Restore the Man

Your Clinical Update on Men's Health

- Thursday 21st June 2012
- Nottingham Belfry Hotel

- Summary of Speaker Presentations

The State of Men's Health in 2012

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Crewe and Macclesfield Hospitals
Senior Research Fellow, Manchester University
Visiting Tutor, St Peters College Oxford

Aims of Testosterone Replacement Therapy (TRT)

- **The primary aim of testosterone replacement therapy is**
  - to return testosterone levels of hypogonadal men back to the normal range
  - to alleviate the symptoms of testosterone deficiency syndrome

- **There are also potential secondary clinical benefits of testosterone replacement therapy when used in symptomatic hypogonadal men**

Life Expectancy

- Men tend to take more risks with their health than women and to consult their doctors less
- Women continue to live longer than men, but the gap has been closing
- Both sexes have shown annual improvements in life expectancy
- But - over the past 27 years the gender gap has narrowed from 6.0 years to 4.2 years

Harbingers of doom.....

- **ED is a marker for CVD, metabolic syndrome and type 2 diabetes**
- **ED is an early marker for Endothelial Dysfunction**
- **ED if ignored can lead to an Early Death**

Pegge NC et al. *Diabet Med* 2006; 23:873-8

TDS is associated with increased mortality

Shores MM et al. *Arch Int Med* 2006;166:1660-5

The Message

- Hypogonadism is a risk factor for cardiovascular disease and for premature death
- Ideally compare current with previous androgen levels
- Estimation of **free** testosterone may be appropriate in South Asian men (given lower SHBG)
- Total testosterone lower in type 2 vs type 1 diabetes
- Late-onset hypogonadism can be defined by the presence of at least three sexual symptoms associated with a total testosterone level of less than 11 nmol/L and a free testosterone level of less than 220 pmol/L (Wu NEJM)

Linking ED, Testosterone and Cardiovascular Disease

Graham Jackson

Consultant Cardiologist

Guy's & St Thomas' Hospital, London, UK.

CONSENSUS

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Erectile dysfunction and coronary artery disease prediction: evidence-based guidance and consensus

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SUMMARY

- A significant proportion of men with erectile dysfunction (ED) exhibit early signs of coronary artery disease (CAD), and this group may develop more severe CAD than men without ED (Level 1, Grade A).
- The time interval among the onset of ED symptoms and the occurrence of CAD symptoms and cardiovascular events is estimated at 2–3 years and 3–5 years respectively; this interval allows for risk factor reduction (Level 2, Grade B).
- ED is associated with increased all-cause mortality primarily due to increased cardiovascular mortality (Level 1, Grade A).
- All men with ED should undergo a thorough medical assessment, including testosterone, fasting lipids, fasting glucose and blood pressure measurement. Following assessment, patients should be stratified according to the risk of future cardiovascular events. Those at high risk of cardiovascular disease should be evaluated by stress testing with selective use of computed tomography (CT) or coronary angiography (Level 1, Grade A).
- Improvement in cardiovascular risk factors such as weight loss and increased physical activity has been reported to improve erectile function (Level 1, Grade A).
- In men with ED, hypertension, diabetes and hyperlipidaemia should be treated aggressively, bearing in mind the potential side effects (Level 1, Grade A).
- Management of ED is secondary to stabilising cardiovascular function, and controlling cardiovascular symptoms and exercise tolerance should be established prior to initiation of ED therapy (Level 1, Grade A).
- Clinical evidence supports the use of phosphodiesterase 5 (PDE5) inhibitors as first-line therapy in men with CAD and comorbid ED and those with diabetes and ED (Level 1, Grade A).
- Total testosterone and selectively free testosterone levels should be measured in all men with ED in accordance with contemporary guidelines and particularly in those who fail to respond to PDE5 inhibitors or have a chronic illness associated with low testosterone (Level 1, Grade A).
- Testosterone replacement therapy may lead to symptomatic improvement (improved wellbeing) and enhance the effectiveness of PDE5 inhibitors (Level 1, Grade A).
- Review of cardiovascular status and response to ED therapy should be performed at regular intervals (Level 1, Grade A).

Review Criteria

We performed an extensive search for articles concerning ED and CAD using multiple sources including PubMed, organizational websites and the expertise of the consensus members. All articles were assessed for levels of evidence and graded accordingly.

Message for the Clinic

ED and CAD frequently coexist. ED may be a marker (warning sign) for occult CAD with a window of opportunity for CAD risk reduction of 2–5 years. All men with CAD should be asked about ED as treatment options are safe and effective for the majority. ED is associated with increased all-cause mortality primarily due to increased cardiovascular mortality. Recognizing this link between ED and CAD may improve lives and also save lives.

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[12]Men's Health Center, The Miriam Hospital, Rhode Island and Family Medicine, Warren Alpert School of Medicine of Brown University, Providence, RI, USA

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Disclosures

G. Jackson has conducted lectures for Lilly and Pfizer during the previous 12 months.

Introduction

Erectile dysfunction (ED) is defined as the persistent inability to achieve and then maintain an erection to permit satisfactory sexual intercourse (1). The severity of ED is classified as mild to severe, according to the International Index of Erectile Function (2). Organic ED (i.e. that with an underlying physical aetiology) and coronary artery disease (CAD) are closely linked, as they are both consequences of endothelial dysfunction, leading to restrictions in blood flow (3,4). Similar risk factors have been identified for both conditions, including obesity, diabetes, smoking, hypertension and dyslipidaemia (5–8).

The aim of this study is to explore the hypothesis that ED is a predictor for CAD and review the

Int J Clin Pract
doi: 10.1111/j.1742-1241.2010.02410.x

Recommendation 1

- A significant proportion of men with erectile dysfunction (ED) exhibit early signs of coronary artery disease (CAD), and this group may develop more severe CAD than men without ED

- (Level 1, Grade A).

Recommendation 2

- The time interval among the onset of ED symptoms and the occurrence of CAD symptoms and cardiovascular events is estimated at 2–3 years and 3–5 years
- This interval allows for risk factor reduction
- (Level 2, Grade B).

Recommendation 3

- ED is associated with increased all-cause mortality primarily due to increased cardiovascular mortality
- (Level 1, Grade A).

Recommendation 4

- All men with ED should undergo a thorough medical assessment, including testosterone, fasting lipids, fasting glucose and blood pressure measurement.
- Following assessment, patients should be stratified according to the risk of future cardiovascular events.
- Those at high risk of cardiovascular disease should be evaluated by stress testing with selective use of computed tomography (CT) or coronary angiography (Level 1, Grade A).

Recommendation 5

- Improvement in cardiovascular risk factors such as weight loss and increased physical activity has been reported to improve erectile function
- (Level 1, Grade A).
- Esposito et al 2004, Revnic 2007,

Recommendation 6

- In men with ED, hypertension, diabetes and hyperlipidaemia should be treated aggressively, bearing in mind the potential side effects
- (Level 1, Grade A).

Recommendation 7

- Management of ED is secondary to stabilising cardiovascular function, and controlling cardiovascular symptoms and exercise tolerance should be established prior to initiation of ED therapy
- (Level 1, Grade A).

Recommendation 8

- Clinical evidence supports the use of phosphodiesterase 5 (PDE5) inhibitors as first-line therapy in men with CAD and co-morbid ED and those with diabetes and ED
- (Level 1, Grade A).
- PDE5Is are contra-indicated in patients taking nitrates and where the cardiac condition precludes sexual activity.

Recommendation 9

- Total testosterone and selectively free testosterone levels should be measured in all men with ED in accordance with contemporary guidelines and particularly in those who fail to respond to PDE5 inhibitors or have a chronic illness associated with low testosterone
- (Level 1, Grade A).

Recommendation 10

- Testosterone replacement therapy may lead to symptomatic improvement (improved wellbeing) and enhance the effectiveness of PDE5 inhibitors
- (Level 1, Grade A).

