Erectile Dysfunction and CVD
– An Affair of the Heart?

Ketan Dhatariya
Consultant in Diabetes NNUH
To Begin With…. 

About \( \frac{2}{3} \) of all men do not discuss ED with their Health Care Professional, but evidence shows that they would like to be asked.

Erectile Dysfunction

- “Inability of the male to attain and maintain erection of the penis sufficient to permit satisfactory sexual intercourse.”
  - NIH Consensus Development Panel on Impotence, 1993

- “The persistent or repeated inability, for at least 3 months duration, to attain and/or maintain an erection sufficient for satisfactory sexual performance (in the absence of an ejaculatory disorder, such as premature ejaculation).”
  - Process of Care Consensus Panel, 1998

- “The consistent or persistent inability to attain and/or maintain a penile erection sufficient for sexual performance.”
  - WHO-ISIR 1st International Consultation on ED, 1999
Causes of Erectile Dysfunction

Diabetes Mellitus 40%
Vascular Disease 30%
Spinal Injury 8%
Endocrine Problems 6%
M.S 3%
Surgery 13%

ONLY ORGANIC CAUSES OF ERECTILE DYSFUNCTION LISTED, OTHER CAUSES INCLUDE PSYCHOGENIC E.D WHICH IS NOT INCLUDED HERE.
Predicted Increase in Prevalence of ED by 2025

Worldwide prevalence will increase from 152 million men in 1995 to 322 million men in 2025

North America: \(\uparrow 9.1\) million

Europe: \(\uparrow 11.9\) million

Asia: \(\uparrow 113\) million

South/Central America and Caribbean: \(\uparrow 15.6\) million

Africa: \(\uparrow 19.3\) million

Oceania: \(\uparrow 0.9\) million

ED: Underdiagnosed & Undertreated

81% of ED is not diagnosed
Only 10-13% of the total ED population is treated

19% Diagnosed (13% Treated)
81% of ED goes undiagnosed

10% reported seeking or receiving treatment
90% men >45 yrs old never seek care for sexual problems

Decision Resources Adaptation of MMAS study 2001
McKinlay JB *Int J Imp Res* 2000
ED Prevalence and Severity

81% of men with ED have only a minimal-to-moderate degree of severity

Feldman et al  J Urol 1994;151:54-61
Age as a Risk Factor for ED: Cologne Male Survey

All odds ratios significantly different from 1.0 ($P<0.0001$).

*Odds ratio=likelihood of an outcome of sexual dysfunction relative to the norm (1.0).

ED Severity Increases with Age and Diabetes Duration

Prevalence of Erectile Dysfunction by Ethnic Origin

Other Risk Factors for ED: Cologne

Male Survey

Odds ratio* vs men aged 30–39 y

Hypertension: 1.58
LUTS: 2.11
Diabetes: 3.95
Pelvic surgery: 6.03

All odds ratios significantly different from 1.0 (P<0.0001).
*Odds ratio=likelihood of an outcome of sexual dysfunction relative to the norm (1.0).
Prevalence of Risk Factors

Total U.S. men ≥ 45 years old: 40,027,000 (1997)

<table>
<thead>
<tr>
<th>ED Risk Factor*</th>
<th>Estimated number of men ≥ 45 years old with risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>3,742,000 (9.3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16,927,000 (42.3%)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>8,525,000 (21.3%)</td>
</tr>
</tbody>
</table>

*Severe depression, HDL-C < 30 mg/dL, and prostatectomy are other key risk factors for ED

## ED Prevalence: Association with Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>ED Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete ED</td>
</tr>
<tr>
<td>Heart Disease (smoker)</td>
<td>57</td>
</tr>
<tr>
<td>Depression (severe)</td>
<td>41</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
</tr>
<tr>
<td>HDL-C &lt; 30 mg/dL</td>
<td>17</td>
</tr>
<tr>
<td>General Population</td>
<td>9.6</td>
</tr>
</tbody>
</table>

Feldman et al J Urol 1994;151:54-61
ED, CVD, and Depression
A Mutually Reinforcing Triad

