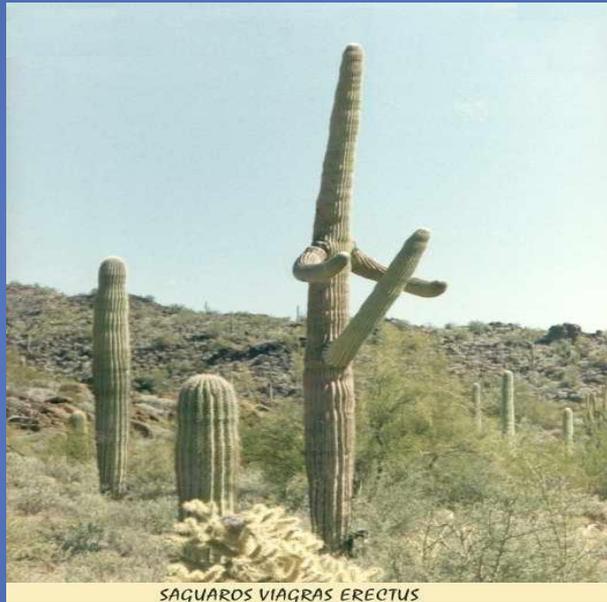


- Measures have been taken, by the Utah Department of Health, Bureau of Health Promotions, to ensure no conflict of interest in this activity.
 - CNE/CEU's are available for this live webinar. You must take the pre and post tests. 80% is required on the post test to receive CNE/CEU's.
 - Certificates will be emailed out to you within two weeks

- Dr. Hotaling has significant training in both the clinical aspects of male fertility and genetic epidemiology and he is currently the only fellowship trained male infertility/andrology expert in Utah. He completed a 6 year residency in urology at the University of Washington, elected to pursue a year of sub-specialty training in male infertility with Craig Niederberger at The University of Illinois Chicago and has a long term research goal of developing novel genetic markers for male infertility that can be used clinically to diagnose and treat this devastating condition. He has seen and performed surgery on hundreds of men with male infertility and is an associate editor of Fertility and Sterility, a premier journal in the field has had significant extramural research funding and has over 25 publications. He obtained an MS in clinical epidemiology in 2010 with a focus on statistical genetics and conducted the first genetic study on erectile dysfunction at the University of Washington. Prior work building the male fertility cryopreservation databank at The University of Washington resulted in his creation of the largest U.S. database of men cryopreserving sperm for cancer. While at The University of Illinois Chicago, he initiated studies on the genetics of male infertility. As part of this collaboration, he established a protocol for the collection and banking of DNA and serum and linkage to a de-identified database, gMR, an infertility specific electronic medical record. gMR allows uniform phenotyping and is going to be used by several members of a CDC working group for research collaboration.

Erectile Dysfunction: Causes and Treatments



James M. Hotaling, MD MSFECSSM

University of Utah, Urology

Center for Reconstructive Urology and Men's Health

801-587-1454

Diabetes Educator Seminar

Overview

- **Intro to ED**
- Diabetes and ED
- Treatment Options
- Future Directions

Goals-Erectile Dysfunction

- What is it?
- Why treat it?
- Who gets it?
- Is it ever dangerous?
- What causes it?
- How is it diagnosed?
- How to treat it?

What is it?

- E.D. is the persistent inability to achieve or sustain an erection sufficient for satisfactory sexual intercourse.
- E.D. can be:
 - A **total** inability to achieve an erection.
 - An **inconsistent** ability to do so; or
 - A tendency to sustain only **brief** erections.

ED is a major issue for baby boomers



ED is common and expensive

- 1 in 5 men over 20 reports ED in the U.S.
- Men increasingly seeking to preserve sexual function and QOL as they age
- If all men in U.S. with ED get treatment, costs will exceed \$10 Bil.

Intro: ED Risk Factors

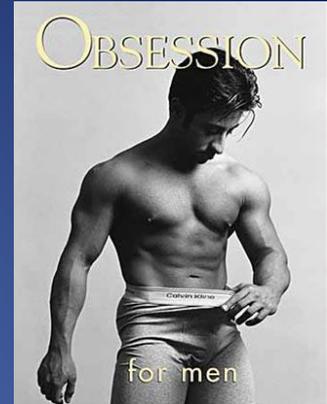
Comorbid State	Odds Ratio (95% CI)
Diabetes	2.69 (1.62,4.46)
Obesity	1.60 (1.10,2.33)
Heart Disease	1.44 (0.87,2.38)
Hypertension	1.56 (1.07,2.29)
Current smoking	1.74 (1.16,2.62)

Referrant for each comorbidity is absence of that comorbidity

Diabetes Epidemic

- Prevalence is increasing worldwide
- 12% of U.S. adults over age 40
- Type 1 diabetes with lifetime risk of 1.3%
- Most of worldwide prevalence is Type 2

Why Be Concerned?

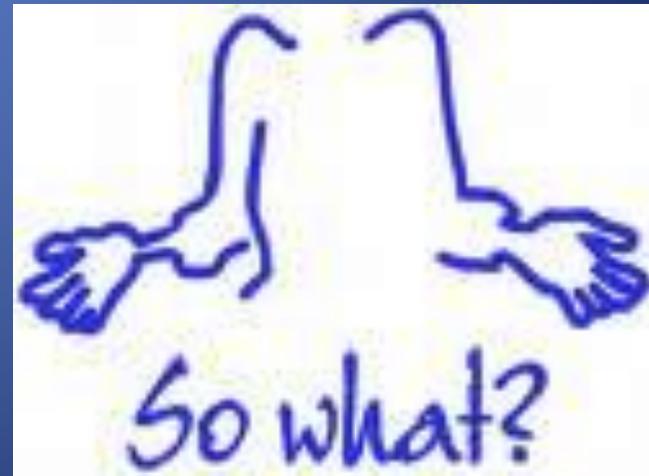


- Affects **quality** of life
- Influences general health perception of men
- Unmet medical need
- May reveal other common disorders that should be treated
 - Hypertension, dyslipidemia, diabetes, major depression

Trudel. *J Sex Marital Ther.* 2002;28:229-249; The National Council on the Aging.
Available at: <http://www.ncoa.org/content.cfm?sectionID=105&detail=128>; Feldman et al.
J Urol. 1994;151:54-61.

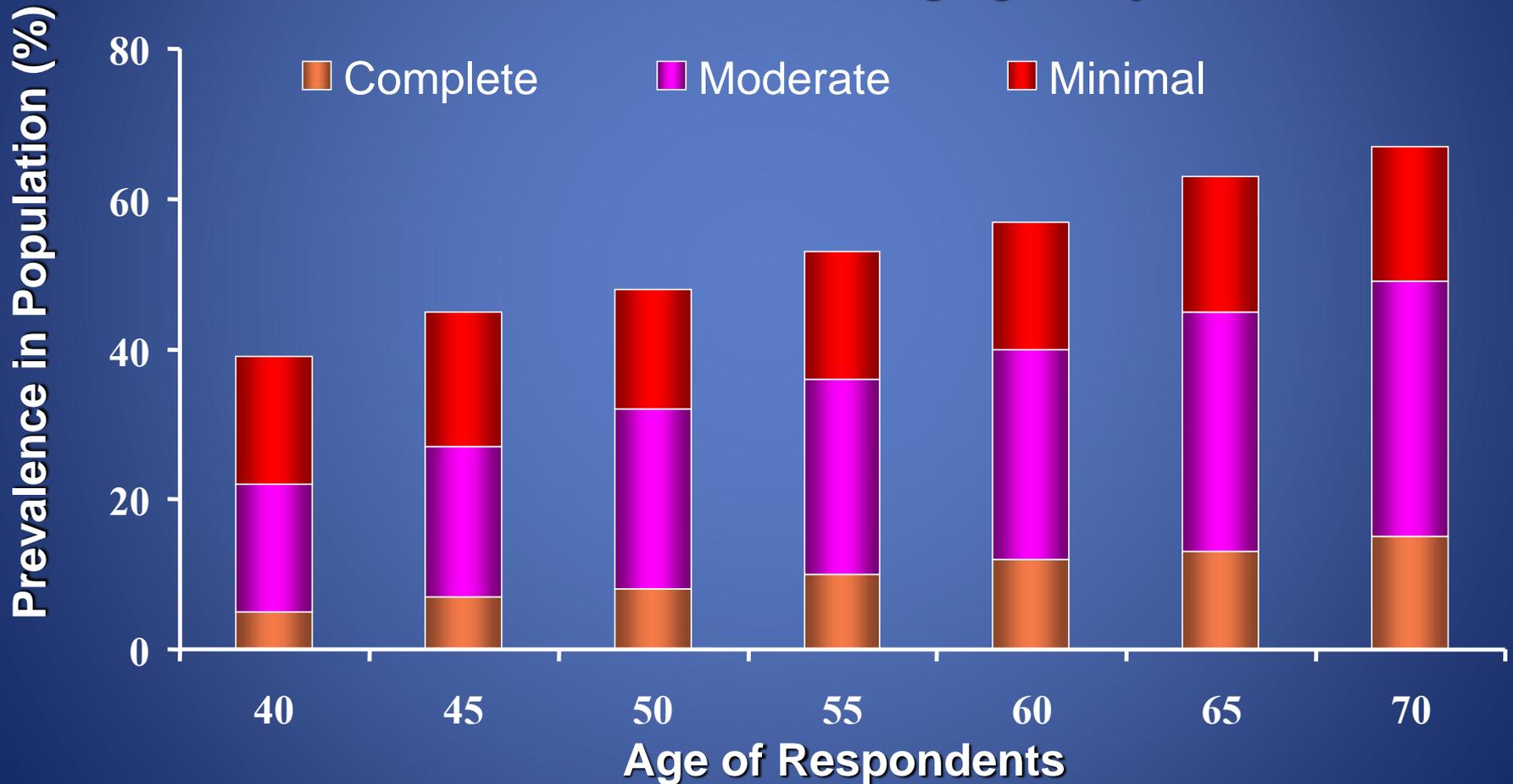
Who cares?

