Secondary Prevention of Bone Disease In Men on Androgen Deprivation Therapy For Prostate Cancer: Quality Improvement Through Implementation of Evidence-Based Bone Health Guidelines

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Androgen deprivation therapy (ADT) is a principle treatment for locally advanced and metastatic prostate cancer, but it is associated with bone loss and increased fracture risk. A urology practice implemented a best practice initiative targeting bone health assessment utilizing evidence-based guidelines.

Key Words: **Androgen deprivation therapy, bone health, prostate cancer.**

Prostate cancer (PCa) is the most common cause of cancer in men in the United States and the second most common cause of all cancer deaths (Siegel, Miller, & Jemal, 2018). One-third of men receive androgen deprivation therapy (ADT), an effective treatment that decreases testosterone, which is the hormone that fuels this cancer. As the foundational treatment for PCa, ADT has associated known, yet manageable, adverse effects. An important ADT-related adverse effect is accelerated bone loss. Higano (2008) reported a 21% to 37% increased fracture risk irrespective of bone metastasis. Bone density loss and heightened fracture risk adversely impact quality of life (QOL), and when combined with increased mortality, make bone health management an important consideration in PCa treatment (Body et al., 2007; Gralow et al., 2013; Liede et al., 2016). Men with PCa are older and at higher risk for low bone density due to age, inadequate nutrition, and potential vitamin D deficiency. These factors result in a higher fracture risk (Allain, 2006; Gralow et al., 2013).

Bone health screening and risk assessment for patients with PCa receiving ADT was identified as a priority practice change at a large suburban urology practice. Initial data showed less than half of providers at the urology practice were addressing bone healthcare needs. Al-Shamsi and colleagues (2012, 2017) noted a similar gap in osteoporosis screening, prevention, and treatment for men on ADT for their locally advanced and metastatic PCa. To

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improve practice, a quality improvement process (QIP) was used to facilitate the adoption of evidence-based bone health guidelines adapted from the National Comprehensive Cancer Network (NCCN) and the American Urological Association (AUA) to optimize the patient's bone health during PCa treatment (Cookson et al., 2013; Cookson, Lowranson, Murad, & Kibel, 2015; Gralow, 2013; NCCN, 2017).

Available Knowledge – Bone Health Guidelines

Bone health guidelines exist spanning the urology and oncology specialties to direct bone health secondary prevention for men with PCa on ADT. However, these guidelines have not been fully embraced in practice (Cookson et al., 2013; 2015; Gralow et al., 2013; Grossmann et al., 2011). Damji, Bies, Alibbas, and Jones (2015) documented poor guideline concordance, noting less than one-third of PCa specialists reported routine measurement of bone mineral density (BMD) prior to the initiation of ADT and no routine BMD measurement one to two years following the initiation ADT, with only 4.6% of respondents using a Fracture Risk Assessment Tool (FRAX®). In this same study, providers identified guideline knowledge but reported lacking the time and supporting structures to promote healthy bone behavior education as barriers to care. Nadler and colleagues (2013) explored osteoporosis knowledge, health beliefs, and healthy bone behaviors in patients on ADT for PCa treatment. Patients lacked basic information about bone health, did not engage in healthy bone behaviors, and were not being screened for fracture risk factors.

Literature Review

A literature review was completed, and available evidence on key components of bone health guidelines was identified and is synthesized. A bone health protocol for best practice for patients with PCa being treated with ADT was developed to help bridge the gap in implementing bone health guidelines (see Figure 1).

Fracture Risk Assessment

Several tools can be used to assess fracture risk. Measurement of BMD to assess fracture risk through the dual energy X-ray absorptiometry (DEXA) scan remains the gold standard to establish the diagnosis of osteoporosis and predict the risk of fracture (Cosman et al., 2014). The FRAX is a 14-item, international, and validated risk assessment tool with high predictive power for fracture occurrence that can easily be incorporated into patient encounters with no added cost (Center for Metabolic Bone Health, n.d.; Dagan, Cohen-Stavi, Leventer-Roberts, & Balicer, 2017). The FRAX tool, when partnered with the DEXA scan, measures fracture risk better than clinical risk factors or BMD alone. The use of the FRAX with the DEXA scan can serve as a surrogate measure of bone health and aid in the identification of men on ADT who would benefit from bone-directed therapies (James et al., 2014; Kawahara et al., 2016; Lee et al., 2011; Leslie et al., 2010; Saylor, Kaufman, Michaelson, Lee, & Smith, 2010). A 2010 position paper from the International Society for Clinical Densitometry (ISCD) and International Osteoporosis Foundation (IOF) supported the use of FRAX without BMD as appropriate when BMD is not readily available or as a means to recognize those individuals who may benefit from a BMD measurement.

Lifestyle Modification

Lifestyle modification has been recommended for patients undergoing ADT. Evidence for lifestyle modification was summarized by Gardner, Livingston, and Fraser (2014) in their systematic review of 10 studies focused on the impact of varied exercise interventions on ADT-induced adverse effects. These researchers noted exercise benefited muscle strength, cardiorespiratory fitness, functional task performance, lean body mass, and improved fatigue. However, the impact on bone health, cardiovascular risk, and QOL was less clear. These authors concluded that appropriately prescribed exercise can decrease a range of ADT-induced side/adverse effects. Results from a randomized clinical trial (RCT) by Cormie and colleagues (2014) concluded supervised exercise with aerobic and resistance exercise when initiating ADT could reduce treatment toxicity. However, no difference in BMD was identified between the treatment groups with the 3-month duration of the trial, limiting detection of changes in BMD. Another RCT evaluated the efficacy of a 6-month dietary and exercise intervention, which helped minimize unwanted body composition change found with ADT. BMD was not measured in this study; however, it had positive implications for survivors of PCa (O'Neill, Haseen, Murray, O'Sullivan, & Cantwell, 2015).

