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Erectile Dysfunction: Inquiry is essential

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Disclosures

- Dr. Köhler – Coloplast Corporation Consultant and Research

Dr. Köhler

- A little Princeton Panel History
- Some ED physiology
- Data linking the penis and the heart
- Psychogenic ED a risk factor too?
- Asking about ED

Princeton Panel History

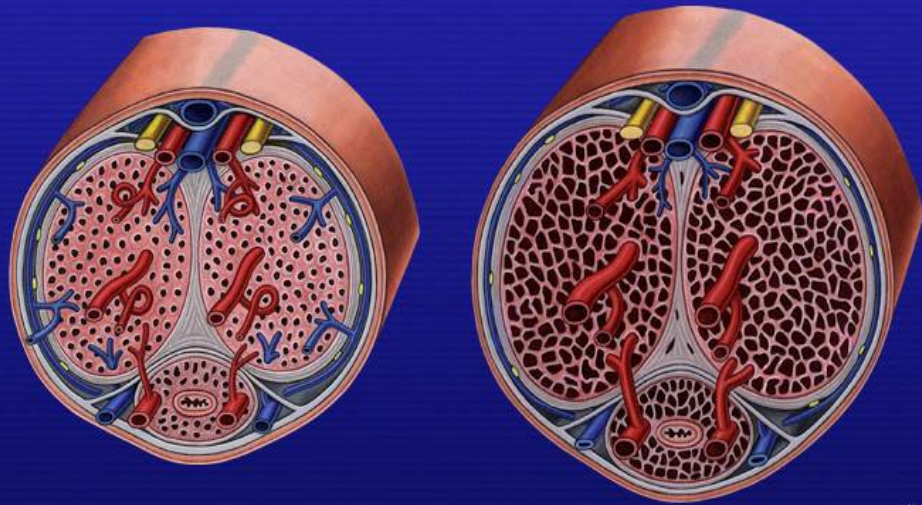
- Started 25 years ago in response to Sildenafil patient deluge
- P1 largely established sex as safe
 - Sex increases US annual baseline risk/year of MI from 1 to 1.01%
 - Risk of sudden cardiac death from sex 1 per 10000 person-years
 - Normal sex 2-3 METS (2 flights of stairs 10 seconds or walk 1 mile flat in 20 minutes)
 - Intense sex 5-6 METS (4 minutes standard Bruce protocol)
- P1-P3 developed recommendations for clinical management of sexual dysfunction in patients with cardiovascular disease using risk stratification based on inquiry of ED & exercise tolerance
- P4 continues development of these recommendations with highlights including use of Coronary Calcium Scores and the role of PDE5 inhibitors



1. DeBusk R, Drory Y, Goldstein I et al. Management of sexual dysfunction in patients with cardiovascular disease: recommendations of The Princeton Consensus Panel. Am J Cardiol 2000; 86: 175-181.
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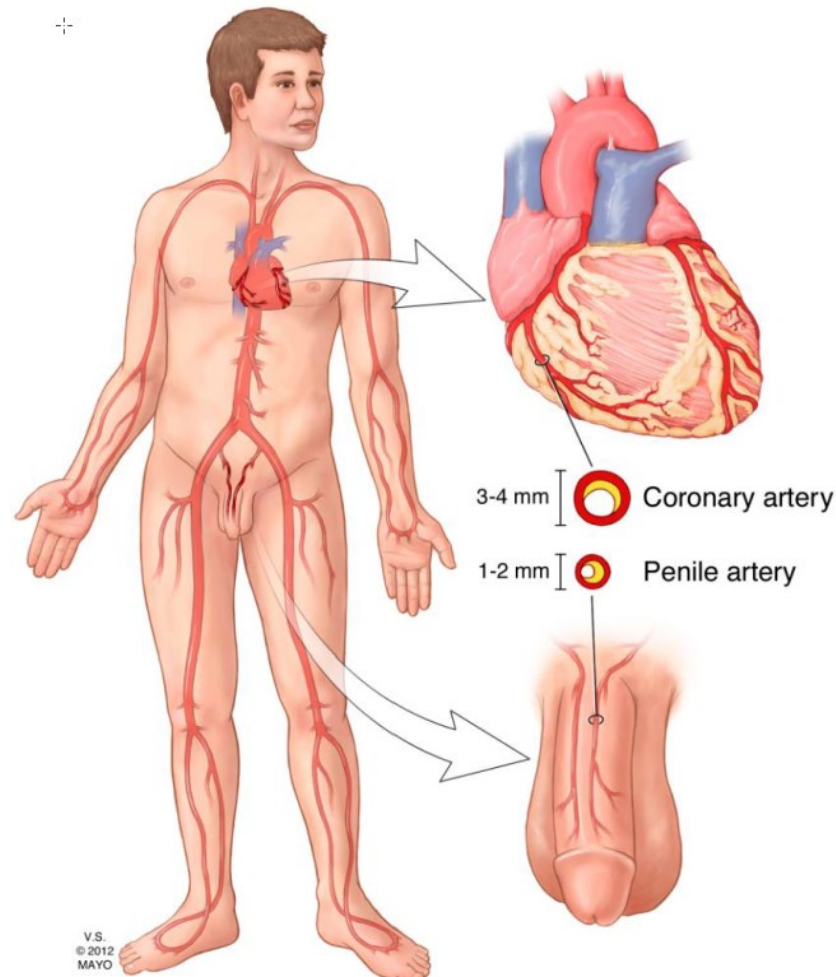
ED Facts & Physiology



