Erectile Dysfunction and CVD – An Affair of the Heart?
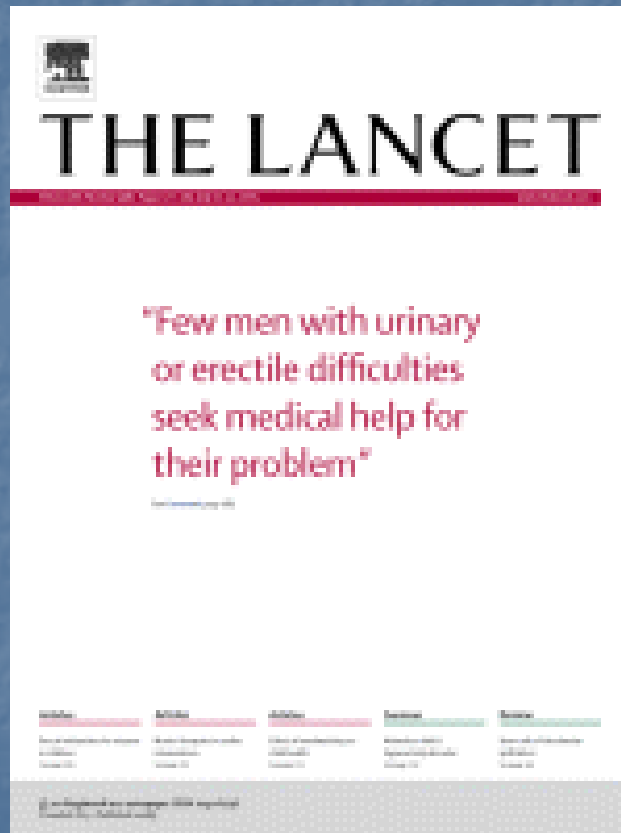
Ketan Dhatariya

Consultant in Diabetes NNUH

To Begin With....

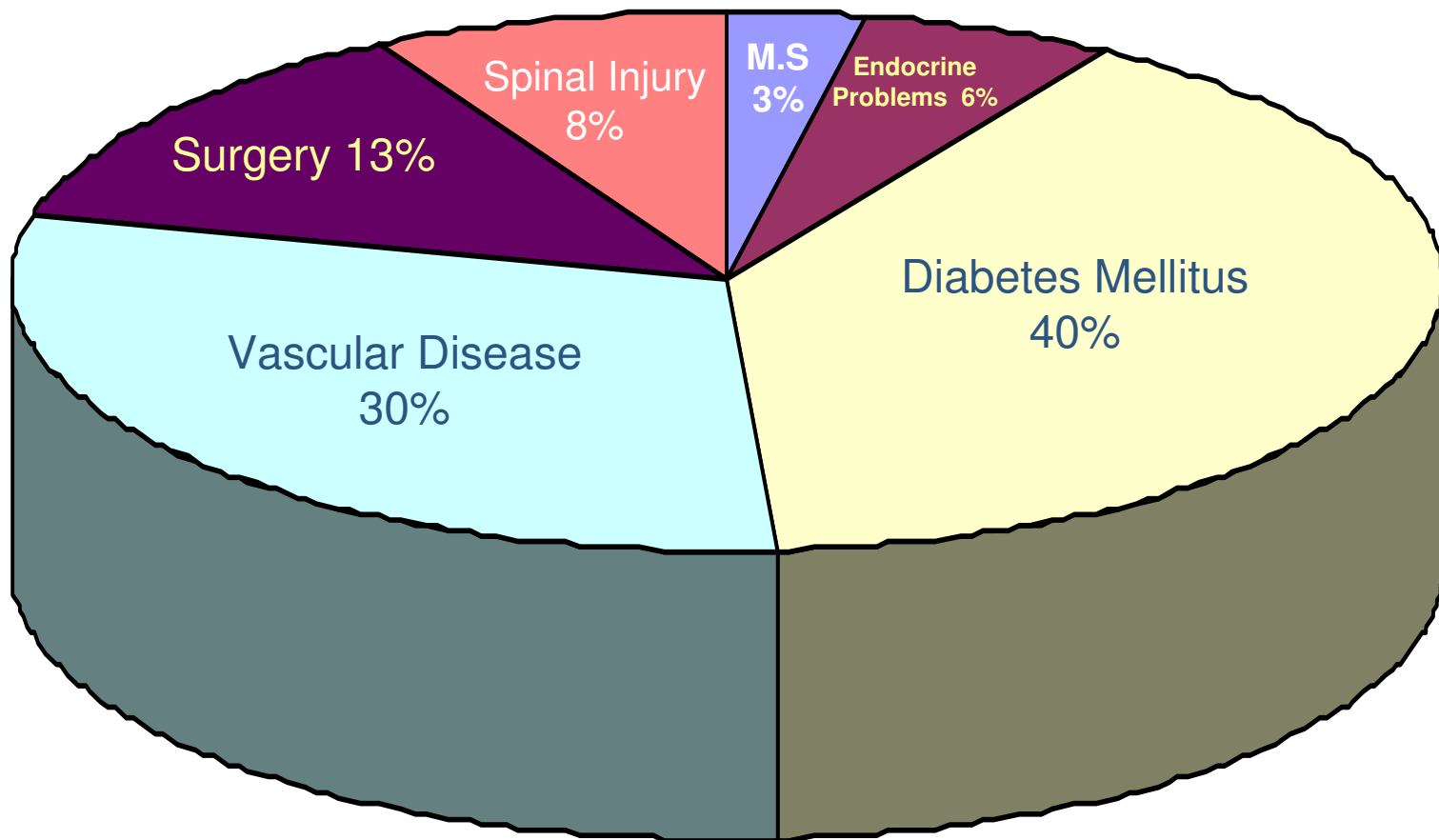"Few men with urinary or erectile difficulties seek medical help for their problem"

About $^2/_3$ of all men do not discuss ED with their Health Care Professional, but evidence shows that they would like to be asked

Rosen RC Lancet 2005;366(9481):183-185

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."

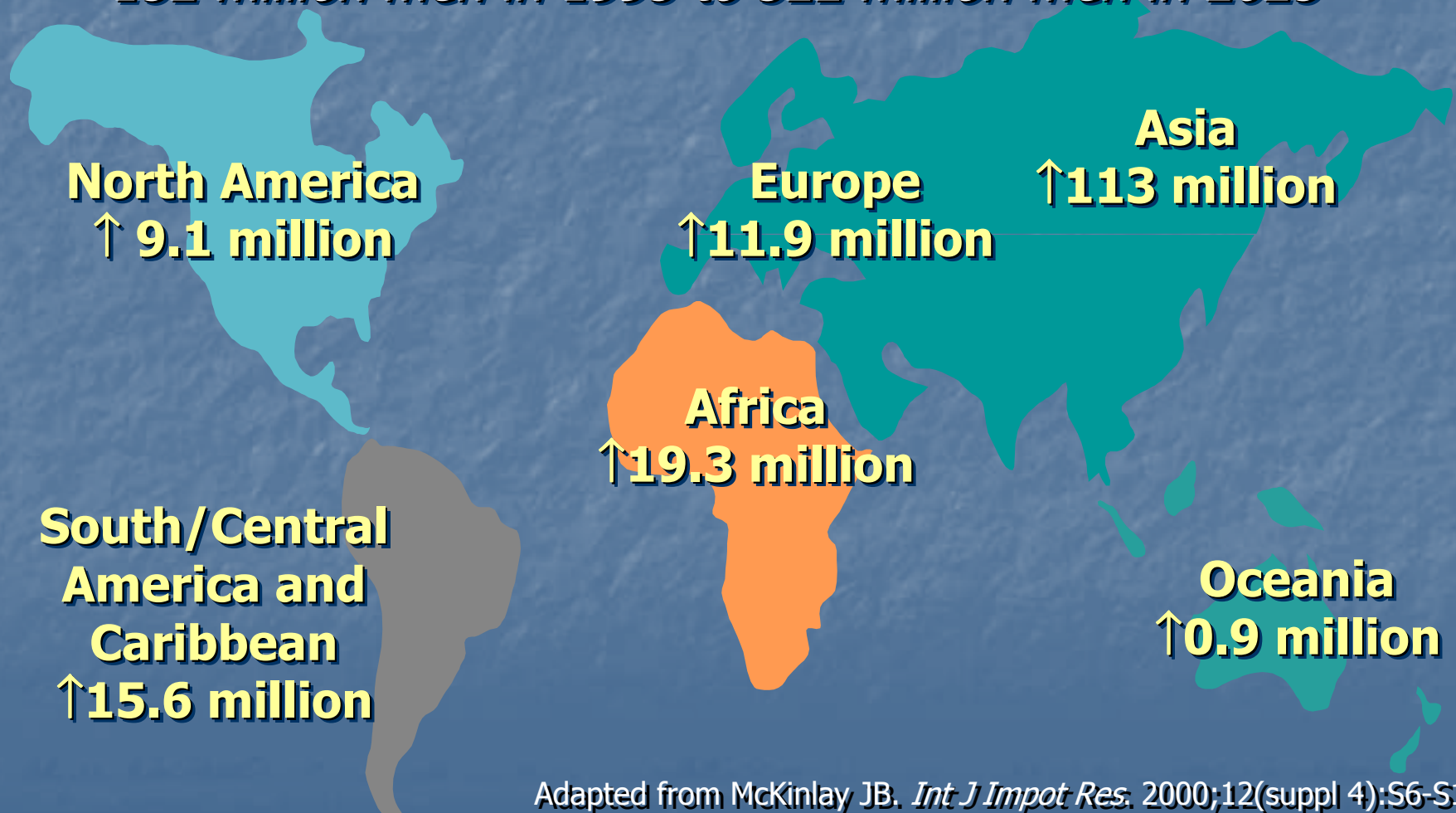 - *WHO-ISIR 1st International Consultation on ED, 1999*

