symptoms and the association of sub-trochanteric femur fracture with bisphosphonates

Ann Intern Med. Doi:10.7326/M14-0317 & Bandolier: What is an NNT? 2009

Repeat Testing/Monitoring

- Most organizations recommend repeat screening every 2 years
- Oregon HERC standards are results-based:
  - ***Normal BMD*:** Every 15 years
  - ***Mild Osteopenia:*** Every 10 years
  - ***Moderate:*** Every 4 years
  - ***Severe Osteopenia/ Osteoporosis:*** Every 2 years
- Serial testing, insufficient evidence for untreated or those on medications

Current State Agency Policy

Description	Medicaid	UMP	DOC	LNI
Screening & Monitoring Tests for Osteopenia/ Osteoporosis	C	C	PA	C

C: Covered
NC: Not covered
PA: Prior authorization required

Screening for Osteopenia/Osteoporosis

Public Employee Benefits (PEBB) & Uniform Medical Plan (UMP)

	2011	2012	2013	Overall	Avg % Chg	
Average Annual Members	212,596	212,684	222,339		2.3%	
Osteoporosis Member Counts	6032	5601	5604	18,948	-5.7%	*
DXA BMD Patients	5933	5102	4658	14,058	-13.4%	*
DXA BMD Tests	6067	5242	4799	16,108	-13.0%	*
Average DXA Encounters per Patient	1.0	1.0	1.0	1.1	0.4%	
Non DXA Tests (not included in totals)	74	83	78	235	1.0%	*
PEBB/UMP Total Paid, All DXA Tests	**$636,180**	**$535,862**	**$497,900**	**$1,669,942**	**-11.4%**	*
Avg Paid/DXA ,Non-Medicare (% of tests)	$121 (86%)	$123 (82%)	$129 (80%)	$124 (83%)	3.3%	

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Screening for Osteopenia/Osteoporosis

Medicaid Fee For Service (FFS) & Managed Care (MC)

	2011	2012	2013	Overall	Avg % Chg	
Average Annual Clients, FFS	473,356	477,727	442,698		-3.2%	
Average Annual Clients, MC	695,591	730,250	800,096		7.3%	
Osteoporosis Client Counts, FFS	1174	994	708	2876	-19.6%	*
Osteoporosis Client Counts, MC	339	351	651	1662	34.0%	*
DXA BMD Patients FFS	2696	2033	1136	5582	-32.7%	*
DXA BMD Patients MC	573	814	1655	2951	60.6%	*
DXA BMD Tests FFS	2828	2143	1175	6146	-32.3%	*
DXA BMD Tests MC	595	851	1726	3172	66.7%	*
Average DXA Encounters/Patient (overall)	1.0	1.1	1.0	1.1		
Non DXA Tests (not included in totals)	28	23	15	113	-27.8%	*
Medicaid Total Paid , All DXA Tests (FFS)	**$171,836**	**$130,550**	**$62,768**	**$365,154**	**-36.7%**	*
Average Paid per Procedure (FFS)	$61	$61	$53	$59	-7.3%	

Screening for Osteopenia/Osteoporosis

DXA CPT Codes	Description	Current Agency Fees		
		PEBB/ UMP*	L&I†	Medicaid‡
77080	DXA BONE DENSITY, AXIAL	$138.48	$84.36	$30.29
77081	DXA BONE DENSITY/PERIPHERAL	$41.01	$46.86	$16.83

***Regence Blue Shield Provider Fee Schedule – effective January 1 2013, MD/DO/DPM Provider rates, Maximum Allowable fee, http://www.hca.wa.gov/ump/documents/Regence_Professional_Fee_Schedule_Jan_2013.pdf, Accessed 10/13/2014. Payment based on the Regence Fee Schedule is subject to all of the terms and conditions of the applicable Regence BlueShield provider agreement, member benefits, Regence BlueShield policies, and all published Regence BlueShield administrative guidelines. Therefore, the appearance of fees for particular procedure codes does not guarantee coverage. Some providers may have contracted fees at different rates.**

†Washington State Labor and Industries Fee Schedules and Payment Policies (MARFS), Fee Schedules and Payment Policies for: 2014, http://www.lni.wa.gov/apps/FeeSchedules/, Accessed 10/12/2014.

‡Washington State Medicaid Rates Development Fee Schedule, July 1, 2014 Physician and Related Services Fee Schedule (Updated October 1, 2014), http://www.hca.wa.gov/medicaid/rbrvs/pages/index.aspx#P, Accessed 10/12/2014.

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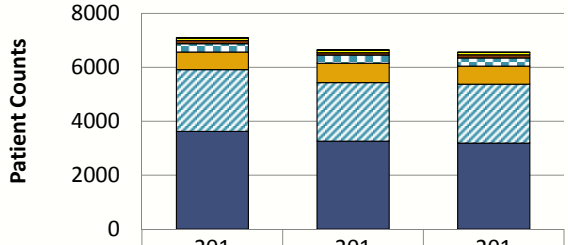
Screening for Osteopenia/Osteoporosis: State Agency Utilization

PEBB/UMP Osteoporosis Patients by Dx type, 2011-2013



	2011	2012	2013
Disuse	8	9	6
Idiopathic	95	94	90
Other: drug induced	119	88	115
Diaphysitic, hypertrophy, polychondritis	309	303	302
Senile osteoporosis	653	715	676
Osteoporosis	2285	2171	2180

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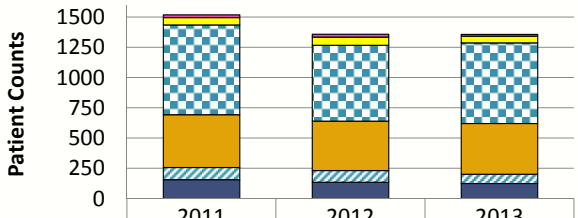
Screening for Osteopenia/Osteoporosis:
State Agency Utilization

Medicaid Total Osteoporosis Patients by Diagnosis Type, 2011-2013



	2011	2012	2013
Disuse	23	24	15
Idiopathic	60	67	55
Diaphysitic, hypertrophy, polychondritis	743	628	668
Senile osteoporosis	437	409	419
Osteoporosis	100	96	77
Other osteoporosis	156	135	124

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Screening for Osteopenia/Osteoporosis:
State Agency Utilization

PEBB/UMP Top Diagnoses

Code	First DXA Tests	Total Paid	Code	Repeat DXA Tests	Total Paid
V82.81	SP SCREENING OSTEOPOROSIS	$315K	**733.9**	DISORDER BONE/CARTILAGE, UNSP	$188K
733.9	DISORDER BONE/CARTILAGE, UNSP	$303K	**733**	UNSPECIFIED OSTEOPOROSIS	$93K
V49.81	ASYMPT POSTMENO STATUS	$86K	**V82.81**	SP SCREENING OSTEOPORSIS	$84K
733	UNSPECIFIED OSTEOPOROSIS	$80K	**V76.12**	SCREEN MAMMOGRAM NEC	$27K
V76.12	SCREEN MAMMOGRAM NEC	$69K	**V49.81**	ASYMPT POSTMENO STATUS	$22K
627.2	SYMPT FEM CLIMACT STATE	$53K	**733.01**	SENILE OSTEOPOROSIS	$17K
627.9	UNSP MENOPAUSAL/POST DSRDR	$25K	**627.2**	SYMPT FEM CLIMACT STATE	$14K
V70.0	RTN GENERAL MEDICAL EXAM	$22K	**627.9**	UNSP MENOPAUSAL/POST DSRDR	$7K
733.01	SENILE OSTEOPOROSIS	$16K	**V70.0**	RTN GENERAL MEDICAL EXAM	$7K

