Under-Diagnosis and Under-Treatment of Osteoporosis and the Importance of Outcomes and Effectiveness Research

Kenneth G. Saag, MD, MSc

Jane Knight Lowe Professor
Vice Chair, Department of Medicine
Division of Clinical Immunology and Rheumatology
Director, Center for Outcomes, Effectiveness Research, and Education (COERE)
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Past president, Board of Trustee, National Osteoporosis Foundation
Consultant: Amgen, Radius, Roche
Royalties: UpToDate
Overview

• How bad is the problem?

• What is the possible impact?

• How do we define quality?

• What has been tried to improve practice in osteoporosis?
  • Provider-directed interventions
  • Patient-directed interventions
  • System interventions
Last month, three professional groups — the American Society for Bone and Mineral Research, the National Osteoporosis Foundation and the National Bone Health Alliance — put out an urgent call for doctors to be more aggressive in treating patients at high risk, and for patients to be more aware of the need for treatment.

“Millions of Americans are missing out on a chance to avoid debilitating fractures from weakened bones, researchers say, because they are terrified of exceedingly rare side effects from drugs that can help them.”
A Crisis in the Treatment of Osteoporosis

Khosla and Shane, 2016
My neighbor Arlyn Riskind, who is 53, has premenopausal osteoporosis, diagnosed nine years ago. She takes low-dose birth control pills to preserve her bone mass and postpone menopause. But after menopause, she knows she “may be soon faced with some decision-making.” And she is quite anxious about it.
Oral Bisphosphonates Use is Declining (alendronate, risedronate, and ibandronate) Use in USA, 2002-2012

Source: IMS Vector One: National, Years 2002-2012 Data Extracted February 2013

Wysowski D. Bone 2012;57: 423
Updated Medicare Data on Drug Rx

Osteoporosis Medications

% Use of PMO Cohort

Calendar Time

Curtis J. et al, personal communication
Declining Bisphosphonate Use in Ontario, CA

Hayes KN  ASBMR 2018
Changing Patterns of Chronic Disease Drug Use in Ontario

a) Benzodiazepine use
b) Diabetes diagnosis
c) Statin use
d) H2RA/PPI use

Hayes KN ASBMR 2018
Osteoporosis Care Lags Behind Other Major Diseases/Conditions (2013 HEDIS HMO data)

- Testing/treatment after a fracture: 29%
- Fall risk discussion: 34%
- COPD spirometry testing: 43%
- Comprehensive diabetes care: 59%
- Fall risk intervention: 62%
- Colorectal cancer screening: 63%
- Controlling high blood pressure: 64%
- Pneumococcal vaccinations (2012): 70%
- Breast cancer screening: 74%
- Beta blockers (post-heart attack): 84%
- Cholesterol management (CVD patients): 87%
- RA anti-rheumatoid therapy: 88%

Temporal Trends in Bisphosphonates vs. FDA Safety Announcements

Safety Announcements

ONJ
Afib
AFF

Bisphosphonates

Other osteoporosis medications

Percentage using medication

Year

Kim S. JBMR 2016;31:1536
"We are failing in our mission to deliver healthcare for those at high risk"

Prof John Kanis, M.D.
International Osteoporosis Foundation
President
Seville, Spain, April 2014
Recent Changing Testing and Fracture Rates in US

11,464 additional hip fractures
$459 million additional expenses
2,293 additional deaths

17.9%
14.8%
13.2%
11.3%
884
738
693
500
550
600
650
700
750
800
850
900

Fractures per 100,000 Women Age 65+

Age-adjusted to the 2014 Age Distribution

Adapted from Lewiecki EM et al. Osteoporos Int. 2018;29:717-722.

11,464 additional hip fractures
$459 million additional expenses
2,293 additional deaths

110%
120%
140%
160%
180%
200%
220%
240%

Percent of Women Age 65+

DXA Medicare Payments

$139

$82

$42

10%
12%
14%
16%
18%
20%
22%
24%
26%

DXA Testing

13.2%
17.9%

Osteoporosis Diagnosis

14.8%
11.3%
More Recent Fracture Trends in US Managed Care Enrollees

Lewiecki EM et al. ASBMR. 2018. Abstract 0742
Increasing Rates of Spine, Femur, and Tib/Fib Fractures in Recent Years

Lewiecki EM et al. ASBMR. 2018. Abstract 0742
Age-Standardized US Hip Fracture Incidence Rates in Women by Race/Ethnicity*

