

# Erectile dysfunction, cardiovascular disease & diabetes

## Living with Diabetes in the 21<sup>st</sup> Century

BY DR PATRICIA SCHARTAU

3RD DECEMBER 2019

GP IN HAMPSTEAD, LONDON

ACADEMIC CLINICAL LECTURER IN PRIMARY CARE AT UCL

NHS ENTREPRENEUR

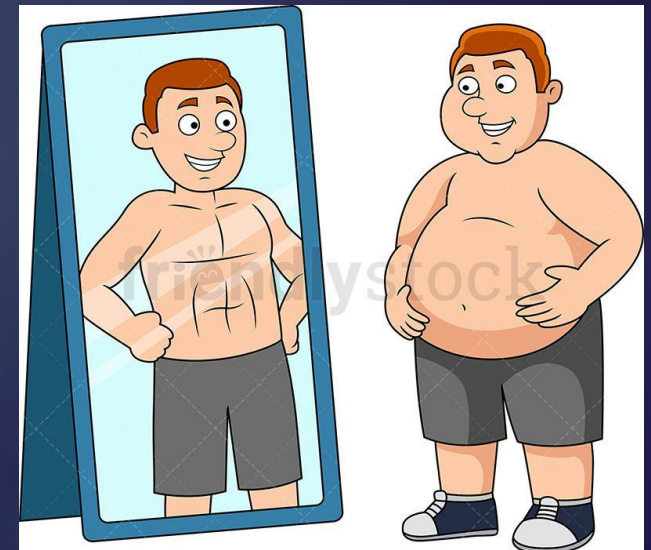


▶ No disclosures



# Case: Rudolf

- ▶ 48y, train driver, husband and father
- ▶ 2 years of increasing tiredness, low mood, reduced sex drive and ED
- ▶ No sign PMHx, non-smoker, alcohol 6 IU/week, OTC Vitamins
- ▶ BMI: 27 ; waist circumference 97.7cm, normal BP and PR
- ▶ Seen GP two years ago: Dx with T2DM and depression
- ▶ ED not addressed, lifestyle measures advocated



# What are the barriers to ED assessment?

Check for updates

InnovAT, 11(5), 269-276

## Erectile dysfunction

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**E**rectile dysfunction is a common, but treatable, condition. Where appropriate, modification of lifestyle factors, medication optimisation and oral pharmacotherapies can be initiated in primary care. Early recognition and management will improve the quality of life of affected individuals and partners, and may avert relationship problems, negative body image and poor mental health. Erectile dysfunction is also an important early warning sign for conditions such as cardiovascular disease. This article considers the aetiology and risk factors for erectile dysfunction, identifies common clinical features, outlines primary care assessment and treatment, and discusses referral criteria. Treatment options available in secondary care are also reviewed.

**The GP curriculum and erectile dysfunction**

*Clinical module 3.07: Men's health* requires GPs to:

- Know that erectile dysfunction is an early warning sign for many conditions including coronary vascular disease, diabetes, depression and lower urinary tract symptoms, occurring on average 5 years prior to the onset of such medical problems

*Clinical module 3.08: Sexual health* requires GPs to:

- Understand that sexual health problems have physical, psychological and social consequences

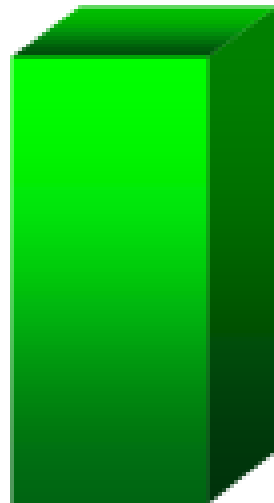
**Definition of erectile dysfunction**

Erectile dysfunction is defined as the inability to achieve and maintain a

patients had an ICD10 (International Classification of Diseases, 10th edition) clinical diagnosis of erectile dysfunction (Nazareth, Boynton, & King, 2005). Another study suggested that 20% of Australians over



# Patients reluctant to talk to their doctors about ED – WHY?



Patients believe ED would not be recognized as a medical problem

Patients fear that discussing sexuality may embarrass their doctors

44% of men attending urologists have ED but fail to mention it - most are too embarrassed

▶ **Doctors equally hesitant to discuss ED with their patients:**

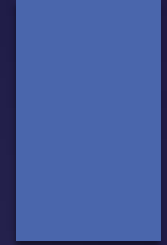
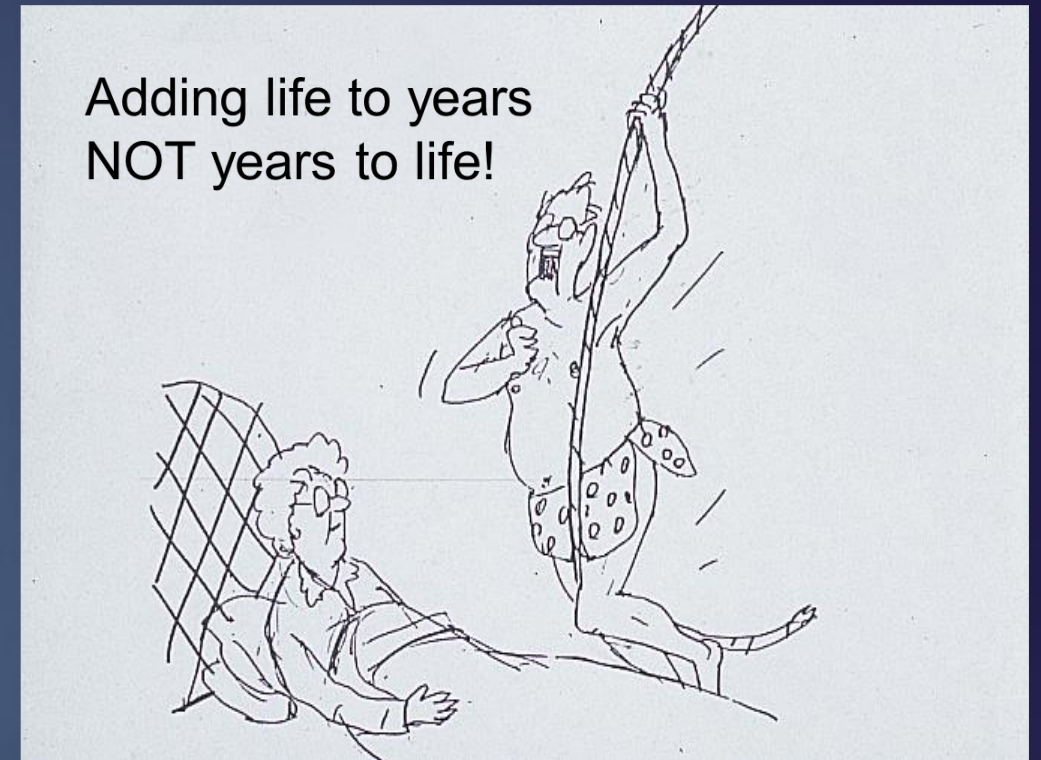
▶ Feel not equipped to address the problem

▶ Waiting for patient to raise the problem

▶ Time pressures

▶ GPs attitudes towards sexuality in older life

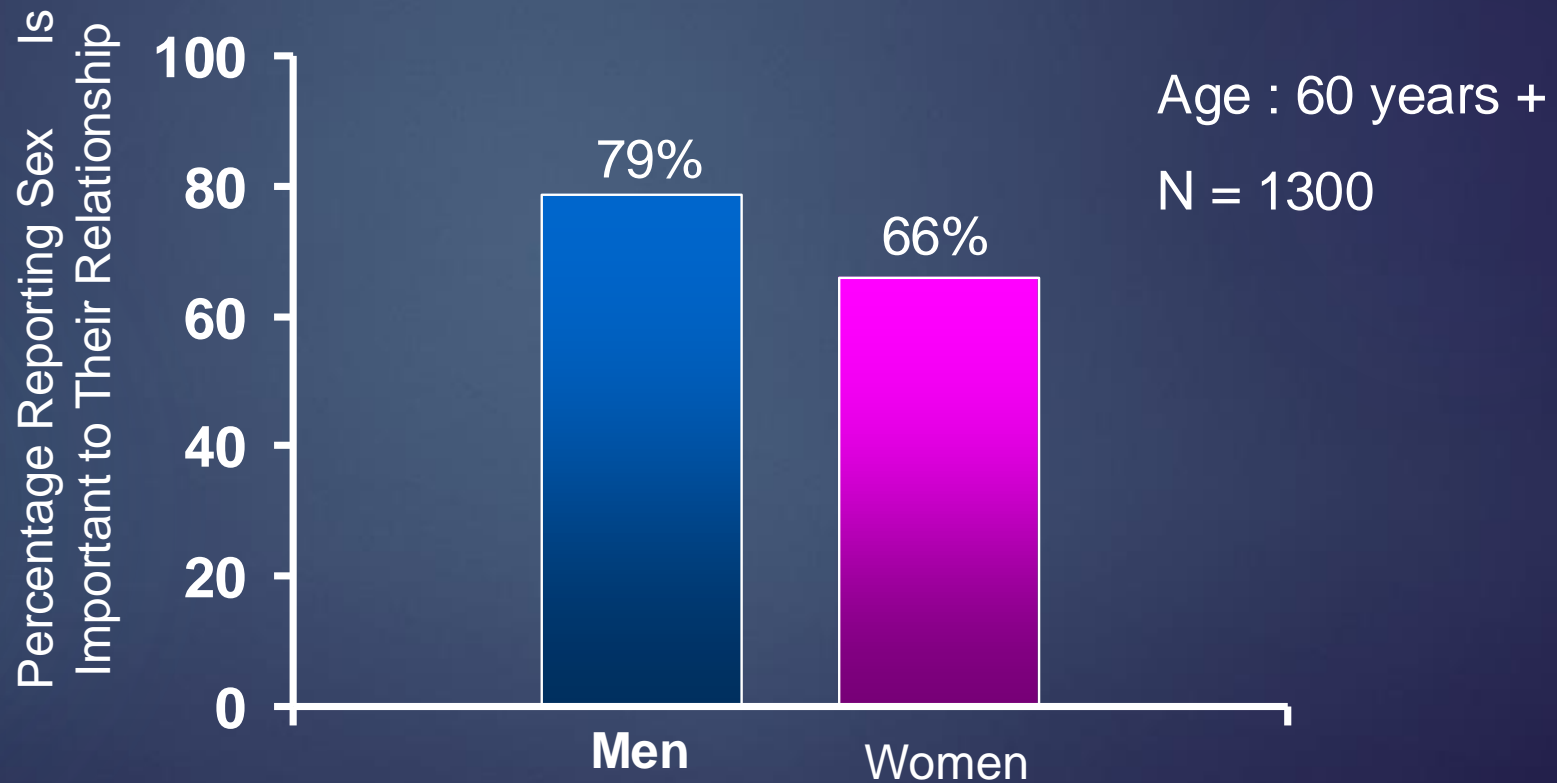
▶ **80% of men with ED would like to talk about it but only if GP raises the subject!**



