

**Testosterone Therapy for Menopausal  
Women**  
**Androgen Insufficiency is *not* a Construct  
of the Pharmaceutical Industry**

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## The making of a disease: female sexual dysfunction

Ray Moynihan

Is a new disorder being identified to meet unmet needs or to build markets for new medications?

The corporate sponsored creation of a disease is not a new phenomenon,<sup>1</sup> but the making of female sexual dysfunction is the freshest, clearest example we have. A cohort of researchers with close ties to drug companies are working with colleagues in the pharmaceutical industry to develop and define a new category of human illness at meetings heavily sponsored by companies racing to develop new drugs. The most recent gathering, featured Pfizer as chief sponsor and Pfizer-friendly researchers as chief speakers. The venue? The Pfizer Foundation Hall for Humanism in Medicine at New York University Medical School.

Since the launch of sildenafil (Viagra) in 1998, more than 17 million men have had prescriptions written for it as a treatment for erectile dysfunction, with Pfizer reporting sales in 2001 of \$1.5bn.<sup>2</sup> The emerging competitors, Bayer's vardenafil and Lilly-ICOS's tadalafil, are likewise expected to have annual markets in excess of \$1bn each.

To build similar markets for drugs among women, companies first require a clearly defined medical diagnosis with measurable characteristics to facilitate credible clinical trials. Over the past six years the pharmaceutical industry has funded, and its representatives have in some cases attended, a series of meetings to come up with just such a definition (table).

### Summary points

Researchers with close ties to drug companies are defining and classifying a new medical disorder at company sponsored meetings

The corporate sponsored definitions of "female sexual dysfunction" are being criticised as misleading and potentially dangerous

Commonly cited prevalence estimates, which indicate that 43% of women have "female sexual dysfunction," are described as exaggerated and are being questioned by leading researchers

Controversy surrounds current attempts to medicalise sexual problems and establish "normative data" for a range of physiological measurements of female sexual response

The role of drug companies in the construction of new conditions, disorders, and diseases needs more public scrutiny

*Mental Disorders*, 4th edition), participants produced a new definition and classification featuring disorders of desire, arousal, orgasm, and pain, to be used in "medical

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# Education and debate

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## The marketing of a disease: female sexual dysfunction

Ray Moynihan

The pharmaceutical industry's dreams of making large profits from treating female sexual dysfunction are starting to look like premature speculation

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Robert Wilson's bestselling book *Feminine Forever* helped persuade the modern world that the menopause was a "disease" of hormone deficiency, to be cured with hormone replacement.<sup>1</sup> The book's 1966 front cover promised, "Every woman no matter what her age, can safely live a fully-sexed life for her entire life," and the hormones sold by Wilson's sponsor duly became best sellers. Forty years later, long term hormone replacement has been exposed as doing more harm than good, drug sales have collapsed, and Wilson's thesis is rightly ridiculed as corporate sponsored disease mongering.<sup>2,3</sup>

In the shadows of this overmedicalisation, the pharmaceutical industry is meeting unexpected resistance to its attempts to sell women the next big profitable "disease," female sexual dysfunction. This condition is claimed by enthusiastic proponents to affect 43% of American women,<sup>4</sup> yet widespread and growing scientific disagreement exists over both its definition and prevalence. In addition, the meaningful benefits of experimental drugs for women's sexual difficulties are questionable, and the financial conflicts of interest of experts who endorse the notion of a highly



however, that the company may have already set aside an initial \$100m (£53m, €76m) to spend on advertising alone.<sup>7</sup> Long before its testosterone patch had even been assessed for approval, the company's global marketing had been strategically targeting health profes-

# Los Angeles Times Magazine

October 2, 2005

## Dr. Berman's Curious Sex Drive

How a former UCLA urologist  
used drug-company money  
to create the 'disease' of  
female sexual dysfunction  
By Anne-Marie O'Connor



The cult of single-gear bikers ~ Making hay from the ADA ~ One high school's driverless education

# Hypoactive Sexual Desire Disorder (HSDD)

Persistent or recurring deficiency (or absence) of sexual fantasies or thoughts and desire for or receptivity to sexual activity that causes personal distress

American Psychiatric Association, DSM-IV. Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> ed. Washington, D.C.: American Psychiatric Press, 1994

