

**RANDOMIZED, PLACEBO-
CONTROLLED, DOUBLE-BLIND,
CROSSOVER DESIGN PILOT
TRIAL OF THE EFFICACY AND
SAFETY OF**

ZESTRA FOR WOMEN™

**IN WOMEN WITH, AND WITHOUT,
FEMALE SEXUAL AROUSAL
DISORDER**

AUTHORS

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Zestra for Women™

- Feminine massage oil developed under the Cosmetics Act
- Enhance sexual pleasure
- Facilitate female sexual arousal
- Ingredients: FDA food additives list , FDA GRAS list, all natural (botanicals)

Zestra for Women™

- Proprietary blend of:
 - Borage seed oil
 - Evening primrose oil
 - Angelica root extract
 - Coleus forskohlii extract
 - Ascorbyl palmitate
 - dl-alpha tocopherol
 - Natural fragrances
- (Patent Pending)

Placebo for Zestra for Women™

- Soybean oil + coloring + fragrance; matches:
 - Odor
 - Color
 - Lubricity
 - Viscosity
 - Absorbency

Methods: study design

- 10 Women with FSAD; 10 women with no FSDs
- Visit 1: Screening, Begin period 1,
 - 5 applicators at home
- Visit 2: Assessment, Begin period 2,
 - 5 applicators at home
- Visit 3: Assessment, Exit

Female Sexual Arousal Disorder

- Persistent or recurrent inability to attain or maintain sufficient sexual excitement, causing personal distress. It may be expressed as a lack of subjective excitement or a lack of genital (lubrication/swelling) or other somatic responses.

Methods: inclusion criteria

- Written, informed consent
- 21 to 65 years
- Without risk of conception
- Stable heterosexual relationship for 1 year
- FSAD: Consensus Panel FSAD for 6 months; previously functional; Normals: No FSDs
- FSAD: $40 \leq \text{FSDS} \leq 60$
- Normals: $\text{FSDS} \leq 40$

Methods: exclusion criteria

- Unresolved sexual trauma or abuse
- Primary anorgasmia, vaginismus, sexual pain disorder, or sexual aversion disorder
- Pregnant or nursing
- Active STD
- Dyspareunia not attributable to vaginal dryness
- Neuroleptics, lithium, bupropion, coumadin

Methods: assessments

Visit 1	Visit 2	Visit 3
FSFI© FSDS©	FSFI© FSDS© FSEP© GAQ© QCTS©	FSFI© FSDS© FSEP© GAQ© QCTS©

Methods: safety endpoints

- Occurrence of any Adverse Events

Methods: efficacy endpoints

- # Satisfactory arousals/adequate attempts (FSEP Q3/Q7)
- Remaining FSEP questions
- FSFI
- FSDS(20)
- GAQ
- QCTS

Female Sexual Encounter Profile (FSEP)©

1. Please circle all activities that apply:
 - A. Genital stimulation by partner
 - B. Masturbation
 - C. Intercourse

Female Sexual Encounter Profile (FSEP)©

2. How would you rate your level of sexual desire during this sexual activity?
 - A. No desire
 - B. Slight desire
 - C. Moderate desire
 - D. High desire

Female Sexual Encounter Profile (FSEP)©

3. Were you satisfied with your arousal
(excitement) during this sexual activity?

Yes

No

Female Sexual Encounter Profile (FSEP)©

4. Did you achieve enough lubrication (wetness) to allow comfortable intercourse (even if you didn't actually have intercourse)?

Yes

No

Female Sexual Encounter Profile (FSEP)©

5. Did you achieve orgasm?

Yes

No

Female Sexual Encounter Profile (FSEP)©

6. How would you rate your level of sexual arousal (excitement) during this sexual activity?
- A. Not at all aroused
 - B. Slightly aroused
 - C. Moderately aroused
 - D. Highly aroused

Female Sexual Encounter Profile (FSEP)©

7. Were conditions appropriate for a satisfactory sexual encounter? (Adequate time, no distractions, etc.)

Yes

No

Results: demographics

Descriptor	Normals	FSAD
Age	43.2 \pm 5.7	44.4 \pm 8.7
Height	166.4 \pm 6.6	163.8 \pm 4.1
Weight	76.3 \pm 17.8	78.7 \pm 18.6
Menarche	12.7 \pm 2.1	13.1 \pm 1.1
1 st Intercourse	18.3 \pm 2.0	17.8 \pm 2.7
Postmenopausal	4/10	3/10
HRT	3/10	3/10
Hormonal Contraception	1/10	4/10
SSRIs	3/10	4/10

Results: demographics

Descriptor	Normals	FSAD
FSDS (20)	11.2 \pm 7.9	45.2 \pm 5.0*
FSFI Total	30.7 \pm 3.0	20.9 \pm 4.3*
FSFI Desire	4.1 \pm 0.9	2.3 \pm 1.4*
FSFI Arousal	5.0 \pm 0.8	2.5 \pm 0.9*
FSFI Lubrication	5.6 \pm 0.8	4.3 \pm 1.7*
FSFI Orgasm	4.9 \pm 1.5	2.6 \pm 1.3*
FSFI Satisfaction	5.2 \pm 1.2	3.4 \pm 0.5*
FSFI Pain	6.0 \pm 0.0	5.8 \pm 0.5

* P < .05

Results: Safety: Adverse Events

- During placebo

- Normals

- Fatigue (moderate)

- FSAD

- Vag irritation (mild)
 - Sinus infection (mod)

- During Zestra

- Normals

- Genital burning (mild)
 - Genital burning (mild)

- FSAD

- Genital burning (mild)