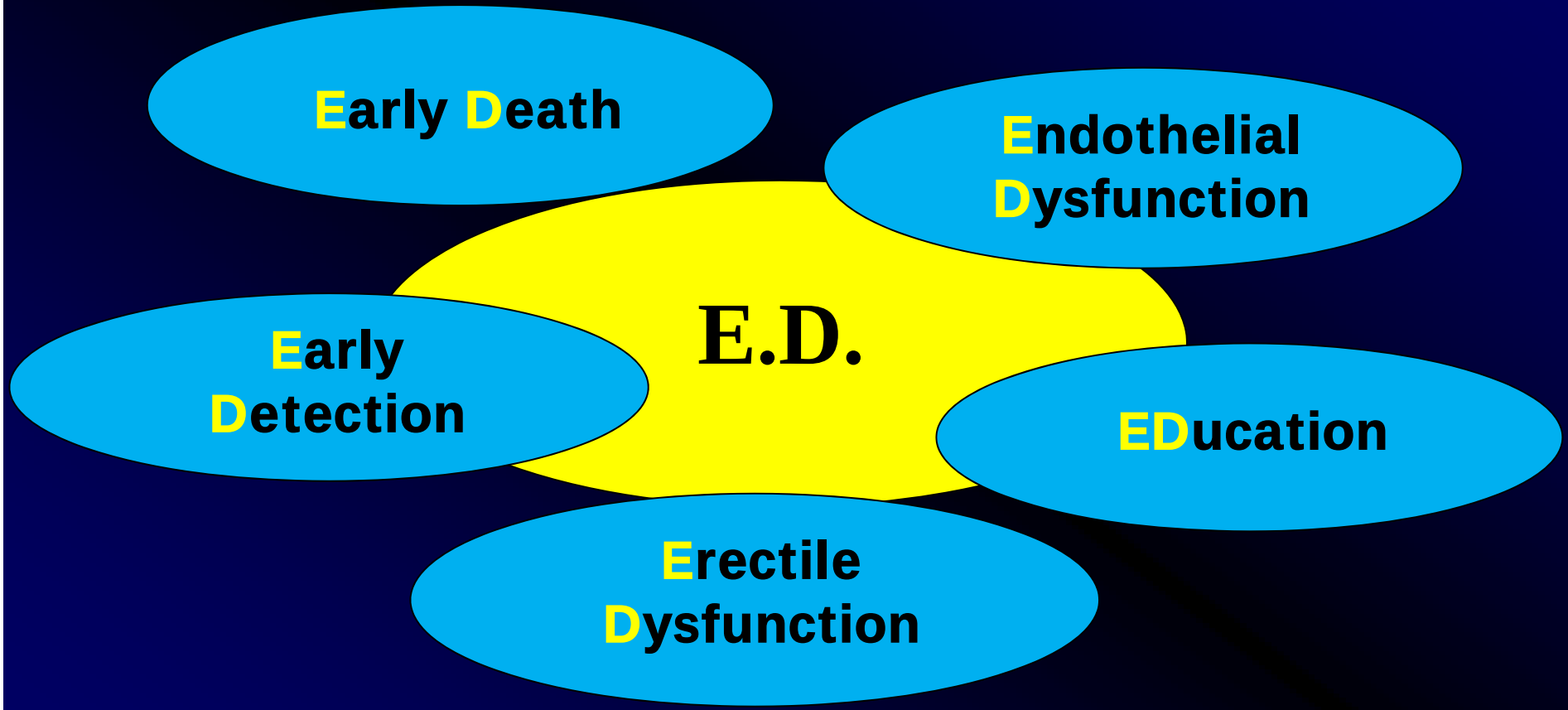
Recommendation 11

- Review of cardiovascular status and response to ED therapy should be performed at regular intervals
- (Level 1, Grade A).

Conclusion

- ED is a cardiovascular equivalent
- We have a time window of 2-5 years to reduce the risk
- Getting it right involves team work between the family doctor, nurse, diabetologist, sexologist, urologist and cardiologist

Take Home Message



Guidelines
and
how do we use them in day to day practice?

Dr. Adrian Heald

Consultant Endocrinologist

Available Guidelines

Bhasin S *et al*.

Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline

J Clin Endocrinol Metab 2010;**95**:2536-2559

Wang C *et al*.

Investigation, Treatment, and Monitoring of Late-Onset Hypogonadism in Males: ISA, ISSAM, EAU, EAA and ASA Recommendations

J Androl 2009;30:1-9

Hatzimouratidis K *et al*.

Guidelines on Male Sexual Dysfunction: Erectile Dysfunction and Premature Ejaculation

Eur Urol 2010;57:804-814

British Society of Sexual Medicine Guidelines on Management of Sexual Problems in Men: The Role of Androgens

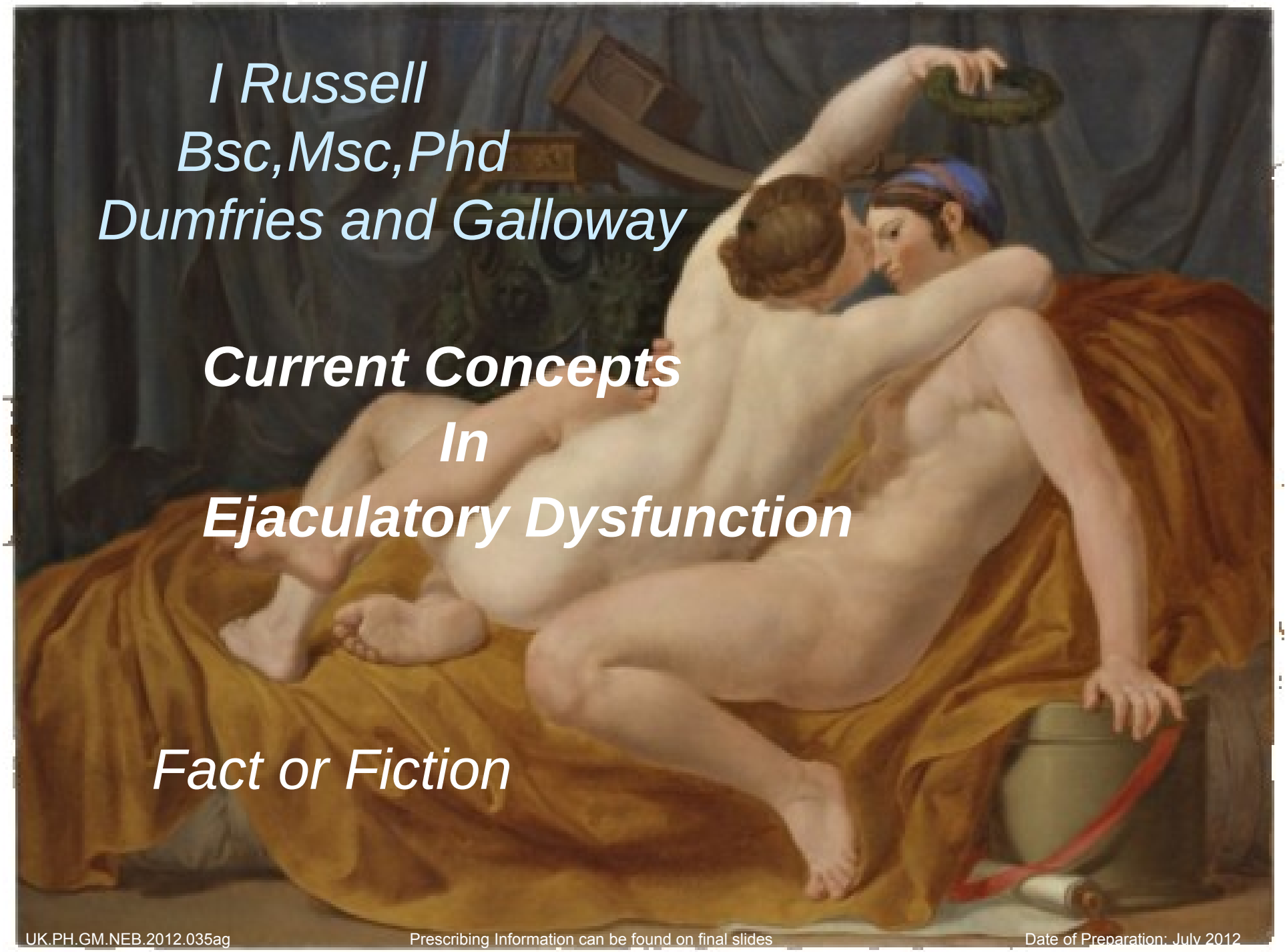
http://www.bssm.org.uk/downloads/UK_Guidelines_Androgens_Male_2010.pdf

Conclusions 1

- Testosterone Deficiency is not rare
- Clinical Guidelines give us a clear framework for the diagnosis and management of testosterone deficiency
- Testosterone deficiency may present with subtle symptoms (LOH)
- Testosterone assays are not always reliable — especially free hormone assays
- Calculated free testosterone is at least as reliable as measured free hormone

Conclusions 2

- When considering therapy symptomatic borderline hypogonadism should be treated as a DEFINED TRIAL PERIOD of 3 Months
- Testosterone Deficiency should be Treated before erectile dysfunction
- Testosterone therapy has a good safety profile and effective but requires on going monitoring for complications
- Newer Preparations give more physiological levels
- Testosterone is not a treatment for ED in Eugonadal men



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Bsc,Msc,Phd
Dumfries and Galloway

Current Concepts In Ejaculatory Dysfunction

Fact or Fiction

Ejaculatory Dysfunction

The most prevalent male sexual disorders are ejaculatory dysfunctions.

Divided into 4 categories:

- Premature ejaculation (PE),
- Delayed ejaculation,
- Retrograde ejaculation,
- Anejaculation/anorgasmia

Ejaculatory Dysfunction

The etiology of ejaculatory dysfunction are numerous and multifactorial:

- Psychogenic,
- Congenital,
- Anatomical,
- Neurogenic,
- Infectious,
- Endocrinological,
- Iatrogenic factors

Secondary to medications may all play a role.

Assessment and Treatment

A sexual history is therefore necessary to uncover the diagnosis. PE can have a significant impact on the quality of life of the patient and his sexual partner, and may lead to psychological distress and loss of self-esteem.

It appears that Ejaculatory Dysfunction has no single etiology, and treatments have been based on both its neurophysiologic and behavioral components

Shabsigh 2010

Treatment

- Psychological/behavioral/sexual counseling therapy
- Stop/Start technique (Masturbatory retraining)
- Topical anesthetics
- Dapoxetine, and other selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants,
- Phosphodiesterase-5 (PDE-5) inhibitors.

