



El Camino Health

Sex and the Heart

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**British Heart
Foundation**

Registered charity in England & Wales (225971) and Scotland (SC039426)



Outline

- Sexual Activity and the Heart
- Erectile Dysfunction
 - Mechanisms
 - Overlap with Heart Disease
 - Treatment with common ED drugs
 - Other heart conditions

The Cardiovascular Response to Sexual Activity – Lab Studies

- Bartlett (1956):
 - studied 3 couples: peak heart rates 170/min
- Masters and Johnson (1966):
 - heart rates in males: 140 – 180/min blood pressure increased by 80/50

Lab studies

- Problems:
 - Non-long-term sexual partners
 - Data were “watched” in the next room
 - Heart rate and blood pressure measured ‘through the wall’

At home studies

- (1970) - 14 men in cardiac rehabilitation wore a 24 hour monitor and engaged in coitus at home with their spouses
 - Older than previous studies (47.5 years)
 - Cardio-respiratory fitness was similar to that reported for ambulatory, middle-aged, normal subjects

Hellerstein and Friedman; Arch Int Med 1970;125:987-999

At home studies

- Mean peak heart rate: 117.4 (range 90 – 144)
- Heart rates during occupational or home recreational activities often exceeded those of sexual activity.

Hellerstein and Friedman; Arch Int Med 1970;125:987-999

At home studies - Impact of Coital Position

- 8 healthy adult males
 - Total of 35 episodes of coitus with spouses in their own homes

Man on top

Woman on top

- HR 114/min

117/min

- BP 163/81

161/77

Bohlen et al., Arch Int Med 1984; 144:1745-1748

Risk of an Acute Cardiac Event

- M. Ueno (1969) reported on 5559 cases of sudden death
 - 34 occurred during or immediately after sex
 - 18 were due to a cardiac cause
 - 27 occurred during extramarital sex

Framingham Heart Study Data

- 50 yr old man – healthy, exercises regularly
 - Absolute chance of MI: 1 / million / hour
 - Double for 2 hrs following coitus
 - Coitus 1/wk
 - 1.01% annual risk compared to 1.00% annual risk without coitus

Muller JE; Am J Cardiol 1999; 84[5B]:2N-5N

Risk of an Acute Cardiac Event

- Relative Risk: 2.5
 - Same for those with prior history of MI and those with no cardiac history
- Coitus was similar to anger in relative risk
- Regular Exercise (3x / week)
 - Eliminated the increase in risk seen with sex

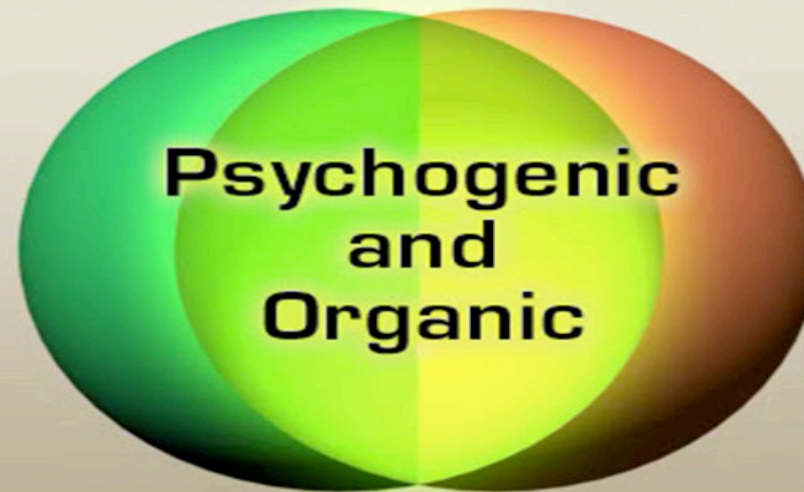
Erectile Dysfunction

Definition: “... the consistent or recurrent inability of a man to attain and/or maintain a penile erection sufficient for sexual activity.”

Lue et al. eds, Sexual Medicine : Sexual Dysfunction in Men and Women. Paris, France: Health Publications: 2004: 605-639.

Classification of ED: Psychogenic and Organic^{1,2}

Combination of Factors
Involved in Most Cases of ED



1. Rosen RC. *Urol Clin North Am.* 2001;28:269-278. 2. Lewis RW et al. In: Lue TF et al, eds. *Sexual Medicine: Sexual Dysfunctions in Men and Women.* Paris, France: Health Publications; 2004:37-72.

Classification of ED: Psychogenic or Organic?