# Why should we ask about ED?



# Quality of Life: Most men & women report sex is important to their relationship





# Physical health

- ▶ **The Duke Longitudinal Study of Ageing (1982)**

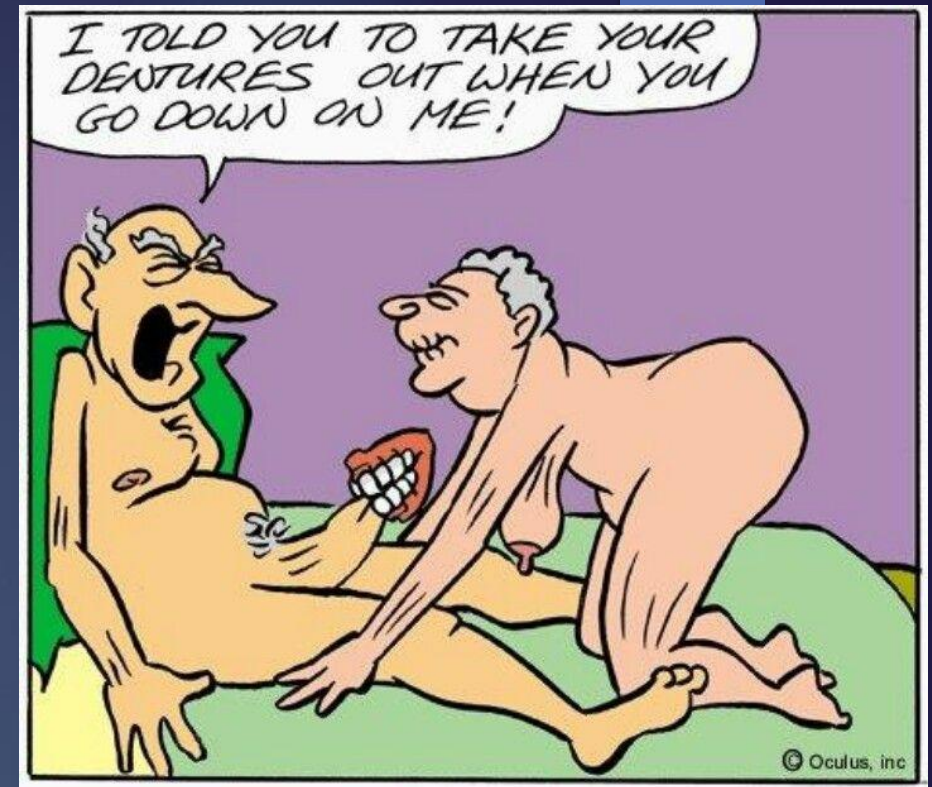
Frequency of intercourse a significant predictor of longevity in men

- ▶ **Swedish Study (1981)**

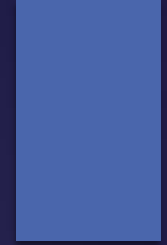
Early cessation of sex associated with premature death

- ▶ **Caerphilly Cohort Study (BMJ 1997)**

50% reduction in cardiac death with more than two orgasms per week



# Physical health

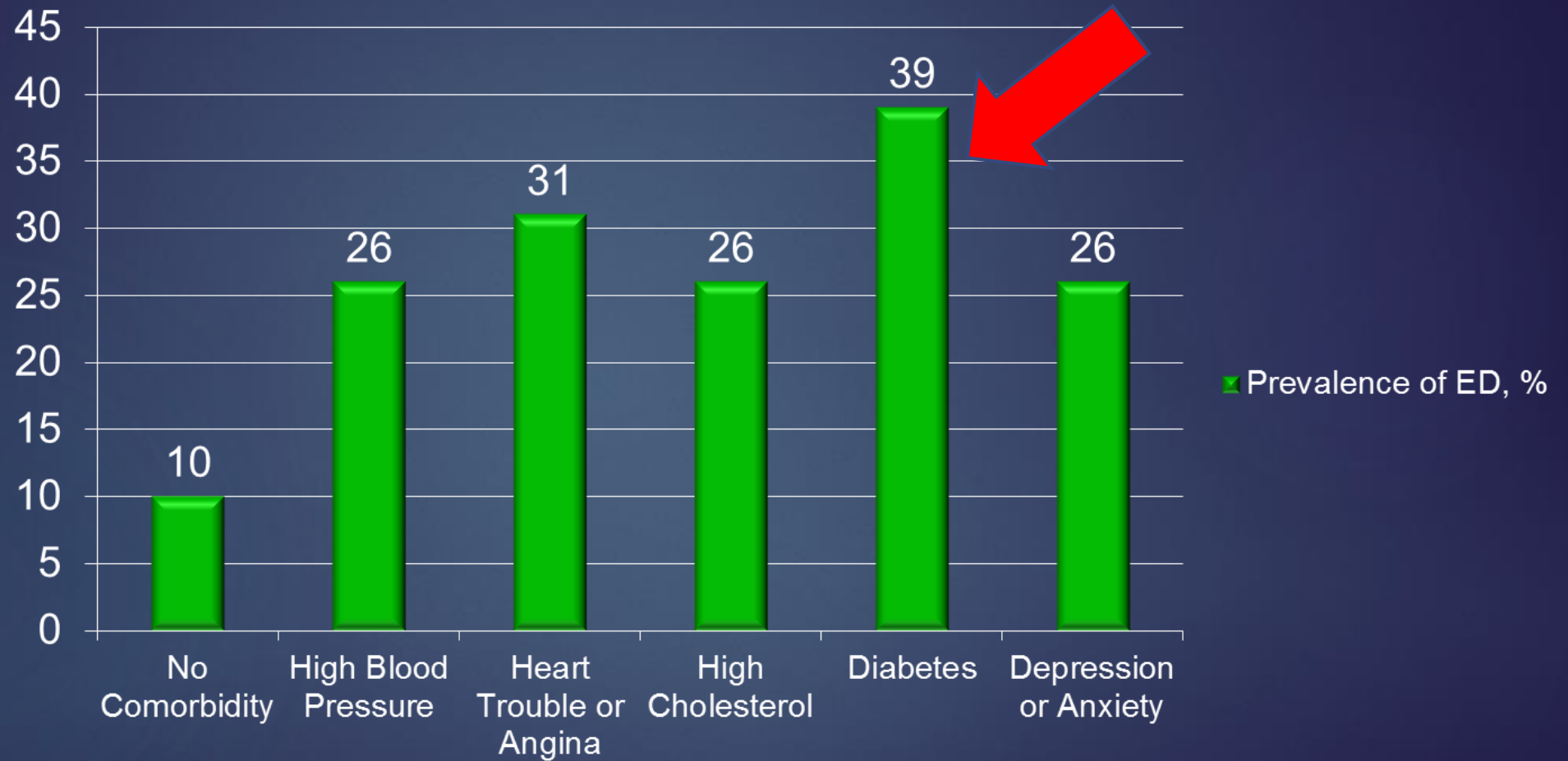


- ▶ **ED is a risk factor for CVD** → Qrisk 3
- ▶ “...equivalent to a current moderate level of smoking. ED confers a 1.46 increased risk for cardiovascular disease”<sup>1</sup>
- ▶ In a younger man, it is associated with a marked increase in the risk of future cardiac events<sup>2</sup>
- ▶ Pro-active management of ED to address other cardiovascular risk factors”<sup>1</sup>

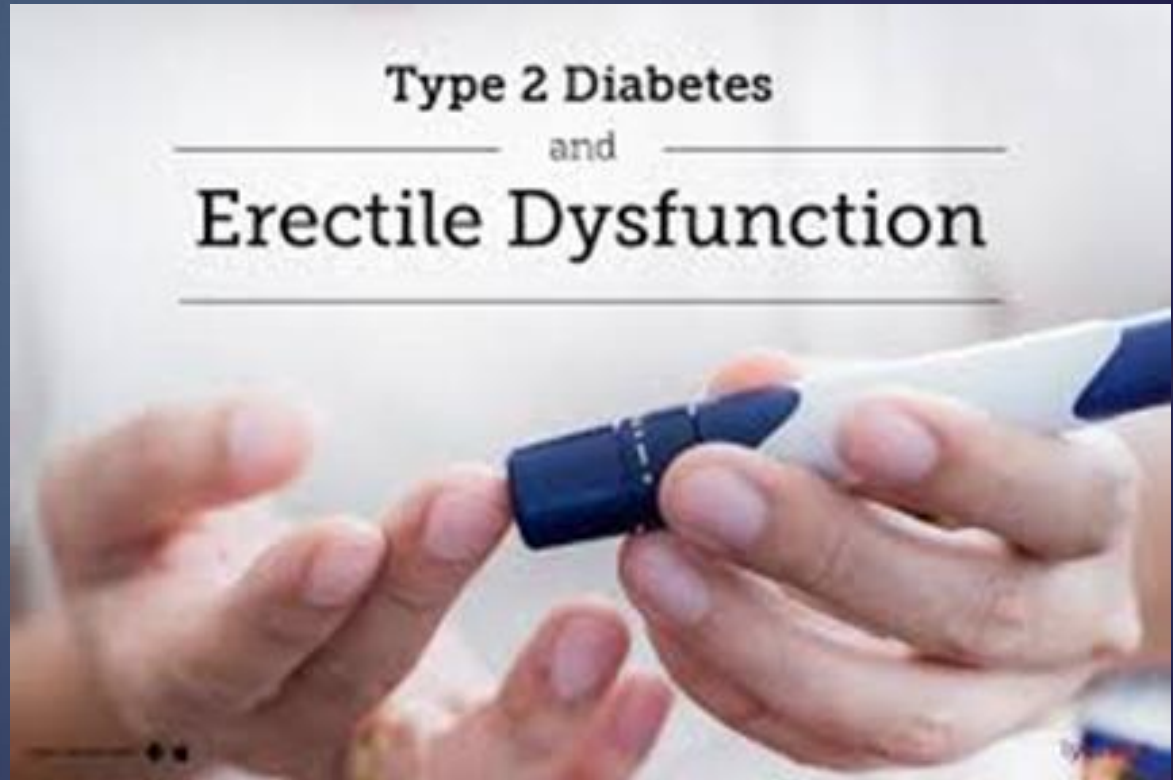
# Artery Size and Atherothrombosis

Artery	Size (mm)	Clinical event
Penile`	1-2	ED
Coronary	3-4	CAD
Carotid	5-7	TIA/Stroke
Femoral	6-8	Claudication