Conclusion

Administration, medications that have shown some success include selective serotonin reuptake inhibitors, tricyclic antidepressants, phosphodiesterase type 5 inhibitors, and topical anesthetics. Behavioral techniques have been the mainstay of treatment, and include techniques to decrease sensory input.

Testosterone & The Prostate

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Swansea

'Restore The Man' - Thursday 21st June, 2012

Summary For BPH

- Hypogonadal men receiving TTh to bring their T level into the normal range often show a transient increase their BPH parameters (PSA/Prostate volume) for the first 3-6 month of treatment
- Increases appear to be towards those levels of the normal controls
- No data to support TTh causing a worsening of their LUTS
- No clear risk of disease progression requiring treatment either pharmacological or surgical

Summary

- The link between lowering T and CaP growth is well established and continues to be used in everyday practice
- The direct link between T and CaP incidence is less clear
- The variable effect explained by saturation model
- No clear evidence that normalising T from a non castrate low level increases CaP incidence or recurrence rates in treated patients

Guidelines

- Guidelines from various medical association and committees exist for TTh
- Wang *(The Aging Male 2008;1:1-8)*
  - ISA, ISSAM, EAU, EAA and ASA recommendations
- Wylie *(Maturitas 2010;67:275-89)*
  - BSSM guidelines

- These uniformly agree there is **no** conclusive evidence
  - TTh increases the risk of developing BPH or CaP
  - TTh converts indolent disease into clinically significant disease
  - TTh in treated patients with CaP only after a prudent period
- Men should be counseled prior to commencing TTh

In Conclusion I

- LOH, BPH and CaP occur in patients with advancing age
- T/DHT are required for normal prostatic development, growth and maintenance
- The recently published data have greatly improved our understanding of the relationship between T levels and BPH/CaP

In Conclusion II

- The theory that TTh invariably enhances BPH or CaP growth has not been substantiated
- Many questions remain unanswered
  - The long term effects of TTh on risk of BPH/CaP
  - The safety in men with prior diagnosis of TTh need to be addressed in appropriate studies
- However in most cases with appropriate pre-treatment assessment and monitoring clinicians should not be reluctant to recommend TTh for symptomatic hypogonadal men

Depression and Diabetes in Men

Prof G I Hackett

Consultant in Sexual Medicine

Clinical Governance Lead South

Staffs Primary Care Trust

Prevalence of Depression in type 2 diabetes

- 10 controlled studies 51,331[1] 1980-2005
- Prevalence 17.6 v 9.8% normal
- Females with diabetes 28% v Men 18% by questionnaire and 26 v 9% by interview[2]
- Odds ratio was 1.9 for Men v 1.3 for Women[1]
- Younger adults particularly vulnerable (twice as men age 35-44 have T2D)[3]
- A 10 yr study of 65,381 women suggested the link was bi-directional[4]

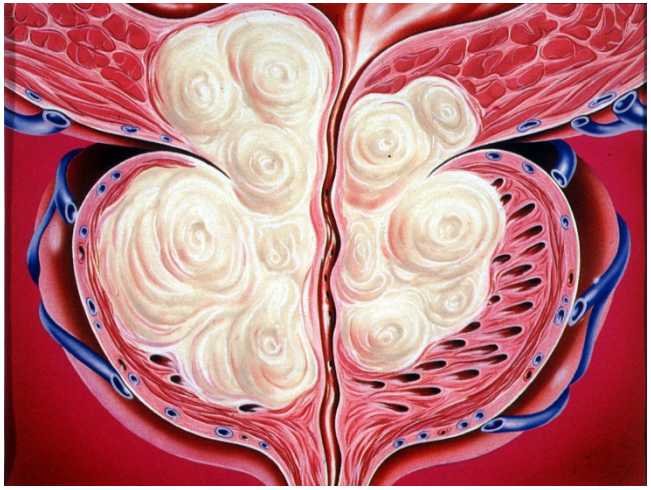
- 1. Ali S, Stone M Diabetic Medicine 2006. 23.11.1165-73
- 2. Anderson RJ Diabetes Care 2001;724:1069-78.
- 3. Zhao et al Public Health 2006 120.696-704
- 4..Pan et al *Arch Intern Med.* 2010;170(21):1884-1891

Depression and Men

- Men are less likely to be diagnosed with depression
- Men are less likely to be treated for depression, with ethnic variations
- Men are less likely to comply with therapy.
- Men are more likely to abuse alcohol
- Men are 3 times more likely to commit suicide. Occupational and ethnic risks.
- (Depression and Men report 2011)

CONCLUSIONS

- Depression is nearly twice as common in T2D than in the non-diabetic population.
- The odds ratio for depression in T2D is significantly higher in men.
- Sexual dysfunction is the co-morbidity most strongly linked with depression in men with T2D
- Testosterone deficiency may be linked with depression and therapy may improve depression but results may take 12 – 18 months.
- The management of depression in men with T2D may be more complex than simply prescribing an antidepressant or CBT.



PSA testing in Primary care

Professor Mike Kirby FRCP

University of Hertfordshire &

The Prostate Centre

London

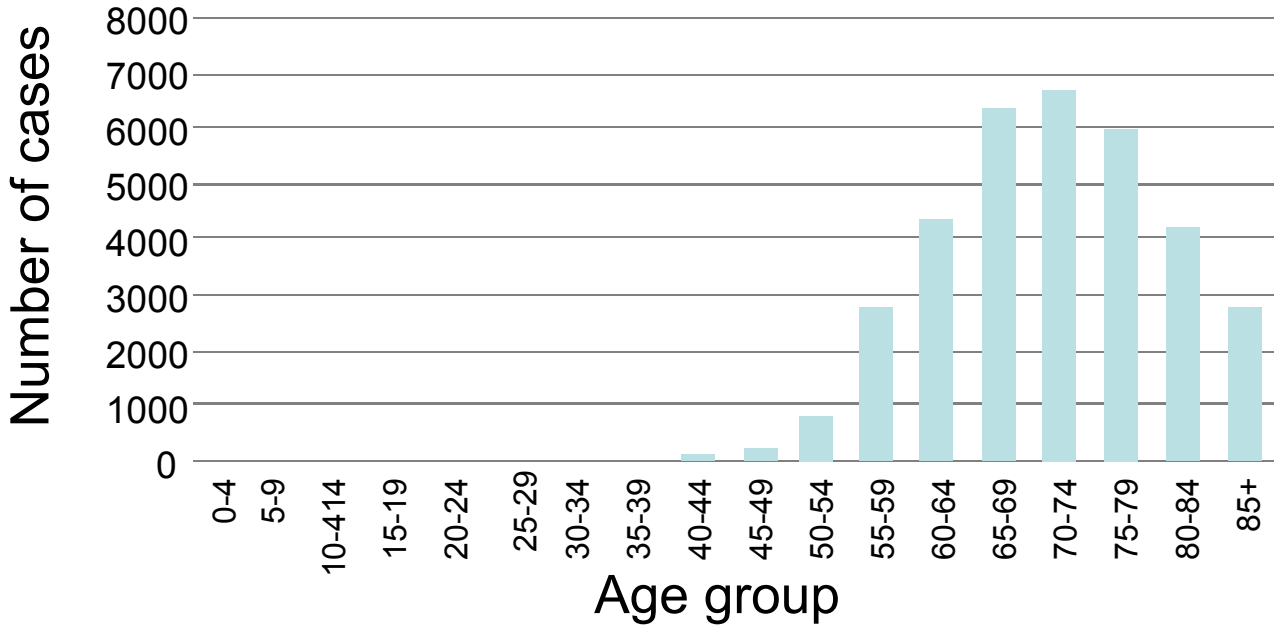
The PCRMP

- **Aims**: The Prostate Cancer Risk Management Programme aims to help the primary care team give clear and balanced information to men who request details about testing for prostate cancer.