Psychogenic

Sudden onset

Complete immediate loss

Morning erections present

**Varies with partner and
circumstance**

Organic

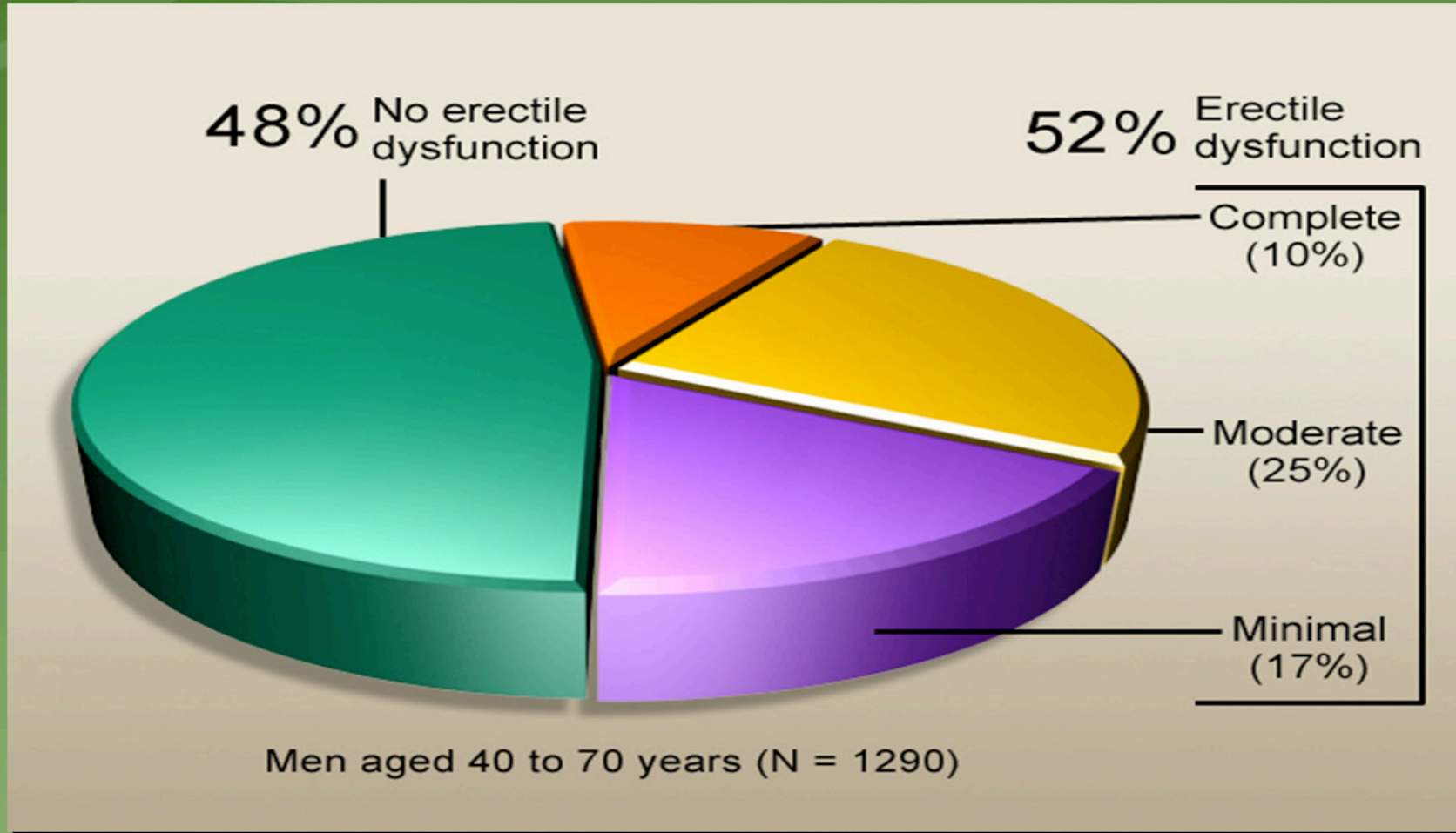
Gradual onset

Incremental progression

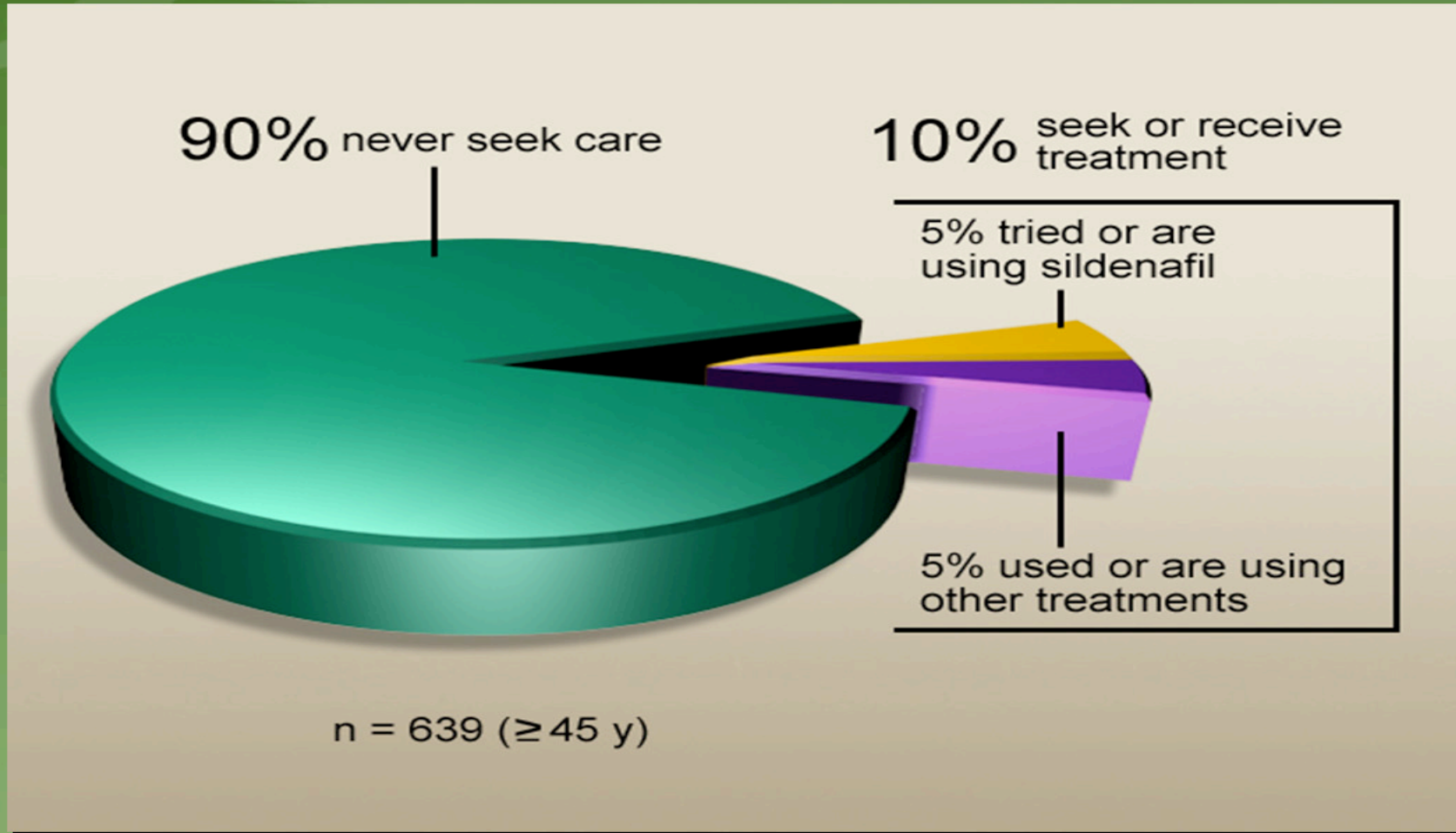
Lack of morning erections

**Lack of erections under
most sexually stimulating
circumstances**

Massachusetts Male Aging Study: Key Prevalence Study of ED



Undertreatment of ED



With permission from McKinlay JB. *Int J Impot Res.* 2000;12(suppl 4):S6-S11. Based on data from the Massachusetts Male Aging Study (MMAS). Source: AARP. *Modern Maturity*, Washington DC, 1999.