Basson R et al. Report of the international consensus development conference of female sexual dysfunction: definitions and classifications. *J Urol* 163:888-93, 2000

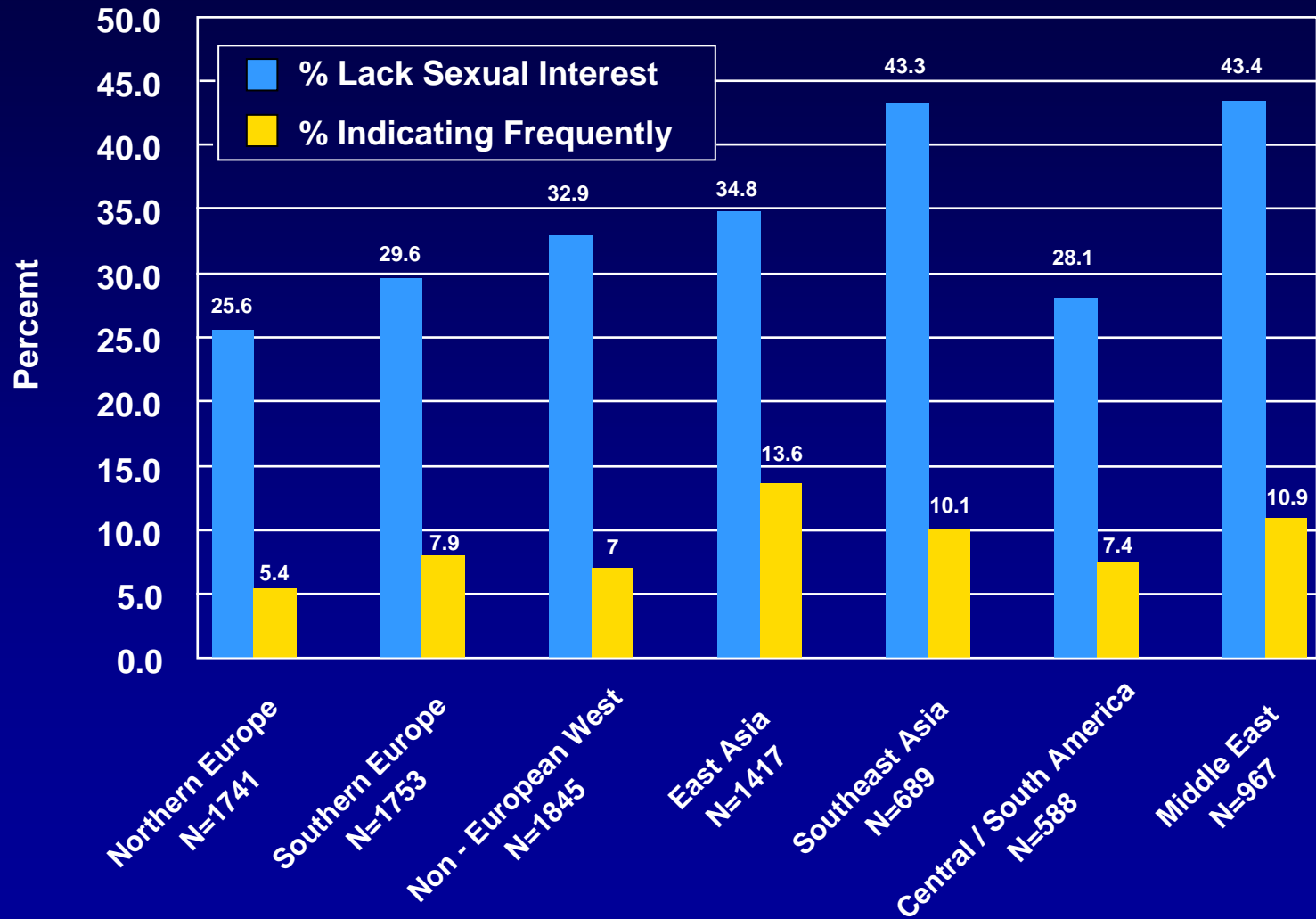
# What the Skeptics Say

- **HSDD is a made-up disease**
  - **Sex problems are normal**
  - **Difficulties become Dysfunctions become Diseases**

