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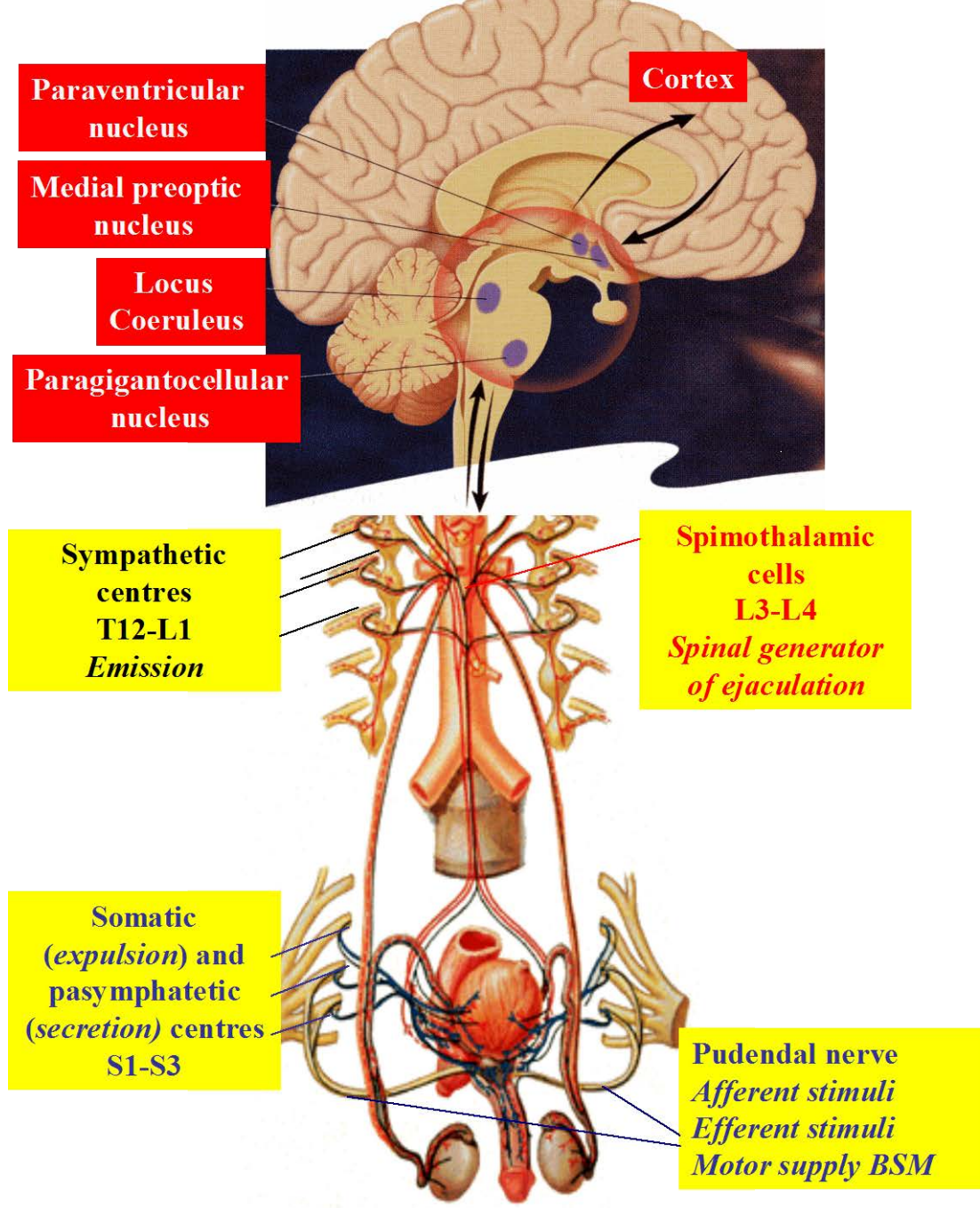
L'eiaculazione precoce

Giovanni Corona MD, PhD

Endocrinology Unit
Medical Department, Ospedale Maggiore
Bologna, Italy
jocorona@libero.it



Corona et al., Nat Rew Urol 2012;9:508

Standard Operating Procedures in the Disorders of Orgasm and Ejaculation

Chris G. McMahon, MBBS, FAChSHM,* Emmanuele Jannini, MD,† Marcel Waldinger, MD, PhD,‡ and David Rowland, PhD§

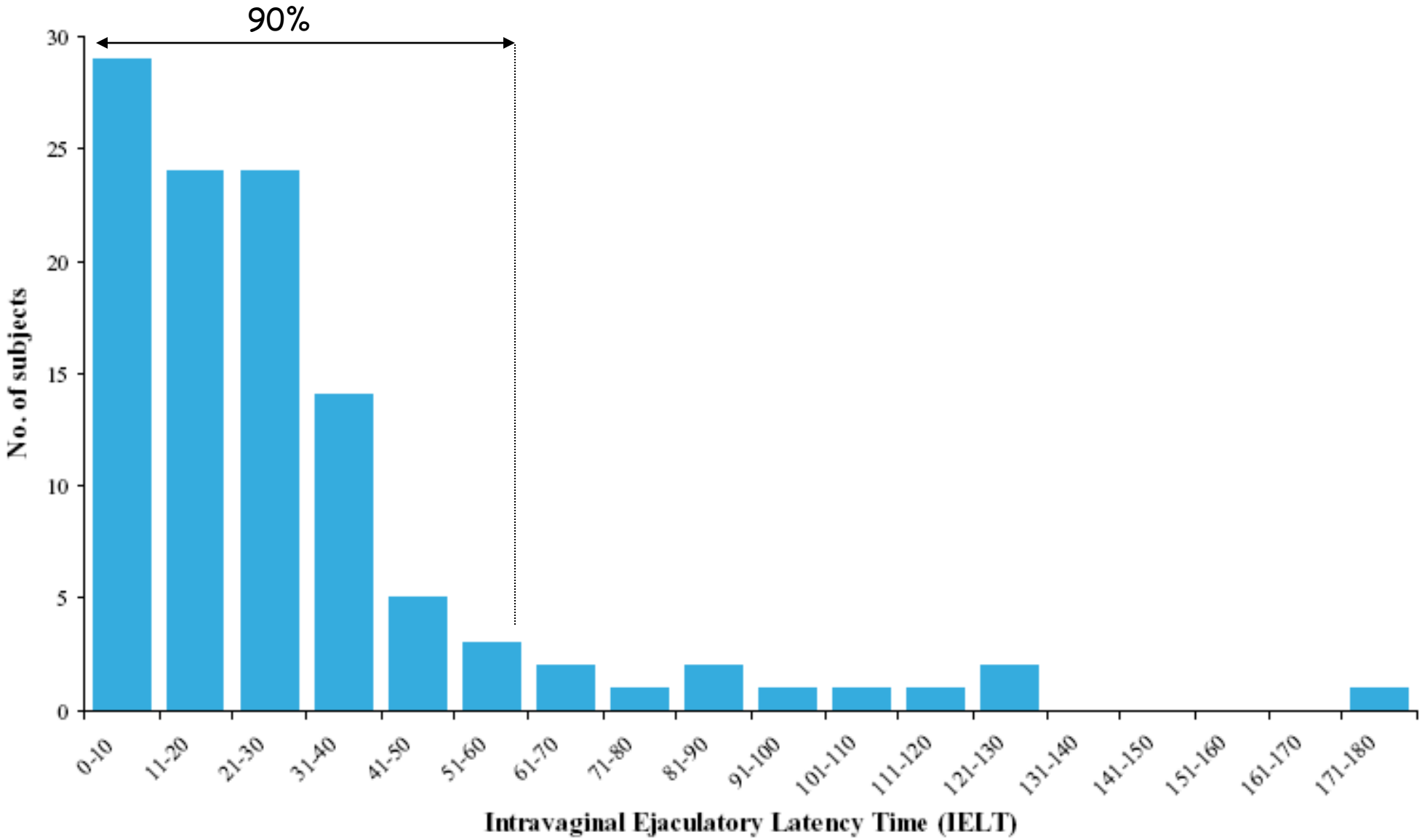
*Australian Centre for Sexual Health, Sydney, Australia; †University of L'Aquila, Endocrinology and Medical Sexology, Experimental Medicine, L'Aquila, Italy; ‡Leyenburg Hospital, Psychiatry and Neurosexology, The Hague, The Netherlands; §Valparaiso University, Psychology, Valparaiso, IN, USA

DOI: 10.1111/j.1743-6109.2012.02824.x

". . . ejaculation which always or nearly always occurs prior to or within about one minute of vaginal penetration, the inability to delay ejaculation on all or nearly all vaginal penetrations, and the presence of negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy"

McMahon et al., J Sex Med. 2013;10:204.

Intravaginal ejaculation latency time measured with stopwatch in 110 men with lifelong premature ejaculation



Waldinger et al., Int J Psychiatry Clin Pract 1998;2:287

Standard Operating Procedures in the Disorders of Orgasm and Ejaculation

Chris G. McMahon, MBBS, FAChSHM,* Emmanuele Jannini, MD,† Marcel Waldinger, MD, PhD,‡ and David Rowland, PhD§

*Australian Centre for Sexual Health, Sydney, Australia; †University of L'Aquila, Endocrinology and Medical Sexology, Experimental Medicine, L'Aquila, Italy; ‡Leyenburg Hospital, Psychiatry and Neurosexology, The Hague, The Netherlands; §Valparaiso University, Psychology, Valparaiso, IN, USA

DOI: 10.1111/j.1743-6109.2012.02824.x

". . . The epidemiological studies demonstrate the varying prevalence estimates ranging from 30% down to 3%.

McMahon et al., J Sex Med. 2013;10:204.

Prevalence of the Complaint of Ejaculating Prematurely and the Four Premature Ejaculation Syndromes: Results from the Turkish Society of Andrology Sexual Health Survey

Ege C. Serefoglu, MD,* Onder Yaman, MD,† Selahittin Cayan, MD,‡ Ramazan Asci, MD,§ Irfan Orhan, MD,¶ Mustafa F. Usta, MD,** Oguz Ekmekcioglu, MD,†† Muammer Kendirci, MD,‡‡ Bulent Semerci, MD,§§ and Ates Kadioglu, MD¶¶

*Kiziltepe State Hospital, Kiziltepe, Mardin, Turkey; †Department of Urology, Faculty of Medicine, Ankara University, Ankara, Turkey; ‡Department of Urology, Faculty of Medicine, Mersin University, Mersin, Turkey; §Department of Urology, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey; ¶Department of Urology, Faculty of Medicine, Firat University, Elazig, Turkey; **Department of Urology, Faculty of Medicine, Akdeniz University, Antalya, Turkey; ††Department of Urology, Faculty of Medicine, Erciyes University, Kayseri, Turkey; ‡‡2nd Urology Clinic, Sisli Etfal Training & Research Hospital, Istanbul, Turkey; §§Department of Urology, Faculty of Medicine, Ege University, Izmir, Turkey; ¶¶Department of Urology, Faculty of Medicine, Istanbul University, Istanbul, Turkey

DOI: 10.1111/j.1743-6109.2010.02095.x

A total of 2,593 couples (mean age, 41.9 ± 12.7 years for males and 38.2 ± 12.1 years for females) were enrolled. Five-hundred twelve subjects (20.0%) complained of ejaculating prematurely.

The median self-estimated IELTs of the patients who described lifelong, acquired or natural variable PE were approximately 1 minute, 1–2 mintues and 2–3 minutes

Serefoglu et al., J Sex Med. 2011;8:540

An Evidence-Based Unified Definition of Lifelong and Acquired Premature Ejaculation: Report of the Second International Society for Sexual Medicine Ad Hoc Committee for the Definition of Premature Ejaculation

Ege Can Serefoglu, MD,* Chris G. McMahon, MD,† Marcel D. Waldinger, MD, PhD,‡ Stanley E. Althof, PhD,§ Alan Shindel, MD,¶ Ganesh Adaikan, PhD,** Edgardo F. Becher, MD,†† John Dean, MD,‡‡ Francois Giuliano, MD, PhD,§§ Wayne J.G. Hellstrom, MD,¶¶ Annamaria Giraldi, MD, PhD,*** Sidney Glina, MD, PhD,††† Luca Incrocci, MD, PhD,‡‡‡ Emmanuele Jannini, MD,§§§ Marita McCabe, PhD,¶¶¶ Sharon Parish, MD,**** David Rowland, PhD,†††† R. Taylor Segraves, MD, PhD,‡‡‡‡ Ira Sharlip, MD,§§§§ and Luiz Otavio Torres, MD¶¶¶¶

1. **Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE).**

2. **The inability to delay ejaculation on all or nearly all vaginal penetrations.**

3. **Negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy.**

Serefoglu et al., J Sex Med. 2014;11:1423

Patient-reported measures of the Premature Ejaculation Profile

Domain	Item	Response options
Perceived control over ejaculation	"Over the past month, was your control over ejaculation during sexual intercourse:"	0: Very poor 1: Poor 2: Fair 3: Good 4: Very good
Personal distress related to ejaculation*	"How distressed are you by how fast you ejaculate during sexual intercourse?"	0: Extremely 1: Quite a bit 2: Moderately 3: A little bit 4: Not at all
Satisfaction with sexual intercourse	"Over the past month, was your satisfaction with sexual intercourse:"	0: Very poor 1: Poor 2: Fair 3: Good 4: Very good
Interpersonal difficulty related to ejaculation*	"To what extent does how fast you ejaculate during sexual intercourse cause difficulty in your relationship with your partner?"	0: Extremely 1: Quite a bit 2: Moderately 3: A little bit 4: Not at all

*For analysis, values for personal distress related to ejaculation and interpersonal difficulty related to ejaculation were reverse coded (i.e., where 0 = "extremely" and 4 = "not at all"), so that lower scores on all measures would represent poorer sexual functioning.

Patrick et al., J Sex Med. 2007;4:780.

Perceived control is better than IELT

	A (base model)	B (proposed model)	C (IELT deleted)
	• Direct effect of IELT on satisfaction with sexual intercourse and personal distress related to ejaculation	• Direct effect of perceived control over ejaculation on satisfaction with sexual intercourse and personal distress related to ejaculation	• Model B with IELT not included
Model fit indices			
Chi square	6.742	7.667	35.664
Degrees of freedom	2	4	5
Probability	0.034	0.105	0.000
CMIN/DF	3.371	1.197	7.133
RMSEA	0.112	0.070	0.181

Paths were constrained by setting the value = 0.
IELT = intravaginal ejaculatory latency time; RMSEA = root mean square error of approximation; CMIN/DF = relative chi-square (minimum sample discrepancy divided by degree of freedom).

Patrick et al., J Sex Med. 2007;4:780.

Aetiology

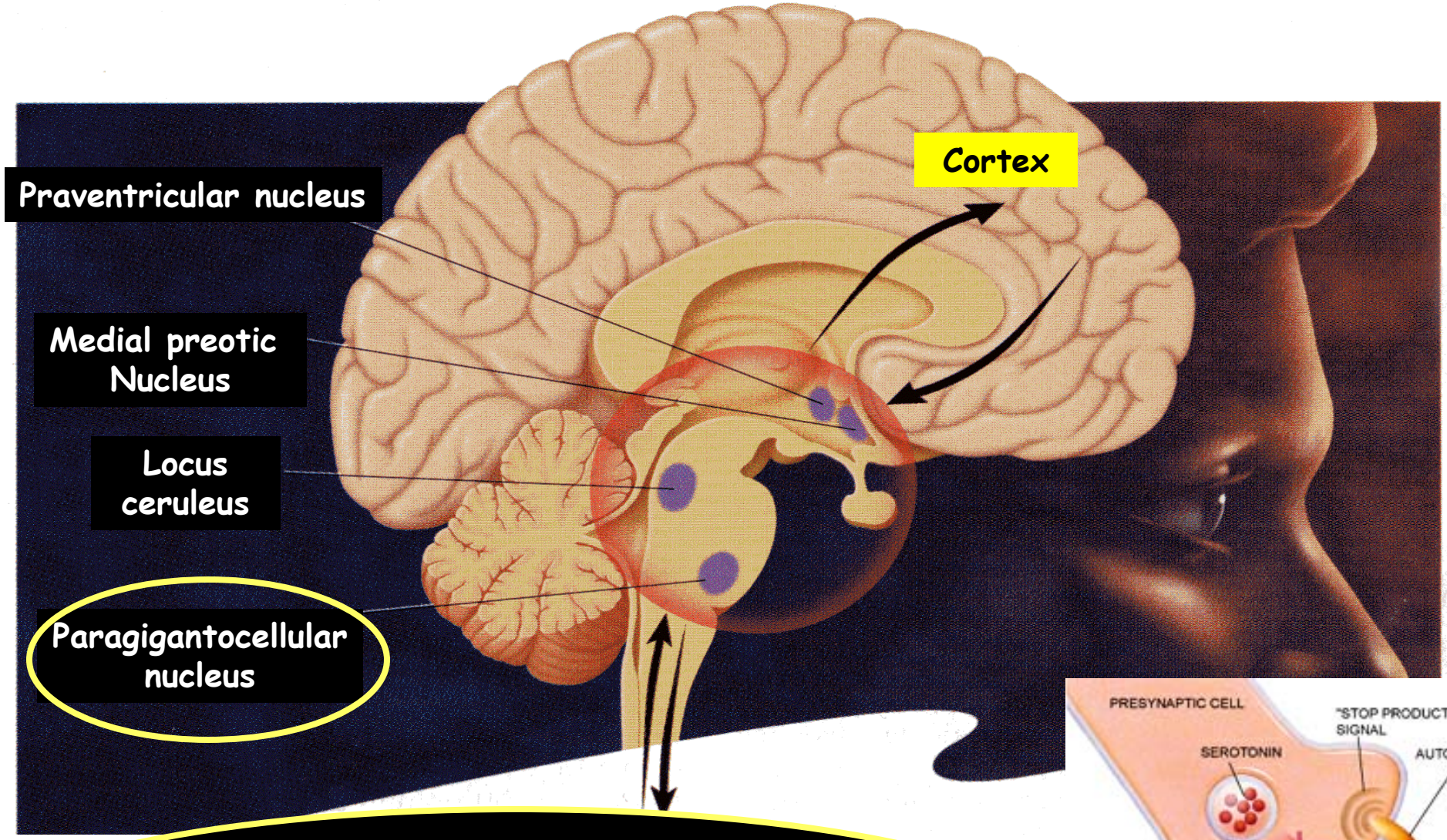
PE
- **Life - long**
- **Acquired**
  - Psychological or relationship problems
  - Organic
    - Urological dysfunctions:
      -Prostatitis
      -ED
    - Hormonal dysfunction

McMahon et al., J Sex Med. 2013;10:204.