Excellent erections require:

1. Adequate active arterial inflow - Meds target here
2. Passive venous compression - Venous leak (Constriction band)
3. Intact Nervous System - Adrenaline matters
4. Adequate testosterone levels - recently T proven safe for MI risk
5. Use it or lose it organ with decreases in length common

Vascular versus non-vascular ED

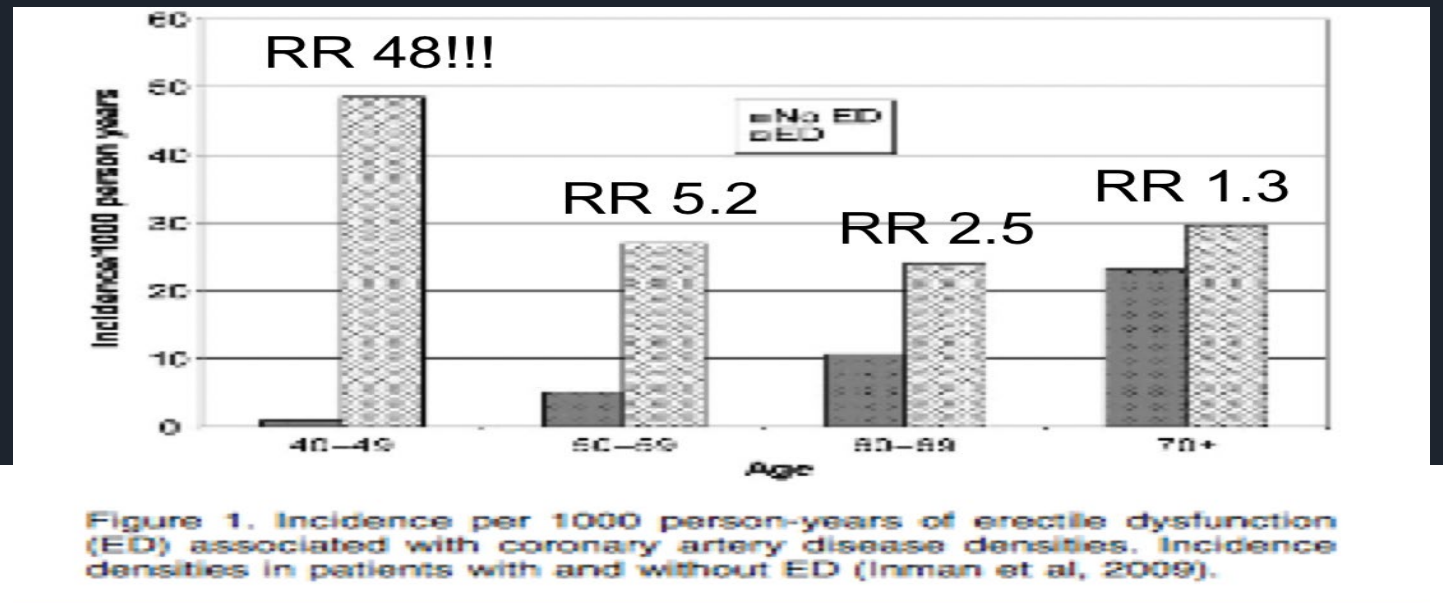


- Historically 90% of ED was “Psychogenic”
- Actually, 90% has organic component
- Most often both co-exist with confidence issues
- Penile blood vessels: 1-2 mm or smaller
- Coronary vessels: 3-4 mm
- Carotids: 5-7 mm
- Femoral vessels: 6-8 mm
- Systematic progressive luminal obstruction of > 50% in these typically results in ED, angina and myocardial infarction, TIA and stroke and intermittent claudication respectively

Progressive vessel narrowing as only mechanism?

- ½ to 2/3 of young men who have an MI have no ED
- Many men with severe ED will never have an MI
- ED Severity is strongly linked with CAD severity and coronary occlusion
- Endothelial dysfunction?
- ED leads to depression and vice-versa
- This can be mitigated with treatment!

Data linking ED & CVD



- Two powerful studies cited in P3 show ED provides a greater CAD predictive capacity in younger men (Inman, 2009²³ & Chew, 2010²⁴).
- The Inman study shows a 50-fold increased risk of cardiac events (which include angina, emergency room visits, interventions and death) for men ages 40-49 with incident ED.