- **Quality** of life, not **quantity**
- Medical care does not always have to center around prolonging life
 - May be for making life worth living!
- Intimacy
- Masculinity



Who gets it?

Massachusetts Male Aging Study



So what's the problem?

- Only 10% ever seek treatment.
- 50% of men discontinue treatment once started.
- **WHY??**



Khampha Bouaphanh / The Star-telegram

Patients Want to Discuss Sexual Health

85%

Patients who believe physicians should inquire about sexual matters

74%

Patients who felt "undersatisfied" by physicians' queries about sexual matters

Failure of physicians to inquire about sexual functioning is a source of dissatisfaction for many male patients

23%

Patients reporting that physician inquired about sexual matters

ED as an Indicator of Undiagnosed Disorders

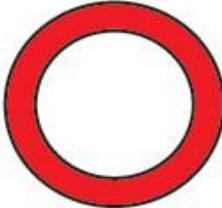
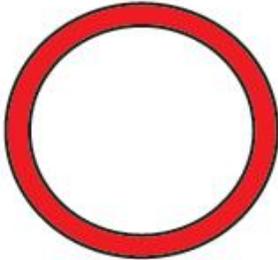
- 178 men evaluated at ED clinic in the United Kingdom
- 65 men (37%) had elevated lipids/cholesterol
 - Of these, 46 (71%) were previously undiagnosed
- 42 men (24%) had diabetes
 - Of these, 6 (14%) were previously undiagnosed
- 35 men (17%) had high blood pressure
 - Of these, 11 (31%) were previously undiagnosed

ED and Cardiovascular Disease (CVD)

- Penile vascular bed is unique, with smaller vessels feeding it
- 57% of men in one study who had had bypass surgery had prior ED
- 64% of men in one study hospitalized for myocardial infarction (MI) had experienced prior ED
- ED is a likely indicator of systemic vascular disease and probably an early warning for increased risk of MI or stroke

Gundle MJ, et al. *Am J Psychiatry*. 1980;137:1591-1594. Jackson G, et al. *Int J Clin Pract*. 1999;53:363-368. Marwick C. *JAMA*. 1999;281:2173-2174. Pritzker MR. Abstract presented at: Proceedings of the American Heart Association; November 7-10, 1999; Atlanta, Ga. Abstract 104561. Wabrek AJ, et al. *Arch Sex Behav*. 1980;9:69-77.

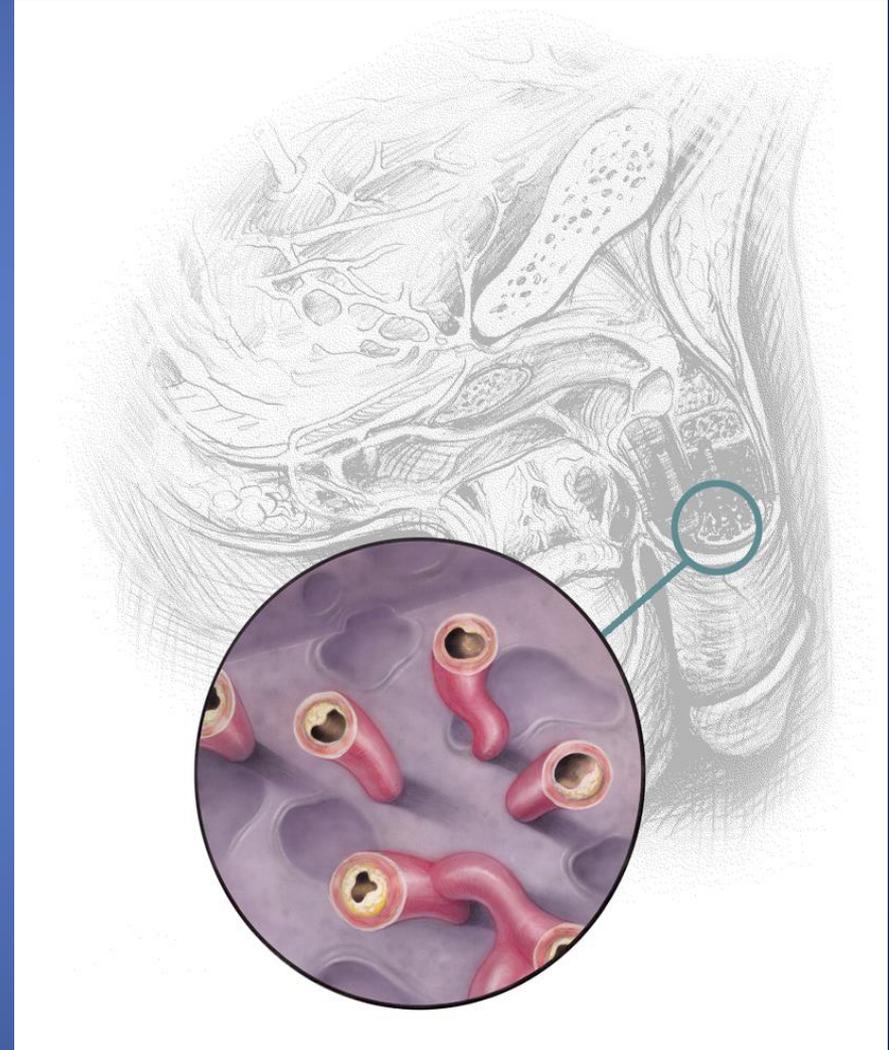
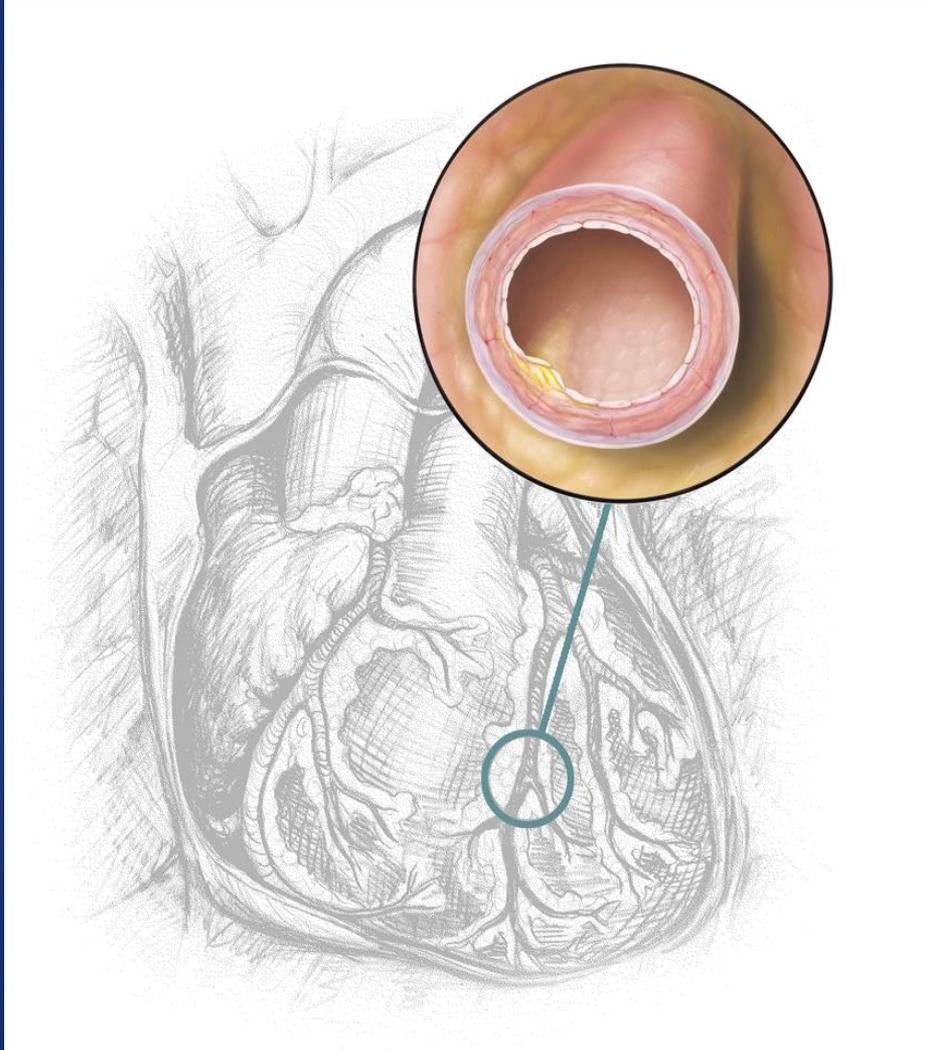
Relative Blood Vessel Sizes