Aetiology

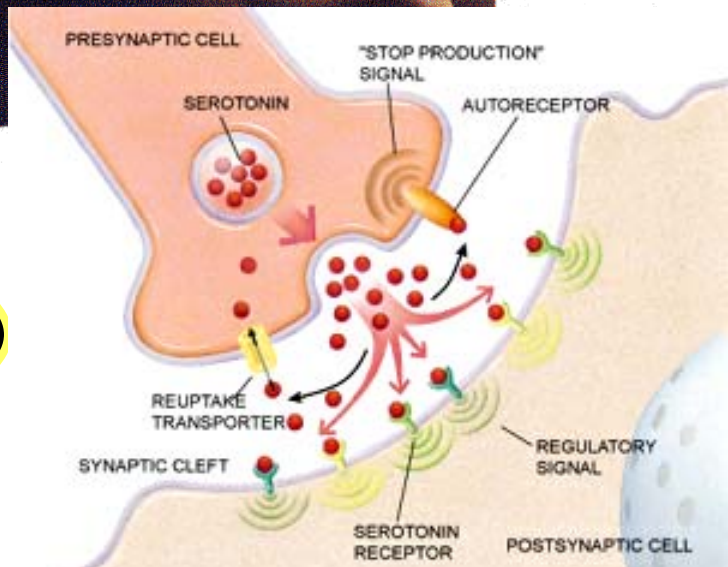
PE { **Life - long**

McMahon et al., J Sex Med. 2013;10:204.



$5HT_{2C}$ $5HT_{1B}$ agonists = delay ejaculation

$5HT_{1A}$ agonists = accelerate ejaculation



Reference	Analyzed SNPs	N. pt/N. ctrl (origin)	Evaluated parameters	Genotype frequency pt/ctrl (%)	Conclusions
Janssen et al., 2009 [21]	5-HTTLPR	89/92 (Holland)	IELT	S = 47/48 L = 53/52 LL = 29/29 SL = 48/45 SS = 22/26	No genotypic difference between pt and ctrl, but SS and SL pt show a IELT longer than LL pt.
Safarinejad, 2009 [22]	5-HTTLPR, rs25531, STin2	227/0 (Iran)	IELT, and sertraline response	LaLa = 26.8 SLa = 31.3 LaLg = 1.8 SLg = 8.4 LgLg = 4.4 SS = 27.3 STin2 10/10 = 25.1 STin2 10/12 = 16.7 STin2 12/12 = 58.42	LaLa e STin2 12/12 pt show a better sertraline response
Ozbek et al., 2009 [23]	5-HTTLPR	70/70 (Turkey)	IELT	LL = 16/17 LS = 30/53 SS = 54/28	S allele is more frequent in pt than in ctrl.
Safarinejad, 2010 [18]	5-HTTLPR, rs25531	82/82 (Iran)	IELT	LaLa = 22/35.4 LaLg = 2.4/6.1 SLa = 24.4/31.7 SS = 35.4/20.7 SLg = 11/4.9 LgLg = 4.9/1.2	SS genotype is more frequent in pt than ctrl. SS, LgLg e SLg genotypes are equivalent and increase a higher risk for EP.

pt = patients; ctrl = controls

Table 5 Data of combined genotypes of the three polymorphic sites of the SLC6A4 gene

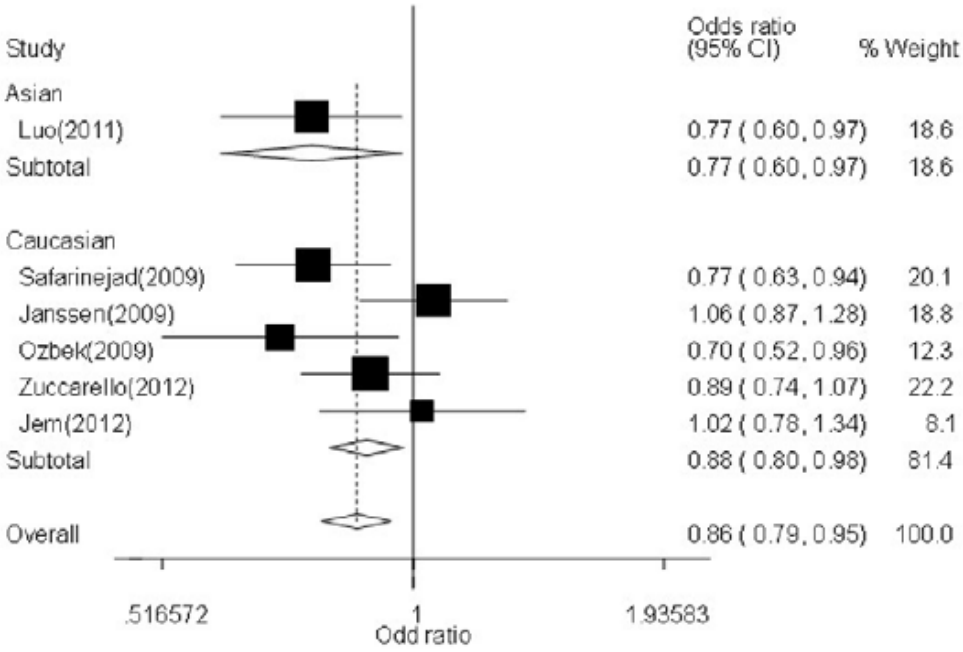
Genotypes	Patients						Controls	
	Total count (N = 121)	Frequency (%)	Primary PE (N = 89)	Frequency (%)	Secondary PE (N = 32)	Frequency (%)	Total count (N = 100)	Frequency (%)
L'L' (LaLa)	23	19.0	16	18.0	7	21.9	23	23
L'S' (LaLg—LaS)	68	56.2	50	56.2	18	56.2	54	54
S'S' (LgLg—LgS—SS)	30	24.8	23	25.8	7	21.9	23	23
L'L' 10/10	6	5.0	5	5.6	1	3.1	3	3
L'L' 10/12	9	7.4	4	4.5	5	15.7	14	14
L'L' 12/12	8	6.6	7	7.9	1	3.1	5	5
L'L' 9/12	0	0	0	0	0	0	1	1
L'S' 9/10	1	0.8	1	1.1	0	0	2	2
L'S								
L'S								
L'S								
L'S								
S'S' 9/10	1	0.8	1	1.1	0	0	0	0
S'S' 9/12	1	0.8	1	1.1	0	0	2	2
S'S' 10/10	3	2.5	1	1.1	2	6.2	1	1
S'S' 10/12	9	7.6	7	7.9	2	6.2	7	7
S'S' 12/12	16	13.2	13	14.6	3	9.4	13	13

L'L' 12/12 and S'S' 10/10 (in bold) are considered the "fastest" and the "slowest" combined genotypes, respectively (see the text for explanation)
L'L' = LaLa; L'S' = LaLg—LaS; S'S' = LgLg—LgS—SS; 9 = STin2.9; 10 = STin2.10; 12 = Stin2.12

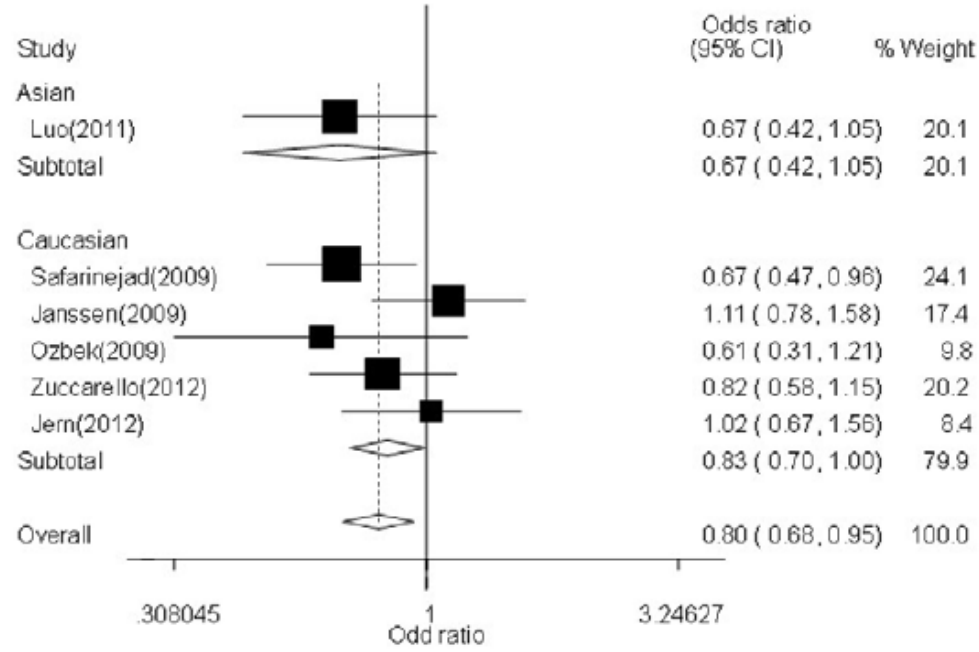
The present results indicate that no difference exists in SLC6A4 polymorphisms frequency between PE patients and controls.

Zuccarello et al., J Sex Med. 2012;9:1659

Forest plot of LPE risk associated with the 5-HTTLPR gene polymorphism (LL vs. SS)



Forest plot of LPE risk associated with the 5-HTTLPR gene polymorphism (LL +LS vs. SS)



Zhu et al., Plose One. 2013;8:e54994

Premature ejaculation

1. Genetic factors might underlie ejaculatory control.

Aetiology

PE

- Life - long
- Acquired
  - Psychological or relationship problems

McMahon et al., J Sex Med. 2013;10:204.

EUROPEAN UROLOGY 51 (2007) 816–824

available at www.sciencedirect.com
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European Association of Urology

Sexual Medicine

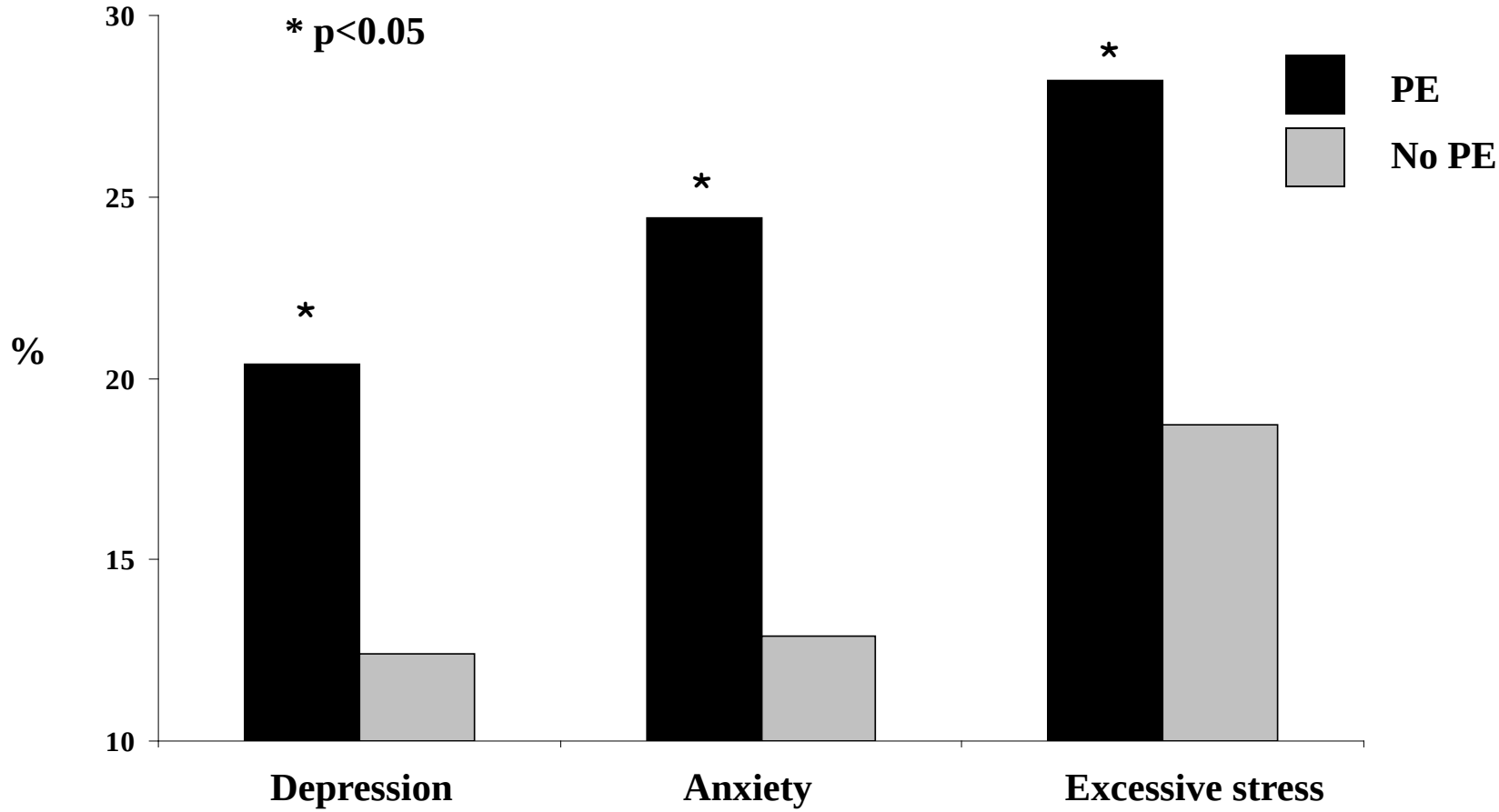
The Premature Ejaculation Prevalence and Attitudes (PEPA) Survey: Prevalence, Comorbidities, and Professional Help-Seeking

Hartmut Porst [a,*], *Francesco Montorsi* [b], *Raymond C. Rosen* [c], *Lisa Gaynor* [d], *Stephanie Grupe* [d], *Joseph Alexander* [d]

Internet-based survey (the PE Prevalence and Attitudes [PEPA] survey) among men ages 18–70 in the United States, Germany, and Italy (n = 12,133 mean age 41.6±11.6 years ols)

Porst et al., Eur Urol. 2007;51:816

Percentages of men reporting comorbid conditions



Porst et al., Eur Urol. 2007;51:816

European Urology

European Urology 46 (2004) 615–622

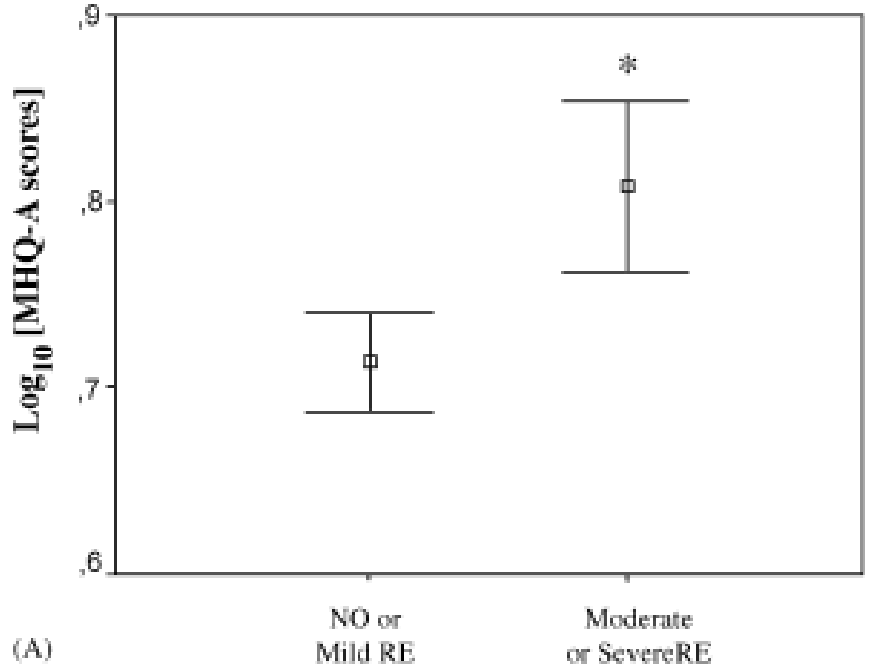
Psycho-Biological Correlates of Rapid Ejaculation in Patients Attending an Andrologic Unit for Sexual Dysfunctions

G. Corona[a,1], L. Petrone[a,1], E. Mannucci[b], E.A. Jannini[c], R. Mansani[a], A. Magini[a], R. Giommi[d], G. Forti[a], M. Maggi[a,*]

[a]*Department of Clinical Physiopathology, Andrology Unit, University of Florence, Viale Pieraccini 6, 50139 Florence, Italy*
[b]*Department of Clinical Physiopathology, Endocrinology Unit, University of Florence, Viale Pieraccini 6, 50139 Florence, Italy*
[c]*Department of Experimental Medicine, Course of Endocrinology and Medical Sexology, University of L'Aquila, L'Aquila, Italy*
[d]*International Institute of Sexology, Florence, Italy*

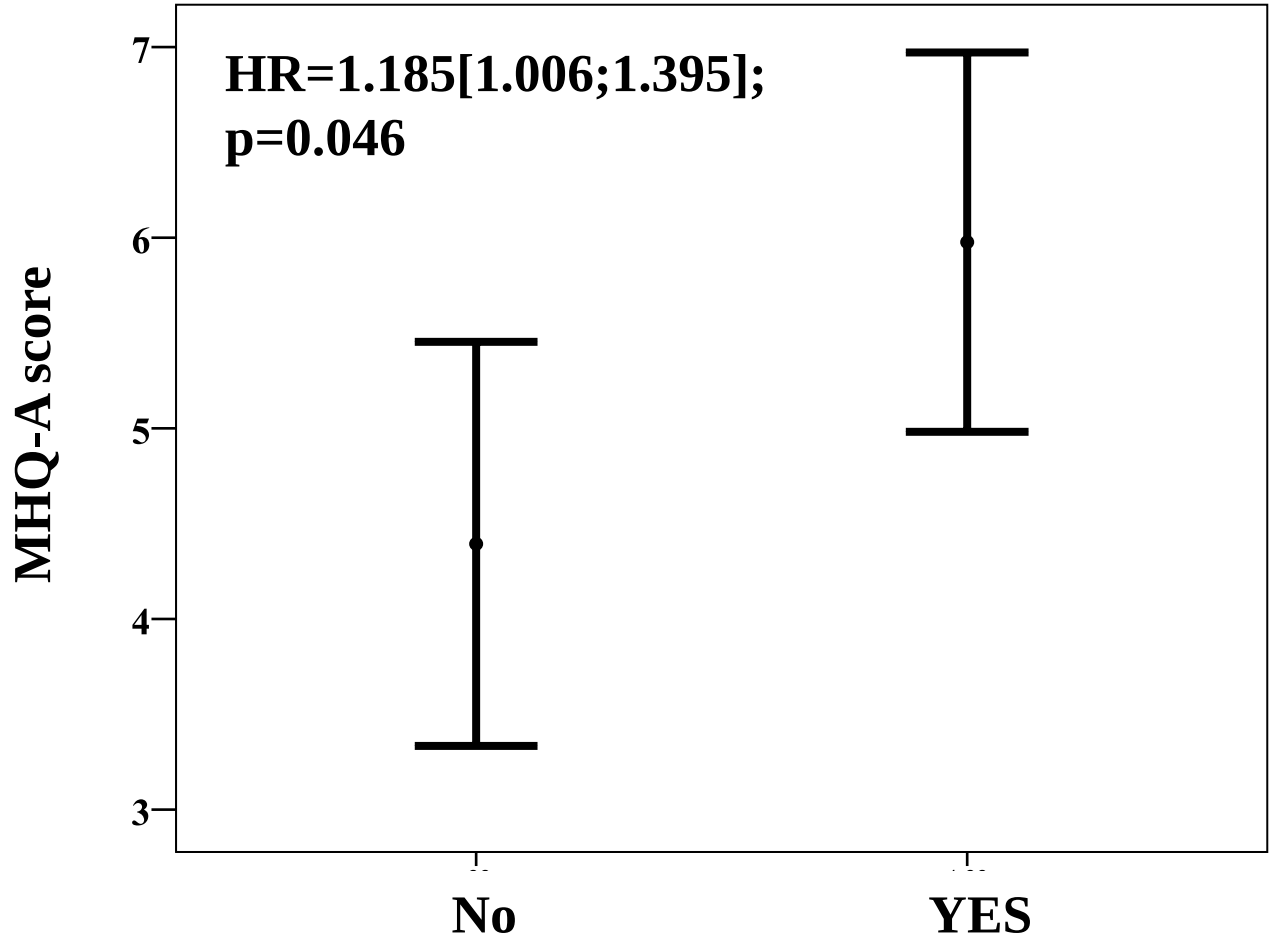
Accepted 1 July 2004

Available online 21 July 2004



(A)