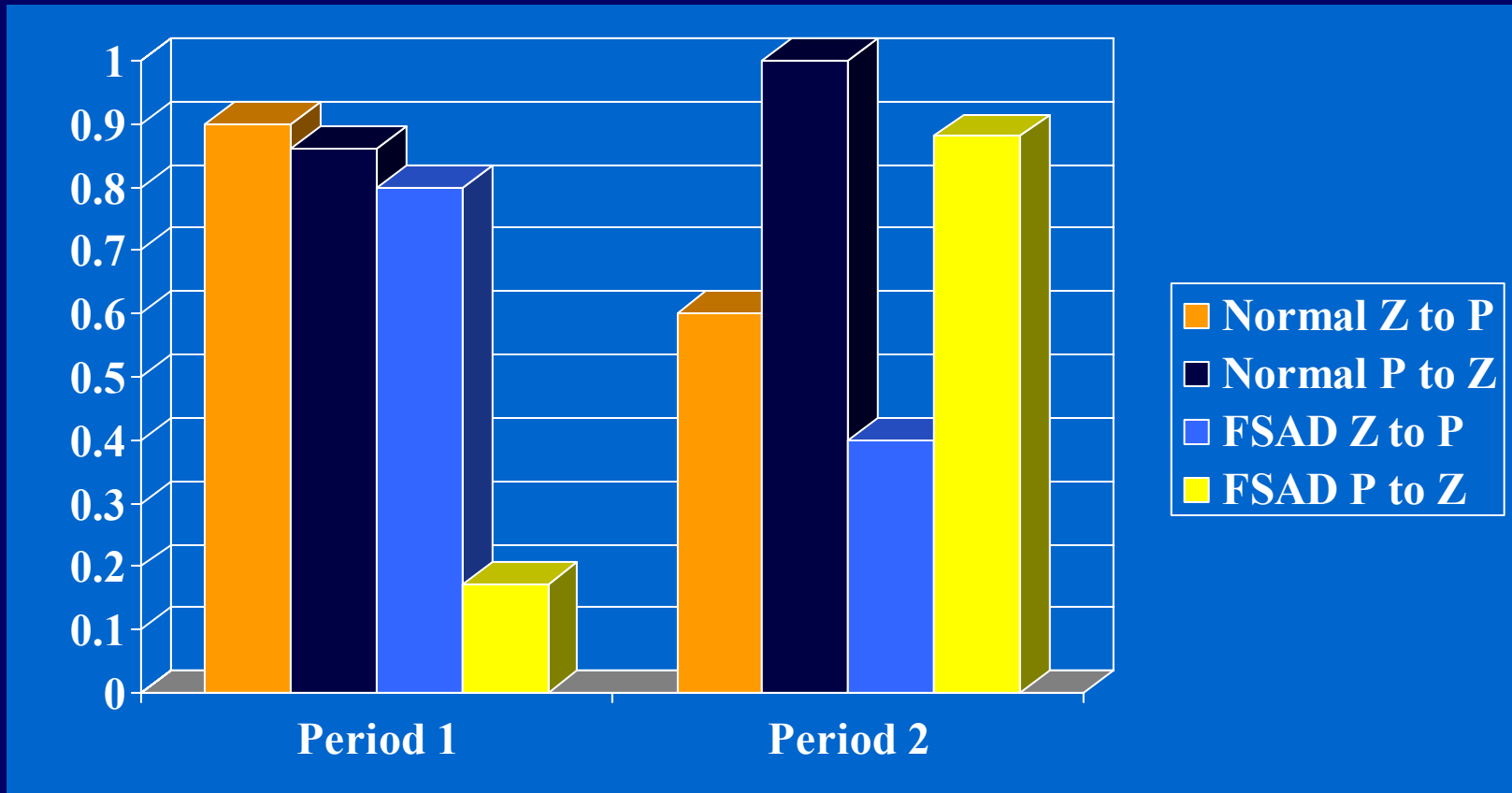
Results: Efficacy

Primary Efficacy: FSEP Q3/Q7

Patients	Sequence	Treatment Period 1	Treatment Period 2
Normals	Zestra - Placebo	0.90 \pm 0.22	0.60 \pm 0.37
	Placebo - Zestra	0.86 \pm 0.41	1.00 \pm 0.0*
FSAD	Zestra - Placebo	0.80 \pm 0.50*	0.40 \pm 0.35
	Placebo - Zestra	0.17 \pm 0.29	0.88 \pm 0.18*

P < 0.05 between groups within treatment period

Results: Efficacy: FSEP Q3/Q7



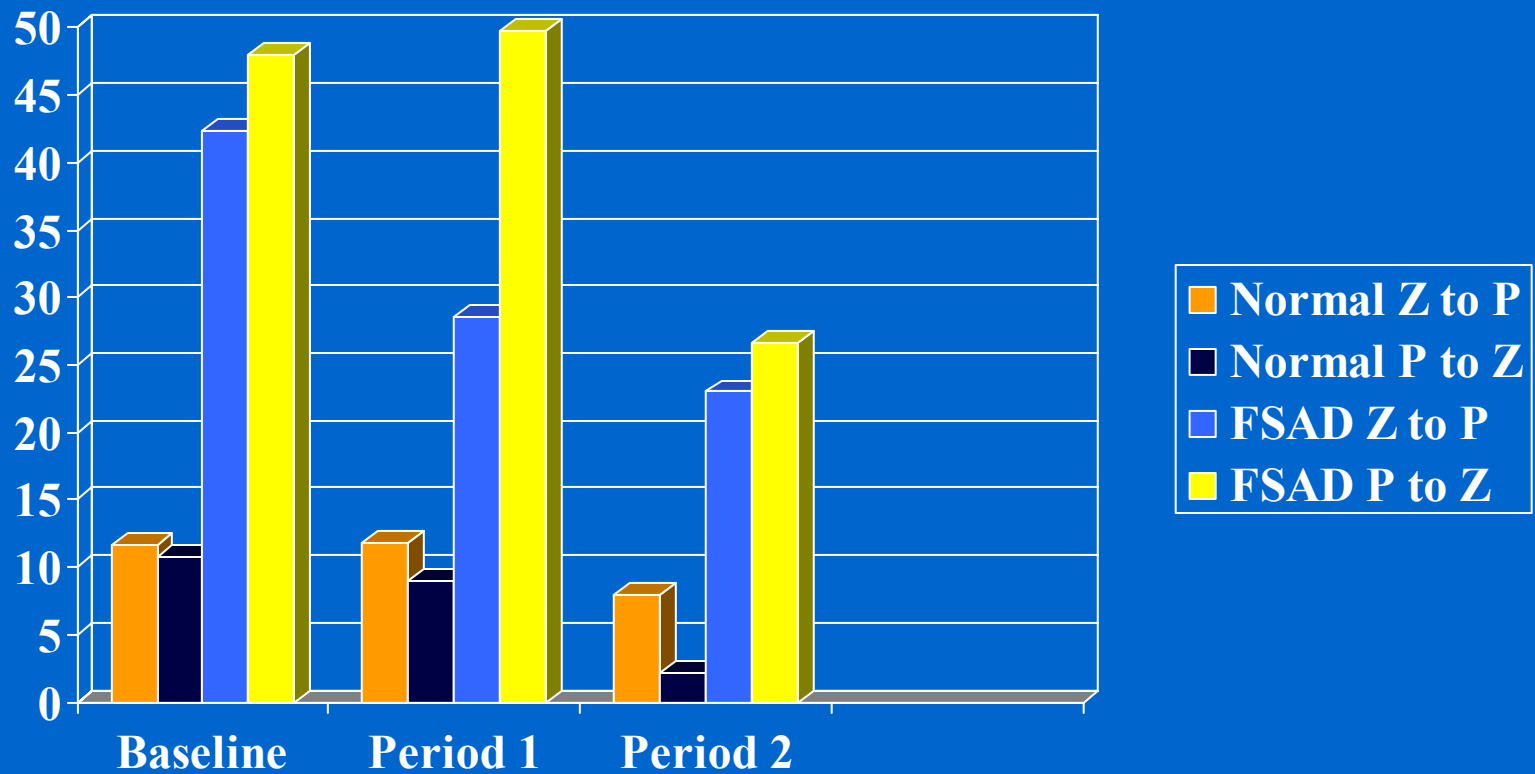
Results: Efficacy: FSDS

Secondary Efficacy: FSDS

Patients	Sequence	Baseline	Treatment Period 1	Treatment Period 2
Normals	Zestra – Placebo	11.6 ± 7.9	11.8 ± 10.6	8.0 ± 8.0
	Placebo - Zestra	10.8 ± 8.9	9.0 ± 10.6	2.2 ± 2.0
FSAD	Zestra – Placebo	42.4 ± 1.1	28.6 ± 14.8*	23.0 ± 13.8
	Placebo - Zestra	48.0 ± 6.0	49.8 ± 4.0	26.6 ± 16.2

