



'Healthy on Hormones': improving the experience of men with advanced prostate cancer

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ABSTRACT

Long-term androgen deprivation therapy (ADT) for advanced prostate cancer can result in significant and distressing side effects and longer-term adverse metabolic effects. A seminar-based service improvement initiative was developed to provide information and strategies to understand ADT, to manage side effects and to provide lifestyle advice regarding cardiovascular and bone issues. The seminars were evaluated with patient questionnaires and were positively received. This approach has proven to be a valuable tool in the care of this patient group.

Key words: Advanced prostate cancer • Androgen deprivation therapy • Metabolic side effects

INTRODUCTION

Over 41 000 men are diagnosed each year with prostate cancer in the UK and at least 20% of these will be diagnosed at an advanced stage (Cancer Research UK 2014a, 2014b), whereas other patients may develop metastatic disease after primary treatment failure. Prostate cancer most commonly spreads to lymph nodes and bone, and once metastasized, is not curable but may be controlled, often for many years. The recent emergence of a number of new therapies for advanced prostate cancer has seen men living for longer with their disease. ADT has been the mainstay of treatment for advanced prostate cancer for over half a century. It is the first treatment given and it is continued after patients become castration refractory alongside other therapies. Huggins and Hodges (1941) first described the androgen dependence of prostate cancer and showed that castration decreased cancer growth. Nowadays this may be achieved by surgical orchidectomy, but more commonly luteinizing-hormone-releasing hormone (LHRH) agonist or antagonists are used.

ANDROGEN DEPRIVATION THERAPY

Testosterone production in men is regulated by the hypothalamus, which releases LHRH in response to low testosterone levels in the blood. LHRH binds to receptors in the pituitary gland, stimulating the release of luteinizing hormone (LH) which in turn acts on the testes causing testosterone production.

LHRH agonists mimic normal LHRH and bind to the LHRH receptors on pituitary cells. This leads to an initial increase in the production of LH, which in turn leads to an increase in testosterone production. Approximately a week after the first injection, chronic exposure results in down regulation of the LHRH receptors which suppresses pituitary LH secretion and eventually testosterone production.

LHRH antagonists are newer drugs with a different mechanism of action. LHRH antagonists block the pituitary gland receptors and as a result, LHRH is unable to bind to these receptors. Consequently, the pituitary gland does not release LH and the testicles therefore do not produce testosterone. Serum testosterone levels drop rapidly, without the initial LH and testosterone surge seen with the agonists.

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SIDE EFFECTS OF ADT

The side effects of ADT can be bothersome and distressing for patients and adversely affect quality of life (Dacal *et al.*, 2006). Intolerable side effects may also affect adherence to treatment, forcing some

men to abandon treatment or decline it through fear. Side effects include reduced or absent libido and erectile dysfunction, hot flushes, gynaecomastia, fatigue, decreased mental sharpness, mood swings and depression (Holzbeierlein *et al.*, 2004; Nelson *et al.*, 2008).

More recently, the literature has also described metabolic complications of ADT which may have serious long-term consequences. The use of ADT is associated with a number of cardiovascular risk factors including obesity (specifically accumulation of subcutaneous fat and loss of lean muscle mass), insulin resistance and dyslipidaemia (Saylor and Smith, 2009; Keating *et al.*, 2010; Jespersen *et al.*, 2013). However, despite data demonstrating the link between ADT and cardiovascular risk factors, there remains debate as to whether ADT is also associated with an increased risk of cardiovascular mortality. However, in the absence of definitive studies, the higher incidence of risk factors for cardiovascular disease in men treated with ADT suggests that there may also be a relationship between ADT and an increased risk of cardiovascular events and death (Levine *et al.*, 2010) although further prospective studies are needed.

Androgens are also key mediators of bone formation. Androgen deprivation decreases osteoblast activity and increases bone resorption by osteoclasts, which leads to a decrease in bone mineral density. In one cross-sectional analysis (Morote *et al.*, 2007), 35.4% of men studied had osteoporosis and 45.2% osteopenia before starting ADT. This rose year on year until after 10 years, none of the men had normal bone mineral density. The risk of sustaining a fracture also increases with longer duration of ADT (Shahinian *et al.*, 2005) and sustaining a fracture is associated with significant increased mortality (Oefelein *et al.*, 2002).

