

Louisa Fleure Prostate Cancer ANP Guys and St Thomas NHS Trust

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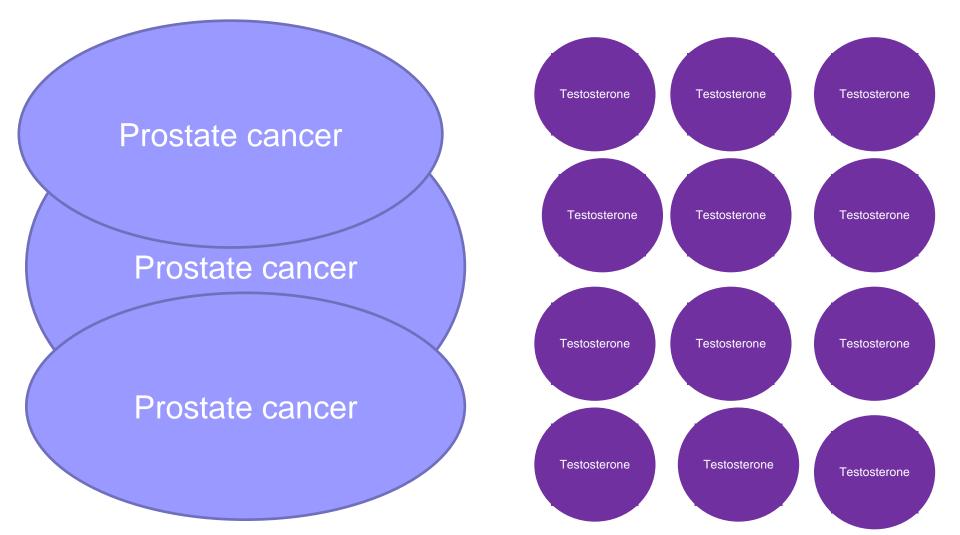
Objectives

- To gain an understanding of ADT and why and how is it used
- To review side effects of ADT and their management
- To review the metabolic effects of ADT
- To review the patient experience on ADT
- To examine how to support patients on ADT
- To review the nursing role in the care of men on ADT

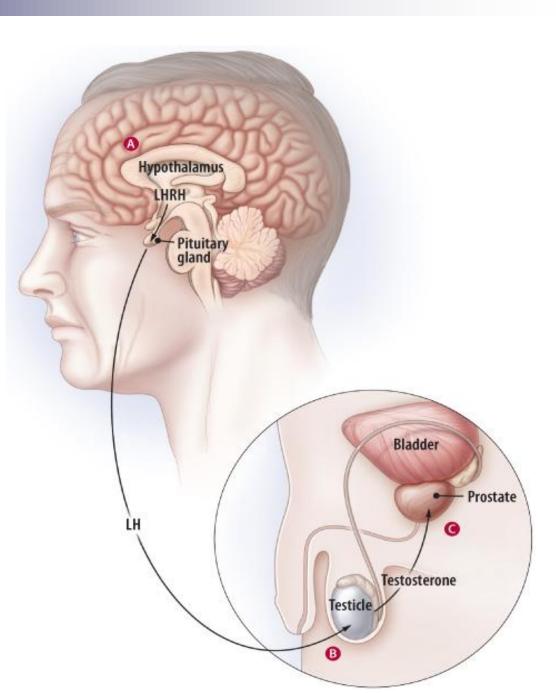
Advanced prostate cancer

- Over 41,000 men are diagnosed each year with prostate cancer in the UK and up to 20% of these will be diagnosed at an advanced stage (Cancer Research UK 2014)
- Metastatic prostate cancer is not curable but may be controlled, often for many years
- In 1941, Huggins and Hodges described the androgen dependence of prostate cancer
- Showed that castrated and oestrogens slowed prostate cancer growth
- The newer treatments now available to men with castration resistant prostate cancer (CRPC) mean that many men are living longer on treatment

Testosterone and prostate cancer



Testosterone production



Hormonal treatments used in the UK

- Surgical castration
- Anti-androgens



LHRH antagonists



LHRH agonists







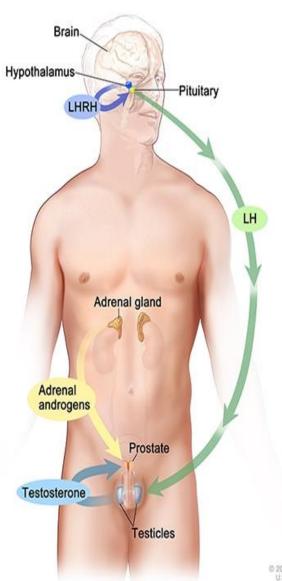
Medical castration

LHRH agonist

- Cause an initial surge in luteinizing hormone (LH), follicle-stimulating hormone (FSH) and, subsequently, testosterone
- Continued overstimulation receptors causes down-regulation
- Leads to castrate levels of testosterone.