P < 0.05 between groups within treatment period

Results: Efficacy: FSDS



Results: Efficacy, Paired Analyses

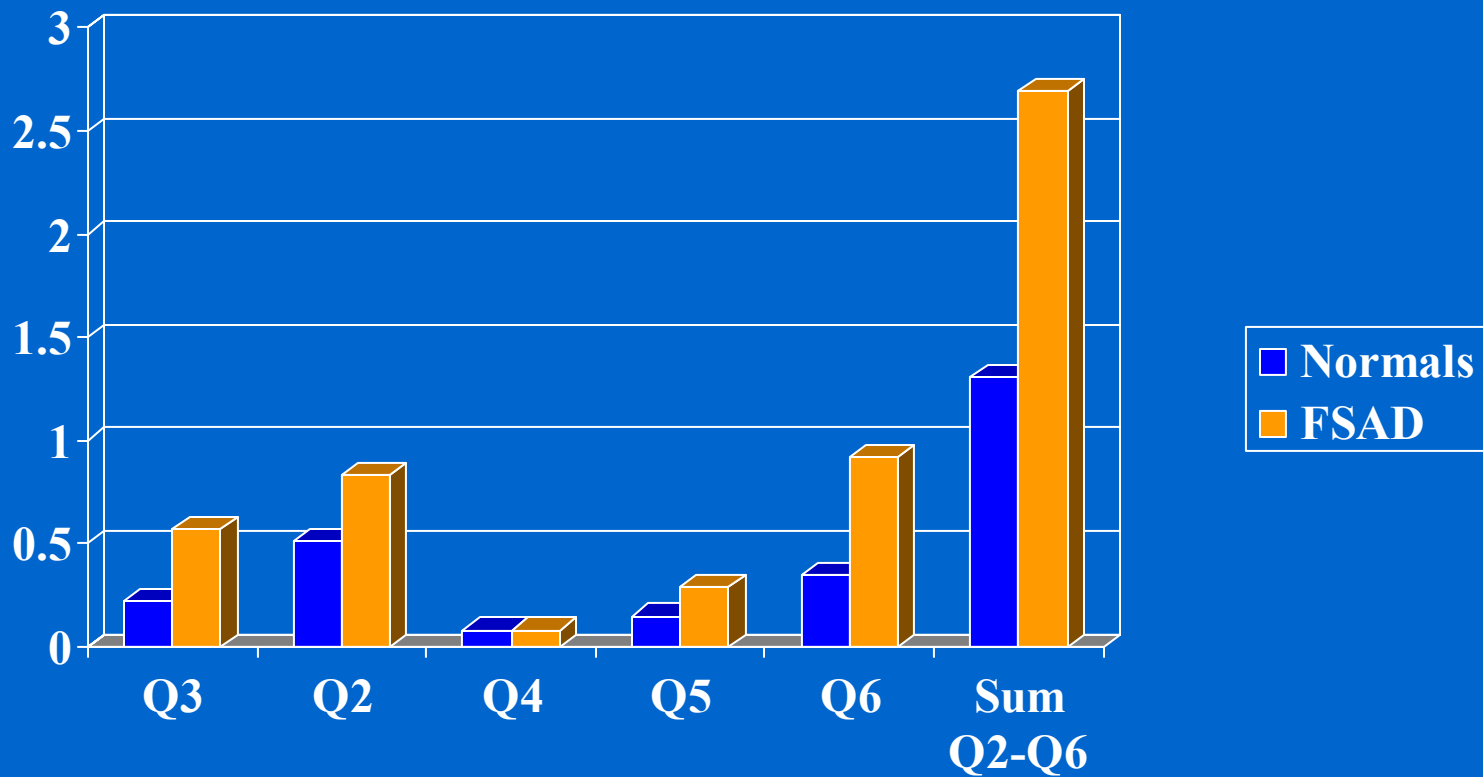
Mean Change (Zestra – Placebo)		
Endpoint	Normals	FSAD
FSEP Q3/Q7	0.22 ± 0.28*	0.57 ± 0.36***
FSEP Q2/Q7	0.51 ± 0.30***	0.83 ± 0.40***
FSEP Q4/Q7	0.08 ± 0.25	0.08 ± 0.17
FSEP Q5/Q7	0.15 ± 0.21	0.29 ± 0.30*
FSEP Q6/Q7	0.35 ± 0.31**	0.92 ± 0.60***
FSEP TOTAL	1.31 ± 1.01**	2.69 ± 1.33***

*P < .05

**P < .01

***P < .001

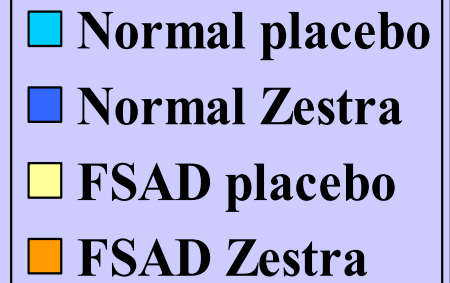
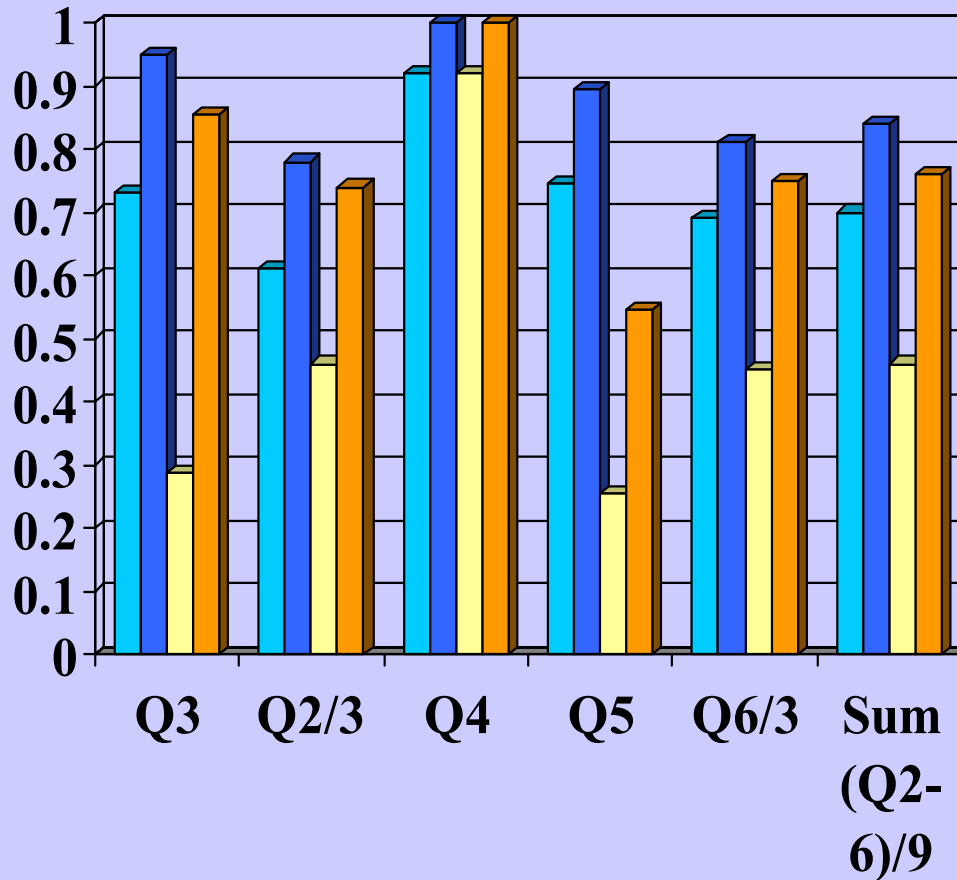
Results: Efficacy: Mean Changes in FSEP Scores



