


And what about Placebo Treatment?

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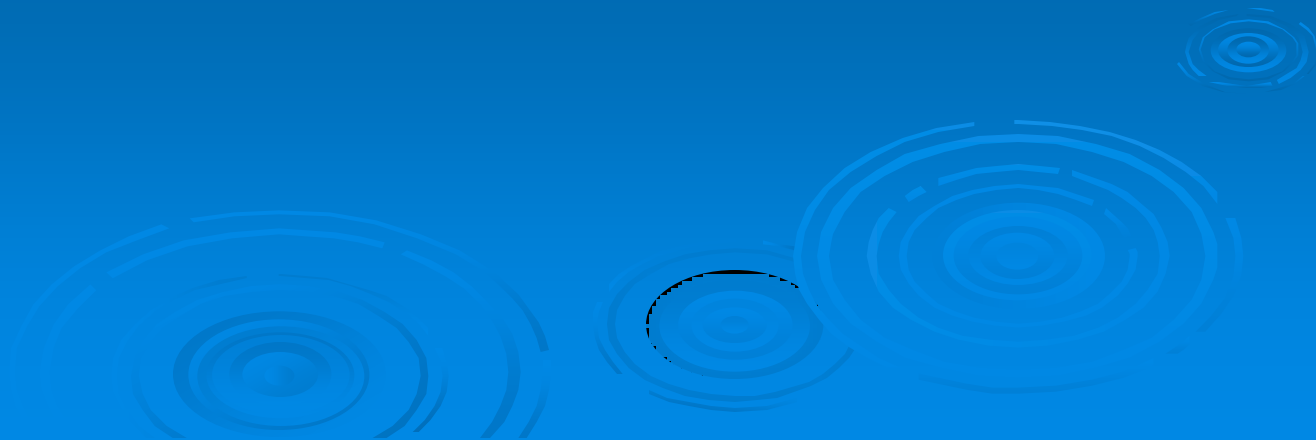
Expectations

- Men and women should have good and exciting sex in all ages...
 - Men should have unlimited erections (and desire).
 - More women should have desire for sex..
 - These should be achieved by pharmacotherapy without significant side effects.
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Aphrodisiacs (by shape)

- Avocado (Mayans and Aztecs)
- Asparagus
- Mango
- Raw eggs
- Ginseng root
- Rhino horn