LHRH antagnoist

Block LHRH-R signalling causing a rapid and sustained inhibition of testosterone, LH and FSH.



Anti-androgens

- Oral compounds classified as:
 - □ steroidal, e.g. cyproterone acetate (CPA),
 - non-steroidal e.g. nilutamide, flutamide and bicalutamide
- Both compete with androgens at the receptor level which lead to an unchanged or slightly elevated testosterone level (ie not castration based therapies)
- The anti-androgen pharmacological side-effects are mainly gynaecomastia (70%) and breast pain (68%)
- Offers bone protection compared with LHRH analogues and probably LHRH antagonists

EAU Guidelines 2015

Anti-androgen monotherapy

- A meta-analysis of eight trials that compared antiandrogens alone with medical or surgical castration found a trend toward shorter overall survival with antiandrogen monotherapy compared with castration that approached, but did not reach, statistical significance (HR 1.22, 95% CI 0.99-1.40) *
- Used principally as an anti flare agent, for MAB or in patients unwilling to accepts sexual side effects of castration based therapies

*Seidenfeld J, Samson DJ, Hasselblad V, et al. Single-therapy androgen suppression in men with advanced prostate cancer: a systematic review and meta-analysis. Ann Intern Med 2000; 132:566.

Aims of ADT

- Although androgen deprivation therapy (ADT) is a palliative, not curative it can:
 - normalize serum levels of prostate specific antigen (PSA) in over 90 percent of patients
 - produce objective tumour responses in 80 to 90 percent.
 - This antitumour activity can improve quality of life (QOL) by reducing bone pain as well as the rates of complications (eg, pathologic fracture, spinal cord compression, ureteral obstruction).

ADT: the evidence

Efficacy of initial ADT

- STAMPEDE: An analysis included data from 917 men with metastatic disease managed with ADT alone with a median follow-up of 20 months.
- □ The median failure-free survival duration following ADT was 20 months
- The median overall survival was 42 months*
- Serum testosterone level The objective of ADT is to lower the serum testosterone level at least to the same extent as that achieved with surgical orchiectomy**
- Historically, this has correlated with a level of 1.7 nmol/L (<50 ng/dL), although contemporary laboratory testing indicates that testosterone levels decline to 0.7 nmol/L (<20 ng/dL) after orchiectomy***

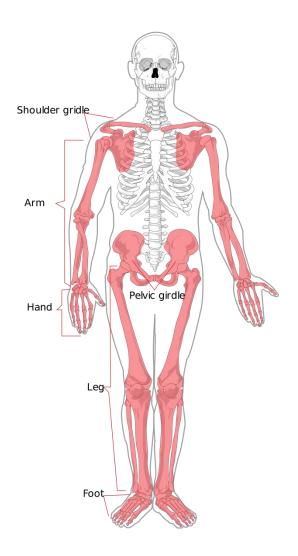
^{*} James ND, Spears MR, Clarke NW, et al. Survival with Newly Diagnosed Metastatic Prostate Cancer in the "Docetaxel Era": Data from 917 Patients in the Control Arm of the STAMPEDE Trial (MRC PR08, CRUK/06/019). Eur Urol 2014.

^{**} Djavan B, Eastham J, Gomella L, et al. Testosterone in prostate cancer: the Bethesda consensus. BJU Int 2012; 110:344.

^{**} Oefelein MG, Feng A, Scolieri MJ, et al. Reassessment of the definition of castrate levels of testosterone: implications for clinical decision making. Urology 2000; 56:1021.