* Standardized to the 65+ population using 2010 US Census data

Wright N. JBMR 2012;27:2325
Changing Patterns of Glucocorticoid Induced Osteoporosis (GIOP) Rx - US HRT + Prescription Bone Rx among New Glucocorticoid Users (n = 5,471)

p < 0.01 for all comparisons

Curtis JR. *Arth Rheum* 2005;52:2485
Temporal Pattern in Osteoporosis Treatment in GIOP in Canada
Low Rates of Rx

Albaum JM. Osteo Int 2015;26:2845
Practice Pattern Variation in GIOP Prevention

Mudano A, J Rheumatol, 28:1298, 2001
Osteoporosis Care Lower Among African American Women with Prior Fractures Compared to Caucasians

- BMD Testing
- Any Prescription
- Estrogen
- Alendronate
- Raloxifene
- Calcitonin
- Calcium
- Vitamin D or MVI

Odds Ratios (95% CI)

How Can We Improve Quality in Osteoporosis?

- New uses for older drugs (efficacy)
- Improve safety of older drugs (safety)
- New(er) drugs/biologics (efficacy)
- Better ways to translate research into practice (effectiveness)
How Can We Improve Quality in Osteoporosis?

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• Improve safety of older drugs (safety)
• New(er) drugs/biologics (efficacy)
• Better ways to translate research into practice (effectiveness)
T2, T3 Research Conceptual Model

Basic Science Knowledge → Clinical Trials → Current Clinical Knowledge

1st Translational Block → 2nd Translational Block → 3rd Translational Block

Policy

Health Care Systems

QI* Early Adoption → QI* Widespread Adoption

Community

Implementation Research

Improved Health Outcomes

*Industrial-style Quality Improvement

Generate new information on benefits, harms, and costs: OBSERVATIONAL

Summarize existing evidence: META-ANALYSIS

DeVELOP MEASURES of clinical performance and patient outcomes

MEASURE VARIATIONS in clinical performance and patient outcomes

TRANSLATE RESEARCH INTO PRACTICE and EDUCATE COMMUNITY

Define the clinical condition

Combine evidence on benefits, harms, costs: ECONOMIC ANALYSIS / GUIDELINES

Generate new information on benefits, harms, and costs: OBSERVATIONAL

Summarize existing evidence: META-ANALYSIS

Evidence Implementation

Evidence Generation

1

2

3

4

5

6
Defining Quality

“Quality is like obscenity: I’ll recognize it when I see it”

Ringel and Vickrey, Arch Neurology, 1997
What Do We Know About Health Care Quality?

- Quality can be measured
- Health care systems must be accountable for quality
- Measurement AND accountability drive improvement
- Consumers want and use information about health care quality
Definition of Quality
Institute of Medicine

• Health services for individuals and populations
• Increase the likelihood of desired health outcomes
• Consistent with current professional knowledge

Institute of Medicine, 2001
“Adults received 55% of recommended care according to 439 process-of-care measures.”
Quality Indicator Development Process

Outreach and Education

Guidelines
- Systematic lit review
- Evidence basis
- Expert panels

Quality indicators
- Develop indicator from GL
- Expert consensus

Quality (performance) measures
- Specify measure
- Test measure in database
Anatomy of a Quality Measure
The Core

• Numerator – what outcome or process of care is the measure trying to address?

• Denominator – what population is the measure focused on?

• Exclusions
  • Medical (contraindication)
  • Patient (patient choice)
  • System (vaccine unavailable)
Quality Measure
National Landscape

Development → NCQA, PCPI, Joint Commission, AHRQ, specialty societies, others

Endorsement → National Quality Forum™ / AQA

Implementation → CMS, private plans, NCQA, medical specialty boards, continuing medical education (CME) developers
HEDIS® Measures for Osteoporosis
Low Rates of Follow-up Intervention

• HEDIS: A set of measures used to assess performance on key measures of clinical effectiveness\(^1\)
  • Process and outcomes measures
  • Standardized member satisfaction survey
  • Used by commercial, Medicare, and Medicaid plans alike
  • Allows plan-to-plan comparison

• Osteoporosis Measure: % of women > 67 years of age who received either a BMD test or an osteoporosis medication within 6 months of fracture\(^2\)

2. The National Committee on Quality Assurance. NCQA Washington, D.C.
# Osteoporosis HEDIS Trends, 2003 - 2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Medicare (PPO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>18%</td>
</tr>
<tr>
<td>2007</td>
<td>18</td>
</tr>
<tr>
<td>2009</td>
<td>18</td>
</tr>
<tr>
<td>2011</td>
<td>19</td>
</tr>
<tr>
<td>2013</td>
<td>22</td>
</tr>
<tr>
<td>2015</td>
<td>33</td>
</tr>
<tr>
<td>2016</td>
<td>34</td>
</tr>
</tbody>
</table>
Quality ID #418 (NQF 0053): Osteoporosis Management in Women Who Had a Fracture