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Screening for Osteopenia/Osteoporosis: State Agency Utilization

Medicaid Top Diagnoses

Code	First DXA Tests	Total Paid	Code	Repeat DXA Tests	Total Paid
733.90	Bone & cartilage dis NOS	$103,292	**733.90**	Bone & cartilage dis NOS	$20,101
V82.81	Screen - osteoporosis	$77,021	**733.00**	Osteoporosis NOS	$14,473
733.00	Osteoporosis NOS	$59,535	**V82.81**	Screen - osteoporosis	$7,097
V49.81	Asympt postmeno status	$35,548	**V49.81**	Asympt postmeno status	$2,836
V76.12	Screen mammogram NEC	$14,606	**V76.12**	Screen mammogram NEC	$1,710
627.2	Sympt fem climact state	$8,726	**205.01**	Act myl leuk w rmsion	$1,235
627.9	Menopausal disordr NOS	$7,399	**204.01**	Act lym leuk w rmsion	$1,207
V58.65	Long-term use steroids	$4,546	**627.2**	Sympt fem climact state	$977
174.9	Malign neopl breast NOS	$4,294	**174.9**	Malign neopl breast NOS	$960
204.01	Act lym leuk w rmsion	$3,403	**204.00**	Ac lym leuk wo achv rmsn	$914

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Screening for Osteopenia/Osteoporosis

Private Payer Examples

- **Aetna:** Covered when medically necessary for members with risk factors, men > 70 years or a history of fragility fractures
- **Oregon HERC:** Women ≥ 65 years and for men or women younger if 10 year risk of major osteoporotic fracture > 10%
- **Group Health/ Regence:** No general coverage policies

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Centers for Medicare & Medicaid Services (CMS)

Issued in 2007. Bone Mass Measurements, BMM, are covered using a bone densitometer, (not photon) or sonometer, every 23 months for any one of the following:

1. Women who are estrogen deficient and at clinical risk based on their history and other findings
2. Individual with vertebral abnormalities on X-ray indicative of osteoporosis, osteopenia or fracture
3. Individuals receiving the equivalent of 5.0 mg prednisone daily for at more than 3 months
4. Individuals with primary hypothyroidism
5. An individual being monitored to assess the response of efficacy of an FDA-approved osteoporosis therapy

Summary

Type of Screen	Finding	Evidence Quality
To prevent fracture in middle aged adults, ≥ 65 yrs -any subgroup effects? perhaps in people > 85yrs.	Favors screening but upper confidence interval limit was (0.99)	Low
To prevent fractures in people taking meds associated with osteoporosis	Found to decrease risks in 2 subgroups of men: those taking ADT and high dose corticosteroids for ulcerative colitis	Low
Does it change clinical management?	In 2 sub groups above more likely to get meds	Low
Does screening change patient behavior?	In one cohort calcium, vit. D intake may increase for a year	Low

Monitoring

Question	Finding	Quality of Evidence
Frequency of Screening	Range of recommendations: 1.1 to 16.8 yrs.	Moderate
Serial Monitoring	Insufficient: lack of evidence	Moderate for one study
Benefit vs. Harm	Safe, technology, some concern about testing and medication effects	Good quality for medication effects
Cost-effectiveness	Cost-effective in women older than 55 yrs and in Canadian study 65 yrs	2 sets of assumptions threshold of willingness to pay for both at $50,000

Number Needed to Screen (NNS), Women

Non-randomized Screening Trial	NNS to prevent 1 hip fracture over 5 years	Systematic Review	NNS to prevent 1 hip fracture over 5 years	Quality of Evidence
Age		**Age**		
55-59 yrs.	1667	**Adults ≥ 65 yrs**		1st Study Low
60-64 yrs.	1000	Overall:	59	
65-69 yrs.	556	Men:	96	2nd Very low
70-74yrs.	323	Women:	46	
75-79 yrs.	238			
		Adults ≥ 85 yrs	7	

Uncertainties

- Who should be screened: Age-based and/or Fracture risk-based?
- How often should screens be repeated as part of serial screening?
- What is the optimal interval for monitoring once on therapy?
- As there is insufficient evidence regarding screening and testing for men, what recommendations should be made for them?
- Prevalence and treatment estimates are difficult to determine for current HCA clients.

State Agency Recommendation

Cover with conditions:

- Women age ≥ 65 yrs, or in younger women with the presence of risk factors suggesting a 10-yr fracture risk of ≥ 9.3%
- Serial screening should not occur more often than every 2 years and in low risk persons, could occur as infrequently as every 10 years
- Once treatment for osteoporosis has begun, serial monitoring is not indicated
- In the setting of a fragility fracture, a DXA scan should not be obtained to confirm the diagnosis of osteoporosis.

Questions?

More Information

http://www.hca.wa.gov/hta/Pages/osteoporosis_testing.aspx

Charissa Fotinos, MD, MSc
Charissa.Fotinos@hca.wa.gov

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Health Technology Assessment

Public Comments:

	Name
1	
2	
3	
4	
5	
6	

No requests to provide public comment on the technology review were received.

Screening and Monitoring Tests for Osteopenia/Osteoporosis

Teresa L. Rogstad, MPH,
Project Leader, Hayes, Inc.
November 21, 2014

Shorthand and abbreviations

- 2010 Nelson review: Evidence review (AHRQ) supporting current USPSTF recommendations

- AACE, American Association of Clinical Endocrinologists
- ACG, American College of Gastroenterology
- ACOG, American College of Obstetricians and Gynecologists
- ACP, American College of Physicians
- ACPM, American College of Preventive Medicine
- ACR, American College of Radiology
- ADT, androgen-deprivation therapy
- AHRQ, Agency for Healthcare Research and Quality
- BMD, bone mineral density
- BMI, body mass index
- CMS, Centers for Medicare & Medicaid Services
- CI, confidence interval
- CS, corticosteroid
- DXA, dual x-ray absorptiometry
- EUA, European Urological Association

Abbreviations (cont.)