Prognostic factors

- SWOG 8894 trial**
 - Performance status (poorer prognosis if PS<1)</p>
 - □ Gleason score (poorer prognosis if Gleason>8)
 - Site of metastases (axial vs appendicular or visceral)
 - Presenting PSA (poorer prognosis if PSA >65ug/l)



*Glass TR, Tangen CM, Crawford ED, et al. Metastatic carcinoma of the prostate: identifying prognostic groups using recursive partitioning. J Urol 2003 Jan;169(1):164-9

Prognostic factors

PSA level after 7 months of ADT may lead to 3 groups with very different survival expectancy**. Median survival is:

75 months if the PSA level < 0.2 ng/mL,
44 months if the PSA < 4 ng/mL
13 months if the PSA is > 4 ng/mL [571]

**Hussain M, Tangen CM, Higano C, et al. Absolute prostate-specific antigen value after androgen deprivation is a strong independent predictor of survival in new metastatic prostate cancer: data from Southwest Oncology Group Trial 9346 (INT-0162). J Clin Oncol 2006 Aug;24(24):3984-90

Prognostic factors

- There may be a relationship between suppression of the serum testosterone and clinical outcome***
 - The risk of dying lowest in those with the greatest suppression of serum testosterone in the first year
 - Compared with a first year minimum testosterone nadir <0.7 nmol/l:</p>
 - Men with a nadir testosterone of 0.7 to 1.7 nmol/L had an increased risk of dying (hazard ratio [HR] 2.08, 95% CI 1.28-3.38), as did those a nadir >1.7 nmol/L (HR 2.93, 95% CI 0.77-4.70)
 - Do you check testosterone?

***Klotz L, O'Callaghan C, Ding K, et al. Nadir Testosterone Within First Year of Androgen-Deprivation Therapy (ADT) Predicts for Time to Castration-Resistant Progression: A Secondary Analysis of the PR-7 Trial of Intermittent Versus Continuous ADT. J Clin Oncol 2015.

Timing of ADT

Symptomatic metastases

For patients with symptomatic metastases, androgen deprivation therapy should be initiated promptly, both to palliate symptoms and to prevent severe complications (eg, pathologic fractures, spinal cord compression)

Asymptomatic metastases

- Treatment for metastatic prostate cancer is not curative and treatment-related side effects can adversely affect quality of life. Therefore, a major question remains for asymptomatic patients whether to start therapy as soon as metastatic disease is diagnosed or whether to delay treatment until significant symptoms are present.
- □ Trials not clear. May be balance of risks vs benefits

Diagnosis: The nursing role



- Support around diagnosis
- Holistic Needs Assessment
- Information about disease, prognosis, treatments
- Management of pathways (staging and MDM discussions etc)
- Consideration of treatment options
 - □ Risks and benefits of treatment
 - Consideration of co morbidities
 - □ Lifestyle and preferences
 - Fear of treatment

Androgen deprivation therapy (ADT) and prostate cancer

- The side effects of ADT can be bothersome and distressing for patients and adversely affect quality of life (Decal et al 2006)
- Intolerable side effects may also affect adherence to treatment, forcing some men to abandon treatment or decline it through fear

Dacal, K., Sereika, S. M., & Greenspan, S. L. (2006). Quality of life in prostate cancer patients taking androgen deprivation therapy. Journal of American Geriatric Society, 54, 85-90

TARGET ORGANS OF TESTOSTERONE

Skin hair growth, balding, sedum production

Liver

synthesis of serum proteins

Male Sexual

Organs

penile growth spermatogenesis prostate growth and function

Bone

accelerated linear growth closure of epiphyses Brain libido, mood

Muscle

increase in strength and volume

Kidney

stimulation of erythropoietin production

Bone Marrow stimulation of stem cells



ADT side effects

Body feminisation

- Genital shrinkage
- Gynecomastia
- Mastodynia
- Weight gain/ body fat redistribution
- Loss of muscle mass
- Loss of body hair
- Hot flushes

Sexual changes

- Erectile dysfunction
- Loss of sexual interest
- Genital shrinkage
- Fatigue
- Orgasm/ ejaculation changes

Cognitive and affective disturbances

- Depression
- Impaired memory and attention
- Fatigue
- Increased emotionality and tearfulness

Metabolic changes

- Risk of developing osteoporosis
- Subsequent increased risk of fracture and associated morbidity and mortality
- Weight gain (mostly as fat)
- Risk of developing insulin resistance
- Increased risk of cardiovascular disease and diabetes



Side effects: The nursing role

- Education about side effects
- Healthy lifestyle advice
- Side effect management
- Support
- Managing non adherence



Approaches to toxicities

- Ignore the problem?
- Minimise the problem?
- Fix the problem?
- Minimise impact?
- Help adapt to change?
- A combination of some of the above?



Managing toxicities and holistic support for men with advanced disease



Assessment and asking the questions

- In consultations
- Support groups
- Seminars/ health and well being events
- Holistic needs assessment



Holistic Needs Assessment

INSTRUCTIONS: For each item below, please tick YES or NO if they have been a concern for you during the past week (including today). Please also tick DISCUSS if you wish to speak about it during your appointment.