- **Contents**:
  - GP booklet
  - Summary card
  - Patient information sheets
  - Cancer Research UK *Prostate CancerStats* sheets

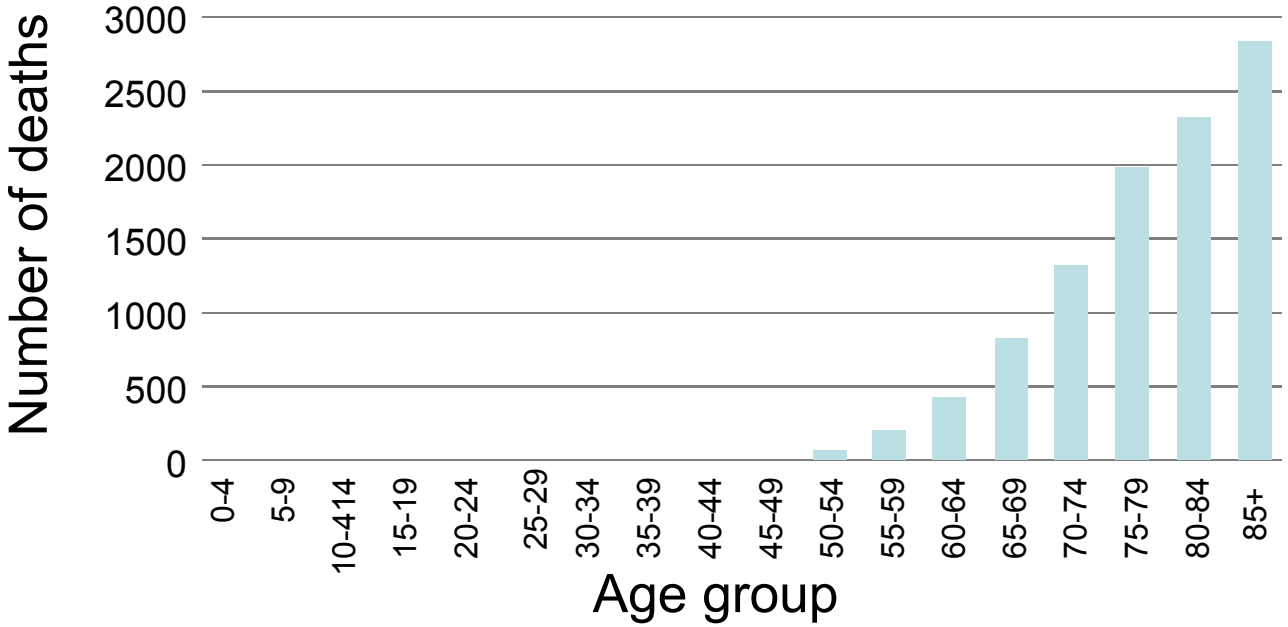
Prostate cancer incidence

- Prostate cancer is the most common cancer in men in the UK
- In 2005, 34,302 men were diagnosed



Prostate cancer mortality

- Prostate cancer is the second most common cause of cancer-related deaths in men in the UK
- Prostate cancer claimed the lives of 10,038 men in the UK in 2006



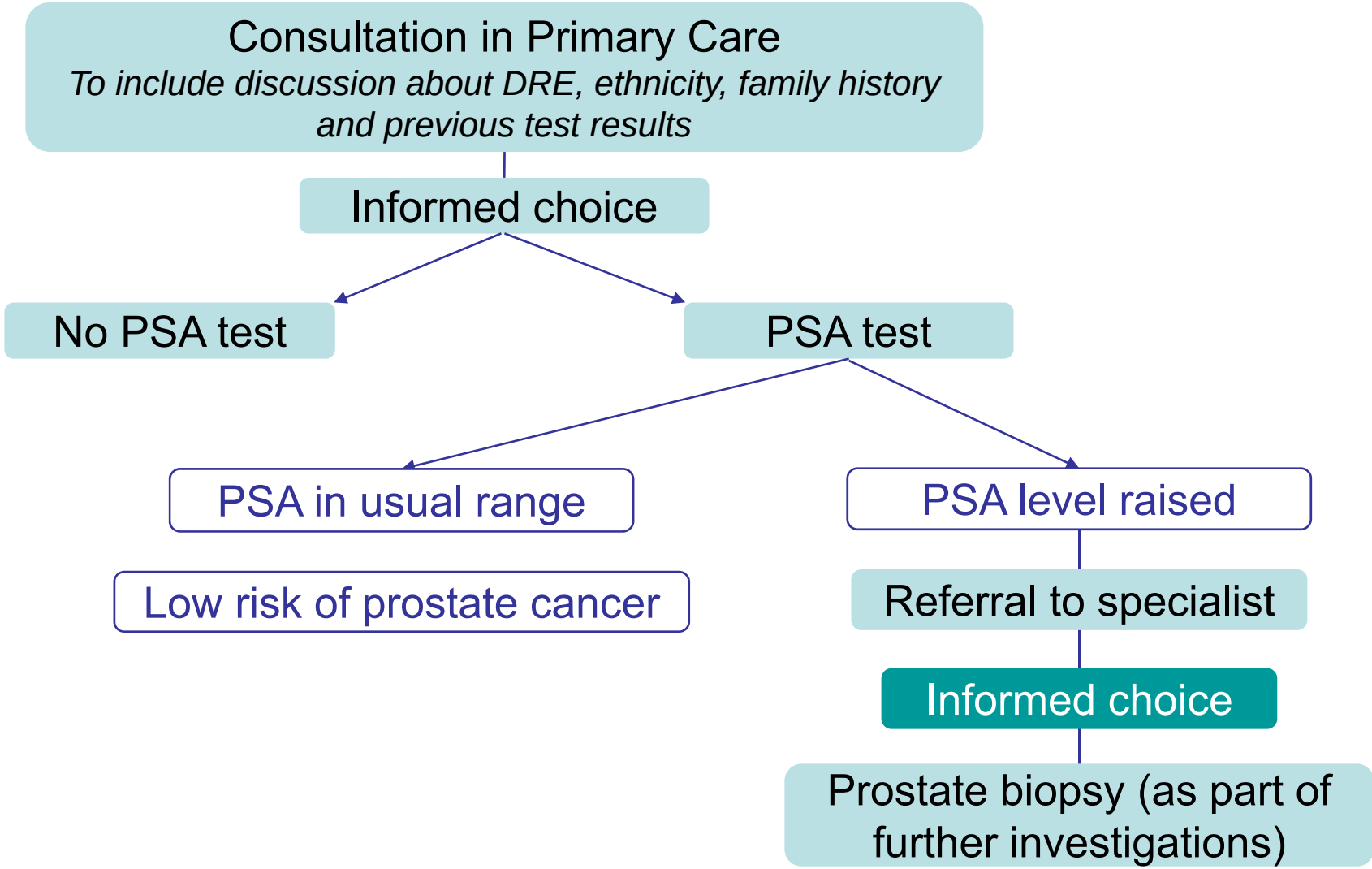
Risk factors for cancer of the prostate

- Age
- Family history
  - 5-10% have an inherited component

Number of first degree relatives diagnosed	Increase in relative risk
1	2.5 fold increasing to 4.3 fold if the relative was under 60 years of age at diagnosis
2	3.5 fold

- Ethnicity
  - risk Black men > White men > Asian/Oriental men
- Diet
  - Lycopenes and possibly selenium may have a protective effect
  - Diet high in protein or calcium from dairy products may increase risk

Use of the PSA test in assessing prostate cancer

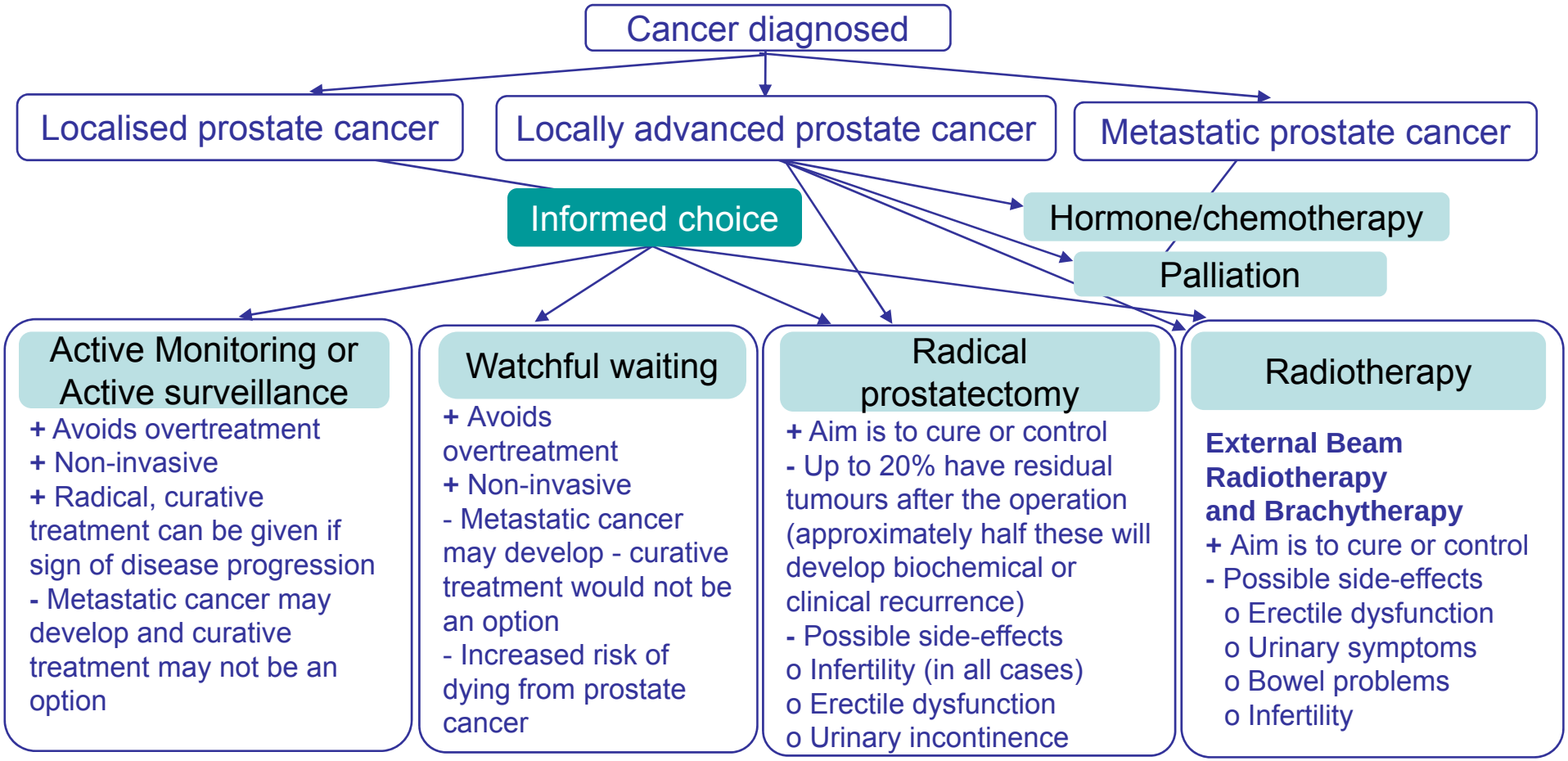


Referral values for total PSA

Age	PSA referral value (ng/mL)
50-59	≥ 3.0
60-69	≥ 4.0
70 and over	> 5.0

- As PSA levels rise with age, the PCRMP recommends the use of age-related referral values
- These levels should be used for all men regardless of their weight

Main options after diagnosis



- Cryotherapy and High Intensity Focussed Ultrasound may be available as part of a clinical trial, but these treatments are not recommended by NICE for routine use.
- PSA levels may be used to monitor disease activity in those with established prostate cancer.