Causes of Erectile Dysfunction

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

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
↑ 9.1 million

Europe
↑11.9 million

Asia
↑113 million

Africa
↑19.3 million

**South/Central
America and
Caribbean
↑15.6 million**

Oceania
↑0.9 million

Adapted from McKinlay JB. *Int J Impot Res*. 2000;12(suppl 4):S6-S11.

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
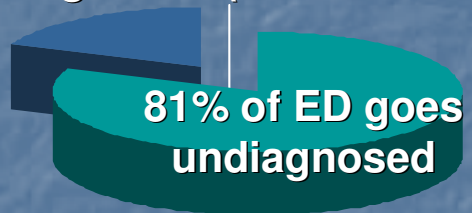
10% reported seeking or receiving treatment

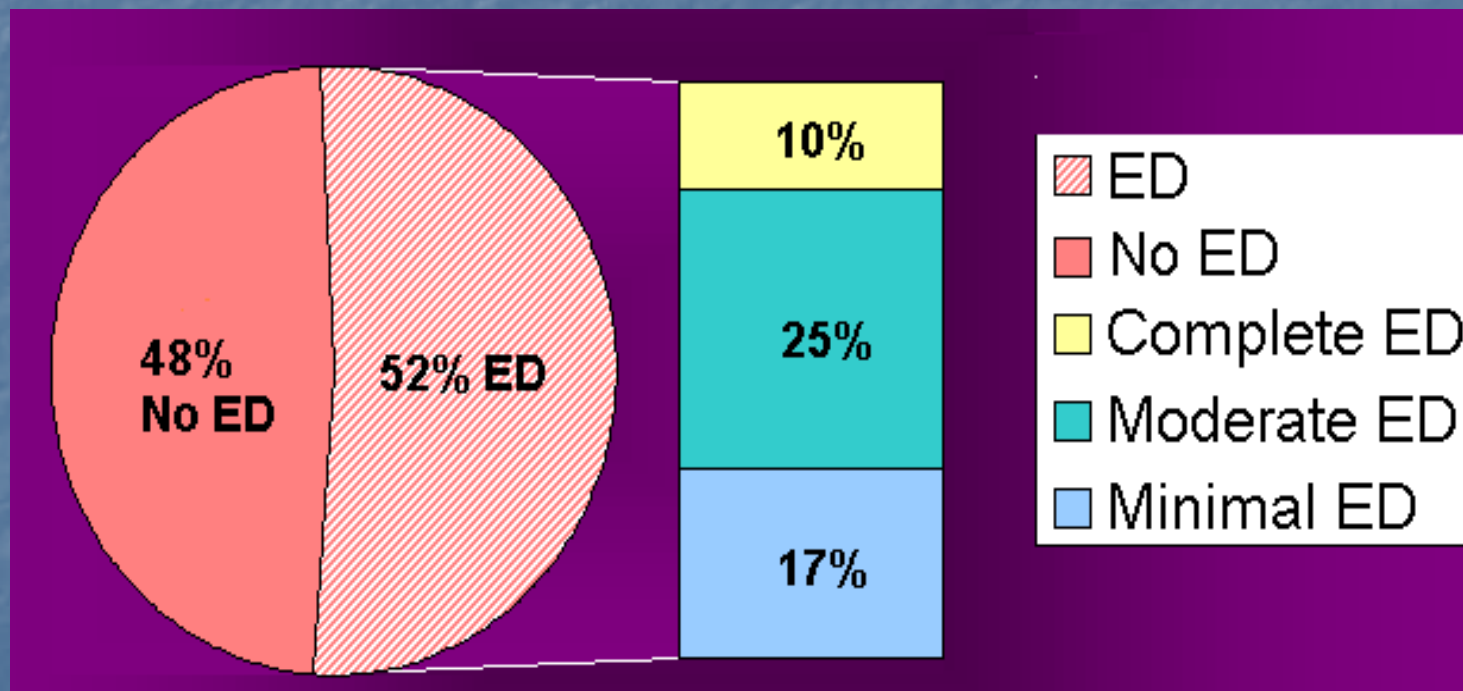*90% men >45 yrs old never seek care for sexual problems*
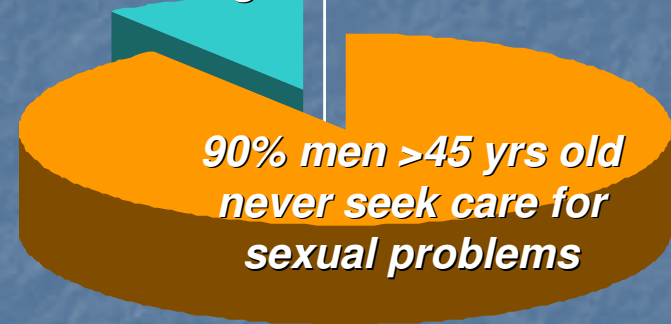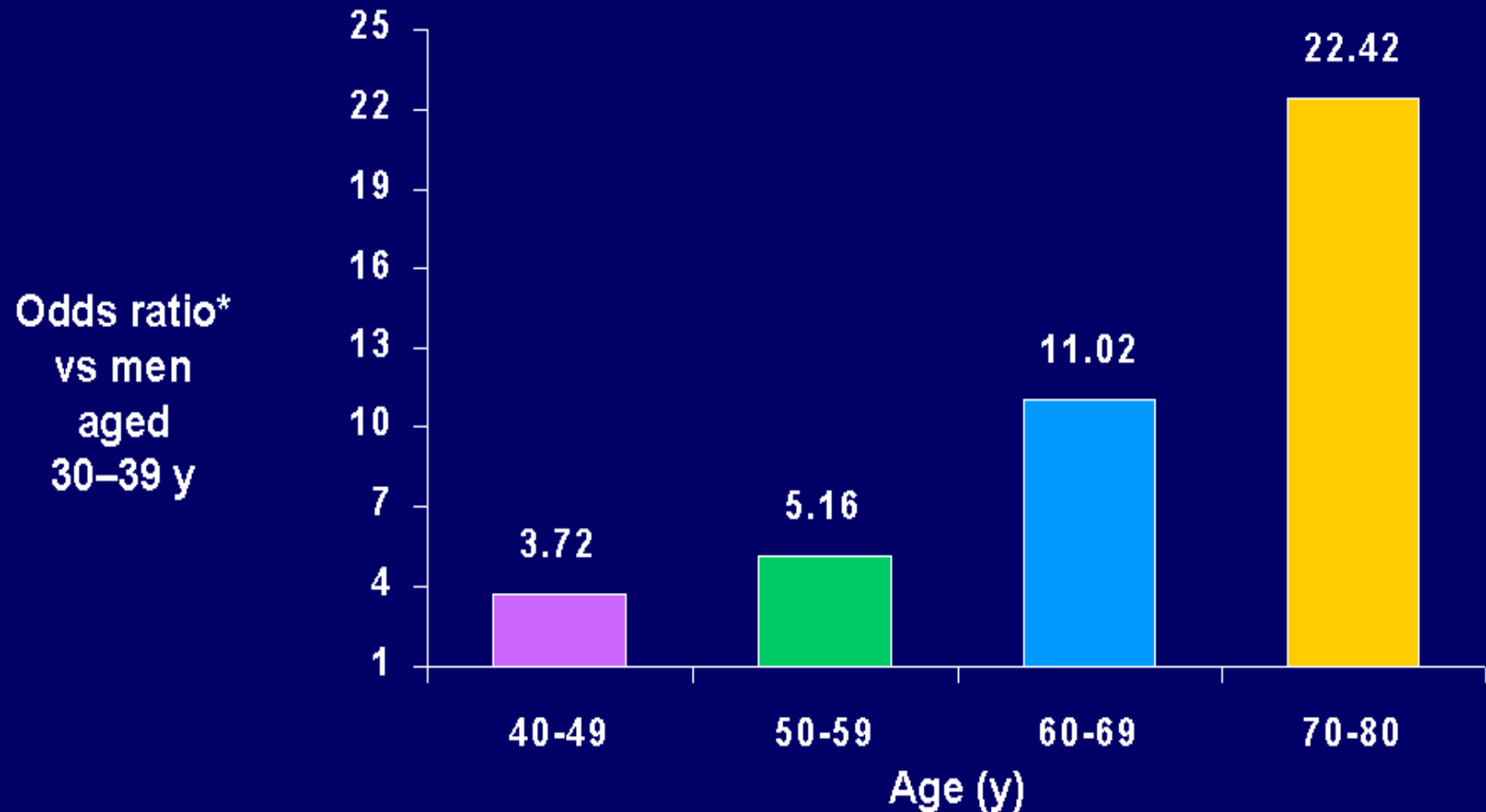
Decision Resources Adaptation of MMAS study 2001