In an updated review, Moyad, Newton, Tunn, and Gruca (2016) reported interventions with exercise, diet, and nutrition supplements, which are easily accessed and available at low cost, can be effective in decreasing ADT-related side/adverse effects of bone health. Generalized exercise guidelines are available and can be individualized to patient needs when possible to assist with maintaining bone health (American Cancer Society, 2017; Segal et al., 2017).

Patient Education

Patient education was also

Figure 1.
Bone Health Protocol Patient on Androgen Deprivation Therapy

A. Non-Metastatic Disease: Imaging (Bone Scan, CT) with No Bone Metastasis

- Baseline DEXA
- Baseline FRAX®
- Education: Androgen deprivation therapy (ADT) effects on bone health and lifestyle modifications (exercise, smoking cessation, minimize alcohol intake, diet. See bone health handout.
- Start calcium 1,200 mg daily and vitamin D 800 IU daily (see handout).
- Labs: Calcium, phosphorous, magnesium; repeat these labs within 14 days of injection; obtain 25-hydroxyvitamin D at baseline.
- Dental clearance: Form signed by dentist. Education on risk of osteonecrosis of jaw (ONJ); reporting dental/jaw pain and dental procedures.
- Insurance authorization for Prolia®, 60 mg subcutaneous every 6 months; obtain consent for Prolia; once approved schedule visit.
- Repeat DEXA yearly (every 1 to 2 years), repeat 25-hydroxyvitamin D with DEXA.

B. Surveillance Non-Metastatic: Prostate-Specific Antigen (PSA) Stable/Lower and No Imaging

- Baseline DEXA if not already obtained.
- Baseline FRAX® if not already obtained; repeat for changes in risk over time.
- Reinforce education regarding effects if ADT on bone health with lifestyle modifications (see handout).
- Continue calcium 1,200 mg daily and vitamin D 800 IU daily (see handout); start if not already taking.
- Follow A above for labs, dental clearance, insurance, Prolia® injections/scheduling and DEXA/repeat labs.

C. PSA Rising +/- New Symptoms: No Imaging

- Obtain imagine (bone scan, CT, other imaging), as indicated.
- If results are negative for metastatic cancer, follow A and B above.
- If results are positive for metastatic cancer, follow D below.

D. Metastatic Disease: Imaging (Bone Scan, CT) with Bone Metastasis

- Education: Risk of fracture with bone involvement and ADT; lifestyle modification – exercise unless contraindicated by nature/extent of bone involvement; smoking cessation, minimize alcohol intake, diet (see handout).
- Start calcium 1,200 mg daily and vitamin D 800 IU daily if not already taking (see handout).
- Labs: Calcium, phosphorus, magnesium at baseline; repeat these labs every 2 to 3 months; more frequently as needed; obtain 25-hydroxyvitamin D at baseline.
- Dental clearance: Form signed by dentist. Education on ONJ risk and reporting dental/jaw pain and dental procedures.
- Castrate-resistant or high clinical risk castrate-sensitive, obtain insurance authorization for Xgeva, 120 mg subcutaneously every 4 weeks; obtain consent for Xgeva; once approved, schedule visit. Prolia, 60 mg subcutaneously every 6 months, if osteopenia/osteoporosis and lower risk clinical castrate-sensitive disease.
- Repeat imaging with bone scan of CT scan for surveillance or new symptoms. FRAX® and baseline DEXA if castrate-sensitive.

Notes: National Comprehensive Cancer Network/National Osteoporosis Foundation: Additional treatment indicated for men when the 10-year probability of hip fracture is greater than or equal to 3% or the 10-year probability of major osteoporosis-related fracture is greater than or equal to 20%.
BMD/DEXA: (Normal within 1 standard deviation (T score – 1 or greater), low bone mass (osteopenia) is 1.0 to 2.5 standard deviations below (T score between -1.0 and -2.5) and osteoporosis is 2.5 or greater standard deviations below (T score -2.5 or less). Additional treatment indicated for osteopenia and osteoporosis – individualize to patient.

identified as an important intervention to support behavior and lifestyle changes. To aid in treatment decisions regarding bone-directed therapies, such as bisphosphonates, Saad and colleagues (2008) emphasized the role of patient education about risk factors to avoid osteoporosis. Bone hygiene and lifestyle modification also included calcium and vitamin D supplementation, smoking cessation, modest alcohol intake, and increasing exercise activity (Body et al., 2007; Gralow et al., 2013; Saad et al., 2008).

Pharmacologic Interventions: Bone-Directed Therapies

Many pharmaceutical bone-directed therapies (BDTs) strengthen bones and decrease skeletal-related events. Several studies provide data supporting the use of the RANK ligand monoclonal antibody denosumab to improve bone density, and decrease bone loss and incidence of new fractures (Saad et al., 2008; Serpa Neto et al., 2012). Edgerdie and colleagues (2012) analyzed BMD in the PCa population after 6-month subcutaneous injections of denosumab and found significantly higher BMD response rates when compared to placebo. Zoledronic acid, an intravenous bisphosphonate, was also effective in preventing bone loss in hypogonadal men (Michaelson et al., 2007). Klotz, McNeill, Kebabdjian, Zhang, and Chin (2013) found that alendronate, a weekly oral bisphosphonate, prevented bone loss associated with ADT. More recently, Campagnaro and colleagues (2018) summarized the current use of BDTs at their institution, including their application of guidelines to PCa in both the castration-sensitive and resistant PCa settings.