References

- PCRMP pack
  - Burford DC, Kirby M, Austoker J. Prostate Cancer Risk Management Programme; an information pack for primary care. Sheffield; NHS Cancer Screening Programmes, 2008
- PCRMP booklet
  - Burford DC, Kirby M, Austoker J. Prostate Cancer Risk Management Programme Information for Primary Care; PSA testing in asymptomatic men. Sheffield; NHS Cancer Screening Programmes, 2008

- To obtain a copy of the pack

  - download from the NHS Cancer Screening Programmes website

  http://www.cancerscreening.nhs.uk/prostate/index.html

  - or contact the Department of Health publications order line quoting PROSCANRMT

    0300 123 1002
    dh@prolog.uk.com
    www.orderline.dh.gov.uk

How a Sex Therapist Does It!

Working with Male Psychosexual Problems

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Nottingham University Hospital Trust
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angelagregory@virginmedia.com

Male Sexual Problems

Erectile Dysfunction

Persistent or re-current inability to attain or maintain and erection for satisfactory completion of sexual intercourse

Premature Ejaculation

Ejaculation prior to, on or soon after penetration occurs. An inability to control the level of sexual arousal

Delayed Ejaculation

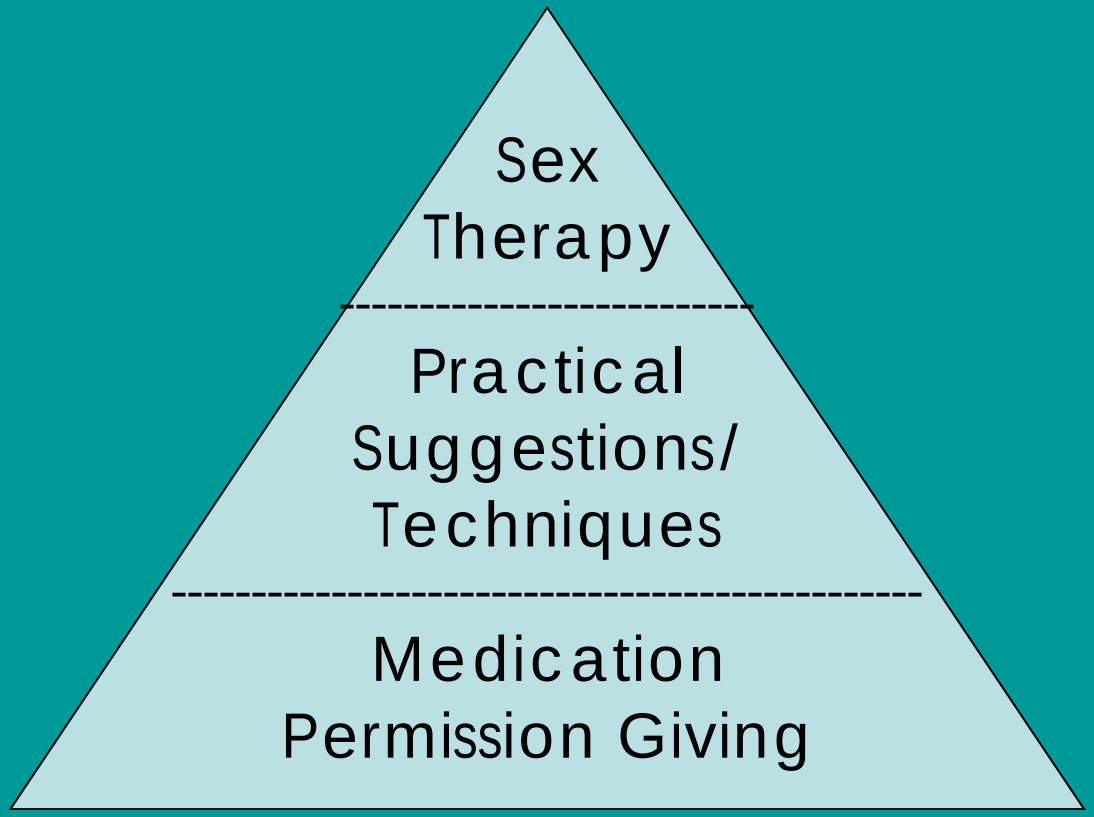
The ejaculatory reflex is inhibited during sexual contact, with or without a partner

Sexual Desire Disorder

Persistent or recurrent deficiency or absence of sexual fantasies or desire for sexual activity that causes marked distress or interpersonal difficulties

DSM 1V Definitions of Psychosexual Dysfunction

Managing Sexual Problems
Levels of Intervention



Take Home Messages

- Anxiety can have a major impact on sexual functioning in men and women, therefore anxiety management techniques can be very useful
- Pelvic floor exercises are very important
- Asking about masturbation matters. Whether a man masturbates, whether he gets a firm erection, whether he can control his arousal, how often he masturbates are useful questions when assessing ED, PE and DE
- Consider checking for testosterone levels in men who present with loss of sexual desire
- Men with organic ED can also have a psychogenic/relationship component to their sexual dysfunction

Useful Websites

- www.cosrt.org.uk
- www.relate.org.uk
- www.sda.uk.net
- www.yourpelvicfloor.co.uk
- www.40over40.com
- www.ErectionAdvice.com
- www.bssm.org.uk
- www.bashh.org