Clinical presentation	Erectile dysfunction	Silent ischemia Stable / Unstable angina AMI	TIA Stroke	Claudicatio intermittens
Artery size (mm)	 <p>Penile artery (1-2)</p>	 <p>Proximal LAD (3-4)</p>	 <p>Internal Carotid (5-7)</p>	 <p>Femoral Artery (6-8)</p>

Atherosclerosis in Coronary Vessels



Atherosclerosis in Penile Arteries



ED as a marker for cardiovascular disease

 ORIGINAL CONTRIBUTION

Erectile Dysfunction and Subsequent Cardiovascular Disease

Ian M. Thompson, MD

Catherine M. Tangen, DrPH

Phyllis J. Goodman, MS

Context The risk factors for cardiovascular disease and erectile dysfunction are similar.

Objective To examine the association of erectile dysfunction and subsequent cardiovascular disease.

ED: A marker of vascular disease ?

- Pritzker – AHA meeting 1999
 - 50 patients requesting sildenafil (Viagra)
 - No patients had known heart disease
 - 35 patients had not seen a physician in 2 years
 - 40 patients had at least one risk factor for cardiac disease
 - 28 patients had treadmill evidence of heart disease
 - 20 patients underwent angiography (13 significant disease)

ED & heart disease

- A survey of 221 men post-heart attack
63% had ED
- For a mean of 5.5 yrs
- Only 58% had spoken to anyone about it
- Only 49% had ever received treatment for ED prior to their heart attack
- ED had worsened in 52% of men after the heart attack

ED: A marker for Diabetes?

- Men with ED twice as likely to have diabetes as those without
- How many men presenting with ED have previously undiagnosed diabetes?
 - 11-12%

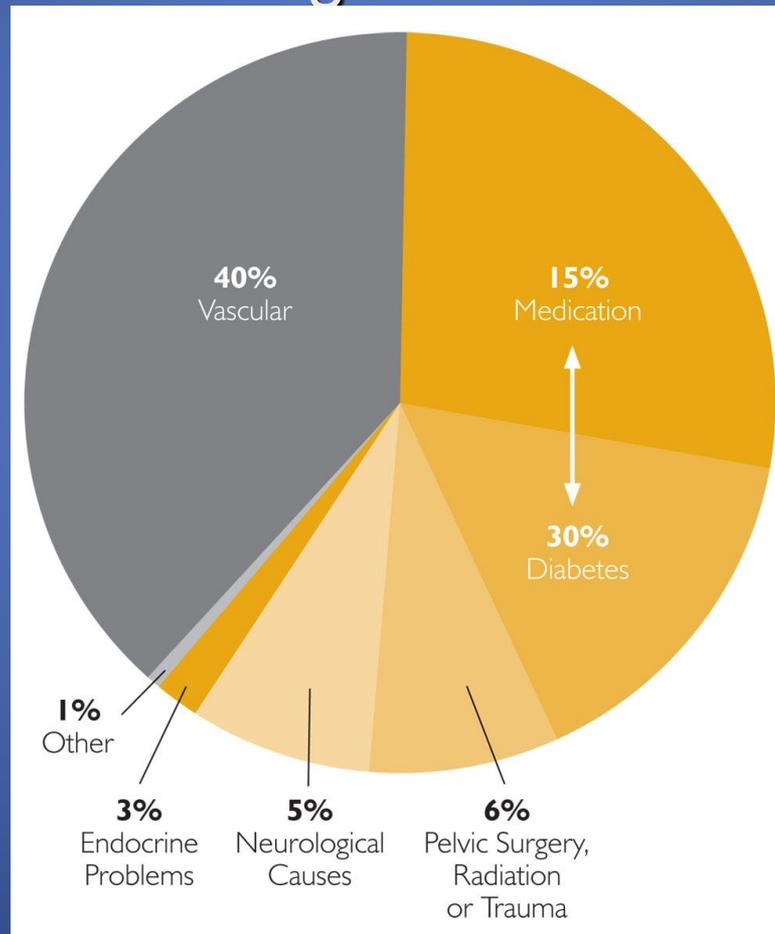
Diabetes and Low Testosterone

- Many men with diabetes have hypogonadism or low testosterone that exacerbates ED
- Up to 10% of men with diabetes have low testosterone
- Low testosterone can be easily treated with testosterone replacement therapy

Diabetes & ED

- Diabetic men are at a high risk of developing ED
- ED is especially common in diabetes, with approximately **35% to 75%** of men having this complication²
- After 60 years of age, **55% to 95%** of men with diabetes are affected by ED²

Main Physical Causes of ED: Percentage Distribution³



Causes of ED

- **Decreased arterial flow (60%)**
 - Diabetes, atherosclerosis, vasculitis, tobacco use
- **Increased venous leakage (10%)**
 - Altered cavernosal tissue (fibrosis, Peyronie's disease, diabetes, tobacco use)
- **Neurogenic (20%)**
 - Diabetes (peripheral), CVA, Parkinson's, Alzheimer's, spinal cord injuries
- **Endocrine (5%)**
 - Hypogonadism, hyperprolactinemia
- **Iatrogenic (5%)**
 - Surgical (radical prostatectomy, rectal surgery, AAA)
 - Medications...



Medications and ED



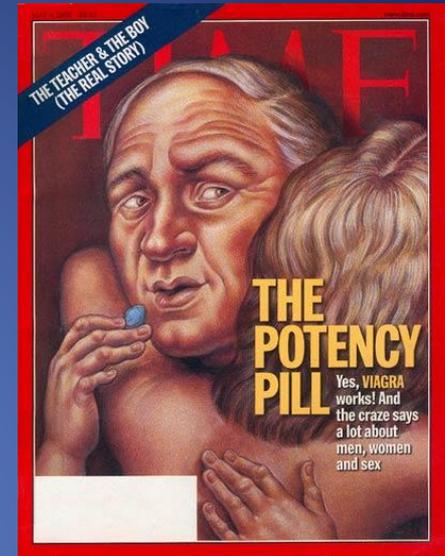
- Antihypertensives
 - Thiazide diuretics, beta-blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors
- Antidepressants
 - Tricyclic antidepressants, SSRIs
- Antiarrhythmics (eg, digoxin)
- Antiandrogens
 - Luprolide, flutamide, finasteride, dutasteride
- H2 receptor antagonists (eg, cimetidine)
- Recreational/Abuse agents
 - Cigarette smoking
 - Cocaine & marijuana

How to diagnose?