- f/u, follow-up
- GL, guideline
- HERC, Health Evidence Review Commission
- HR, hazard ratio
- IBD, inflammatory bowel disease
- ICSI, Institute for Clinical Systems Improvement
- ISCD, International Society for Clinical Densitometry
- NAMS, North American Menopause Society
- NOF, National Osteoporosis Foundation
- NS, (statistically) nonsignificant
- OP, osteoporosis
- QALY, quality-adjusted life-year
- RCT, randomized controlled trial
- SR, systematic review
- USPSTF, United States Preventive Services Task Force
- WHO, World Health Organization

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Presentation overview

- Background
- Scope, Methods, and Search Results
- Findings
- Practice Guidelines and Payer Policies
- Overall Summary and Discussion

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Background

Osteoporosis/low bone mass

- Prevalence in Americans older than 50 years
  - Men:
    - OP, 4%
    - Low bone mass, 38%
  - Women
    - OP, 16%
    - Low bone mass, 61%
- *Low bone mass = osteopenia*
- DXA
  - BMD
  - "Gold standard"
  - DXA-measured BMD predicts fracture risk

Definitions

WHO: Postmenopausal Women and Men > 50 Years Old	
T-score ≥ -1.0	Normal
T-score above -2.5 to -1.0	Low bone mass (osteopenia)
T-score ≤ -2.5	Osteoporosis
T-score ≤-2.5 with ≥ 1 fractures	Severe or established osteoporosis
Compared with young adult reference population, same sex.	
ISCD*: Premenopausal Women, Men < 50 Years Old, Children	
Z-score > -2.0:	BMD within the expected range
Z-score ≤ -2.0:	Low BMD for chronological age
Compared with age-, sex-, and ethnicity-matched reference population.	

**ISCD = International Society for Clinical Densitometry*

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Osteoporosis-Related Fracture

- *Osteoporotic/fragility/low trauma/low impact*
- Lifetime risk in white women: ~50%
- Economic burden in U.S., per year
  - 432,000 hospital admissions
  - 2.5 million medical office visits
  - ~180,000 nursing home admissions
- Hip fractures: greatest morbidity/mortality
  - Excess 1-year mortality: 8.4%-36%
  - Mortality higher in men than women

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Risk prediction

- 2010 Nelson review
  - Osteoporosis: 14 validated tools
  - Fracture: 11 validated tools
    - May or may not include BMD
  - Simpler tools ≈ more complex tools
- FRAX (WHO) for fracture risk http://www.shef.ac.uk/FRAX/tool.jsp
  - Most common in the literature
  - Use with or without BMD scores
  - Basis of current USPSTF recommendations
  - Accuracy for prediction of fracture*
    - Any osteoporotic fracture: 0.54–0.78
    - Hip fracture: 0.65–0.81

**Area under the (receiver operating characteristics) curve (AUC)*

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Components of FRAX

• Current age • Sex • Weight • Height • Prior osteoporotic fracture (clinical or asymptomatic) • Parental history, hip fracture	• Current smoking • Oral glucocorticoids* • Rheumatoid arthritis • Secondary causes† • Alcohol intake (≥ 3 drinks/day) • Femoral neck BMD if available‡

*Current exposure or past exposure for > 3 months at the equivalent of > 5 milligrams of prednisone)

†Insulin-dependent type 1 diabetes, osteogenesis imperfecta in adults, untreated longstanding hyperthyroidism, hypogonadism or premature menopause (age < 45 years), chronic malnutrition or malabsorption, chronic liver disease

‡Total hip BMD may be entered, but femoral neck measurement is preferred; the tool will compute a risk estimate without BMD data.

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Treatment of OP to prevent fracture

- Not effective: Vitamin D and calcium; exercise
- Threshold for OP medications (any of the following)
  - Clinical or radiographic fracture of spine or hip
  - T-score ≤ -2.5 (DXA)
  - Osteopenia *and*
    - *Either* 10-year 3% risk hip fracture (FRAX)
    - *Or* 10-year 20% risk major osteoporotic fracture (FRAX)
- Efficacy of OP medications in
  - ✓Postmenopausal women: Several classes (2 AHRQ evidence reviews)
    - May not be generalizable to typical clinical populations
  - Men: Inconclusive (3 SRs)
  - ✓ Rheumatoid arthritis, especially using glucocorticoids (1 SR)
  - ✓ Spinal cord injury (1 SR)

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USPSTF recommendations for screening for osteoporosis

2002

- Screen women age ≥ 65 years
- Screen women age 60-64 years at increased risk
- No recommendations for other women; men not considered

2010 (impetus for current report)

- Screen women age ≥ 65 years without previous known fractures or secondary causes of osteoporosis. (Grade B recommendation)
- Screen women age < 65 years whose 10-year fracture risk is ≥ that of 65-year-old white woman without additional risk factors.* (Grade B recommendation)
- No recommendation for men who have no previous known fractures or secondary causes of osteoporosis. (Grade I for insufficient evidence)
- No formal recommendation regarding optimal intervals

**Risk for 65-year-old white woman, no additional risk factors: 9.3% according to FRAX*

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USPSTF recommendations

- Rationale
  - Reliable tools: OP and fracture risk assessment
  - Evidence that OP treatment reduces fracture risk
  - Both demonstrated by 2010 Nelson review (AHRQ)
- Unanswered questions, impetus for report
  - Non-RCT studies or new RCTs that assess impact of screening?
  - New/missed evidence on optimal screening or monitoring intervals?
  - Evidence for perimenopausal women or individuals with osteoporosis-inducing conditions?
  - Cost/cost-effectiveness?

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Scope, Methods, and Search Results

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PICO

- **Population**: Adult men and women.
- **Interventions**: BMD testing with DXA.
- **Comparisons**: Clinical assessment of fracture risk or treatment success without BMD testing.
- **Outcomes**: Health outcomes such as fractures, fracture-related morbidity, fracture-related mortality; intermediate outcomes such as clinical management decisions and patient behavior; harms associated with screening, including potential harms resulting from OP treatment; cost and cost-effectiveness.

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Key Questions

1. Is there **direct evidence that screening** for osteoporosis and low bone density **improves** health **outcomes**, clinical management decisions, or patient choices?

   1a. For individual patients—and do these outcomes vary according to age, sex, or other risk factors for BMD or fracture?

   1b. In populations*—and do these outcomes vary by population characteristics?

*Individual- or group-level data for an entire community or region to assess the effect of a public health program, as opposed to data from a clinic setting or from a community sample.

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Key Questions (cont.)

2. Is there direct evidence that **monitoring (serial testing)** for osteoporosis and low bone density **improves** health **outcomes**, clinical management decisions, or patient choices?
   - 2a. For individual patients—and do these outcomes vary according to age, sex, other risk factors (including previous BMD measurements), treatment status, or testing interval?
   - 2b. In populations—and do these outcomes vary according to population characteristics or testing interval?
   - 2c. What is the **minimum interval required to detect transition** from normal or low BMD to osteoporosis, or to assess treatment effect?
3. What is the **number needed to screen (NNS)** to prevent 1 fracture in subgroups defined by age, sex, and other risk factors?
4. Are bone density tests **safe** and what are the potential downstream adverse effects?
5. What are the **costs and cost-effectiveness** of osteoporosis screening and monitoring?

