Nutrition Education for Osteoporosis Prevention in Men With Prostate Cancer Initiating Androgen Deprivation Therapy

Heather Millar, RD, MSc, and Joyce Davison, RN, PhD

Osteoporosis is a common side effect of treatment with androgen deprivation therapy (ADT) in men with prostate cancer. ADT may prolong survival; however, deterioration of bone mass density occurs soon after initiation. A systematic review of current literature revealed the importance of adequate nutrition during treatment with ADT to reduce the risk of osteoporosis. More specifically, this literature stressed achieving adequate intake of calcium and vitamin D through a combination of supplements and food. The necessity of providing nutrition education to patients with prostate cancer at initiation of ADT was identified. Healthcare professionals, including nurses, oncologists, and dietitians, can be instrumental in identifying patients with prostate cancer initiating ADT who are at risk for osteoporosis. Research on nutrition and lifestyle modification interventions to maintain bone health and reduce fracture risk for patients initiating ADT is limited. Additional research is required to develop and evaluate nutrition education interventions that will reduce the risk and prevent osteoporosis in men on ADT.
ADT for osteoporosis prevention (Malcolm et al., 2007). Adequate nutrition is required by patients using bisphosphonates because they are ineffective in promoting bone health if the dietary reference intake for calcium and vitamin D is not met concurrently (Holzbeierlein, 2006). Also, bisphosphonates can cause low serum calcium, phosphate, and magnesium levels, as well as vitamin D deficiency (Saad, Abrahamsson, & Miller, 2009; Saad et al., 2006; Weingard, 2006), providing additional evidence to support adequate intake of those essential nutrients while using bisphosphonates. In general, many men with prostate cancer do not consume adequate amounts of vitamin D and calcium (Smith et al., 2001; Wiens & Barr, 2012).

The purpose of this review was to summarize and synthesize the current evidence to support the need for nutrition counseling in patients with prostate cancer on ADT. The review will provide healthcare professionals with supporting evidence, offering direction for the development of a patient education intervention to reduce the risk of men developing osteoporosis during ADT.

Methods

A systematic review of the literature in the PubMed and CINAHL® databases of publications from 2000–2010 was conducted. The authors selected those years to provide a current review that included the most recent research. A search strategy was developed with the help of a health sciences librarian to identify potentially relevant studies. Medical Subject Headings (MeSH terms) related to prostate cancer (termed prostatic neoplasms), androgen deprivation therapy (termed androgen antagonists and/or antineoplastic agents, bormonal) and nutrition education (termed diet) were used to search for articles on this topic. PubMed was searched first, and 68 articles were identified. The same search terms were entered into CINAHL® and one more article was identified. Limits were set to human studies, English language, and a publication date from 2000–2010. The limits excluded 29 of the 69 previously identified studies.

Abstracts were screened to determine which articles discussed diet and humans and eliminated molecular- or cellular-level studies and animal studies. This step eliminated an additional 15 studies. The 25 remaining studies were reviewed in their entirety and 13 articles that more specifically discussed nutrition for osteoporosis prevention or management for men with prostate cancer on ADT were identified and included in the systematic review. A final review of the reference lists of those 13 additional articles revealed 4 more studies that fit the topic and inclusion criteria and were included in the systematic review. The final article included in the review was an unpublished article at the time of review that also fit the topic and inclusion criteria. The articles were evaluated for quality and strength of the evidence using the Johns Hopkins Nursing Evidence-Based Practice guidelines (Newhouse, Dearholt, Poe, Pugh, & White, 2001). Of the 18 articles reviewed, one was a randomized, controlled trial in progress; three were nonexperimental studies; five were systematic reviews or expert opinion; and nine were literature reviews or background articles. Table 1 contains a synopsis of the articles listed in order of level of evidence. Articles with the strongest evidence are listed first.