Results: Efficacy: Mean FSEP Scores

	Q2	Q3	Q4	Q5	Q6	Σ Q2-6
Normal: Placebo	1.8 \pm .5	.7 \pm .3	.9 \pm .3	.7 \pm .3	2.1 \pm .5	6.3 \pm 1.4
Normal: Zestra	2.3 \pm .5***	1.0 \pm .2*	1.0 \pm .0	.9 \pm .2	2.4 \pm .5**	7.6 \pm 1.2**
FSAD: Placebo	1.4 \pm .6	.3 \pm .3	.9 \pm .2	.3 \pm .3	1.3 \pm .6	4.2 \pm 1.6
FSAD: Zestra	2.2 \pm .6***	.9 \pm .3***	1.0 \pm .0	.5 \pm .4*	2.3 \pm .7***	6.9 \pm .7***
*P<.05 **P<.01 ***P<.001						

Results: Efficacy: Normalized Mean FSEP Scores

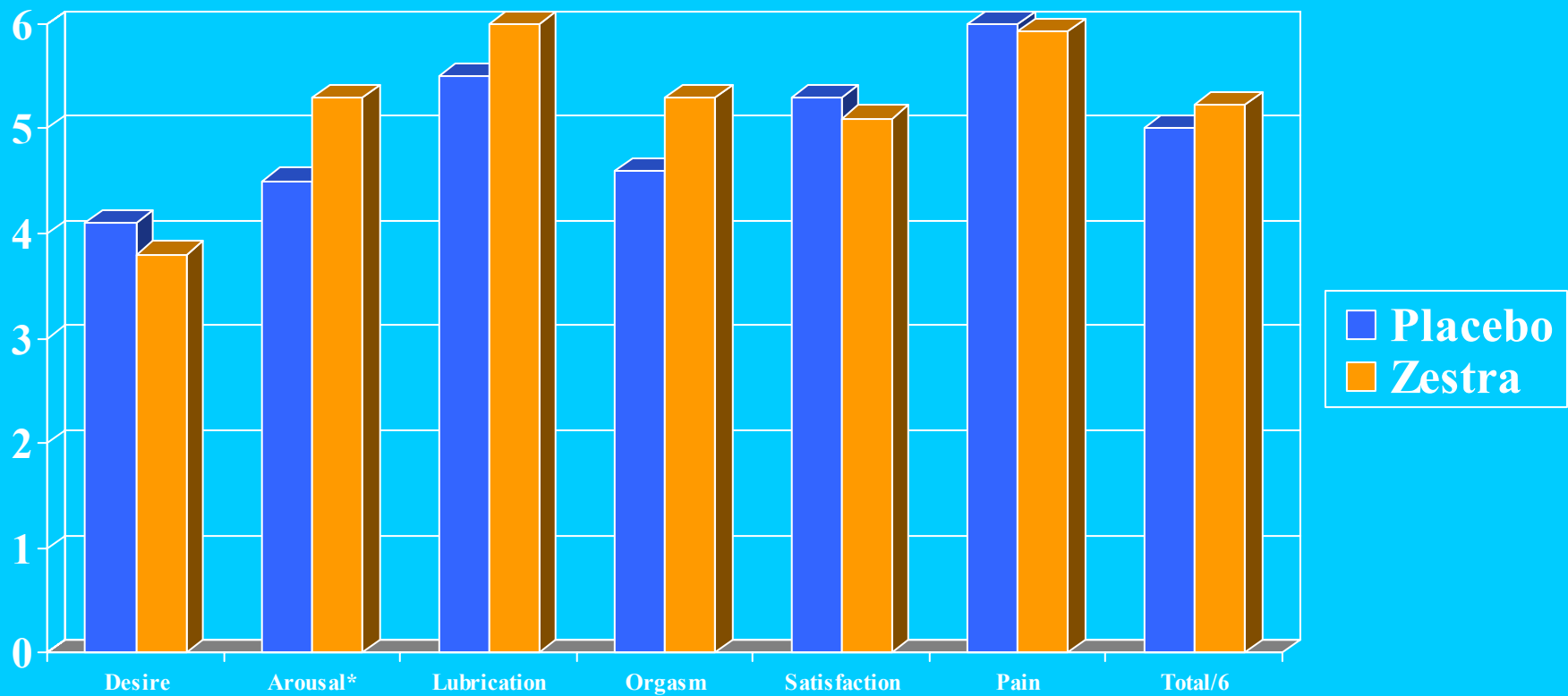


Results: Efficacy: Normals

Endpoint	Placebo	Zestra
FSFI DESIRE	4.1 \pm 0.8	3.8 \pm 0.9
FSFI AROUSAL	4.5 \pm 0.9	5.3 \pm 0.9*
FSFI LUBRICATION	5.5 \pm 1.0	6.0 \pm 0.0
FSFI ORGASM	4.6 \pm 1.5	5.3 \pm 1.0
FSFI SATISFACTION	5.2 \pm 0.9	5.1 \pm 1.4
FSFI PAIN	6.0 \pm 0.0	5.9 \pm 0.3
FSFI TOTAL	30.0 \pm 3.8	31.4 \pm 3.0
FSDS	8.5 \pm 8.9	7.0 \pm 8.8