These unwanted effects of ADT can affect adherence to treatment and quality of life, but can also cause longer-term morbidity and mortality associated with cardiovascular risk factors and osteoporosis. Some men report being poorly informed about side effects (Walker *et al.*, 2011) and knowledge about side effect management may be limited. Many men with prostate cancer receiving ADT do not receive appropriate screening or information about bone health (Nadler *et al.*, 2013). It is therefore essential that we give some thought to how we can improve the patient experience of treatment and try to minimize some of the longer-term metabolic risks.

SELF EFFICACY AND CANCER

Self-efficacy for cancer patients has been described as an individual's confidence in managing disease-related

symptoms (Campbell *et al.*, 2004). Self-efficacy has been shown to be a strong indirect predictor of quality of life for men with advanced prostate cancer. In addition, partners are also negatively affected by the disease and can influence patient outcomes (Kershaw *et al.*, 2008). Providing interventions to promote and improve self-efficacy can therefore be identified as a key aim when planning specialist nursing interventions for men with advanced prostate cancer. Kershaw *et al.*, (2008) also found that patients with advanced disease had a better quality of life if they used active coping. Active coping strategies are an individual's efforts to eliminate, circumvent or lessen the effects of the stressor (Zabalegui, 1999), so providing solution focused education regarding side effects may be useful.

Aims

The aim of this nurse-led service development, therefore, was to offer men a group-based seminar, which enabled them:

- To understand their treatment and its side effects, and offer advice regarding side effect management
- To suggest simple lifestyle changes to mitigate longer-term metabolic effects
- To empower men to engage with primary care and take an active part in their monitoring and care

The seminar development

Clinical nurse specialists (CNSs) traditionally carry out counselling about treatments and side effects during one-to-one consultations. Whilst this model has many benefits, it was recognized that a seminar approach would allow access to other experts, and allow patients to share their concerns and anxieties with others in

10.00-10.30	Tea and registration
10.30-11.00	Introduction to Hormone therapy and side effects
11.00-11.45	Staying healthy: Diet
11.45- 12.30	Staying healthy: Exercise
12.30-13.00	Relaxation and stress management
13.00	Questions and close

Figure 1 Timetable for first seminar.

Table 1 Preventative strategies for cardiovascular disease and osteoporosis

Recommendations to prevent bone loss (National Osteoporosis Foundation http://nof.org/learn/prevention accessed 5/2/14)	Recommendations to reduce cardiovascular risk (British Heart Foundation www.bhf.org.uk/heart-health/prevention/healthy-eating.aspx accessed 5/2/14)
Men older than 50 years: calcium 1200 mg/d and vitamin D3 800–1000 IU/d DXA scan monitoring Treat osteoporosis with bisphosphonates (alendronate or zoledronic acid) Consider treating patients with osteopenia and other risk factors (FRAX) –10-year probability of hip fracture $\geq 3\%$ –10-year probability of major osteoporosis-related fracture $\geq 20\%$ Encourage cardiovascular and weight-bearing & resistance exercise Limit alcohol and caffeine consumption Smoking cessation	<p>Eat healthily</p> <ul style="list-style-type: none"> plenty of fruits and vegetables plenty of starchy foods such as bread, rice, potatoes and pasta. Choose wholegrain varieties wherever possible some milk and dairy products some meat, fish, eggs, beans and other non-dairy sources of protein only a small amount of foods and drinks high in fats and/or sugar. <p>Be physically active Smoking cessation Reduce alcohol consumption Maintain a healthy weight Keep blood pressure, diabetes and cholesterol under control</p>

Table 2 Lifestyle measure in the management of Cardiovascular and osteoporosis risk

Lifestyle measure	Osteoporosis	Cardiovascular disease/ metabolic syndrome
DIET	Diet high in calcium and vitamin D	Diet low in saturated fats and high in fibre
EXERCISE	Resistance exercise	Aerobic exercise
WEIGHT	Healthy BMI	Healthy BMI
SMOKING	Advise smoking cessation	Advise smoking cessation
ALCOHOL	Moderate intake	Moderate intake

BMI, body mass index.

a similar situation, Group seminars have been used successfully within the department for some time to deliver information to patients about to undergo radical prostatectomy and had been positively evaluated by attendees (Kinsella *et al.*, 2012)

A seminar was developed by the CNS in Advanced Prostate Cancer to educate men with metastatic prostate cancer on ADT and its side effects, prevention and management (Figure 1). Men on ADT were identified and invited to attend the seminar by mail, at outpatient appointments, through fliers in the urology and oncology departments and through the existing patient support group.