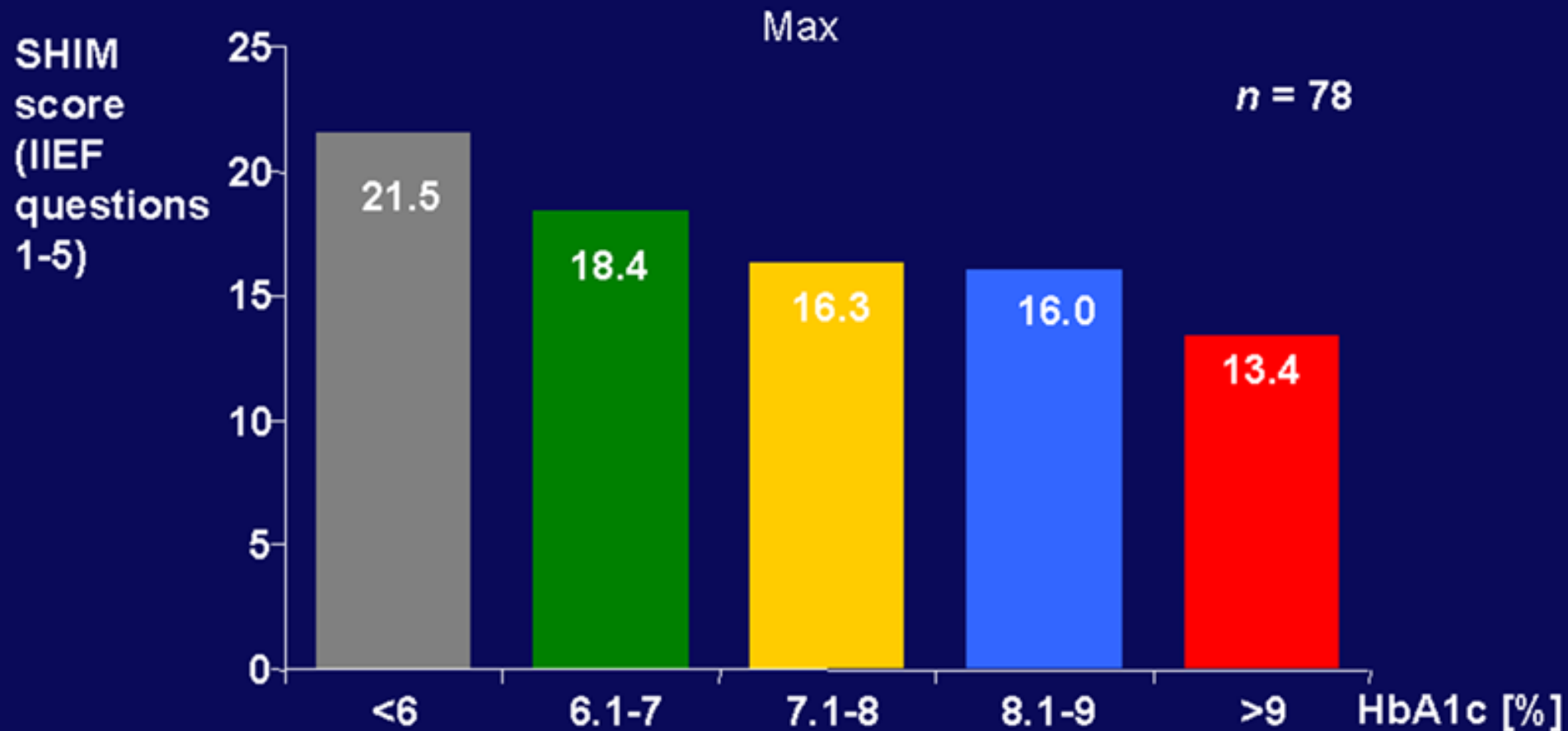
# Prevalence of ED in men with co-morbidities



# T2DM, ED & TD



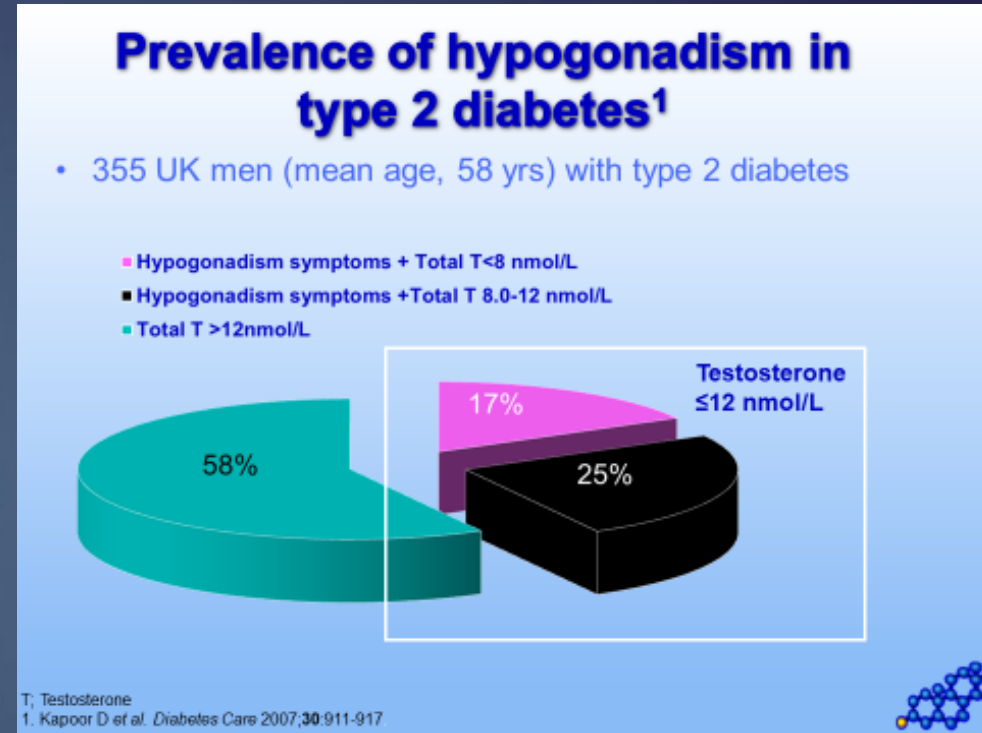
# Correlation between ED and glycaemic control



Romeo J *et al.* *J Urol* 2000; 163: 788-91.

▶ T2DM on the rise: >3 million with DM diagnosis in the UK, 90% T2DM

▶ **Prevalence of ED in men with T2DM:**  
Range of 32 – 90%<sup>1</sup>



▶ **ED pathophysiology:** Micro and macrovascular, endocrine and neuropathic disease<sup>2</sup>

▶ ED is an early marker and independent risk factor for CVD<sup>3</sup> and a predictor of T2DM<sup>4</sup>



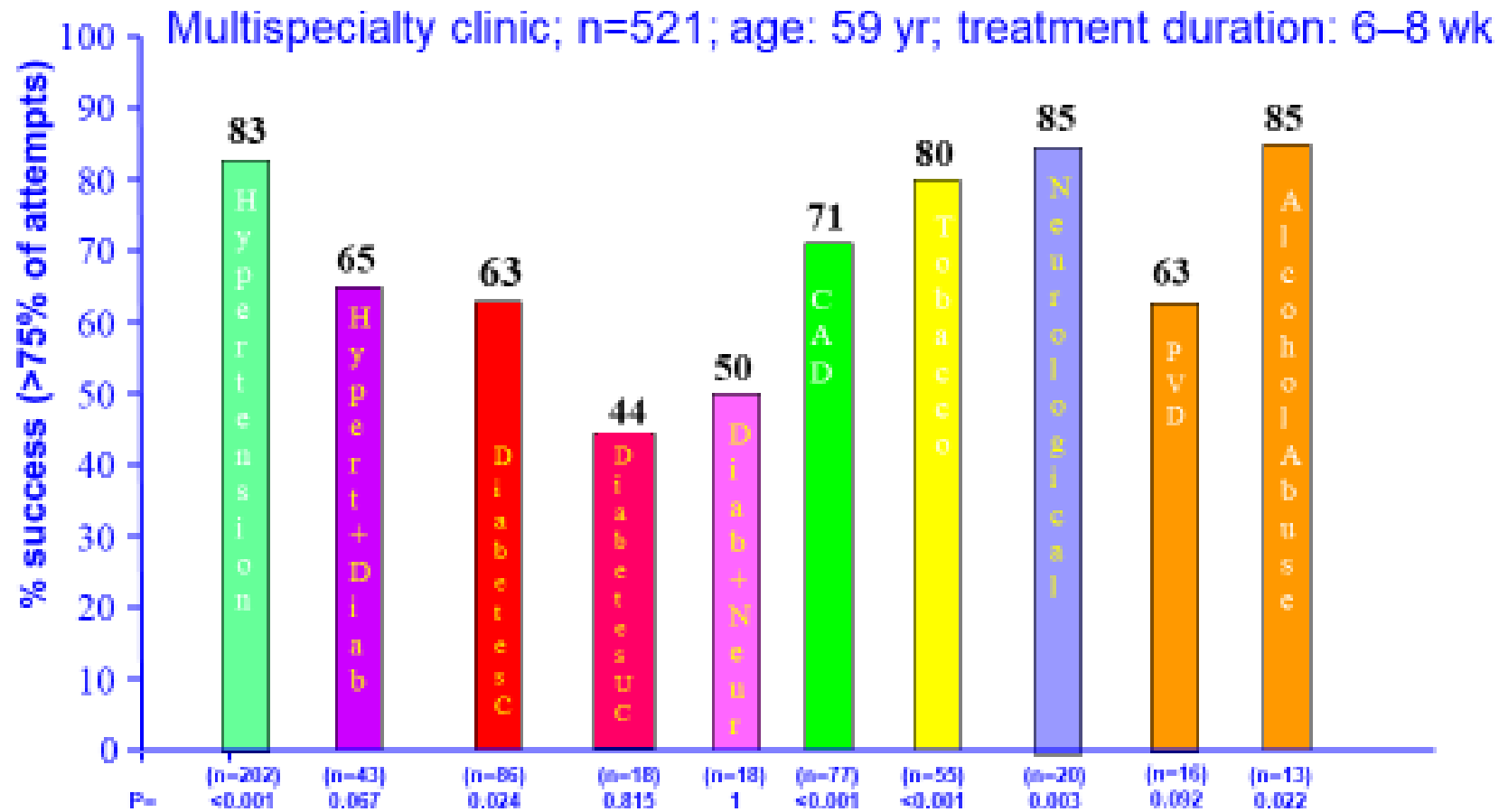
- ▶ ED is 3-4 times more common in men with T2DM<sup>5,6</sup>
- ▶ Severity correlates with diabetic control
- ▶ 40% of T2DM patients have low total testosterone (TD)  
→ independently predicts mortality in T2DM; treatment-resistant ED<sup>5,6</sup>

1. Kamenov, Z.A. (2015). *Exp Clin Endocrinol Diabetes*, 123, 141-58.
2. Hackett, G., Heald, A.H., Sinclair, A. et al. (2016a). *Clin Pract*, 70, 244-53.
3. Kirby, M. & Hackett, G. (2017). *International Journal of Clinical Practice*, 72:e13054. doi.org/10.1111
4. Mazzilli, R.J., Elia, M., Delfino, F. et al. (2015). *Clin Ther*, 166, e317-20
5. Chiles, K.A. (2016). *Transl Androl Urol*, 5, 195-200
6. Hackett, G. (2016). *British Journal of Diabetes*, 16, 52-57. doi:10.15277/bjd.2016.076