TABLE 1. Relative Risks for Men With Erectile Dysfunction

	Relative risk	95% Confidence Interval	P Value
Overall	1.48	1.25 – 1.74	< .001
Coronary Heart Disease	1.46	1.31 – 1.63	< .001
Stroke	1.35	1.19 – 1.54	< .001
All cause mortality	1.19	1.05 – 1.34	< .005

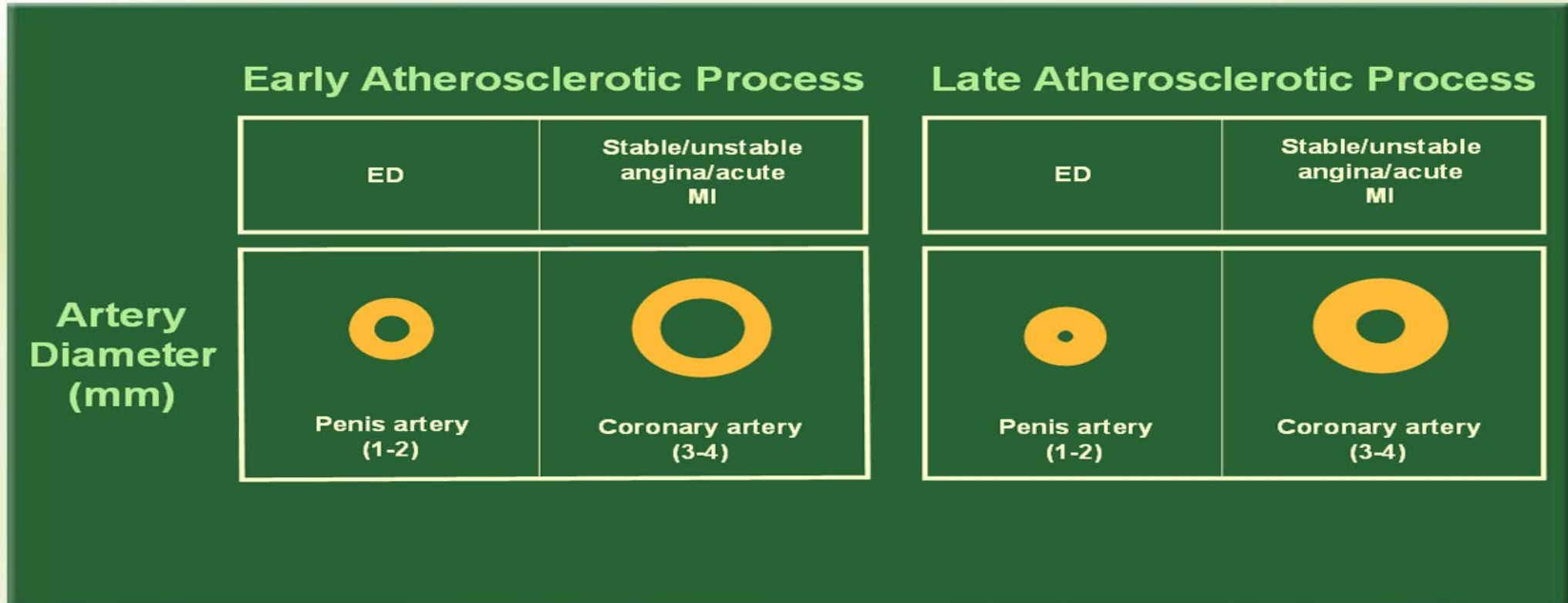
Erectile dysfunction and risk of cardiovascular disease meta-analysis of prospective cohort studies. *J Am Coll Cardiol.* 2011;58(13):1378-1385.