Review of the Evidence

Vitamin Supplementation

The review of the evidence revealed that nutrition, including vitamin D and calcium supplementation, plays an important role in maintaining bone health in men on ADT. A need to increase patient awareness surrounding this issue does exist. In the articles reviewed, recommendations for calcium and vitamin D supplementation for men on ADT were prevalent. Not all authors provided dosing for supplementation, but those who did provided amounts that ranged from 1,000–1,500 mg calcium per day and 400–800 IU of vitamin D per day (Berruti et al., 2002; Chang, 2003; Eastham, 2007; Holzbeierlein, 2006; Holzbeierlein, Castle, & Thrasher, 2004; Israeli, Ryan, & Jung, 2008; Lebret et al., 2010; Moyad, 2005; Smith, 2002a, 2002b, 2003; Tombal, 2009). The reviewed literature highlighted the importance of timing for calcium and vitamin D supplementation and recommended starting at the initiation of ADT (Chang, 2003; Davison et al., 2009; Davison, Wiens, & Cushing, 2011; Eastham, 2007; Holzbeierlein, 2006; Holzbeierlein et al., 2004).

Lifestyle Modification

In addition to calcium and vitamin D recommendations for men on ADT, other lifestyle modifications were commonly suggested to reduce the risk of osteoporosis. The most common recommendations from the articles were limiting intake of caffeine to less than 400 mg per day, keeping alcohol consumption in moderation (less than two drinks per day), and participating in weight-bearing and resistance exercise (Chang, 2003; Davison et al., 2011; Eastham, 2007; Haseen, Murray, Cardwell, O’Sullivan, & Cantwell, 2010; Holzbeierlein, 2006; Holzbeierlein et al., 2004; Moyad, 2005; Smith, 2002a; Tombal, 2009; Weingard, 2006). A diet also was suggested; however, specifics of what this diet included were not described (Haseen, Murray, Cardwell, et al., 2010; Moyad, 2005; Weingard, 2006).

The importance and necessity of providing education to patients with prostate cancer initiating ADT regarding vitamin supplementation and other lifestyle modifications were identified. Weingard’s (2006) literature review suggests education regarding regular exercise, decreasing alcohol and caffeine intake, and vitamin supplementation along with a proper diet can help prevent bone loss and reduce risk of fracture; however, no research studies in the current review supported Weingard’s suggestion. The studies by Lebret et al. (2010) and Davison et
<table>
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<th>Study</th>
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<td>Davison et al., 2011</td>
<td>Quasi-experimental study; investigation of calcium and vitamin D intakes before and after a patient nutrition education intervention using a two-part survey questionnaire</td>
<td>Calcium and vitamin D intake among men on ADT may be inadequate and no different than the general population. Providing information on lifestyle and dietary changes while on ADT may be more effective if delivered at the initiation of therapy.</td>
<td>Generalizability of results to a broader group of men is limited. Larger sample is needed to detect significant differences.</td>
<td>Strength: II Quality: B</td>
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<td>Haseen, Murray, Cardwell, et al., 2010</td>
<td>Systematic review for articles through January 2009 of the effect of ADT on body composition in men with prostate cancer</td>
<td>Significant increases in body weight, BMI, percentage body fat, and declines in lean body mass were reported in patients with prostate cancer on ADT. These changes occur early in treatment. Exercise and low-calorie diet should be encouraged at the beginning of treatment to minimize change in body composition.</td>
<td>Mainly Caucasian participants in studies; inadequate adjustments of confounders in primary studies</td>
<td>Strength: III Quality: A</td>
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<td>Panju et al., 2008</td>
<td>Prospective match-cohort study of health outcomes of men starting ADT. Data collected through clinical interviews and charts were reviewed to elicit information including calcium and vitamin D intake and the use of medications.</td>
<td>The minority of patients were being informed of bone-specific side effects of ADT, and lifestyle and pharmacologic interventions to prevent declines in BMD were uncommonly recommended. A need was identified to increase awareness and create clinical practice guidelines.</td>
<td>Descriptive statistics, no statistically significant data identified</td>
<td>Strength: III Quality: B</td>
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<td>Lebret et al., 2010</td>
<td>Nonexperimental longitudinal survey; 91 of 128 urologists and 287 of 585 patients evaluated an educational toolkit designed for patients with prostate cancer about to receive ADT at two different time points.</td>
<td>Information supplied in toolkit on diet and exercise was well received by patients and clinicians and met a need. Implementation rate was high. Guidance on exercise and diet (based on recommendations for reducing metabolic syndrome, promoting cardiovascular health, and preventing prostate cancer) may need updating with new evidence.</td>
<td>Nongeneralizable; short follow-up period, potential of response bias</td>
<td>Strength: III Quality: C</td>
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<td>Diamond et al., 2004</td>
<td>Systematic review and expert opinion; PubMed, Cochrane, and Lab published abstracts were reviewed and expert opinion included to develop a clinical algorithm for managing bone health in high-risk men initiating ADT for prostate cancer.</td>
<td>Adequate calcium intake and vitamin status should be ensured in all men on ADT. Based on published data, pamidronate and zoledronic acid are the best agents for effective prevention of osteoporosis in men on ADT.</td>
<td>Methodologic limitations were not disclosed.</td>
<td>Strength: IV Quality: A</td>
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<td>Chang, 2003</td>
<td>Literature review; risk of osteoporosis associated with the use of ADT in prostate cancer and prevention of bone loss and fractures.</td>
<td>Osteoporosis can be associated with long term ADT. Moderation of alcohol consumption and 1,200 mg calcium and 600–800 IU vitamin D supplements daily should be recommended at the start of ADT. Bisphosphonates may be beneficial in preventing and treating osteoporosis.</td>
<td>Undefined search strategy</td>
<td>Strength: IV Quality: B</td>
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<td>Eastham, 2007</td>
<td>Literature review; ADT-related bone loss in prostate cancer, current treatments, and emerging therapies</td>
<td>ADT adversely affects bone health. Patient education of risk, lifestyle modification, and bisphosphonate therapy can improve outcomes. Lifestyle modification recommendations for men initiating ADT include avoidance of excessive alcohol and caffeine, 1,200 mg calcium supplement daily in divided oral dose, and vitamin D supplementation of 400–800 IU per day.</td>
<td>Insufficient identification of limitations and strengths of studies evaluated</td>
<td>Strength: IV Quality: B</td>
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ADT—Androgen deprivation therapy; BMD—bone mineral density; BMI—body mass index; RCT—randomized, controlled trial