Clinical Considerations: Dental and Laboratory Screening and Monitoring

Leng and Lentsch (2018) described the complicated clinical considerations required for the use of BDT as including a need for dental care, attention to renal function, hypocalcemia, and vitamin D deficiency. Before BDT is initiated, dental screening with education surrounding dental care with a comprehensive dental examination and completion of preventive dental work are recommended to help minimize the occurrence of osteonecrosis of the jaw (ONJ), an infrequent but clinically serious adverse event associated with BDT (Campisi et al., 2014; Hinchy et al., 2013; Rosella et al., 2016; Ruggiero et al., 2009; Ruggiero, Dodson, & Fantasia, 2014).

The current body of evidence provides guidelines with interventions to support best practice for secondary prevention of bone disease for at-risk men on ADT for their PCa. The eCQI Resource Center of the Centers for Medicare & Medicaid Services (CMS) identified bone density evaluation for patients with PCa, and as of 2018, receiving ADT is a clinical quality improvement measure for practice (CMS Office of the National Coordinator of Health Information Technology, 2018).

Methods

Context

This QIP was conducted at a large suburban urology practice in the western United States with an interprofessional team of healthcare providers. The team included an oncology nurse practitioner, urologists, urology physician assistants, registered nurses, medical assistants, medical records staff, information technology personnel, and administrative staff. The QIP took place within the Comprehensive Prostate Cancer Clinic (CPCC); data were collected from April 2017 through January 2018 and stored on a password-protected, secure Microsoft® Excel spreadsheet. Manual chart review within the electronic medical record (EMR) (Allscripts®) and Precision Point Specialty (PPS) Analytics™ software was used to identify and track patients who were potential candidates for BDT and the components of bone health protocol. Men at any stage of PCa receiving intermittent or continuous ADT at all three clinic locations were included in this QIP.

Methodology

Plan-Do-Study-Act (PDSA) methodology served as the guide for the planning, practical application, implementation, and evaluation of the bone health QIP (Langley et al., 2009). Specific aims of the project were to improve secondary prevention of bone disease as measured by increased use of the FRAX tool (0% to 75%) and DEXA scanning for BMD (40% to 75%) for men on ADT for their PCa seen in the practice. The FRAX tool and the DEXA scan served as surrogate measures for bone disease. The use of the FRAX tool was a novel intervention to the practice.

Interventions and Study Of the Interventions

The CPCC first created a bone health protocol (see Figure 1) based on national evidence-based bone health guidelines in conjunction with a needs assessment and observation of baseline practice metrics and bone health processes at this urology practice setting. PDSA cycles were utilized to implement and operationalize components of the bone health protocol, and were based on a needs assessment from root cause analysis with an Ishikawa diagram (Phillips & Simmonds, 2013), along with a driver diagram, which served as a blueprint that directed and prioritized action items. This included the use of the FRAX tool for initial fracture risk assessment with a laboratory panel with several iterations, including coding for billing. An existing dental clearance form was revised and updated. A one-page bone health education handout was developed and revised to direct key lifestyle components that corresponded with process measures (lifestyle, exercise, calcium and vitamin D intake, smoking cessation, and minimizing alcohol intake). PDSA cycles are described in a PDSA Series Summary Table (see Appendix A).

This QIP project began by obtaining baseline data from PDSA cycles that focused on current bone healthcare practice in men receiving ADT and concluded after a 10-month period in which change was tracked over the course of the project implementation. The QIP team identified enablers and barriers to care, and the bone health protocol was revised with provider feedback. Patients were screened for fracture risk with the FRAX tool, DEXA scan to assess for osteopenia and osteoporosis, and bone scan for those at risk for bone metastasis. Subsequent PDSA cycles included the build and testing of an EMR-embedded bone health laboratory panel, patient education handout, and a revised dental clearance form. The handout included lifestyle modifications specific to the protocol, such as calcium and vitamin D supplementation, smoking cessation, moderate alcohol intake (less than two drinks a day), exercise, dietary, and fall precaution recommendations for optimal bone health. This handout corresponded with known risk factors noted on the FRAX and corresponded to key lifestyle process measures of the QIP. Remaining and ongoing PDSA cycles looked at the roll out of PPS Analytics software, denosumab ordering and documentation process, and bone health quality measures for sustainability.