# Why HSDD is Not a Made-Up Condition

- Low libido causing distress is not new
- Defined as a disorder in the *International Classification of Diseases* and the American Psychiatric Association's *Diagnostic and Statistical Manual*
- 5-10% of women world-wide say they have low libido “frequently”

# Prevalence of Low Libido Among Women 40-80 Years



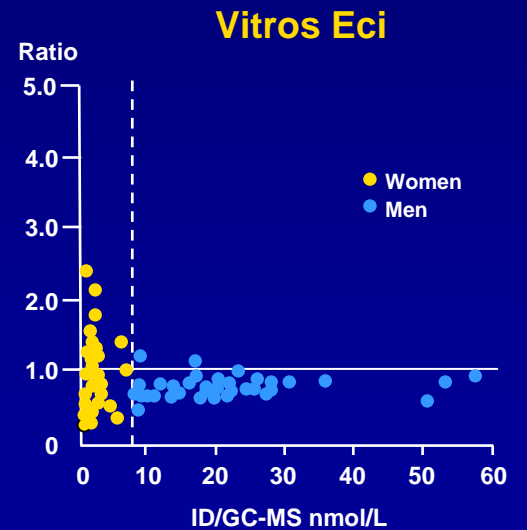
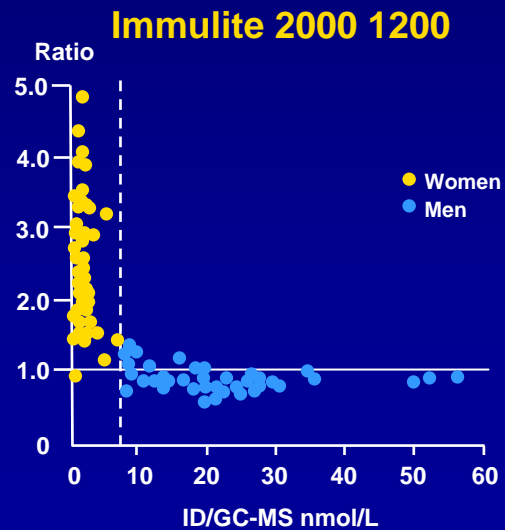
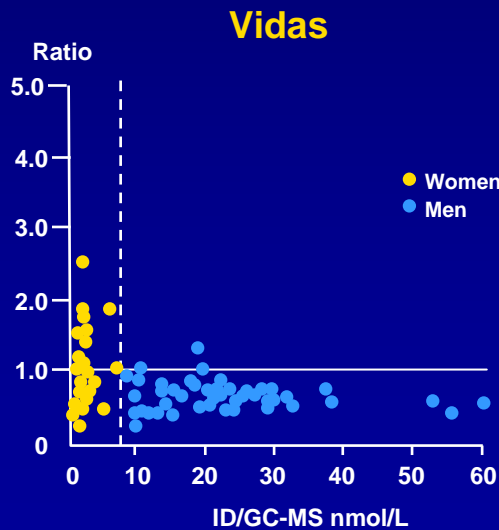
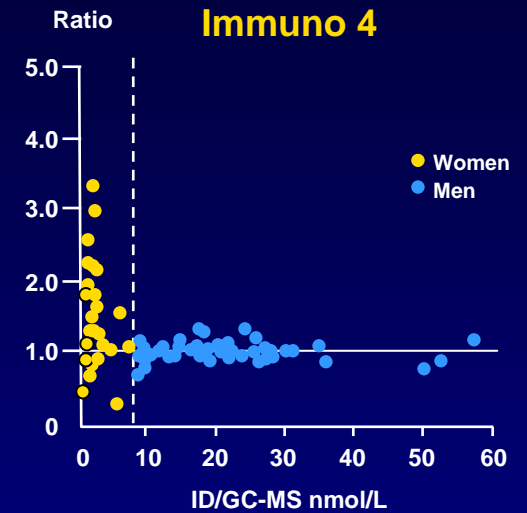
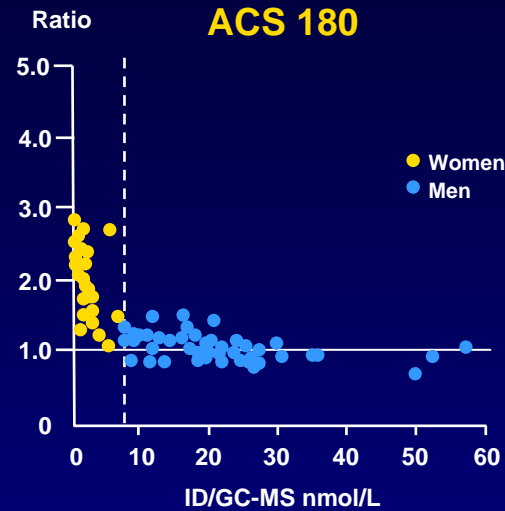
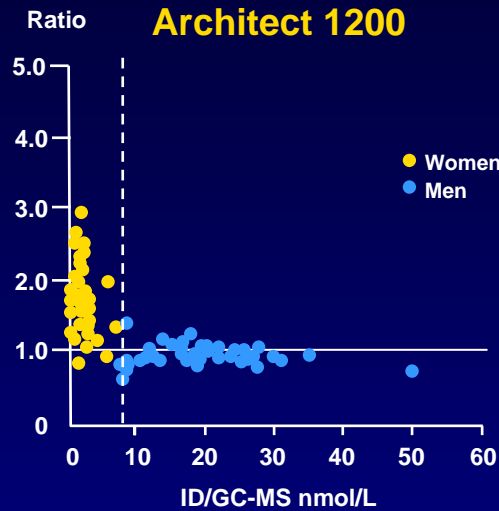
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- **Testosterone levels do not discriminate between women with normal or low libido**