- This risk was attenuated with older decades presumably to competing non-vascular ED risk factors.

1. Inman BA, Sauver JL, Jacobson DJ, et al. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. *Mayo Clin Proc.* 2009;84(2):108-113.
2. [Kew-Kim Chew](#), [Judith Finn](#), [Bronwyn Stuckey](#), [Nicholas Gibson](#), [Frank Sanfilippo](#), [Alexandra Bremner](#), [Peter Thompson](#), [Michael Hobbs](#), [Konrad Jamrozik](#). Erectile dysfunction as a predictor for subsequent atherosclerotic cardiovascular events: findings from a linked-data study. *J Sex Med.* 2010 Jan;7(1 Pt 1):192-202.

Data linking ED & CVD

Table 4

Time interval between manifestation of erectile dysfunction (ED) and first atherosclerotic cardiovascular (CV) events subsequent to manifestation of ED

Time interval from manifestation of ED (years)	Atherosclerotic CV events subsequent to manifestation of ED		
	N	Cumulative N	Cumulative %
≤2	13	13	4.2
2.1-5	25	38	12.3
5.1-10	77	115	37.3
10.1-15	119	234	76.0
15.1-20	45	279	90.6
>20	29	308	100.0
Median 11.9	Mean 11.2	Standard deviation 6.9	

- Here cardiac events were much more stringent and serious excluding angina and ER visits.
- The net RR of cardiac events for all men in the study < 70 was 2.2 and was inversely correlated to age.
- Notably, cardiac events occurred in 4.2% of men within 2 years of incident ED and 12.3% of men at 5 years.
- This 5-year event percentage is very similar to 11% cardiac events found in the PCPT³