- Patient History
 - Duration of problem, specific problem with erection
 - Life changes/Social factors
 - Nocturnal erections
 - Other medical problems / medications /social habits
- Physical Exam
- Questionnaires



How to treat?



- Medications

- Pills

- Sildenafil (Viagra)

- Vardenafil (Levitra)

- Tadalafil (Cialis)

- Intraurethral pills (MUSE)

- Penile injections (Caverject, Bimix, Trimix)

- Non-medication

- Vacuum erection devices

- Surgery

Treatment-Do Nothing

- Watch and Wait
 - Rat models: penile cell death
 - Human studies: decrease in length and girth

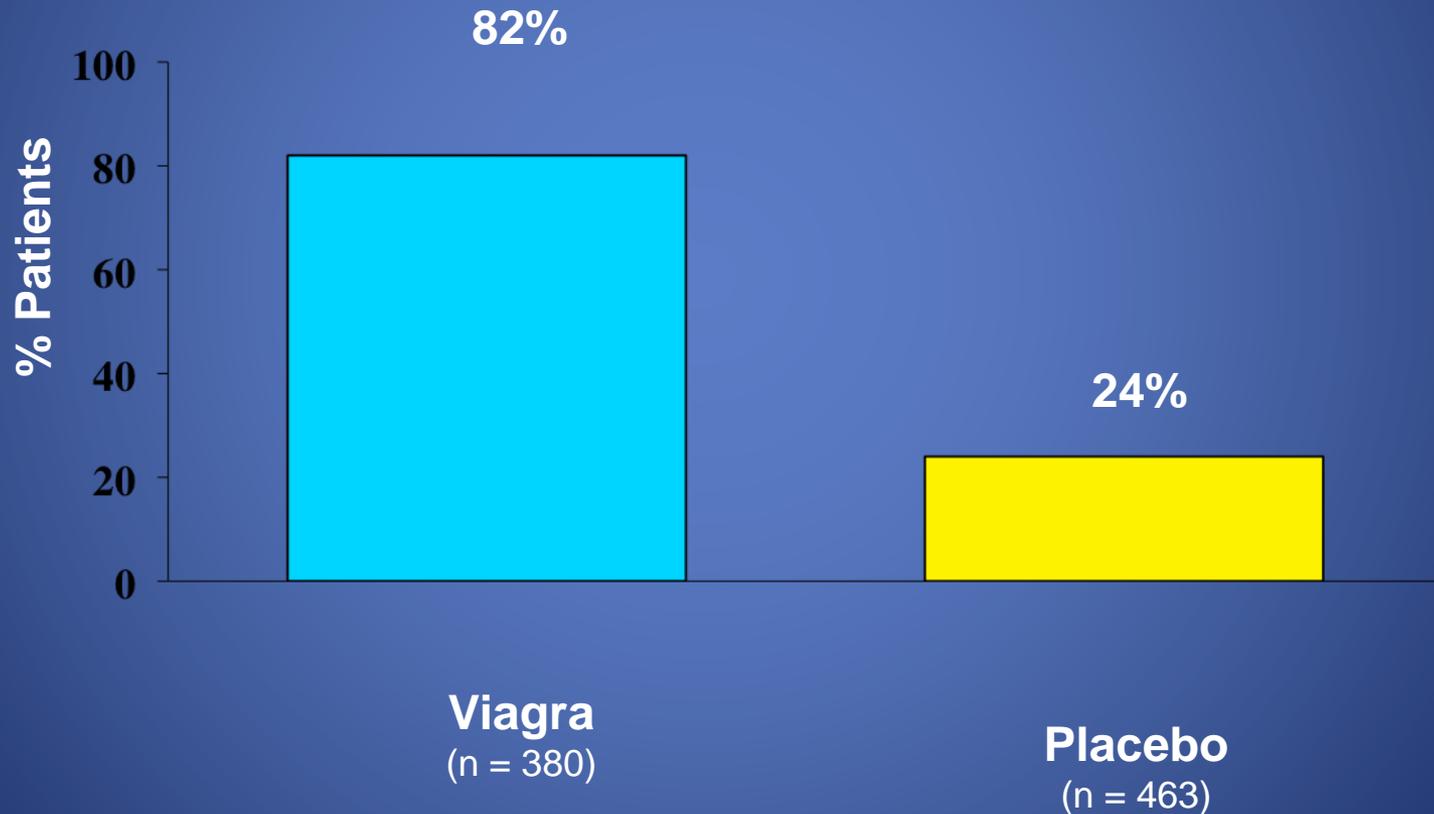
**Small penis?
Have I got
a car for you.**



If you're going to overcompensate, then by all means, overcompensate.
Loaded '89 911 Carrera 4. Call (312) 552-1676. Ask for Tiny.

JOE'S PORSCHE 

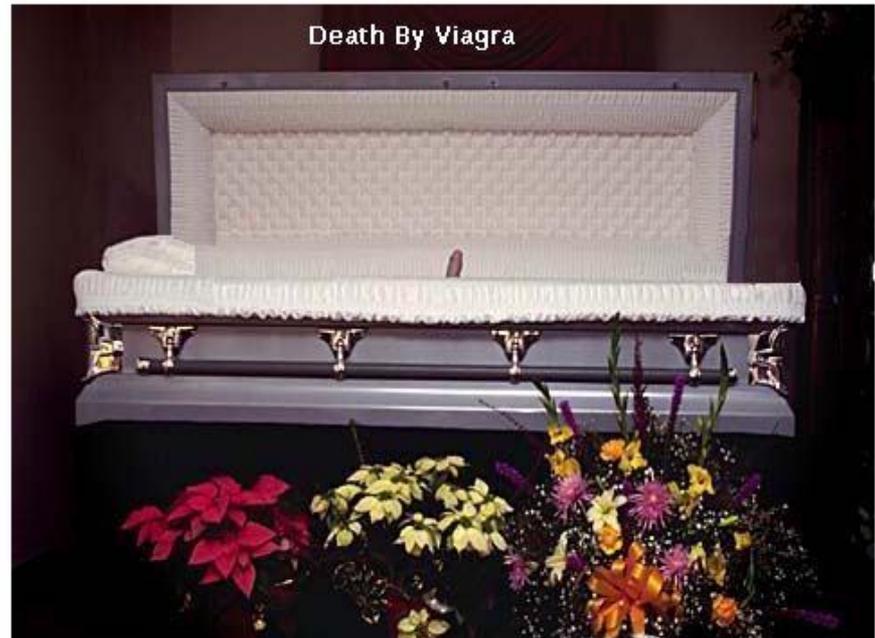
Patients Reporting Improved Erections Across All Degrees of ED Severity



Contraindication:

Nitrates

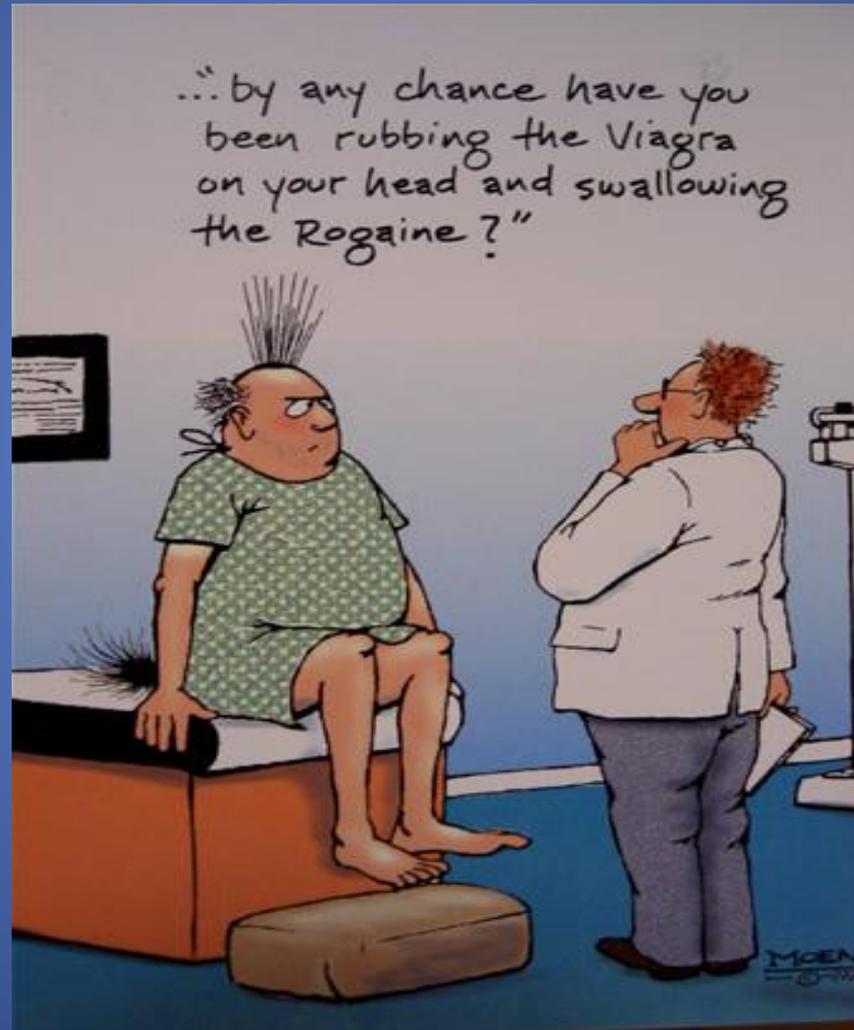
- For all of the drugs
- May make blood pressure drop dangerously low



Keys to using pills successfully:

- Sexual stimulation is necessary
- Take prior to meal or after light snack
- May not work 1st few times
- Treat other medical conditions
 - Stop smoking, increased exercise, etc.
- 30% of men have side effects
 - Only a few stop medications because of side effects

If pills do not work?



Vacuum Erection Device (VED): Basic Principles



- Externally applied device mechanically effects penile blood engorgement
- Cylinder/pump placed over penis creates closed chamber; pump creates vacuum, drawing blood into corpora cavernosa
- Constrictive elastic ring then placed at base of penis to restrict flow of suctioned blood

VED: Profile

- Efficacy¹
 - Uniformly produces erection
 - Low satisfaction rate²
- Advantages^{2,3}
 - On-demand use
 - No systemic side effects
 - Cost
- Disadvantages^{2,3}
 - Cumbersome
 - Unnatural erection
 - Must be in stable relationship
 - Possible side effects may include
 - Bruising/burst blood vessels
 - Penile pain
 - Ejaculatory blockage
 - Numbness
 - Penile hinging

Second-Line Therapy: Intracavernosal Injection

- Lack of response to oral therapy^{1,2}
- Contraindications to specific oral drugs¹
- Adverse reactions/intolerance to oral drugs¹
- More reliable, instant, predictable erection
- Patient preference



1. Recommendations of the 1st International Consultation on Erectile Dysfunction.
In: Jardin A, et al, eds. *Erectile Dysfunction*. Plymouth, United Kingdom: Health Publication,
Ltd; 2000:711-726. 2. Shabsigh R, et al. *Urology*. 2000;55:477-480.

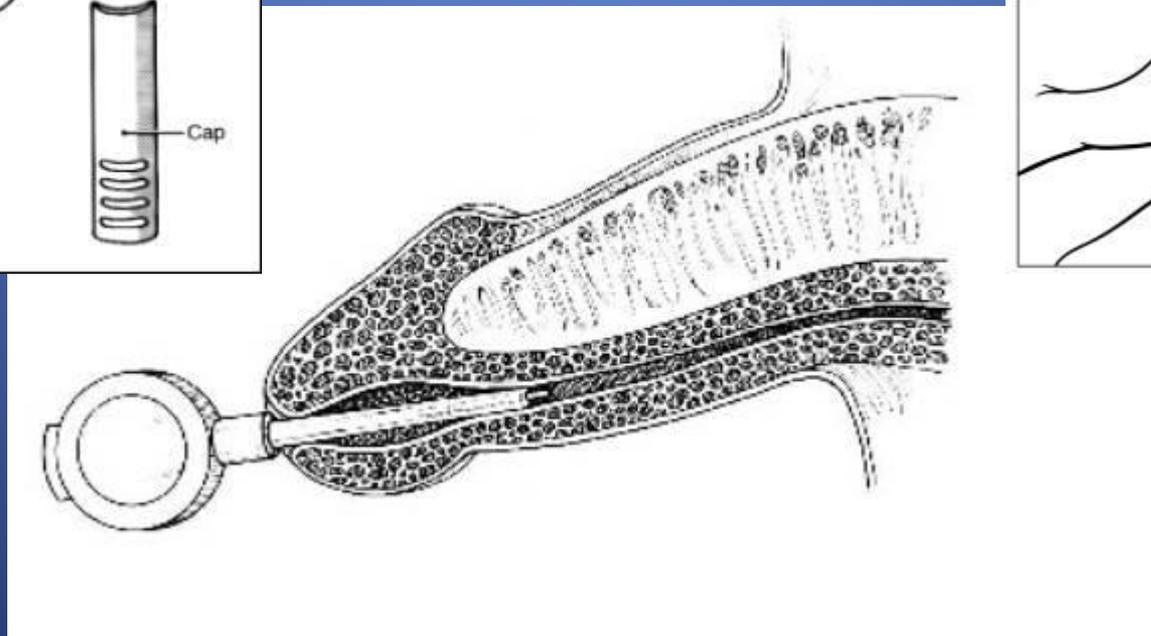
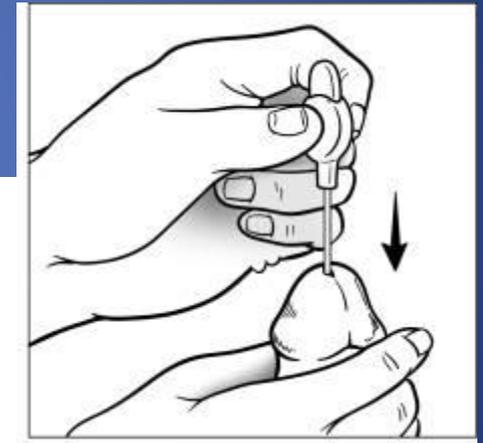
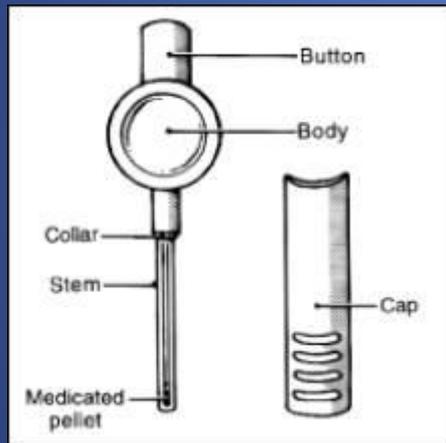
Penile Injection Therapy: Advantages

- Highly effective
- Mimics natural physiology of erection
- No effect on sensation, ejaculation
- Higher level of discretion, thus spontaneity

Penile Injection Therapy: Disadvantages

- Poor long-term tolerability (dropout rate >60%)
- Bruising, prolonged erection, scarring in penis, pain at injection site, penile deformity (rare)
- Cumbersome, especially for patients with poor manual dexterity/vision or severe obesity
- Requires training, follow-up, and dosing adjustments

Intraurethral Alprostadil (MUSE)



Intraurethral Alprostadil (MUSE): Advantages

- Alleviates need for needles/injections
- High safety, local therapy, no systemic side effects
- No effect on sensation, ejaculation
- No fibrosis, prolonged erections, or curvature

Intraurethral Alprostadil (MUSE): Disadvantages

- Transient penile burning in at least 32%
- Less effective than injection therapy
- Patients with poor manual dexterity/vision or severe obesity may find administration difficult
- Technique must be taught
- Expensive