Appendix A.
Plan-Do-Study Act Summary Series Table

PDSA Cycles	Aim	Measure of Success	Major Cycle Activity (Bulleted Discussion)	Results/Plan
1. Plan: Perform Ishikawa diagram, needs assessment. Form team.	AIM: Identify current practice patterns and needs to roll out bone protocol.	Fishbone diagram and needs assessment performed. Build bone health team.	Observe current practice patterns. Identify enablers and barriers to care and education needs.	Prioritize operationalization of bone health protocol and strategies for roll out, teaching, use of protocol in clinic.
2. Plan: Bone health protocol updates and revisions based on evidence.	AIM: Create evidence-based bone health protocol.	Bone health protocol accurate, algorithm directs appropriate care.	Review of national guidelines, review of the literature. Feedback and updates based on revisions.	Current revision from June/July 2017 available on the shared drive, written copies to all teams, practice sites. Ongoing education updates and use of protocol based on patient scenarios. Included revision of existing dental clearance form.
3. Plan: Embed FRAX® tool in electronic medical record (EMR). Create FRAX® tool and Bone Health choice in Health Maintenance.	AIM: Initiate use of the FRAX® Tool: Plan with staff for use of new tool; location in EMR.	FRAX® tool identified in EMR and results easily retrieved and identified by staff. FRAX® performed on 75% of patients.	Meet with medical records/IT regarding the develop/test FRAX® form and Bone Health choice in health maintenance in EMR. Develop plan to share change to staff.	FRAX® tool can be located and is being scanned correctly under documents; underway. FRAX® results entered under Bone Health within Health Maintenance in EMR. DEXA results also located here. Weekly Comprehensive Prostate Cancer Clinic (CPCC) meetings; monthly team meetings as needed.
4. Plan: Identify labs needed for bone health protocol and create a panel. Test and finalize revision to lab panel.	AIM: Create a bone health lab panel to order appropriate labs per bone health protocol.	Laboratory panel use with appropriate labs chosen and correct billing codes 90% of the time. Decrease miscoded bone lab orders pre/post lab panel by 50%.	Review laboratory guidelines and those for bone-directed therapies. Feedback and revisions on laboratory panel with providers/staff. Calls to laboratory companies to verify test components and coding.	Initially, differences with basic metabolic panel (BMP) between laboratory companies were found, along with miscoded magnesium route and vitamin D coding, which impacted laboratory draws and billing, and were corrected. Reviewed Medicare website. Laboratory panel use easier for providers, adds little time to visit. Some patients required recoding (errors) for insurance coverage.
5. Plan: Gather existing materials and develop bone health education resources. Implement use of educational materials at patient visits.	AIM: Improve patient education for bone health on androgen deprivation therapy (ADT) by developing bone health education handout and resources.	Bone health education toolkit reviewed and resources available for patient education. Measure: Bone health education received by 75% of patients.	"Managing Bone Health on Androgen Deprivation Therapy" handout draft created and revised.	Single page "Managing Bone Health" good overview; patients like it; available on shared drive. Lupron industry pamphlet complex. "Promoting Wellness in Prostate Cancer Patients" (Moyad) book provides good overview of cancer and bone health. Chemocare handout easy to understand. ManPlan online exercise resource well received by some but not all men. Ongoing evaluation of online support groups, find local/national resources. Created Urology Associates handout on local/online support services.

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Appendix A. (continued)
Plan-Do-Study Act Summary Series Table

PDSA Cycles	Aim	Measure of Success	Major Cycle Activity (Bulleted Discussion)	
6. Plan: Utilize PPS Analytics software tool to improve care of prostate cancer patients bone health. Check data accuracy from Allscripts and PPS Analytics.	AIM: PSA, bone health agents, DEXA tracked accurately in PPS Analytics and EMR.	Accurate reporting and data capture of DEXA and bone scan, bone health medications in PPS Analytics.	Early meetings/webinar with PPS Analytics before purchase for training, troubleshoot, and onboard. ID champions. Roll out PPS Analytics to other teams, staff.	Data pulls from EMR required some revisions in the process staff enter information (prostate-specific antigen [PSA], medications, etc.) and special data scanning to capture old laboratory values performed. Analytics not yet fully functional for bone health monitoring. Identify staff to run and monitor reports. Continue PPS Analytics training. **Next Steps:** Arrange consultant visit training in Spring 2018. PPS Analytics upgrading functionality of bone health components at their level currently.
7. Plan: Develop reminder system for ordering denosumab. Trial new denosumab ordering reminder system.	AIM: Patients receive denosumab treatment per protocol.	Denosumab dose is available at patient visit 100% of the time.	Meetings with nursing/staff current process for tracking and ordering denosumab. Cost, inventory, authorization on file.	Nursing staff will drive to bring missing dose from office to office. Developed appointment type for denosumab (Prolia®, Xgeva®). Identified reports available in Allscripts™.
8. Plan: Develop EMR-embedded Centers for Medicare & Medicaid Services (CMS) dual energy X-ray absorptiometry (DEXA) quality measure 2018. Trial if Urology Associates agrees to CMS DEXA measure.	AIM: Establish EMR DEXA quality measure to meet CMS requirements.	In planning.	Initial and follow up emails to director, practice manager and IT manager.	Tentative plan for late 2018 or 2019 EMR metric roll out.
9. Plan: Create a denosumab nursing administration sheet.	AIM: Nursing assessment safety measure prior to denosumab administration.	In planning.	Meetings and discussion with practice manager, IT, nursing regarding.	Agreement template needed to assess for protocol compliance for dental and laboratory parameters, development of new symptoms.

Outcome and Process Measures

The primary outcome measure was FRAX scoring appropriately performed on 75% of patients with PCa on ADT not taking bisphosphonates or denosumab. The secondary outcome measure was BMD through DEXA scan performance on 75% of appropriate patients with PCa on ADT, up from a baseline of 40%.

Lifestyle modifications measurement was the first of two process measures and had three components: exercise recommendations, smoking cessation, and minimizing alcohol intake. This was measured by documentation of discussion during a patient visit and provision of the bone health patient education handout, with a goal of reaching 75% of patients on ADT. BDT measurement was the second process measure with two components: 1) 90% of patients were appropriately prescribed and taking calcium and vitamin D, with documentation on the medication list; and 2) 90% of patients received BDT per bone health guidelines (an increase from baseline 40%) based on FRAX and BMD findings.