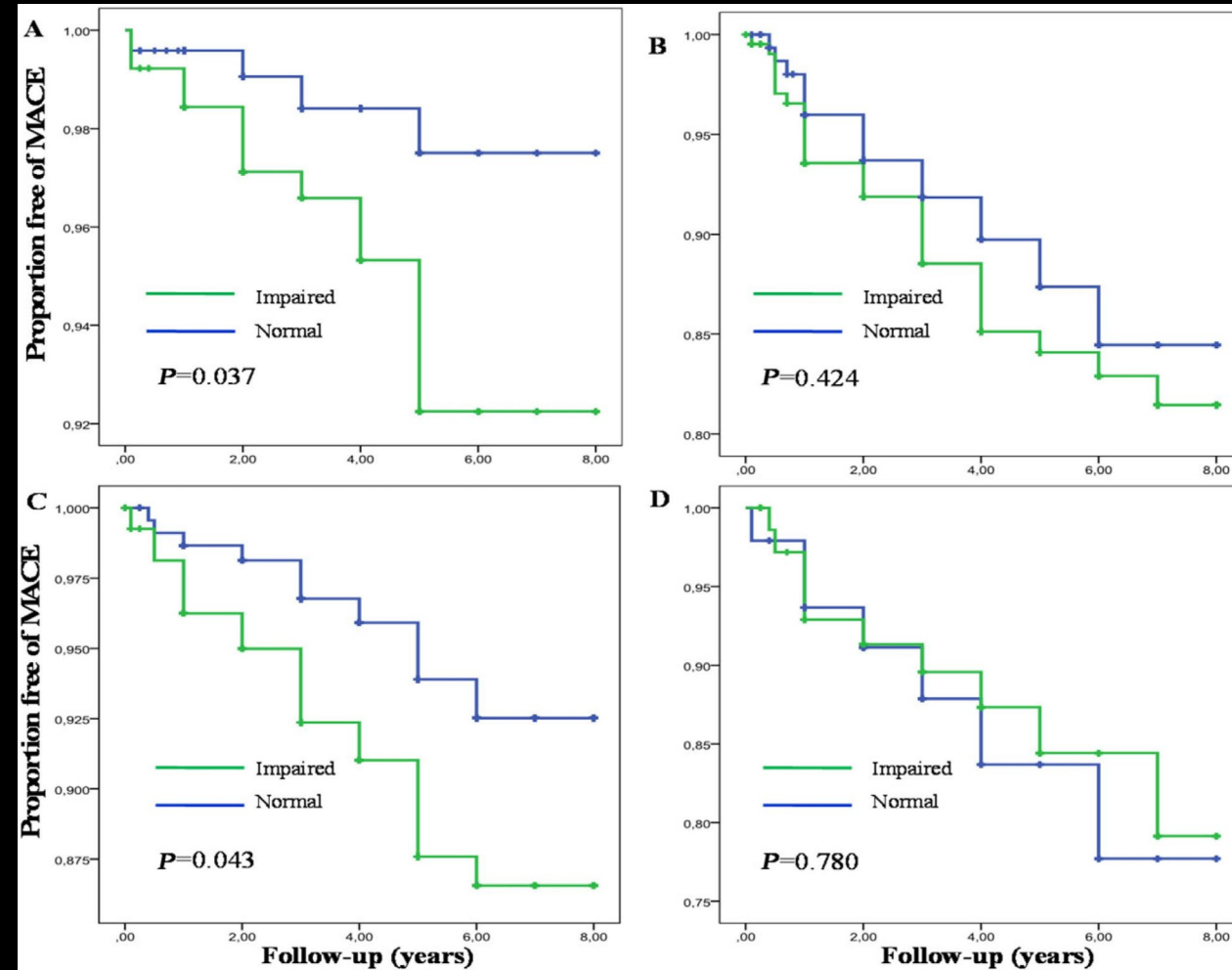
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3. [Ian M Thompson](#), [Catherine M Tangen](#), [Phyllis J Goodman](#), [Jeffrey L Probstfield](#), [Carol M Moinpour](#), [Charles A Coltman](#). Erectile dysfunction and subsequent cardiovascular disease. JAMA. 2005 Dec 21;294(23):2996-3002

Data linking ED & CVD

- Masturbation-induced erections and cardiovascular events¹⁹ :
 - In contrast, a unique study examining the association between impaired masturbation-induced erections and incidence of cardiovascular events showed a HR = 3.35, P = 0.032 only in the youngest patients (<55 years old) and HR = 2.11 , P = 0.049 in nondiabetic subjects.



Data linking ED & CVD

- Banks et al (2013) provides conflicting results compared to Inman & Chew: only after adjusting for confounding: younger age did not predict greater CV events²⁷.