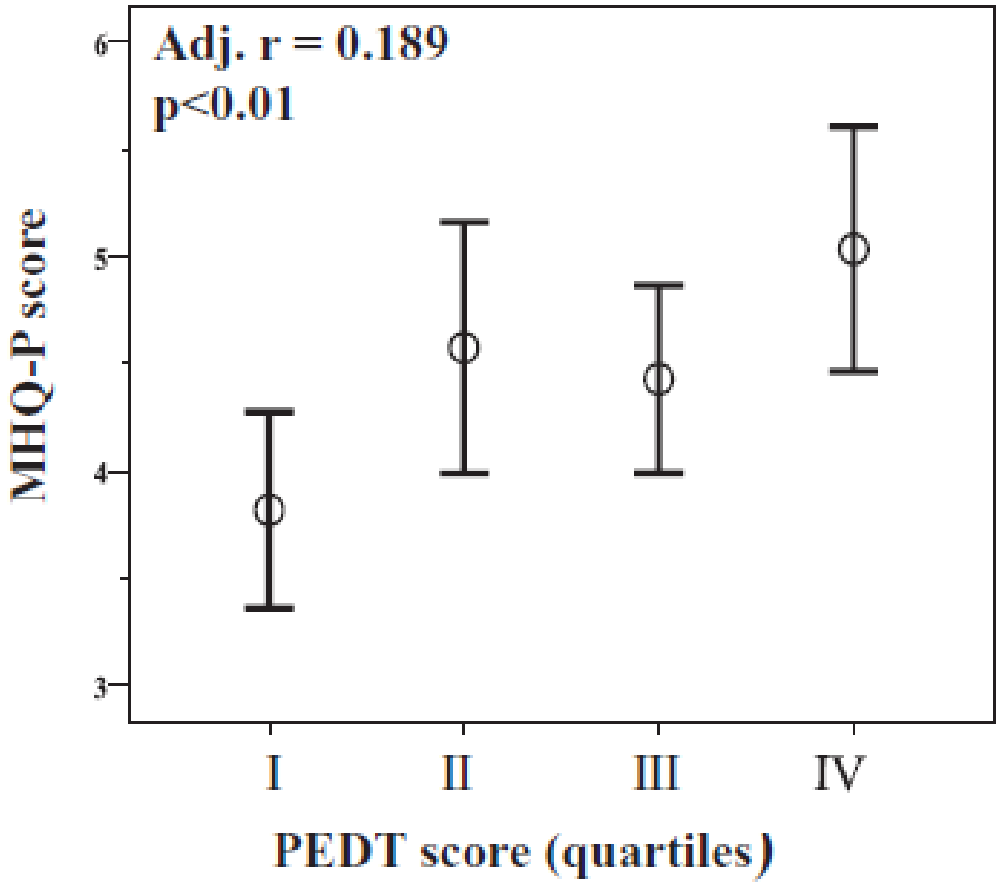
Anxiety symptoms (MHQ-score) in subjects with or without PE according to Premature Ejaculation Diagnostic Tool (PEDT) score



Adjusted for age

Clinical Correlates of Erectile Dysfunction and Premature Ejaculation in Men with Couple Infertility

Francesco Lotti, MD,* Giovanni Corona, MD,*† Giulia Rastrelli, MD,* Gianni Forti, MD,* Emmanuele A. Jannini, MD,‡ and Mario Maggi, MD*



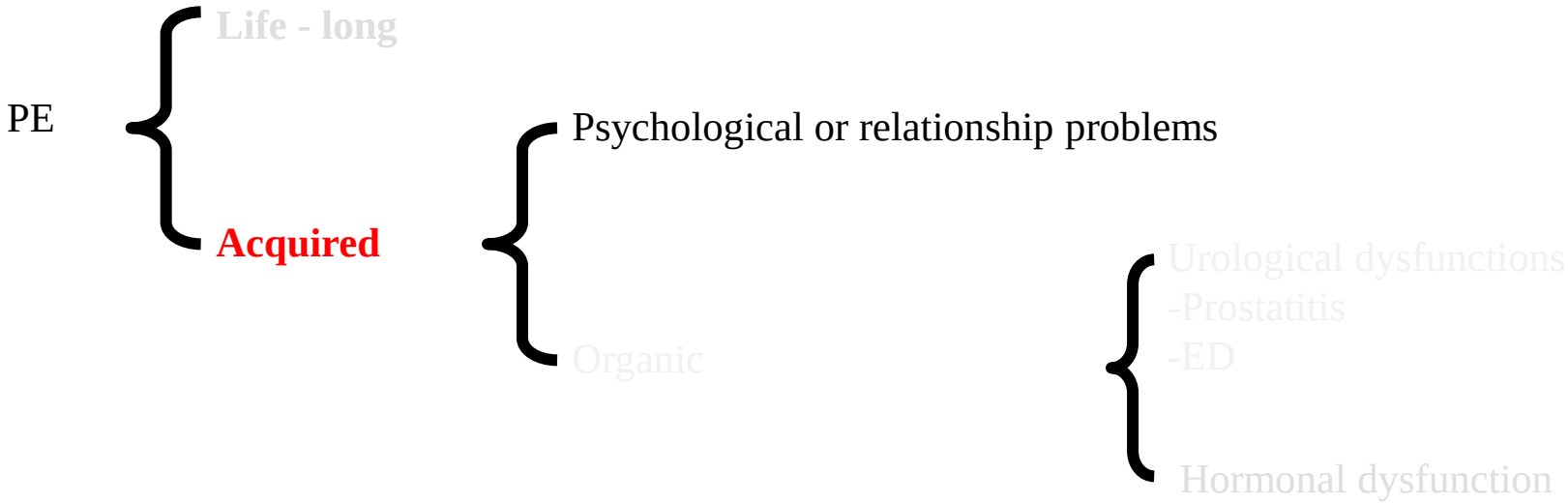
Consecutive series of 244 men (mean age 35.2 ± 7.8) with couple infertility

Lotti et al., J Sex Med. 2012;9:2698.

Premature ejaculation

1. **Genetic factors might underlie ejaculatory control.**
2. **Anxiety symptoms are associated with PE**

Aetiology



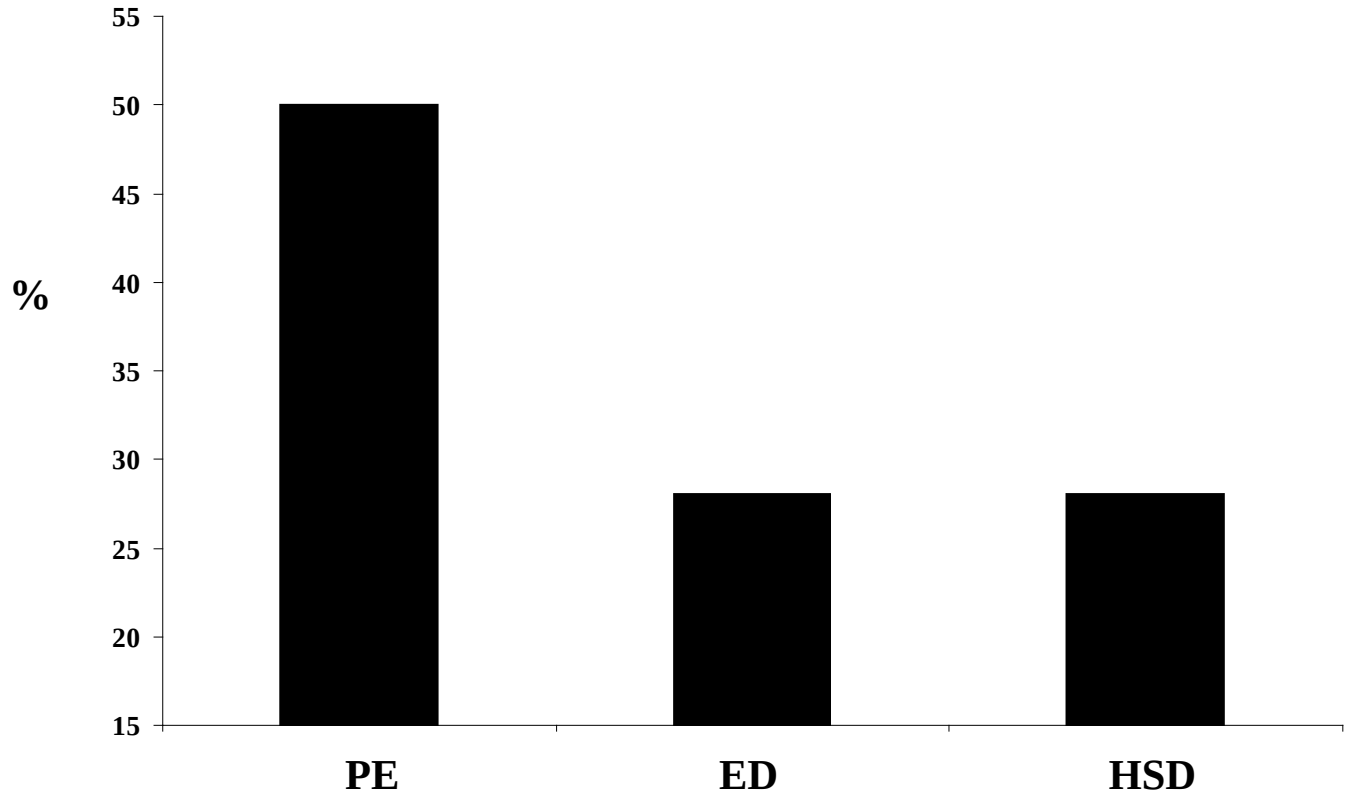
McMahon et al., J Sex Med. 2013;10:204.

ORIGINAL ARTICLE

The frequency of sexual dysfunctions in male partners of women with vaginismus in a Turkish sample

S Dogan[1] and M Dogan[2]

[1]*Department of Psychiatry, GOP Hospital and Bogazici University Mediko-Sosyal Center, Istanbul, Turkey and*
[2]*Department of Psychiatry, Esenler Hayat Hospital, Istanbul, Turkey*

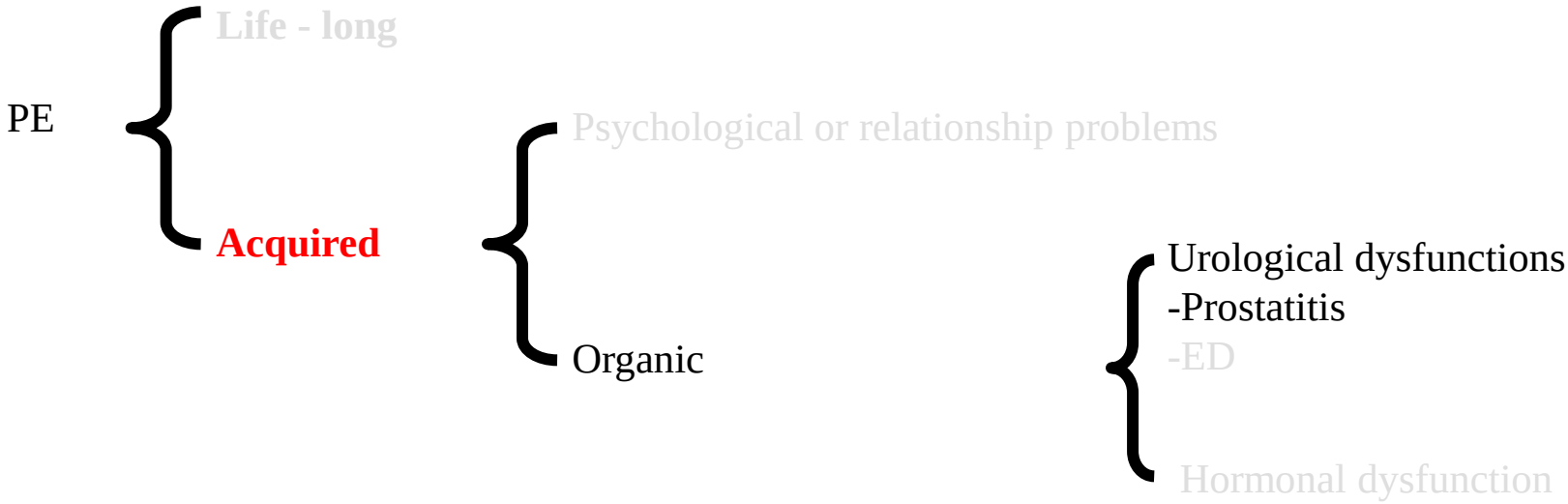


Dogan &Dogan., Int J Impot Res. 2008;20:218

Premature ejaculation

1. **Genetic factors might underlie ejaculatory control.**
2. **Anxiety symptoms are associated with PE**
3. **PE is a couple problem**

Aetiology



McMahon et al., J Sex Med. 2013;10:204.

ADULT UROLOGY

PREVALENCE OF CHRONIC PROSTATITIS IN MEN WITH PREMATURE EJACULATION

EMILIANO SCREPONI, ELEONORA CAROSA, SAVINO M. DI STASI, MARIO PEPE, GIUSEPPE CARRUBA, AND EMMANUELE A. JANNINI

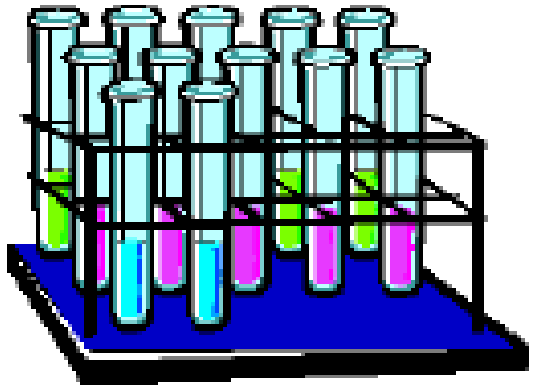
ABSTRACT

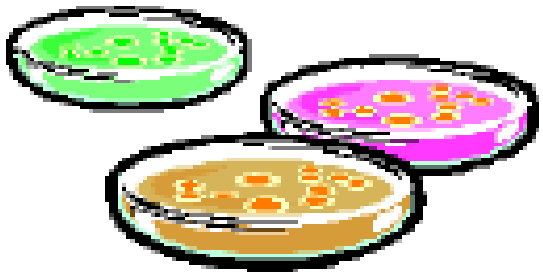
Objectives. To investigate the prevalence of chronic prostatitis in men with premature ejaculation. The etiology of premature ejaculation is currently considered psychological in nature. However, the possibility that urologic, hormonal, or neurologic factors may contribute to this condition should be considered in its management.

Methods. We evaluated segmented urine specimens before and after prostatic massage and expressed prostatic secretion specimens from 46 patients with premature ejaculation and 30 controls by bacteriologic localization studies. The incidence of premature ejaculation in the subjects with chronic prostatitis was also evaluated.

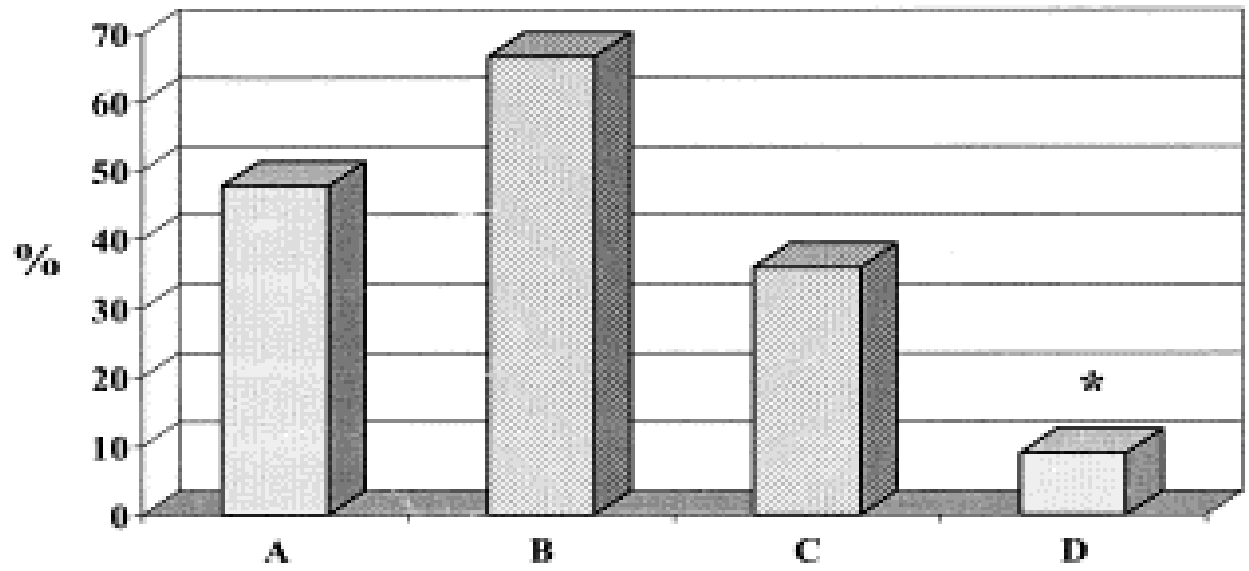
Results. Prostatic inflammation was found in 56.5% and chronic bacterial prostatitis in 47.8% of the subjects with premature ejaculation, respectively. When compared with the controls, these novel findings were statistically significant ($P < 0.05$).

Conclusions. Considering the role of the prostate gland in the mechanism of ejaculation, we suggest a role for chronic prostate inflammation in the pathogenesis of some cases of premature ejaculation. Since chronic prostatitis has been found with a high frequency in men with premature ejaculation, we stress the importance of a careful examination of the prostate before any pharmacologic or psychosexual therapy for premature ejaculation. UROLOGY **58**: 198–202, 2001.