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<td>Isareli et al., 2008</td>
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<td>Systematic review; PubMed search using terms and keywords relating to bone loss in men with prostate cancer on ADT</td>
<td>Calcium (1,200–1,500 mg per day) and vitamin D (400–600 IU per day) supplements are considered an essential component of ADT-induced bone loss prevention. Most evidence to date supports bisphosphonates for prevention of ADT-induced bone loss.</td>
<td>Insufficient evaluation of strengths and limitations of studies reviewed</td>
<td>Strength: IV Quality: B</td>
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<td>Berruti et al., 2002</td>
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<td>Background article; review of treatment of prostate cancer, bone loss induced by ADT, management of osteopenia/osteoporosis induced by ADT including general preventative measures of nutrition and exercise and the use of antiresorptive drugs (bisphosphonates)</td>
<td>Optimizing diet is important but can not completely prevent bone loss. Calcium intake should be 1,200–1,500 mg per day. Bisphosphonates can prevent treatment-related bone loss. Research is needed to determine whether bisphosphonates can prevent adverse skeletal events.</td>
<td>Undefined search strategy; lacking evaluation of included studies</td>
<td>Strength: IV Quality: C</td>
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<td>Moyad, 2005</td>
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<td>Expert opinion; 10 steps to promote general health during ADT</td>
<td>Education should be provided regarding dietary and lifestyle changes to promote general health. Specifically, calcium and vitamin D supplements (1,000–1,500 mg per day and 400–800 IU per day, respectively), exercise, weight loss, and diet changes to reduce cardiovascular disease risk.</td>
<td>Potential biases were not acknowledged.</td>
<td>Strength: V Quality: A</td>
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<td>Smith, 2002a</td>
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<td>Literature review; osteoporosis and other adverse body composition changes during ADT for prostate cancer</td>
<td>Diet and lifestyle may contribute to bone loss during ADT. Supplemental calcium and vitamin D are recommended. Smoking cessation, moderate alcohol, and weight-bearing exercises also are recommended.</td>
<td>Undefined search strategy</td>
<td>Strength: V Quality: B</td>
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<tr>
<td>Literature review; osteoporosis during ADT for prostate cancer</td>
<td>ADT accelerates bone loss. Diet, lifestyle, and treatment-related loss of lean body mass contribute to fracture risk. Supplemental vitamin D (400 IU per day) and calcium (1,200–1,500 mg per day) are recommended. Pamidronate can prevent bone loss during ADT.</td>
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<tr>
<td>Literature review; diagnosis and management of treatment-related osteoporosis in men with prostate cancer</td>
<td>ADT accelerates bone loss. Diet, lifestyle, and treatment-related loss of lean body mass contribute to fracture risk. Supplemental vitamin D (400 IU per day) and supplemental calcium (1,200–1,500 mg per day) are recommended. Bisphosphonates prevent bone loss and increase BMD during ADT.</td>
<td>Undefined search strategy; biases not acknowledged</td>
<td>Strength: V Quality: B</td>
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<td>Tombal, 2009</td>
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<td>Literature review; a holistic approach to ADT</td>
<td>Side effects of ADT should be monitored and appropriately managed and treated, including proper counseling, if necessary. Dietary advice may help to minimize metabolic changes, anemia, and osteoporosis. Physical exercise may prevent or minimize side effects of ADT. All ADT-treated men aged 65 years and older should receive supplementary calcium and vitamin D to prevent osteoporosis.</td>
<td>Undefined search strategy; limited identification of limitations and strengths of studies evaluated</td>
<td>Strength: V Quality: B</td>
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ADT—androgen deprivation therapy; BMD—bone mineral density; BMI—body mass index; RCT—randomized, controlled trial