*** P < .05**

Results: Efficacy: FSFI; Normals



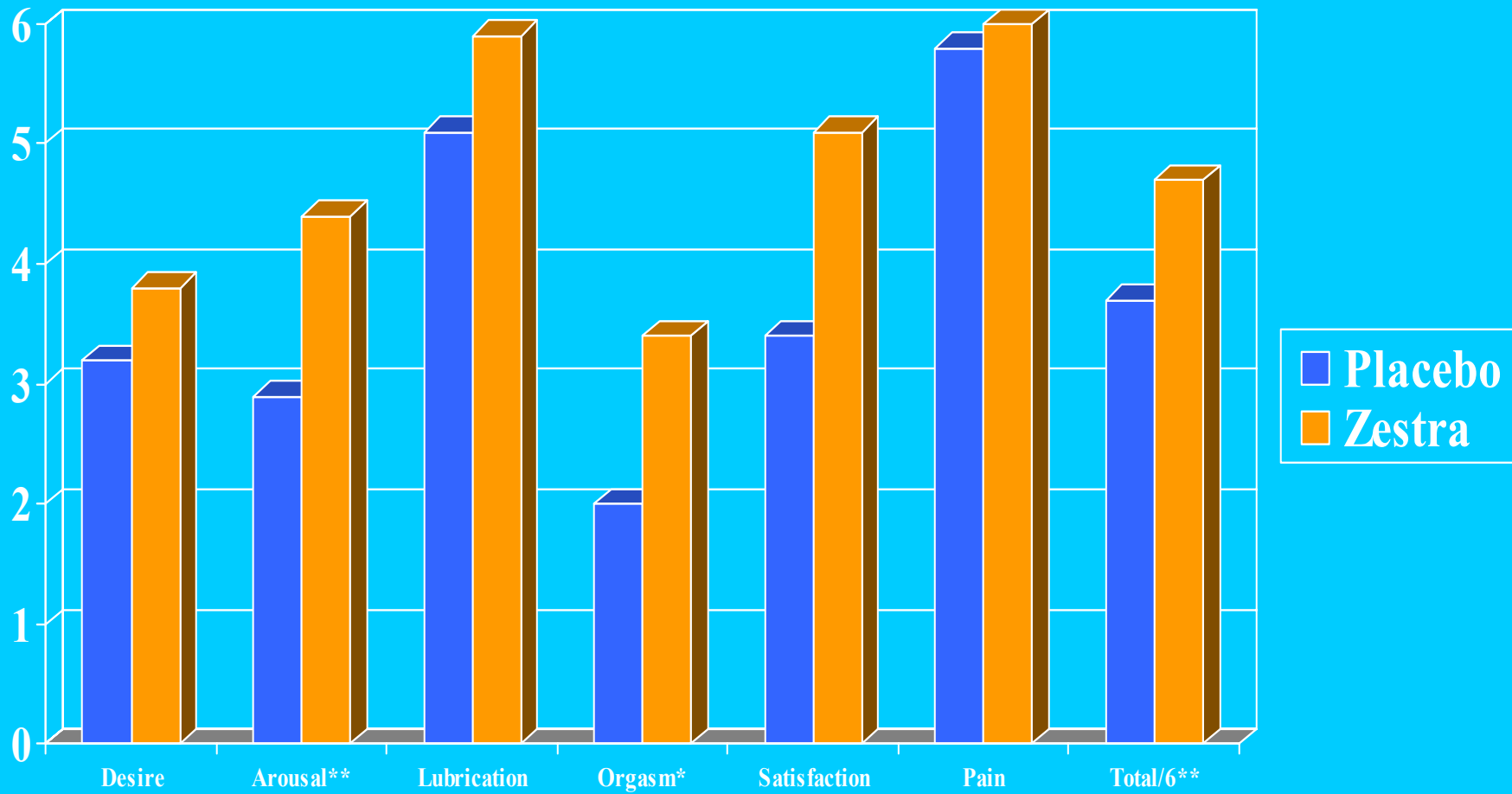
Results: Efficacy: FSAD

Endpoint	Placebo	Zestra
FSFI DESIRE	3.2 \pm 1.3	3.8 \pm 0.7
FSFI AROUSAL	2.9 \pm 1.0	4.4 \pm 1.0**
FSFI LUBRICATION	5.1 \pm 1.5	5.9 \pm 0.3
FSFI ORGASM	2.0 \pm 1.1	3.4 \pm 1.9*
FSFI SATISFACTION	3.4 \pm 1.2	5.1 \pm 1.4
FSFI PAIN	5.8 \pm 0.5	6.0 \pm 0.1
FSFI TOTAL	22.3 \pm 4.5	28.0 \pm 4.0**
FSDS	36.4 \pm 17.1	27.6 \pm 14.7