	<u>Events (No ED/ED)</u>	<u>RR*</u>	<u>RR# (95% CI)</u>	<u>Heterogeneity (p-value)</u>
Age 45-54 years	59/16	2.63	1.56 (0.88-2.77)	0.2
Age 55-64 years	102/54	2.06	1.57 (1.11-2.21)	
Age 65-74 years	103/99	1.37	1.04 (0.78-1.38)	
Age 75+ years	56/321	1.53	1.43 (1.07-1.92)	

- The Banks study is extremely well powered with 123,775 patients (n=1660 Chew, n=1402 Inman).
- At study start men responded to a single ED question for which answers were coded into none, mild, moderate, and severe ED.

Banks E, Joshy G, Abhayaratna WP, Kritharides L, Macdonald PS, et al. (2013) Erectile Dysfunction Severity as a Risk Marker for Cardiovascular Disease Hospitalisation and All-Cause Mortality: A Prospective Cohort Study. PLOS Medicine 10(1): e1001372. <https://doi.org/10.1371/journal.pmed.1001372>
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Literature Update
since P3 Publication about age effect

- Figure demonstrates increased RR for men with and without known baseline CVD of several condition with ED severity including all-cause mortality, and novel findings of heart failure and AV and left bundle branch block.

Banks E, Joshy G, Abhayaratna WP, Kritharides L, Macdonald PS, et al. (2013) Erectile Dysfunction Severity as a Risk Marker for Cardiovascular Disease Hospitalisation and All-Cause Mortality: A Prospective Cohort Study. PLOS Medicine 10(1): e1001372. <https://doi.org/10.1371/journal.pmed.1001372>
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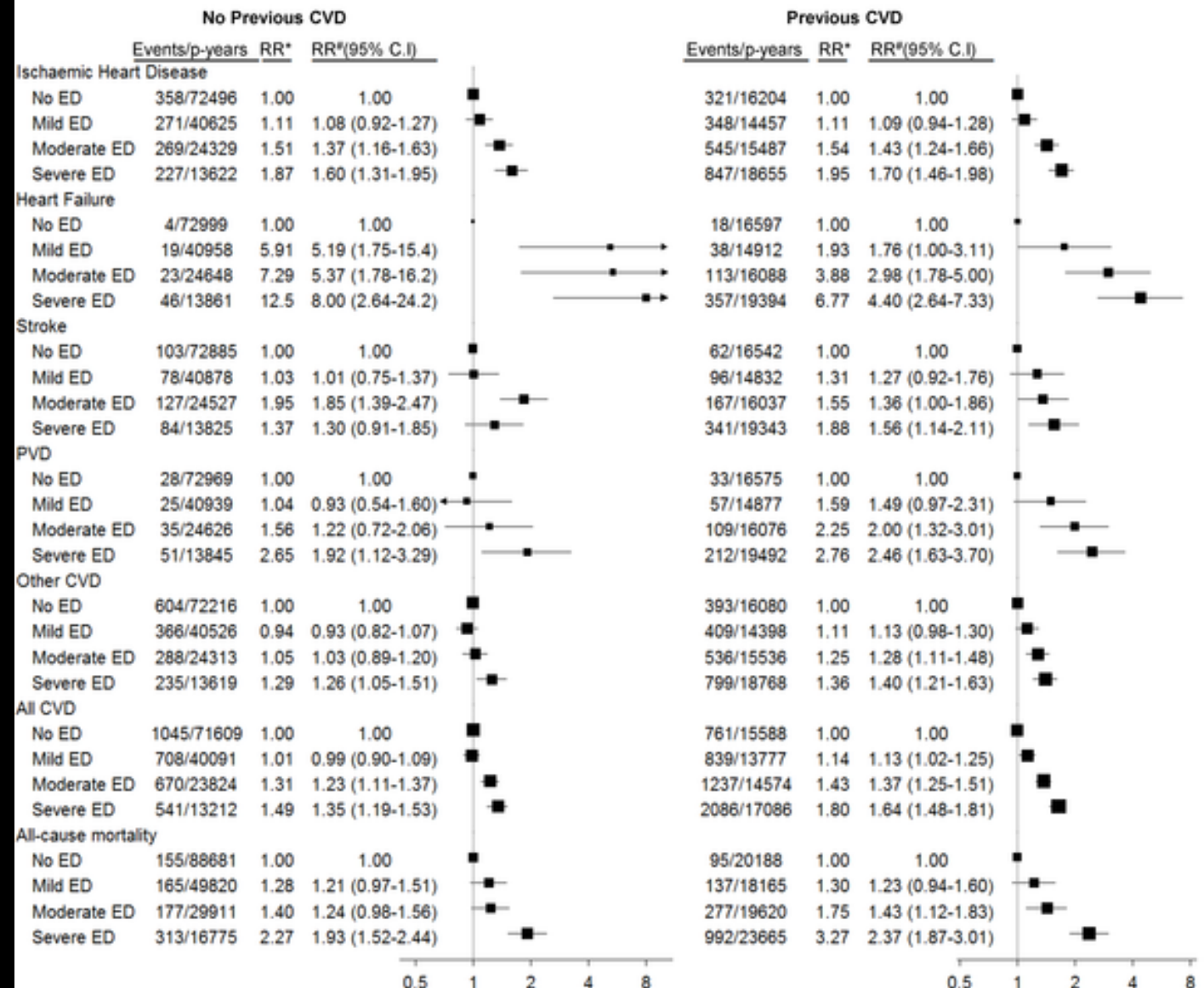