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

Differentiation Between Penile and Coronary Vasculature

Artery-size hypothesis

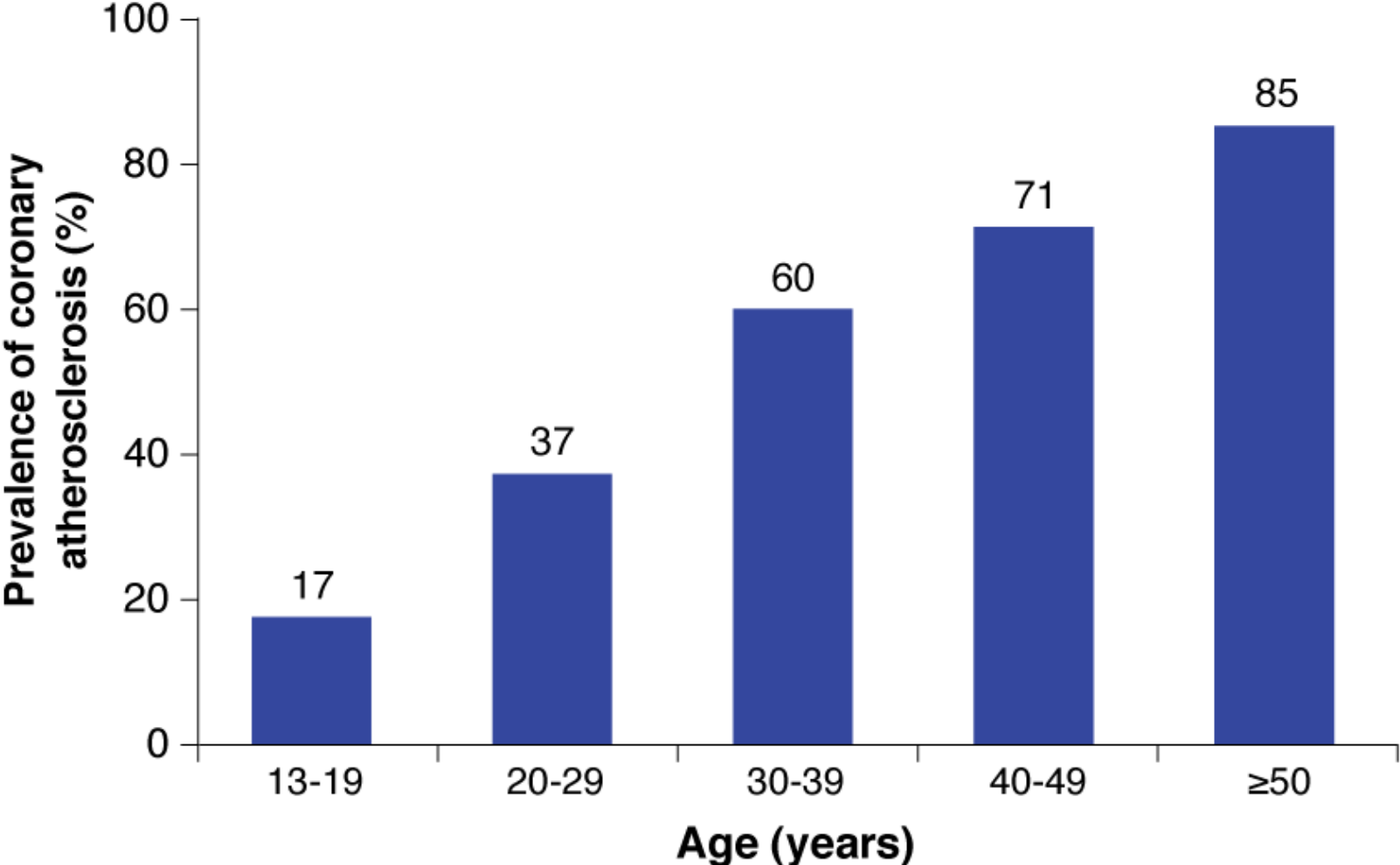


MI=myocardial infarction.

Adapted with permission from Montorsi P et al. *Curr Opin Urol*. 2004;14:361-365.

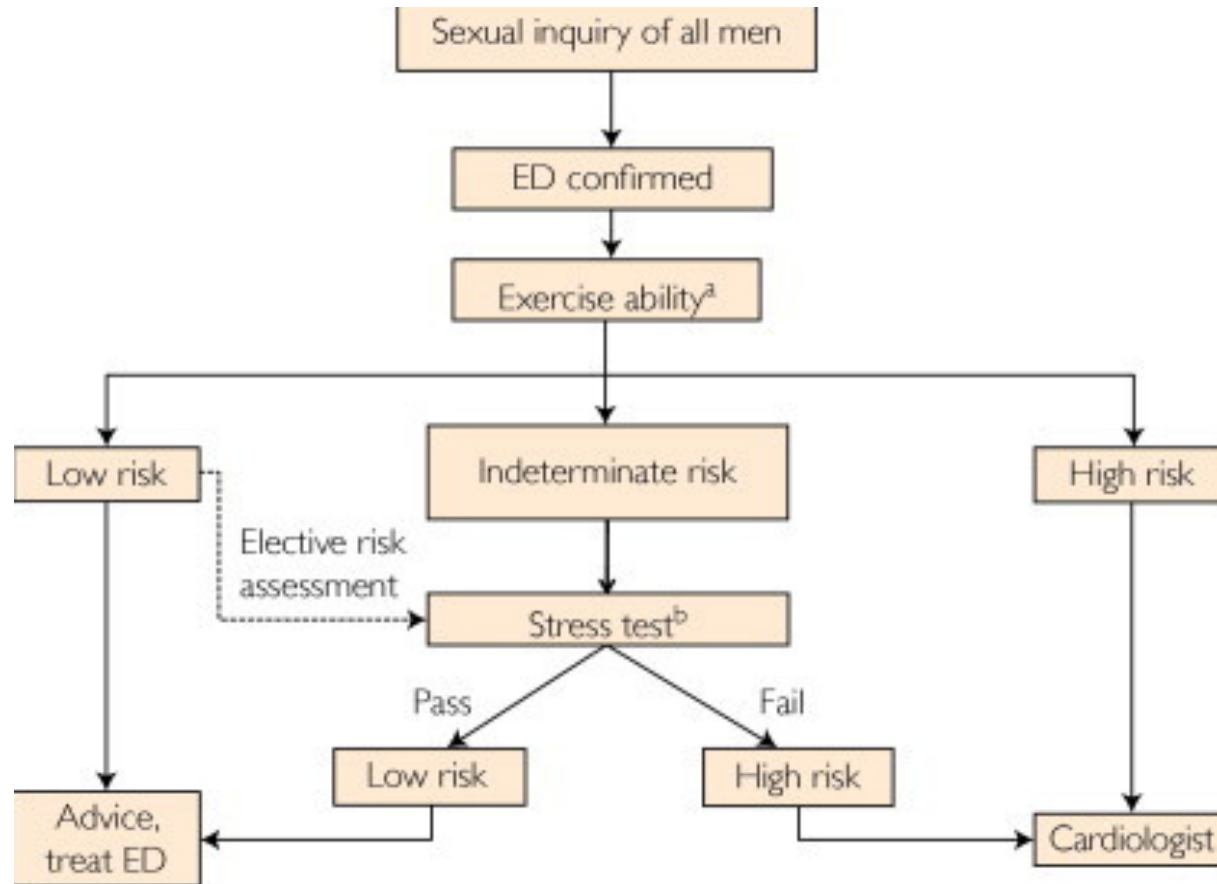


Atherosclerosis: When Does It Begin?



Data from 262 heart transplant donors.
Sites with intimal thickness ≥ 0.5 mm were defined as atherosclerotic.

The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease



ED and Cardiovascular Disease

- ED provides an opportunity for CVD risk reduction.
- ED not only shares risk factors with CVD but also is, in itself, an independent marker of increased risk for CVD.
- ED is a marker of significantly increased risk of CVD, coronary artery disease (CAD), stroke, and all-cause mortality.

Mayo Clinic Proc. August 2012; 87(8):766-778

Major Risk Factors for ED: Antihypertensive Medications

- ◆ Diuretics and β -blockers associated with highest incidence of ED and α -blockers with lowest incidence in 1 study¹
- ◆ Other findings indicate that thiazide diuretics pose greater risk than β -blockers^{2,3}
- ◆ In contrast, use of ACE inhibitors found not to increase ED risk⁴

1. Burchardt M et al. *J Urol.* 2000;164:1188-1191. 2. Kloner RA. *J Clin Hypertens.* 2000;2:33-36.
3. Grimm RH Jr et al. *Hypertension.* 1997;29:8-14. 4. Rosas SE et al. *Kidney Int.* 2001;59:2259-2266.