Concerns Thermometer		Practical Concerns	Yes	No	Discuss	Physical Concerns	Yes	No	Discuss	
" I am coping well"		Caring responsibilities				High Temperature				
Yes	No 🗌	Housing or Finances				Wound Care				
		Transport or parking								
Please circle the number		Work or education				Passing Urine				
that best describes how		Information Needs				Constipation or Diarrhorea				
much distress you have						Indigestion				
been feeling in the last		Family Concerns				Nausea or vomiting				
week, including today.		Relationship with children								
Extreme		Relationship with partner				Eating or appetite				
Distress No Distress		Relationship with others				Changes in taste				
	9-					Sore or dry mouth				
	7-	Emotional Concerns								
	6-	Loneliness or isolation				Feeling swollen				
	5-	Sadness or depression				Breathlessness				
	3-	Worry, fear or anxiety				Pain				
	2-	Anger, frustration or guilt				Dry, itchy or sore skin				
		Memory or concentration				Tingling in hands or feet				
		Hopelessness				Hot flushes				
		Difficulty making plans								
		Sexual concerns				Bathing or dressing				
OFFICE USE ONLY						Moving around				
		Spiritual Concerns				Fatigue				
		Loss of faith or other				Sleep problems				
Patient ID:		spiritual concern								
		Loss of meaning or				Communication				
Preferred n	ame:	purpose in life				Personal appearance				
Pathway stage:		Regret about the past				Other medical condition				
Date:						(NCCN Guidelines®) for Distress Management (V.3.				
Staff ID:		Cancer Network, Inc. Available at: NCCN.org. Accessed [25th May 2012] To view the most recent and complete version of the NCCN Guidelines®, go on-line to NCCN.org Additional permissions from Guy's & St Thomas' Charity: Guy's and St Thomas' NHS Foundation Trust. Kings Health Partners Integrated Cancer Centre: The Royal Marsden NHS Foundation Trust.								

Available at: www.londoncanceralliance.nhs.uk/media/20657/hna_lca_final.pdf

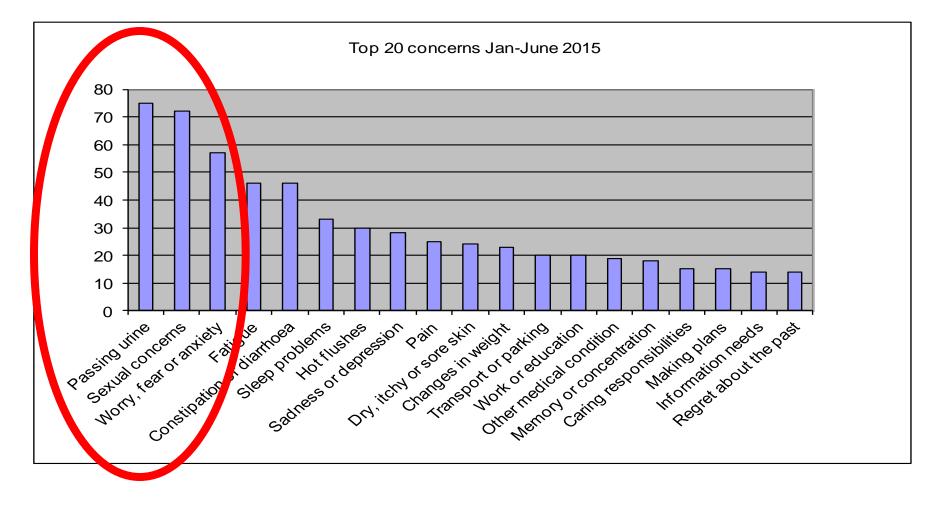
Holistic needs assessment

Your four main conce	erns are: (In discuss	ion with you health professional)
1.	,	
2.		
3.		
4.		
4.		
Would you like help	with these?	
	No 🗆	
Yes 🗆		
Would you be interes	sted in any complem	entary therapy e.g. massage, reflexology?
	• •	entary merapy e.g. massage, renexblogy:
Yes 🗆	No 🗆	
Would you like furthe	r information on:	
	Emotional/psychol	• • • • • • • • • • • • • • • • • • • •
	Yes □	No 🗆
	Benefits	
		N -
	Yes □	No 🗆
	Support Groups	
	Yes D	No 🗆
ls there anything els	a about which you w	ould like information?
Yes 🗆 No 🗆		

HNAs

- Not ADT or prostate specific
- But does cover broadly sexual issues, relationship issues, cognitive changes
- May provide a framework
- Focus on effects of treatment (patient focus rather than disease)

Concerns reported in HNAs



Assessing the impact

- People vary greatly on how they interpret physical side effects.
- What is worse?
 - Hair loss?
 - □ Gynecomastia?
 - Mastalgia?
 - □ Erectile dysfunction?
 - □ Loss of libido?
 - Loss of mental sharpness
 - □ Weight gain?