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).
Braun M et al. *Int J Impot Res*. 2000;12:305-311.

ED Severity Increases with Age and Diabetes Duration

Prevalence of Erectile Dysfunction by Ethnic Origin

Holden et al Lancet 2005;366(9481):218-224

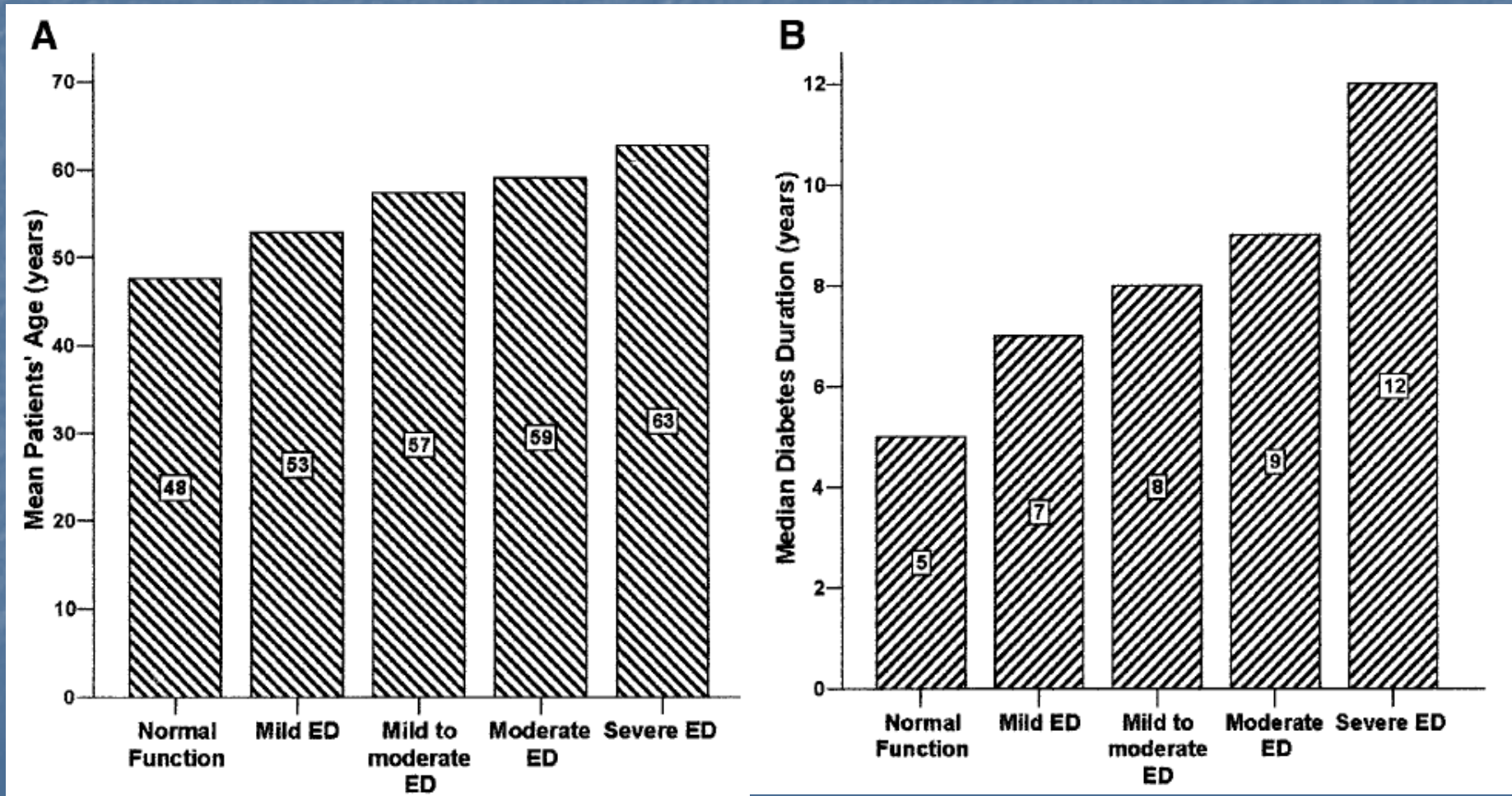# Other Risk Factors for ED: Cologne Male Survey