# **HSDD is Found in Conditions Associated With Low Testosterone**

- **Surgical removal of both ovaries**
- **Pituitary disease**
- **Destruction of the adrenal glands**
- **Oral estrogen use after natural  
menopause**

# Comparison of Total T Methods



# What the Skeptics Say

- HSDD is a made-up disease
  - Sex problems are normal
  - Difficulties become Dysfunctions become Diseases
- Testosterone levels do not discriminate between women with normal or low libido
- **Data showing efficacy and safety of testosterone Rx tainted by conflicts-of-interest of investigators**
- **There is a big market for lifestyle drugs**

**Moynihan R, The making of a disease: female sexual dysfunction, BMJ 326:45-7, 2003**

**“A cohort of researchers with close ties to drug companies are working with colleagues in the pharmaceutical industry to develop and define a new category of human illness at meetings heavily sponsored by companies racing to develop new drugs.”**

# Testosterone as a Treatment for HSDD

- **Used well before the pharmaceutical industry was interested** (Greenblatt RB. Androgenic therapy in women. *Endocrinology* 2:665-6. 1942)
- **1<sup>st</sup> randomized, double-blind, placebo controlled trial reported in 1950** (Greenblatt et al. Evaluation of estrogen, androgen, and estrogen-androgen combination and a placebo in the treatment of menopause. *JCEM* 10:1547-58, 1950)
- **Estratest<sup>®</sup> (esterified estrogens+methyltestosterone) on the market since 1964 for treatment of menopausal vasomotor symptoms**

# Testosterone as a Treatment for HSDD

- In 2003, 21% of total prescriptions for branded male testosterone products were written for women (145,000 prescriptions), and in 2002-3 there were 1,315,000 prescriptions written for compounded or generic testosterone products for women (National Disease and Therapeutic Index, IMS Health, 2003)
- Multiple randomized, double-blind placebo-controlled trials with testosterone have shown it to be effective in women with HSDD