No validated questionnaire or survey instrument that can be used to predict who will find which changes most and least distressing.

ADT and holistic support for men with advanced disease

Giving information and support

When
Where
How
How often
Different for all



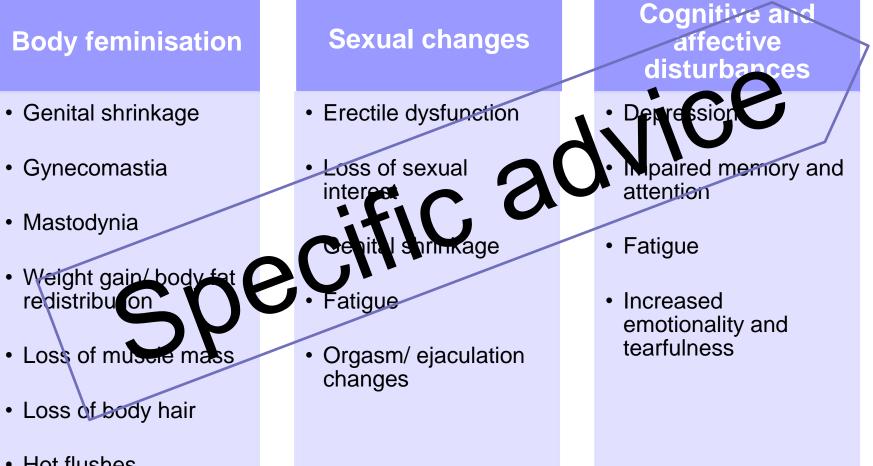
ADT and holistic support for men with advanced disease

- Health and wellbeing
 - 🗆 Diet
 - Exercise
 - Benefits include metabolic but also psychological
 - Relaxation
 - Stress management

Referral when

- necessary
 - Psychologist
 - Dietician
 - Physiotherapist
 - 🗆 Chaplain
 - Local groups

ADT side effects



Hot flushes

Metabolic changes

- Dyslipidaemia
- Insulin resistance & Diabetes
- Obesity (central fat and loss of muscle mass)
- Osteoporosis

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			

Recommendations to Prevent Bone Loss (National Osteoporosis Foundation <u>http://nof.org/learn/prevention</u> accessed 5th February 2014) Recommendations to reduce cardiovascular risk (British Heart Foundation <u>www.bhf.org.uk/heart-health/prevention/healthy-eating.aspx</u> accessed 5th February 2014)

NICE 2014 Osteoporosis

- Do not routinely offer bisphosphonates to prevent osteoporosis in men with prostate cancer having androgen deprivation therapy
- Consider assessing fracture risk in men with prostate cancer who are having androgen deprivation therapy, in line with Osteoporosis (NICE clinical guideline 146)
- Offer bisphosphonates to men who are having androgen deprivation therapy and have osteoporosis
- Consider denosumab for men who are having androgen deprivation therapy and have osteoporosis if bisphosphonates are contraindicated or not tolerated

Body feminization

The American Cancer Society claims that..."Men who no longer have their testicles or who are on hormone therapy drugs often feel like 'less of a man.' This is a myth. Manhood does not depend on hormones, but on a lifetime of being male."

From: Sexuality and Cancer: For the man who has cancer and his partner. American Cancer Society, 2009.

Body feminization

 ADT often challenges men's core identity, leaving many...feeling like they are at the border of masculinity: not fully masculine nor feminine, but undefined

> "Whenever I saw my body, I wondered, 'Who am I? A woman? A man? It's a very confusing situation. I believe I'm neither one thing nor another; that's the only way I can think about myself without becoming confused. To tell the truth, at first, every time I looked at myself [in the mirror] I became depressed."

Navon L & A Morag (2003) Advanced prostate cancer patients' ways of coping with the hormonal therapy's effect on body sexuality and spousal ties. *Qualitative Health Research*,13:1378-1392.