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Searches

- SRs, meta-analyses, economic evaluations, GLs published last 10 years
  - Searched July 8 to August 1, 2014
- Primary studies (PubMed)
  - Searched June 12 (exception, July 17 for KQ#3)
- Final update searches
  - August 4, 2014

Results: 10 studies total

- **KQ #1a** (effectiveness of screening):
  - General: 2 RCTs; 1 nonrandomized trial; 1 quasi-randomized trial
  - OP-inducing medications: 2 retrospective cohort studies
- **KQ #2a** (effectiveness, monitoring/serial testing) – 0
- **KQ #1b, #2b** (population-wide) – 0
- **KQ #2c** (minimum interval)
  - Screening – 2 longitudinal studies
  - Treatment monitoring – 0
- **KQ #3** (NNS)
  - General: 1 nonrandomized screening study; analysis, 2010 Nelson review
  - OP-inducing medications: 2 retrospective cohort studies
- **KQ #4** (safety) – 0 with direct evidence
- **KQ #5** (cost-effectiveness) – 2 economic evaluations

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Quality assessment aligns with GRADE system (Appendix II)

- Individual **study** appraisal
  - *Are the findings **valid**?*
    - Study design, execution, and analysis (checklist)
    - Internal validity (minimization of bias)
    - *Good–Fair–Poor–Very Poor*
- Evaluation of **body of evidence** for each outcome
  - *How **confident** are we that this evidence answers the Key Question?*
    - Domains:
      - –Study design and weaknesses
      - –Quantity/precision of data
      - –Publication bias
      - –Applicability to PICO
      - –Consistency, study findings
    - *High–Moderate–Low–Very Low*

Findings

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Key Findings for KQ#1:Effectiveness of screening

Outcome	Findings	# Studies, Overall Quality
Fracture prevention	• *May* reduce risk in middle-aged/older adults	2 studies, low
	• *May* be more effective, advanced age	2 studies, very low
	• *May* reduce risk with use of OP-inducing drugs	2 studies, low
	• *May* be more effective with greater intensity of medication use	1 study, low
Prescription of OP medication	• *May* cause increase	3 studies, low
OP-preventing behavior	• Minimal or no effect	2 studies, low
NOTE: No studies assessed population-wide impact (KQ #2b).		

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Key Question #1a: Screening may reduce fracture risk, middle-aged/older adults

Evidence	Relative Risk of Fracture, Screened vs Unscreened (statistically significant results bolded)
2 fair experimental studies (n=7907) **Low Overall Quality** (fair study quality; few studies, imprecision)	**Kern 2006 (nonrandomized trial; men and women, age ≥ 65 years; f/u 5 years):** Overall adjusted HR: **0.64 (CI, 0.4-0.99**) Unadjusted cumulative incidence: 4.8% vs 8.2% **Barr 2010 (RCT; women; age 45-54 years; f/u 9 years):** *Overall adjusted HR:* Intention-to-treat: 0.791 (CI, 0.600-1.042) Treatment-received: 0.759 (NS) Per-protocol HR: **0.734 (CI, 0.546-0.988; *P*=0.041)** Unadjusted cumulative incidence: 8.9% vs 9.4% Uncertain generalizability to clinical populations.

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KQ #1a: Screening effectiveness may be greater with advanced age

Evidence	Relative Risk of Fracture, Screened vs Unscreened (statistically significant results bolded)
2 fair experimental studies (n=7907) **Very Low Overall Quality** (fair studies; imprecision, indirect comparisons)	**Kern 2006 (nonrandomized, fair; men and women, age ≥ 65 years; f/u 5 years) (HR):** Overall: **0.64 (CI, 0.4–0.99)** Women: 0.61 (CI, 0.35–1.06); Men: 0.68 (CI, 0.32–1.42) Age 65–74 years: 0.73 (CI, 0.29–1.87) Age 75–84 years: 0.82 (CI,0.47–1.44) Age ≥ 85 years: **0.22 (CI, 0.06–0.79)** **Barr 2010 (RCT, fair; women, age 45–54 years; f/u 9 years) (HR):** Intention-to-treat: 0.791 (CI, 0.600–1.042) All results represent an adjusted comparison.

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KQ #1a: Screening may reduce fracture risk, use of OP-inducing medications

Evidence	Relative Risk of Fracture (statistically significant results bolded)
2 fair retrospective cohort studies (n=7168) **Low Overall Quality** (fair study quality, few studies; only 2 medications, exclusion of women)	**Zhumkhawala 2013 (1432 men, ADT; f/u 2–3 years)**: Adjusted HR (control vs screened): **4.19 (CI, 1.92–9.13)** Unadjusted cumulative incidence rates (control vs screened):5.1% vs 18.1% **Khan 2014 (5736 men, ulcerative colitis with varying intensities of CS; f/u 3 years):** Adjusted HR (screening vs no screening) for fragility fracture: **0.5 (CI, 0.3–0.9; *P*=0.03)** Unadjusted cumulative incidence rates (screening vs no screening): 1.6% vs 2.8%

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KQ #1a: Screening effectiveness may vary according to CS exposure

Evidence	Relative Risk of Fracture, Screened vs Unscreened (statistically significant results bolded)
1 retrospective cohort study (n=5736) **Low Overall Quality** (fair study quality, only 1 study)	**Khan 2014 (5736 men with ulcerative colitis with varying intensities of CS; f/u 3 years):** *Interaction between DXA screen and CS exposure (incidence risk ratio):* Low CS exposure: No difference Moderate: 0.44 (NS) High: 0.38 **(*P*=0.02)**

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KQ #1a: Screening may increase OP treatment

Evidence	% Patients, Screened vs Unscreened (statistically significant results bolded)
3 studies (n=7168) (1 RCT,* 2retrospective cohort) **Low Overall Quality** (fair study quality; unknown differences in appropriateness of treatment)	***Barr 2010 (2604 women, age 45-54 years; f/u 9 years)** Hormone replacement therapy: **52.4%, 44.5% (*P*<0.01)** Vitamin D: **24.2%, 12.5% (*P*<0.01)** Calcium: **20.0%, 14.1% (*P*<0.01)** **Zhumkhawala 2013 (1432 men undergoing ADT; f/u 2-3 years):** OP drugs: **29% vs 3% (*P*<0.0001)** **Khan 2014 (5736 men; ulcerative colitis with varying intensities of CS; f/u 3 years):** OP medication, excluding hormone replacement therapy: 36.6%, 21.6% (*P*<0.001) Vitamin D-calcium: 32.9%, 13.4% (*P*<0.001)

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KQ #1a: OP-preventing behavior in older adults, no/minimal effect of screening

Evidence	Results, Screened vs Unscreened (statistically significant results bolded)
2 experimental studies (n=399) **Low Overall Quality** (1 good, 1 poor study; small quantity data, short f/u)	**Sedlak 2007 (RCT, good; 203 postmenopausal women; f/u 1 year):** Total calcium intake over 1 year (screened, wait-list) (units unclear; assumed to be IUs* per day): **786, 668 (global *P*<0.001)** Exercise: No change over time in either group **Doheny 2011 (quasi-RCT, poor; men ≥ 50 years, f/u 1 year):** Mean # mins of vigorous activity: 22, 19 (NS) Mean # mins walking: 15.3, 13 (NS) Calcium: No group or knowledge effect

**IU=International Unit*

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Key Findings for KQ #2c: Minimum interval for screening/testing