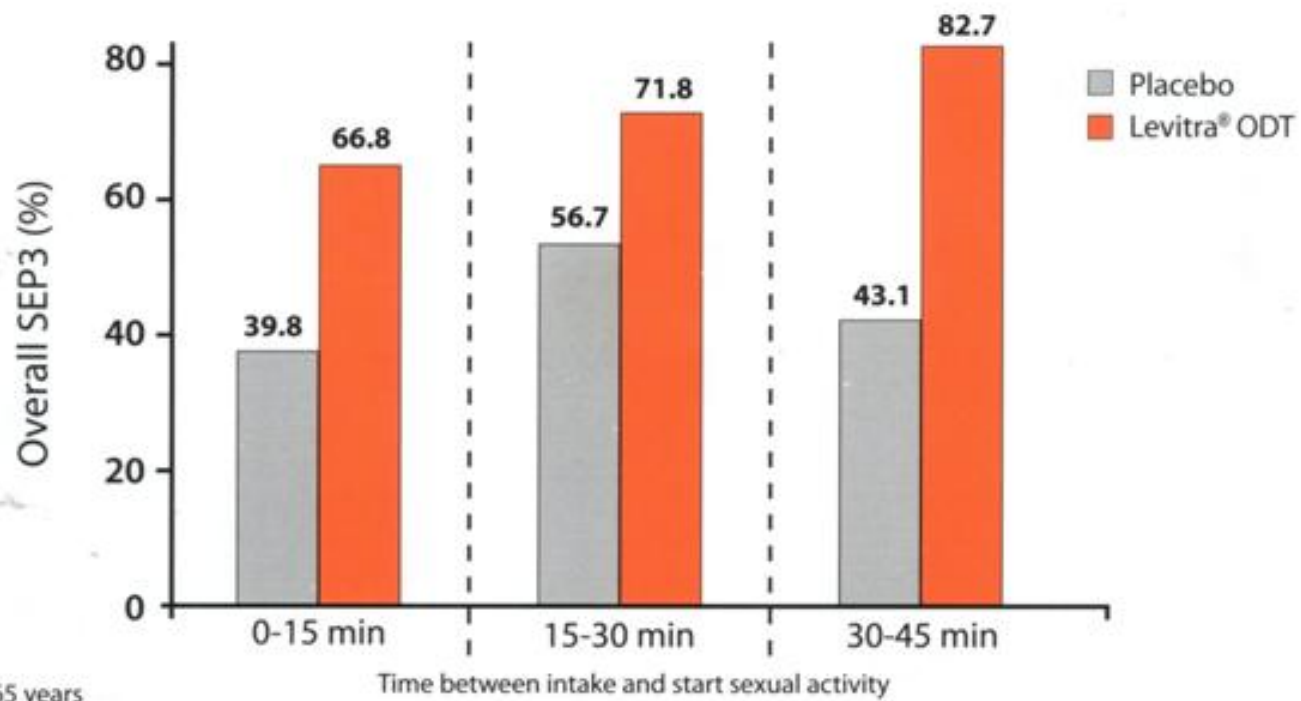
Oysters



Spanish Fly (Lytta Vesicatoria)



LEVITRA® ODT



* Men aged < 65 years

Improvement by placebo in studies of PDE-5 Inhibitors

23 - 47% satisfied erection

54.5% improved erection



Vardenafil improves patient satisfaction with erection...

	10mg	20mg	placebo
Intercourse satisfaction (IIEF)	10.3	10.3	7.7
Orgasmic function	7.1	6.9	5.3
Overall satisfaction	7.1	7.1	5.2

J. Sex. Med. 2004

Placebo and severity of ED (Vs. tadalafil 20 mg)

Mild ED	33%	(72%)
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Moderate ED	19%	(65%)
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Severe ED	9%	(49%)
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Efficacy of vardenafil for the treatment of ED in men with hypertension

A meta-analysis: 8 clinical trials

Vardenafil n=498 placebo n=341

IIEF-EF at week 12: 16.4-26.1 for vardenafil
1.3-17.8 for placebo

Ability to obtain erection (SEP2)

Vardenafil 57.2-92.2% placebo 32-66.9%

Ability to maintain erection (SEP3)

Vardenafil 41.7-88.2% placebo 20.5-51.4%

The management of erectile dysfunction with placebo only: does it work?

123 ED patients randomly assigned to 3 groups:

G1 – was informed to be receiving a substance for ED

G2 – they could be receiving an active drug or placebo

G3 – was conscious to be using placebo

Assessment: after 8 weeks by IIEF-EF and Quality of erection questionnaire

Results: ED severity improved in all 3 groups

G1 = 31.7%, $p=0.039$;

G2 = 36.8%, $p=0.028$;

G3 = 36.8%, $p=0.002$;

Improvement of Quality of Erection Score: G2 and G3

De Araujo et al, J Sex Med, 2009

Premature Ejaculation

1. PSD 502 Vs placebo (baseline 0.6 min.)
3.8 min Vs 1.1 min

Dinsmore and Wyllie BJU Int. April 2009

2. Dapoxetine Vs placebo (n-1238)
perceived control over ejaculation +↓ personal distress
Dapoxetine 60 mg as needed- 47.6% Placebo- 21.7%

Kaufman et al BJU Int. March 2009

3. Dapoxetine Vs placebo (n-618)
Mean average IELT: baseline 0.9 min
Dapoxetine 30 mg= 3.2 min Dapoxetine 60 mg=3.5 min
placebo = 1.9 min

Buvat et al, Eur Urol, Jan 2009

Premature Ejaculation (Cont.)

4. Tadalafil and fluoxetine

Placebo- 49.9 sec to 67.8 sec ($p=0.042$)