Body feminization

- Listen for the cues
- Acknowledge
- Listen
- Assess impact
- Adaptation, acceptance and some problem solving

Body feminization

Gynaecomastia and	Preventive management through radiation treatment
mastodynia	Binding/camouflage
	 Selective oestrogen receptor modulators (e.g. tamoxifen)
	Mastectomy/liposuction
Weight gain and loss	 Increased physical activity
of muscle mass	 Also may have impact on mood
Hot flushes	Identifying and modifying trigger factors
	Medroxyprogertserone, SSRIs, venlafaxine,
	Diaphragmatic breathing/paced respiration
	Visualisation/ relaxation
Genital shrinkage	 Pharmacological and physical ED treatments

NICE 2014 Hot flushes

- Offer medroxyprogesterone (20 mg per day), initially for 10 weeks, to manage troublesome hot flushes caused by long-term androgen suppression and evaluate the effect at the end of the treatment period
- Consider cyproterone acetate or megestrol acetate[6] (20 mg twice a day for 4 weeks) to treat troublesome hot flushes if medroxyprogesterone is not effective or not tolerated
- Tell men that there is no good-quality evidence for the use of complementary therapies to treat troublesome hot flushes.

Triggers



Common triggers include:

□ Spicy food

- Alcohol
- Caffeine

□ Stress

Smoking

Hot rooms and hot weather

Managing your environment

- Sip cold or iced drinks
- Dress in layers, so you can take clothes off as you get warmer.
- Wear cotton, linen or rayon, rather than synthetic fabrics or wool.
- Avoid polo neck tops and wear open-neck shirts where possible.
- Keep your home cool. Turn down the heating or use a fan. You may also find it helpful to carry a hand held battery operated fan when you go out. Even cheap paper fans can help.
- Wear cotton pyjamas or a nightshirt. If you perspire a lot at night, your nightclothes are easier to change than the sheets.
- Use cotton sheets only, not synthetics
- Take a cool or lukewarm shower before bed instead of a hot one.
- Use of a cooling pillow insert, such as a "Chillow Pillow"
- Put a towel on your bed if you sweat a lot at night

Smoking

- If you smoke, try to stop. Help is available to everyone free on the NHS
- Please ask your nurse or doctor t refer you to the Smoking Cessation Programme, or see your GP or local pharmacist
- You can also contact the National Quitline on

0800 169 0169

Managing stress

- Many people notice that stress can increase the frequency and severity of their hot flushes.
- There are various ways to reduce stress including relaxation exercises, massage and meditation.
- Complementary therapies include aromatherapy and reflexology, relaxation and stress management courses
- These services are free of charge for cancer patients and their carers
- Some small studies have suggested that acupuncture may also be helpful

Managing the impact

- Speak to other men
- Counselling
- Relaxation, breathing, visualisation



May get better with time

NICE 2014 Gynaecomastia

- For men starting long-term bicalutamide monotherapy (longer than 6 months), offer prophylactic radiotherapy to both breast buds within the first month of treatment.
- If radiotherapy is unsuccessful in preventing gynaecomastia, weekly tamoxifen should be considered.

Sexual changes with ADT

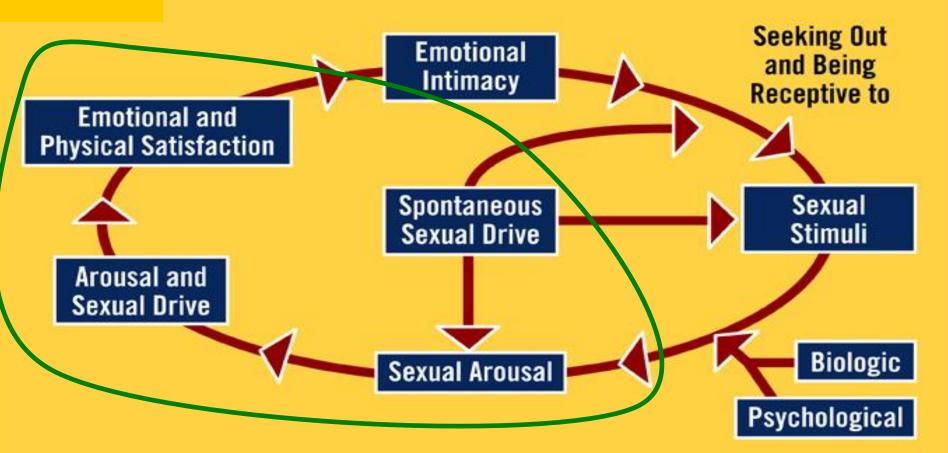
- Most men on ADT experience nearly complete loss of sexual interest.
- ~15% still report being sexually active at some level—and are capable of having orgasms even without erections
- Sole focus on erections is unlikely to be successful and may make problem worse
- Communication: what do you want?
- Adaption to change and acceptance
- Moving forward