2018 OPTIONS FOR INDIVIDUAL MEASURES: REGISTRY ONLY

MEASURE TYPE

• % women age 50-85 who fracture and who either had:
  • 1) Bone mineral density test or
  • 2) Prescription for a drug to treat osteoporosis in the six months after fracture

• Submitted after each fracture
• Anticipated that clinicians who treat any fracture except fractures of the finger, toe, face or skull will submit measure
• Fracture identified by either an ICD-10CM diagnosis code for fracture and a CPT service code OR an ICD-10-CM diagnosis code for fracture and CPT procedure code for surgical treatment of fractures
“Performance measurement is a necessary but not sufficient foundation to drive and sustain improvements in patient care. Improvements in the quality and affordability of care will occur only when this information is actually used.”

Standforquality.org
Building a Foundation for High Quality, Affordable Health Care: Linking Performance Measurement to Health Reform

Institute of Medicine, 2006
Qualified Clinical Data Registries (QCDR)

A single, secure data feed from multiple EHRs

RHEUMATOLOGY INFORMATICS SYSTEM for EFFECTIVENESS
NOF/NBHA QCDR

QCDR (Custom) Measures
- Hip Fracture Mortality Rate (IQI 19) (NOF6) (Group Reporting)
- Osteoporosis: percentage of patients, any age, with a diagnosis of osteoporosis who are either receiving both calcium & vitamin D intake, & exercise at least once within 12 months. (NOF7)
- Median Time to Pain Management for Long Bone Fracture (NOF 12)
- Osteoporosis: Management Following Fracture of Hip, Spine or Distal Radius for Men and Women Aged 50 Years and Older (NOF 13)

MIPS Quality and Electronic Clinical Quality Measures (eCQMs)
- Screening for Osteoporosis for Women Aged 65–85 Years of Age Q#039, NQF 0046
- Medication Reconciliation Post-Discharge Q#046, NQF 0097
- Care Plan Q#047, NQF 0326
- Osteoarthritis (OA): Function and Pain Assessment Q#109
- Preventive Care and Screening: Influenza Immunization Q#110, NQF 0041
- Osteoporosis Management in Women Who Had a Fracture Q#418, NQF 0053
- Functional Status assessment for Total Hip Replacement Q#376
- Falls: Screening for Future Fall Risk Q#318, NQF 0101
The Quality Problem In Osteoporosis
Why Most Clinicians Don’t Recognize High Risk patients and Provide Osteoporosis Management?

• **Primary prevention (no prior fractures)**
  - BMD testing confusion and (increasing) scarcity
  - FRAX or other risk prediction tools not routinely used/understood
  - Uncertainty regarding treatment (risks vs benefits)

• **Secondary prevention (prior fracture)**
  - Orthopaedic surgeons reluctance to treat osteoporosis
  - Osteoporosis prescribers not alerted to fracture occurrence
  - Uncertainty regarding treatment (risk vs benefits)
The diagram below is designed to demonstrate visually the different approaches available in clinical research, relationships among the different approaches, and the relationships among clinical research approaches, bench research, and public health.

This diagram is based on the report written by members of the Clinical Research Roundtable of the Institute of Medicine and published in the March 12, 2003 issue of *JAMA*.
What Is Outcomes Research?  
Basic Tenets

- Outcomes, not geography or ethnicity, should determine which treatment a patient receives.
- Variations in practice are associated with differences in patient outcomes.
- Patient values and preferences should be incorporated into clinical decision making.
Implementation Research

• At the intersection between research and quality improvement (QI)
• Uses methods from health services research (HSR) and qualitative methods
• Translation science that goes beyond the bedside
Implementation Research

The scientific study of methods to promote the rapid uptake of research findings, and hence to reduce inappropriate care and improve the health of individuals and populations.
Beta blockade achieved in animals (Powell, 1958)

Propranolol tested in humans and considered for MI and HTN (Black, 1964)

Norwegian and BHAT trials post-MI (1981-82)

Braunwald states it's a good idea (1984)

Definitive evidence based on 60 trials in 25k pts (Yusuf, 1985)

ACC/AHA Endorses as a Quality Indicator (1996)

NCQA Retires as Quality Indicator (2007)

20% get a beta-blocker post-MI

40% 60% 80% 90%

Beta-Blockers After a Heart Attack Reduce Mortality by 25%

T-1 translation (10 years)

T-2 translation (20 years)

Underuse "Care-Gap"
Approaches to Evidence Implementation Research

- Printed Materials
- Traditional Continuing Education
- Outreach Visits
- Audit & Feedback
- Intensive Conferencing
- Computerized Tools
- Local Opinion Leaders
- Multi-faceted Approaches
Model for Quality Improvement

AIM STATEMENT
★ What are we trying to accomplish?