Two components for patient safety were established as important balancing measures prior to initiating BDT: 1) dental clearance obtained, and 2) appropriate bone health labs obtained and verified. To minimize the occurrence of osteonecrosis of the jaw, healthcare providers had to verify that a dental clearance form was completed. Providers were asked to query patients if they were experiencing dental, jaw or mouth pain, or had any jaw complaints at visits. To avoid electrolyte abnormalities associated with BDT, providers had to verify that appropriate labs (calcium via comprehensive metabolic panel, magnesium, phosphorous, and vitamin D 25-hydroxy) had been drawn and were within treatment parameters before BDT was prescribed. In addition, dental and electrolyte abnormalities were planned to be monitored on 100% of patients on BDT.

Analysis

Data were stored in Microsoft Excel on the secure server and de-identified prior to transfer to SSPS© Version 24 for analysis (IBM Corporation, 2016). Process control methods were used for outcome and process measures, and reported on a run chart with data points added to charts monthly. Pre- and post-intervention process data were reported with descriptive statistics using frequencies and percentages reported on the outcome and process measures. Changes and trends from interventions were detected on an annotated run chart. PDSA-driven interventions employed during the QIP were evaluated to track their monthly impact on the percentage of change in achieving QIP AIMS (see Figure 2) (Perla, Provost, & Murray, 2013). Fifty percent (50%) of CPCC patients were targeted to complete a baseline Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) QOL questionnaire to help direct future patient-centered, management of symptoms impacting QOL (Chang et al., 2011).

Ethical Considerations

This QIP was reviewed and deemed quality improvement and exempt from Institutional Review Board approval. No conflicts of interest were identified; no funding was received for this QIP.

Results

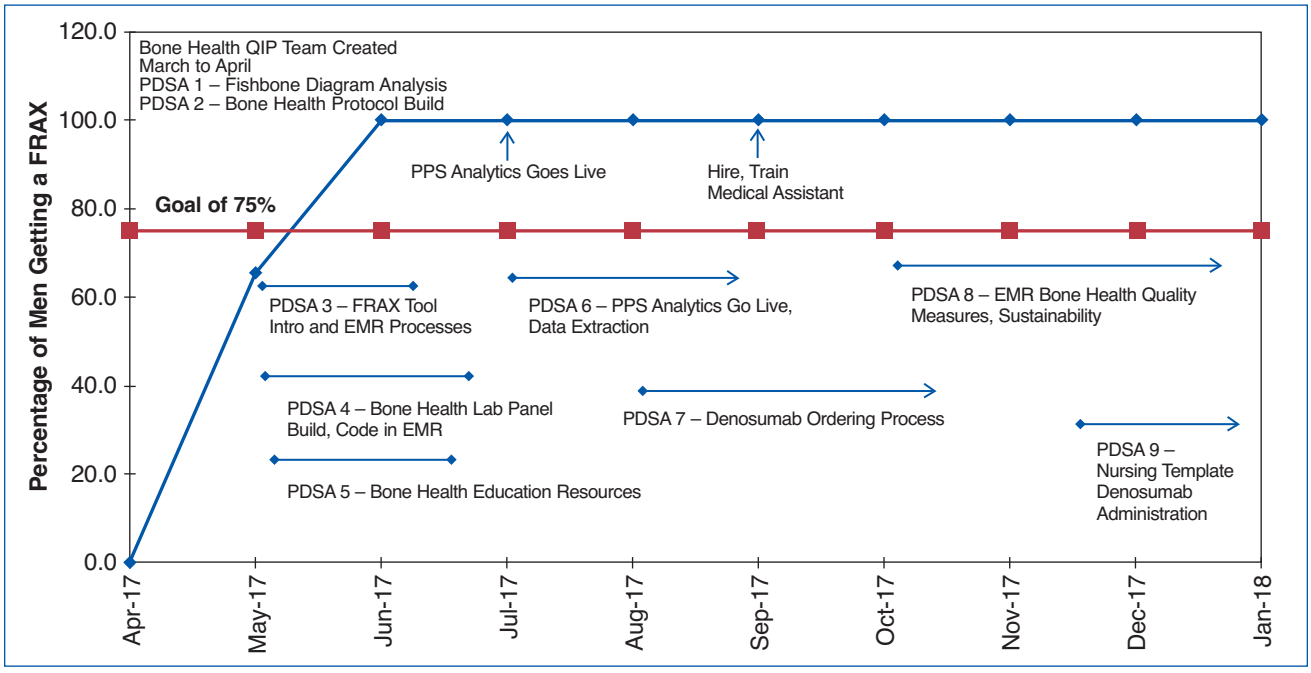
PDSA cycles were undertaken in a 10-month period in which the bone health protocol components were operationalized. A total of 173 men were evaluated in the CPCC and were predominantly insured, Caucasian, overweight men with an average age of 75 years. These patients had higher risk and higher stage of PCa, and 20% were noted to have hormone-resistant disease. Table 1 provides detailed demographic and descriptive data. The timeline and description of these nine PDSA cycles is embedded on the run charts for the primary outcome measures of FRAX and DEXA scan use (see Figures 2 and 3, and Appendix A).

There was early improvement, which was sustained over the course of the QIP, with both the FRAX tool and DEXA scan use meeting the goal of 75%. FRAX use went from 0% in April 2017 to just over 60% by May 2017 to 100% screening by June 2017, where it remained. Hip fracture risk was higher than the risk of major osteoporotic fracture risk in our patient population. DEXA scanning increased from the baseline of 40% between January to April 2017, to just below 60% in May 2017 to over 90% by June 2017, then to 100% screening by July 2017, where it remained for the duration (see Figures 1 and 2, and Table 2).