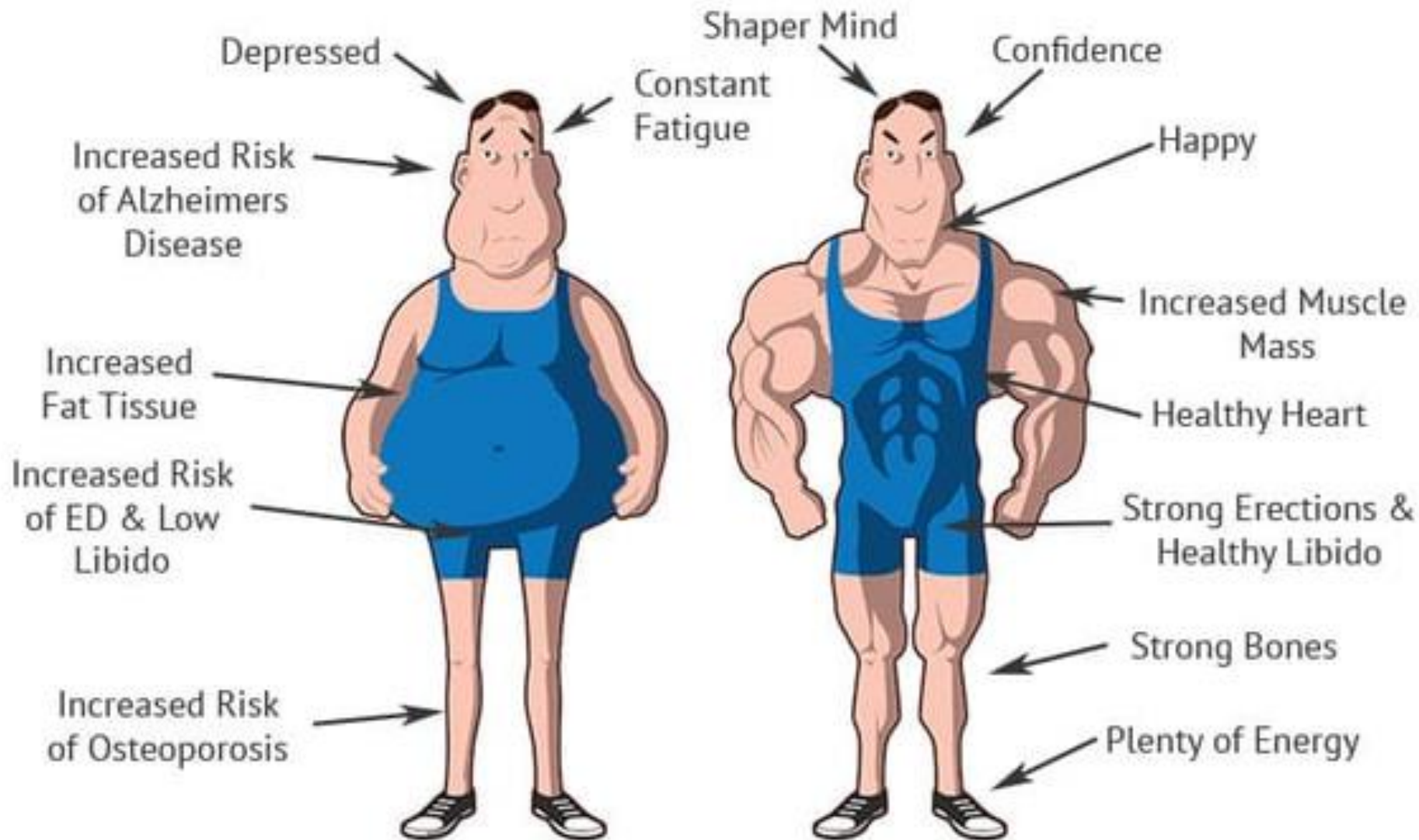
## Success of Sildenafil in Patients with Risk Factors or Concomitant Conditions (%)



\*Uncontrolled

Guay et al. J Andrology 2001;22(5):793–797

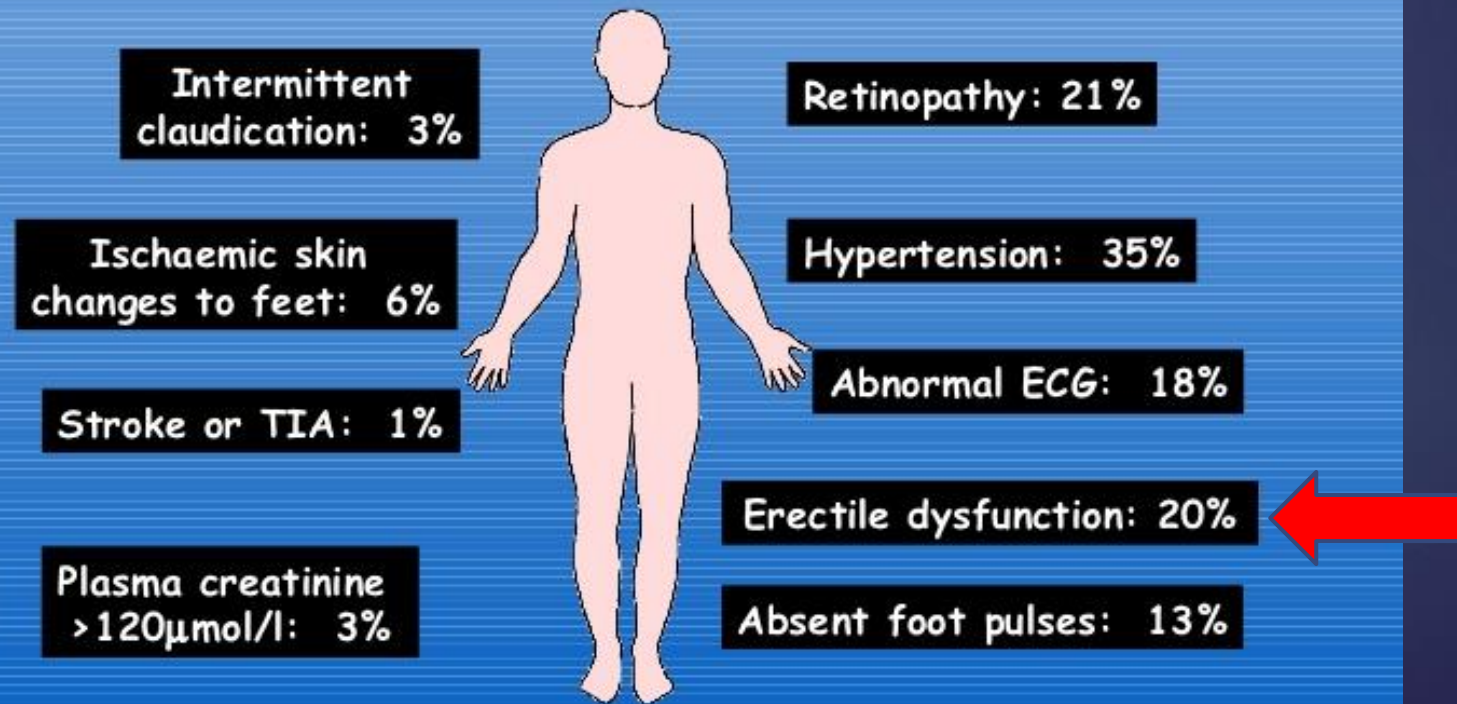
# Benefits of Optimal Testosterone



# Complications at diagnosis of T2DM

## Complications at Diagnosis

50% of newly presenting people with type 2 diabetes already have one or more complications at diagnosis



# Phosphodiesterase type-5 inhibitor use in type 2 diabetes is associated with a reduction in all-cause mortality

Simon G Anderson,<sup>1,2</sup> David C Hutchings,<sup>1</sup> Mark Woodward,<sup>2,3</sup> Kazem Rahimi,<sup>2</sup> Martin K Rutter,<sup>4,5</sup> Mike Kirby,<sup>6</sup> Geoff Hackett,<sup>7</sup> Andrew W Trafford,<sup>1</sup> Adrian H Heald<sup>8,9</sup>

Anderson SG, et al. *Heart* 2016;**0**:1–7. doi:10.1136/heartjnl-2015-309223



## ABSTRACT

**Objective** Experimental evidence has shown potential cardioprotective actions of phosphodiesterase type-5 inhibitors (PDE5is). We investigated whether PDE5i use in patients with type 2 diabetes, with high-attendant cardiovascular risk, was associated with altered mortality in a retrospective cohort study.

**Research design and methods** Between January 2007 and May 2015, 5956 men aged 40–89 years diagnosed with type 2 diabetes before 2007 were identified from anonymised electronic health records of 42 general practices in Cheshire, UK, and were followed for 7.5 years. HRs from multivariable survival (accelerated failure time, Weibull) models were used to describe the association between on-demand PDE5i use and all-cause mortality.

**Results** Compared with non-users, men who are prescribed PDE5is (n=1359) experienced lower percentage of deaths during follow-up (19.1% vs 23.8%) and lower risk of all-cause mortality (unadjusted HR=0.69 (95% CI: 0.64 to 0.79); p<0.001). The reduction in risk of mortality (HR=0.54 (0.36 to 0.80); p=0.002) remained after adjusting for age, estimated glomerular filtration rate, smoking status, prior cerebrovascular accident (CVA) hypertension, prior myocardial infarction (MI), systolic blood pressure, use of statin, metformin, aspirin and  $\beta$ -blocker medication. PDE5i users had lower rates of incident MI (incidence rate ratio (0.62 (0.49 to 0.80), p<0.0001) with lower mortality (25.7% vs 40.1% deaths; age-adjusted HR=0.60 (0.54 to 0.69); p=0.001) compared with non-users within this subgroup.

**Conclusion** In a population of men with type 2 diabetes, use of PDE5is was associated with lower risk of overall mortality and mortality in those with a history of acute MI.

# Mortality data of men with Type 2 Diabetes mellitus receiving PDE5 Inhibitors followed for approximately 4 years (N= 175)

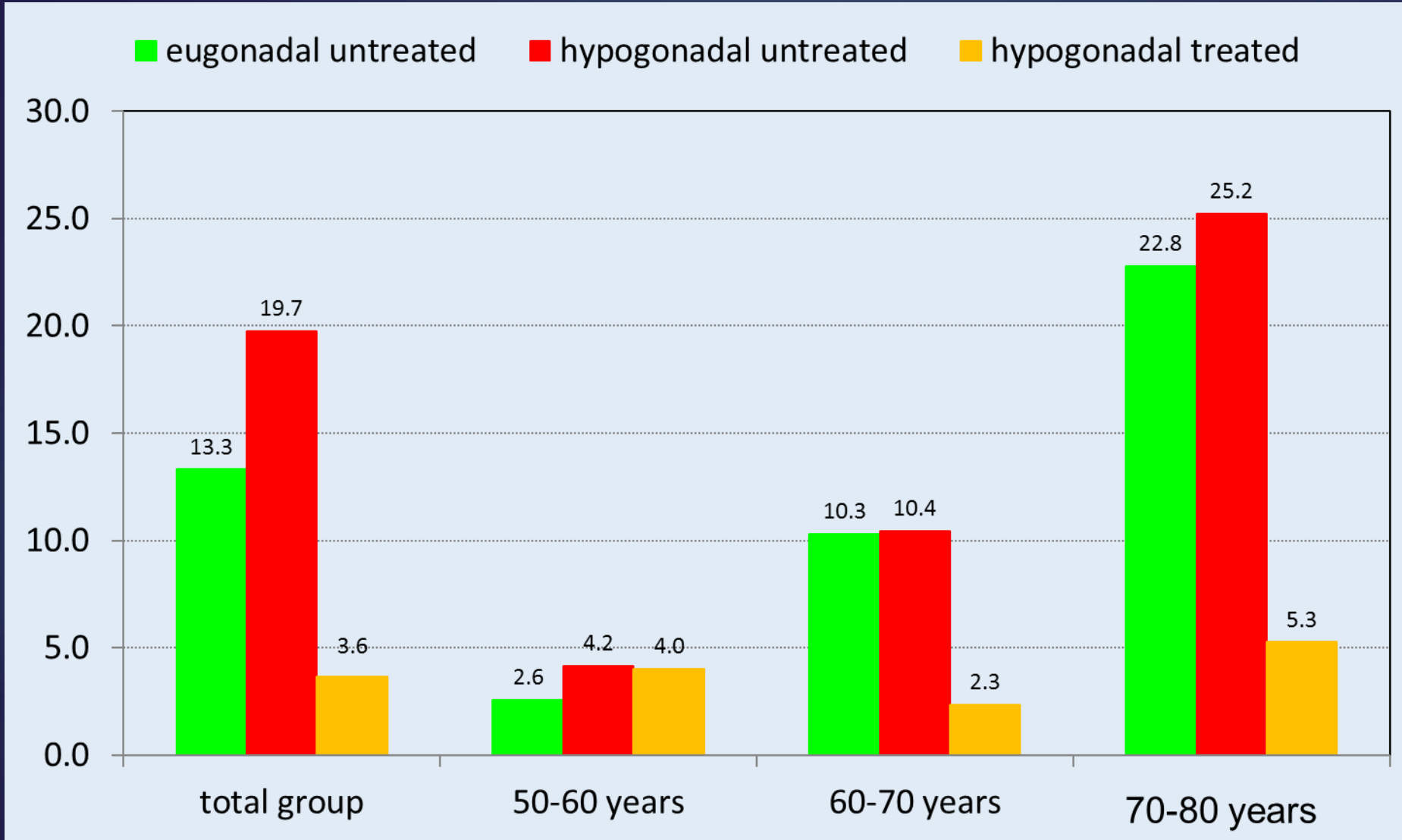


**Table 1** Demographic and mortality data of total study group and when classified by testosterone baseline and individual treatment categories