MEASURE
★ How will we know if a change is an improvement?

PI TOOLS
★ What changes can we make that will result in an improvement?

PDSA
★ Tests of change
Potential sequelae of the “NIKE approach”?  
- Widespread adoption of ineffective programs  
- Unintended harms  
- Opportunity costs  
- Loss of MD and RN goodwill (i.e., social capital)  
- etc.
Implementation Research vs. QI

- Generalizability is a consideration (so is “All quality is local”)
- Context is frequently health care system and policy, not just local
- Theory-driven vs. “Shot-gun”
- Emphasis is on knowledge and action, not just results
Strategies for Overcoming Barriers to Improve Quality

4 Levels

- Individual clinicians
- Patients
- Health care system interventions
- Health care financing reform
### Implementation Science

#### Levels of Targets

<table>
<thead>
<tr>
<th>Levels of Targets</th>
<th>Pro’s</th>
<th>Con’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual Clinicians and Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health Care System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health Care Financing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Heterogeneity in Osteoporosis Implementation Studies

- Rigor of study design
- Targets: providers, patients, health systems, health care financing, and mixed
- Primary vs. Secondary prevention
- Timing to fracture event
- Initiating vs. sustaining testing/therapy
- Osteoporosis sub-types
- Type of health care coverage/systems
Provider Interventions
Pervasive Care-Gap Between What Doctors Know and What They Do

- Reviewed studies with both self-report and practice audits:
  - Median difference (care-gap) = 28%
  - MDs overestimate own guideline adherence 88% of time

Designing Evidence-Based Interventions to Overcome Barriers to Best Practice

- **Physician level**
  - Lack of knowledge; **lack of time**; clinical inertia

- **Patient level**
  - **Lack of information**; symptomatic vs preventive care bias; preferences, demands, expectations; non-adherence

- **System level**
  - **Lack of information systems** (i.e., registries with real time reminders); access; reimbursement

Majumdar S. CMAJ 2003;169:30
Majumdar S. JACC 2004;43:1738
Thank you for your participation in AQAF’s *quality improvement efforts*. In this report, we are pleased to provide you with feedback that includes benchmarks (dark blue bars). They are intended to provide you with practical goals. You may be above the benchmark in some aspects of care and below in others.

*See back of brochure for definition of indicators*
Achievable Benchmarks Improve Process of Care Over Conventional Feedback

Odds Ratios: Intervention vs. Control*

*Receipt of therapy at follow up for intervention vs control physicians after adjusting for (1) baseline performance (2) nesting of pts within MDs and (3) MD characteristics

Kiefe C. JAMA 2001;285:2871
UAB GIOP Group RCT Study Design

Control Arm (n = 75)
Unrelated CME Module
Follow up DXA Screening and Rx Rate

Intervention Arm (n = 75)
Internet GIOP Intervention

Aetna U.S. Healthcare Population

Doctors Prescribing Steroids
High-risk Steroid Users
Baseline DXA Screening and Rx Rate

Curtis JR. Arch Int Med 2007; 167:591
GIOP Internet Intervention

- Access via e-mail
- Tailored presentation
- Case-based interactive learning
- Personal data feedback using Achievable Benchmark of Care (ABC™)
- Improvement “toolbox”
- Printable CME certificate
- Continued exposure to combat “decay”

Kiefe C. JAMA 2001;285:2871
## GIOP Group RCT Results

### % Receipt

<table>
<thead>
<tr>
<th>Intent-To-Treat</th>
<th>Intervention (n = 76 docs)</th>
<th>Control (n = 73 docs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD</td>
<td>19</td>
<td>21</td>
<td>NS</td>
</tr>
<tr>
<td>Prescription Rx</td>
<td>26</td>
<td>24</td>
<td>NS</td>
</tr>
<tr>
<td>Per Protocol*</td>
<td>(n = 27 docs)</td>
<td>(n = 18 docs)</td>
<td></td>
</tr>
<tr>
<td>BMD</td>
<td>26</td>
<td>16</td>
<td>0.04</td>
</tr>
<tr>
<td>Bisphos Rx</td>
<td>24</td>
<td>17</td>
<td>0.09</td>
</tr>
<tr>
<td>BMD or Rx</td>
<td>54</td>
<td>44</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Completed all 3 modules

Curtis JR. Arch Int Med 2007; 167:591
Review of Glucocorticoid-Induced Osteoporosis (GIOP) Interventions (n = 7 Studies)