Population	Findings	# Studies , Overall Quality
Screening, age > 60 years (without OP at last screening and without risk factors other than age)	Repeat screening generally does not improve estimation of fracture risk for **several years** after initial screening. Exceptions: Very elderly with ≥ substantial osteopenia at the time of the previous screen. Evidence-based, precise schedule not possible	2 studies, moderate
Screening, age < 60 years or perimenopausal women **Monitoring, OP treatment** **Factors other than age or treatment status**		Insufficient evidence (no studies)

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KQ #2c: Older adults; no transition to OP or fracture for ≥ several years; exception, advanced age and substantial osteopenia

Evidence	Study Results (statistically significant results bolded)
2 longitudinal cohort studies (n=5707) **Moderate Overall Quality** (good studies; heterogeneity in and lack of validation of models, and imprecision for individuals with normal or near-normal BMD)	***Frost 2009 (750 men and 1003 women, age ≥ 60 years and no OP at baseline; Australia):*** *Time in years to reach 20%, 10-year risk of OP and/or clinical fracture:* Men, Longest: Screened at age 60, T-score 0: 15.0+ (90% CI, **14.3**–15.0+) † Men, Shortest: Screened at age 80, T-score -2.2: 2.9 (90% CI, **2.6**–3.8) Women, Longest: Screened at age 60, T-score 0: 14.1 (90% CI, **12.7**–15.0+)† Women, Shortest: Screened at age 80, T-score -2.2: 2.4 (90% CI, **2.2**–2.6) *Authors advised using lower CI bound as guide. †F/u did not go beyond 15 years. See next 2 slides.

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Frost 2009 in other words

- Repeat screening at < 2 years would have utility for no individuals.
- Repeat screening at < 3 years would have utility only in elderly adults with substantial osteopenia:
  - Men age 80 years, T-score ≤ -2.2 at the time of the last screening.
    - Younger men or men with higher T-scores would not reach the treatment threshold for an average of ≥ 3 years.
  - Women age 75 years, T-score ≤ -2.0 at the time of the last screening.
    - Younger women or women with higher T-scores would not reach the treatment threshold for an average of ≥ 3 years.
  - Women age 80 years, T-score ≤ -1.5 at the time of the last screening.
    - Younger women or women with higher T-scores would not reach the treatment threshold for an average of ≥ 3 years.

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KQ #2c: Older adults; no transition to OP or fracture for ≥ several years; exception, advanced age and substantial osteopenia (cont.)

Evidence	Study Results
2 longitudinal cohort studies (n=5707) **Moderate Overall Quality** (good studies; heterogeneity in and lack of validation of models, and imprecision for individuals with normal or near-normal BMD)	**Gourlay 2012 (4957 women, age ≥ 67 years and no OP at baseline; U.S.):** *Adjusted time in years for 10% women to develop OP or have fracture or treatment, by OP status at last screen:* Normal BMD (T-score ≥ -1.00): **16.8** (CI, 11.5-24.6) Mild osteopenia (T-score -1.01 to -1.49): **17.3** (CI, 13.9-21.5) Moderate osteopenia (T-score -1.50 to -1.99): **4.7** (CI, 4.2-5.2) Advanced osteopenia (T-score -2.00 to -2.49): **1.1** (CI, 1.0-1.3) See previous 2 slides.

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KQ #2c: Other policy-relevant information

- Numerous additional studies were not designed to estimate intervals
- But provided substantial evidence that
  - Change in BMD is poor predictor of change in fracture risk
  - Unless risk was high at last screen
- Same finding in small # studies in patients who
  - Had discontinued OP treatment
  - Had risk factors other than age or treatment status

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Key Findings for KQ #3: Number-needed-to-screen (NNS)

Population	Findings	# Studies, Overall Quality
Older adults	NNS may diminish with age NNS hip > NNS any fracture Very serious inconsistency precludes reliable numerical estimates	2 studies Women, low overall quality Men, very low overall quality
Using OP-inducing medications	Men taking ADT for prostate cancer NNS=26 Men taking glucocorticoids for ulcerative colitis, NNS=278 Screening effect was dose-dependent. NNS dose-dependent?	1 study, each medication Very low overall quality
Other Subpopulations: Insufficient evidence (no studies)		

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KQ #3: In older adults NNS may diminish with age; considerably greater for prevention of hip fracture than for any OP fracture

Evidence	NNS
1 screening trial; calculations from 1 good-quality SR **Low Overall Quality (women)** (small # analyses, fair-quality study with imprecision [Kern 2006], indirect evidence [Nelson 2010a/2010b], inconsistency) **Very Low Overall Quality (men)** (potentially confounded data from single study)	**Kern 2006 (nonrandomized trial, fair; men and women, age ≥ 65 years):** NNS to prevent 1 hip fracture over 5 years: Overall: 59 Men: 96 Women: 46 Adults age ≥ 85 years: 7 **Nelson 2010 (SR, special analysis; women, age ≥ 55 years):** NNS to prevent 1 fracture over 5 years (any fracture, hip fracture): Age 55-59 years: 278, 1667 Age 60-64 years: 187, 1000 Age 65-69 years: 103, 556 Age 70-74 years: 61, 323 Age 75-79 years: 43, 238

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KQ #3: NNS, OP-inducing medications

Evidence	NNS
2 retrospective cohort screening studies **Very Low Overall Quality** (fair study quality; unknown applicability to full spectrum of medications, only 1 study for each medication, NNS by dose not possible, possible confounding, no data for women)	**Zhumkhawala 2013 (1432 young to old men undergoing ADT; f/u 2-3 years, mean 3.2):** For prevention of 1 hip fracture over 3 years: 26 **Khan 2014 (5736 young to old men with ulcerative colitis with varying intensities of CS; f/u mean 3 years):** For prevention of 1 hip fracture over 3 years: 278

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KQ #4: Safety (background information)

- Radiation exposure from DXA scan
  - Less per scan than with chest x-ray or mammogram
  - Concern if scanning is repeated over a lifetime
- Potential for inappropriate treatment or missed opportunities for treatment if:
  - False-positive or false-negative scan results
  - Incorrect risk assessment for OP prior to screening or for fracture after screening.
  - Actual data not available.
- Serious adverse events have been reported with OP medication use
  - But rare or without proven causality.
  - See Table 6 in report.

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KQ #5: Cost/cost-effectiveness

- Cost of DXA scan
  - $98 assumed in U.S. economic evaluation (Nayak 2011)
  - Medicare reimbursement reportedly lower now
  - WA State Agency Utilization Data
    - $104 (PEBB/UMP)
    - $124 (non-Medicare PEBB/UMP)
    - $59 (Medicaid)
- Cost-effectiveness in men
  - Insufficient evidence (no evaluations with adequate model)

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KQ #5: Cost/cost-effectiveness

- Cost-effectiveness in women
  - 1 U.S. and 1 Canadian evaluation
  - Threshold of $50,000/QALY
  - Cost-effective in older women
    - Age ≥ 55 years (U.S.)
    - Age ≥ 65 years (Canada)
  - Mixed findings for age < 65 years
    - Cost-effective at ages as young as 55 years (U.S.)
    - Not cost-effective at age 40-64 years (Canada)
  - **Caution:** Empirical evidence for screening effectiveness is of low quality
- Cost-effectiveness in other populations; cost-effectiveness of serial screening or monitoring
  - Insufficient evidence (no evaluations)

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KQ #5: Cost-effectiveness in older women, Nayak 2011 (U.S.)