Prostatitis



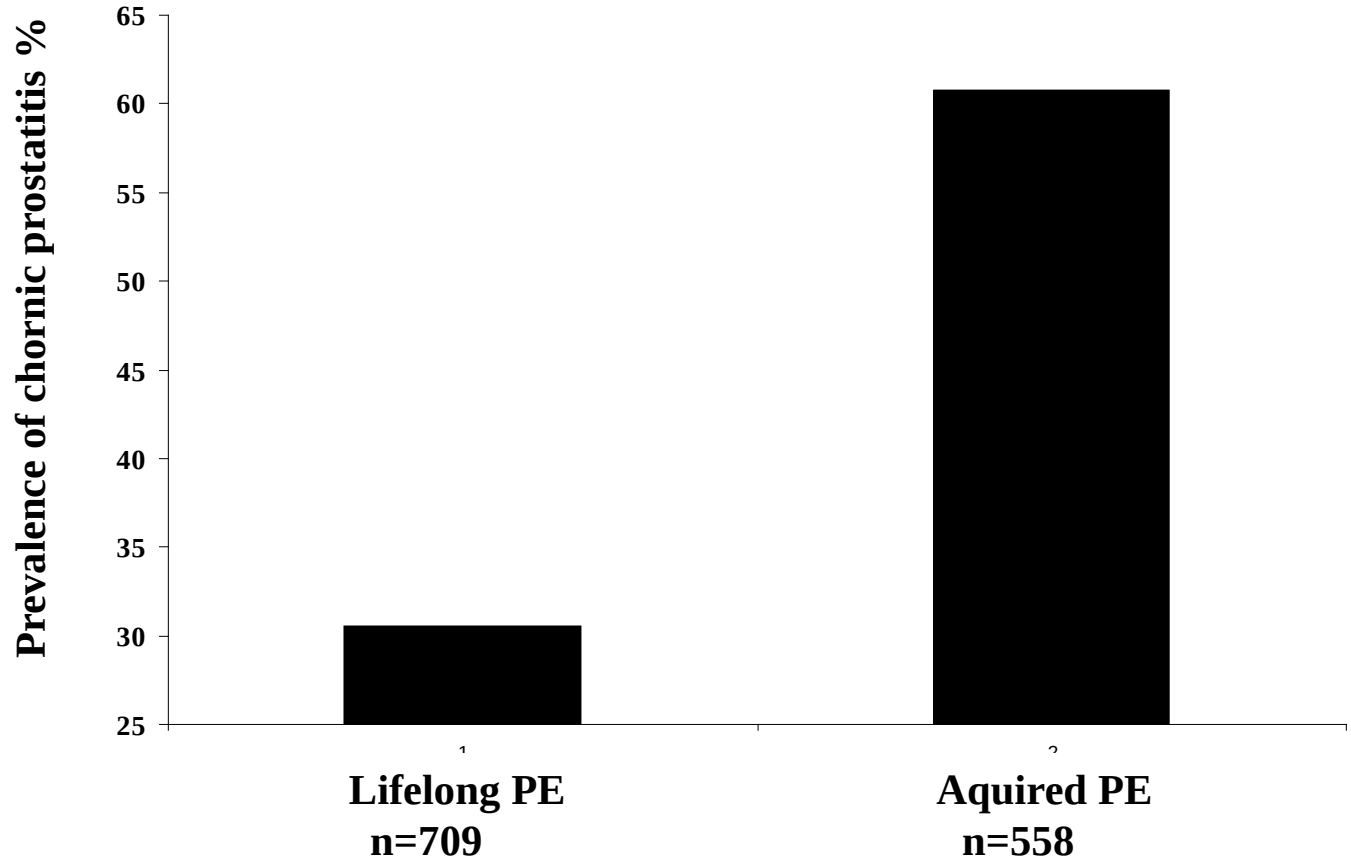
A	B	C	D
EP Total n=46	EP Prim. n=21	EP Second. n=25	Healthy Control n=30

Screponi et al., Urology 2001;58:198

Distribution and Factors Associated with Four Premature Ejaculation Syndromes in Outpatients Complaining of Ejaculating Prematurely

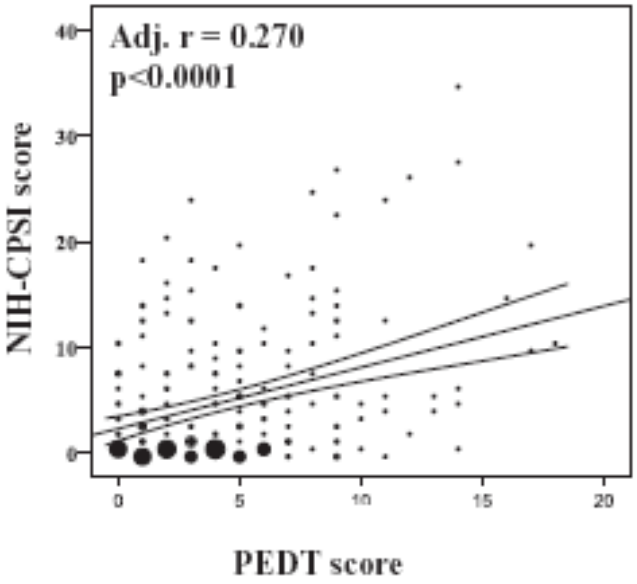
Xiansheng Zhang, MD, PhD, Jingjing Gao, MB, Jishuang Liu, MM, Lei Xia, MM, Jiajia Yang, MB, Zongyao Hao, MD, PhD, Jun Zhou, MM, and Chaozhao Liang, MD, PhD

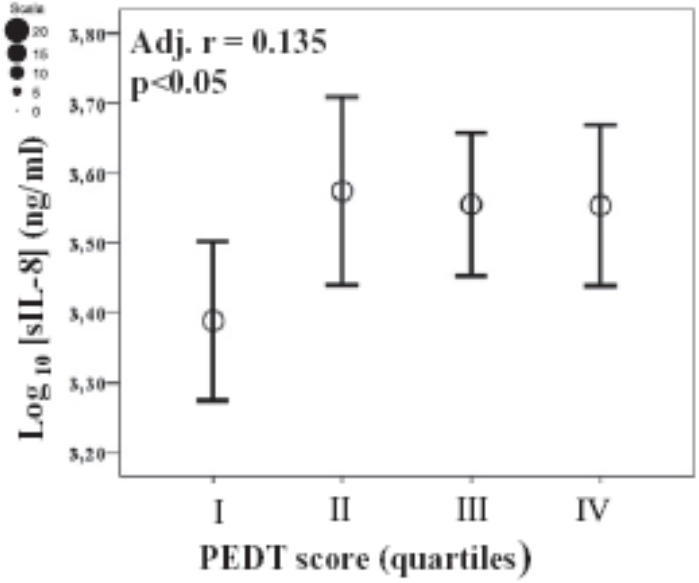
Department of Urology, The First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China

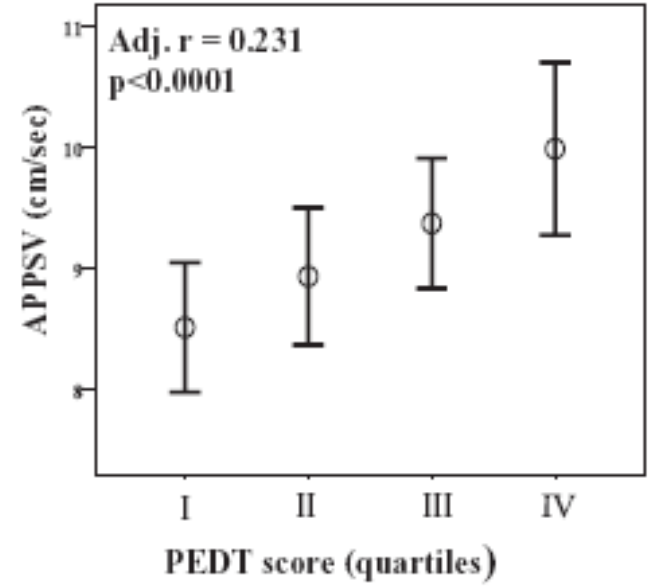


Zhang et al., J Sex Med. 2013;10:1603

Consecutive series of 244 men (mean age 35.2 ± 7.8) with couple infertility







Lotti et al., J Sex Med. 2012;9:2698.

Premature ejaculation

1. **Genetic factors might underlie ejaculatory control.**
2. **Anxiety symptoms are associated with PE**
3. **PE is a couple problem**
4. **Prostatitis are frequently associated with acquired PE**

Antibiotic Treatment Can Delay Ejaculation in Patients with Premature Ejaculation and Chronic Bacterial Prostatitis

. J Sex Med 2007;4:491–496.

AbdelRahman El-Nashaar, MD,* and Rany Shamloul, MD†

*Department of Andrology, Sexology and STDs, Cairo, Egypt; †Department of Physiology, University of Saskatchewan, Saskatoon, Canada

DOI: 10.1111/j.1743-6109.2006.00243.x

Table 3 Patient and control group results

	Patient (N = 74)*		Control (N = 20)
Age (mean ± SD, years)	40.2 ± 6.3		38.3 ± 2.9
Duration of complaint (mean ± SD, months)	14.1 ± 2.3		12.8 ± 2.1
Sexual intercourse (mean ± SD)	2.5 ± 1.3		2.9 ± 1.4
Prostatic culture			
Eschericia coli	(32/74) 43.2%		(9/20) 45%
Enterococci	(24/74) 32.4%		(5/20) 25%
Pseudomonas aeruginosa	(18/74) 24.3%		(6/20) 30%
	TR (N = 62)	NR (N = 12)	No treatment
IELT (mean ± SD)			
Baseline	1.1 ± 0.2	1.4 ± 0.1	1.3 ± 0.4
After 1 month of treatment	2.9 ± 0.3**	1.5 ± 0.3	1.2 ± 0.1
After 4-month follow-up	2.8 ± 0.2**	N/A	N/A

*$P > 0.05$; **$P < 0.05$, vs. baseline.
TR = treatment responsive; NR = treatment nonresponsive; N/A = not available; IELT = intravaginal ejaculatory latency time.

145 men with acquired PE→64.8% bacterial prostatitis (94 subjects)

Fluoroquinolone–macrolide combination therapy for chronic bacterial prostatitis: retrospective analysis of pathogen eradication rates, inflammatory findings and sexual dysfunction

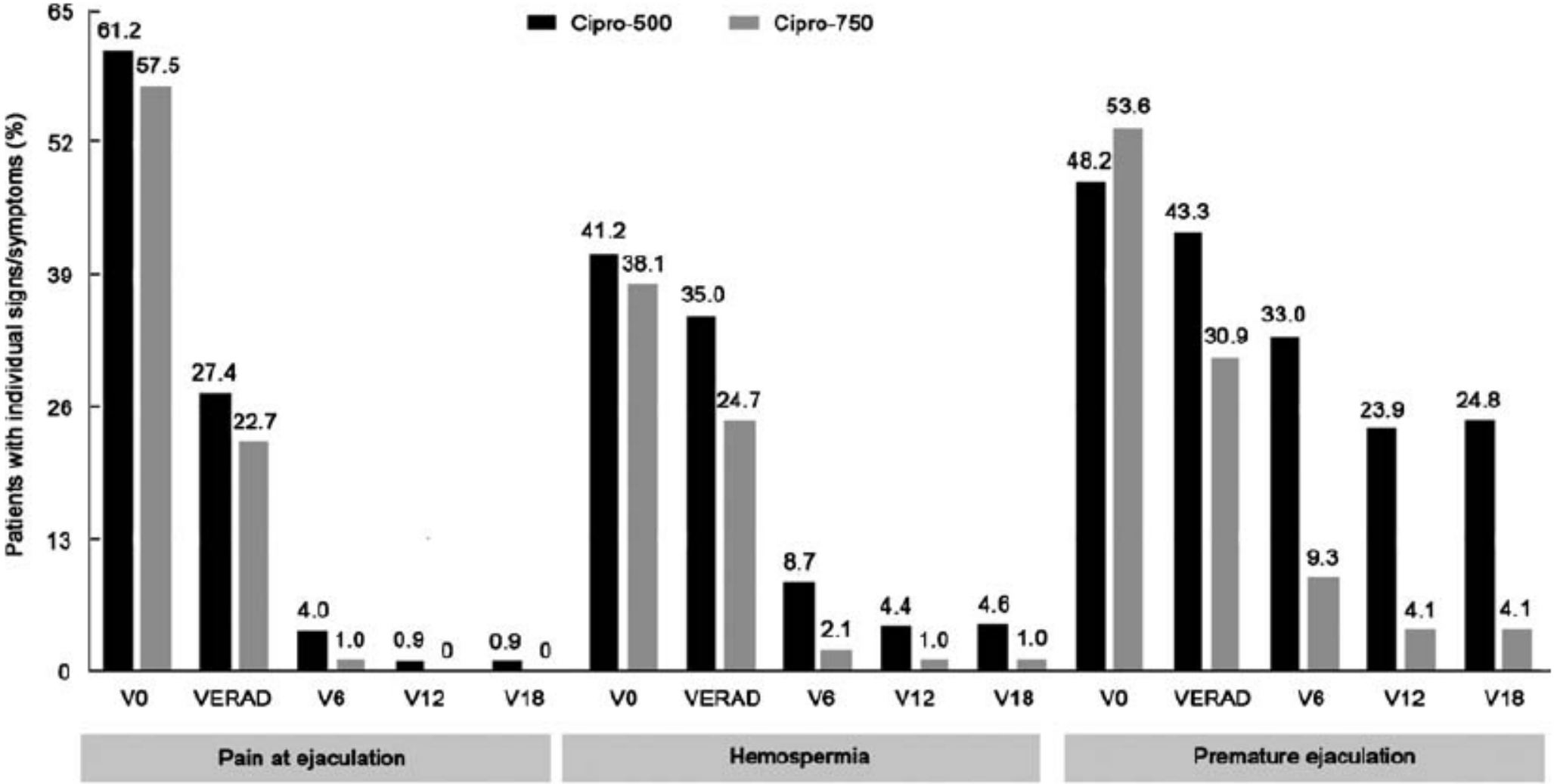
Vittorio Magri[1], Emanuele Montanari[2], Višnja Škerk[3], Alemka Markotić[3], Emanuela Marras[4], Antonella Restelli[5], Kurt G Naber[6] and Gianpaolo Perletti[4]

	Patient cohort	*Cipro-500*[b] *(n=170)*		*Cipro-750*[a] *(n=97)*	
Demography	Mean/median age	45/41		46/45	
Microbiological presentation at baseline	Single-agent infection, *n* (%)	132	(77.65)	83	(85.56)
	Two pathogens, *n* (%)	30	(17.65)	13	(13.40)
	Three pathogens, *n* (%)	8	(4.70)	1	(1.03)
	Total multiple infections, *n* (%)	38	(22.35)	14	(14.43)
	χ^2 (single-agent *vs.* multiple infections)		2.16 (P=0.14)		
Microbiological outcome after therapy	Eradication, *n* (%)	106	(62.35)	75	(77.32)
	Eradication with superinfection, *n* (%)	16	(9.41)	8	(8.25)
	Bacteriological success, *n* (%)	122	(71.76)	83	(85.57)
	Persistence, *n* (%)	47	(27.65)	12	(12.37)
	Persistence with superinfection, *n* (%)	1	(0.59)	2	(2.06)
	Bacteriological failure, *n* (%)	48	(28.24)	14	(14.43)
	X^2 (eradication *vs.* persistence)		8.57 (P=0.003)		
	χ^2 (bacteriological success *vs.* failure)		5.9 (P=0.015)		

[a] A cohort of patients treated with once-daily 750-mg ciprofloxacin for 4 weeks.

[b] A cohort of patients treated with once-daily 500-mg ciprofloxacin for 6 weeks.

Magri et al., Asian J Androl. 2013;13:819



Magri et al., Asian J Androl. 2013;13:819

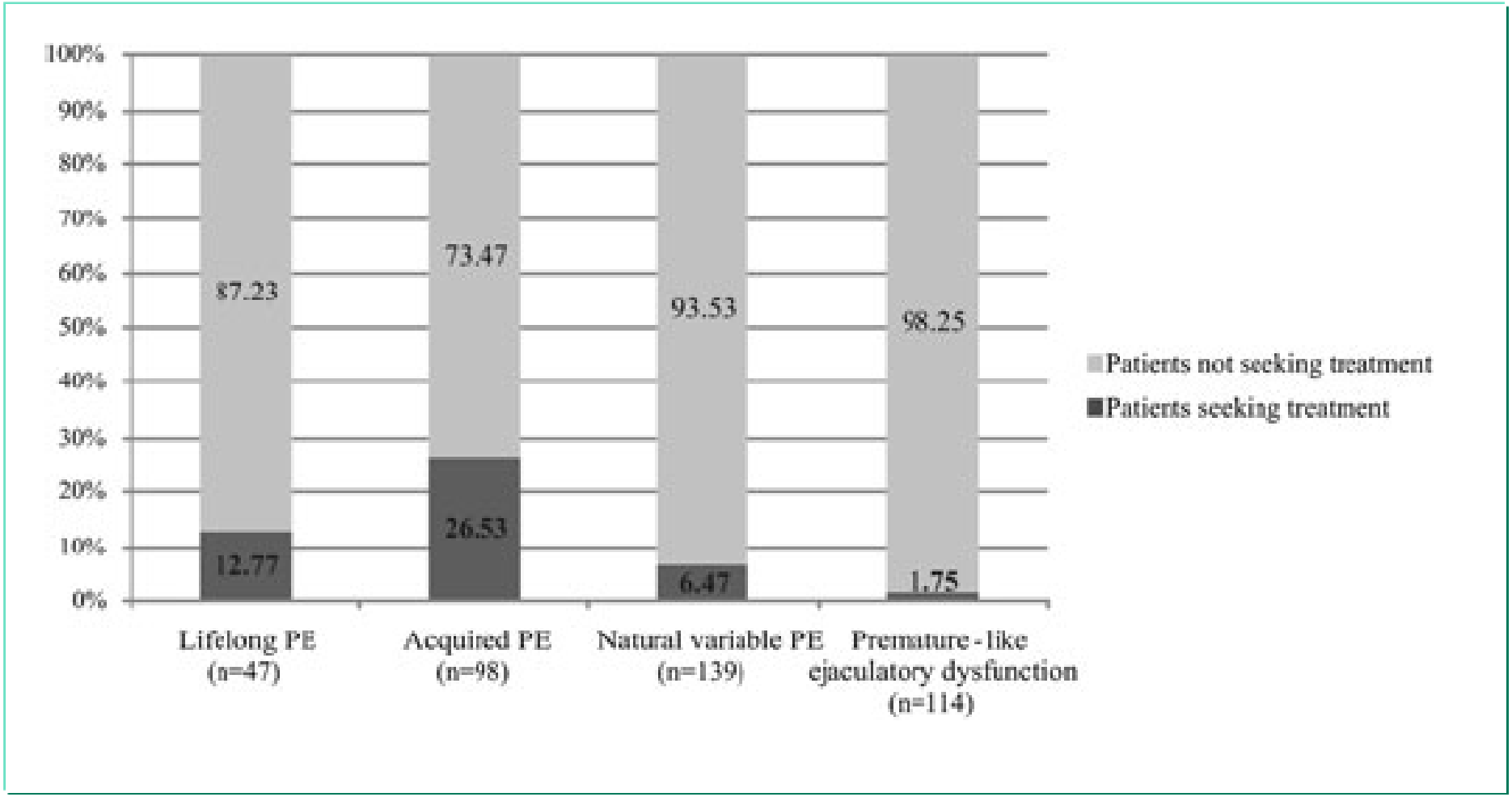
Premature ejaculation

1. **Genetic factors might underlie ejaculatory control.**
2. **Anxiety symptoms are associated with PE**
3. **PE is a couple problem**
4. **Prostatitis are frequently associated with acquired PE**
5. **Antibiotic treatment improve prostatitis-related PE**