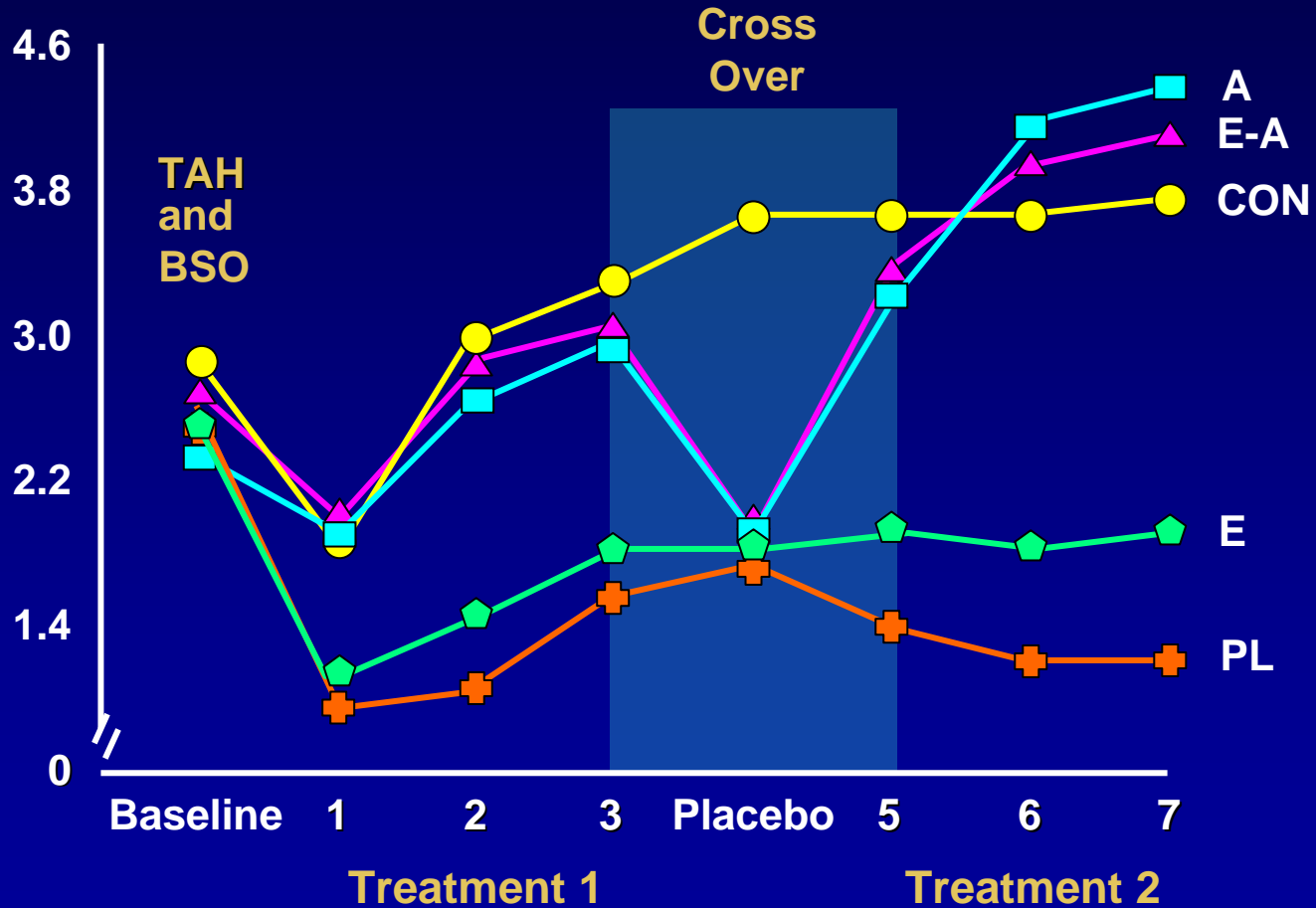
# Androgen and Sexual Motivation

- Randomized, double-blind, placebo-controlled crossover
- N = 43 before and after surgical menopause; sexual function not classified
- Rx: TAH control; TAH + BSO: Placebo, E, E + A, or A
- Duration: 3 mo
- Sexual function tool: daily menopausal rating scale
- Results: ↑ desire, fantasy, arousal
  - No change in coital or orgasmic frequency

TAH = total abdominal hysterectomy, BSO = bilateral salpingo-oophorectomy, E = estrogen, A = androgen