Major Risk Factors for ED: Lifestyle Issues

- ◆ Lack of exercise/sedentary lifestyle^{1,2}
- ◆ Obesity¹⁻³
- ◆ Heavy drinking^{1,3}
- ◆ Recreational drugs³
- ◆ Cigarette smoking^{1,3}

Causes of ED: Vascular Factors

- ◆ **Atherosclerosis¹⁻³ and associated risk factors^{4,5}**
 - **Smoking^{4,6}**
 - **Diabetes⁵**
 - **Dyslipidemia⁵**
 - **Hypertension⁵**
- ◆ **Venous leaks^{7,8}**
- ◆ **Pelvic or perineal trauma⁷**
 - **Perineal arterial compression from cycling⁹**

1. Miller TA. *Am Fam Physician*. 2000;61:95-104, 109-110. 2. NIH Consensus Development Panel on Impotence. *JAMA*. 1993;270:83-90. 3. Azadzo KM et al. *J Urol*. 1998;160:2216-2222. 4. Kaiser FE et al. *J Am Geriatr Soc*. 1988;36:511-519. 5. Lue TF. *N Engl J Med*. 2000;342:1802-1813. 6. McVary KT et al. *J Urol*. 2001;166:1624-1632. 7. Munarriz RM et al. *J Urol*. 1995;153:1831-1840. 8. DePalma RG et al. *J Vasc Surg*. 1989;10:117-121. 9. Sommer F et al. *Eur Urol*. 2001;39:720-723.





Causes of ED: Penile Injury or Disease

- ◆ Trauma^{1,2}
- ◆ Priapism³
- ◆ Peyronie's disease⁴
- ◆ Anatomic abnormalities^{4,5}

1. Azadzo KM. *J Androl.* 2004;25:382-388. 2. Lewis RW et al. In: Lue TF et al, eds. *Sexual Medicine: Sexual Dysfunctions in Men and Women.* Paris, France: Health Publications; 2004:37-72. 3. Chun J, Carson CC. *Urol Clin North Am.* 2001;28:249-258. 4. Lue TF. *N Engl J Med.* 2000;342:1802-1813. 5. Miller TA. *Am Fam Physician.* 2000;61:95-104, 109-110.



Causes of ED: Medications

- ◆ Antihypertensives¹⁻³
 - Diuretics²
 - Beta-blockers³
- ◆ Selective serotonin-reuptake inhibitors (SSRIs)¹⁻⁴
- ◆ Hormonal agents (eg, antiandrogens)^{1-3,5}
- ◆ Protease inhibitors⁶
- ◆ Cytotoxic agents^{5,7,8}
- ◆ H₂ antagonists^{2,3,5}

1. Lue TF. *N Engl J Med*. 2000;342:1802-1813. 2. Ricci E et al. *Int J Impot Res*. 2003;15:221-224. 3. Fogari R et al. *Curr Hypertens Rep*. 2002;4:202-210. 4. Nurnberg HG et al. *JAMA*. 2003;289:56-64. 5. Lewis RW et al. In: Lue TF et al, eds. *Sexual Medicine: Sexual Dysfunctions in Men and Women*. Paris, France: Health Publications; 2004:37-72. 6. Schrooten W et al. *AIDS*. 2001;15:1019-1023. 7. Chatterjee R et al. *Bone Marrow Transplant*. 2000;25:1185-1189. 8. Lewis RW. *Urol Clin North Am*. 2001;28:209-216.



Analysis of Risk Factors and Incident CVD in Men Without ED at Baseline

- ◆ Incident ED had a strong impact on subsequent development of CVD compared with risk factors such as family history, smoking, and dyslipidemia
- ◆ ED may be an early indicator of CV clinical events in some men
- ◆ ED should prompt assessment and treatment for CV risk factors