- **Education-based interventions** (n = 5)
  - RCTs (n= 2) focused on physicians - NS
  - Non-randomized educational interventions (n = 2) - NS
  - RCT focused on pharmacists and patients - increased calcium supplementation in the intervention vs. control arm (55.7% vs. 31.6%, p < 0.05)

Tory HO. *Semin Arthritis Rheum* 2015;44:483
Tasmanian GIOP Intervention

- Non-randomized, pre-/post with controls
- Intervention in Northern Tasmania
  - Educational Material/Guidelines and Academic Detailing
  - GPs (n = 200), Pharmacists (n = 81)
  - 113 pts
- Southern Tasmania “control”
- Changes in GIOP Prevention in Hospitalized Patients
  - Any GIOP Rx: ↑ 31 to 57%
  - Bisphosphonates: ↑ 6 to 24%

Naughton M. J Rheumatol 2004;31:550
Effect of 2 Interventions on Osteoporosis Testing and Treatment After Vertebral Compression Fracture Reported on CXR

- *P < 0.001 for physician vs control
- †P = 0.01 for physician + patient vs physician

Majumdar S. Am J Med 2012;125:929
Alternate Evidence Implementation Approaches in Osteoporosis

System

Patient

Physician/Provider
Patient Interventions
Patient Activation after DXA Result Notification (PAADRN) Study Design

- Pragmatic Randomized controlled trial
- Unit of randomization and analysis: Study Participants and Providers
- Two Arms
  - Usual Care
  - Tailored letter containing DXA test information and educational brochure
- Power based on n = 7500 participants (7,749 randomized)

Cram P. Osteoporos Int 2016; 27: 3513
PAADRN- Results

• 6,728 (86.8%) completed 12-week follow-up.
  • 84% women
  • 77% White
  • Mean age 66.5 years
• At follow-up: 65.4% of intervention and 64.4% of control patients on guideline concordant therapy (P=0.41)*
• Intervention patients more likely to know DXA results (69.7% vs 56.8%; p<0.001)
• Intervention patients more likely to speak to their physician about DXA results (61% vs 57.3%; p=0.02)

*significant effect at one of three study sites (p<0.05).

Cram P. Osteoporos Int 2016; 27: 3513
Narrative Communication
Why Give Stories to Patients?

- Narrative Content (story line)
- Production Quality
- Persuasive Subtext
- Homophily (similarity between characters and participants)

- Transportation (absorption in story line)
- Identification with Characters in Narrative

- Change in Attitudes & Behavior

Slater M. *Communication Theory*. 2002;12 :173
“The power of narratives to change belief has never been doubted and has always been feared.”

Green MC. J Personality Social Psychology 2000; 79 :701
Improving Blood Pressure Medication Adherence
Culturally Sensitive Intervention (CSI)
Cooper Green Jefferson County Hospital

<table>
<thead>
<tr>
<th></th>
<th>Baseline systolic BP</th>
<th>3-Month Follow-up systolic BP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>132.5 mmHg</td>
<td>127.5 mmHg</td>
</tr>
<tr>
<td>Control</td>
<td>131.1 mmHg</td>
<td>132.2 mmHg</td>
</tr>
</tbody>
</table>

Benefit greatest among those with uncontrolled BP at baseline (-17 mmHg intervention, -7 mmHg control, \( p = 0.03 \))

* \( p = 0.04 \), intervention vs. control

Houston T. Ann Int Med 2011;154:77
Steroids and Fractures
## Improving GIOP Treatment Rates

**Internet-based Video Intervention In Chronic Steroid Users from MEDCO**

(“Light Touch, Low Cost”)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Total N</th>
<th>% Osteoporosis Rx at 180 days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intent-to-treat</strong></td>
<td>3018</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>Per protocol</strong></td>
<td>1780</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>“Self-click”</strong></td>
<td>87</td>
<td>5.7%</td>
</tr>
<tr>
<td><strong>Usual care (control)</strong></td>
<td>1641</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

* Per protocol indicates a measurable exposure to the online intervention video

**Self-click indicates that person self-clicked on web link to watch video

Warriner A. J Rheumatol 2015;42:1478
Activating Patients to Reduce OsteoPorOsiS (APROPOS)

- Subset of Global Longitudinal Registry of Osteoporosis in Women (GLOW) study population
  - US women 55+ yrs
  - Self-report of fracture on any GLOW survey
  - No current osteoporosis Rx
- Randomized Controlled Trial of patient activation approach
  - Usual Care (n = 1342)
  - Online/DVD tailored educational intervention (n = 1342)
  - Power 80%, alpha = 0.05, min detectable difference = 4%
    - N_{adj} per treatment group = 850