Medicare coverage allows for DEXA scans every two years for men over 70 years of age, or earlier for those receiving medication with agents known to impact bone health or chemotherapy for their prostate cancer (American Bone Health, 2018). Insurance coverage was not a barrier for the population we screened during this QIP; however, we did not have to justify repeat DEXA prior to 24 months in the timeframe of our project. Those who did not complete the FRAX or DEXA were noted to have other urgent clinical matters, not be appropriate for screening due to goals of care or advanced age, already be on BDT, or have bone metastasis found on bone scan (see Table 2). The bone health process takes several months to complete, so a few men had testing ordered that was not yet performed.

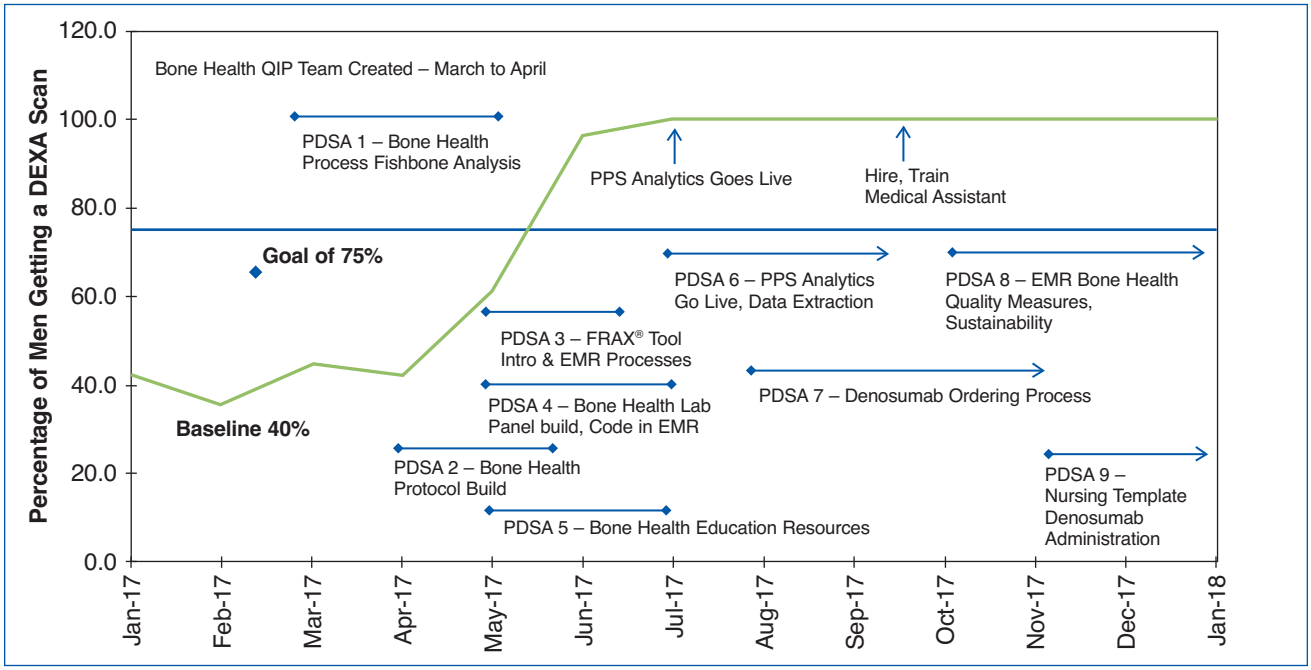
Process measures goals showed mixed results (see Table

Figure 2.
Bone Health Run Chart: Percentage of Men with Prostate Cancer on ADT Getting a FRAX® 5/1/17 to 1/31/18



Note: Percentage of men getting FRAX® includes men who have received FRAX scoring and those who are not appropriate for FRAX® scoring.

Figure 3.
Bone Health Run Chart: Percentage of Men with Prostate Cancer on ADT Getting a DEXA Scan 1/1/17 to 1/31/18



Note: Men getting a DEXA includes the following: DEXA ordered and done, those screened and DEXA ordered but not done yet, and those screened not appropriate for DEXA to be performed.

Table 1.
Demographic and Descriptive Statistics for Patients

	Mean (*SD*) Range
Current Age	75.07 (8.871) 51-96
Age Diagnosed	69.27 (8.886) 51 to 92
Body Mass Index	27.32 (4.83) 16.05 to 48.82
Cancer Stage	***n*** **(%)**
Stage I	4 (2.3)
Stage II	51 (29.5)
Stage III	23 (13.3)
Stage IV	66 (38.2)
Unknown Stage (no Stage IV)	29 (16.8)
National Comprehensive Cancer Network Risk Category	**Frequency *n* (%)**
Very Low	2 (1.2)
Low	3 (1.7)
Intermediate	35 (20.2)
High	31 (17.9)
Very High	76 (43.9)
Unknown	26 (15.0)
Hormone Resistance Status	***n*** **(%)**
Hormone Sensitive	137 (79.2)
Hormone Resistant	35 (20.8)

Table 2.
Outcomes Measures: FRAX® and DEXA Usage

Outcome Measures (*N*=173)	Result	*N* (%)
FRAX® Assessment	Performed	130 (75.2)
	Not Performed	43 (24.8)
FRAX® Hip Fracture Risk	Greater ≥ 3%	77 (44.5)
	Less < 3%	53 (30.6)
	Not Performed	43 (24.9)
FRAX® Major Osteoporotic Risk	Greater ≥ 20%	13 (7.5)
	Less < 20%	117 (67.6)
	Not Performed	43 (24.9)
DEXA Bone Mineral Density	Normal	42 (24.3)
	Osteopenia	48 (27.7)
	Osteoporosis	15 (8.7)
	Other	68 (39.3)

Notes: All patients were screened for bone health with FRAX® and DEXA. Reasons the FRAX® was not performed included: Not indicated bone metastasis, on bone-directed therapy (BDT), advanced age (not valid greater than 90 year of age), DEXA results on file, other urgent issues during visit. Reasons for no DEXA performed included: Not indicated bone metastasis, on BDT (*N*=29/16.8%), declined/ defer to other provider or later date (*N*=11/6%), goals of care (advanced age/ dementia) (*N*=5/3%), ordered, not yet done/ pending other imaging (*N*=8/5%), Of the 39.3% listed as other under DEXA, more than half of these appropriately did not obtain the actual DEXA scan.