	Total group	Normal T/untreated	Low T/untreated	Low T/treated	PDE5I/untreated	PDE5I/treated
Patients	857	320	362	175	682	175
Age at initial visit (mean/SD) – years	63.5/11.7	64.2/11.1	65.5/11.8	58.3/11.0	64.7/11.8	58.9/9.9
Age at final visit/death (mean/SD) – years	67.4/11.7	68.3/11.1	69.2/11.7	62.0/11.0	68.6/11.7	62.7/10.1
Statin treated at final visit/death (%)	662 (77.3)	247 (77.2)	282 (77.9)	133 (76.0)	535 (78.5)	127 (72.6)
<b>Data at initial visit (n)</b>						
BMI (kg/m <sup>2</sup> )	31.2/5.7 (843)	29.8/4.7 (312)	31.8/5.9 (356)	32.6/6.4 (175)	31.2/5.8	31.4/5.3
HbA1c (%)	7.4/1.4 (710)	7.3/1.3 (289)	7.5/1.5(297)	7.6/1.3 (124)	7.4/1.4	7.5/1.1
Cholesterol (mean/SD) – mmol/l	4.2/1.0 (726)	4.1/0.9 (289)	4.1/1.0 (305)	4.5/1.1 (132)	4.1/1.0	4.3/1.1
TG (mean/SD) – mmol/l	1.8/1.2 (703)	1.6/0.9 (288)	1.9/1.2 (291)	2.2/1.5 (124)	1.8/1.1 (703)	1.9/1.4 (130)
HDL cholesterol (mean/SD) – mmol/l	1.2/0.4 (701)	1.2/0.3 (286)	1.1/0.3 (295)	1.2/0.7 (120)	1.2/0.4 (573)	1.1/0.5 (128)
Systolic BP (mean/SD) – mmHg	138.8/16.4 (851)	136.4/15.9 (318)	139.4/16.8 (358)	141.8/16.1(175)	138.7/16.8 (677)	138.9/15.2 (174)
Diastolic BP (mean/SD) – mmHg	78.7/10.3 (851)	77.8/9.9 (318)	78.3/10.4 (358)	81.4/10.4 (175)	78.1/10.4 (677)	81.1/9.4 (174)
Total testosterone – nmol/l	11.9/5.2 (833)	16.5/4.2 (309)	9.0/3.2 (351)	9.6/4.3 (173)	11.8/5.1 (663)	12.3/5.7 (170)
Free testosterone – pmol/l	194.5/111.2 (337)	288.0/71.0 (120)	163.2/82.2 (78)	131.3/99.0 (139)	206.5/106.3 (256)	156.5/118.2 (81)
<b>Mortality data</b>						
Number of deaths	103	36	61	6	100	3
Follow-up (mean/SD) – years	3.8/1.2	4.1/1.2	3.6/1.2	3.72/1.07	3.81/1.24	3.9/1.1
% Mortality	12.0	11.3	16.9	3.4	14.7	1.7
<b>% Mortality (n) – age categories (initial visit)</b>						
50–60 years	2.9 (173)	3.5 (57)	3.0 (67)	2.0 (49)	3.6 (112)	1.6 (61)
60–70 years	7.5 (294)	8.4 (119)	8.7 (115)	3.3 (60)	8.0 (236)	1.7 (58)
70–80 years	20.7 (222)	20.5 (88)	23.9 (109)	8.0 (25)	22.4 (201)	4.8 (21)
% major adverse coronary events (MACE)	6.8	7.5	6.6	5.7	7.3	4.6
% prostate related events	2.7	2.8	2.8	2.3	3.1	1.1

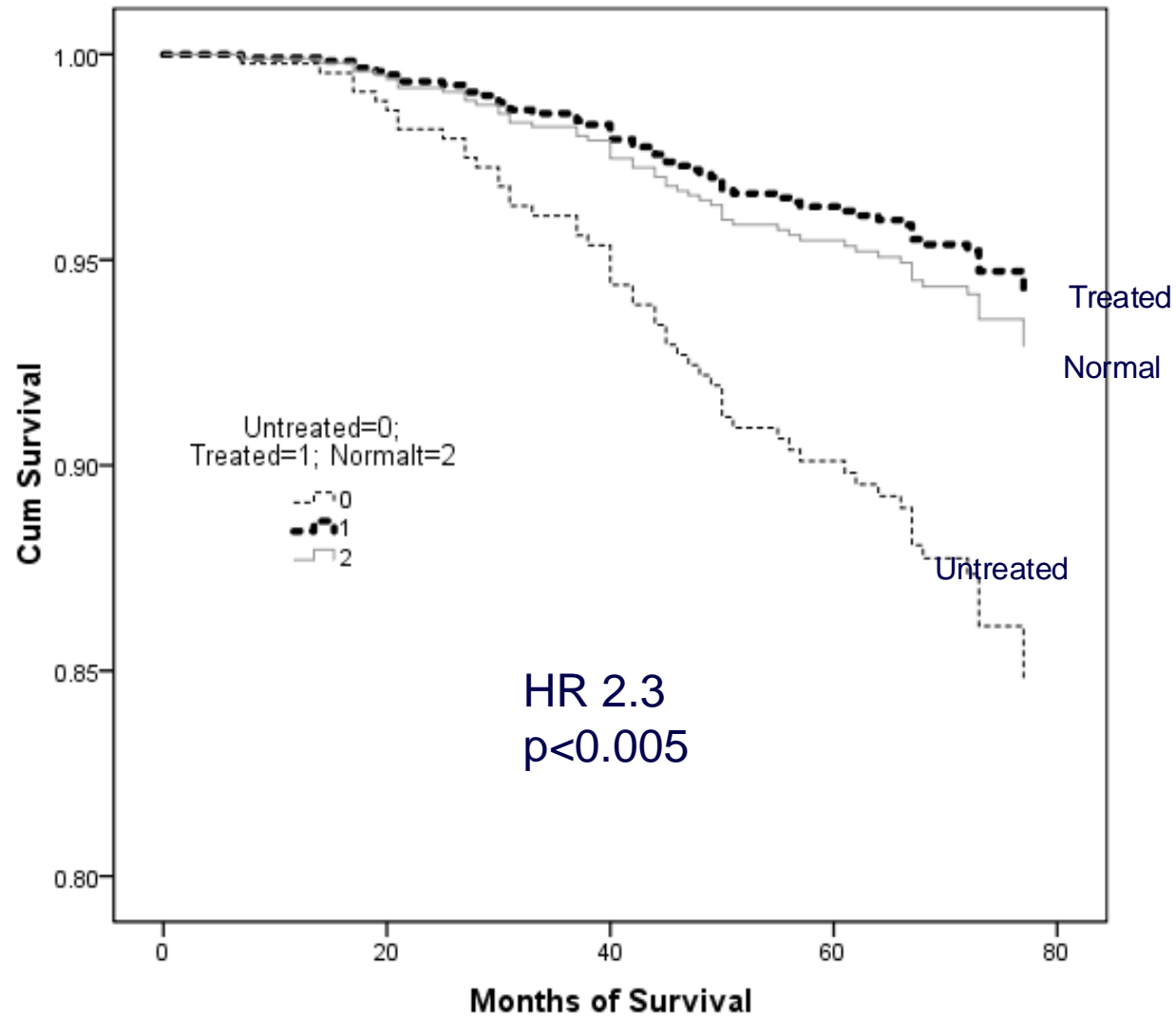
**HR: 0.21, CI: 0.066–0.68**

# Mortality data of men with Type 2 Diabetes mellitus not receiving PDE5 Inhibitors followed for approximately 4 years (N= 682)



**HR: 0.38, CI: 0.16–0.90**

# Effect of TRT on 6 year mortality in men with T2DM



# T2DM, ED, Hypogonadism



- ▶ Guidance T2DM: ED & TD
- ▶ **National & international:** All men with T2DM should be asked annually about ED, investigated and treated accordingly, and have their serum testosterone levels measured
- ▶ Opportunity to screen for (and treat) metabolic and cardiovascular health
- ▶ Financial incentive (QOF) to assess and diagnose ED in UK primary care (2013/14)



## QOF 2013/14: ED in T2DM

DM015. The percentage of male patients with diabetes, on the register, with a record of being asked about erectile dysfunction in the preceding 12 months <i>NICE 2012 menu ID: NM51</i>	4	40–90%
DM016. The percentage of male patients with diabetes, on the register, who have a record of erectile dysfunction with a record of advice and assessment of contributory factors and treatment options in the preceding 12 months <i>NICE 2012 menu ID: NM52</i>	6	40–90%