NICE 2014 sexual dysfunction

- Before starting androgen deprivation therapy, tell men and, if they wish, their partner, that long-term androgen deprivation will cause a reduction in libido and possible loss of sexual function
- Advise men and, if they wish, their partner, about the potential loss of ejaculation and fertility associated with long-term androgen deprivation and offer sperm storage.
- Ensure that men starting androgen deprivation therapy have access to specialist erectile dysfunction services.
- Consider referring men who are having long-term androgen deprivation therapy, and their partners, for psychosexual counselling
- Offer PDE5 inhibitors to men having long-term androgen deprivation therapy who experience loss of erectile function
- If PDE5 inhibitors fail to restore erectile function or are contraindicated, offer a choice of: intraurethral inserts penile injections penile prostheses vacuum devices.

Sexual Response Cycle



Basson R. Med Aspects Hum Sex. 2001;41-42. Basson R. Human sex-response cycles. J Sex Marital Therapy. 2001;27:33-43. Adapted with permission.

Kingsberg SA, Knudson G.

COMMUNICATION

Recognition that there is a loss which may need to be acknowledged Acceptance that sex no longer part of relationship/life

ge

Adaptat

Erection restoring treatments (but only once above addressed)

Sexual changes

Erectile dysfunction	 Standard pharmacologic and physical ED treatments But an ED treatment that is not fully effective but only partially effective can do more harm than good. It can erode a patient's confidence in his sense of virility and masculine capability Redefinition or reframing of sexual activities (e.g. non-penetrative sexual activity)
	Renegotiated or novel sexuality
Loss of sexual desire	Special effort to enhance displays of physical affection
	Counselling to recruit past sexual fantasies and explore expanding erogenous zones
	Use of erotic material to enhance sexual arousal
Delayed or absent orgasm	Use of lubricants for increased stimulation without skin irritation
	Use of vibrator/sex toys to combat fatigue
	Reframing of the sexual experience — shared intimacy rather than focus only on reaching orgasm (sensate focus)
Infertility	Assess importance for all patients regardless of age
	Sperm banking for those interested

Sexual changes: our issues

- Health professionals willingness to discuss
- Embarrassment of lack of knowledge
- The setting in which these ideas are presented to them (i.e., in a clinic room, in a sexual function clinic, or at a non-clinical sex workshop)
- May be appropriate to refer for specialist psychosexual counselling for advice and also regarding adapting to change

Cognitive and affective symptoms

Depression	
Changes in emotionality	CounsellingExercise
Tension, anxiety, fatigue and irritability	Pharmacological therapiesSupport (peer, family, professional)
Decline in spatial reasoning, spatial abilities and working memory	Relaxation and stress management techniques

NICE 2014 Fatigue

- Tell men who are starting androgen deprivation therapy that fatigue is a recognised side effect of this therapy and not necessarily a result of prostate cancer
- Offer men who are starting or having androgen deprivation therapy supervised resistance and aerobic exercise at least twice a week for 12 weeks to reduce fatigue and improve quality of life

ADT and holistic support for men with advanced disease

Giving information and support

When
Where
How
How often
Different for all



The issues we faced

- Most education and support was being given 1:1 in consultations or over the phone
- Often in the context of a nurse led clinic also dealing with treatment response or disease progression
- Information not always retained
- Referrals often not taken up



Is there another additional way to deliver information and support?

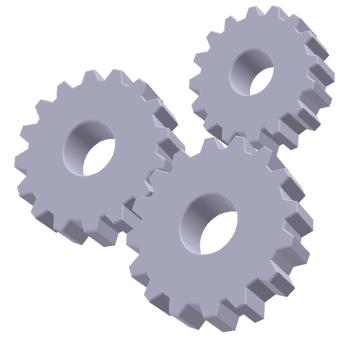
- Pre treatment seminars already running
- Support group well established
- Patients responded positively to the idea

- Somewhere away from a "clinic setting" where we met men as delegates rather than patients
- A focus on living well rather than disease