3). Lifestyle modification surpassed the goal of 75%, with 92.5% receiving education. Oral calcium intake was reported at 61.3% and vitamin D intake at 69.9%, and did not achieve the goal of 90%. Poor adherence has been identified as a problem because patients may decline or discontinue supplementation and intake of calcium and vitamin D for men on ADT; osteopenia and osteoporosis through initial screening by BMD has been reported as low at 50% (Al-Shamsi et al., 2012, 2017). All patients appropriate for BDT were offered treatment, which met the goal of 100%. A few patients declined treatment or were not candidates due to poor dental status and no plans to seek dental care. Of the 175 men screened; 44 men received BDT, with 33 of these patients receiving their BDT as denosumab at the urology practice site. The remaining 11 men received BDT at outside practices. No fractures were documented in the time of this QIP.

The goal of 100% for this bone laboratory panel as a balancing measure was not met; 2 of the 33 men receiving BDT at this urology clinic were missing a bone laboratory panel component (see Table 4). When the deficit was found, the missing laboratory component was then ordered and the two patients contacted. Coding issues with the vitamin D component of the bone laboratory panel created financial concerns for men early in this QIP process, and three did not obtain this level or required billing to be resubmitted to cover the expense. Dental clearance was obtained on the 33 men receiving BDT, which met this safety measure at 100%. One patient receiving ADT by an outside provider was reported to have developed ONJ.

The EPIC-CP questionnaire (Chang et al., 2011) was completed by 71% (*N*=122) of patients seen in the CPCC, with 189 forms

Table 3.
Process Measures: Lifestyle Modification, Calcium and Vitamin D, and Bone-Directed Therapy

Lifestyle Modification Education (Goal 75%) (Smoking Cessation, Exercise Recommendations, Minimize Alcohol Intake and Calcium and Vitamin D Recommendations)	*N* (%)
No	13 (7.5)
Yes	160 (92.5)

Note. Reasons education was not received: visit preceded formal education process/handout, other pressing issues at visit, advanced age, and goals of care.

Taking Supplements and Documented	Calcium *N* (%) Goal 90%	Vitamin D *N* (%) Goal 90%
No	62 (35.9)	52 (30.1)
Yes	106 (61.3)	121 (69.9)
Other	5 (2.9)	NA

Notes. Though calcium and vitamin D were documented when yes selected the dosing was unknown for calcium (*n*=61 [35.3%]) and vitamin D (*n*=46 [26.2%]) and dosing reported with wide ranges (calcium 200 mg to 2,000 mg; vitamin D 200 IU to 50,000 IU).

Bone-Directed Therapy (BDT) Goal 90%	*N* (%)
Denosumab (Prolia®)	13 (7.5)
Denosumab (Xgeva®)	23 (13.0)
IV-Zoledronic Acid (Zometa®)	3 (1.7)
Oral (bisphosphonate)	5 (2.8)
No BDT *	129 (75.0)

Notes. All candidates (100%) screened and offered BDT if indicated; *N*=44 on BDT, 33 received denosumab at the urology practice. Other BDT delivered at outside providers. Some candidates declined BDT or were not candidates due to dental problems.

*BDT does not include calcium/vitamin D supplementation.

returned because some men completed the form more than once. This met the goal of EPIC-CP completion on 50% of patients seen during the QIP. Scoring is on a 5-part Likert scale from no problem, very small problem, small problem, moderate problem, to a big problem. Only the vitality/hormonal symptom score results will be reported here to emphasize symptom burden in men on ADT (see Table 5). Hot flashes and breast tenderness or enlargement were reported as moderate or big problems by 21.7% of men. Fatigue was also a moderate or big problem for 30.2% of men. Feeling depressed was noted as a moderate or big problem for 6.4% who completed the survey. The vitality/hormonal symptom score burden was high, and feeling depressed and lack of energy can limit physical activity levels. These symptoms and the urinary, bowel, and sexual health concerns of men on ADT reported on the EPIC-CP responses can also be future targets for evidence-based algorithms to direct care.

Discussion

The bone health protocol was complex and took up to three to four months to complete, in addition to requiring ongoing

Table 4.
Balancing Measures: Bone Health Laboratory Panel and Dental Clearance

Bone Health Lab Panel Goal 100%	Panel Obtained	Partial Panel	No Panel
Denosumab (Prolia® and Xgeva®) *n*=36* *Receiving denosumab; 29 had labs at the urology practice; 2 had partial labs at the urology practice; 5 had labs at outside provider.	32	2 (missing laboratory ordered)	2 (outside provider provided medication)

Note. All patients receiving denosumab at the practice site had a bone health lab panel obtained or were pending missing laboratory component.

Dental Clearance Goal 100%	*N* (%)
No	4 (2.3)
Yes	33 (19.1)
Other	136 (78.6)

Note. No responses included invasive dental work; a move out of state and not a candidate for bone-directed therapy (BDT). Other responses included BDT provided at an outside provider, patient edentulous, or not currently a candidate for BDT so not indicated. All patients receiving BDT at clinic site had dental evaluation. One patient receiving BDT at an outside site developed osteonecrosis of the jaw.