# Revitalise audit

- ▶ David, J. et al. (2017)
- ▶ 13 GP practices across the UK
- ▶ N = 3185

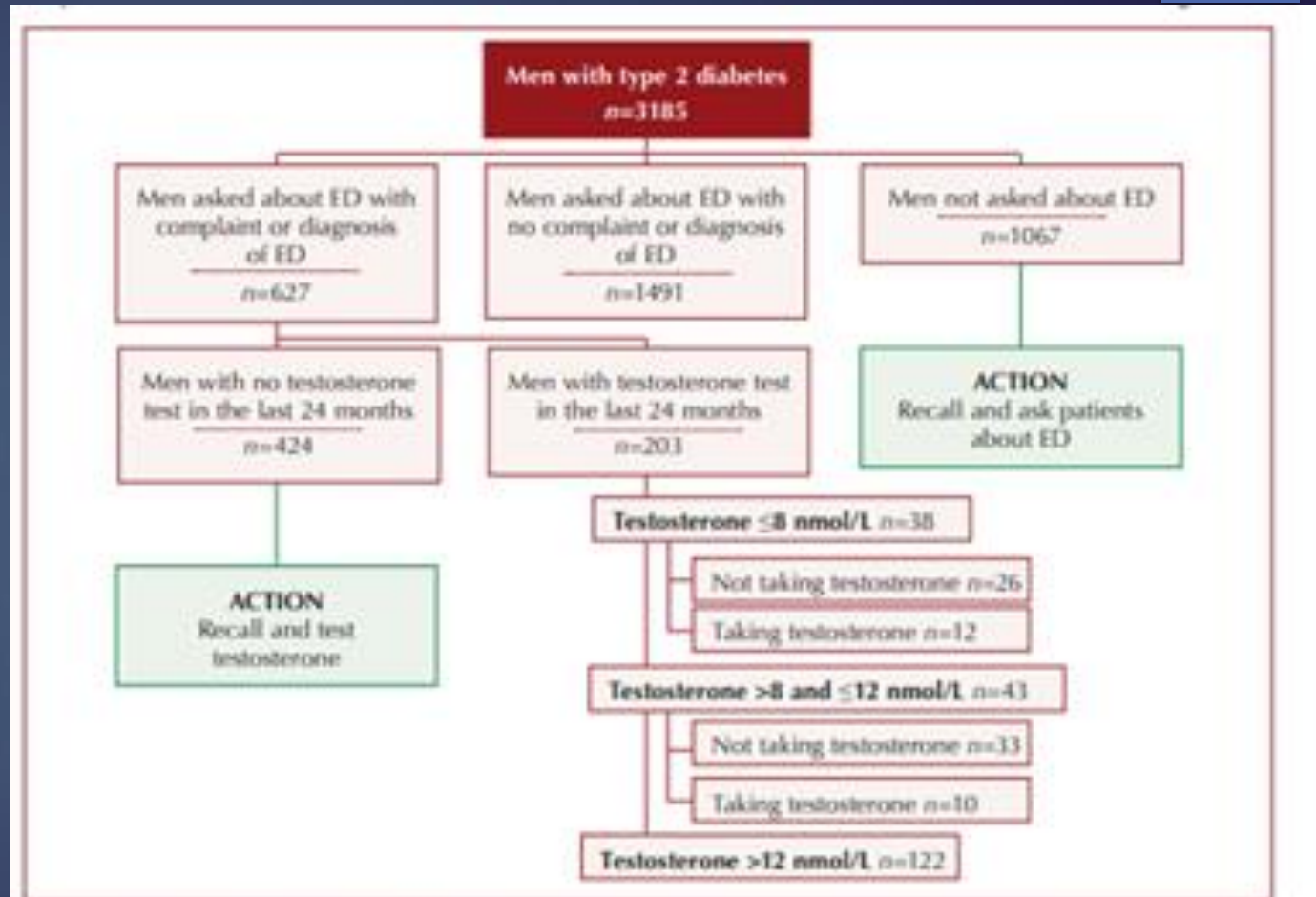


Figure 1. Disposition of men with type 2 diabetes from 13 GP practices. ED=erectile dysfunction.

# Revitalise audit

## Results:

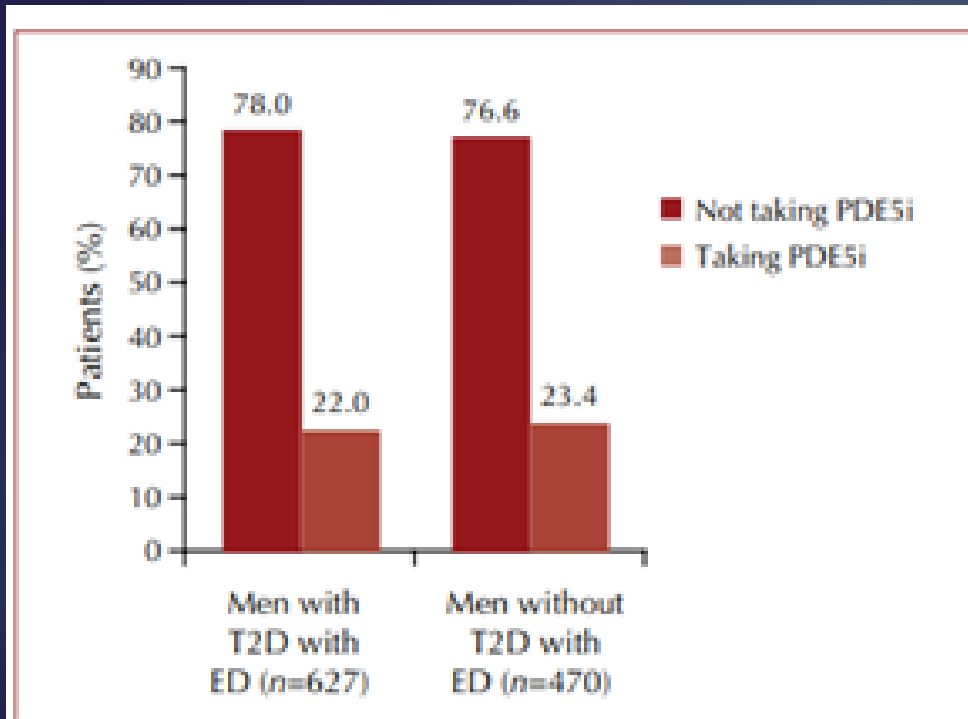


Figure 2. Use of phosphodiesterase type 5 inhibitors (PDE5i) in men with or without type 2 diabetes with erectile problems. ED=erectile dysfunction; T2D=type 2 diabetes.

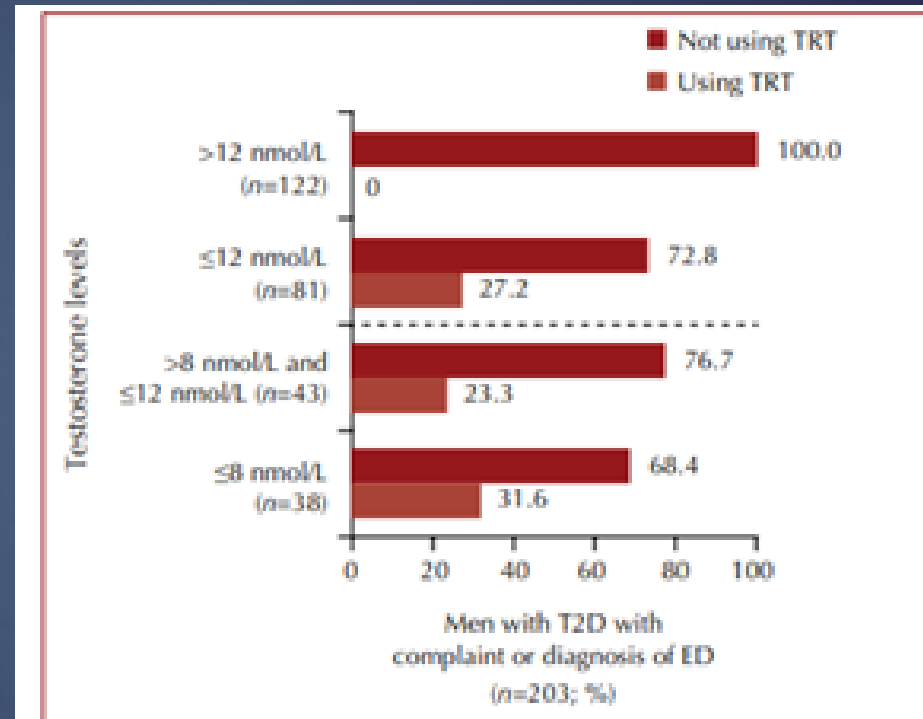
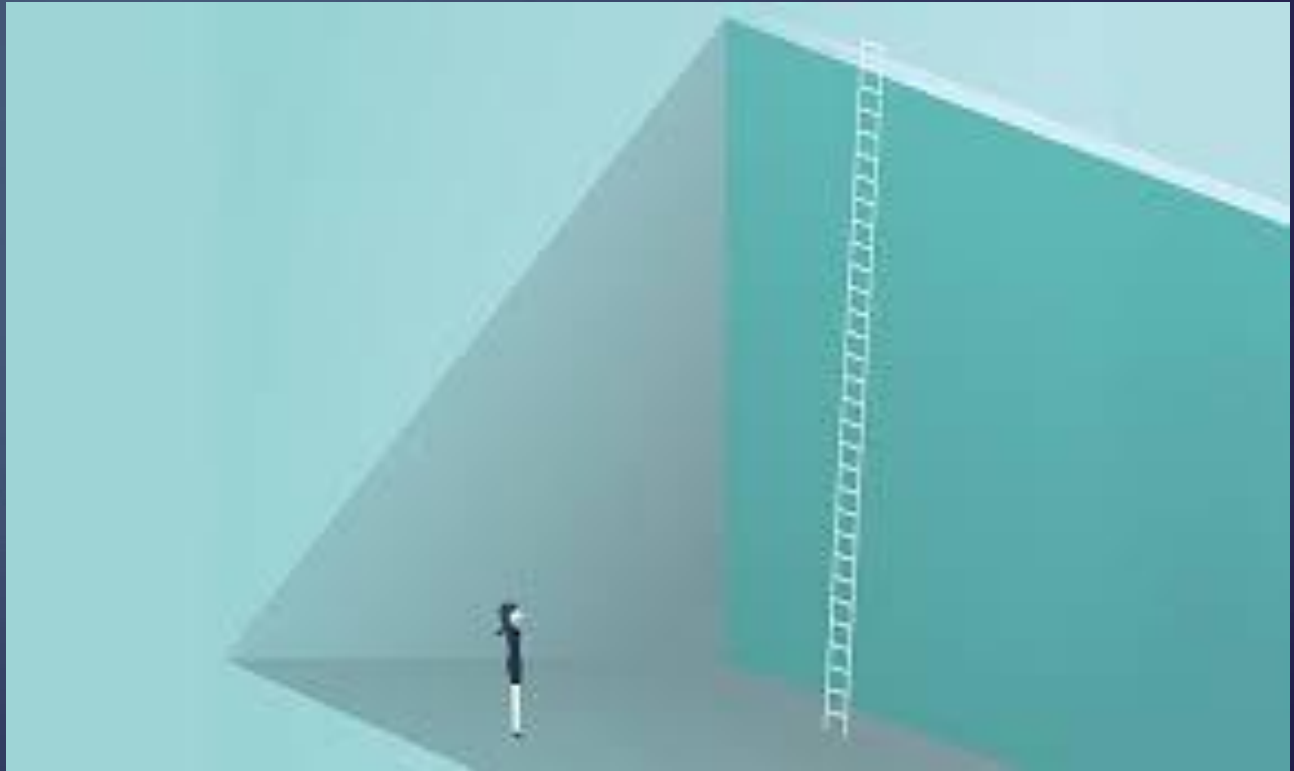


Figure 3. Testosterone levels and use of testosterone replacement therapy in men with type 2 diabetes with erectile problems. ED=erectile dysfunction; T2D=type 2 diabetes; TRT=testosterone replacement therapy.

**Conclusion:** Need for improvement of clinical Mx in men with and without T2DM at risk of ED/TD

What are the barriers to TD assessment and management?



▶ Feel not equipped to address or manage the problem

▶ Time pressures

▶ ?GPs attitudes towards TRT?