Testosterone, Metabolic Syndrome and Type 2 Diabetes

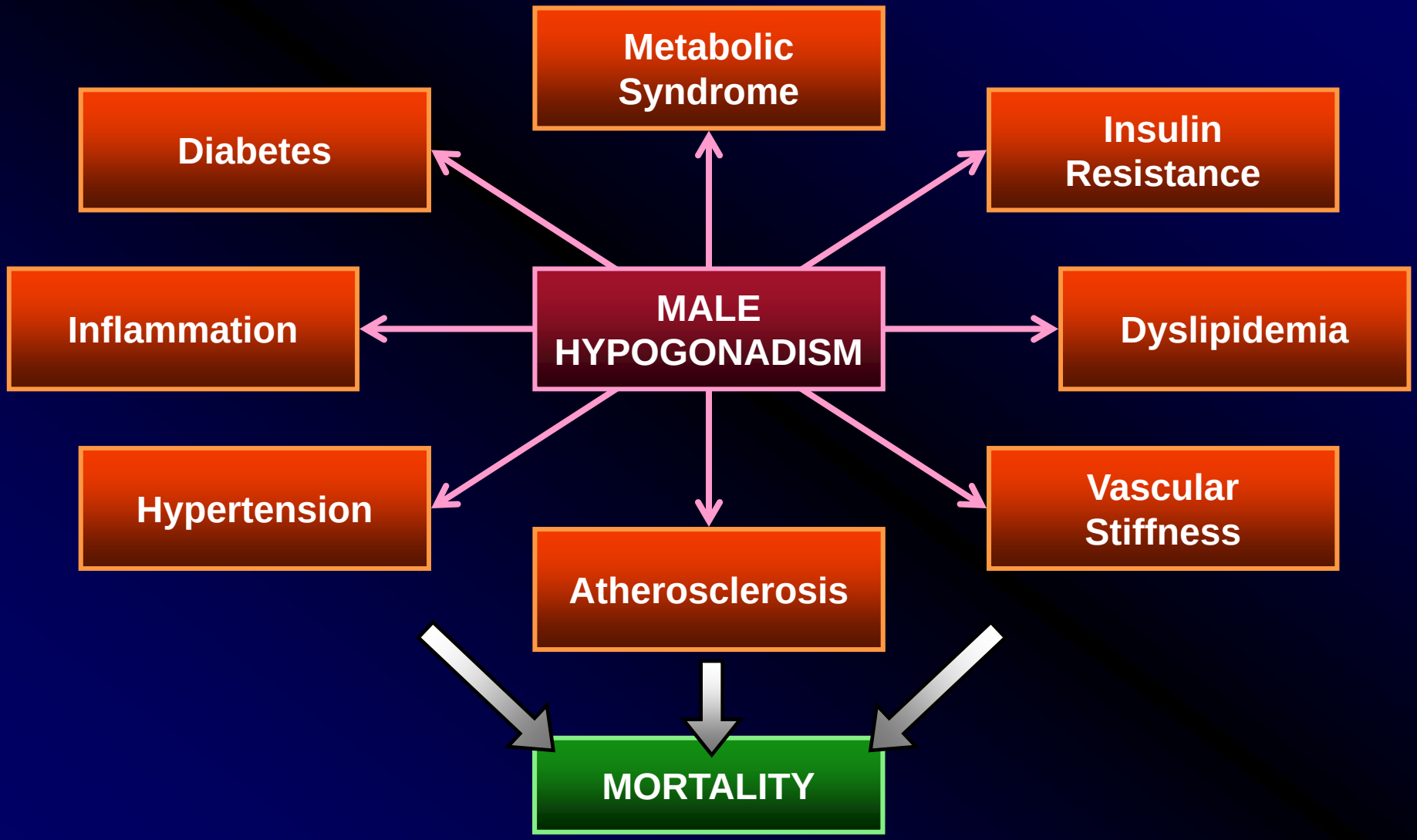
Prof Geoff Hackett

Consultant in Urology/Andrology
Good Hope Hospital
Birmingham

Aims of Testosterone Replacement Therapy (TRT)

- **The primary aim of testosterone replacement therapy is**
  - to return testosterone levels of hypogonadal men back to the normal range
  - to alleviate the symptoms of testosterone deficiency syndrome
- **There are also potential secondary clinical benefits of testosterone replacement therapy when used in symptomatic hypogonadal men**

New Spectrum of Cardiovascular Complications of Low Testosterone Levels



Maggio M and Basaria S Int J Impot Res 21: 261-264 (2009)

Low Testosterone predicts T2D

1 **MMAS** (Stellato) 1709 men (40- 70) Follow Up 9 yrs (table)

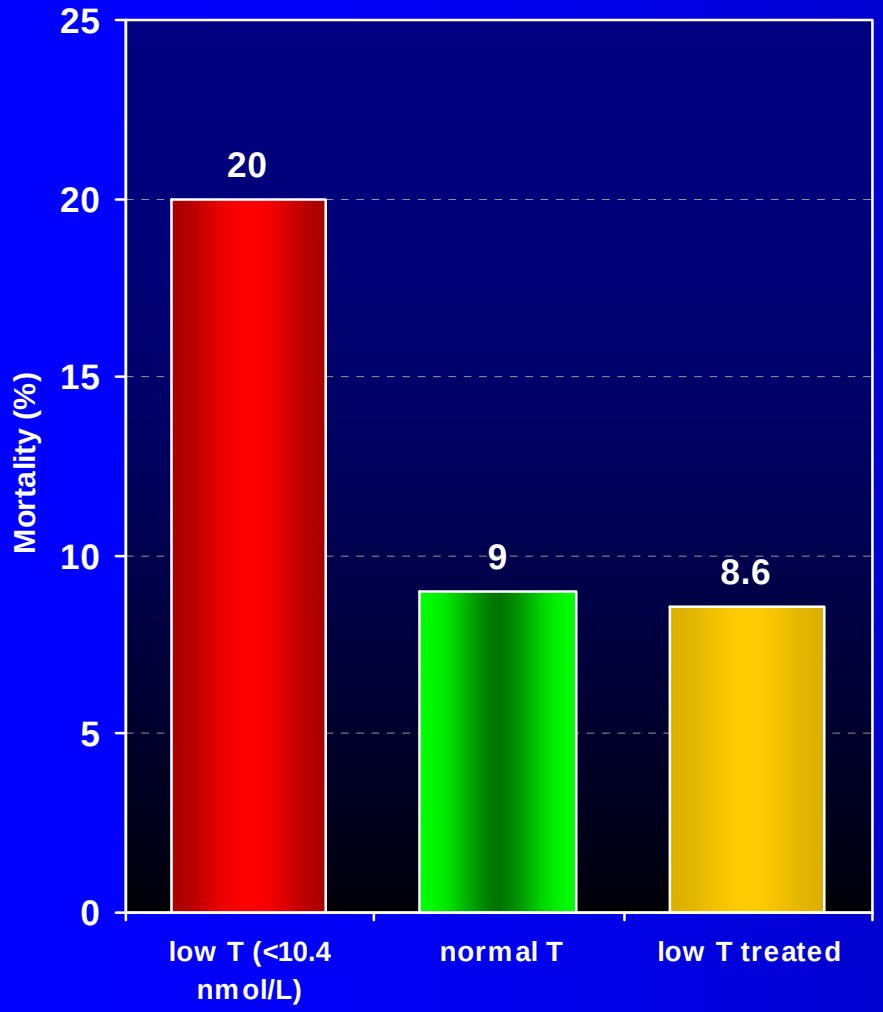
2 **Rancho Bernardo (Oh et al)** 294 M 233 women (55-89) FU 8yrs

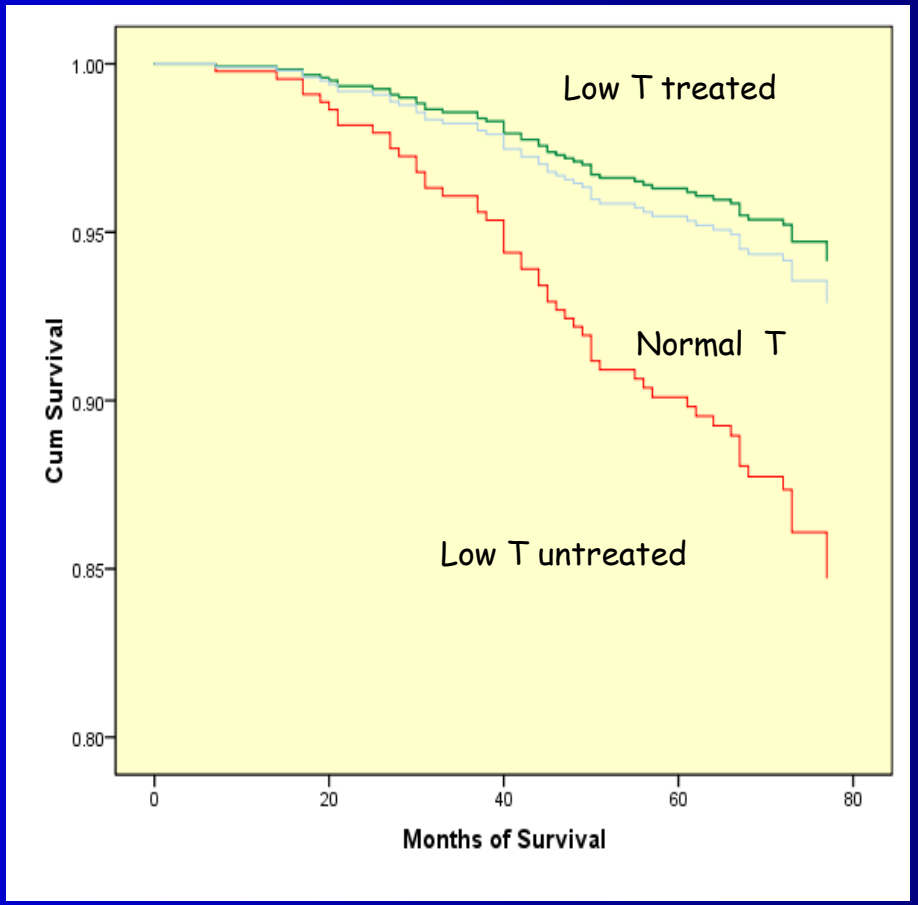
3 **NHANES-III (Selvam et al)** 1413 men (>20) 10 yr follow up Men in towest terile of TT and FT -4 times more likely to develop T2D independent of obesity and ethnicity

FACTOR	T2D	No-T2D	p
TT	15.2	18.2	<0.001
FT	0.28	0.34	0.004
SHBG	24.4	32.3	<0.001
Hypogon <10.4 nmol/l	**15.1%**	**3.3%**	**<0.001**
HTN	48.1%	23.8%	<0.001
Moderate Exercise	64.8	68	0.24
Depress	18.9%	8.5%	0.02
BMI	31.0	26.9	<0.001

- 1 Diabetes Care 2000 Apr; 23(4) :490-4. 2 Diabetes Care 2002 Jan;25(1):55-60 3 *Diabetes Care* 30:23-84, 2007

Low Testosterone Predicts Increased Mortality and Testosterone Therapy Improves Survival in 587 Men with Type 2 Diabetes (mean Follow-up: 5.8 years)