Figure: Relative risk of grouped CVD admissions and all-cause mortality since baseline, according to severity of erectile dysfunction at baseline.

*RR adjusted for age only. #RR adjusted for age, tobacco smoking, alcohol consumption, marital status, income, education, physical activity, BMI, diabetes, and current treatment for hypertension and hypercholesterolemia. RRs are plotted on a log scale and are represented with squares with areas inversely proportional to the variance of the logarithm of the RR, providing an indication of the amount of statistical information available; 95% CIs are indicated by horizontal lines. ED, erectile dysfunction; PVD, peripheral vascular disease.

All Studies linking ED & CVD

Authors/Date	Study Population	Study Design/Data Collection	Main Findings
Thompson 2005 (1)	Placebo treated men aged 55+ (N=9500) in US prostate cancer prevention trial.	Longitudinal assessment of ED, labs w/ clinical f/u from 1994-2003.	Men with incident ED have higher risk of CV events comparable to smoking or family hx of MI.
Montorsi 2006 (2)	Italian community sample of men (N=285) with ED and CAD.	Cross-sectional comparison of CAD risk in men w/ and w/o ED.	In patients with observable CAD, ED onset precedes CAD by approximately 2-3 years.
Schouten 2008 (3)	Dutch, community sample (N=1248) of men aged 50-75 yo without CVD during baseline period (1995-1998).	Longitudinal f/u up to 8 yrs. Extensive annual data collection.	Men with ED at baseline predicts cardiac events at f/u. Dose response effect - more severe ED predicts more CV events irrespective of age & other risk factors.
Gazzaruso 2008 (4)	Italian men with T2DM (N=291) w/ silent CAD.	Longitudinal f/u to 48 months.	ED associated with increased MACE (HR=2.1). PDE-5 use associated with lower rates of MACE.
Inman 2009 (5)	Olmsted County longitudinal study of US men aged 40-70yo from 1996-2005 (N=1402).	Longitudinal study of male health in general population.	ED associated with an approximately 80% higher risk of later CAD - stronger effect in younger men.
Chew 2010 (6)	Western Australian men with ED (N=1660) & w/o CVD at baseline, aged 45-70.	Retrospective linked data design health records for f/u.	Incidence of atherosclerotic CV events in men with ED were twice the rate observed in general male population (SIRR 2.1; 95% CI 1.9, 2.4)
Banks 2013 (7)	Australian men in national health survey from 2006-2009 (N=95,038).	Proportional hazard modeling of ED on CV outcomes.	ED strongly predictive of subsequent CV events and death in men w/ and w/o prior CV history.
Uddin 2018 (8)	Sub-sample (N=1914) of US men in multi-ethnic atherosclerosis (MESA) study from 2000-2012.	Proportional hazard modeling of ED effects on CV outcomes.	Strong, independent effects of ED on subsequent CV after multiple controls for other potential causes.
Adam 2020 (9)	Male participants (N=573) of mixed ages in epidemiological studies in 4 European countries.	Systematic review and meta-analysis of pooled data from 4 separate studies.	ED is highly significant harbinger of CVE's after controlling for all other risk factors.