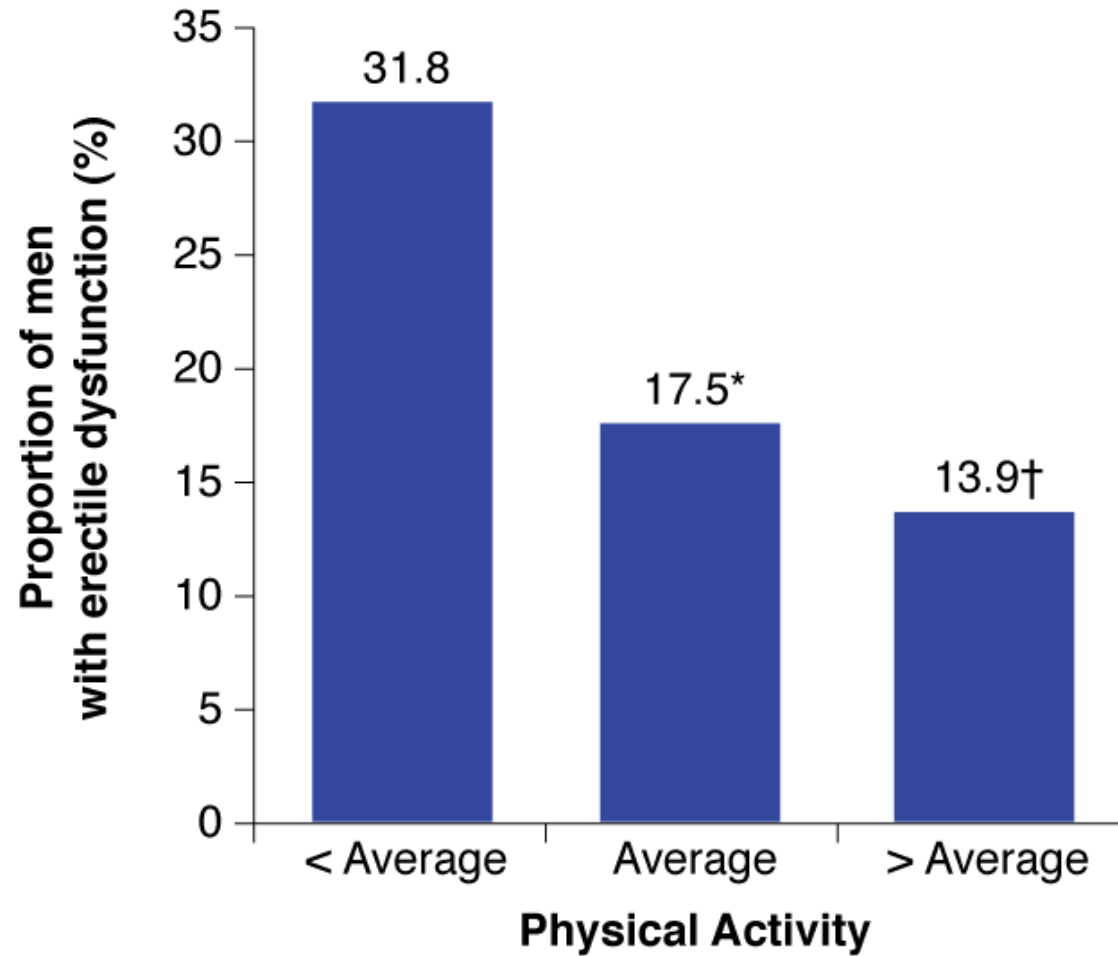
Risk Factors for ED and CVD

- ◆ **Patients with significant risk factors for both diseases or CVD should be evaluated for ED¹**
 - **A study of men with chronic, stable CAD showed that 75% had ED (severe for 25%)¹**
- ◆ **Similarly, men presenting with ED should be screened for CVD²**

Treatment of Erectile Dysfunction

- Risk Factors
 - Lifestyle Modification
 - Cessation of Smoking
 - Exercise
 - Mediterranean Diet
 - Control of HTN / Cholesterol / Diabetes

Physical Activity and Prevalence of Erectile Dysfunction



*Odds ratio = 0.46 (CI, 0.27-0.76).

†Odds ratio = 0.35 (CI, 0.22-0.54).



Erectile Dysfunction and a Mediterranean Diet

- In this current perspective we analyzed the role of Mediterranean diet in sexual function and particularly in erectile dysfunction (ED), according to the latest scientific evidence.
- We conducted a systematic search of relevant full-length papers identified during the time period from January 2010 to the present.
- Our findings suggest that the encouragement of a healthy lifestyle, such as Mediterranean Diet promotion, could be an attractive dietary approach to prevent ED and preserve sexual function.

Di Francesco et al. Cent European J Urol. 2017; 70: 185-187



Treatment of Erectile Dysfunction

- Change Cardiac Drugs
 - Thiazide Diuretics (HCTZ, Chlorthalidone)
 - Digoxin
 - Beta-blockers

Treatment of Erectile Dysfunction

- Phosphodiesterase 5 Inhibitors
 - Viagra (sildenafil), Cialis (tadalafil), Levitra (vardenafil)
- Alprostadil
 - Self injection
 - Urethral suppository
- Testosterone
- Penis pump
- Penile Implant





1999 ACC/AHA Expert Consensus Document: Use of Sildenafil (Viagra®) in Patients with Cardiovascular Disease

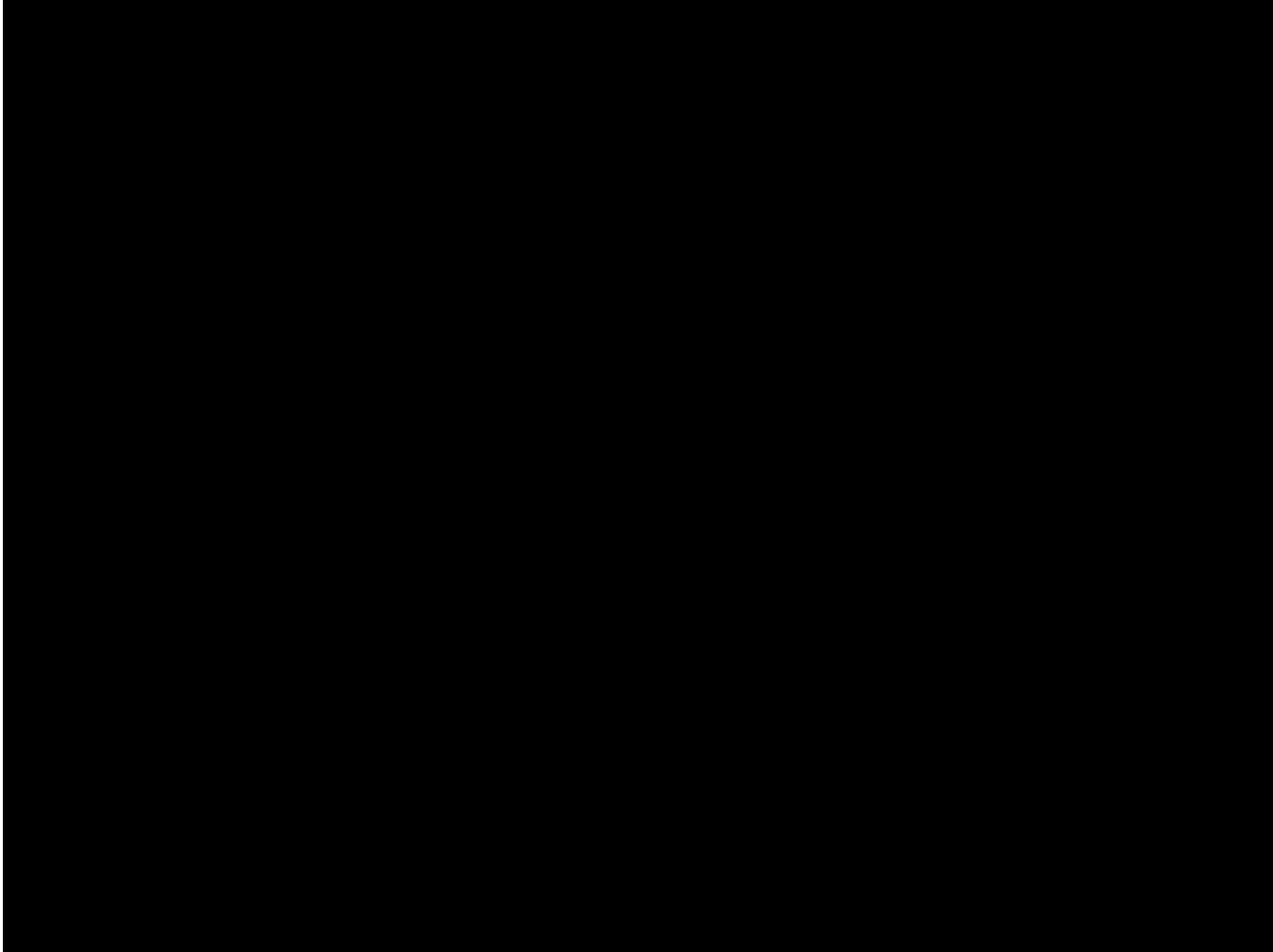
Summary Table of Clinical Recommendations