Aetiology

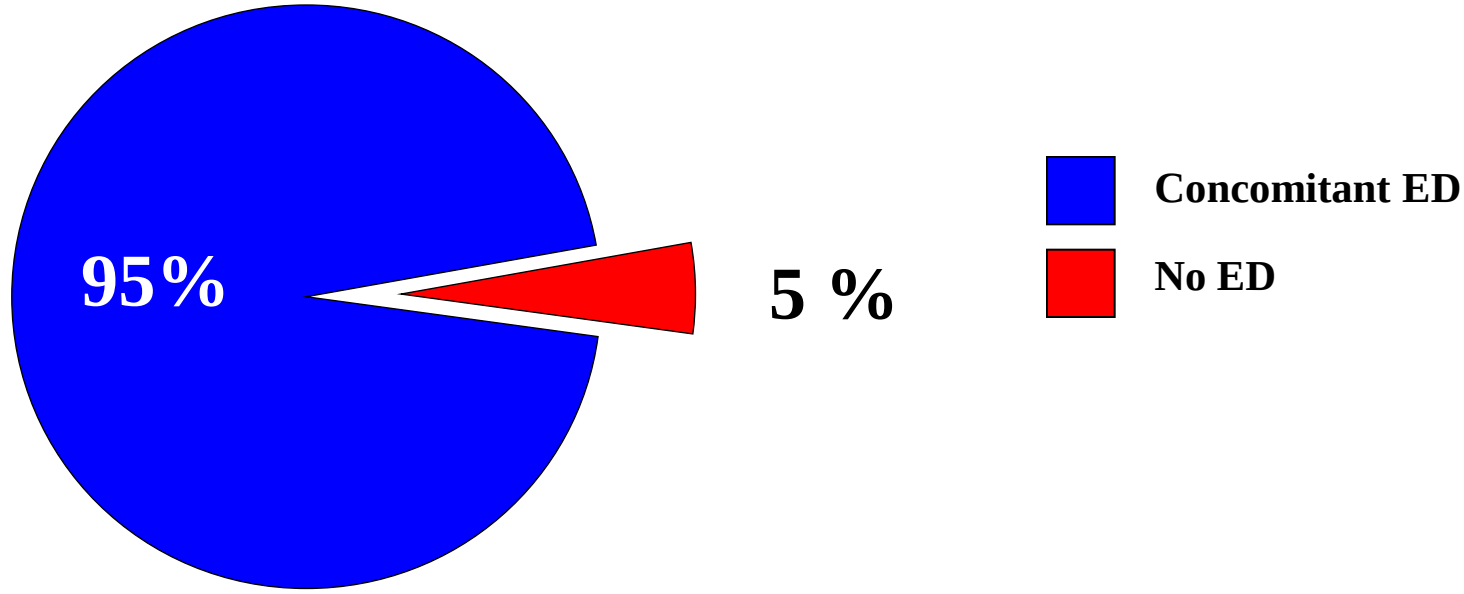
PE
- Life - long
- **Acquired**
  - Psychological or relationship problems
  - Organic
    - Urological dysfunctions:
      - -Prostatitis
      - -ED
    - Hormonal dysfunction

McMahon et al., J Sex Med. 2013;10:204.



Serefoglu et al., J Sex Med. 2011;8:540

Prevalence of ED in patients with PE

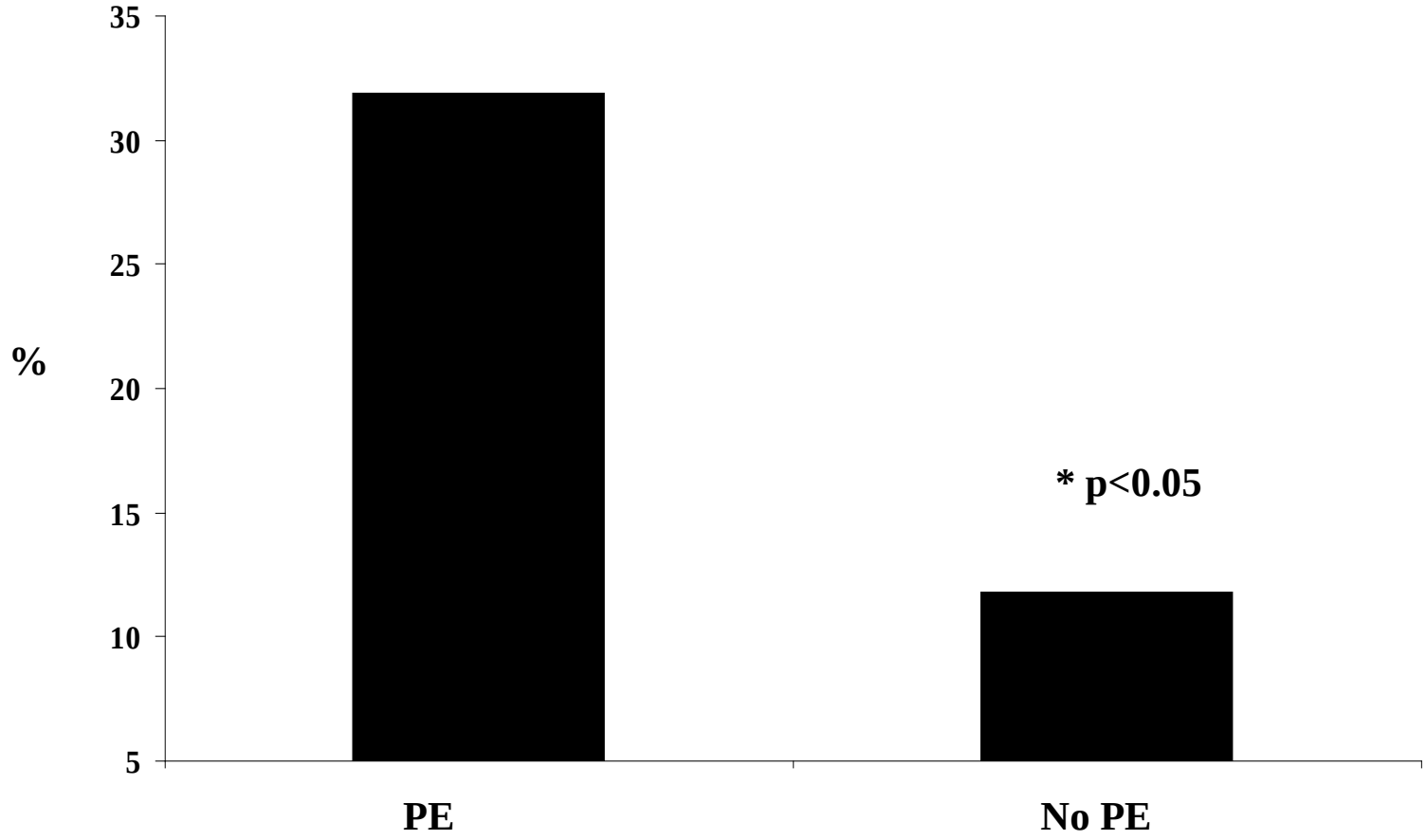


Although PE is considered the most common sexual problem in men

"The vast majority of patients do not seek help for PE until it is comorbid with ED"
(Waldlinger, 2002).

Corona et al., Eur. Urol. 2004; 46: 615

Percentages of men reporting erectile dysfunction : PEPA study

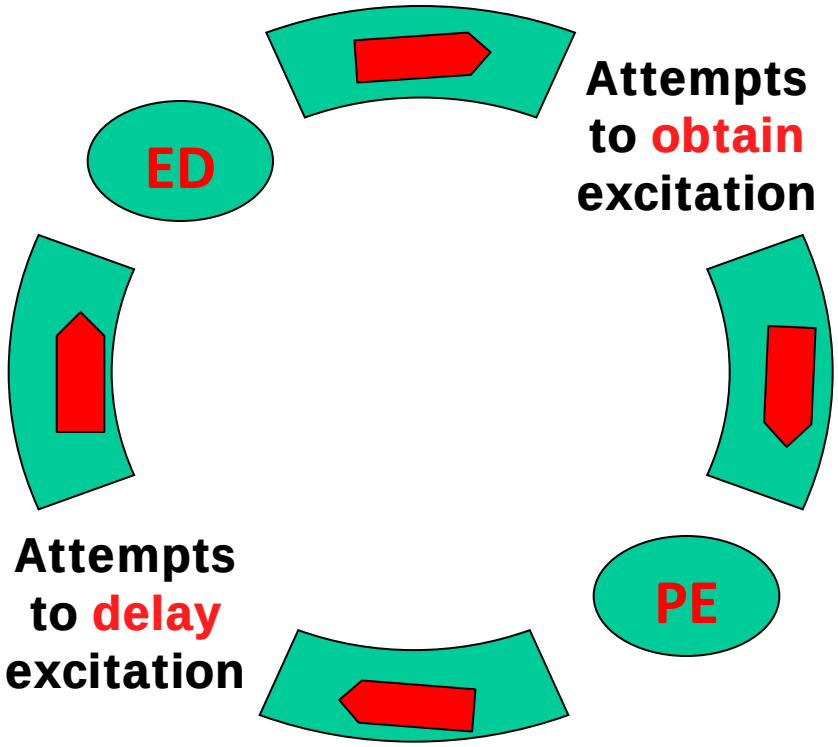


Porst et al., Eur Urol. 2007;51:816

Correlation between ejaculatory and erectile dysfunction

E. A. JANNINI,* F. LOMBARDO† and A. LENZI†

international journal of andrology, 28 (Suppl. 2): 40–45 (2005)

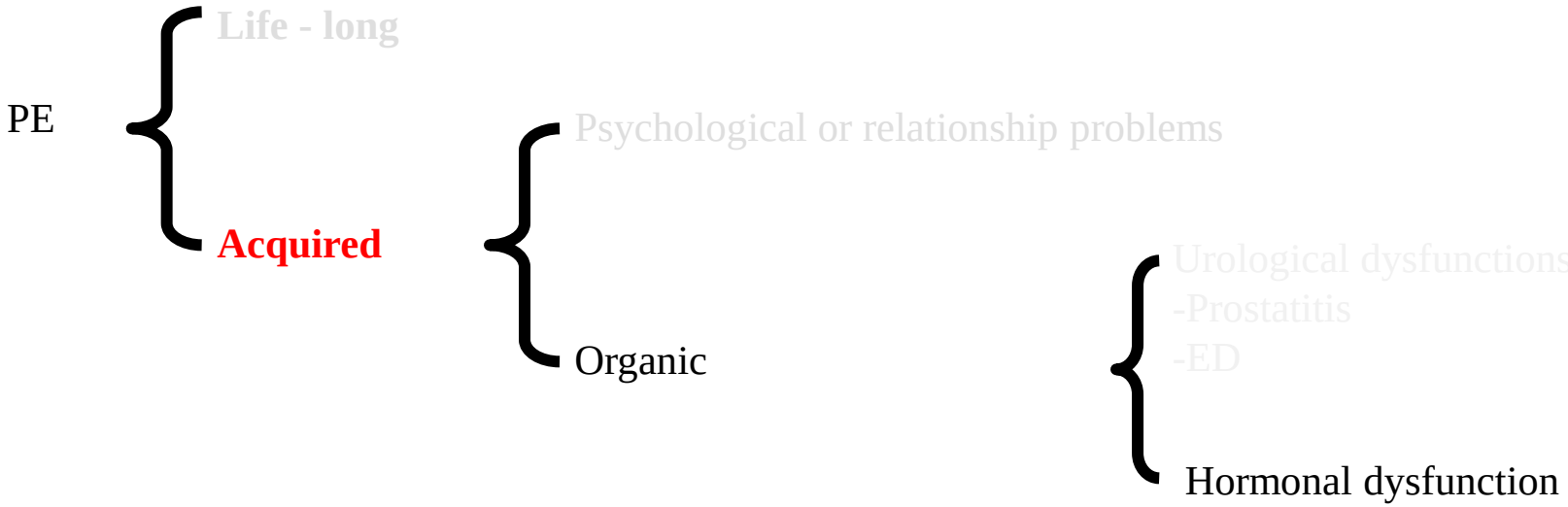


Possible relationship between ED and PE

Premature ejaculation

1. **Genetic factors might underlie ejaculatory control.**
2. **Anxiety symptoms are associated with PE**
3. **PE is a couple problem**
4. **Prostatitis are frequently associated with acquired PE**
5. **ED is frequently associated with PE ins subjects seeking medical care**

Aetiology



McMahon et al., J Sex Med. 2013;10:204.

Hormonal control of ejaculation: outline

- **Thyroid hormones**
- **Testosterone**
- **Prolactin**

Hormonal control of ejaculation: outline

- **Thyroid hormones**
- **Testosterone**
- **Prolactin**

European Urology

European Urology 46 (2004) 615–622

755 male subjects with sexual dysfunction

Psycho-Biological Correlates of Rapid Ejaculation in Patients Attending an Andrologic Unit for Sexual Dysfunctions

G. Corona[a,1], L. Petrone[a,1], E. Mannucci[b], E.A. Jannini[c], R. Mansani[a], A. Magini[a], R. Giommi[d], G. Forti[a], M. Maggi[a,*]

[a]*Department of Clinical Physiopathology, Andrology Unit, University of Florence, Viale Pieraccini 6, 50139 Florence, Italy*
[b]*Department of Clinical Physiopathology, Endocrinology Unit, University of Florence, Viale Pieraccini 6, 50139 Florence, Italy*
[c]*Department of Experimental Medicine, Course of Endocrinology and Medical Sexology, University of L'Aquila, L'Aquila, Italy*
[d]*International Institute of Sexology, Florence, Italy*

Accepted 1 July 2004

Available online 21 July 2004

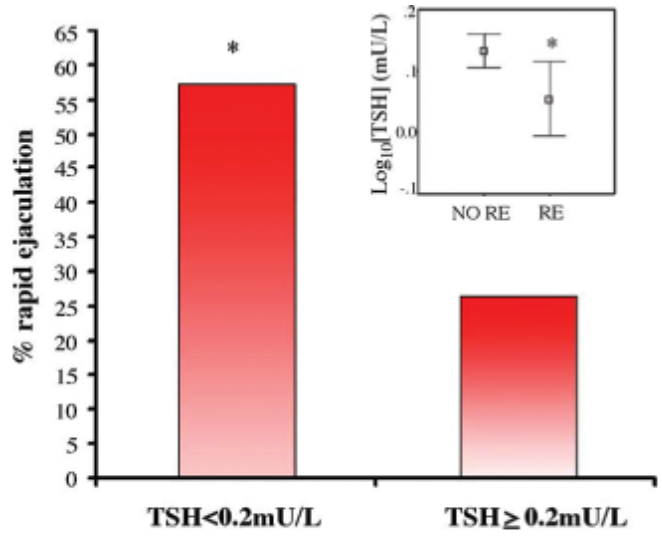


Fig. 2. Prevalence of rapid ejaculation (%) in hyperthyroid (TSH <0.2 mU/L) and euthyroid patients. Inset: Log_{10} [TSH], expressed as mean and 95% confidence of the mean, in patients reporting and not reporting rapid ejaculation (RE) (*$p < 0.05$).

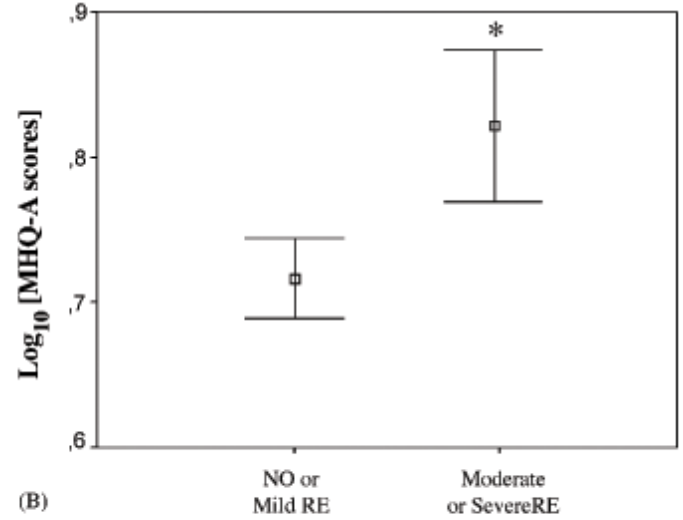


Fig. 3. Free-floating anxiety symptoms (Log_{10} [MHQ A-scores], expressed as mean and 95% confidence of mean, in patients reporting moderate or severe rapid ejaculation (RE) in comparison to the rest of the sample. A: all patients; B: patients with erectile dysfunction (* $p < 0.05$).