Danila M. Contemp Clinical Trials Com 2016; 4:14
Danila M. JBMR 2018;33:763
Percentage of Participants Interacting with APROPOS Intervention Website by Contact Information

- **Email only:** 44.6% (75/168)
- **Phone and Email:** 45.8% (216/472)
- **Overall:** 27.6% (370/1342)
- **Phone only:** 11.9% (51/427)
- **No Phone or Email:** 10.2% (28/275)

Danila M. ASBMR, 2015
UAB APPROPOS Tailored Intervention

Level I
- Intervention N = 1342
- No Barriers Ranked N = 860

Level II
- Other Barriers ID’d on Survey
  - YES
  - Stage of Change
    - Level III
      - Previous Treatment (Tx)
        - NO
        - Risk awareness N = 84
      - Contemplative N = 32
        - YES
        - Pre-contemplative N = 268
          - YES
          - Risk awareness N = 47
          - NO
          - Tx options & Supplements not enough N = 47
        - NO
        - Tx options & Supplements not enough N = 47
      - NO
      - Tx options & Supplements not enough N = 47
    - NO
    - Tx options & Supplements not enough N = 47
  - NO
  - Recommendation N = 37

Level III
- Concern about long-term AEs (Patients’ views about osteo and therapy scale) N = 392
  - YES
  - Tx options with revised intro
    - NO
    - Tx options with revised intro
  - Supplements not enough & Concerns about meds
    - YES
    - Tx options with revised intro
    - NO
    - Tx options with revised intro
- Addressing identified barriers N = 364
- ONJ & Supplements not enough N = 118

VIDEO SEGMENTS
Appropos Tailored Video
Osteonecrosis of the Jaw
APROPOS Results

- No differences in treatment rates between intervention and control arms in ITT population
- More individuals in the intervention arm shifted from pre-contemplative to contemplative stage of behavior change relative to usual care
- Increased reports of treatment-related barriers including ONJ, difficulty taking medication, and GI/stomach in intervention group
- Subgroup and per protocol analyses showed increased DXA testing in intervention arm
  - No prior DXA
  - Providing an email address
  - Measurable exposure to intervention

Danila M. Contemp Clinical Trials Com 2016; 4:14
Danila M. JBMR 2018;33:763
<table>
<thead>
<tr>
<th>Reference</th>
<th>Intervention</th>
<th>Sample size</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tüzün et al. 2013</td>
<td>Telephone calls, interactive education</td>
<td>Intervention (N = 226)</td>
<td>Intervention: Self-reported persistence and compliance = 152 (50.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (N = 222)</td>
<td>Control: Self-reported persistence and compliance = 149 (49.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(p = 0.862)</td>
</tr>
<tr>
<td>Solomon et al. 2012</td>
<td>Telephone-based counseling/motivational interviews by health educator</td>
<td>Intervention (N = 1046)</td>
<td>Intervention: MPR = 49% (IQR 7, 88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (N = 1041)</td>
<td>Control: MPR = 41% (IQR 1.5, 86.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(p = 0.074)</td>
</tr>
<tr>
<td>Bianchi et al. 2015</td>
<td>Educational booklets, calendar alarms (Grp 2) Added Phone call reminders (Grp 3)</td>
<td>Group 2 (N = 110)</td>
<td>Group 2: 90.1% persistent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group 3 (N = 111)</td>
<td>Group 3: 84.6% persistent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (N = 113)</td>
<td>Control: 92.0% persistent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(p=0.288)</td>
</tr>
<tr>
<td>Cizmic et al. 2015</td>
<td>Interactive voice response followed by reminder letter</td>
<td>Intervention (N = 126)</td>
<td>Intervention: 48.8% bisphosphonates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (N = 118)</td>
<td>Control: 30.5% bisphosphonate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OR = 2.17, 95% CI 1.29-3.67</td>
</tr>
</tbody>
</table>
“Activating Patients” to Increase Osteoporosis Treatment Initiation

- Multi-stage, complex pathway to change process
- Involves patient and clinician
- Success may depend in part on how far down pathway you start
System Interventions
Improving Care of Osteoporosis: Multi-Modal Intervention to Increase Testing and Treatment (ICOMMIITT)

Interventions at the Patient and System Level

UAB: K Saag, A Warriner, R Outman, J Curtis, J Bodon, J Allison, M Safford, T Houston

KPGA: D Roblin, J Calvi, J Ren

KPNW: A Feldstein, M Rix, A Rosales
Improving Care of Osteoporosis: Multi-Modal Intervention to Increase Testing and Treatment (ICOMMIITT)