Mattis et al., Urol Int. 2008

5. Venlafaxine Vs Placebo

1.7 fold vs. 1.6 fold

6. Tramadol Vs. Placebo

20 sec to 243 Vs. 34 sec

Waldinger et al, 1998

Rosen and Associates

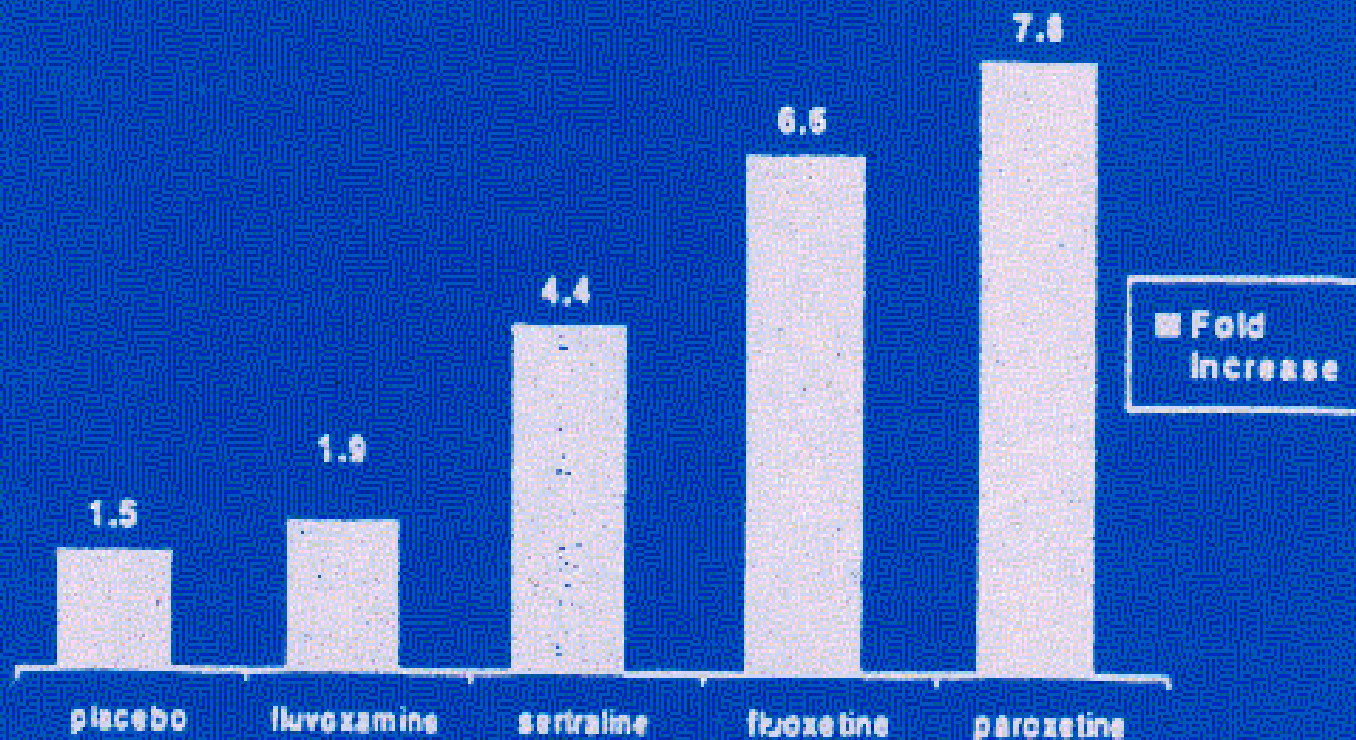


FIG. 1. Fold increase in IELT in a 6-week, placebo-controlled study of SSRIs in 71 men with primary premature ejaculation <1 minute.

Buspirone treatment in Sexual Dysfunction induced by SSRI's

<u>Author</u>	<u>N</u>	<u>Response</u>
Norden (1994)	16	11/16 (69%)
Landen et al (1999)	117	Buspirone - 58% Placebo - 30%
Michelson et al (2000)	57 women	No difference between Buspirone, Amantadine and Placebo (27%)