Malleable Implant

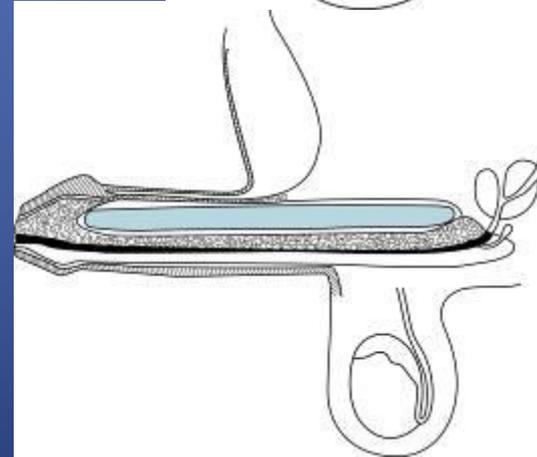
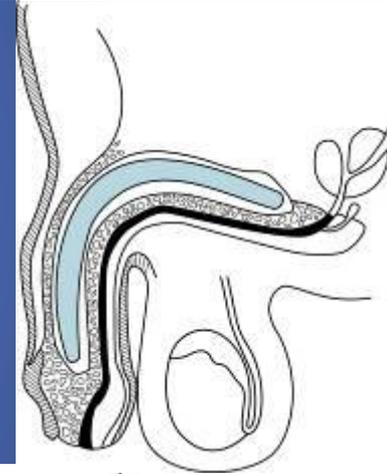


Advantages:

- Easy for you or your partner to activate
- Good option for men with limited dexterity
- Totally concealed in body
- The simplest surgical procedure
- Least expensive prosthesis

Disadvantages

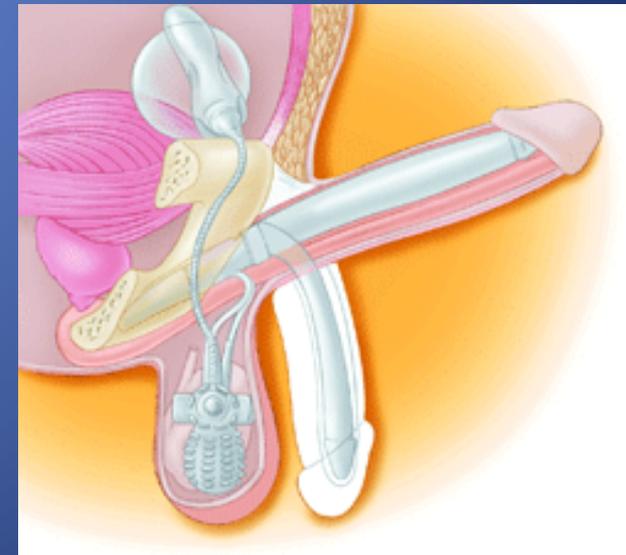
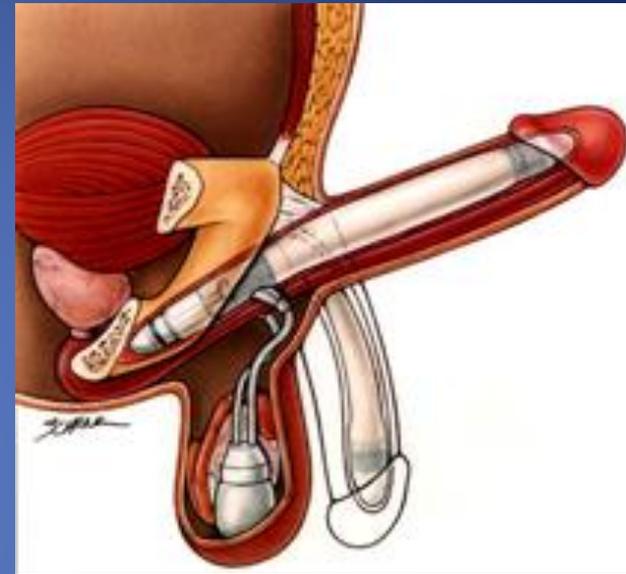
- Stays firm when not in erect position
- May “show” through clothes



Inflatable Penile Prosthesis (IPP)

Advantages:

- Easy to use
- One-step deflation
- Totally concealed in body
- Natural flaccidity compared to non-inflatable implants
- Acts and feels more like a natural erection
- More firm and full than other implants
- Feels softer and more flaccid when deflated



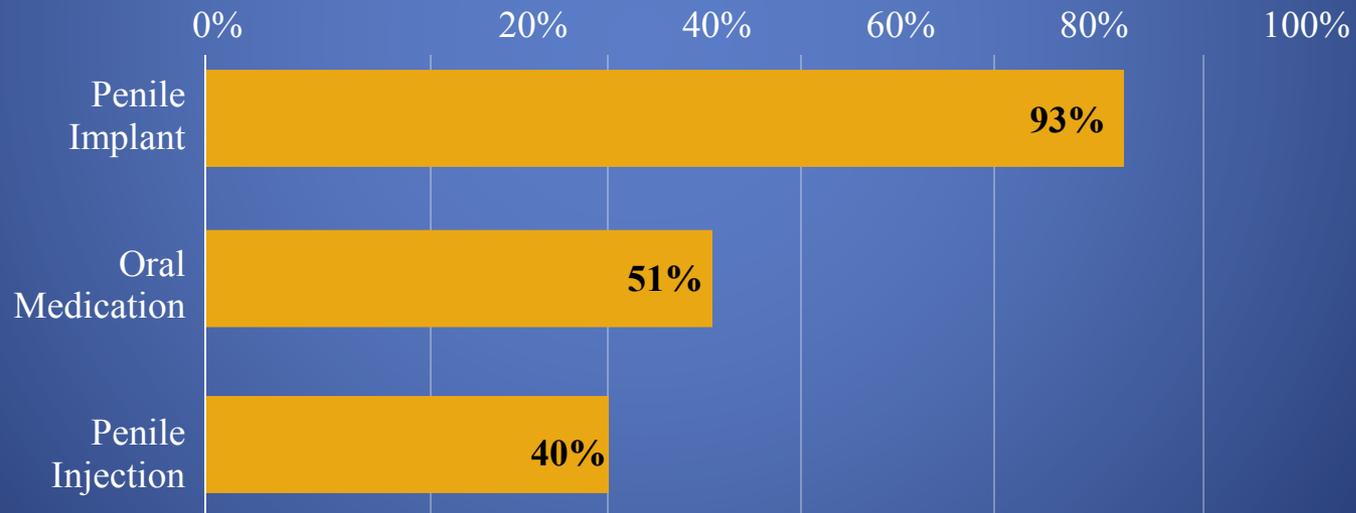
Penile Prosthesis

Pros

- Highest patient satisfaction rate
- 7 to 10 years average functional prosthesis life
- Higher spontaneity
- Discreet, normal appearance
- Erection longevity controllable
- Normal sensation/orgasm
- Significant clinical data on procedure and results