Table 5.
Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP): Vitality/Hormonal Symptom Score

Vitality/Hormonal Symptom Score (*N*=189)	No Problem *N* (%)	Very Small Problem *N* (%)	Small Problem *N* (%)	Moderate Problem *N* (%)	Big Problem *N* (%)	Left Blank/NA *N* (%)
Hot flashes or breast tenderness or enlargement	94 (49.7)	28 (14.8)	20 (10.6)	26 (13.8)	15 (7.9)	6 (3.2)
Feeling depressed	127 (67.2)	23 (12.2)	19 (10.1)	6 (3.2)	6 (3.2)	8 (4.2)
Lack of energy	58 (30.7)	26 (13.8)	45 (23.8)	33 (17.5)	24 (12.7)	3 (1.6)

Notes. *N*=189 questionnaires; *N*=122 (71%) completed; *N*=51 (29%) did not complete; some completed more than once. Goal 50% of patients seen in Comprehensive Prostate Cancer Clinic (CPCC) would complete the EPIC-CP.

monitoring. QIP methodology with PDSA cycles was helpful in operationalizing the bone health protocol within this urology practice and guide practice change.

This success of this QIP can be adapted to other urology and cancer clinics to promote bone health care with allocation of dedicated staff and resources to implement and monitor components of a bone health protocol. Primary aims of FRAX and DEXA use met their goal over the 10-month course of this QIP, as did process measures for lifestyle and BDT, and balancing measure of dental clearance. The process measure of calcium and vitamin D supplementation intake was not met, but may have been unrealistic and the focus of a more in-depth PDSA addressing motivational factors that impact adherence (Conti et al., 2012). The balancing measure for bone health labs was not met because two partial bone health labs were found and then re-ordered. This component was complex due to several reasons, including labs obtained through outside providers and delays when waiting until the next scheduled lab draw to coincide with a three-month interval prostate specific antigen (PSA) test.

The strength of this project was the understanding that urology staff and the health provider team had surrounding the "burning platform" to improve bone health for patients on ADT. The urology practice supported the process by creating a dedicated clinic with an advanced practice nurse with QIP and leadership training, an information technology champion, and resources to support the project. Patients were receptive to education regarding bone health as a part of their care.

Interpretation, Strengths, And Limitations

Quality improvement methodology partnered well with the successful implementation of a bone health protocol based on evidence to guide practice change in this large urology practice. Multiple competing stressors and staff turnover factored into the implementation timeline, but this is a reality of improvement processes. All provider team members did not refer equally to the CPCC, and not all of the estimated 308 potential patients, based on 2016 baseline data for men on ADT, were seen. Addressing referral patterns and revisiting any perceived barriers will be important next steps to capture data on all men on ADT at the practice site (Damji et al., 2013, Nadler et al., 2015).

Continuing to embed components of the protocol within the EMR will assist with sustainability and monitoring over time. Bone health evaluation takes several months to complete, which requires resources for ongoing evaluation, education, monitoring, and follow-up of protocol components. In addition, duration of ADT and risk versus benefit discussions regarding the decisions to initiate BDT are complex and were not captured during this QIP.

A gap in care remains for screening, prevention, and treatment of men on ADT. Any man receiving ADT should be screened for osteopenia and osteoporosis (Al-Shamsi et al., 2012, 2017). A recent randomized clinical trial found that educational strategies to improve bone health are feasible and improve ordering of BMD. More study was needed to identify optimal education strategies (Alibhai et al., 2018). At this project site, the initial clinic visit provided time to screen with FRAX and review a one-page education handout and found improved BMD testing over baseline measures. Bultijnck and colleagues (2018) found that use of a clinical pathway to manage ADT-related side/adverse effects in men with PCa improved implementation of evidence-based healthcare strategies, including bone health. This QIP utilized a bone health protocol for men on ADT and could be

expanded in a similar fashion to address other ADT-related side/adverse effects in this population as a next step. Baseline EPIC-CP results obtained in this QIP identified problematic symptoms that impact QOL that can be targeted for future improvement. Budgeting for bone health care, tracking both clinical and financial outcomes can help meet practice metrics to comply with reporting regulations, remain fiscally viable, and address provider satisfaction to meet the quadruple aim (Manchanda, 2018).

Conclusions

Bone health is an important component of the care of men with PCa on ADT and can be delivered within urology, oncology, and other specialty practices by targeting this gap in care through the implementation of evidence-based bone health guidelines. Dedicated resources are needed to implement, maintain, and sustain this practice change (Alihhai et al., 2018, Al-Shamsi et al., 2012, 2017; Bultijnck et al., 2018). The FRAX tool is a no-cost, initial screening tool available online to assess fracture risk that can be easily offered at office visits and help identify at-risk patients not found with DEXA screening (James et al., 2014). This QIP found hip fracture risk to be substantial with 44.5% of men with risk at greater than or equal to 3% on FRAX, the measure corresponding with significant 10-year probability of a hip fracture.

Sustaining gains in bone health care achieved with this QIP will require ongoing leadership to envision, empower, encourage, and enlist staff (Buchard, 2014). The bone health protocol will require review and revision as new evidence emerges. Calcium and vitamin D dosing and adherence strategies are evolving. Follow up of bone health labs, dental clearance, and exercise recommendations require more study. Finally, partnerships with primary care to promote bone health education of this PCa patient on ADT is an important survivorship issue for future development within the community (Choi et al., 2013). ◙

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