Placebo treatment in women

196

Bradford and Meston

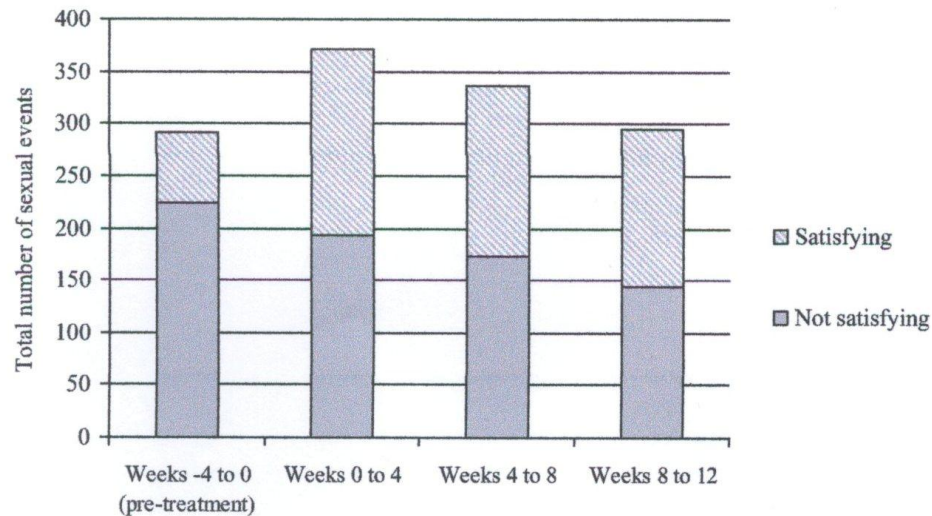


Figure 2 Sexual event frequency (all participants) by time and satisfaction rating.

Characteristics of women with FSD responding to placebo

- Placebo affects all types of FSD excluding pain
- The less satisfied the woman is from sexual relationship prior to treatment, the more she responds to placebo
- Decrease in distress during treatment indicates improvement in sexual functioning
- The factors predicting placebo response were increase in number of satisfying sexual encounters
- The fact that they had to have at least 3 sexual relationships per week, and to document them, increased awareness to their sexual sensations in genitals, leading to increase in sexual thoughts and desire

Bradford & Metson JSM, 2007

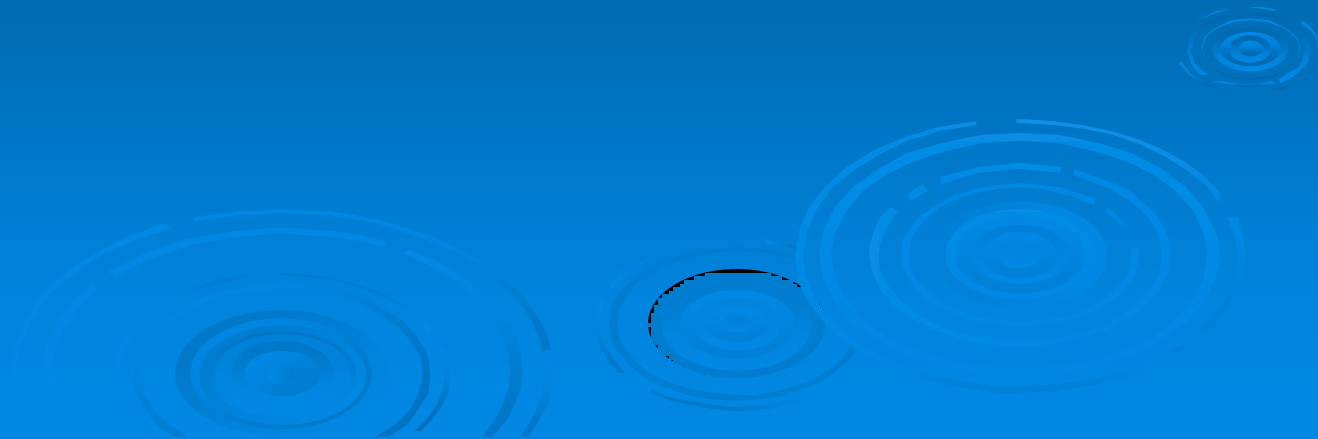
Placebo effect on FSFI score a Cialis- Placebo study in women

- During the month prior to study – 17
- Baseline after 4 weeks – 23.5
- After 8 weeks – 22.5
- End of treatment – 24 ($p < 0.001$)
- At end of treatment 30% of women scored more than 26 – no FSD!

Conclusion of the study

- High placebo effect was observed in women with FSD
- Older, married women with longer duration of relationships – more sensitive to placebo
- Placebo caused improvement in quality of couple relationship during 8 weeks of treatment correlating with improvement in sexual functioning

Why do people respond to placebo?