UCL

Title: Recent trends in incidence of recorded erectile dysfunction, hypogonadism, phosphodiesterase type 5 inhibitor prescriptions and testosterone replacement therapy in patients with Type 2 diabetes in a primary care setting

# Aims & Methodology



- ▶ Aim: Explore the effects of QOF on ED/TD assessment, diagnoses & management in T2DM patients
- ▶ Data source: The health improvement network (THIN) UK primary care database
- ▶ Study design: Retrospective cohort study
- ▶ Study population: Cohort of males (aged  $\geq 18$ y) diagnosed with T2DM and contributing to UK primary care electronic health records between 1999-2016
- ▶ Analysis: STATA15: Adjusted incident ratios (IRRs) using multivariate Poisson regression

# Analysis (1)

<b>N = 110,423</b>	<b>Mean age: 60y</b>
ED Assessment	53,003 (48%)
ED Diagnosis	14,355 (13%)
PDE5i prescriptions	10,623 (74%)

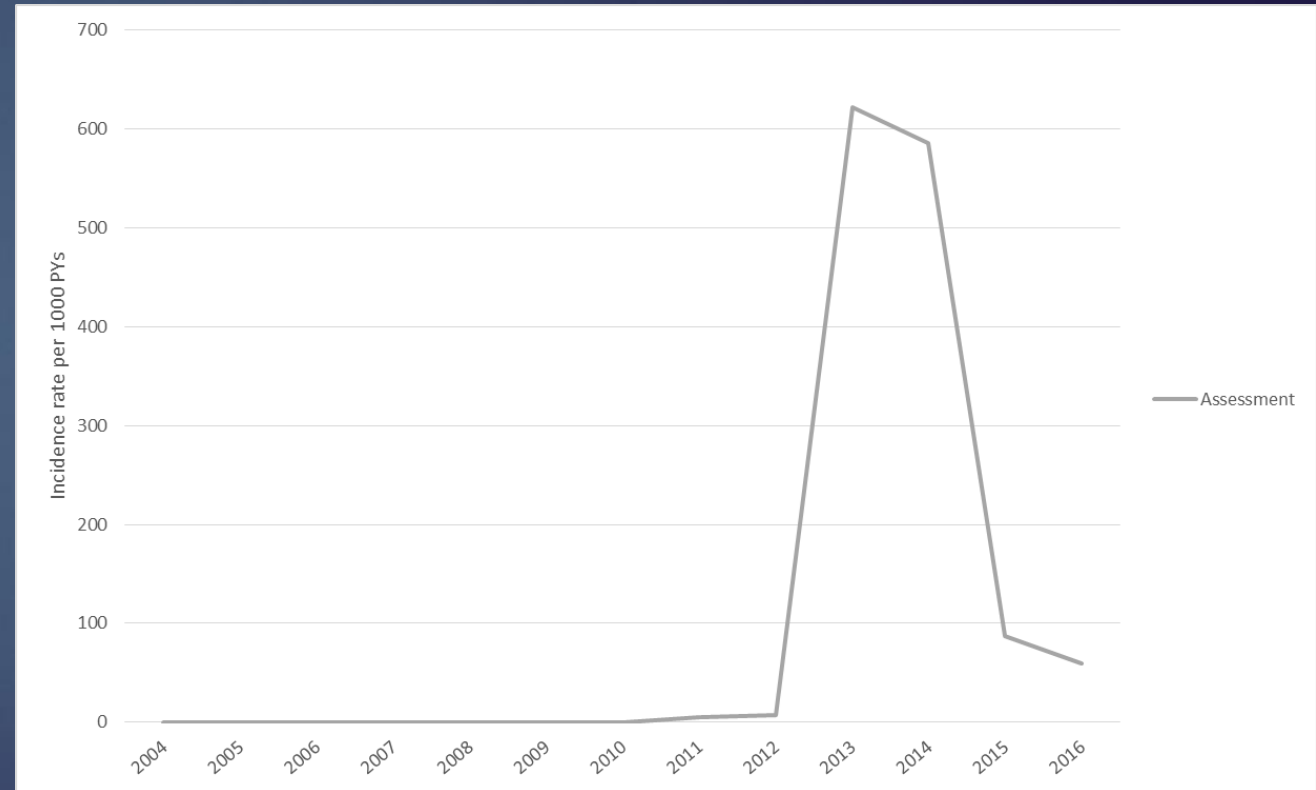


Figure 1. Time trends for ED assessment.



# Analysis (2)

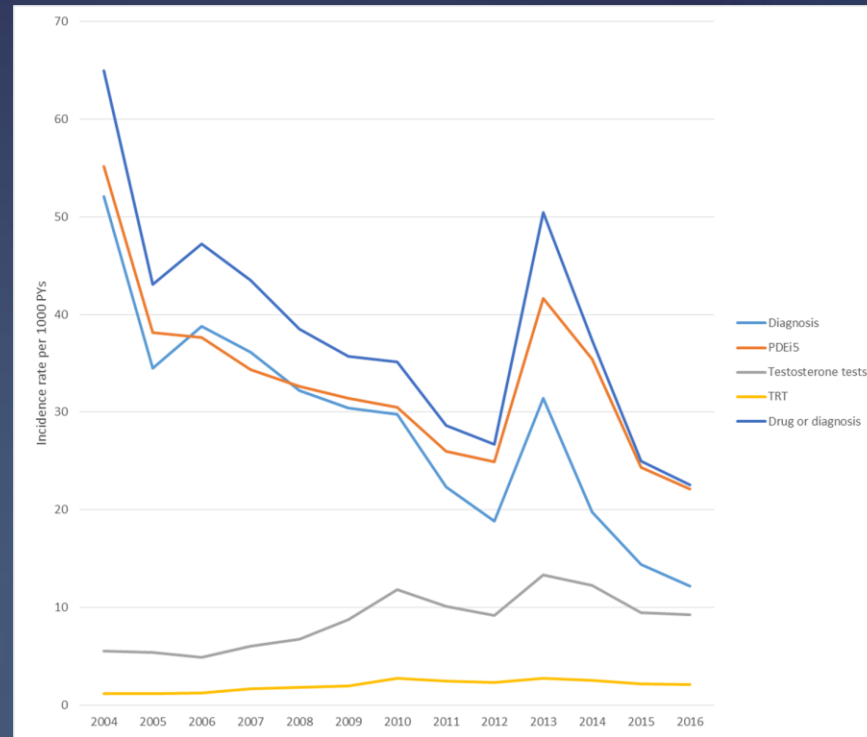


Figure 2. Time trends for ED diagnosis, testosterone testing and TRT/PDE5is prescriptions

- **ED assessment:** Adj Incident rate (IR) ↑ from 7.6 to 620 per 1000 PYAR from 2012 to 2013 (95% CI: 7.0- 8.3)  
↓ to 54 per 1000 PYAR in 2015
- **ED diagnoses:** IR doubled from 2012 to 13 (IRR 2.0; CI: 1.8 – 2.1)

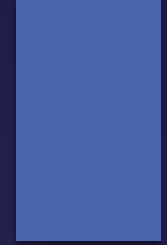
# Analysis (3)- Cross-sectional and multi-variate



## ➤ Testosterone:

- Of 1187 men with T2DM and newly diagnosed ED in 2015, 213 (18%) had at least one testosterone measurement, 45 (21%) of these had a serum testosterone  $\leq 8$ nmol/L, of which 9 (20%) received TRT
- Significant effect of age on ED assessment, diagnosis and PDE5i prescriptions ( $p < 0.001$ ) with most assessments, diagnoses and PDE5is prescriptions done in the 55-60y old age group

# Discussion & Conclusions



- ▶ Prevalence of recorded ED (13%) lower than reported in the literature
- ▶ ↓ PDE5i prescription rate
- ▶ Testosterone testing not common practice; ↓ TRT prescription rate
- ▶ Triad between ED, TD & CVD in pts with T2DM → early screening & treatment

# The GP and Sexual Problems – Just a matter of time?

- ▶ Overall, we are doing ok
- ▶ Time may be a factor, but not the only one
- ▶ To improve diagnosis/management of ED/TD in T2DM pts:
  - incorporation of guidelines into GP framework
  - financial incentives
  - solid GP education

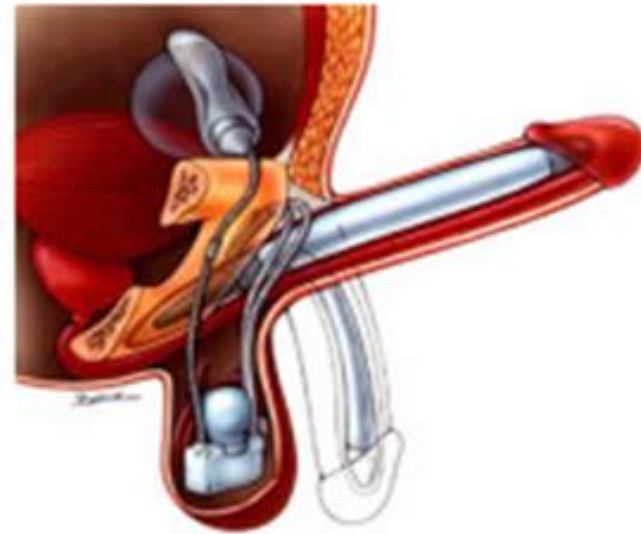
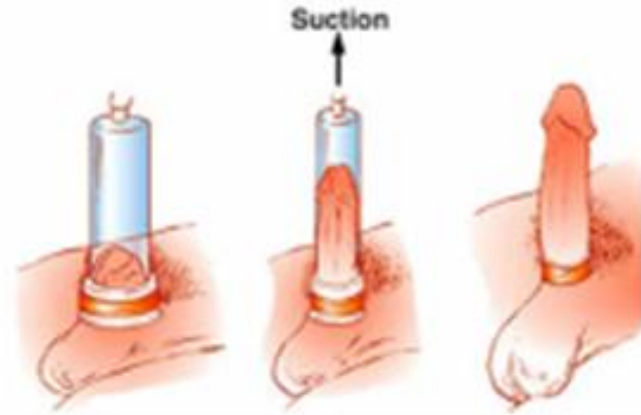




# ED Mx:

## Combination therapy

- PDE5 inhibitors (daily)
- Pelvic floor exercises
- Exercise regimes
- If failure to respond to PDE5,
- **Check testosterone**
- VED
- MUSE
- IC injections
- Penile prostheses



# TD Mx:

## A practical guide on the assessment and management of testosterone deficiency in adult men

Based on the 2017 British Society for Sexual Medicine (BSSM) guidelines on adult testosterone deficiency, with statements for UK practice<sup>1</sup>



### Why does it occur?

Testosterone deficiency (TD), also known as hypogonadism, may result from:<sup>2-4</sup>

- Problems with the testes [primary (hypergonadotropic) TD]
- Problems with the hypothalamus and pituitary gland [secondary (hypogonadotropic) TD]
- Problems with the hypothalamus/pituitary and testes (combined primary and secondary TD)
- Impaired action/suppression of testosterone

### How is it diagnosed?

- The diagnosis of symptomatic TD requires the presence of characteristic signs and symptoms,<sup>2,5-8</sup> PLUS reduced serum concentrations of total testosterone (TT) or free testosterone (FT)<sup>9</sup>

#### Psychological

- Changes in mood (e.g. anger, irritability, sadness, depression)
- Decreased well-being/poor self-rated health
- Diminished cognitive function (including impaired concentration, verbal memory and spatial performance)

#### Cardiometabolic

- Increased body mass index (BMI)/obesity
- Visceral obesity
- Metabolic syndrome
- Insulin resistance and type 2 diabetes