Limitations	Results
Multiple data sources. Possible overestimation, effectiveness of treatment. Assumes all at T-score threshold will receive treatment.	**Women age ≥ 55 years; 7 screening strategies compared with usual care:*** *Best strategy overall (most effective and still within WTP* threshold):* Initiate at age 55; DXA screen; treat if T-score ≤ -2.5; screen every 5 years **$45,450/QALY** ($48,581 in 2014 USD) *Usual care = treat only after OP fracture

**WTP=willingness-to-pay*

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KQ #5: Cost-effectiveness in older women, Nshimyumukiza 2013 (Canada)

Limitations	Results
No consideration of medication AEs. May not be generalizable to (a) screening programs without prevention program or (b) screening followed by treatment based on T-score rather than a multifactorial risk tool.	**Women age ≥ 65 years; 12 programs of universal screening* plus universal primary prevention, compared with no program:†** *Program to avert greatest # fractures; add most QALYs:* BMD/CAROC* plus universal primary prevention with physical activity + vitamin D + calcium: ICER = $60,205/averted fracture ($55,019, 2014 USD) (Sensitivity analysis: 63% probability of ≤ $50,000 per averted fracture) ICUR = **$55,300/QALY** ($50,537, 2014 USD) (Sensitivity analysis: **75% probability of ≤ $50,000 per QALY**) *Universal screening = initial screen with 1 follow-up DXA at 2 or 5 years, depending on risk †No program = possible DXA scan and treatment after fracture

CAROC=Canadian Association of Radiologists and Osteoporosis Canada fracture risk assessment tool

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Practice Guidelines and Payer Policies

Selected Payer Policies	
Screening covered with conditions • Estrogen deficiency • Depo-Provera contraception (injections) • Men age > 70 or age 50 years with risk factors • Men, ADT • Men, hypogonadism • Radiographic signs of OP or low bone mass • Fragility fracture • Glucocorticoids for > 3 months • Celiac sprue • Primary hyperparathyroidism • Women age ≥ 65 years, 10-year risk of major fracture ≥ 9.3%	Aetna, CMS Aetna Aetna Aetna Aetna Aetna Aetna, CMS Aetna, CMS Aetna Aetna, CMS Oregon HERC
Treatment monitoring (OP medications) covered	Aetna, CMS
Screening/monitoring typically every 2 years, more frequently if: • Initiate OP treatment monitoring • Glucocorticoids for > 3 months • Anticonvulsants for > 3 months • Uncorrected primary hyperparathyroidism Screening every 2-15 years depending on BMD status (Gourlay et al., 2012)	Aetna, CMS Aetna, CMS Aetna, CMS Aetna Aetna Oregon HERC
DXA and others; CMS puts some limits on others DXA	Aetna, CMS Oregon HERC
No relevant policy	GroupHealth, Regence

CMS policy

- National Coverage Determination (NCD) for Bone (Mineral) Density Studies (150.3)
  - Version 2 transferred conditions for coverage of bone mass measurements to CMS Manual System (January 2007)
- No evidence analysis
  - NCD 150.3 Version 1 (1998–2006)
  - NCD 150.3 Version 2 (2007–present)
  - Current Bone Mass Measurements section of CMS Manual System

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Practice Guidelines, Generally Healthy Populations (11 Guidelines)	
Screening in Women (9 GLs)	Age ≥ 65 years* Age < 65 years with risk factors* 3 of 9 GLs: all women during menopausal transition
Screening in Men (8 GLs)	Age ≥ 70 years (7 GLs)* Age < 70 years (or age 50–69) with risk factors (7 GLs)† Insufficient evidence (USPSTF)
Follow-Up Screening	Mixed recommendations (1–5 years)
OP Treatment Monitoring (7 GLs)	Every 1–2 years or until BMD stabilizes

*Consistent with low-quality evidence of effectiveness in middle-age/older adults; most evidence pertains to women.
†Consistent with low-quality evidence of fracture prevention in men taking OP-inducing drugs (wide age range).

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Practice Guidelines, Special Medical Conditions (3 Guidelines)	
Screening (2 GLs)	Severe late-onset hypogonadism (1 guideline) Glucocorticoid therapy for ≥ 3 months (2 GLs)* IBD plus risk factors (1 GL)* Single factor such as ADT may be sufficient cause (1 GL)*
Serial Testing (1 GL)	Patients taking glucocorticoids:* Every 6 months during OP treatment Yearly for OP screening

*Consistent with low-quality evidence of effectiveness in presence of OP-inducing medications.

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Overall Summary and Discussion

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Final Summary: Screening effectiveness

- Not well established
  - But some positive empirical evidence (postmenopausal women, use of glucocorticoids or ADT)
- May increase with age or greater use of OP-inducing medication
- Supported by 2 economic evaluations, older women
- Individuals with normal BMD/mild osteopenia unlikely to reach treatment threshold for several years
  - In absence of risks such as glucocorticoid use
- No direct empirical basis
  - Precise age or risk profile to prompt screening
  - Precise screening intervals
- Consensus (professional groups)
  - Start at age 65 in women, age 70 in men
  - Earlier in the presence of risk factors
  - None regarding screening intervals

Final Summary: Effectiveness of OP treatment monitoring

- No empirical evidence
- No analysis of intervals
- Consensus
  - Every 1-3 years or until BMD stabilizes
- However,
  - BMD change is a poor predictor of fracture risk
  - Standard practice is to discontinue treatment after 5 years

Additional research needed for all Key Questions

- Screening and serial screening/testing
  - Very large observational studies (cohort design), pragmatic RCTs
  - Assess reduction in fracture risk
  - Optimal age and risk profile to start
- Populations other than postmenopausal women
  - Men
  - Perimenopausal women
  - Non-white populations
- Longitudinal studies to determine the screening/testing interval
  - U.S. populations
  - Standardized approach
- Additional cost-effectiveness studies
  - Preferably trial-based