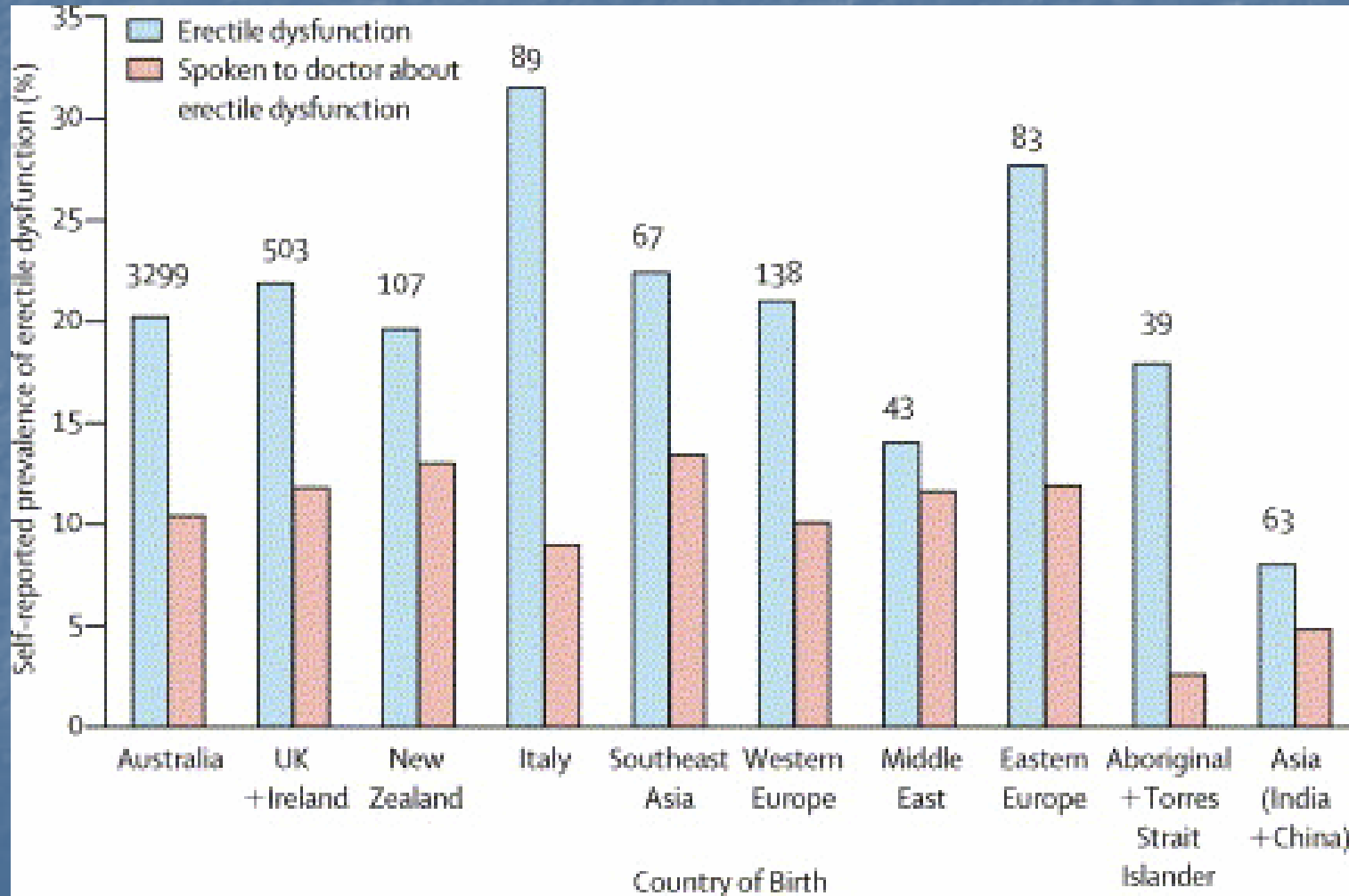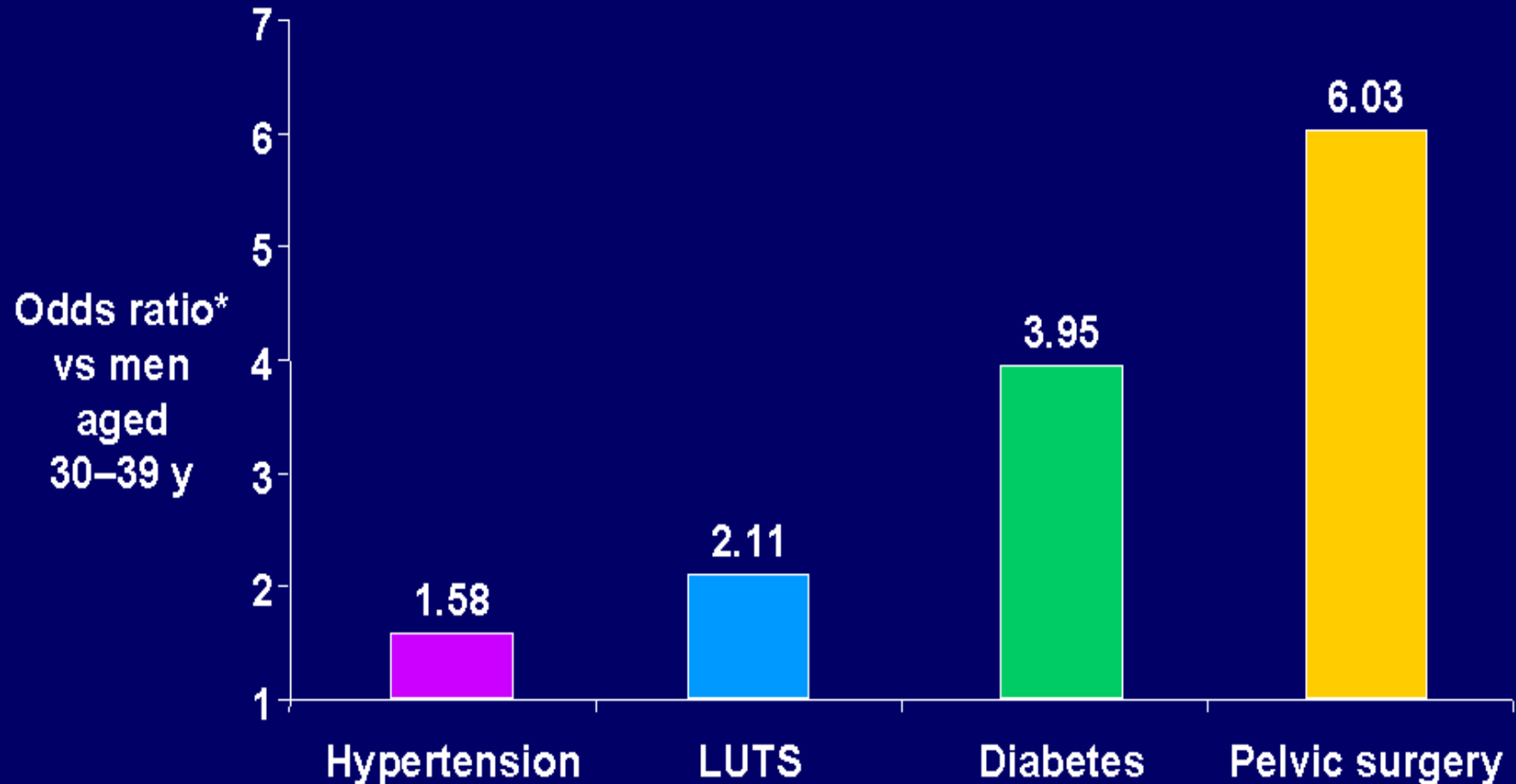
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*Odds ratio=likelihood of an outcome of sexual dysfunction relative to the norm (1.0).
Braun M et al. *Int J Impot Res*. 2000;12:305-311.

Prevalence of Risk Factors

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

ED Risk Factor*	Estimated number of men ≥ 45 years old with risk factor
Diabetes	3,742,000 (9.3%)
Hypertension	16,927,000 (42.3%)
Heart disease	8,525,000 (21.3%)

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

ED Prevalence:
Association with Risk Factors

Risk Factor	ED Prevalence (%)	
	Complete ED	Moderate-to-Complete ED
Heart Disease (smoker)	57	78
Depression (severe)	41	90
Diabetes	28	56
Hypertension	20	40
HDL-C < 30 mg/dL	17	48
General Population	9.6	35