- Partnership with Kaiser Permanente of Georgia and Kaiser Northwest
- Multi-Modal Intervention
  - System (practice redesign strategy, BMD testing alert)
  - Patient (education and activation, improve patient-provider communication)
  - Provider (web-based CME) (control)
DXA Self-Referral Significantly Increased Testing Rates
(Kaiser Permanente Health Systems)

KPNW
N = 8879

Warriner AH. *Medical Care*, 2014;52:743

KPG
N = 3249

Warriner AH. *JBMR*, 2012.;27:2603
## Recent System Interventions for Adherence

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Intervention</th>
<th>Sample size</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stuurman-Bieze et al. 2014</td>
<td>1° prevention</td>
<td>Pharmacist-delivered medication monitoring and counseling</td>
<td>Intervention (N = 495) Historical control (N = 442)</td>
<td>Intervention: 19.0% discontinued medications or non-adherent Control: 32.8% discontinued medications or non-adherent (p&lt;0.001)</td>
</tr>
<tr>
<td>Majumdar et al. 2017</td>
<td>2° prevention</td>
<td>Catch-a-Break: “Type C” FLS program</td>
<td>Intervention (N = 4633) Simulated control (N = 2690)</td>
<td>Intervention: 17.5% (95% CI 15.6–19.4) bisphosphonates Rx Simulated Control: 13.2% (95% CI 12.4–14.0) bisphosphonate Rx (p &lt; 0.001)</td>
</tr>
<tr>
<td>Ganda et al. 2014</td>
<td>2° prevention</td>
<td>“Type A” FLS program in Group A Intervention (6 visits with FLS)</td>
<td>Intervention (N = 49) Control (N = 53)</td>
<td>Intervention: MPR = 0.78 (IQR, 0.50–0.93) Control: MPR = 0.79 (IQR, 0.48–0.96) (p=0.68)</td>
</tr>
</tbody>
</table>
Review of GIOP Interventions (n = 7 Studies)

- **Education-based interventions (n = 5)**
  - RCTs (n= 2) focused on physicians - NS
  - RCT focused on pharmacists and patients - increased calcium supplementation in the intervention vs. control arm (55.7% vs. 31.6%, p < 0.05)
  - Non-randomized educational interventions (n = 2) - NS

- **Non-randomized, uncontrolled studies of system changes (n = 2)**
  - Increased concomitant prescriptions of glucocorticoids and calcium (37- 49%, p < 0.0001) and vitamin D (38-53%, p < 0.0001) using computerized order entry system
  - Dedicated clinical team - increased vitamin D levels from 19.5 to 29.4 (p = 0.001) and improved GIOP-related habits

Tory HO. *Semin Arthritis Rheum* 2015;44:483
Screening in the Community to reduce fractures in Older women with OP (SCOOP) Trial

- Two-arm randomised controlled Trial
  - Compared a screening programme using the Fracture Risk Assessment Tool (FRAX) vs. Usual management
  - In screening group, treatment recommended in women identified to be at high risk of hip fracture, according to FRAX 10-year hip fracture probability
  - Letter to patient and to GP with FRAX results
- Primary outcome
  - Proportion of individuals who had one or more osteoporosis-related fractures over a 5-year period
- Pre-specified secondary outcomes
  - Proportions of participants who had at least one hip fracture, any clinical fracture, or mortality
  - Effect of screening on anxiety and health-related quality of life
SCOOP Study

Participant Flow

Women 70–85 yrs from 100 primary care practices (n = 52,033)

Eligible subjects (n = 38,031)

Consenting participants (n = 13,029)

Randomisation (n = 12,495)

Post-Randomisation Exclusions (n=12)

SCREENING n = 6,233

CONTROL n = 6,250

Shepstone L. Lancet 2018; 391: 741
SCOOP Study

Osteoporotic-related Fractures

HR = 0.95 (95% CI 0.85 - 1.03)

Shepstone L. *Lancet* 2018; 391: 741
SCOOOP Study

Percentage of participants with prescription anti-osteoporosis medication

Shepstone L. Lancet 2018; 391: 741
SCOOOP Study

Shepstone L. *Lancet* 2018; 391: 741

HR = 0.72 (95% CI 0.59 - 0.89)
SCOOP Conclusion

• Community based UK screening program was feasible, generally well received
• No evidence of overall fracture risk reduction, mortality, or quality of life
• Evidence that medication prescribing increased and hip fractures could be reduced

Shepstone L. Lancet 2018; 391: 741
Fracture Liaison Services (FLS) in an “Open” System

- Study design: Pre-post comparison of fracture care before and after FLS program
- Pre-FLS: Retrospective chart review for 6 months after fracture (N=344)
- Post-FLS: Prospective assessment for 6 months after fracture (N=148)
- Facilities: 3 independent health care systems
  - A, B, C that serve 450-600 adults hospitalized with low-trauma fractures
  - Open System: payers, hospitals, patients and physicians not closely aligned