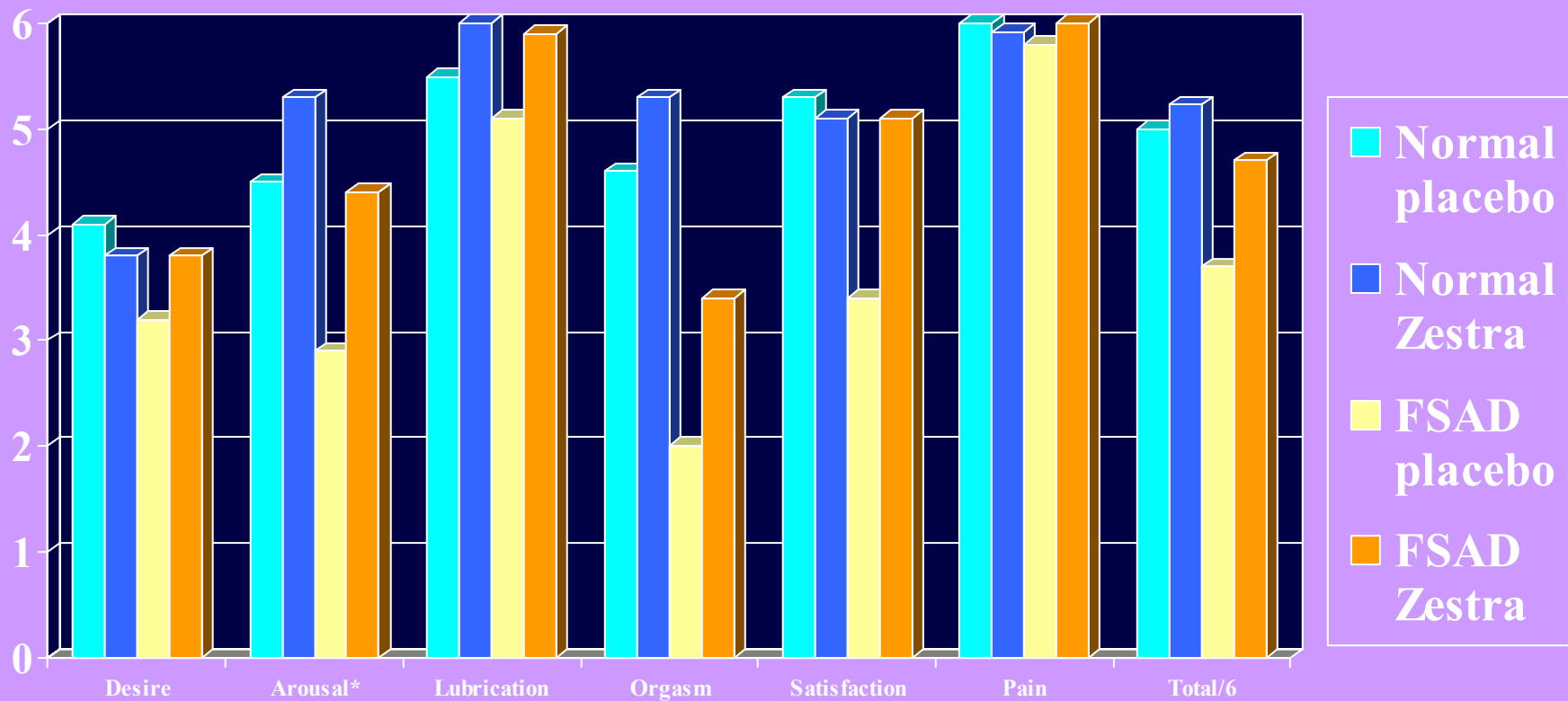
* P < .05

** P < .01

Results: Efficacy: FSFI; FSAD



Results: Efficacy: FSFI



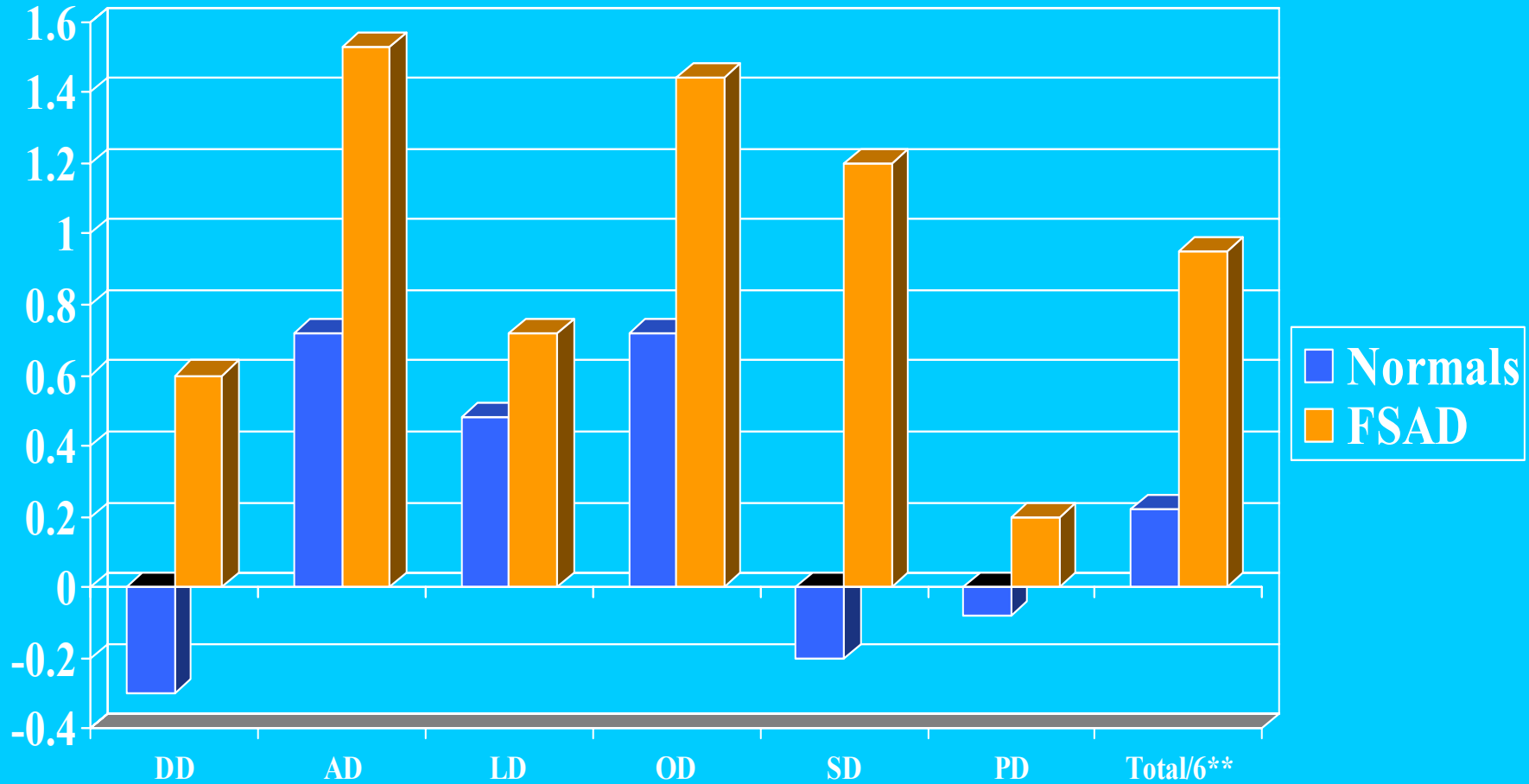
Results: Efficacy: Mean Changes in FSFI

Endpoint	Normals	FSAD
FSFI DESIRE	$-.30 \pm 1.0$	$.6 \pm 1.4$
FSFI AROUSAL	$.72 \pm .8^*$	$1.5 \pm 1.5^{**}$
FSFI LUBRICATION	$.48 \pm 1.0$	$.7 \pm 1.5$
FSFI ORGASM	$.72 \pm 1.1$	$1.4 \pm 1.4^*$
FSFI SATISFACTION	$-.20 \pm 1.3$	1.2 ± 1.3
FSFI PAIN	$-.08 \pm 0.3$	$.2 \pm 0.4$
FSFI TOTAL	1.34 ± 3.4	$5.69 \pm 5.1^{**}$
FSDS	-1.5 ± 10.0	-8.8 ± 19.3

*** P < .05**

**** P < .01**

Results: Efficacy: Mean Changes in FSFI



Results: Efficacy: Global Assessment

Question 1

- GAQ 1: While using the study medication, did you feel that your level of sexual arousal (excitement) improved?
 - 0 Not at all
 - 1 A little, but barely noticeable
 - 2 Somewhat
 - 3 Quite
 - 4 Greatly