# Sexual Desire

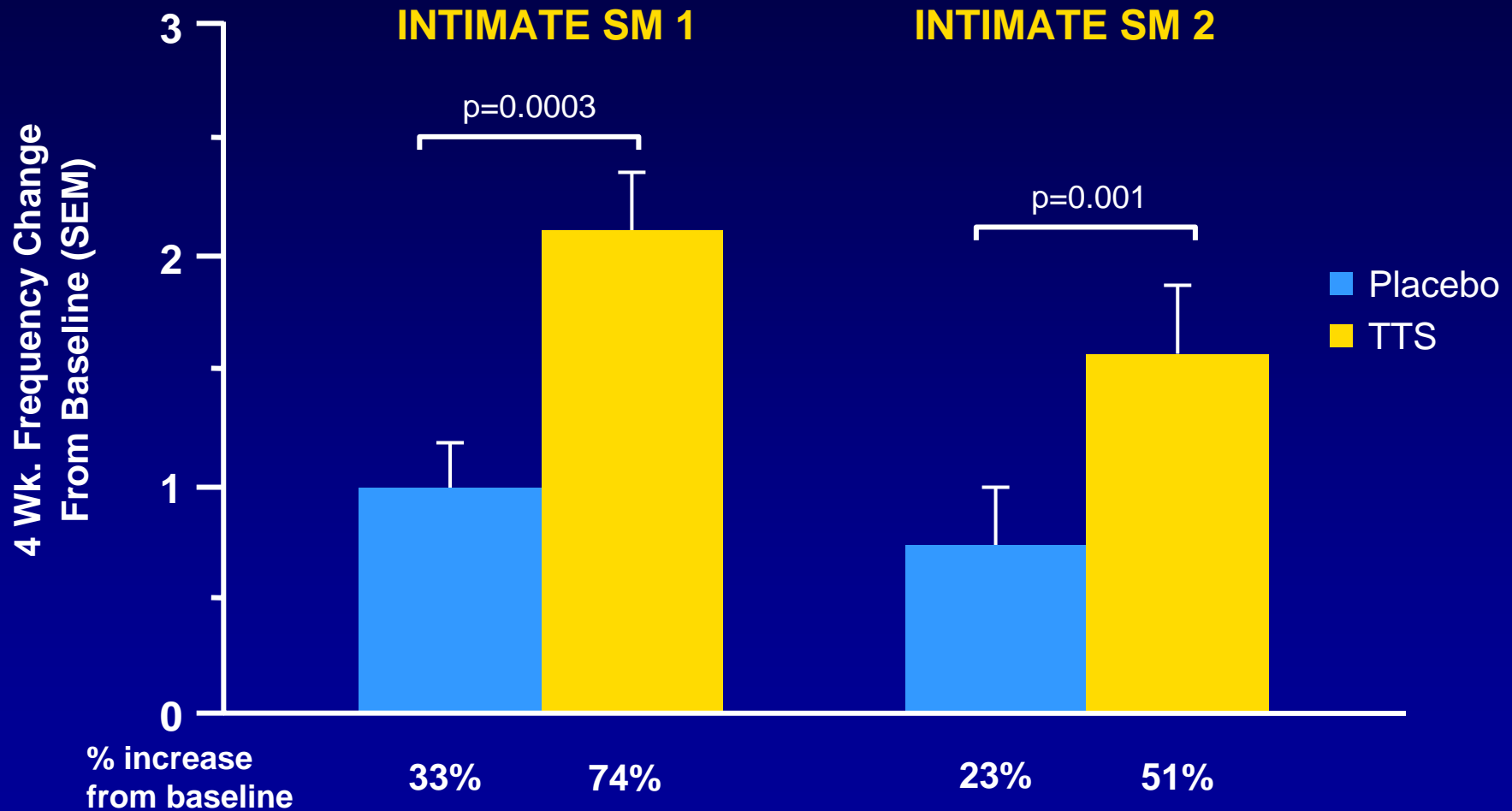
Mean level per 24 hours



# Transdermal Testosterone

- Two Phase III randomized, double-blind, placebo controlled, parallel studies (INTIMATE SM 1 & SM 2)
- SM 1 N=562; SM 2 N=533
- Rx: 300 mcg/day testosterone via patch
- Duration: 6 months
- Sexual Function Tools: Sexual Activity Log; Profile of Female Sexual Function; Personal Distress Scale
- Results: ↑ activity, desire, arousal, orgasm, pleasure, responsiveness; ↓ distress