Response to Placebo - causes

- Expectation of the patient (for reward): Activation of the reward circuitry through the release of dopamine.
- Non specific elements of treatment: Increases attention to the couples' relationship and unrealistic expectations.
- patient's response to therapist's attention
 - In research – more intense visits

Correlates of diminished sexual responsiveness in females

- Relationship duration
- Number of young children
- Marital discord
- Symptoms of anxiety and depression
- Age

Dunn , J Sex Marit Ther 2000; Klusmann et al, Arch Sex Behav;
Basson et al, J Sex Med 2004; Eplov et al, J Sex Med 2006

Relationship duration and desire

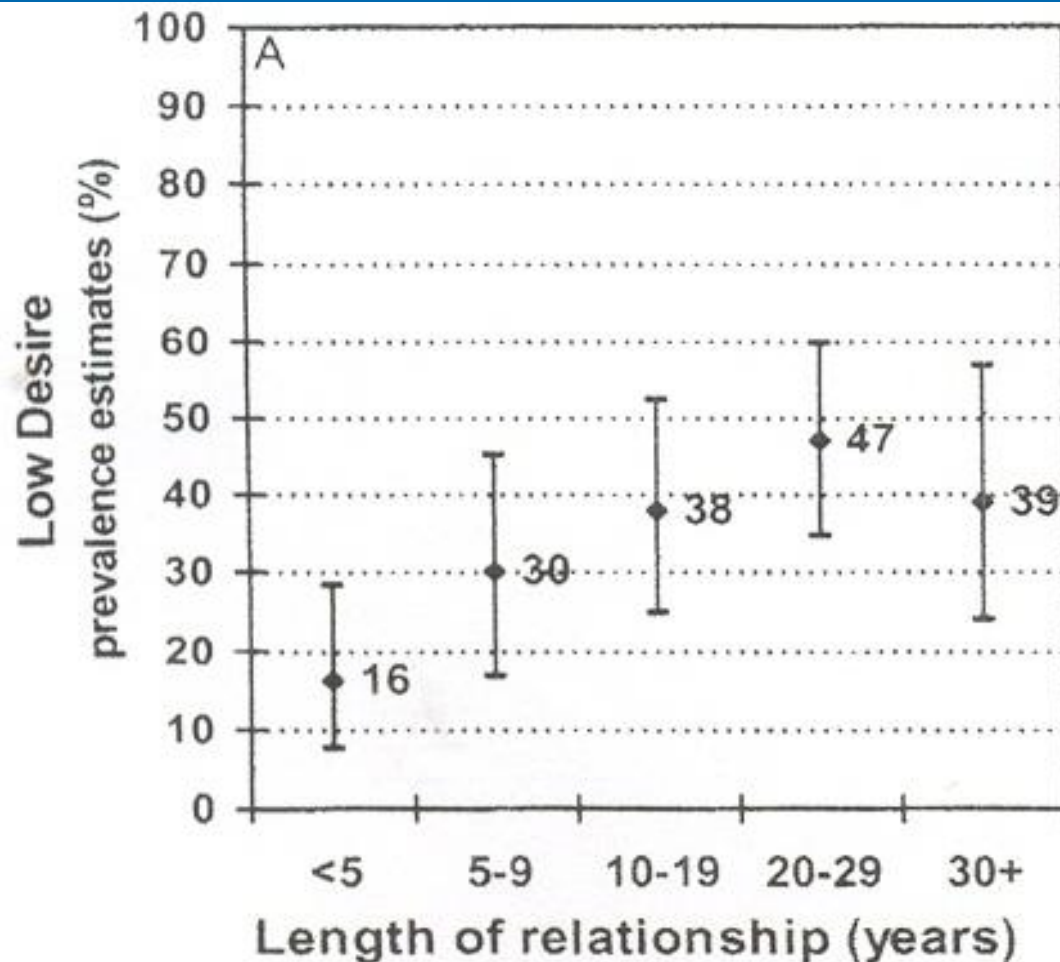
- Percent reporting wanting to have sex often