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al. (2011) also supported the need for nutrition and exercise education in patients with prostate cancer initiating ADT. Lebret et al.'s (2010) survey demonstrated that patient education does not need to be provided traditionally by a healthcare professional, but also may be effective through delivery in a toolkit format.

**Medication**

To date, evidence indicates bisphosphonates such as pamidronate and zoledronic acid are the best agents for preventing treatment-related bone loss during ADT, and taking them may improve patient outcomes (Diamond, Higano, Smith, Guise, & Singer, 2004; Eastham, 2007). Patients should take 1,200–1,500 mg of calcium and 400 IU of vitamin D concomitantly with bisphosphonates to provide nutrients essential to bone formation (Holzbeierlein, 2006). In the literature reviewed, bisphosphonates were the main pharmacologic agent recommended to prevent bone loss in men on ADT; however, other pharmacologic agents are available for this purpose and are in use, one of which is denosumab (Lee, Saylor, & Smith, 2011).

**Clinical Implications**

Osteoporosis is common in patients with prostate cancer on ADT. ADT-associated bone loss adversely affects bone health and patient quality of life by increasing risk of skeletal-related events (Davison et al., 2011). Low bone mineral density is a risk factor for mortality assumed to be related to comorbidities in affected patients; consequently, ADT-associated bone loss also may impact survival in men on ADT (Johnell et al., 2004). Recognizing that risk as patients initiate ADT therapy may help manage those potential side effects (Lebret et al., 2010). Front-line care providers, including nurses, physicians, and pharmacists, have an influential role in raising awareness of the associated issues with ADT.

The literature has identified that patients require guidance to follow a nutritionally complete diet while on ADT, which includes meeting their nutrition requirements for calcium and vitamin D and keeping caffeine and alcohol intake to moderate amounts. The most effective way to provide that education has yet to be identified. A toolkit of information used in a study by Lebret et al. (2010) has shown success, and research is currently in progress to develop a more comprehensive toolkit.
underway to assess a six-month individually tailored home-based nutrition and exercise plan (Haseen, Murray, O’Neill, O’Sullivan, & Cantwell, 2010; Lebret et al., 2010).

Through screening, oncology nurses, dietitians, and oncologists can be instrumental in identifying patients with prostate cancer at risk for osteoporosis. By initiating a discussion regarding calcium and vitamin D intake when a patient on ADT visits the injection clinic, the importance of proper nutrition to maintain bone health and reduce risk of bone fracture may be highlighted. Nutrition and lifestyle modification interventions provided by healthcare professionals, including dietitians and exercise therapists, should be made available to patients initiating ADT. Oncologists and oncology nurses have important roles of beginning the discussion of osteoporosis prevention and making appropriate referrals to the interventions available.

**Conclusion**

Nurses, oncologists, and dietitians are fundamental in identifying men with prostate cancer on ADT who are at risk for osteoporosis. Interdisciplinary healthcare professionals, including dietitians and exercise therapists, can offer specialized knowledge for development and facilitation of a nutrition and lifestyle modification intervention for patients initiating ADT. The evidence provided through this systematic review outlines key actions that can be taken by healthcare professionals to reduce the risk of osteoporosis in that patient population.

**References**


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