Feldman et al J Urol 1994;151:54-61

ED, CVD, and Depression
A Mutually Reinforcing Triad

Medications

Lifestyle factors

ED

CVD & DM

Depression

Psychosocial factors

Demographic factors

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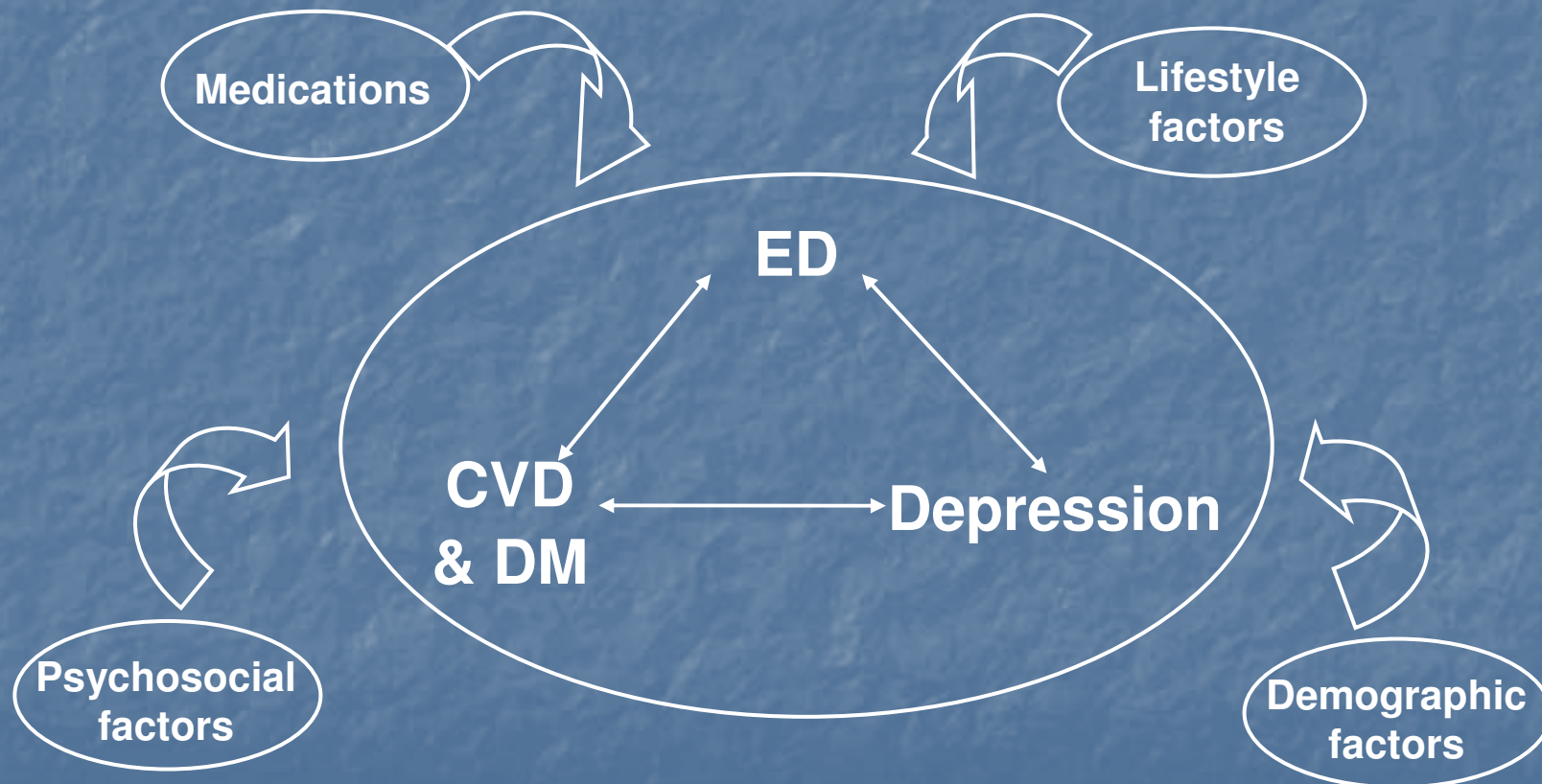
Comorbidities in Ageing Males
ED and Diabetes

- 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

Hatzichristou D et al 1994 Neuro-Med
Johannes CB et al J Urol 2000;163:460
DCCT Ann Intern Med 1995;122:561-568

Vascular Complications Of Type 2 Diabetes At The Time Of Diagnosis

Retinopathy[1]   **39%**

Nephropathy[2]   **18%**

Erectile dysfunction[1]   **20%**

Ischaemic skin changes (foot)[1]   **6%**

Abnormal vibration threshold (foot)[1]   **7%**

7%   **Cerebrovascular disease[3]**

18%   **Abnormal ECG[1]**

35%   **Hypertension[1]**

4.5%   **Intermittent claudication[3]**

13%   **Absent foot pulses[1]**
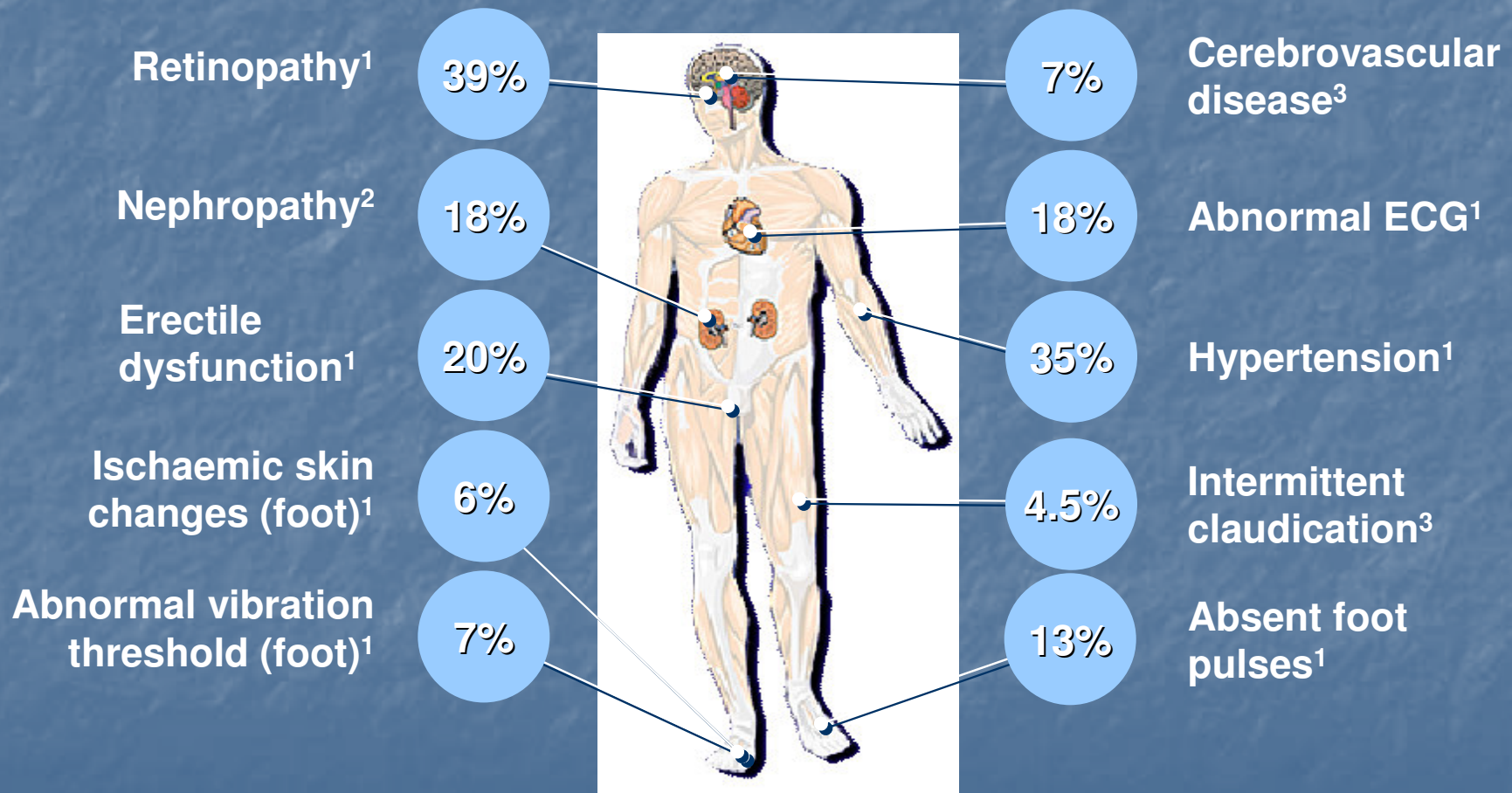
1. UKPDS 33 Lancet 1998;352(9193):837-853
2. The Hypertension in Diabetes Study Group. J Hypertension 1993;11:30–17
3. Wingard DL et al Diabetes Care 1993;16:1022–5