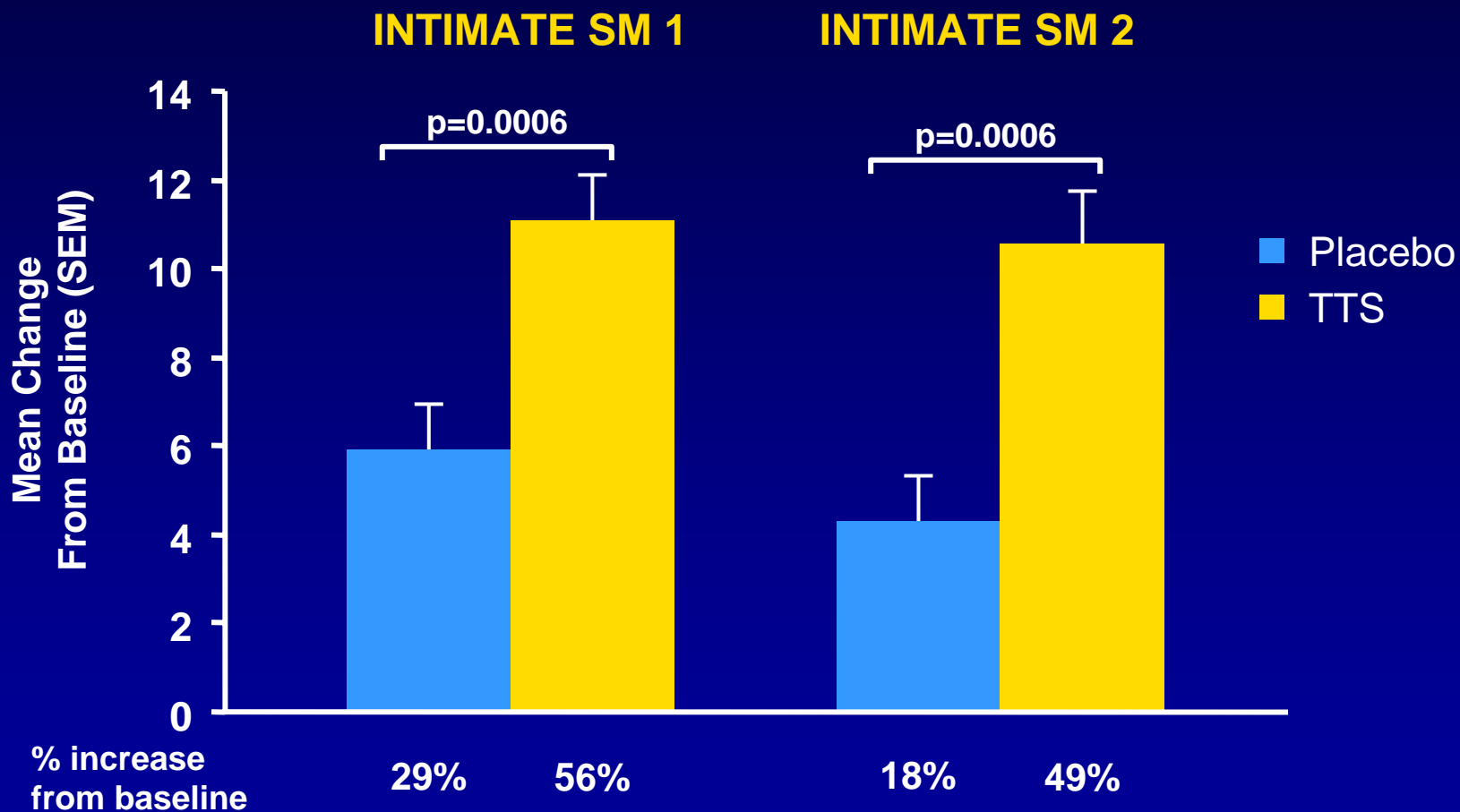
# Increases in Total Satisfying Sexual Activity at 24 Weeks from SAL<sup>®</sup>