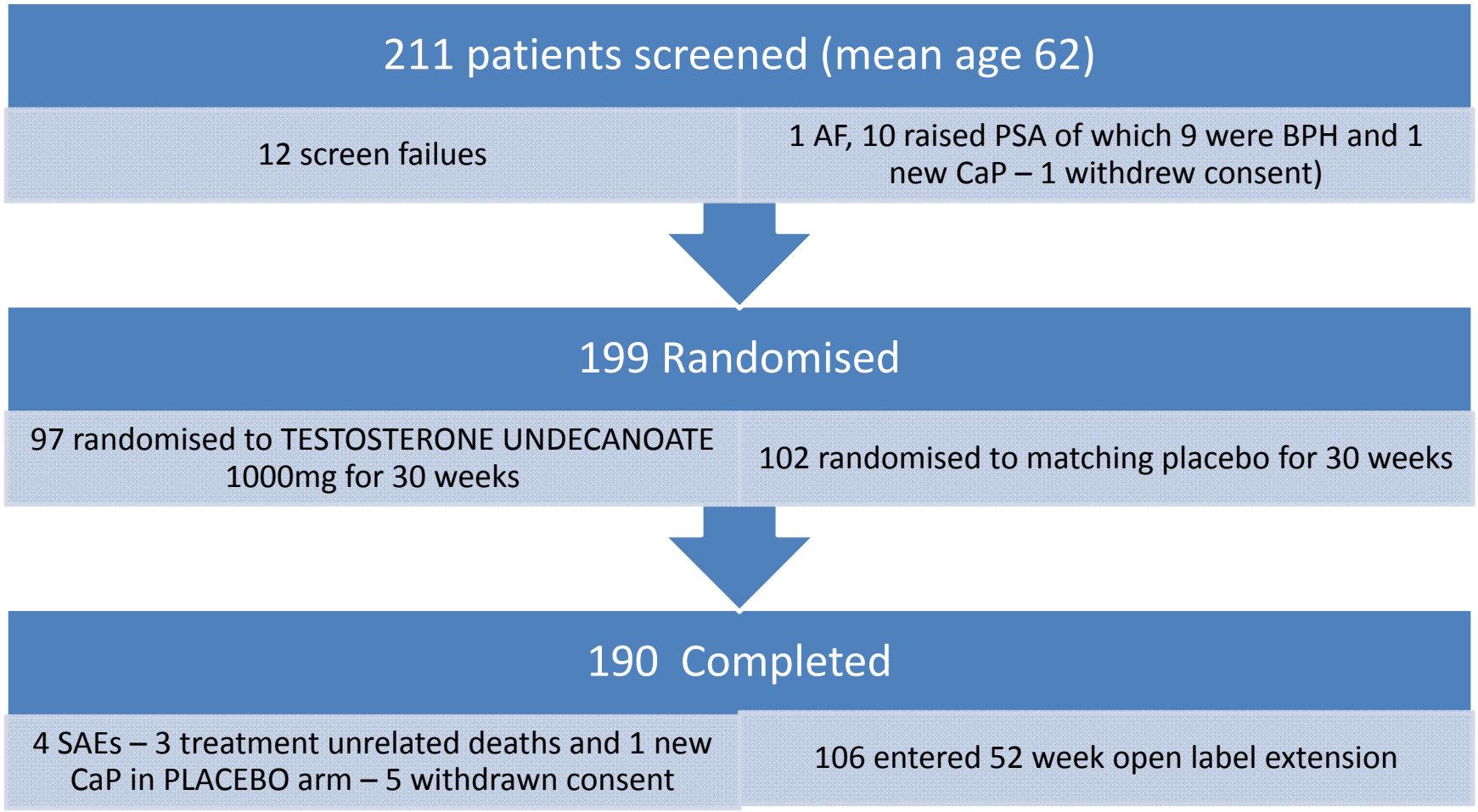




Muraleedharan V et al. Endocr Abstracts 25: P 163 (April 2011)

The BLAST study

A 30 week double blind placebo controlled study of long acting testosterone undecanoate versus placebo in men with type 2 diabetes



BLAST Conclusions

Long Acting TU was associated with significant:

- Reduction in HbA1c – especially poorly controlled men.
- Waist circumference (Weight and BMI in non-depressed men)
- Increase in all domains of the IIEF (except depressed men)
- Improved AMS, Anxiety and Global Efficacy scores
- **Improvements were most marked in men over 60 - these men had less obesity and higher rises in TT and TT**
- **Less marked reponse in depressed men.**
- **Marked treatment benefits were seen extending to 12 and 18 months**

Testosterone and components of the metabolic syndrome

- Testosterone replacement therapy shows potential improvements in some components of the metabolic syndrome compared to placebo/non-testosterone replacement therapy:
  - Fasting plasma glucose
  - Insulin resistance (HOMA-IR)
  - Triglycerides
  - Waist circumference

TESTOGEL PRESCRIBING INFORMATION

Testogel® (testosterone) Prescribing Information

(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: One sachet contains 50mg testosterone in 5g colourless gel.

Indication: Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests.

Posology and method of administration: Cutaneous use.

Adults and Elderly men: One 5g gel sachet daily. Dose can be adjusted in 2.5g gel steps, to a maximum of 10g gel daily. Once sachet is opened, apply immediately onto clean, dry healthy skin over both shoulders or both arms or abdomen. Do not apply to genital areas.

Children: Not for use in children. Not evaluated clinically in males under 18.

Contra-indications: Known or suspected prostate or breast cancer. Hypersensitivity to testosterone or any constituents of the gel.

Warnings and precautions: Use only if hypogonadism has been demonstrated and if other etiology has been excluded. Not to be used for male sterility or impotence. Before therapy exclude prostate cancer. Androgens may accelerate the progression of sub-clinical prostatic cancer and benign prostatic hyperplasia. Examine prostate and breast at least annually, or twice yearly in elderly or at risk patients (clinical or familial factors). Use with caution in cancer patients at risk of hypercalcaemia (and associated hypercalciuria), due to bone metastases. Regular monitoring of serum calcium concentration is recommended in these patients. Testogel® may cause oedema with or without congestive cardiac failure in patients with severe cardiac, hepatic or renal insufficiency. In this case, stop treatment immediately. Use with caution in patients with ischaemic heart disease, hypertension, epilepsy and migraine. Periodically check testosterone concentrations, haemoglobin, haematocrit, liver function (tests), and lipid profile. Possible increased risk of sleep apnoea especially if obesity or chronic respiratory disease present. Improved insulin sensitivity may occur. Irritability, nervousness, weight gain, prolonged or frequent erections may indicate excessive androgen exposure requiring dose adjustment. If severe application site reactions occur, discontinue if necessary. Testosterone may produce a positive reaction in anti-doping tests. Testosterone gel can be transferred to others by close skin to skin contact and can lead to adverse effects (inadvertent androgenisation) if repeated contact occurs. Inform patient of transfer risk that is prevented by clothing or washing of application site. In vitro absorption studies suggest patients observe at least 6 hours between gel application and showering, though occasional baths or showers taken between 1 and 6 hours should not significantly influence treatment. Testogel® should not be prescribed for patients who may not comply with safety instructions (e.g. severe alcoholism, drug abuse, severe psychiatric disorders).

Interactions: Interactions reported with oral anticoagulants, ACTH or corticosteroids, and thyroxin binding globulin in laboratory tests.
Pregnancy and lactation: Not for use in women. Pregnant women must avoid any contact with Testogel® application sites.
Undesirable effects: Most common (10%) – application site reaction, erythema, acne, dry skin. Common – changes in laboratory tests, headache, prostatic disorders, gynaecomastia, mastodynia, dizziness, paraesthesia, amnesia, hyperaesthesia, mood disorders, hypertension, diarrhoea, alopecia, urticaria. Serious side effects – *cf. CI/Warnings and Precautions - in addition* liver function test abnormalities, hypersensitivity reactions. Other side effects – Prostate cancer risk in association with testosterone therapy is inconclusive. Hepatic neoplasm rarely associated with excessive dosages of testosterone. Nervousness, depression, hostility, priapism, reversible interruption or reduction of spermatogenesis and urinary retention have been reported following testosterone oral or injectable treatment. Prescribers should consult the SmPC in relation to other side effects.
Overdose: Excessively high plasma testosterone concentration is unlikely using the transdermal route.
Legal Category: POM.

Package Quantities and Basic NHS Costs: £31.11 per pack of 30 x 5g sachets
MA Number: PL 16468/0005
Further information available from: Bayer Schering Pharma, Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA United Kingdom. Telephone: 01635 563000.
Date of preparation: January 2010

Testogel® is distributed by Bayer plc, Bayer House, Strawberry Hill, Newbury, RG14 1JA. Trading as Bayer plc, Bayer Schering Pharma.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax.: 01635 563703, Email: phdsguk@bayer.co.uk

NEBIDO PRESCRIBING INFORMATION

Nebido® 1000 mg/4 ml, solution for injection (testosterone undecanoate) Prescribing Information

(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: 1ml of solution contains 250 mg of testosterone undecanoate, corresponding to 157.9 mg of testosterone. Each 4ml ampoule of solution contains 1000 mg of testosterone undecanoate.

Indication: Testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests.

Posology and method of administration: Strictly for intramuscular use. *Application:* Inject Nebido® extremely slowly. One ampoule (1000mg) is injected intramuscularly every 10 to 14 weeks. Nebido® should be injected deeply into the gluteal muscle, and must be administered very slowly. Special care should be taken to avoid intravasal injection. The contents of an ampoule should be injected intramuscularly immediately after opening the ampoule – refer to the SmPC or PIL for instructions on opening the ampoule safely. *Starting treatment:* Measure serum testosterone levels before the start and during initiation of treatment. If appropriate, first injection interval may be reduced to a minimum of 6 weeks. *Maintenance:* Injection interval within 10 to 14 week range. Monitor serum testosterone and symptoms regularly; adjust injection interval as appropriate.