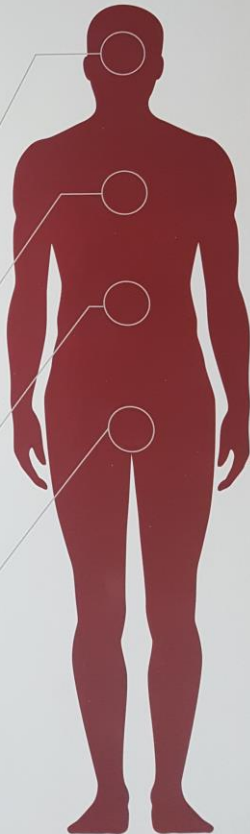
#### Physical

- Decreased body hair
- Gynaecomastia
- Decreased muscle mass and strength
- Hot flushes/sweats
- Sleep disturbances
- Fatigue
- Osteoporosis/height loss/low trauma fractures

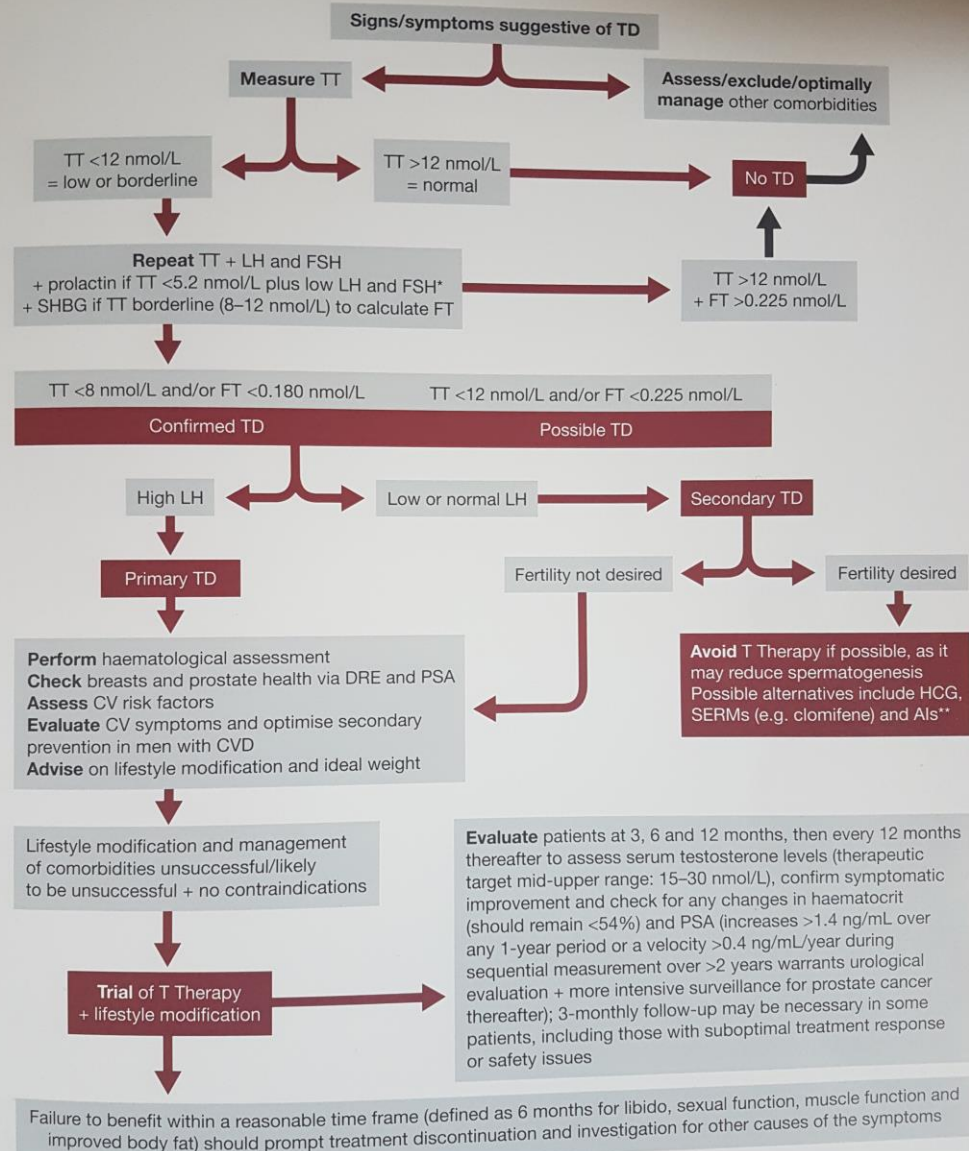
#### Sexual

- Delayed puberty
- Small testes
- Infertility
- Decreased sexual desire and activity
- Decreased frequency of sexual thoughts
- Erectile dysfunction (ED)
- Delayed ejaculation
- Decreased volume of ejaculate
- Decreased or absent morning/night-time erections

- The 3 most common symptoms of TD are ED, loss of early morning erections and low sexual desire – men often present with sexual dysfunction and a desire for treatment



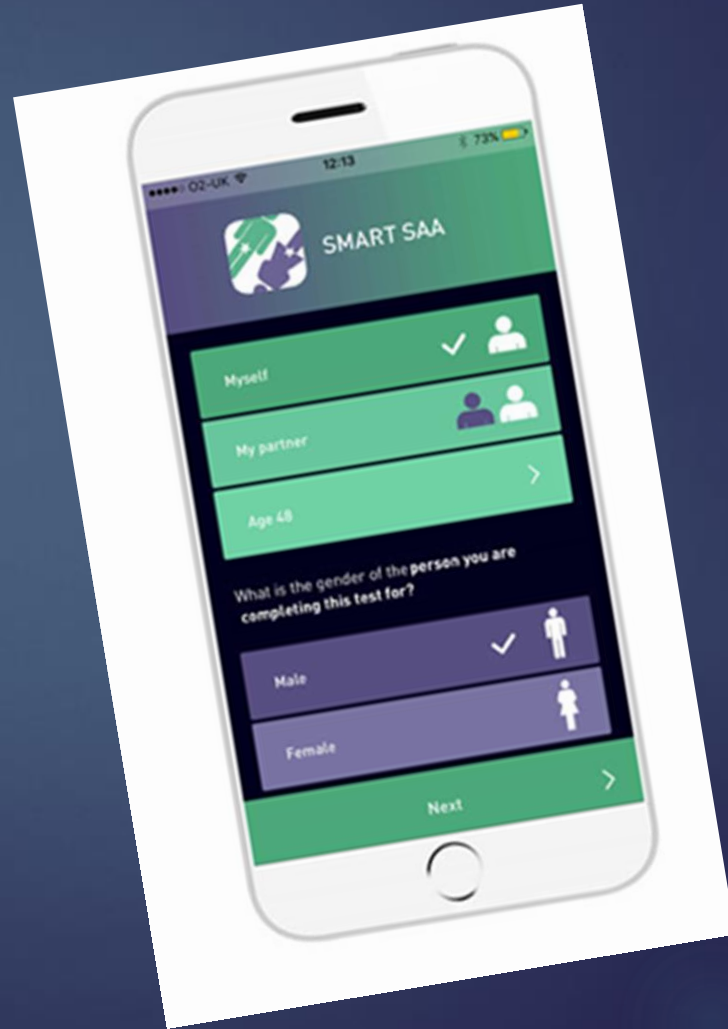
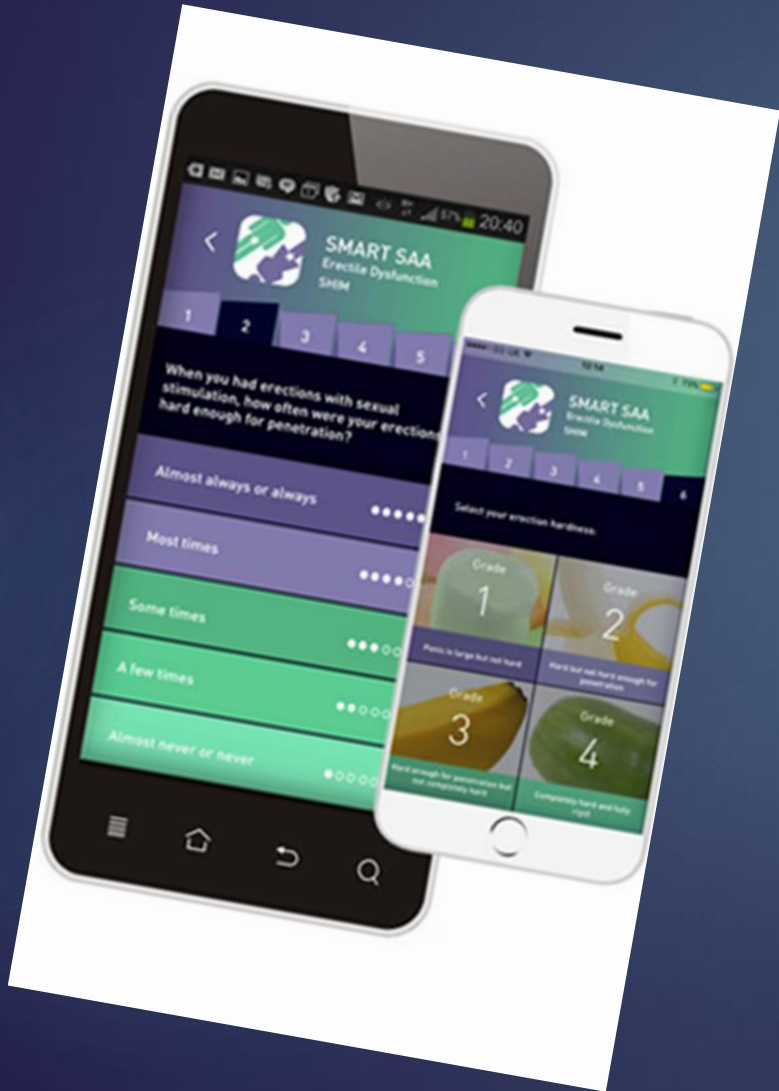
## Diagnosing and managing TD in adult men<sup>2,7,9,12,13</sup>



Adapted from Minhass and Mulhall, 2017.<sup>2</sup>  
 AI – aromatase inhibitor, CV – cardiovascular, CVD – cardiovascular disease, FSH – follicle-stimulating hormone, FT – free testosterone, HCG – human chorionic gonadotropin, LH – luteinising hormone, MRI – magnetic resonance imaging, PSA – prostate-specific antigen, SERM – selective oestrogen receptor modulator, SHBG – sex hormone-binding globulin, T therapy – testosterone therapy, TT – total testosterone.  
 \*For men with TT levels < 5.2 nmol/L plus low LH and FSH or increased prolactin levels, refer to endocrinology or arrange a pituitary MRI scan to exclude a pituitary adenoma.<sup>2,14</sup>  
 \*\*These drugs should not be used if pituitary function is compromised. SERMs and AIs are not currently licensed for TD.

Smart SAA:

<https://sexualadviceassociation.co.uk/app/>





# Take home message:

- ▶ ED assessment, diagnosis & management is important in relation to QoL, underlying physical health, and risk factor management
- ▶ ED is independent risk factor for cardiovascular events, risk amplified in DM
- ▶ TD is common in DM → independently predicts mortality and treatment resistant ED
- ▶ BSSM Primary Care Guidelines: For ED/TD
- ▶ Various additional options to treat ED in secondary care



Thank you!

NO pills - NO exercise  
In only ONE Month  
You Can do it too



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Now!!!

Photoshop Courses  
The best tool to change your body