Greenspan S. Osteo Int. 2018;29:953
Fracture Liaison Service (FLS) Results in a “Open” System

The Impact of the FLS Program

<table>
<thead>
<tr>
<th>% Receiving Test or Treatment</th>
<th>Pre FLS</th>
<th>Post FLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD Test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D Assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D/Calcium Prescribed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacologic Therapy Prescribed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Greenspan S. Osteo Int. 2018;29:953
• To evaluate cost-effectiveness of Fracture Liaison Service (FLS)
• To test cost-effectiveness under a universal vs targeted (based on DXA) approach
• Examine sensitivity of findings to:
  • Target population (prior hip fracture only; hip, vertebral, or wrist fracture)
  • Cost of FLS
  • Efficacy in increasing bisphosphonate use
  • Cost of medications (IV Zol)
### FLS Economic Results

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>Delta Cost</th>
<th>Delta QALY</th>
<th>ICER ($/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>-7</td>
<td>0.004</td>
<td>Cost saving</td>
</tr>
<tr>
<td><strong>One Way Sensitivity Analyses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FLS cost at $205</td>
<td>93</td>
<td>0.004</td>
<td>24,933</td>
</tr>
<tr>
<td>OP med costs at $250</td>
<td>54</td>
<td>0.004</td>
<td>14,513</td>
</tr>
<tr>
<td>2nd fx rates reduced by 10%</td>
<td>17</td>
<td>0.005</td>
<td>4,072</td>
</tr>
<tr>
<td>BIS disutility included</td>
<td>11</td>
<td>0.003</td>
<td>3,971</td>
</tr>
<tr>
<td>FLS treatment rates 66%</td>
<td>-145</td>
<td>0.008</td>
<td>Cost saving</td>
</tr>
<tr>
<td><strong>Multi Way Sensitivity Analyses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FLS $205, OP med $250</td>
<td>141</td>
<td>0.004</td>
<td>37,729</td>
</tr>
<tr>
<td>Worst case analysis 1</td>
<td>207</td>
<td>0.003</td>
<td>68,124</td>
</tr>
<tr>
<td>Worse case analysis 2</td>
<td>226</td>
<td>0.002</td>
<td>112,877</td>
</tr>
</tbody>
</table>

Solomon D. *JBMR* 2014;29:1667
Pooled Absolute Effects (risk difference) on Osteoporosis Rx From 9 Secondary Prevention RCTs (intervention vs usual care)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intervention</th>
<th>Usual care</th>
<th>Risk Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Miki 2008</td>
<td>15</td>
<td>26</td>
<td>7.3%</td>
</tr>
<tr>
<td>Rozental 2008</td>
<td>8</td>
<td>27</td>
<td>7.9%</td>
</tr>
<tr>
<td>Davis 2007</td>
<td>15</td>
<td>28</td>
<td>9.4%</td>
</tr>
<tr>
<td>Gardner 2005</td>
<td>10</td>
<td>36</td>
<td>9.5%</td>
</tr>
<tr>
<td>Majumdar 2007</td>
<td>56</td>
<td>110</td>
<td>12.0%</td>
</tr>
<tr>
<td>Cranney 2008</td>
<td>35</td>
<td>125</td>
<td>145</td>
</tr>
<tr>
<td>Majumder 2008</td>
<td>30</td>
<td>137</td>
<td>135</td>
</tr>
<tr>
<td>Feldstein 2006 (1)</td>
<td>50</td>
<td>210</td>
<td>101</td>
</tr>
<tr>
<td>Solomon 2007</td>
<td>6</td>
<td>134</td>
<td>1</td>
</tr>
</tbody>
</table>

20% (10-30%)

Total (95% CI)
- Total events: 833, 689, 100%
- Heterogeneity: Tau² = 0.02; Chi² = 66.69, df = 8 (P < 0.00001); I² = 88%
- Test for overall effect: Z = 3.83 (P = 0.0001)

Little EA. *Implement Sci* 2010;5:80
Summary of Evidence Implementation Research in Osteoporosis

- Defining quality is necessary first step
- Increasing armamentarium of evidence implementation interventions
- System approaches largely superior to approaches targeting patients or providers alone
- Implementing evidence at community level is not easy
  - Technology offers promises, context and engagement are key
  - “Teachable moment” is optimal (secondary prevention)
  - Multi-modal approaches often work better, but one size fits none
  - Approaches SHOULD BE tested
Adopting Ineffective Programs
Be Skeptical About Uncontrolled Studies

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