The seminar was planned initially as a half-day event and subsequently as a full-day event, and took place on a separate day to scheduled outpatient visits in a

11.30-12.00	Tea and registration
12.00-12.30	Introduction to Hormone therapy and side effects
12.30- 12.45	Managing hot flushes
12.45-13.15	Managing mind and mood changes
13.15-13.40	Erection dysfunction
13.40- 1355	Ask the panel
13.55- 14.25	Break for refreshments
14.25- 15.10	Staying healthy: Exercise
15.10-15.55	Staying healthy: Diet
15.55-16.10	Tea/coffee
16.10-16.30	Finance and benefits
16.30-1700	Relaxation and stress management
17.00	Questions and close

Figure 2 Sample timetable for subsequent seminars.

non-clinical area. The first session of the seminar was delivered by the CNS and discussed cancer, the role of testosterone in health and the role of testosterone in prostate cancer and the rationale for ADT, along with common side effects.

The following sessions held by a dietician and physiotherapists looked at the role of diet and exercise in maintaining good cardiac and bone health along with the need to engage with primary care in monitoring cardiac risk factors. Preventative strategies for both cardiovascular disease and osteoporosis were gathered from the National Osteoporosis Foundation and the British Heart Foundation (Table 1). The common lifestyle strategies are shown in Table 2 and were integrated into these lifestyle sessions.

Finally, a therapist from the cancer information centre talked about managing stress, concluding with a relaxation exercise.

The seminar was evaluated with a patient questionnaire and the attendees were asked to suggest other topics that they would like to see included in the programme. The content was subsequently expanded to include specific side effect management (hot flushes and erectile dysfunction) and an interactive session on mood and mind changes delivered by a psychologist. This session explored the cognitive changes associated with ADT and the impact and coping mechanisms for the groups. Finally, a session covering advice about finance and benefits was added (Figure 2). The

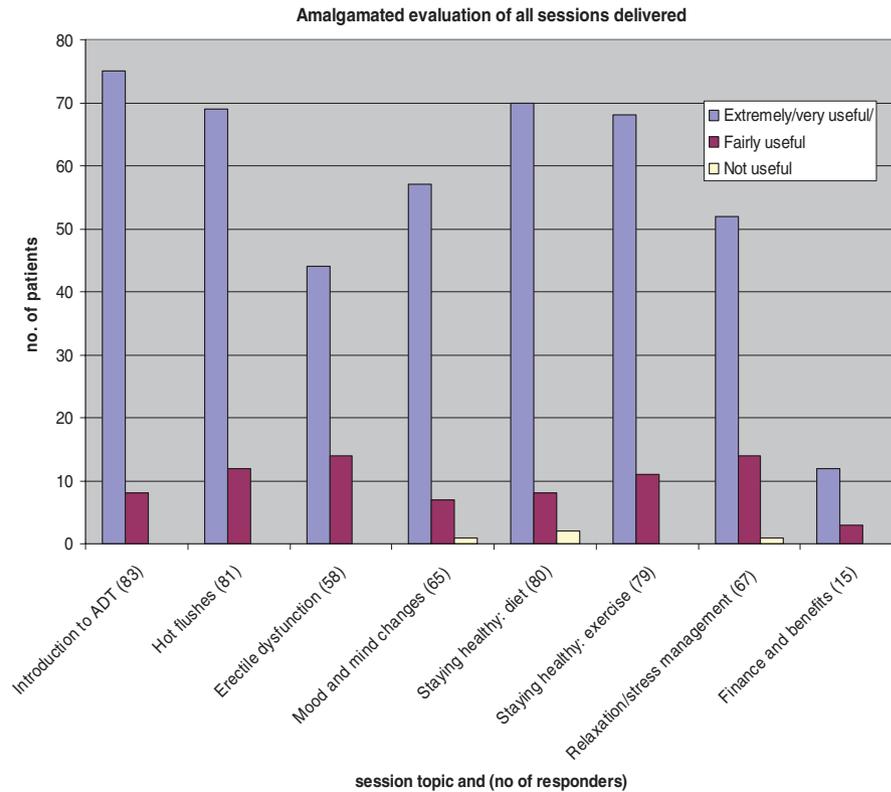


Figure 3 Evaluation of all sessions delivered.

second, third and fourth seminars were similarly evaluated by patients, with additional questions exploring whether responders felt that their behaviour (diet and exercise) would change as a result of attending the seminar

Evaluation

A total of 101 men and 18 partners have attended the seminars, and 83 evaluations were completed (74 men with prostate cancer and 9 partners)