ED, CVD, and Depression
A Mutually Reinforcing Triad

Medications
Lifestyle factors
Psychosocial factors
Demographic factors

ED
CVD & DM
Depression

Goldstein I Am J Cardiol 2000;86:41F-45F
Comorbidities in Ageing Males

**ED and Diabetes**

- Prevalence of ED in diabetes is very high 35%-75%
- ED occurs in 50% of people with diabetes within 10 years of diagnosis
- ED my be the presenting symptom of diabetes in up to 12%
- Incidence of ED in diabetes is also high.
- MMAS: age-adjusted probability of complete ED in men with diabetes three times higher compared to those with diabetes
- Glycaemic control prevents or postpones neuropathy
- Smoking doubles the risk of ED

Johannes CB et al J Urol 2000;163:460
Vascular Complications Of Type 2 Diabetes At The Time Of Diagnosis

1. Retinopathy\(^1\) 39%
2. Nephropathy\(^2\) 18%
3. Erectile dysfunction\(^1\) 20%
4. Ischaemic skin changes (foot)\(^1\) 6%
5. Abnormal vibration threshold (foot)\(^1\) 7%
6. Cerebrovascular disease\(^3\) 7%
7. Abnormal ECG\(^1\) 18%
8. Hypertension\(^1\) 35%
9. Intermittent claudication\(^3\) 4.5%
10. Absent foot pulses\(^1\) 13%

1. UKPDS 33 Lancet 1998;352(9193):837-853
Erectile Dysfunction and Atherosclerosis: Shared Risk Factors

<table>
<thead>
<tr>
<th>Coronary artery disease</th>
<th>Erectile Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age</td>
<td>• Age</td>
</tr>
<tr>
<td>• Dyslipidemia</td>
<td>• Dyslipidemia</td>
</tr>
<tr>
<td>• Hypertension</td>
<td>• Hypertension</td>
</tr>
<tr>
<td>• Diabetes</td>
<td>• Diabetes</td>
</tr>
<tr>
<td>• Smoking</td>
<td>• Smoking</td>
</tr>
<tr>
<td>• Sedentary lifestyle</td>
<td>• Sedentary lifestyle</td>
</tr>
<tr>
<td>• Obesity</td>
<td>• Obesity</td>
</tr>
<tr>
<td>• Depression</td>
<td>• Depression</td>
</tr>
<tr>
<td>• Male gender</td>
<td>• Coronary artery disease, peripheral vascular disease</td>
</tr>
</tbody>
</table>
ED is Associated with Premature Death

The presence of ED is predictive of:

- All-cause death (hazard ratio [HR] 1.84, 95% confidence interval [CI] 1.21 to 2.81, \( P=0.005 \))
- CV related death (HR 1.42, 95% CI 1.04 to 1.94, \( P=0.029 \))
  - CV death (HR 1.93, 95% CI 1.13 to 3.29, \( P=0.016 \))
  - MI (HR 2.02, 95% CI 1.13 to 3.58, \( P=0.017 \))

Böhm M et al Circulation 2010;121:1439-1446
Vascular Outcomes of Endothelial Insults: The ED Connection

Precursors

Diabetes
Hypertension
Vasoconstriction

Oxidative stress

Endothelial cell injury

Erectile dysfunction
Atherosclerosis
Thrombosis

Outcomes

Dzau VJ et al Am J Cardiol 1997;80(9A):33I-39I
Can Sexual Dysfunction in a Vascular Patient be Treated?

- Is sex safe – generally?
- Is sex safe – for the individual?
- Can we treat ED safely in patients with established CVD or those at high risk of CVD (e.g. with diabetes)?
Energy Requirements of Sexual Activity

- In general, the physiological cost of sexual activity with the usual partner is similar to that of exercise of mild-to-moderate intensity in most middle-aged men, with or without coronary artery disease.