Simon, *JCEM* 2005; 90:5226

Buster, *Obstet Gynecol* 2005; 105:944

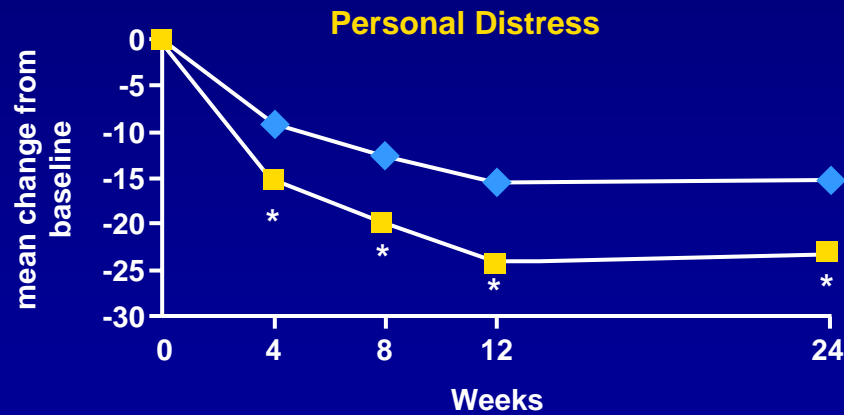
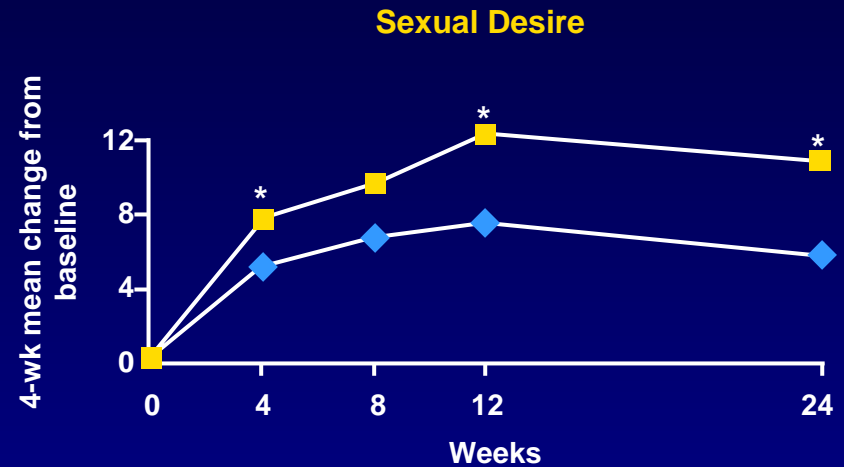
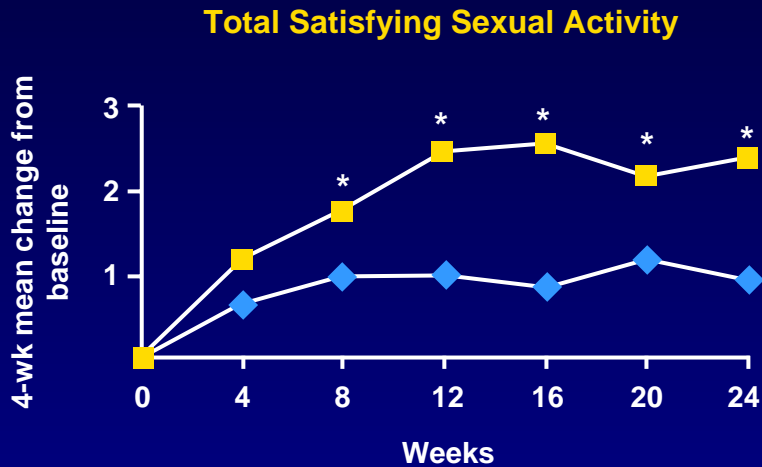
# Increase in Desire at 24 Weeks from PFSF<sup>®</sup>



Simon, *JCEM* 2005; 90:5226

Buster, *Obstet Gynecol* 2005; 105:944

# Change in 4-Week Efficacy Parameters Over 24 Weeks



■ = testosterone ♦ = placebo

# Conclusions

- **Hypoactive Sexual Desire Disorder is a real clinical disorder and occurs with conditions known to be associated with low testosterone levels**
- **Testosterone is an effective treatment of HSDD after other conditions (e.g. depression, marital discord) are ruled out**
- **If approved, the pharmaceutical industry will probably market HSDD and testosterone through the use of key opinion leaders, educational brochures, CME, websites, white papers, and possibly directly to consumers, *but* that does not make the condition or its therapy constructs of the pharmaceutical industry**

Man



ON



OFF

*Keith Long 1988-2001*

Woman

ON

OFF