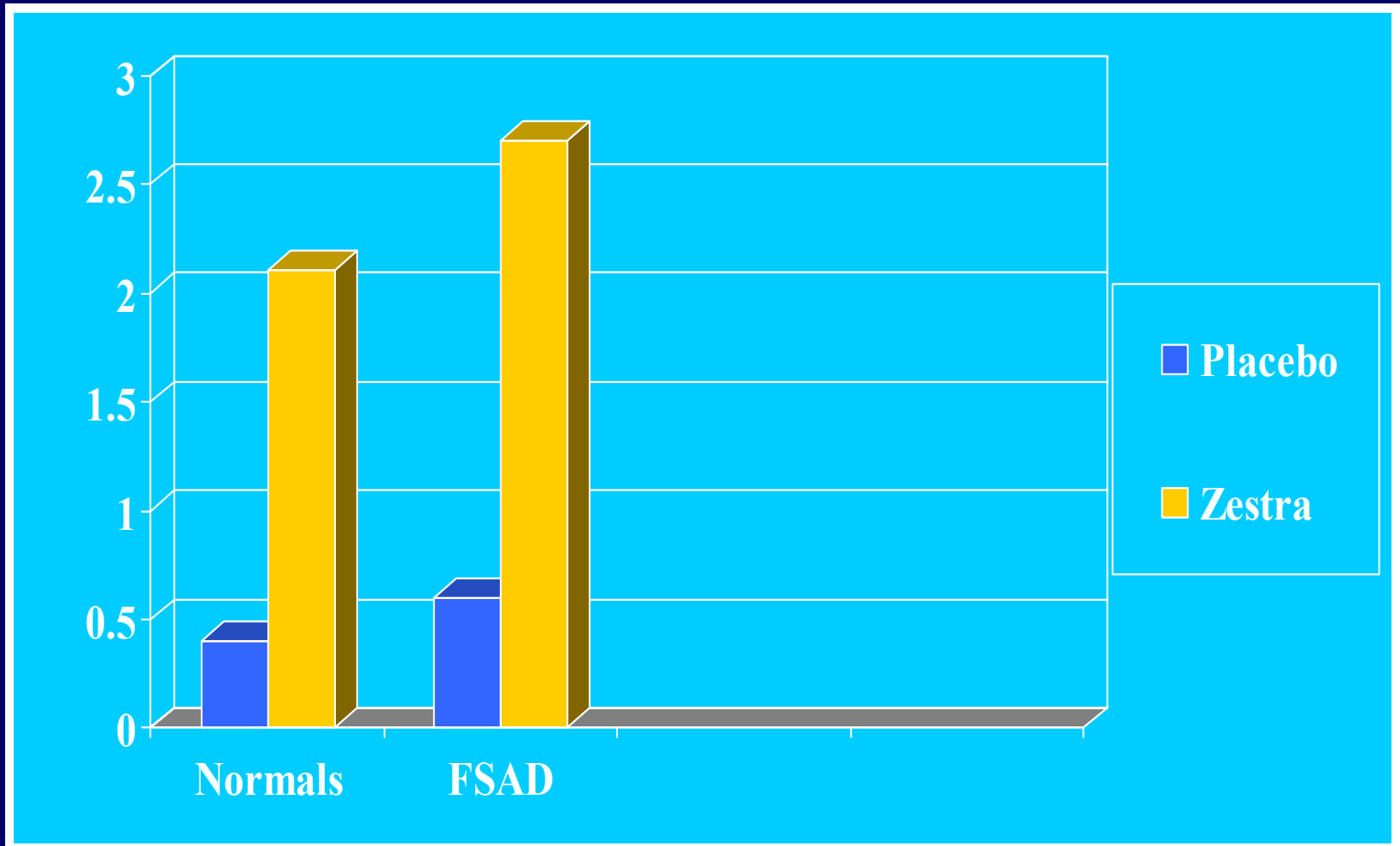
Results: Efficacy: Global Assessment

Question 1

Patients	Placebo	Zestra
Normals	0.4 ± 0.5	$2.1 \pm 1.4^{**}$
FSAD	0.6 ± 0.8	$2.7 \pm 1.3^{**}$

****P<0.01**

Results: Efficacy: Global Assessment Question 1



Results: Efficacy: Global Assessment

Question 1

- GAQ 2: While using the study medication, did you feel that your sexual pleasure was enhanced?
 - 0 Not at all
 - 1 A little, but barely noticeable
 - 2 Somewhat
 - 3 Quite
 - 4 Greatly

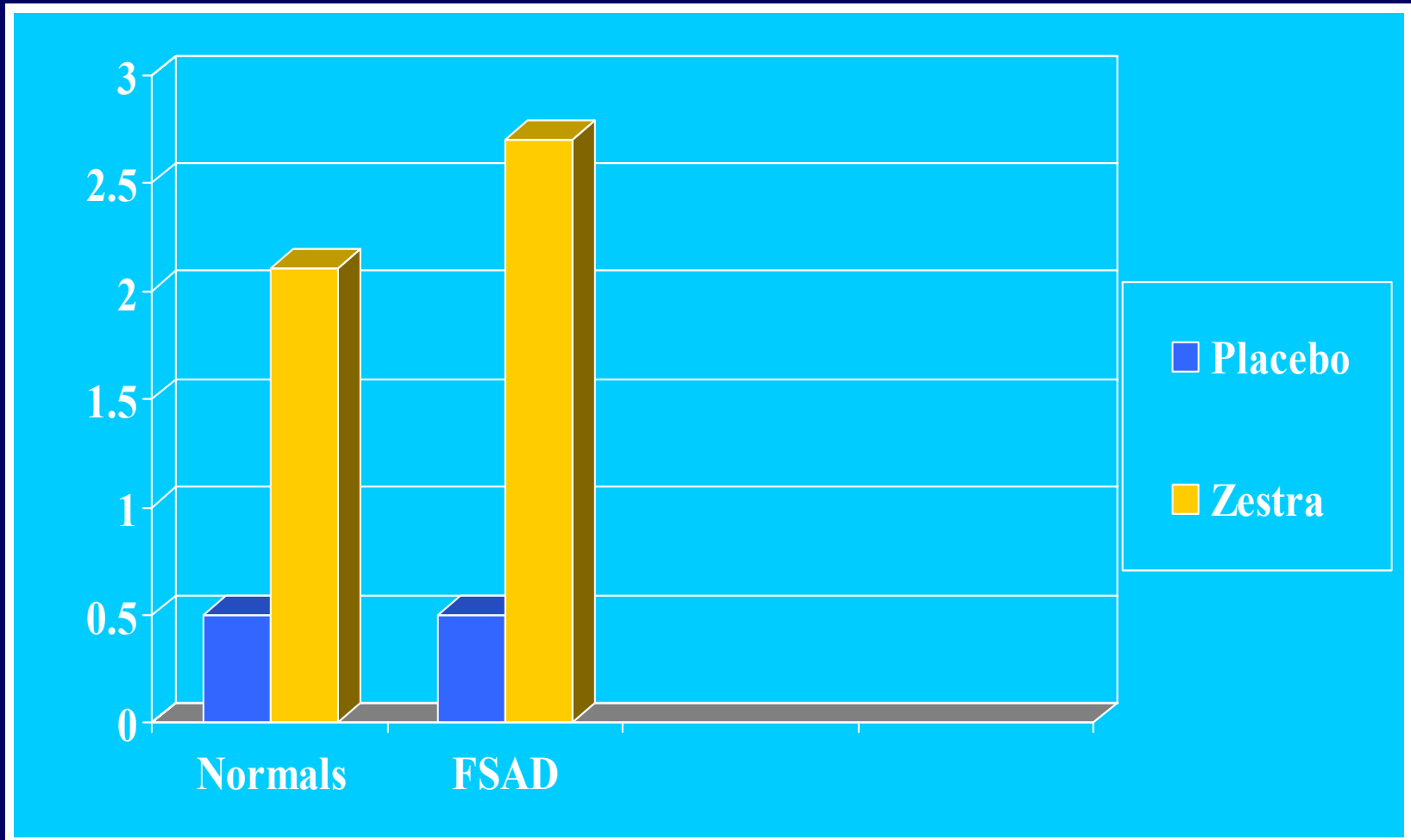
Results: Efficacy: Global Assessment

Question 2

Patients	Placebo	Zestra
Normals	0.5 ± 0.5	$2.1 \pm 1.2^{**}$
FSAD	0.5 ± 0.7	$2.7 \pm 1.1^{***}$