METS = Metabolic Equivalent of Task Units

Jackson et al Int J Clin Practice 2002;56;663-671
**METS equivalents as a guide to relating daily activity to sexual activity**

*ENERGY EXPENDITURE IN RESTING STATE METS = 1*

<table>
<thead>
<tr>
<th>Activity</th>
<th>METS Expended</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIFTING AND CARRYING OBJECTS (9-20kg)</td>
<td>4-5 METS EXPENDED</td>
</tr>
<tr>
<td>WALKING 1.6km (1 MILE) LEVEL GROUND (20 MINUTES)</td>
<td>3-4 METS EXPENDED</td>
</tr>
<tr>
<td>GOLF</td>
<td>4-5 METS EXPENDED</td>
</tr>
<tr>
<td>GARDENING (DIGGING)</td>
<td>3-5 METS EXPENDED</td>
</tr>
<tr>
<td>D.I.Y</td>
<td>4-5 METS EXPENDED</td>
</tr>
<tr>
<td>LIGHT HOUSEWORK (e.g. IRONING / POLISHING)</td>
<td>2-4 METS EXPENDED</td>
</tr>
<tr>
<td>HEAVY HOUSEWORK (e.g. SCRUBBING FLOORS, CLEANING WINDOWS)</td>
<td>3-6 METS EXPENDED</td>
</tr>
</tbody>
</table>

Jackson et al Int J Clin Practice 2002;56;663-671
METS During Sex

MEASURES FOR COUPLES IN A LONG STANDING RELATIONSHIP

Average peak heart rate: 110–130 beats/min
Average peak systolic blood pressure: 150–180 mm Hg
Average metabolic expenditure

- 2-3 METS before orgasm
- 3-4 METS during orgasm
- 5-6 METS upper range

Jackson et al Int J Clin Practice 2002;56;663-671
Sildenafil Experience: Unsuccessful Intercourse

Fink HA et al Arch Intern Med 2002;162:1349-1360

- **Placebo**
  - Mild to moderate ED
    - N=1359
  - Severe ED
    - N=3265*

- **Sildenafil**
  - Mild to moderate ED
    - N=1359
  - Severe ED
    - N=3265*

*Double counted the men in crossover trials

72% Did Not Succeed, 28% Successful
63% Successful, 37% Did Not Succeed
11% Successful, 81% Did Not Succeed
47% Successful, 53% Did Not Succeed
Sildenafil Efficacy in Diabetes

Has the treatment you have been taking over the past 4 weeks improved your erections?

*P<0.001 vs placebo

Rendell MS et al JAMA 1999;281:421-426
Vardenafil Efficacy in Diabetes

Has the treatment you have been taking over the past 4 weeks improved your erections?

*P<0.001 vs Placebo

Goldstein I et al Diabetes Care 2003;26:777-773
Has the treatment you have been taking over the past 4 weeks improved your erections?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Placebo</th>
<th>10 mg</th>
<th>20 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Answering Yes</td>
<td>25%</td>
<td>56%</td>
<td>64%</td>
</tr>
</tbody>
</table>

n= 71, 73, 131
Questions on Sexual Patterns

- What proportion of patients are able to plan or predict their sexual activity:
  - 2 hours ahead?
  - 6 hours ahead?
  - 12 hours ahead?
  - 24 or 36 hours ahead?

- What proportion of these patients are willing to take a drug based on this expectation of sexual activity?
Restoring Natural Intercourse Patterns

Night/Evening: 48% Male, 39% Female
Afternoon: 16% Male, 19% Female
Morning: 5% Male, 7% Female
No Set Pattern: 30% Male, 34% Female

Changes in Patterns of Treatment Over 6 Months

Significantly more new to ED treatment patients started on tadalfil remained on their original therapy vs. sildenafil or vardenafil

NICE on Erectile Dysfunction

- Ask annually

- If there are no contraindications, offer a PDE 5 (lowest cost drug first)

- If unsuccessful, offer other medical, surgical, or psychological management
But What is ‘Low Cost’?

- Acquisition cost?
- Costs associated with frequent consultations?
- Costs associated with secondary care referrals?
Recent Data

- 2 Birds with 1 stone?
  - Sildenafil treatment at 50 mg tds for 1 year in people with stable, chronic heart failure improved functional capacity and clinical status

Gauzzi et al Circulation: Heart failure 2011;4:8-17
ABCD position statement on the management of hypogonadal males with type 2 diabetes

K Dhatriya*, D Nagi, TH Jones; on behalf of the Association of British Clinical Diabetologists (ABCD)
In Summary

- ED is common in men with diabetes
- Treatment is often delayed
- Give the treatment time to work (or fail!)
- CVD is also VERY common
- ED is a strong predictor of early cardiovascular morbidity and mortality
- Aggressive CV risk reduction is necessary in men with ED
The Ultimate Goal?

Thank you for your attention
Any Questions?