Erectile Dysfunction and Atherosclerosis:
Shared Risk Factors

Coronary artery disease	Erectile Dysfunction
• Age	• Age
• Dyslipidemia	• Dyslipidemia
• Hypertension	• Hypertension
• Diabetes	• Diabetes
• Smoking	• Smoking
• Sedentary lifestyle	• Sedentary lifestyle
• Obesity	• Obesity
• Depression	• Depression
• Male gender	• Coronary artery disease, peripheral vascular disease

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 → Oxidative stress ← Dyslipidaemia

Hypertension → Oxidative stress ← Tobacco

Oxidative stress → Endothelial cell injury

Endothelial cell injury → Vasoconstriction

Endothelial cell injury → Atherosclerosis

Endothelial cell injury → Erectile dysfunction

Endothelial cell injury → Thrombosis

Outcomes

Dzau VJ et al Am J Cardiol 1997;80(9A):33I-39I
Goldstein I Int J Impot Res 2000;12(suppl 4):S147-S151

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)

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

METS During Sex

<u>MEASURES FOR COUPLES IN A LONG STANDING RELATIONSHIP</u>
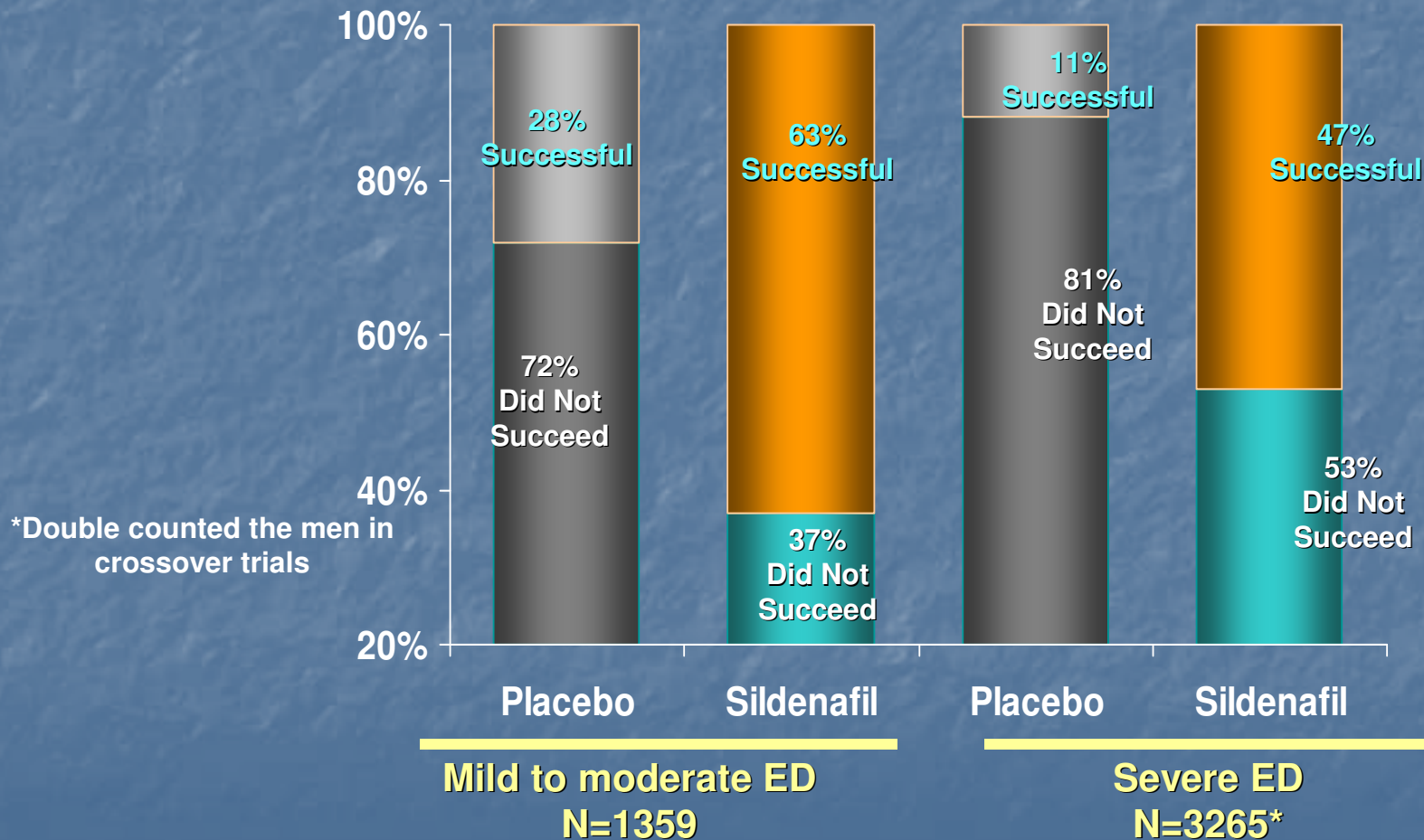
Average peak heart rate: 110–130 beats/min