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ORIGINAL ARTICLE

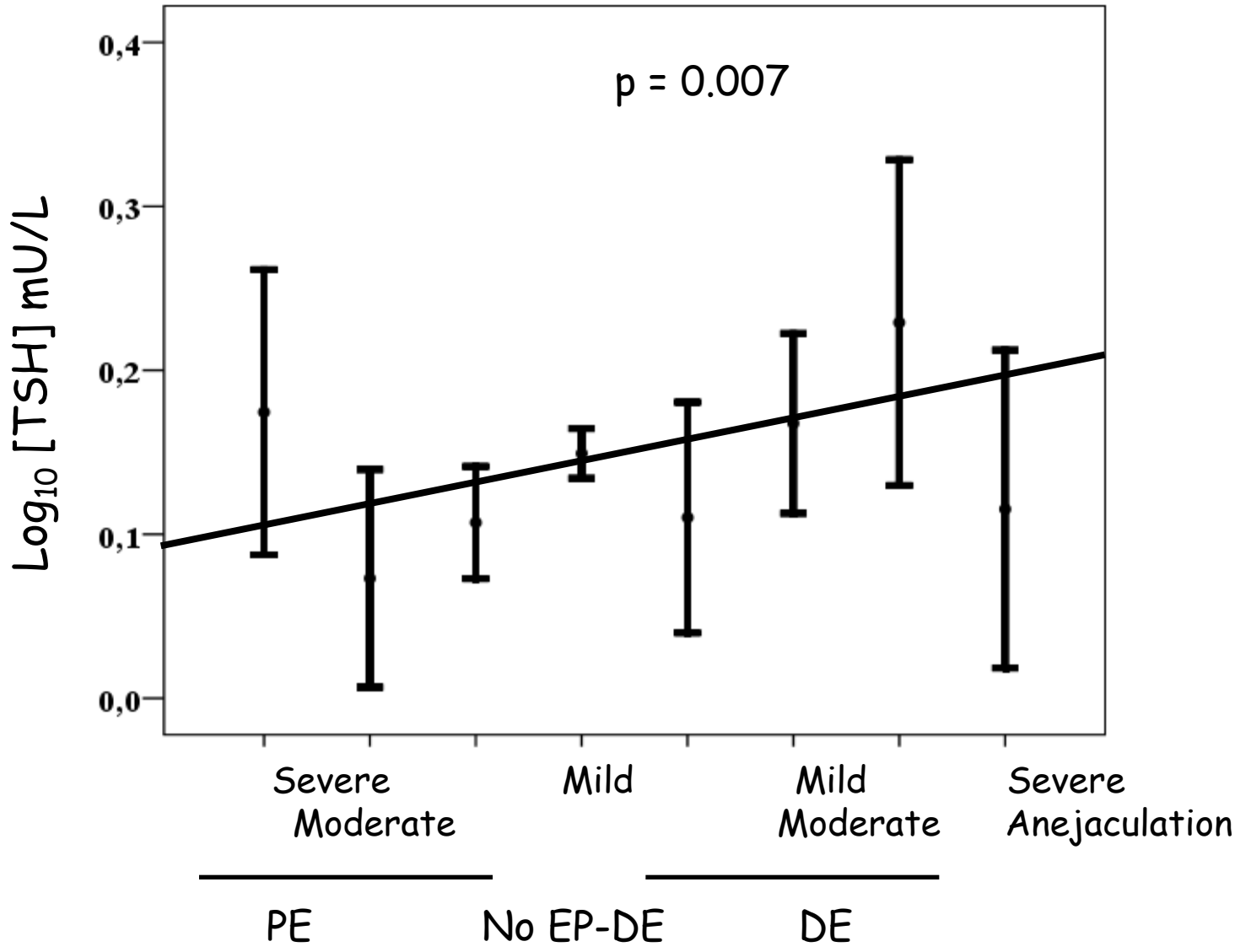
Premature and delayed ejaculation: two ends of a single continuum influenced by hormonal milieu

G. Corona,*† E. A. Jannini,‡ F. Lotti,* V. Boddi,* G. De Vita,* G. Forti,* A. Lenzi,§ E. Mannucci¶ and M. Maggi*

*Department of Clinical Physiopathology, Andrology Unit and Endocrinology, University of Florence, Florence, Italy, †Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, Italy, ‡School of Sexology, Department of Experimental Medicine, University of L'Aquila, L'Aquila, Italy, §Department of Medical Pathophysiology (DFM-Fisiopatologia Medica), Sapienza University, Rome, Italy, and ¶Diabetes Section Geriatric Unit, Department of Critical Care, University of Florence, Florence, Italy

n=2652; mean age 51.6±13.0 years

Corona et al. Int J Androl. 2010;33:1



Corona et al. Int J Androl. 2010;33:1

Hormonal control of ejaculation

1. **Thyroid hormones modulate ejaculatory reflex.**

Thyroid-Stimulating Hormone Assessments in a Dutch Cohort of 620 Men with Lifelong Premature Ejaculation without Erectile Dysfunction

Marcel D. Waldinger, MD, PhD,*† Aeilko H. Zwinderman, PhD,‡ Berend Olivier, PhD,†§ and Dave H. Schweitzer, MD, PhD¶

*Department of Psychiatry and Neurosexology, HagaHospital Leyenburg, The Hague, The Netherlands; †Department of Psychopharmacology, Faculty of Pharmaceutical Sciences and Rudolf Magnus Institute for Neurosciences, Utrecht University, Utrecht, The Netherlands; ‡Department of Medical Statistics, Clinical Epidemiology and Biostatistics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; §Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA; ¶Department of Internal Medicine and Endocrinology, Reinier de Graaf Groep, Delft-Voorburg, The Netherlands

Conclusion. Thyroid-stimulating hormone distribution was analyzed in a cohort of Dutch men with lifelong premature ejaculation and no erectile dysfunction. According to statistical analysis, there appeared to be no interaction between this ejaculatory complaint and the prevalence of thyroidal dysfunction. However, further studies are needed to gain more insight into the role of thyroid dysfunction and regulation of ejaculation time.

Waldinger et al., J Sex Med 2005;2:865

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No association between PE and thyroid hormones in subjects with lifelong PE

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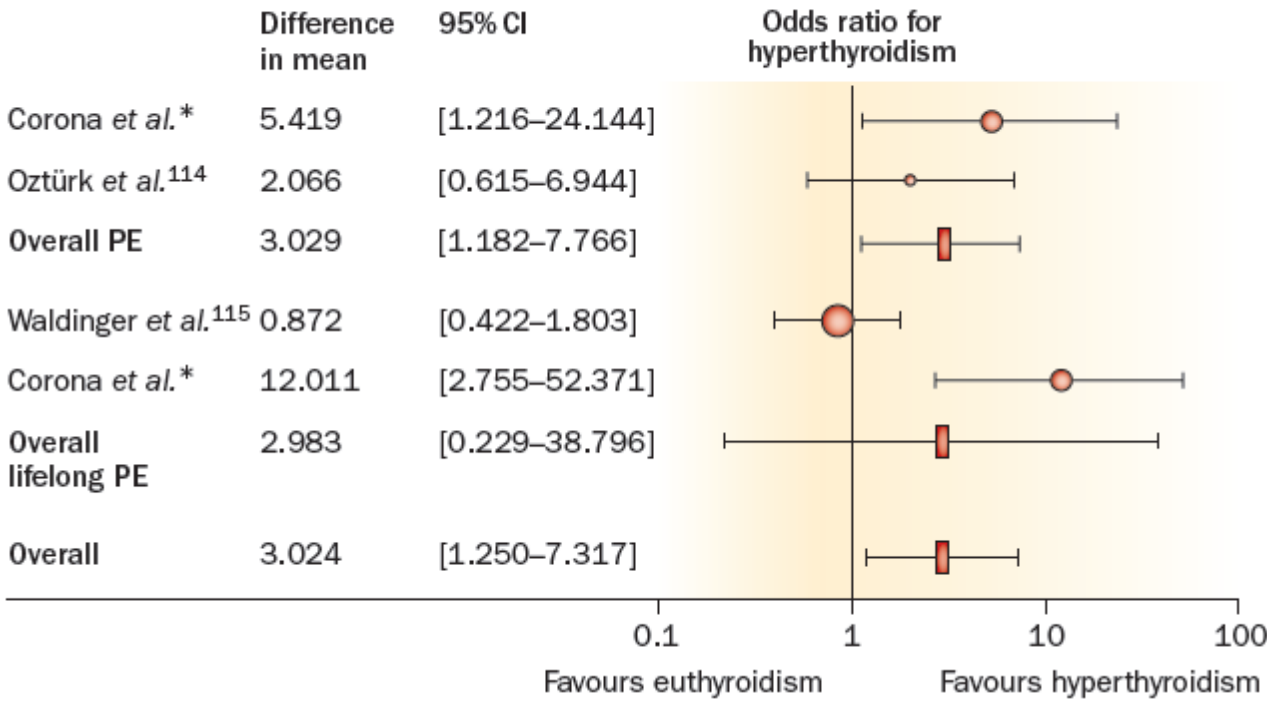
Waldinger et al., J Sex Med 2005;2:865

The hormonal control of ejaculation

Giovanni Corona, Emmanuele A. Jannini, Linda Vignozzi, Giulia Rastrelli and Mario Maggi



Corona et al., Nat Rew Urol 2012;9:508

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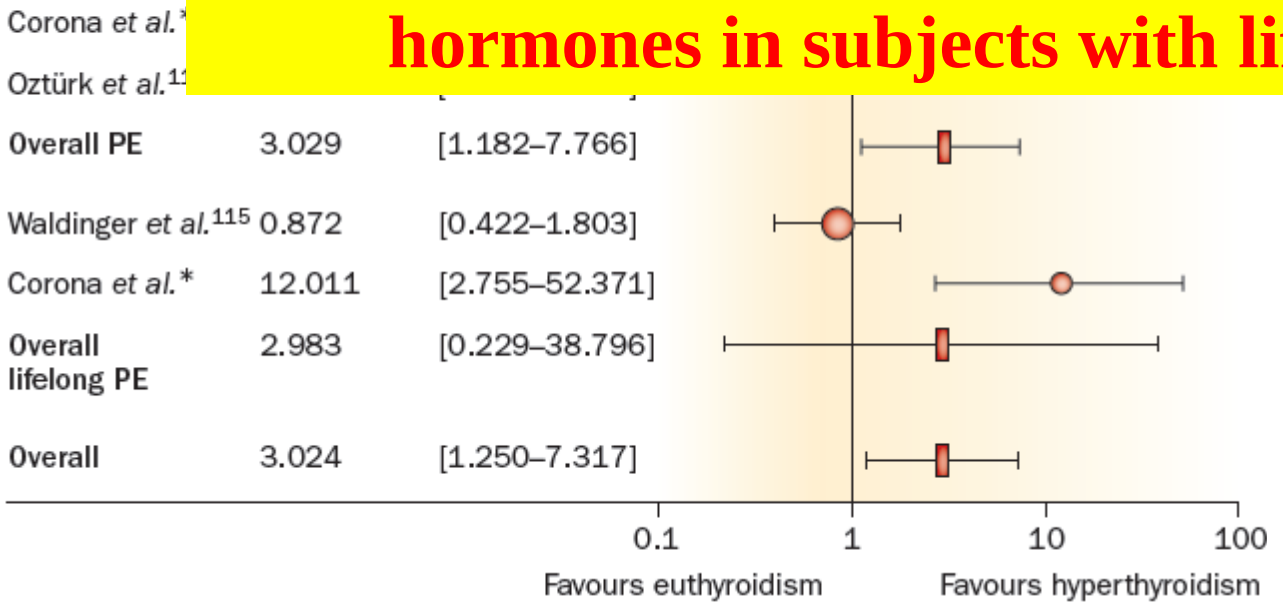
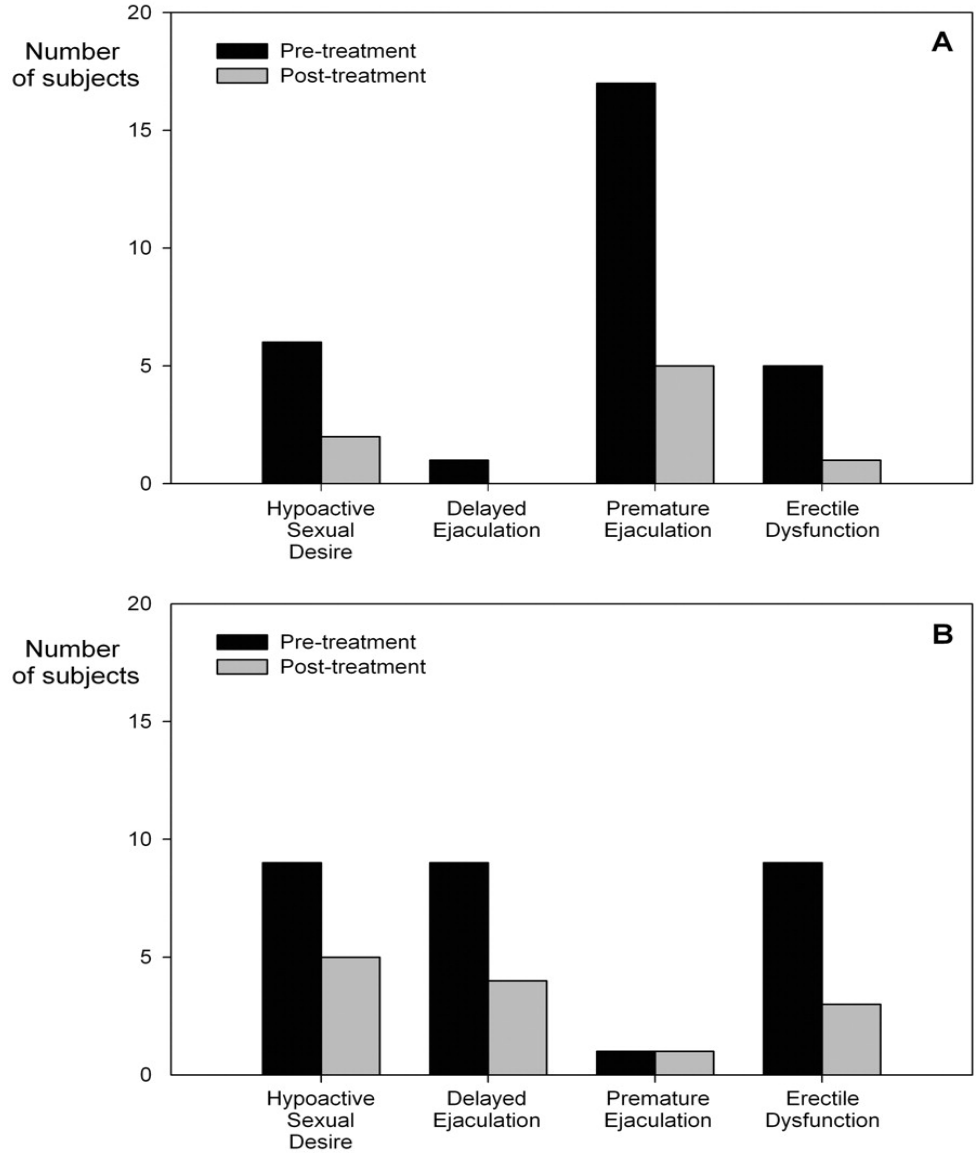


Corona et al., Nat Rew Urol 2012;9:508

Hormonal control of ejaculation

1. **Thyroid hormones modulate ejaculatory reflex.**
2. **Hyperthyroidism is a cause of acquired PE**

Prevalence of sexual dysfunction before and after recovery from hyperthyroidism (A) and hypothyroidism (B)



Carani et al., J Clin Endocrinol and Metab 2005;90:6472

Hormonal control of ejaculation

1. **Thyroid hormones modulate ejaculatory reflex.**
2. **Hyperthyroidism is a cause of acquired PE**
3. **Treatment of hyperthyroidism or hypothyroidism improves ejaculatory problems**

Investigation of the Neural Target Level of Hyperthyroidism in Premature Ejaculation in a Rat Model of Pharmacologically Induced Ejaculation

Asif Cahangirov, MD,* Ahmet Cihan, MD,* Nergis Murat, PhD,† Omer Demir, MD,* Guven Aslan, MD,* Sedef Gidener, MD,* and Ahmet Adil Esen, MD*

*Department of Urology, School of Medicine, Dokuz Eylul University, Izmir, Turkey; †Department of Pharmacology, School of Medicine, Dokuz Eylul University, Izmir, Turkey

DOI: 10.1111/j.1743-6109.2010.02042.x J Sex Med 2011;8:90–96

Conclusion

Elevated thyroid hormone level triggers shortened ejaculation latency time in male rats. Hyperthyroidism affects both phases of ejaculatory process. Spinal transection of the rats resolves the effects of thyroid hormone on ejaculation parameters. Effects of hyperthyroidism on ejaculation pathways probably take place mainly in the supraspinal centers.

J Sex Med 2011;8:90–96

Table 1 The comparison of ejaculation parameters between spinal transected control and hyperthyroid rats

	Control rats			Hyperthyroid rats			Group1 vs. Group 3	Group 2 vs. Group 4
	Group 1 (Spinal Intact)	Group 2 (Spinal Tx)	*P*	Group 3 (Spinal Intact)	Group 4 (Spinal Tx)	*P*	*P*	*P*
SV tonic pressure maximum amplitude (mmHg)	1.0 ± 0.1	1.7 ± 0.2	0.007	2.3 ± 0.3	1.5 ± 0.2	0.047	0.001	$P > 0.05$
SV phasic contraction number	33.0 ± 5.5	14.7 ± 3.9	0.021	57.5 ± 3.1	13.3 ± 4.0	<0.001	0.003	$P > 0.05$
SV phasic contraction maximal amplitude (mmHg)	4.6 ± 1.5	3.4 ± 0.7	0.495	21.1 ± 6.4	7.9 ± 3.4	0.100	0.031	$P > 0.05$
Interval between SV and BS muscle contraction	9.3 ± 1.3	8.7 ± 1.0	0.712	5.1 ± 0.4	8.7 ± 1.1	0.011	0.009	$P > 0.05$
BS muscle EMG AUC (10^{-4} Vsec)	4.8 ± 0.6	7.9 ± 2.9	0.316	13.6 ± 3.7	9.6 ± 4.1	0.478	0.038	$P > 0.05$
Ejaculation latency time (sec)	426 ± 49.6	1,229 ± 79.1	<0.0001	261 ± 7.3	1,087 ± 151.5	0.002	0.008	$P > 0.05$

SV = seminal vesicle; EMG = electromyographic.

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Hormonal control of ejaculation: outline

- Thyroid hormones
- **Testosterone**
- Prolactin

Psychobiological Correlates of Delayed Ejaculation in Male Patients With Sexual Dysfunctions

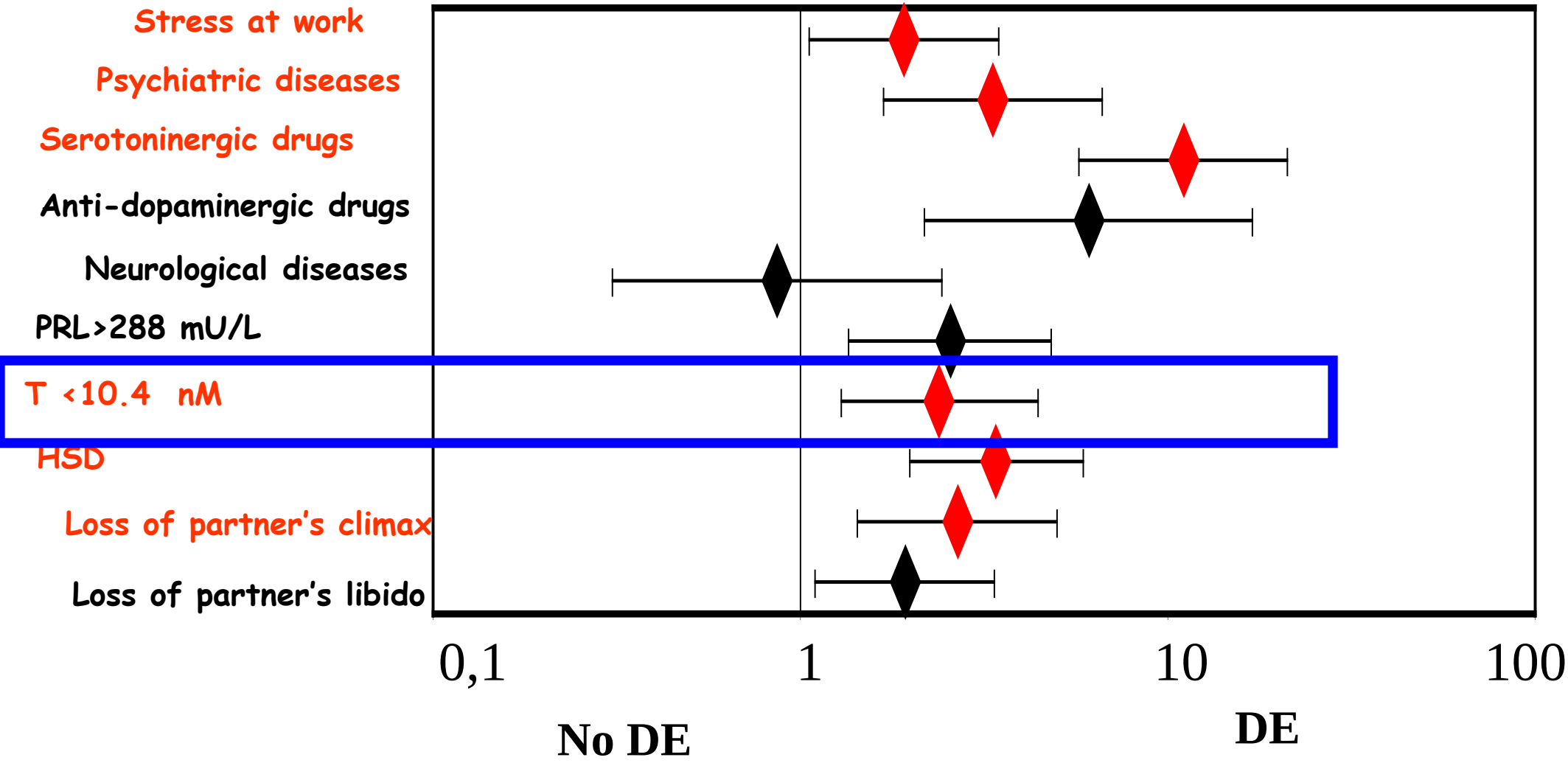
GIOVANNI CORONA,*† EDOARDO MANNUCCI,‡ LUISA PETRONE,* ALESSANDRA D. FISHER,* GIANCARLO BALERCIA,§ GIUSEPPE DE SCISCIOLO,|| ALESSANDRO PIZZOCARO,¶ ROBERTA GIOMMI,# VALERIO CHIARINI,† GIANNI FORTI,* AND MARIO MAGGI*