***Paediatric population*:** Not for use in children. Not evaluated clinically in males under 18.

***Geriatric patients*:** Based on limited data, no dose adjustment is considered necessary.

Contra-indications: Androgen-dependent prostate cancer or breast cancer. Past or present liver tumours. Hypersensitivity to testosterone or any of the excipients. Not for use in women.

Warnings and precautions: Use only if hypogonadism has been demonstrated and if other etiology has been excluded. Limited experience in patients over 65. Before therapy exclude prostate cancer. Examine prostate and breast at least annually, or twice yearly in elderly or at risk patients (clinical or familial factors). Periodically check testosterone concentrations, haemoglobin, haematocrit and liver function tests. Androgens may accelerate the progression of sub-clinical prostate cancer and benign prostatic hyperplasia. Use with caution in cancer patients at risk of hypercalcaemia (and associated hypercalciuria), due to bone metastases. Regular monitoring of serum calcium concentration is recommended in these patients. Rarely, liver tumours (both benign and malignant) have been reported. Include liver tumour in differential-diagnostic considerations if severe upper abdominal complaints, liver enlargement or signs of intra-abdominal haemorrhage occur. Efficacy and safety of Nebido® has not been demonstrated in patients with hepatic and renal impairment, therefore testosterone replacement therapy should be used with caution in these patients. Nebido® may cause oedema with or without congestive cardiac failure in patients with severe cardiac, hepatic or renal insufficiency, or in patients with ischaemic heart disease. In this case, stop treatment immediately. Use with caution in patients predisposed to oedema, with epilepsy, migraine or blood clotting irregularities. Improved insulin sensitivity may occur. Irritability, nervousness, weight gain, prolonged or frequent erections may indicate excessive androgen exposure requiring dose adjustment. Pre-existing sleep apnoea may be potentiated. Testosterone may produce a positive reaction in anti-doping tests. Not suitable for developing muscles or increasing fitness in healthy individuals. Withdraw treatment if symptoms of excessive androgen exposure persist or reappear.

Interactions: Interactions reported with oral anticoagulants (requires dose monitoring), ACTH or corticosteroids, and thyroxin binding globulin in laboratory tests.

Pregnancy and lactation: Not for use in women.

Effects on ability to drive and use machines: None known.

Undesirable effects: Common – injection site pain, acne, polycythaemia, increased weight, hot flush, increased prostate specific antigen, abnormal prostate examination, benign prostate hyperplasia and various injection site reactions. Serious side effects – *cf. CI/Warnings and Precautions* – in addition, hypersensitivity, cardiovascular disorder, depression, aggression, hypertension, liver function test abnormalities, urinary retention, prostatic intraepithelial neoplasia and prostatitis. Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhidrosis, chest pain, dizziness, paraesthesia or syncope. Suspected anaphylactic reactions after Nebido injection have been reported. Other side effects - The following adverse reactions have been reported under treatment with testosterone-containing preparations: nervousness, hostility, sleep apnoea, various skin reactions including seborrhoea, increased frequency of erections, in rare cases, priapism, and, in very rare cases, jaundice. Therapy with high doses of testosterone preparations commonly reversibly interrupts or reduces spermatogenesis, thereby reducing the size of the testicles. Prescribers should consult the SmPC in relation to other side effects.

Overdose: Reduce dose or terminate therapy.

Incompatibilities: Must not be mixed with other medicinal products.

Legal Category: POM.

Package Quantities and Basic NHS Costs: 1 x 4ml ampoule (£80.00).

MA Number(s): PL00010/0549.

Further information available from: Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire, RG14 1JA, United Kingdom. Telephone: 01635 563000.

Date of preparation: December 2011.

Nebido® is a registered trademark of the Bayer Group.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax.: 01635 563703, Email: phdsguk@bayer.co.uk

LEVITRA® PRESCRIBING INFORMATION

Levitra® film-coated tablets and Levitra® orodispersible tablets (vardenafil)
Prescribing Information
(Refer to full Summary of product Characteristics (SmPC) before prescribing)
Presentation: Levitra® film-coated tablets: 5/10/20mg vardenafil (as hydrochloride). Levitra® orodispersible tablets: 10mg vardenafil (as hydrochloride).
Indication: Treatment of erectile dysfunction. To be effective, sexual stimulation is required.
Posology and method of administration: Film-coated: 10mg approximately 25–60 minutes before sexual activity. Based on efficacy and tolerability, dose may be increased to 20mg or decreased to 5mg. Maximum dose is 20mg/day. Can be taken with or without food. Onset of activity may be delayed if taken with a high fat meal. *Orodispersible: 10mg approximately 25–60 minutes before sexual activity.* Maximum dose is 10mg/day. Can be taken with or without food, but not with liquid. *Elderly men (>65 years): No dose adjustment required, though increase to a* maximum 20mg film-coated tablets dose should be carefully considered depending on individual tolerability. *Hepatic and renal impairment: Consider* starting with 5mg dose film-coated tablets in patients with mild–moderate hepatic impairment or severe renal impairment. Max dose in patients with moderate hepatic impairment is 10mg film-coated tablets. Orodispersible tablets should not be used in patients with moderate to severe hepatic impairment or with end-stage renal failure. *Paediatrics: Not indicated for individuals <18 years of age. Use with other medicinal products: In combination with moderate CYP3A4* inhibitors, the dose should not exceed 5mg film-coated tablets.
Contra-indications: Hypersensitivity to vardenafil or to any excipients; coadministration with nitrates/nitric oxide donors (such as amyl nitrite); loss of vision in one eye due to NAION; men for whom sexual activity is inadvisable; severe hepatic impairment; end-stage renal disease requiring dialysis; hypotension (BP <90/50 mmHg); recent stroke or myocardial infarction (≤6 months); unstable angina; known hereditary retinal degenerative disorders; concomitant use of potent CYP3A4 inhibitors ketoconazole and itraconazole (oral form) in men older than 75 years; concomitant use of potent HIV protease inhibitors.
Warnings and Precautions: Given cardiac risk associated with sexual activity, consider cardiovascular status. Vardenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Patients with left ventricular outflow obstruction can be sensitive to the actions of PDE5 inhibitors. Use with caution in patients with anatomical deformation of the penis or conditions which predispose to priapism. Combination with other treatments for erectile dysfunction, including Levitra® orodispersible, is not recommended. Concomitant use of alpha-blocker therapy may lead to symptomatic hypotension, consider only if therapy is stable, initiate vardenafil at a starting dose of 5mg film-coated tablets and consider a time separation of dosing. Concomitant use with potent CYP3A4 inhibitors should be avoided. Dose adjustement might be necessary when given concomitantly with moderate CYP3A4 inhibitors, e.g. erythromycin or clarithromycin. Avoid grapefruit or grapefruit juice. Prolongation of QTc interval – avoid use in patients with relevant risk factors. In case of sudden visual defect, treatment should be stopped. Administration to patients with bleeding disorders or active peptic ulceration should be considered carefully. Orodispersible tablets contain aspartame and sorbitol.
Interactions: CYP3A4 inhibitors may reduce vardenafil clearance. Nicorandil may have a serious interaction with vardenafil due to the nitrate component. Prescribers should consult the SmPCs for full details on interactions.
Fertility, pregnancy and lactation: Not indicated for use in women; no fertility data available.
Effects on ability to drive and use machines: Patients should be aware of how they react to Levitra® before driving or operating machinery.
Undesirable Effects: Headache. Common: Flushing, dizziness, nasal congestion, & dyspepsia. Serious side effects: *cf. CI/Warnings and Precautions – in addition: Ventricular tachy-arrythmias, chest pain,, angina pectoris,* myocardial infarction, gastritis, seizure, somnolence, syncope, amnesia, paraesthesia/dysaesthesia, priapism, NAION, visual defects, increased intraocular pressure, sudden deafness, allergic reaction, allergic oedema and angioedema. Incidence of ADRs (especially "dizziness") slightly higher in patients with history of hypertension. Serious cardiovascular events, including cerebrovascular haemorrhage, sudden cardiac death, transient ischaemic attack, unstable angina & ventricular arrhythmia reported post-marketing in temporal association with another medicinal product in the same class. Prescribers should consult the SmPC in relation to other side effects.
Overdose: Doses of 40mg twice daily have been associated with severe back pain without any muscle or neurological toxicity. Standard supportive measures should be adopted. Renal dialysis is not expected to accelerate clearance.
Legal Category: POM.
Package Quantities and Basic NHS Costs: Film-coated: 4 x 5mg (£7.56), 8 x 5mg (£15.12), 4 x 10mg (£14.08), 8 x 10mg (£28.16), 4 x 20mg (£23.48), and 8 x 20mg (£46.96). *Orodispersible: 4 x 10mg* (£17.88).
MA Number(s): EU/1/03/248/001-015.
Further information available from: Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA, United Kingdom, Telephone: 01635 563000.
Date of revision: April 2012.
Levitra® is a registered trademark of Bayer AG.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax.: 01635 563703, Email: phdsguk@bayer.co.uk