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

*Double counted the men in crossover trials

Mild to moderate ED N=1359

Severe ED N=3265*

Placebo — 28% Successful, 72% Did Not Succeed

Sildenafil — 63% Successful, 37% Did Not Succeed

Placebo — 11% Successful, 81% Did Not Succeed

Sildenafil — 47% Successful, 53% Did Not Succeed

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

Sildenafil Efficacy in Diabetes

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

% Answering Yes at 12 weeks

- Placebo
- Sildenafil, 100 mg

56*

10

n=127   n=131
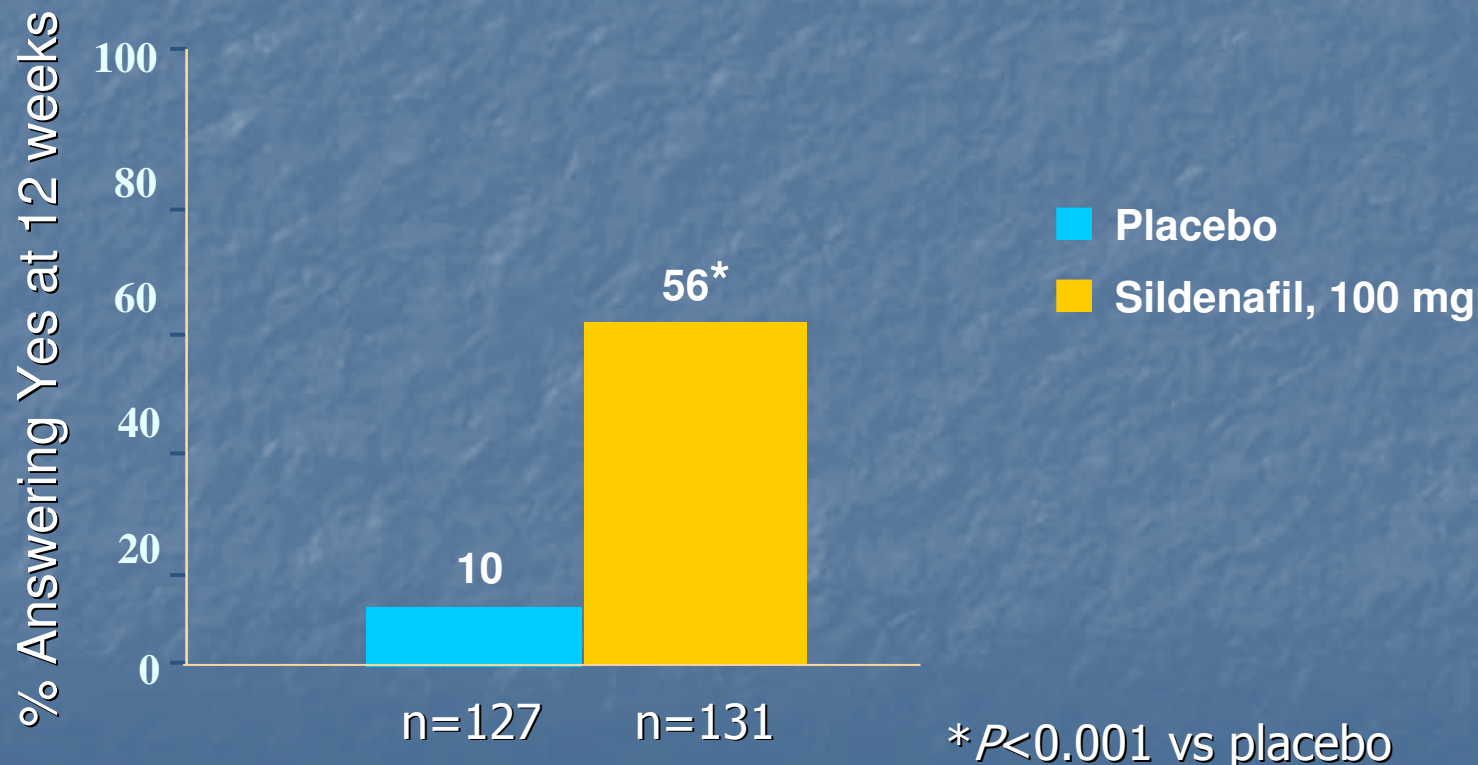
*P<0.001 vs placebo

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?
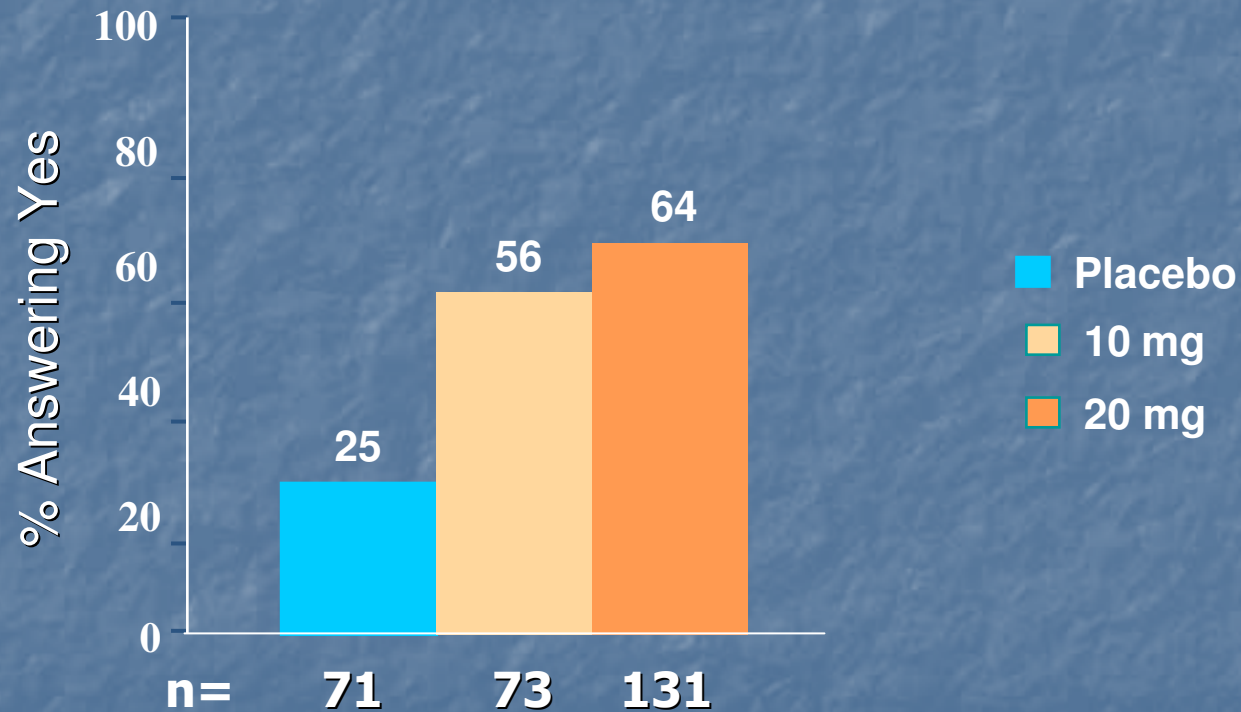

% Answering Yes

- **Placebo** (blue)
- **10 mg** (light orange)
- **20 mg** (orange)

72*
57*
13

n=   122   131   127
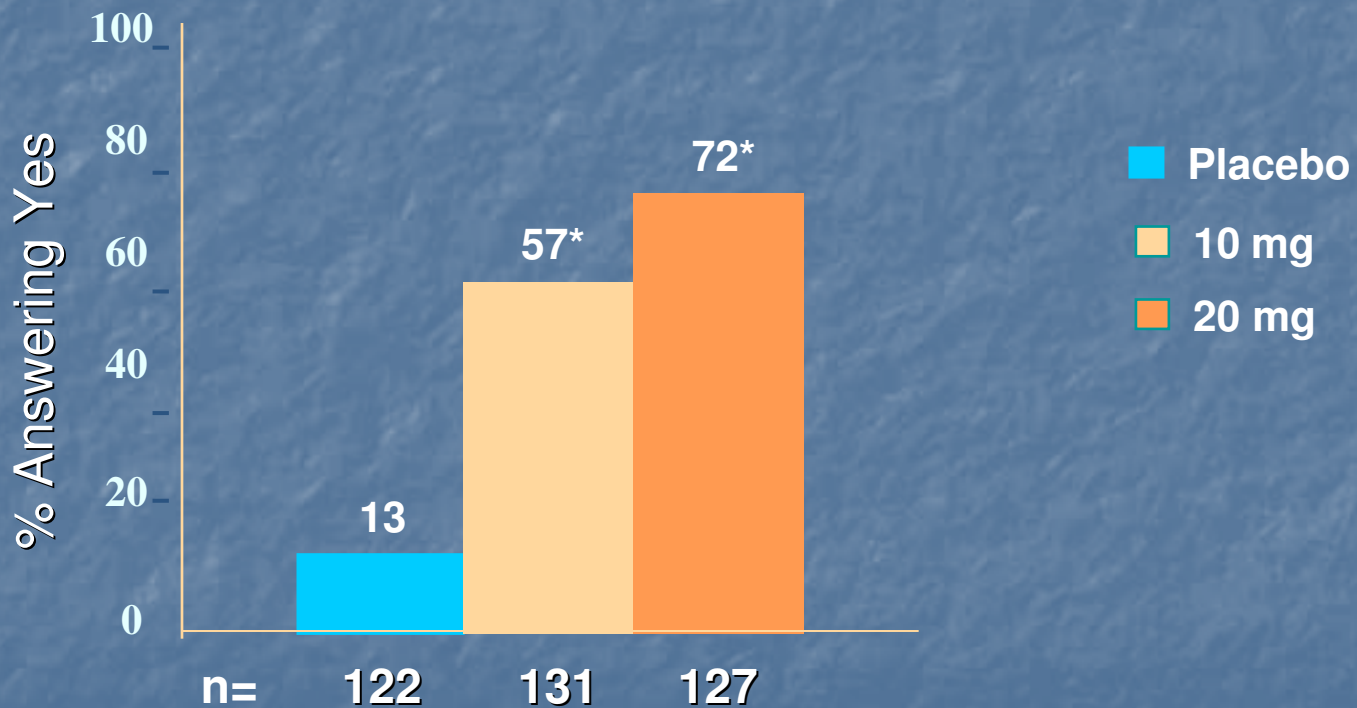
*P<0.001 vs Placebo