*From the *Andrology Unit, Department of Clinical Physiopathology, University of Florence, Italy; †Endocrinology Unit, Maggiore-Bellaria Hospital Bologna, Italy; ‡Diabetes Section Geriatric Unit, Department of Critical Care, University of Florence, Italy; §Endocrinology Unit, Polytechnic University of Marche Ancona, Italy; ||Spinal Unit, Neurophysiopathology Service, University of Florence, Italy; ¶Humanitas Clinical Institute, Rozzano, Milan, Italy; and #International Institute of Sexology, Florence, Italy.*

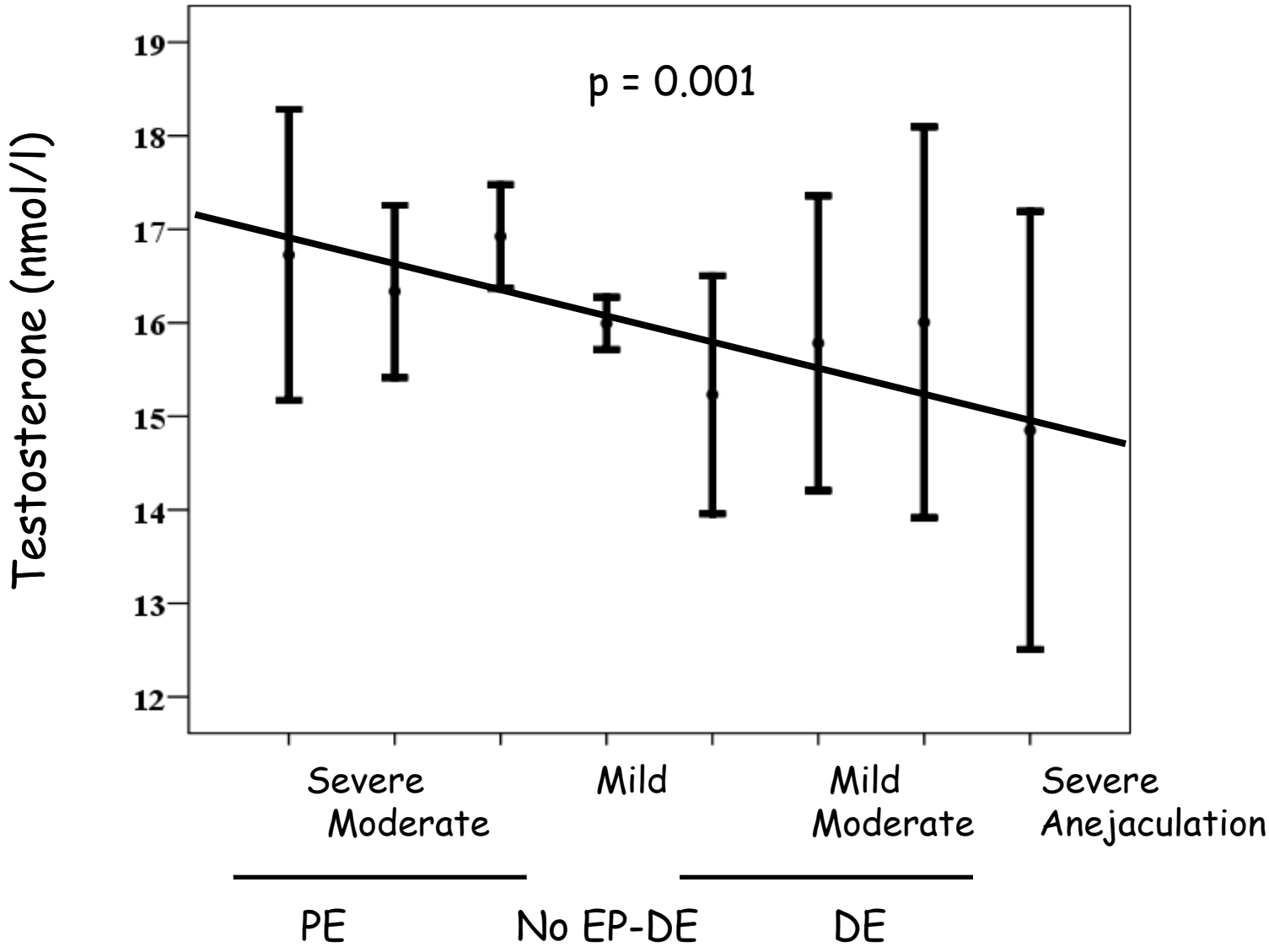
n=1632; mean age 50.1±12.0 years

Corona et al. J Androl. 2006;27:453

Relative risk for the parameters correlated to delayed ejaculation (DE) after adjustment for confounding factors

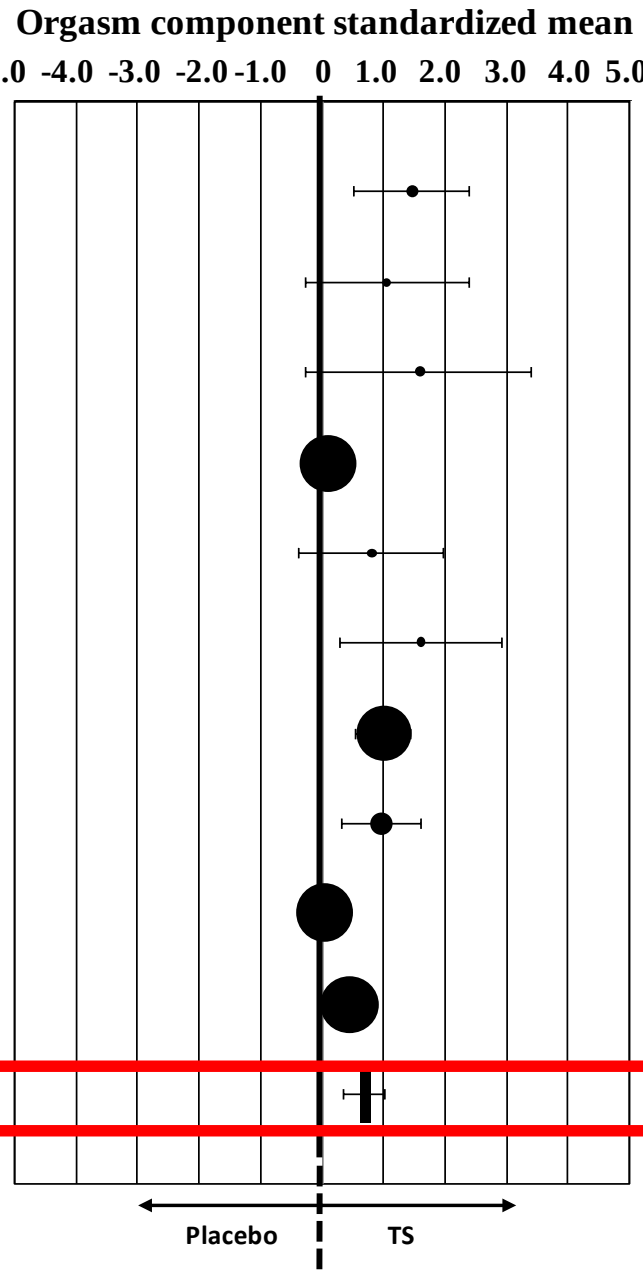


Corona et al. J Androl. 2006;27:453



Corona et al. Int J Androl. 2010;33:1

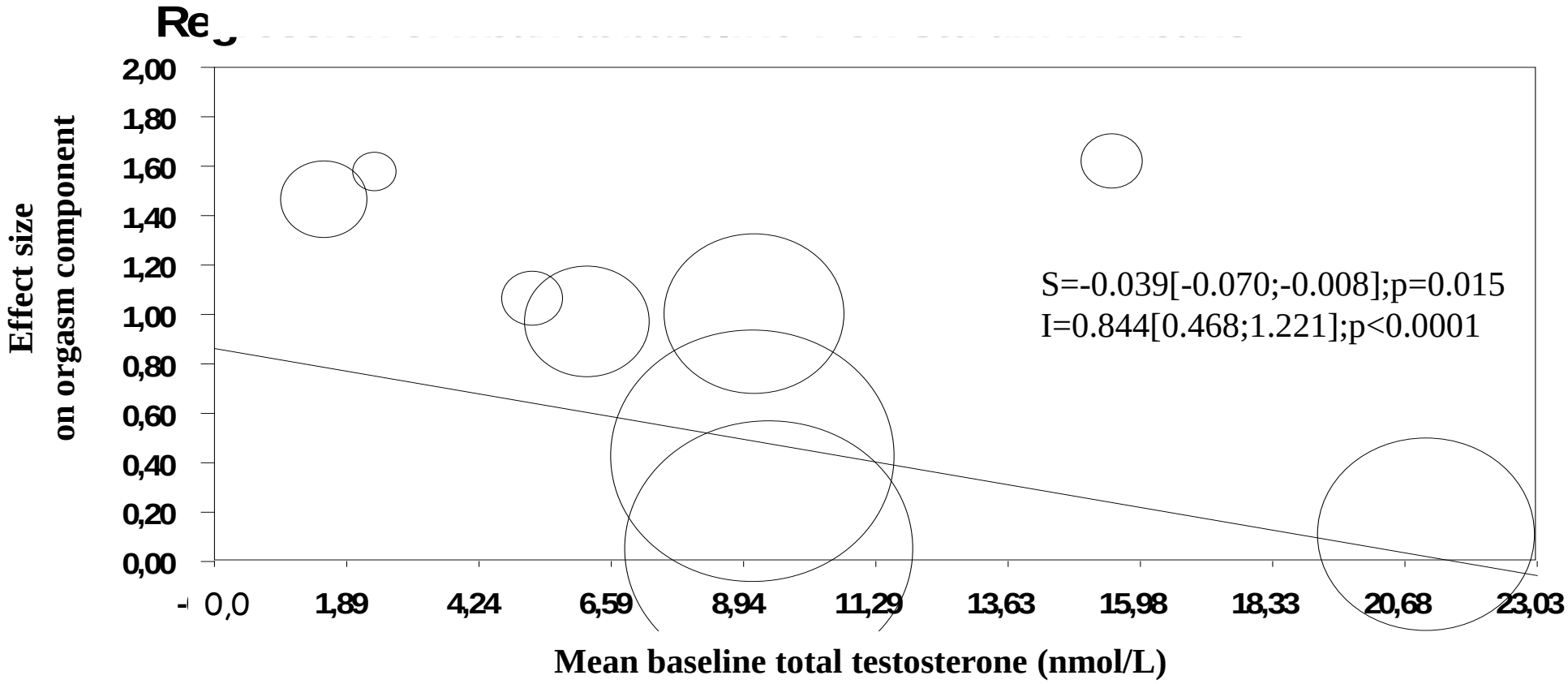
Effect size (with 95%CI) of testosterone supplementation (TS) versus placebo on orgasm component



Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Skakkebaek et al., 1981	1,46	0,52	2,40	0,00
Davidson et al., 1979	1,06	-0,26	2,39	0,12
Kwan et al., 1983	1,58	-0,26	3,41	0,09
Gluud et al., 1988	0,11	-0,27	0,49	0,58
Carani et al., 1990	0,79	-0,38	1,97	0,19
Schiavi et al., 1997	1,62	0,30	2,94	0,02
Cavallini et al., 2004	1,00	0,54	1,46	0,00
Chaing et al., 2009	0,97	0,31	1,62	0,00
Jones et al., 2011	0,05	-0,24	0,34	0,74
Hackett et al., 2013	0,42	0,13	0,72	0,00
Overall	**0.68**	**0.34**	**1.02**	**0.001**

Corona et al., J Sex Med. 2014;11:1577

Meta-regression analysis for total testosterone



Corona et al., J Sex Med. 2014;11:1577

Hormonal control of ejaculation

1. **Thyroid hormones modulate ejaculatory reflex.**
2. **Hyperthyroidism is a cause of acquired PE**
3. **Treatment of hyperthyroidism or hypothyroidism improves ejaculatory problems**
4. **Testosterone modulates ejaculatory reflex**

Hormonal control of ejaculation: outline

- Thyroid hormones
- Testosterone
- **Prolactin**

Hypoprolactinemia: A New Clinical Syndrome in Patients with Sexual Dysfunction

Giovanni Corona, MD,*,** Edoardo Mannucci, MD,† Emmanuele A Jannini, MD,‡ Francesco Lotti, MD,* Valdo Ricca, MD,§ Matteo Monami, MD,† Valentina Boddi, MD,* Elisa Bandini, MD,* Giancarlo Balercia, MD,¶ Gianni Forti, MD,* and Mario Maggi, MD*

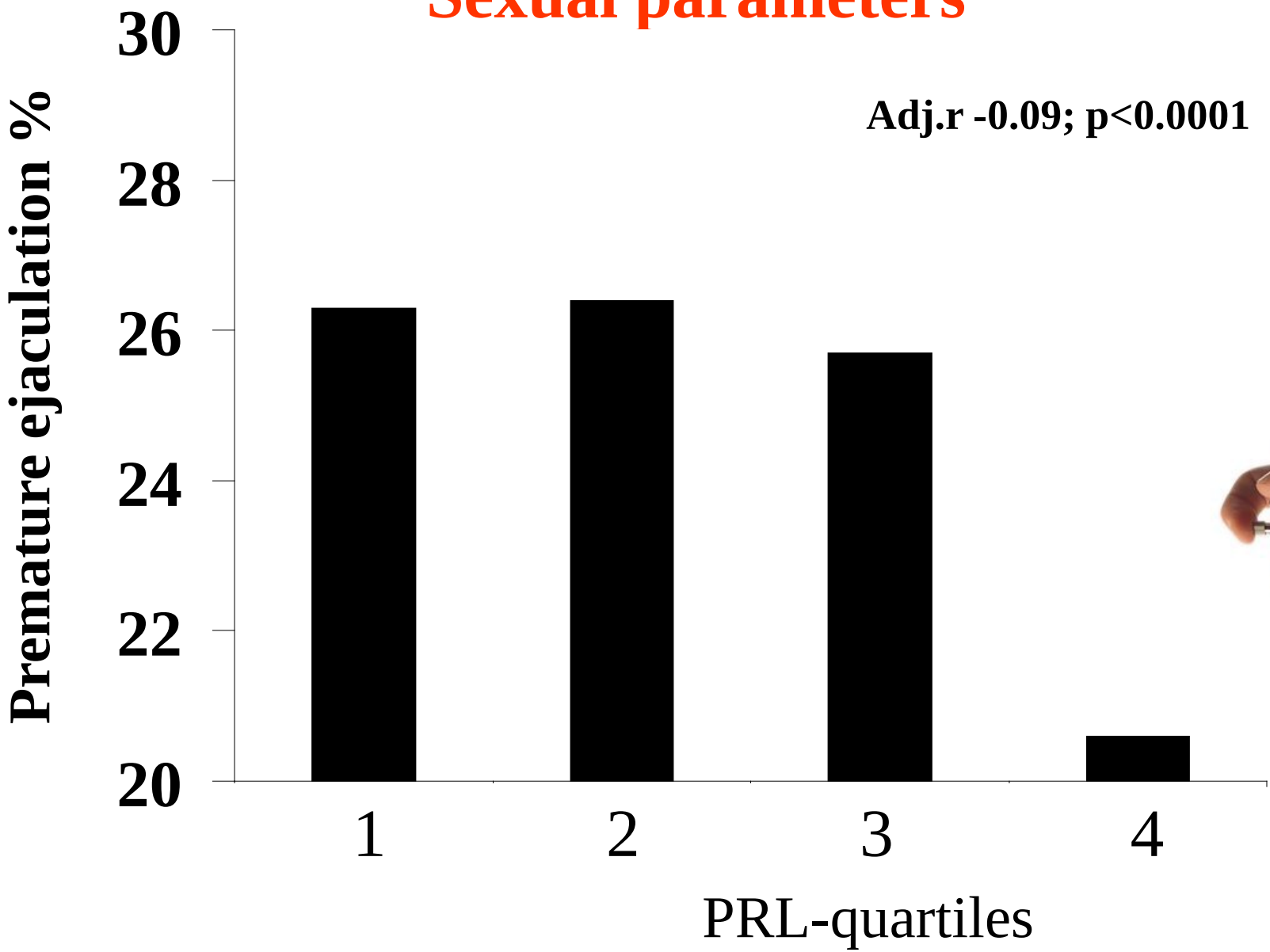
*Andrology Unit, Department of Clinical Physiopathology, University of Florence, Florence, Italy; †Diabetes Section Geriatric Unit, Department of Critical Care, University of Florence, Florence, Italy; ‡Department of Experimental Medicine, School of Sexology, University of L'Aquila, L'Aquila, Italy; §Psychiatry Unit, Department of Neurological and Psychiatric Sciences, University of Florence, Florence, Italy; ¶Endocrinology Unit, Polytechnic University of Marche, Ancona, Italy; **Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, Italy

DOI: 10.1111/j.1743-6109.2008.01206.x

A consecutive series of 2,496 male patients (w/o hyperprolactinemia and medication) attending the outpatient clinic for sexual dysfunction at the University of Florence, Florence, Italy