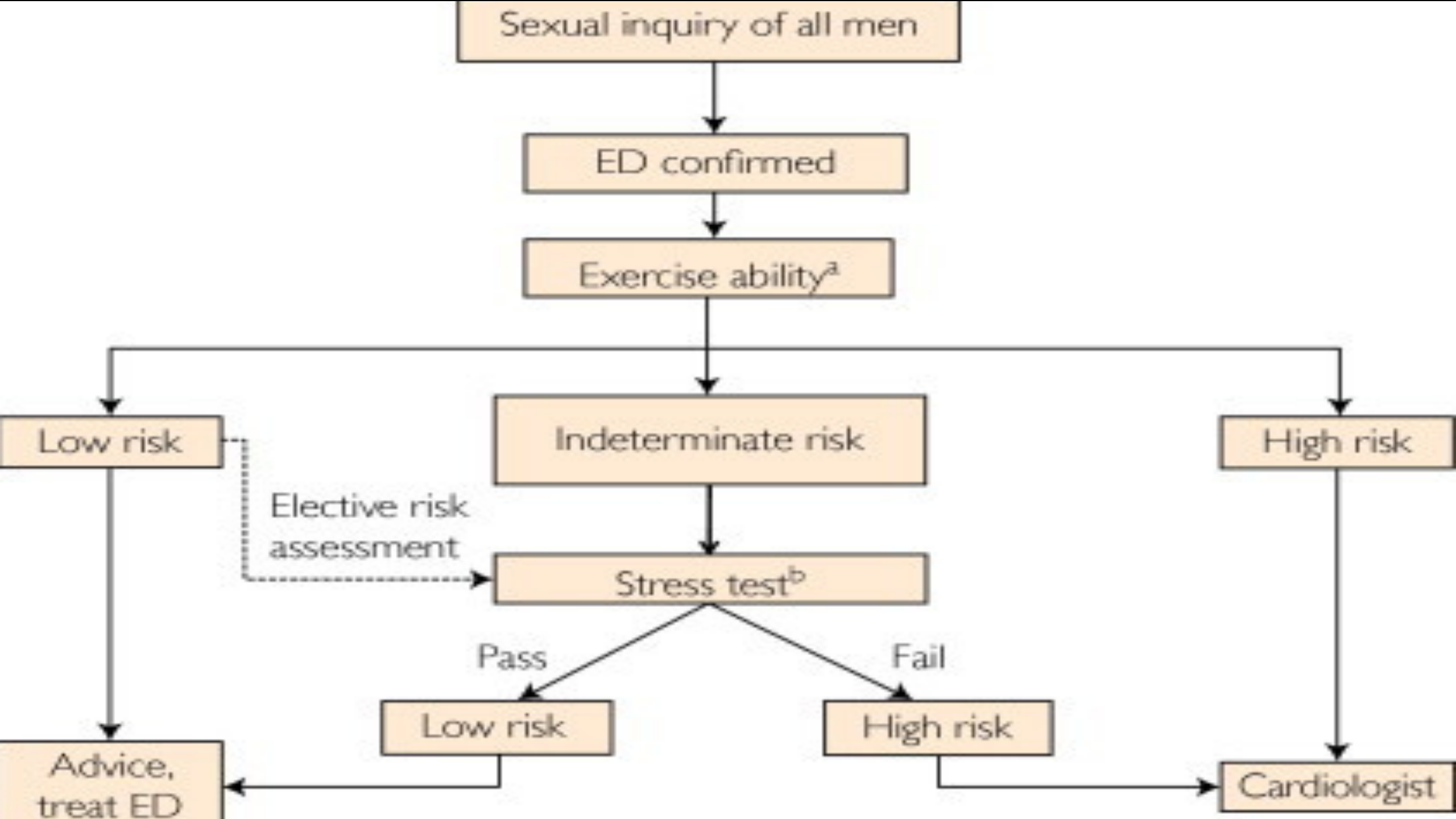
Use of Viagra® clearly contraindicated

- Concurrent use of nitrates

Cardiovascular effects of Viagra® may be potentially hazardous (use dependent on individual clinical assessment)

- Patients with active coronary ischemia who are not taking nitrates (eg, positive exercise test for ischemia)
- Patients with congestive heart failure and borderline low blood pressure and borderline low volume status
- Patients on a complicated, multidrug, antihypertensive program
- Patients taking drugs that can prolong the half-life of Viagra®





Endogenous Testosterone Levels and Cardiovascular Risk: Meta-Analysis of Observational Studies.

- The relationship between endogenous testosterone levels and cardiovascular (CV) risk in men is conflicting.
- After screening, 37 observational studies, published between 1988 and 2017 including 43,041 subjects with a mean age of 63.5 years and mean follow-up of 333 weeks, were considered.
- Low endogenous Testosterone at enrollment predicted overall and CV mortality, as well as CV morbidity.

Corona et al. Endogenous Testosterone Levels and Cardiovascular Risk: Meta-Analysis of Observational Studies. J Sex Med 2018;15:1260-1271

Testosterone and Cardiovascular Risk: Meta-Analysis of Interventional Studies.

- After screening, 15 pharmaco-epidemiological and 93 RCT studies were considered. The analysis of pharmaco-epidemiological studies documented that Testosterone therapy reduces overall mortality and CV morbidity.
- Data from Randomized Clinical Trials suggest that treatment with Testosterone is not effective in reducing CV risk, however, when Testosterone therapy is correctly applied, it is not associated with an increase in CV risk and it may have a beneficial effect in some sub-populations.

Corona et al. Testosterone and Cardiovascular Risk:
Meta-Analysis of Interventional Studies. J Sex Med 2018;15:820-838.