ITT, 12 weeks, completers

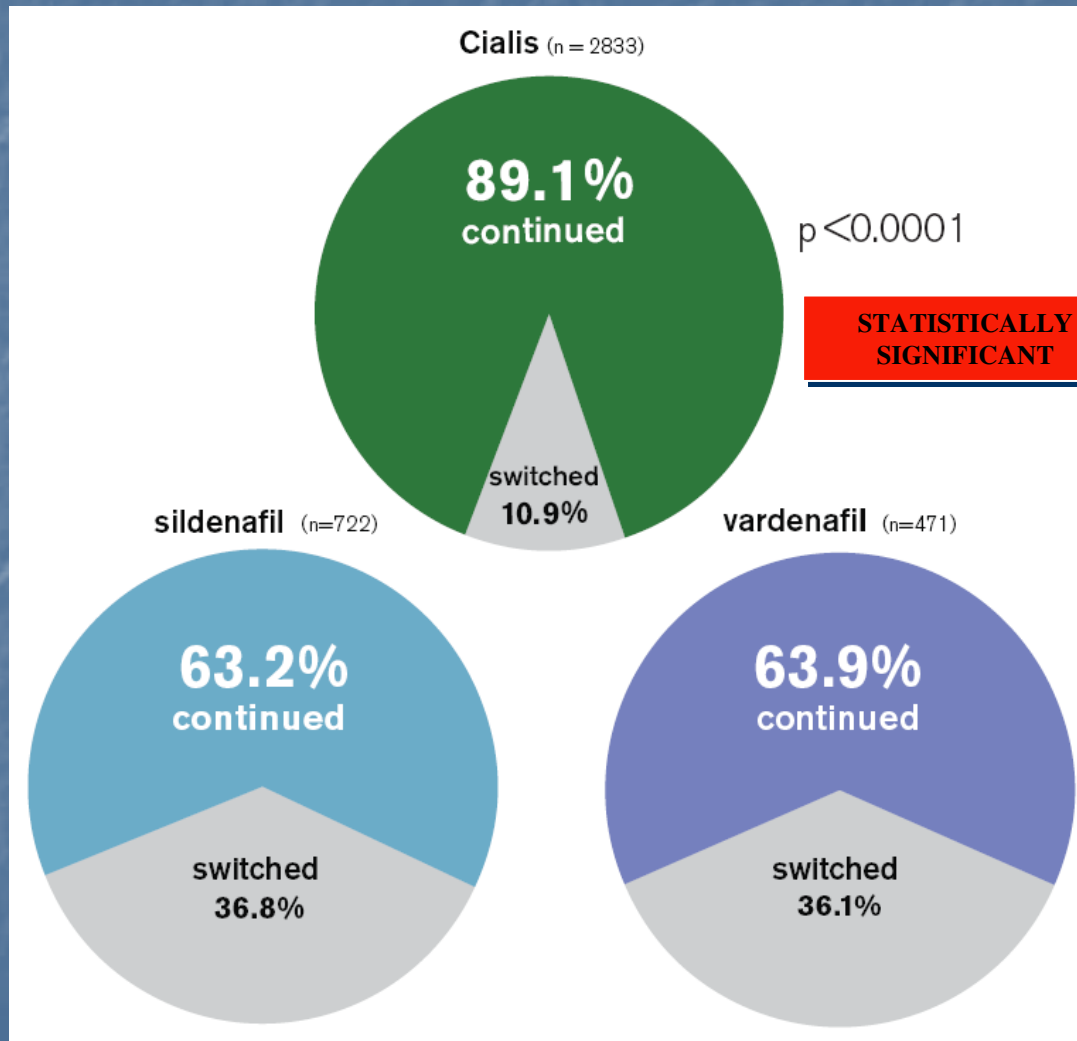Goldstein I et al Diabetes Care 2003;26:777-773

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

Fisher W et al J Sex Med 2005;2:675–84
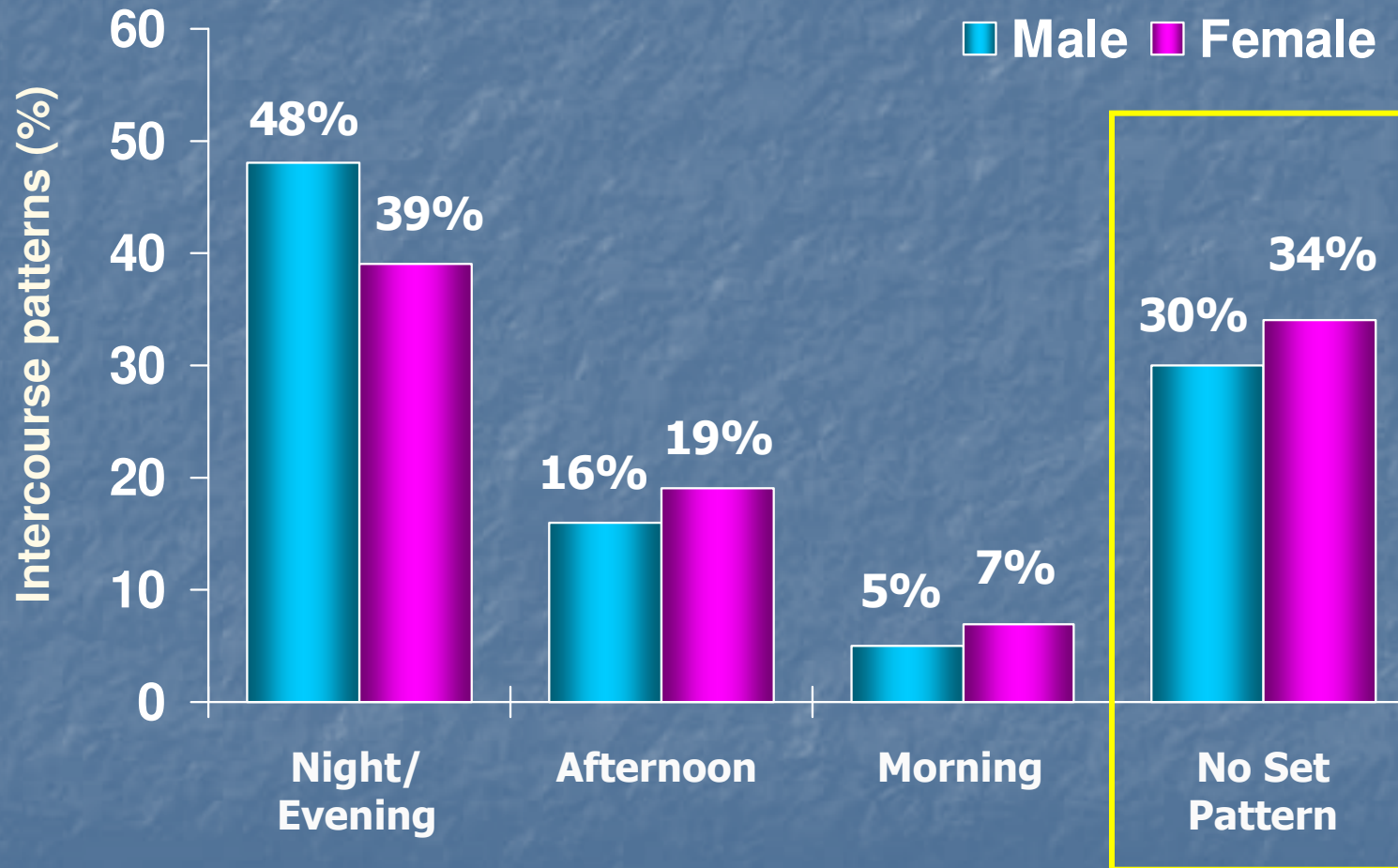
Changes in Patterns of Treatment Over 6 Months

Cialis (n = 2833)

89.1% continued

p<0.0001

STATISTICALLY SIGNIFICANT

switched 10.9%

sildenafil (n=722)

63.2% continued

switched 36.8%

vardenafil (n=471)

63.9% continued

switched 36.1%

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

Hatzichristou D et al Int J Clin Pract 2007;61:1850-1862

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

Look Out For This

ABCD position statement on the management of hypogonadal males with type 2 diabetes

K Dhatariya*, 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?