	< 1 yr	1-3 yr	> 3 yr
Men	76%	74%	76%
Women	65%	44%	26%

Klusman , Arch Sex Behav 2002

Length of relationship and decrease in sexual desire - women

J Sex Med 2008; 1681-1693



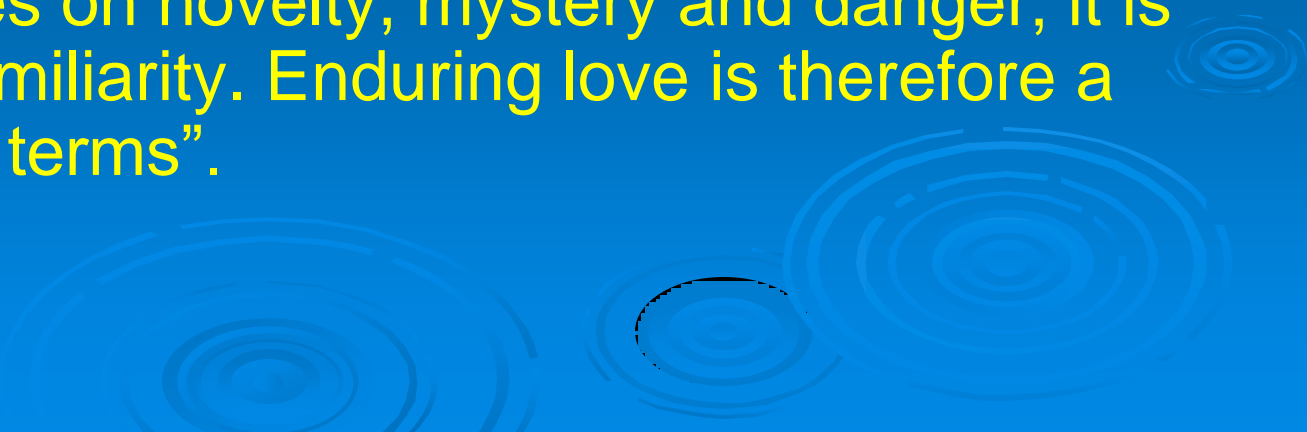
Stephen Mitchell

Can Love Last? The Fate of Romance Over Time (2002)

Inherent difficulties in combining desire and long-term love.

“Authentic romance is hard to find and even harder to maintain. It easily degrades into something else. Much less captivating, much less enlivening, ..., predictable companionship, or hatred, guilt, and self pity...

Romance thrives on novelty, mystery and danger; it is dispersed by familiarity. Enduring love is therefore a contradiction in terms”.



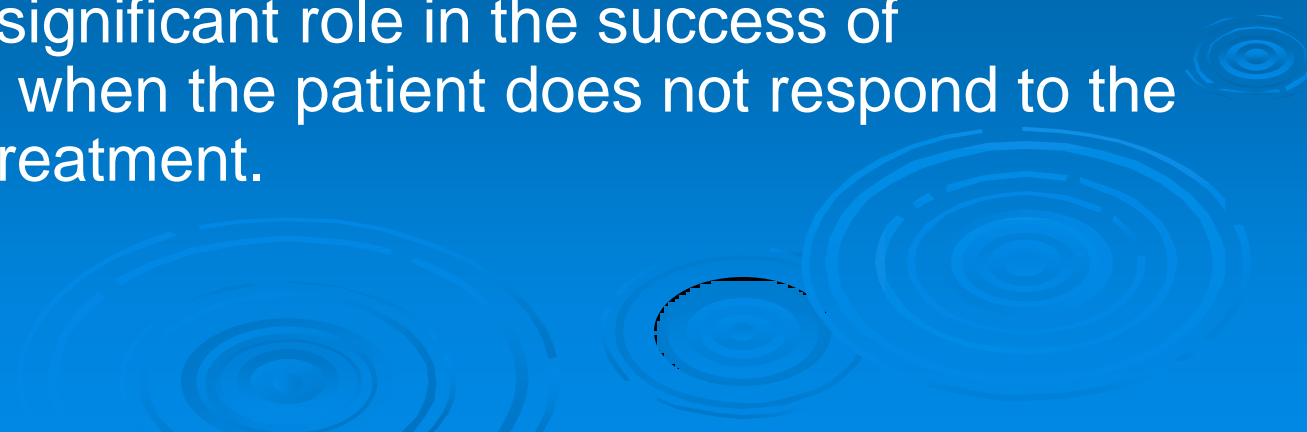
“The opposite of love is not hate,
it's indifference.

The opposite of life is not death,
it's indifference.”

Elie Wiesel



Conclusion

1. Response to placebo in ED is at a rate of 20-25%
 2. Better response in mild ED with shorter duration
 3. Placebo treatment in premature ejaculation prolongs ejaculation by 1.6-1.9 fold
 4. In women, greater placebo response in desire disorders and less in arousal
 5. Married women responded to placebo better than unmarried
 6. Beliefs and expectations of both, therapist and patients may play a significant role in the success of intervention when the patient does not respond to the first line of treatment.
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Thank You