- The first seminar: 20 men and 5 partners attended and 18 attendees completed evaluation forms (15 patients and 3 friends/partners).
- The second seminar: 22 patients and 4 partners attended and 19 attendees completed evaluation forms (17 patients and 2 friends/partners)
- The third seminar: 25 men and 5 partners attended and 21 attendees completed evaluation forms (19 patients and 2 friends/partners)
- The fourth seminar: 34 men and 4 partners attended and 25 attendees completed evaluation forms (23 patients and 3 friends/partners)

Responders were asked to rate how useful they found each session. The results for the four seminars are shown in Figure 3. Of the responses received, the

majority found the sessions extremely or very useful. A small number of responders added comments that some sessions were not personally relevant to them (e.g. erectile dysfunction or finance) but they were happy for them to be included on the programme. Attendees were also asked to rate whether they felt that the lifestyle sessions on diet and exercise would make them change the way that they ate or exercised. Whilst this does not measure actual change, the majority of responders again felt that the sessions would or might encourage them to change the way they ate and exercised (Figure 4).

Importantly, all responders said that they would recommend the seminar to other men on ADT. Attendees were also encouraged to offer free-text comments about the seminars. Comments included: 'Great stuff', 'This has put years on my life expectancy', 'Excellent – I would recommend to everyone', and 'I understand so much more about my treatment and feel much less scared now'

CONCLUSION AND IMPLICATIONS FOR PRACTICE

Attendance at the seminar is recorded in the patient's electronic notes. This is then referenced at subsequent

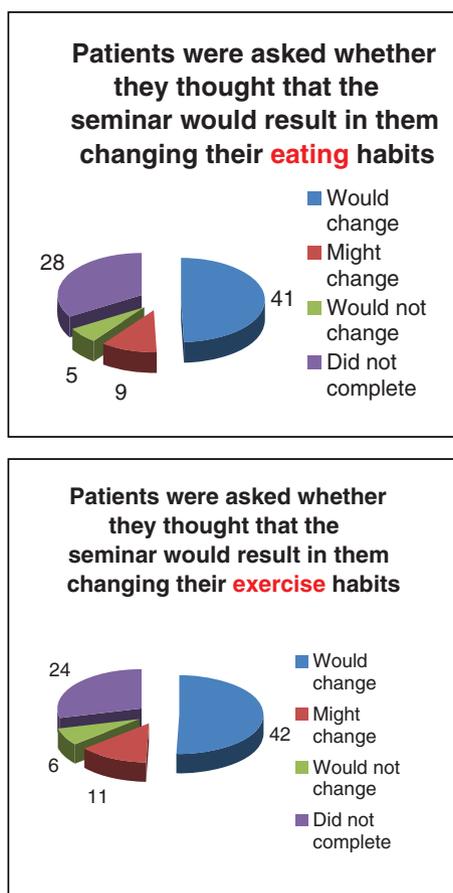


Figure 4 Rating whether sessions would result in behaviour change.

clinic visits and progress towards diet and exercise targets explored, along with targeted questions about engagement with primary care for blood pressure and cholesterol monitoring. It is recognized that some men may benefit from further one-to-one support. The seminar introduces men to both the issues affecting them and the specialist professionals and services available, and men are encouraged to ask for referral for further tailored help, if required. Attendance is also communicated to GPs, along with information about risk factors associated with ADT to encourage partnership between men and their primary care team.

The seminars were well attended and evaluated and have evolved with patient feedback. The service continues to develop and aims to be offered to all men treated with ADT once established on treatment. We are also considering introducing a support group specifically for men with advanced prostate cancer as many attendees have specifically requested more sessions. Further work is required to evaluate whether lifestyle classes result in long-term behavioural change in patients.

ADT adversely affects quality of life, and these seminars may be one method to empower men to improve their long-term health, and their experience of living with ADT. As we know more and more about the long-term toxicities and metabolic effects of ADT, we cannot ignore the health education needs of this group of men.

WHAT IS KNOWN ABOUT THIS TOPIC

- Androgen deprivation therapy (ADT) is the mainstay of treatment for men with advanced prostate cancer but can cause distressing side effects, which adversely affect quality of life.
- The long term metabolic effects of ADT can affect cardiovascular risk factor and bone health and may lead to long term morbidity.

WHAT THIS PAPER ADDS

- This paper discusses and evaluates a practical, seminar based service development to help men understand their treatment and its side effects, to deliver lifestyle advice and promote self efficacy and engagement with treatment and health.

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