EVIDENCE FOR CONTAMINATION OF HERBAL ERECTILE DYSFUNCTION PRODUCTS WITH PHOSPHODIESTERASE TYPE 5 INHIBITORS

NEIL FLESHNER,^{*,†} MELISSA HARVEY,[‡] HANS ADOMAT,[‡] CATHERINE WOOD,[‡]
ANDY EBERDING,[‡] KAREN HERSEY[‡] AND EMMA GUNS[‡]

From Princess Margaret Hospital, University of Toronto, Toronto, Ontario (NF, MH, KH) and The Prostate Centre at Vancouver General Hospital, University of British Columbia, Vancouver, British Columbia (HA, CW, AE, EG), Canada

ABSTRACT

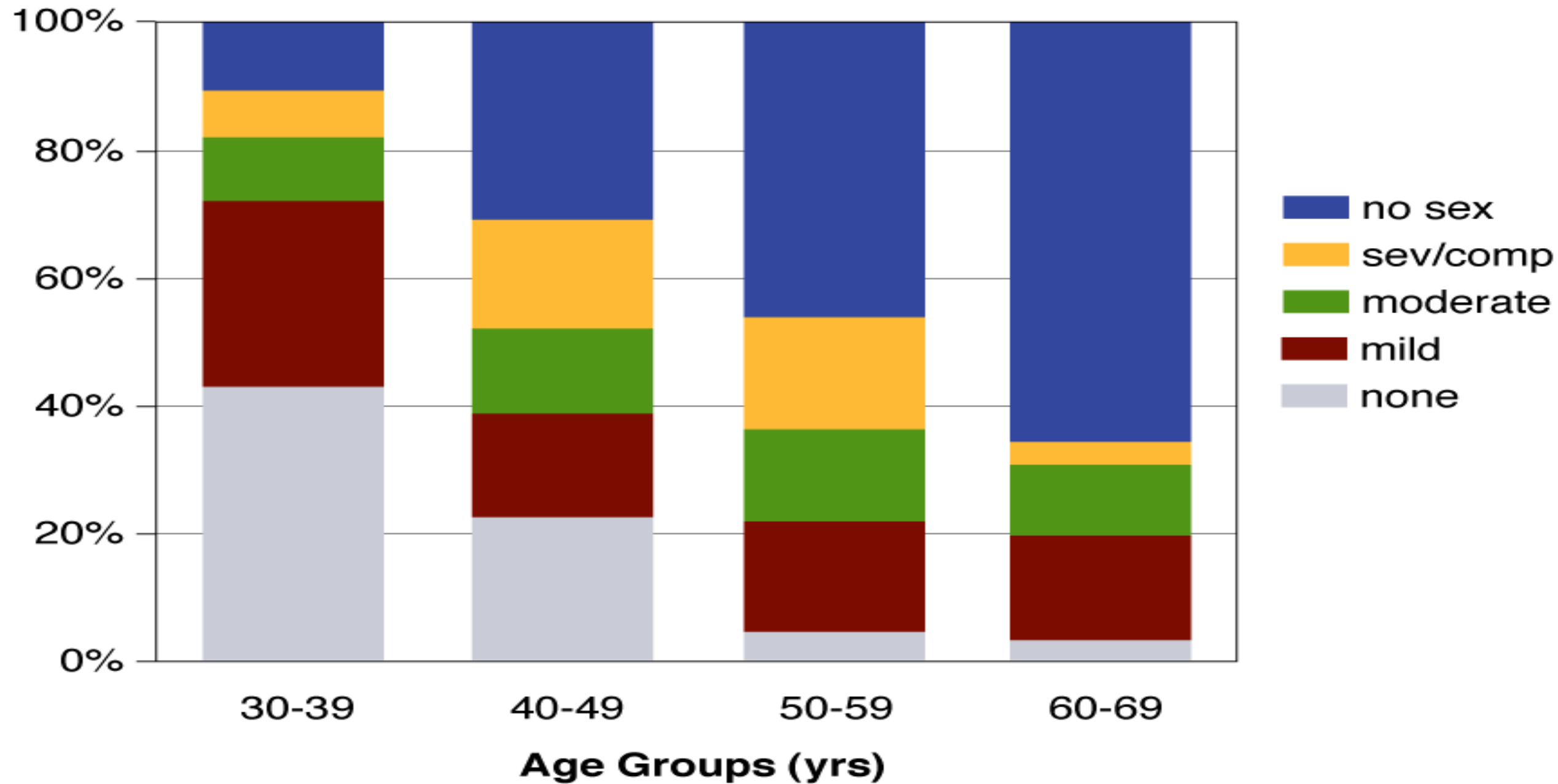
Purpose: We determined if pharmacological dosages of phosphodiesterase type 5 inhibitors (PDE5) inhibitors were present within a group of natural products marketed for the treatment of erectile dysfunction.

Materials and Methods: Seven herbal products marketed for the treatment of erectile dysfunction were purchased via the Internet or at local health food stores. Specimens were batched, relabeled and blindly analyzed for contamination with PDE5 inhibitors. High performance liquid chromatography and mass spectrometry were used to detect evidence of contamination with sildenafil, tadalafil or vardenafil.

Results: Of the 7 tested products 2 contained pharmacological dosages of sildenafil and tadalafil. Contamination with vardenafil was not identified. Mean dosages of sildenafil and tadalafil were 30.2 and 19.7 mg, respectively.

Conclusions: A significant proportion of natural products marketed for erectile dysfunction contains PDE5 inhibitors. Although marketed as natural products devoid of adverse effects, these agents are known to have potentially fatal drug interactions with nitrates. Better regulation of the natural health products industry is urged.

Erectile Dysfunction by Age



Smoking

- Smoking increases the risk of moderate to severe ED by 2-fold.
- The association between smoking and ED is likely due to impairment of endothelium-dependent smooth muscle relaxation.
- The risk of ED in ex-smokers is inversely related to the number of years since the patient quit smoking.

McVary et al. J Urol 2001; 166: 1624-1632
Bortolotti et al. Eur Urol 2001; 40:392-396

Condition	%
Heart Disease	52.3
Diabetes Mellitus	49.3
Hypertension	35.4
Obesity	23.5
Smoking	15.0