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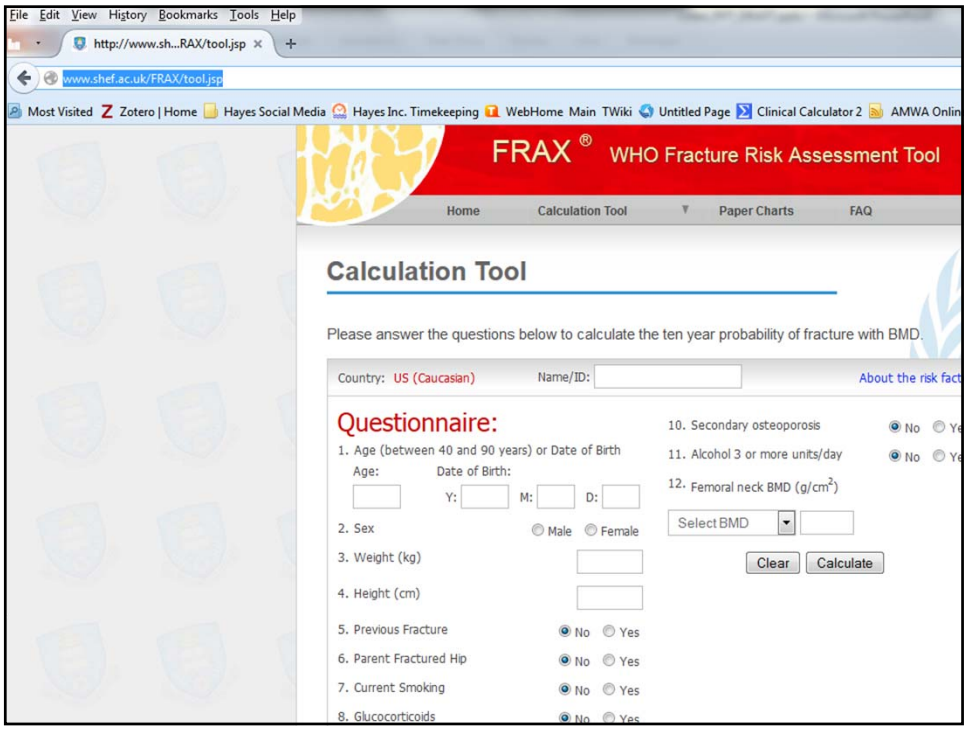
Extra Slides

Precision of DXA

- BMD changes occur slowly
- Precision varies across machines, facilities, and operators
- Least significant change (LSC) calculated for each machine and operator
- For repeat scan, same machine and operator
  - BMD change is considered statistically significant and due in part to biological change if it exceeds LSC
  - Best if patients are monitored on same machine

Other risk factors supported by systematic reviews

- Nutritional deficiencies
- Lack of physical activity
- Genetic diseases
- Gastrointestinal disorders
- Hematologic disorders
- Anticonvulsant medications
- Aromatase inhibitors (used for treating breast cancer)
- Cystic fibrosis
- Inflammatory bowel disease
- Celiac disease



Practice guidelines

Quantity and Quality of GLs	Recommendations, Screening in Women
9 (AACE, ACOG, ACPM, ACR, ICSI, ISCD, NAMS, NOF,* USPSTF) 2 Good, 4 Fair, 1 Poor, 2 Not Rated	**Age < 65 years** Screen (BMD) postmenopausal women with risk factors. E.g., if 10-year fracture risk > 9.3% (risk for 65-year-old white woman with no additional risk factor) (ICSI and USPSTF). Exceptions: ACR (poor) policy additionally applies to women in menopausal transition; no additional risk factors. ISCD (not rated) and NOF (poor) also advise screening during menopausal transition if risk factors are present. **Age ≥ 65 years** Screen (BMD) all women Exception: ACR recommendation (poor) applies to all women age ≥ 50 years

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Practice guidelines

Quantity and Quality of GLs	Recommendations, Screening in Men
7 (ACP, ACPM, ACR, Endocrine Society, ISCD, ICSI, NOF*) 3 Good, 1 Fair 2 Poor, 1 Not Rated	**Age < 70 years** Screen (BMD) men age <70 or age 50-69 years with risk factors for fracture. ICSI: "consideration" Endocrine Society: "weak recommendation" Risk factors identified by ≥1 guideline: Low BMI, weight loss, physical inactivity, CS use, ADT, fragility fracture. **Age ≥ 70 years** Screen (BMD) all men age ≥ 70 years. ICSI: "consideration" Endocrine Society: "weak recommendation"
1 (USPSTF) – Good	Insufficient evidence

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Practice guidelines

Quantity and Quality of GLs	Recommendations, Follow-up Screening After Initial Screen
5 (AACE, ACR, NAMS, ISCD, USPSTF) 2 Good, 2 Fair, 1 Not Rated	**AACE (good), ACR (fair), NAMS (fair):** Every 1–5 years, depending on risk factors and T-score in patients with risk factors or low BMD (osteopenia) at last scan. **ISCD (not rated):** Monitor BMD if evidence of bone loss would result in treatment. **USPSTF (good):** Lack of evidence regarding appropriate intervals.

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Practice guidelines

Quantity and Quality of GLs	Recommendations, Treatment Monitoring
7 (AACE, ACOG, ACR, Endocrine Society, ISCD, ICSI, NAMS, NOF) 1 Good, 3 Fair, 2 Poor, 1 Not Rated	**Overall:** Every 2 years (3 GLs), every 1–2 years (3 GLs), or no interval specified (1 statement). **Some GLs:** DXA discontinued or performed less frequently if BMD improves or stabilizes and no new risk factors. **ISCD:** More frequent for conditions associated with rapid bone loss, e.g., glucocorticoid therapy.

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Practice guidelines

Quantity and Quality of GLs	Recommendations, Screening in Special Situations
1 (poor) (ACG: Ulcerative Colitis)	Consider DXA in IBD patients: (1) with risk factors for OP (e.g., smoking, low body mass, sedentary lifestyle, hypogonadism, family history, nutritional deficiencies); (2) age ≥ 60 years; (3) using corticosteroids > 3 months
1 (fair) (EUA: Male Hypogonadism)	Adult men with established severe hypogonadism (late-onset) for concomitant OP. (Severe was not defined.)
2 (good) (American College of Rheumatology, ICSI: Patients Taking Glucocorticoids)	Baseline DXA before starting glucocorticoid for an anticipated ≥ 3 months. American College of Rheumatology: Consensus-based recommendation. ICSI: Strong recommendation with moderate-quality evidence .
1 (good) (ACP)	In certain situations, a single risk factor, e.g., ADT, may be sufficient reason to screen (not a formal recommendation).

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Practice guidelines

Quantity and Quality of GLs	Recommendations, Monitoring in Special Situations
1 (good) (American College of Rheumatology: Patients Taking Glucocorticoids)	Consider serial BMD testing for patients receiving glucocorticoid therapy for ≥ 3 months. As often as 6 months for treatment of OP, yearly for prevention of OP.

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USPSTF recommendations: Findings of 2010 Nelson (AHRQ) review

For men and postmenopausal women without known fracture

- Effectiveness/harms of screening
  - No RCTs
- Simple fracture risk tools ≈ more complex tools (generalizable to clinical populations?)
- Repeat measurement up to 8 years after initial scan (Hillier et al., 2007)
  - Did not improve accuracy of fracture prediction
- Bisphosphonates, parathyroid hormone (PTH), raloxifene, and estrogen
  - Reduce primary vertebral fractures in postmenopausal women
  - Sensitivity analyses: Bisphosphonates also reduce nonvertebral fractures in this population.
- Safety of OP medications
  - Some serious AEs reported

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on three questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective[1] as expressed by the following standards[2]:

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms[3]:

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

[1] Based on Legislative mandate: See RCW 70.14.100(2).

[2] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

[3] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

Using Evidence as the Basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. Availability of Evidence:

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. Sufficiency of the Evidence:

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence[4] using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- The amount of evidence (sparse to many number of evidence or events or individuals studied);
- Consistency of evidence (results vary or largely similar);
- Recency (timeliness of information);
- Directness of evidence (link between technology and outcome);
- Relevance of evidence (applicability to agency program and clients);
- Bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. Factors for Consideration - Importance

At the end of discussion a vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- Risk of event occurring;
- The degree of harm associated with risk;
- The number of risks; the burden of the condition;
- Burden untreated or treated with alternatives;
- The importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- The degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- Value variation based on patient preference.