Table 1: ED as a harbinger for CVD: Supportive epidemiologic findings

Abbreviations: ED = Erectile dysfunction; CVE= Cardiovascular Events; CVD=Cardiovascular Disease; CAD=Coronary Artery Disease; MACE=Major Adverse Cardiovascular Events; MESA=Multi-Ethnic Study of Atherosclerosis; SIRR: Standardized Incidence Rate Ratio

Psychogenic ED predicts CAD?!?

- ED may be a harbinger of increased CVD risk, not dissimilar to the risk level for vasculogenic ED!!!
- A large meta-analysis in 2017 reported that psychogenic ED was associated with an increased risk of CVD (pooled odds ratio [OR] 1.57, 95% confidence interval [CI] 1.20–2.05), after adjusting for traditional cardiovascular risk factors such as age, smoking, hypertension, and diabetes.
- Similar findings were seen in a large 2021 meta-analysis
- Overall, these studies suggest that psychogenic ED may be a risk factor for CVD, independent of a potential vascular component, and that men with psychogenic ED may benefit from cardiovascular risk assessment and management.
- More research is needed to further elucidate the relationship between psychogenic ED and CVD.

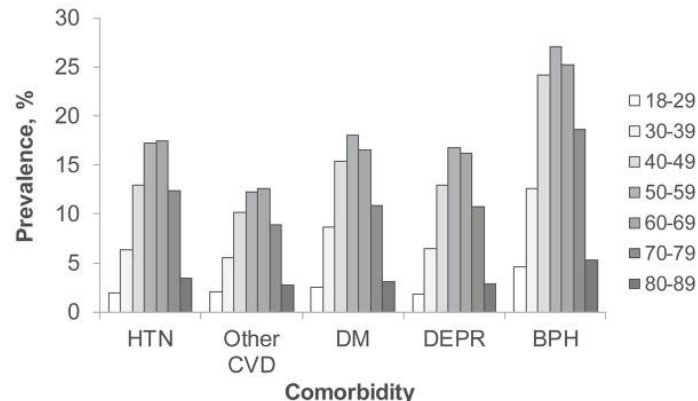
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How to inquire?

- Do you have any problems with sex?
 - “When you experience erections with sexual stimulation, how often are your erections firm enough for penetration?”
 - “During intercourse, how often are you able to maintain your erections following penetration with your partner?”
 - “Does failure to do so cause you or your partner any level of distress?”
- Important to differentiate between how (obtain, maintain or both), with whom (partnered vs. non-partnered) and when (relation to ejaculation)

The Stakes as why to inquire

- Cardiovascular disease (CVD) is a leading cause of death in which half of all men who die suddenly never have CVD symptoms
- The majority of men who have a heart attack have normal cholesterol
- Between one third to half of all men < age 45 and 90% of older men > 65 who had a heart attack and survived had at least mild ED
- Erectile dysfunction often predates the first MI by 2-5 years
- Cardiac events occur in 4.2% of men within 2 years of incident ED and 12.3% of men at 5 years



Mulhall JP, Luo X, Zou KH, Stecher V, Galaznik A. Relationship between age and erectile dysfunction diagnosis or treatment using real-world observational data in the USA. *Int J Clin Pract.* 2016 Dec;70(12):1012-1018. doi: 10.1111/ijcp.12908. PMID: 28032424; PMCID: PMC5540144.

Conclusions

- ED inquiry offers a unique opportunity to diagnose and intervene for CAD
- Definitive evidence links ED and CAD
- This relationship may extend beyond vascular mechanisms as psychogenic ED also predicts CAD
- Younger age gives us a better opportunity to impact change and sexual function is a great fulcrum for lifestyle change
- Thus, all men regardless of age should be asked about ED

References for ED & CAD Table

1. [Ian M Thompson](#), [Catherine M Tangen](#), [Phyllis J Goodman](#), [Jeffrey L Probstfield](#), [Carol M Moinpour](#), [Charles A Coltman](#). Erectile dysfunction and subsequent cardiovascular disease. JAMA. 2005 Dec 21;294(23):2996-3002.
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