Satisfaction with treatment options

Overall Patient Satisfaction with ED Treatments



Penile Prosthesis

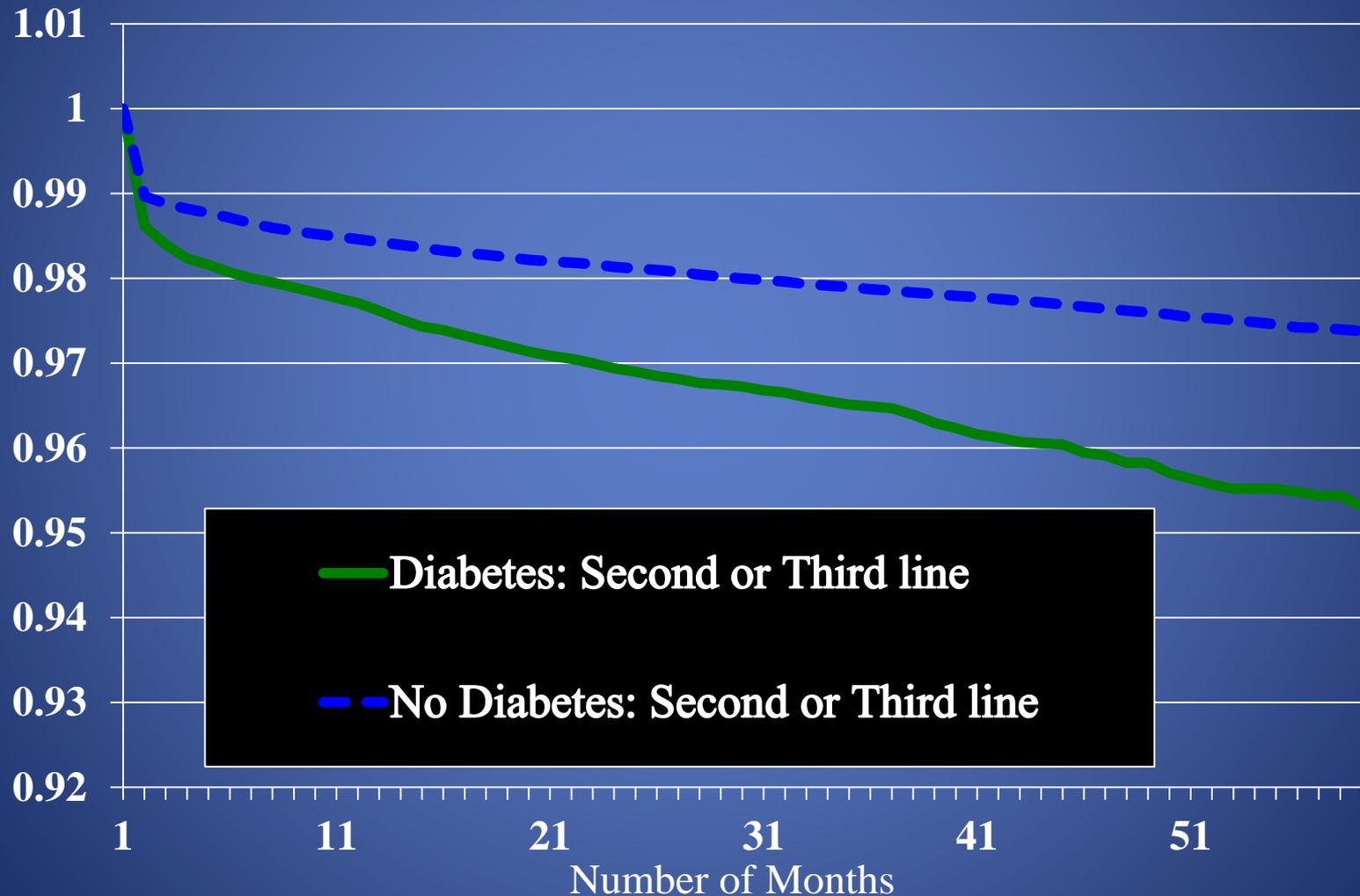
Cons

- Eliminates the possibility of the return of natural erections
- If an infection occurs, the implant may have to be removed
- Cost?
- May cause the penis to become shorter
- In rare cases, may cause lasting pain
- Mechanical failure

UDA Costs of ED in Diabetes

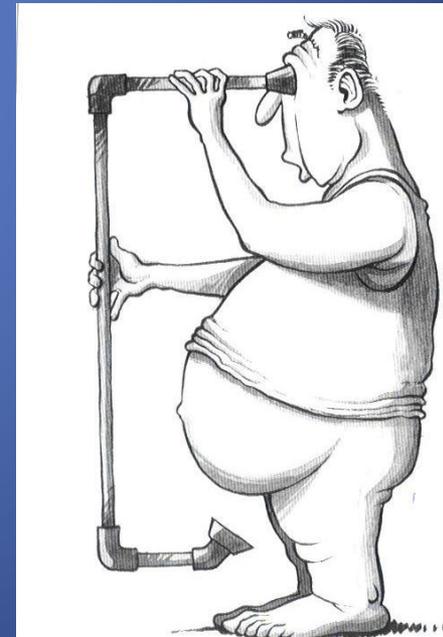
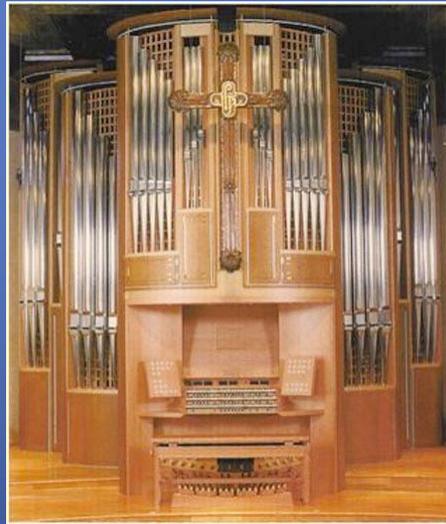
- Inovus I3 claims database queried '02-'06
- ED therapies compared between men with and without pre-existing diabetes
 - Primary (PDE5i)
 - Secondary (injectables)
 - Tertiary (prosthesis)
- 136,306 men with ED; 19,236 with DM

Increased risk of therapeutic progression in patients with DM



Reasons for Dissatisfaction With Penile Implant

- Loss of penile length
- Unrealistic expectations



ED Tx do not treat pathophysiology

1. Phosphodiesterase type 5 inhibitors (PDE5i)
2. Intracavernosal Therapy
3. Inflatable Penile Prosthesis

Efficacy?

70%

50% in
diabetics

70% but
up to 68%
self d/c

85%



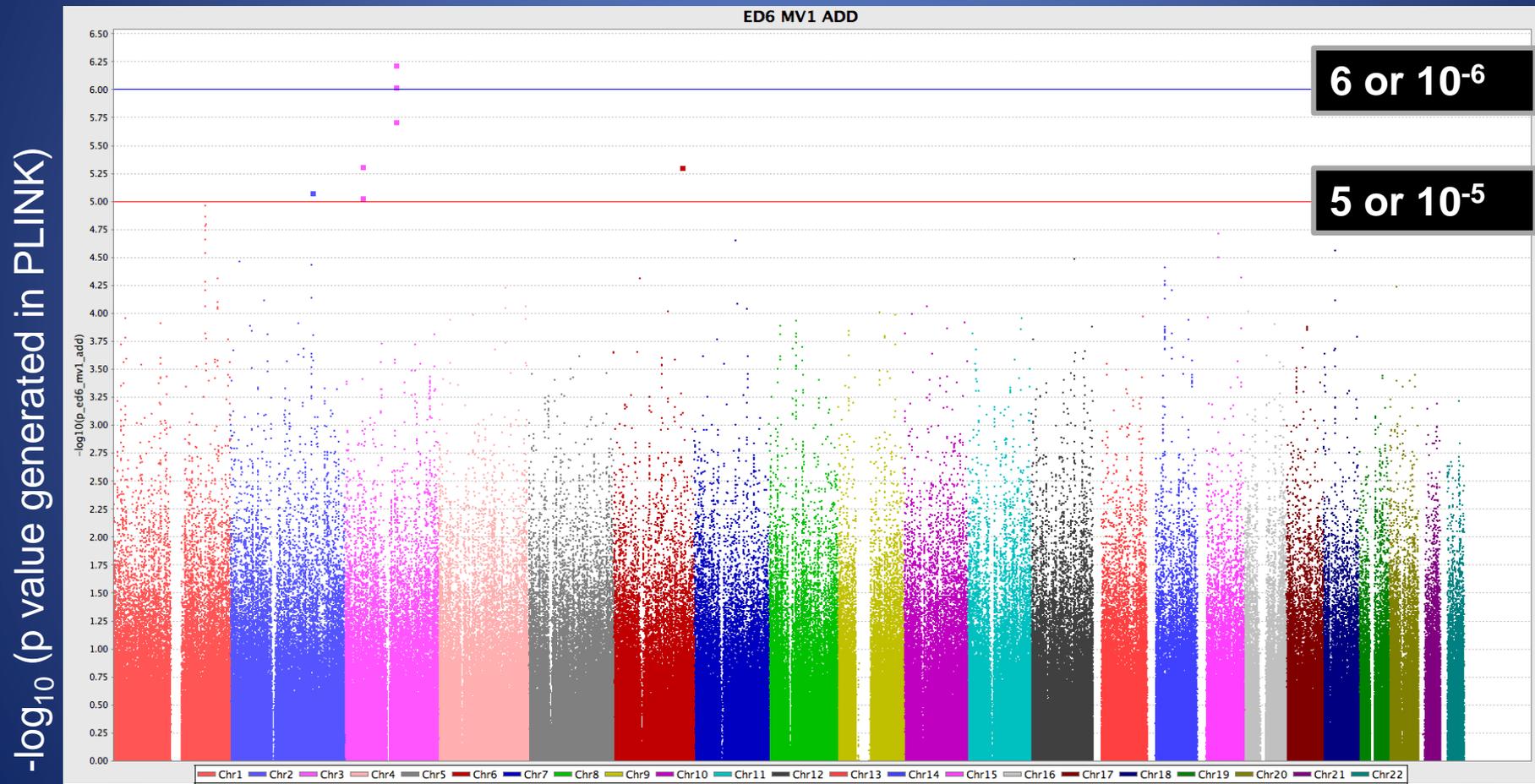
Pilot Genome-Wide Association Search Identifies Potential Loci for Risk of Erectile Dysfunction in Type 1 Diabetes Using the DCCT/EDIC Study Cohort