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

Safety Outcomes	Safety Evidence
Radiation exposure	
Efficacy – Effectiveness Outcomes	**Efficacy / Effectiveness Evidence**
Fracture incidence	
Clinical Management Decisions	
Behavior Modification	
Special Population / Considerations Outcomes	**Special Populations/ Considerations Evidence**
Age	
Sex	
BMD status	
Medication use (e.g., steroids)	
Cost	**Cost Evidence**
Cost	
Cost-effectiveness	
Cost-utility	

Medicare Coverage and Guidelines

[From Evidence Report, page 38]

- A CMS National Coverage Determination (NCD) for Bone (Mineral) Density Studies (150.3), which was issued in January 2007, documented the transfer of conditions for coverage of bone mass measurements to the CMS Manual System. A document on Bone Mass Measures in the Manual System states that effective January 1, 2007, bone mass measurement is covered, generally every 2 years but subject to certain conditions. Neither the NCD nor the Manual System provides the rationale or evidence base for these policies.

[From Evidence Report, page 36]

Table 8. Summary of Practice Guideline Recommendations

Key: AACE, American Association of Clinical Endocrinologists; ACG, American College of Gastroenterology; ACOG, American College of Obstetricians and Gynecologists; ACP, American College of Physicians; ACPM, American College of Preventive Medicine; ACR, American College of Radiology; ADT, androgen-deprivation therapy; BMD, bone mineral density; BMI, body mass index; DXA, dual x-ray absorptiometry; EUA, European Urological Association; GL, guideline; IBD, inflammatory bowel disease; ICSI, Institute for Clinical Systems Improvement; ISCD, International Society for Clinical Densitometry; NAMS, North American Menopause Society; NOF, National Osteoporosis Foundation; OP, osteoporosis; USPSTF, United States Preventive Services Task Force

Quantity of Individual GLs	Individual GL Quality*	Recommendations
Screening in Postmenopausal Women <65 Yrs of Age		
9 (AACE, ACOG, ACPM, ACR, ICSI, ISCD, NAMS, NOF*, USPSTF)	2 Good 4 Fair 1 Poor 2 Not rated	Postmenopausal women age <65 yrs should have BMD screening if they have risk factors for fracture. For example, ICSI and USPSTF recommend screening if 10-yr fracture risk exceeds 9.3% (risk for 65-year-old white woman with ≤1 additional risk factor). *Exceptions:* ACR (poor) policy applies to women in menopausal transition and does not require risk factors other than menopause. ISCD (not rated) and NOF (poor) also advise screening during menopausal transition if risk factors are present.
Screening in Women ≥65 Yrs of Age		
9 (AACE, ACOG, ACPM, ACR, ICSI, ISCD, NAMS, NOF*, USPSTF)	2 Good 4 Fair 2 Poor 1 Not rated	All women age ≥65 yrs should have BMD screening. (ACR recommendation applies to all women age ≥50 yrs.)
Screening in Men <70 Yrs of Age		
7 (ACP, ACPM, ACR, Endocrine Society, ISCD, ICSI, NOF*)	3 Good 1 Fair 2 Poor 1 Not rated	Men age 50-69 yrs should have BMD screening if they have risk factors for fracture. *(Presented as a consideration, not a recommendation, by ICSI; and as a weak recommendation by the Endocrine Society.)* Risk factors identified by ≥1 GL: Low BMI, weight loss, physical inactivity, corticosteroid use, ADT, fragility fracture.
1 (USPSTF)	1 Good	Evidence is insufficient to support a recommendation.

Quantity of Individual GLs	Individual GL Quality*	Recommendations
Screening in Men ≥70 Years of Age		
7 (ACP, ACPM, ACR, Endocrine Society, ISCD, ICSI, NOF*)	3 Good 1 Fair 2 Poor 1 Not rated	All men age ≥70 yrs should have BMD screening. *(Presented as a consideration, not a recommendation, by ICSI; and as a weak recommendation by the Endocrine Society.)*
1 (USPSTF)	1 Good	Evidence is insufficient to support a recommendation.
Follow-Up Testing After Initial Screen		
5 (AACE, ACR, NAMS, ISCD, USPSTF)	2 Good 2 Fair 1 Not rated	AACE, ACR, NAMS: Every 1-5 yrs, depending on risk factors and T-score in patients with risk factors or low BMD (osteopenia) at last scan. ISCD: To monitor BMD if evidence of bone loss would result in treatment. USPSTF: Lack of evidence regarding appropriate intervals.
Treatment Monitoring		
7 (AACE, ACOG, ACR, Endocrine Society, ISCD, ICSI, NAMS, NOF)	1 Good 3 Fair 2 Poor 1 Not rated	Typical: BMD monitoring recommended every 2 yrs (3 GLs), every 1-2 yrs (3 GLs), or without specification of interval (1 position statement). Some GLs add that DXA can be discontinued or performed less frequently if BMD improves or stabilizes and there are no new risk factors. The ISCD recommends more frequent monitoring for conditions associated with rapid bone loss, e.g., glucocorticoid therapy.
Screening in Special Situations		
1 (ACG: Ulcerative Colitis)	1 Poor	DXA screening should be considered in IBD patients: (1) with risk factors for OP such as smoking, low body mass, sedentary lifestyle, hypogonadism, family history, and nutritional deficiencies; (2) age ≥60 yrs; (3) using corticosteroids >3 months consecutively or recurrently.
1 (EUA: Male Hypogonadism)	1 Fair	Adult men with established severe hypogonadism (late-onset) should be screened for concomitant OP. (*Severe* was not defined.)
2 (American College of Rheumatology, ICSI: Patients Taking Glucocorticoids)	2 Good	Baseline DXA *recommended* for patients before starting glucocorticoid for an anticipated ≥3 months. (Considered a consensus-based recommendation *by American College of Rheumatology but a strong recommendation with moderate-quality evidence by ICSI.*)
1 (ACP)	1 Good	In certain situations, a single risk factor, e.g., ADT, may be sufficient reason to screen (*not a formal recommendation*).
Treatment Monitoring in Special Situations		
1 (American College of Rheumatology: Patients Taking Glucocorticoids)	1 Good	Serial BMD testing should be *considered* for patients receiving glucocorticoid therapy for ≥3 months. As often as 6 months for treatment of OP, yearly for prevention of OP.

Clinical Committee Findings and Decisions

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
  - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
  - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?

Next Step: Cover or No Cover
If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions
If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
    - Refer to evidence identification document and discussion.
    - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
    - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
    - What are the known conditions/criteria and evidence state
    - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Clinical Committee Evidence Votes

First Voting Question
The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	**Equivalent** (yes)	**Less** (yes)	**More** (yes)
Effective				
Safe				
Cost-effective				

Discussion
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second Vote
Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered _____ Covered Unconditionally _____ Covered Under Certain Conditions

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.