P<0.01 *P<0.001

Results: Efficacy: Global Assessment Question 2



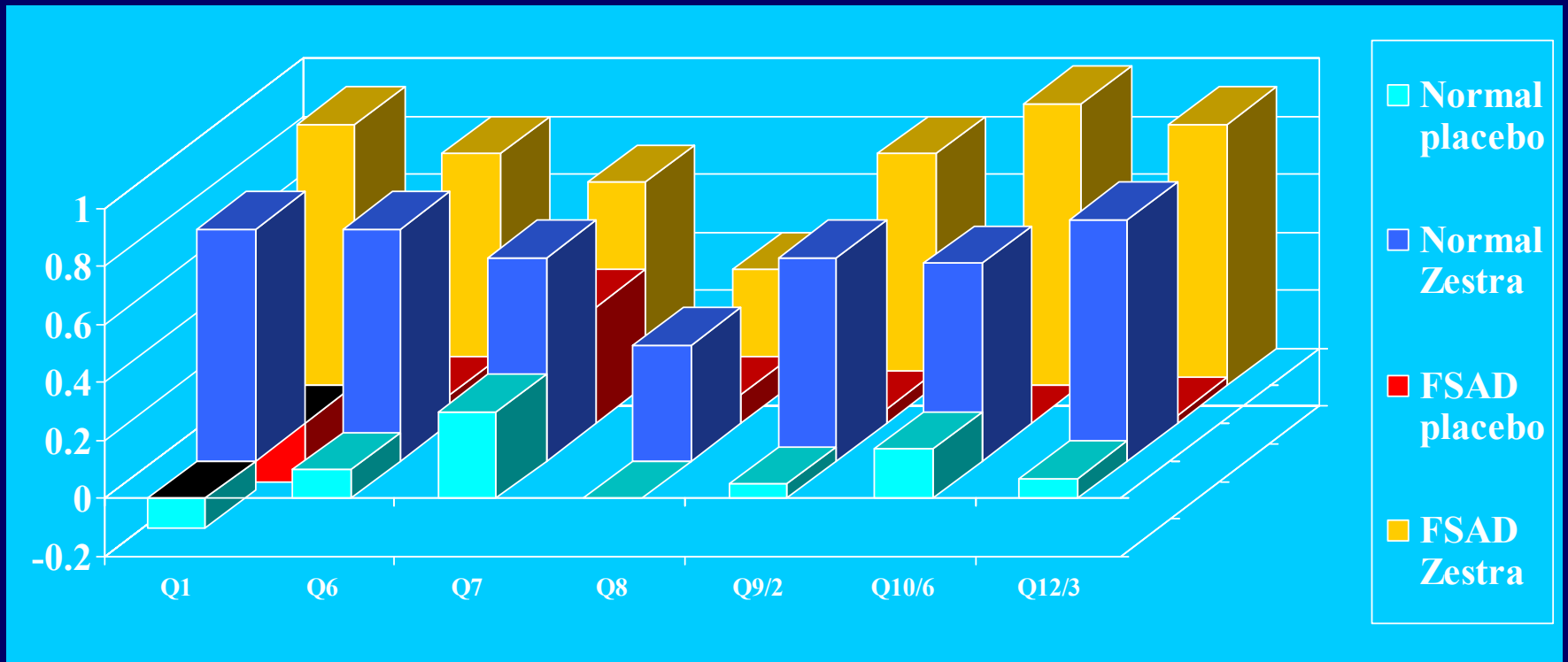
Results: Efficacy: QualiLife Consumer Testing Survey

- Questions 1, 6, 7, 8, 9, 10, and 12 are quantitative.
- Q1 addresses genital sensation.
- Q6 addresses pleasure with sexual activities.
- Q7 addresses lubrication.
- Q8 addresses ability to have orgasms.
- Q9 addresses enhancement of sexual experience.
- Q10 addresses willingness to purchase product.
- Q12 asks how much patient would pay for product.

Results: Efficacy: QualiLife Consumer Testing Survey

QCTS Question	Normal Placebo	Normal Zestra	FSAD Placebo	FSAD Zestra
Q1: sensation	$-.1 \pm .3$	$.8 \pm .4^{***}$	$-.2 \pm .4$	$.9 \pm .3^{***}$
Q6: pleasure	$.1 \pm .3$	$.8 \pm .4^{**}$	$.1 \pm .3$	$.8 \pm .4^{**}$
Q7: lubrication	$.3 \pm .5$	$.7 \pm .5$	$.4 \pm .5$	$.7 \pm .5$
Q8: orgasm	$.0 \pm .5$	$.4 \pm .5^*$	$.1 \pm .3$	$.4 \pm .5$
Q9: enhanced	$.1 \pm .7$	$1.4 \pm 1.0^{**}$	$.1 \pm .3$	$1.6 \pm .8^{***}$
Q10: purchase	1.0 ± 1.9	$4.1 \pm 1.9^*$	0.0 ± 0.0	$5.8 \pm .9^{****}$
Q12: price	$.2 \pm .3$	$2.5 \pm 3.1^*$	$.1 \pm .3$	$2.7 \pm 3.1^*$
*P<.05 **P<.01 ***P<.001 ****P<.0001				

Results: Efficacy: QualiLife Consumer Testing Survey



Summary of Results: Efficacy

PAIRED ANALYSES

Group	FSEP					FSFI							FSDS	GAQ		QCTS						
	Q2	Q3	Q4	Q5	Q6	D	A	L	O	S	P	T		1	2	1	6	7	8	9	10	12
N	3	1	0	0	2	0	1	0	0	0	0	0	0	2	2	3	2	0	1	2	1	1
F	3	3	0	1	3	0	2	0	1	0	0	2	0	2	3	3	2	0	0	3	4	1

0 = NS 1 = P<.05 2 = P<.01 3 = P<.001 4 = P<.0001

Conclusions

- Zestra for Women™ is safe under these conditions of use.
- Zestra for Women™ improves level of desire in normal and FSAD women.
- Zestra for Women™ increases satisfaction with arousal in normal and FSAD women.
- Zestra for Women™ improves level of arousal in normal and FSAD women.
- Zestra for Women™ increases frequency of orgasm in FSAD women.
- Zestra for Women™ improves arousal in normal and FSAD women.
- Zestra for Women™ enhances sexual pleasure in normal and FSAD women.