Aims of the seminar

- To understand 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

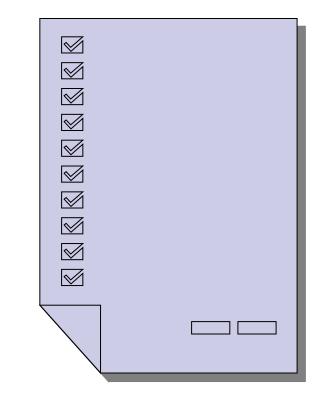


09.30-1000	Tea and registration
10.00-10.30	Introduction to Hormone therapy and side effects
10.30-11.00	Managing hot flushes
11.00-11.30	Erectile dysfunction
11.30-11.50	Tea break
11.50-12.35	Managing mood and mind changes
12.35-12.50	Trials and the biobank
12.50-13.00	Ask the Panel
13.00-13.45	Lunch
13.45-14.15	Staying healthy: Diet
14.15- 14.45	Staying healthy: Exercise
14.45-15.15	Finance and benefits
15.15-16.00	Tea/coffee
16.00-16.30	Hormone therapywhat comes next?
16.30-17.00	Relaxation and stress management
17.00	Questions and close

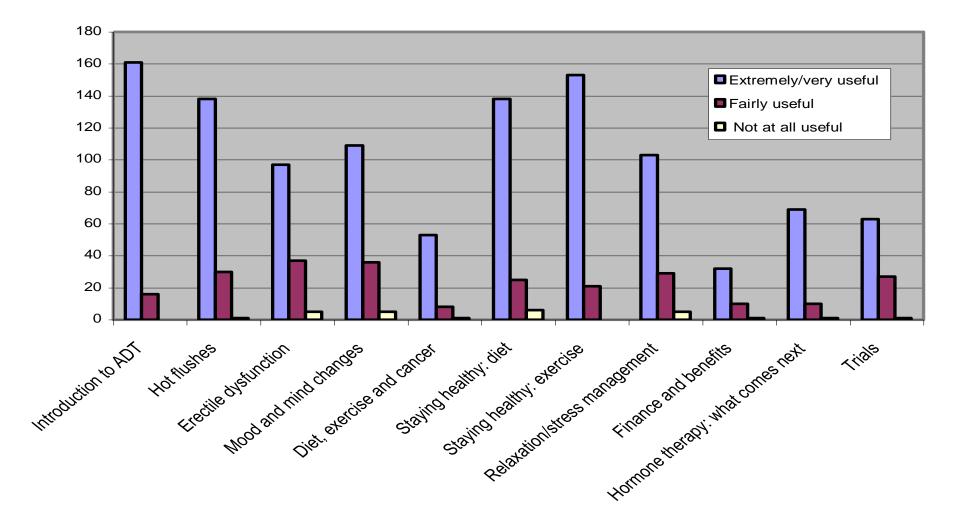
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Evaluation

- A total of 191 men and 45 friends/partners have attended the seminars
- 180 evaluations were completed (157 men with prostate cancer and 23 partners)

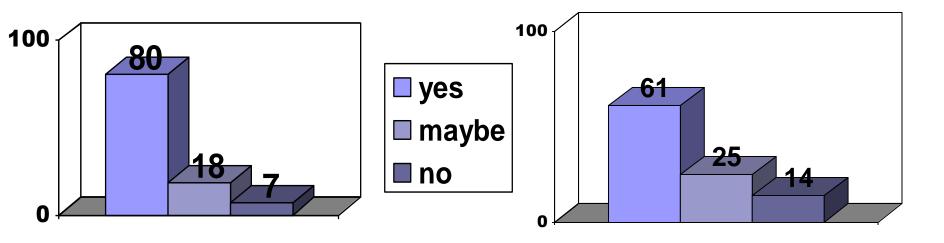


Evaluation of sessions



Evaluation: making changes

- Patients were asked whether they thought that the seminar would make them change their exercise habits
- Patients were asked whether they thought that the seminar would make them change their diet



All responders said that they would recommend the seminar to other men on ADT.

I am so glad that there are things I can do to feel better

Excellent- I would recommend to everyone

I understand so much more about my treatment and feel much less/ scared now/

I was too embarrassed to ask questions myself but I was able to listen to all the other men and learnt so much

I cried when I heard that other people were going through the same things everyone should have as we were

I think

this at the

start of

treatment

This has put years on my *life expectancy*

ADT and the nursing role



Key principles in managing side effects

- Be proactive
- Be aware of cues and respond to them
- Affects more than the man (remember the wider network including partners and family)
- Different people need different approaches: do we have different models of support and help?
- Think about timing, setting and delivery of your information
- Be truthful yet positive

Summary

- ADT is an important treatment for advanced prostate cancer
- It is important to understand the rational for use and it's risks and benefits
- ADT side effects can affect the way a man views his whole self, so needs a whole person approach
- May involve strategies to promote adaptation to change just as much as quick fixes