James M. Hotaling, Daryl R. Waggott, Jack Goldberg, Gail Jarvik, Andrew D. Paterson, Patricia A. Cleary, John Lachin, Aruna Sarma, Hunter Wessells*,† and the DCCT/EDIC Research Group

From the Departments of Urology (JM, HW) and Medical Genetics (GJ), University of Washington School of Medicine and Department of Epidemiology (JG) and Diabetes Research Center (HW), University of Washington, Seattle, Washington, Dalla Lana School of Public Health, University of Toronto (ADP), Program in Genetics and Genomic Biology, Hospital for Sick Children (ADP) and Samuel Lunenfeld Research Institute, Mount Sinai Hospital (DRW), Toronto, Ontario, Canada, George Washington University, The Biostatistics Center (JL), Rockville, Maryland, and Department of Urology, University of Michigan (AS), Ann Arbor, Michigan

8 or 10^{-8}

Manhattan Plot

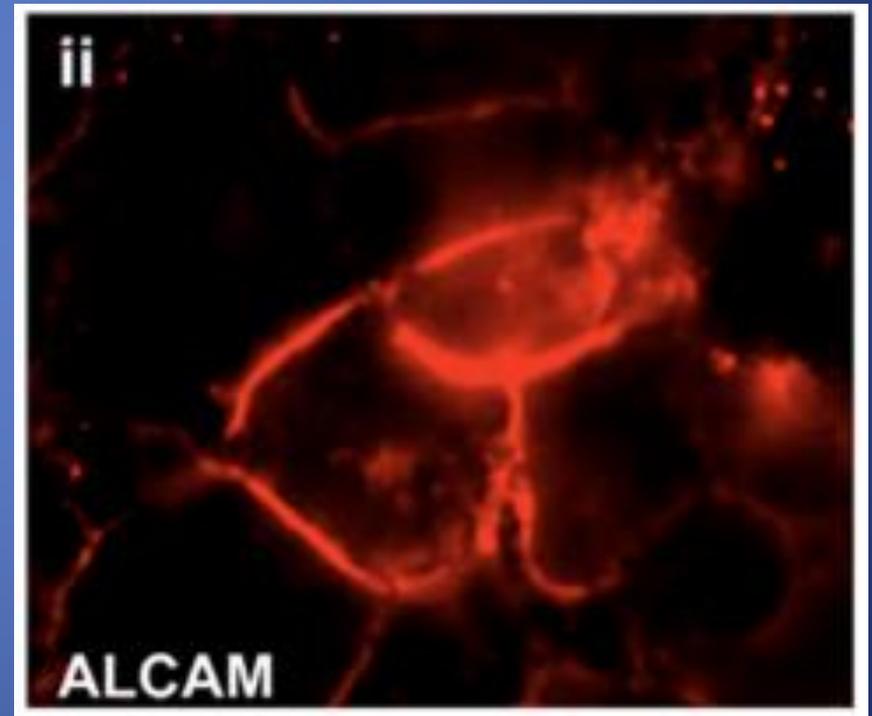


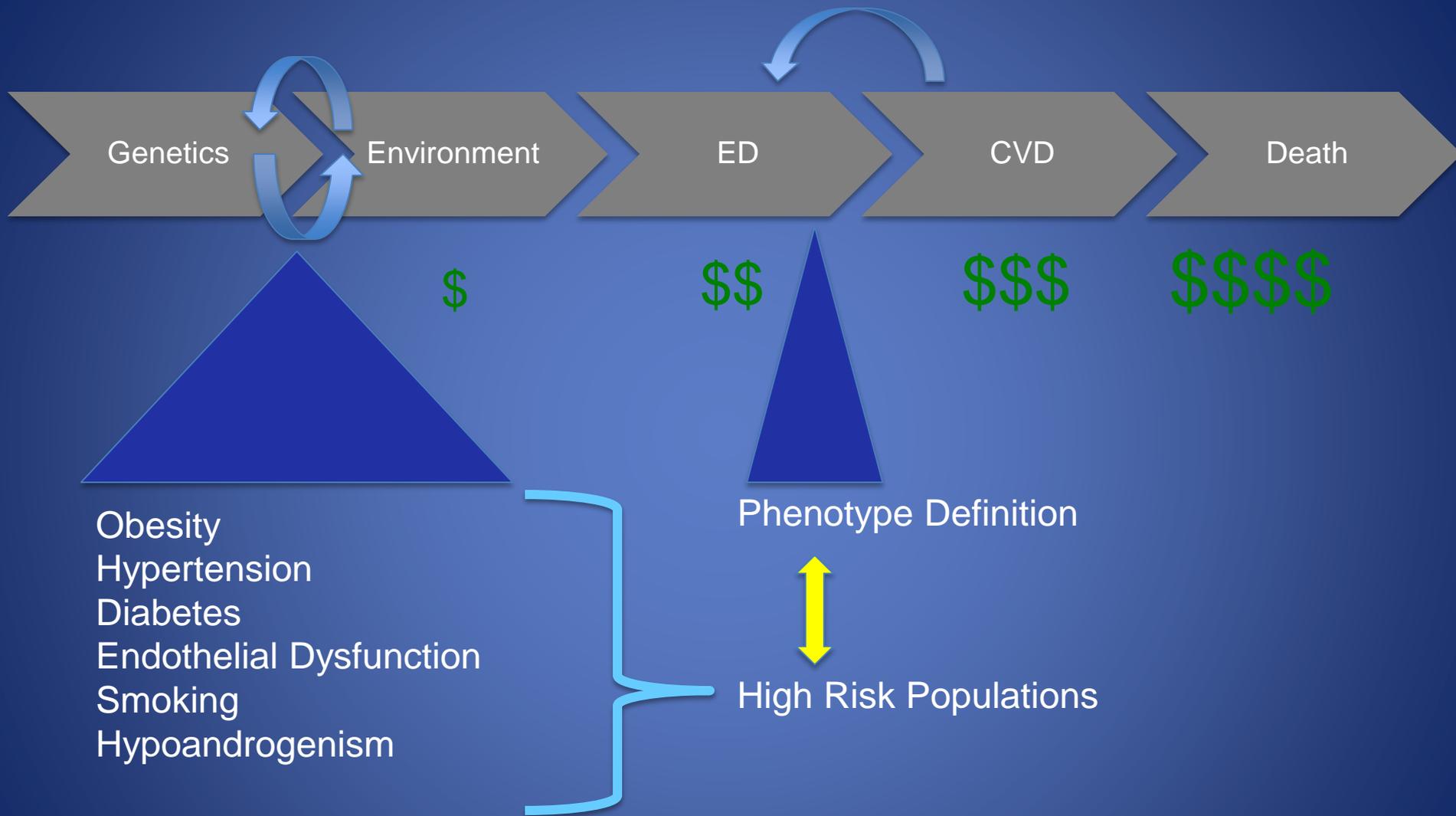
Location on Chromosome (each color is a separate Chromosome)

Top Hits: ALCAM

(rs981023 $p=6.98 \times 10^{-7}$ & rs1920201 $p=8.60 \times 10^{-7}$)

- Activated Leukocyte Cell Adhesion Molecule (CD166)
- Cell surface immunoglobulin Involved in transendothelial cell migration





Genetics

Environment

ED

CVD

Death

\$

\$\$

\$\$\$

\$\$\$\$

Obesity
Hypertension
Diabetes
Endothelial Dysfunction
Smoking
Hypoandrogenism

Phenotype Definition

High Risk Populations

Summary

- ED is common
- ED is not just “in your head”
- ED is associated with many medical conditions
- ED is **VERY TREATABLE**
- There is no reason to suffer, especially in silence

QUESTIONS?