Corona et al., J Sex Med. 2009;6:1457

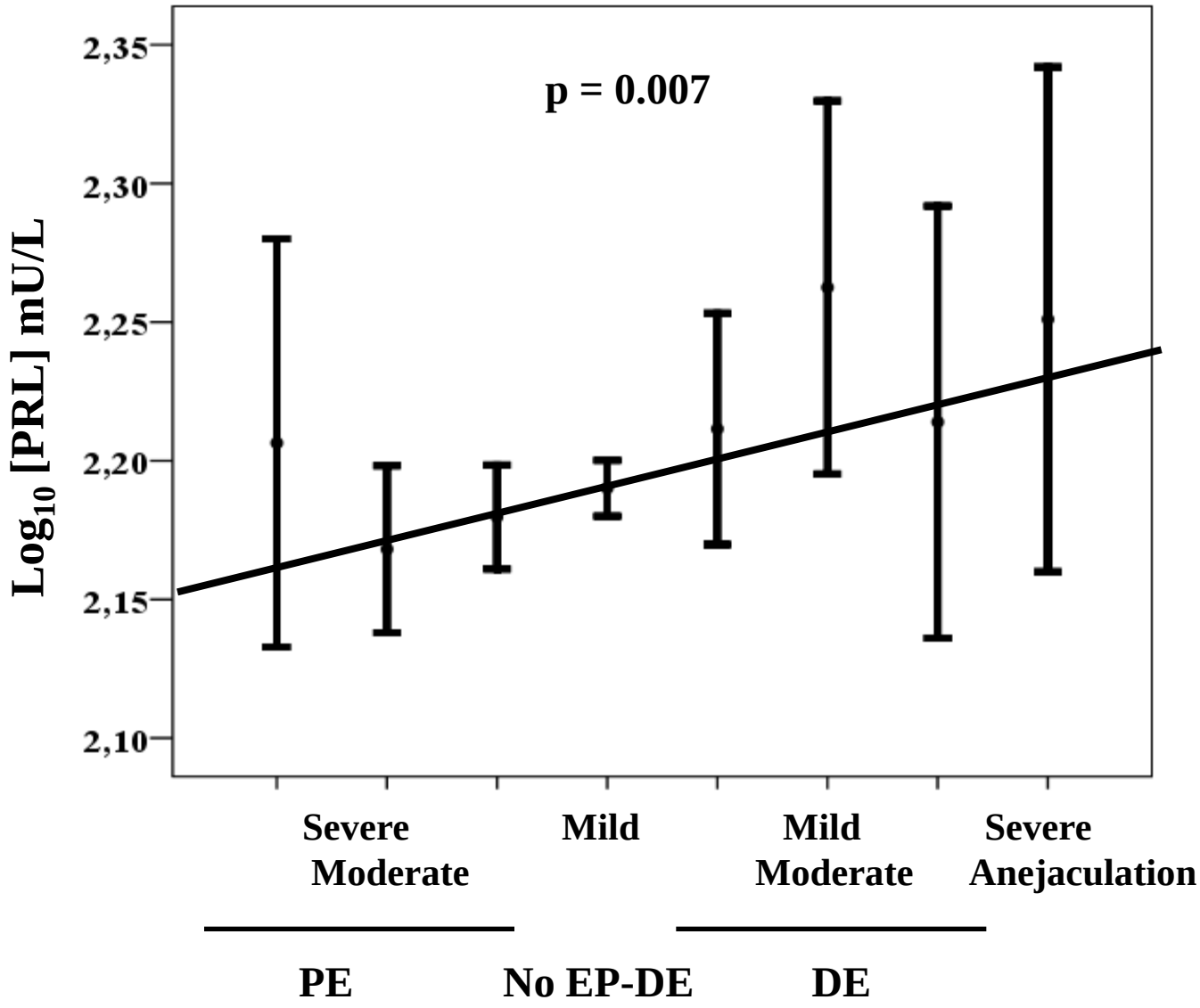
Sexual parameters



Adj.r -0.09; p<0.0001

Adjusted for
- age
- Smoking
- BMI
- Medicaments

Corona et al., J Sex Med. 2009;6:1457



Corona et al. Int J Androl. 2010;33:1

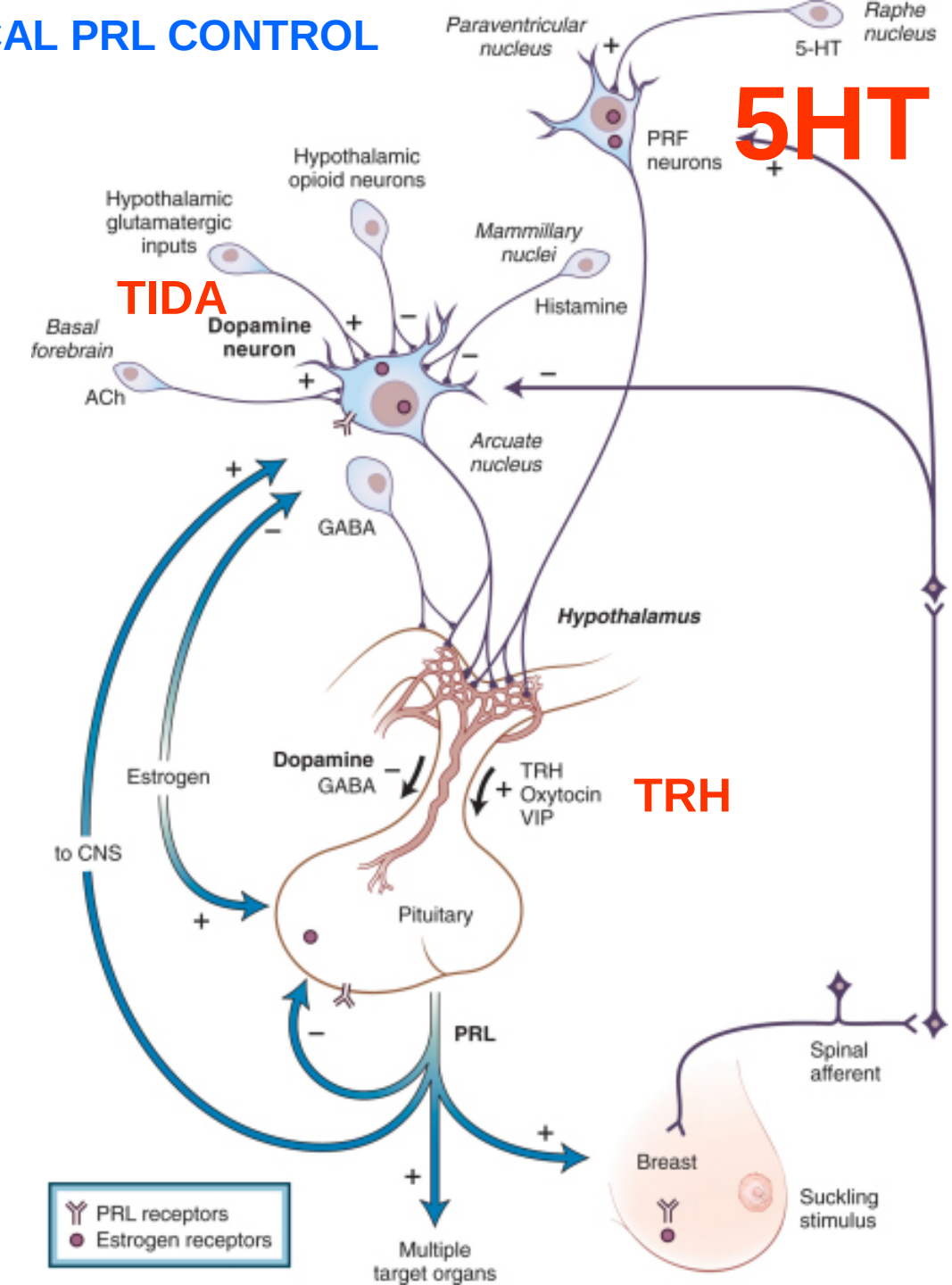
NEUROENDOCRINOLOGICAL PRL CONTROL

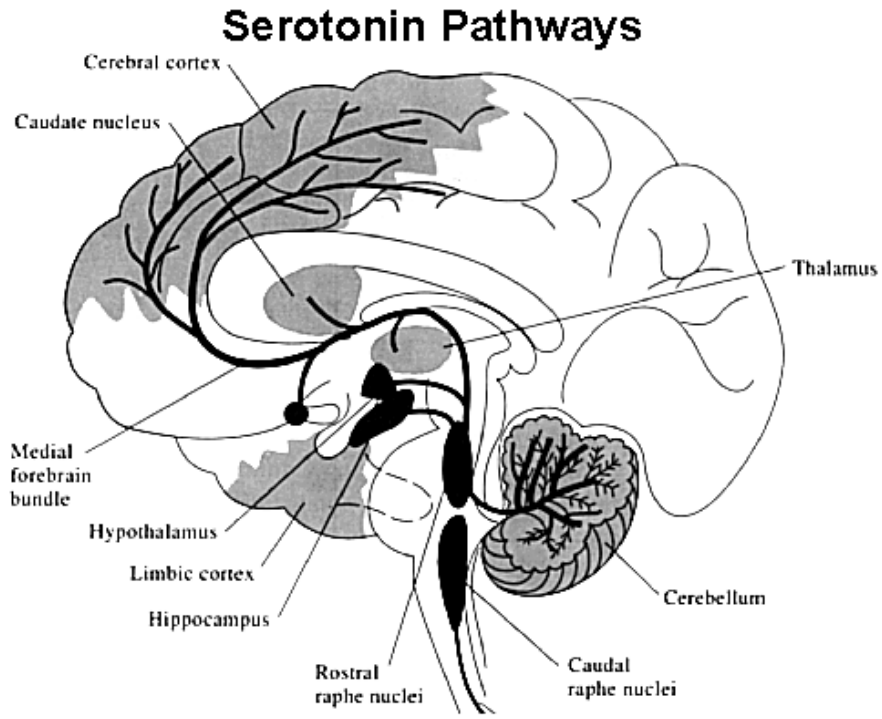
Prolactin-inhibiting factors

- **DA (tuberohypophyseal TIDA system)**
- endothelin-1
- TGFβ1

Prolactin-releasing factors

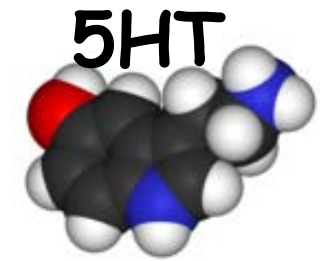
- **5HT**
- **TRH**
- VIP
- Oxytocin
- EGF
- Basic FGF
- Opioid

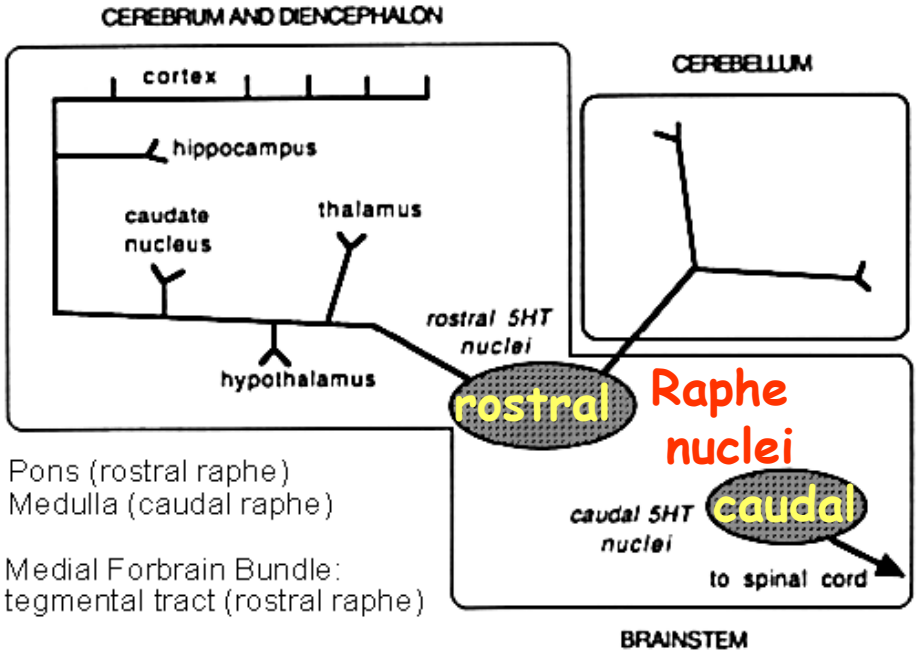




Biological functions of 5HT in CNS:

- ↓ Sexual responsiveness
  - ↓sexual desire
  - ↑Ejaculatory time
- ↑ Mood
- ↓ Food intake
- ↑ Metabolism



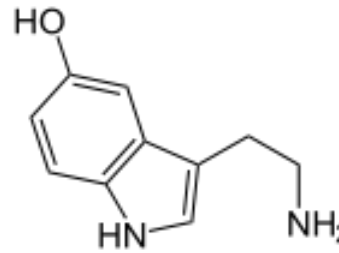


Hyposerotonergic tone:

- decreased orgasm

- anxiety & depression

- metabolic syndrome



Salivary Prolactin as a Marker for Central Serotonin Turnover

Stephen G. Lindell, Stephen J. Suomi, Susan Shoaf, Markku Linnoila,† and J. Dee Higley

*Central nervous system (CNS) serotonin deficits have been linked to many pathological behaviors in both human and nonhuman primates. The plasma prolactin response to fenfluramine has been widely used to assess CNS serotonin functioning in humans. Prolactin is also found as an integrated measure in saliva. We hypothesized that salivary prolactin concentrations would correlate positively with cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid (5-HIAA) in rhesus monkeys. Twenty-seven adult male and female rhesus macaques (*Macaca mulatta*) were sampled for concurrent saliva, blood, and CSF. Saliva and blood serum were assayed for prolactin concentrations, and CSF was assayed for 5-HIAA, homovanillic acid (HVA), and 3-methoxy-4-hydroxyphenylglycol (MHPG). Salivary prolactin concentrations were positively correlated with CSF 5-HIAA concentrations. No other relationships between any of the measures, including that between salivary prolactin and serum prolactin, were found to be statistically significant. These findings suggest the possibility of using salivary prolactin concentrations as an index of CNS serotonin turnover in humans.* Biol Psychiatry 1999;46: 568–572 © *1999 Society of Biological Psychiatry*

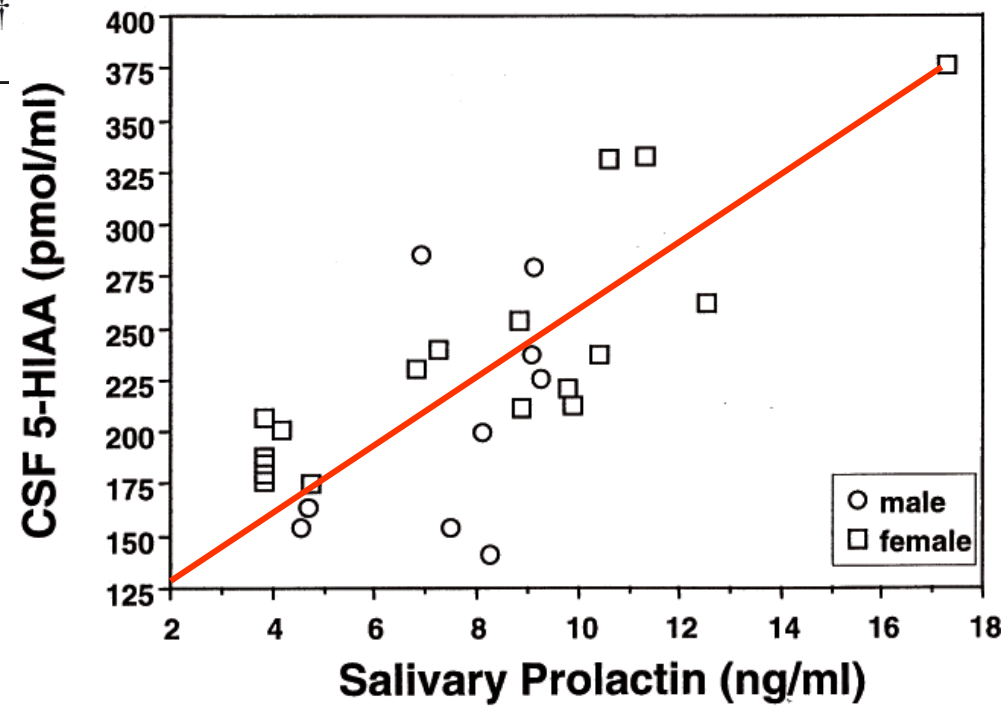


Figure 1. Correlation between cerebrospinal fluid 5-hydroxyindoleacetic acid (CSF 5-HIAA) and salivary prolactin concentrations in male (-E-) and female (-G-) rhesus monkeys ($r = .75$, $p < .0002$). Individuals ($n = 6$, all females) with salivary prolactin concentrations below the assay level of detection (3.84 ng/ml) were assigned this value. The correlation was still significant ($r = -.68$, $p < .0004$) when the highest salivary prolactin concentration was removed.

Salivary Prolactin as a Marker for Central Serotonin Turnover

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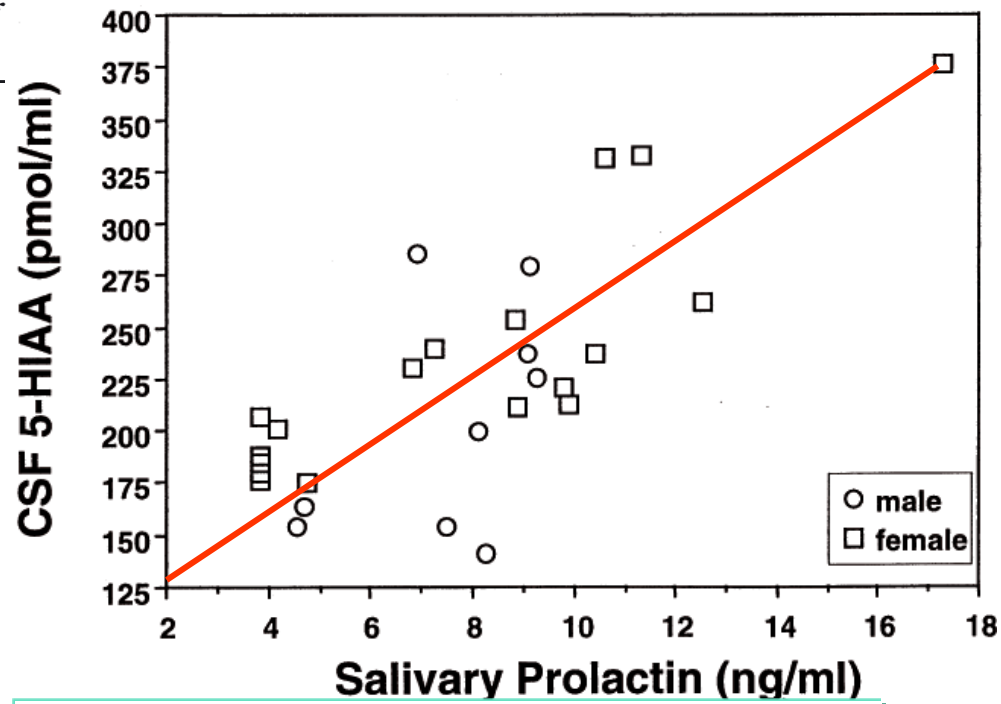
Hypoprolactinemia= Hyposerotonergic tone



HYPOTHESIS?

roxyin-
ncentra-
= .75,
$p < .0002$). Individuals ($n = 6$, all females) with salivary prolactin concentrations below the assay level of detection (3.84 ng/ml) were assigned this value. The correlation was still significant ($r = -.68$, $p < .0004$) when the highest salivary prolactin concentration was removed.

Comparisons between subjects with prolactin-secreting pituitary adenomas (8 micro and 5 macroadenomas) and age-BMI-smoking habit- testosterone matched controls (1:5 ratio).

	Case patients	Controls	p<
Age (years)	47.8±12.2	46.8±11.0	ns
BMI (Kg/m^2)	27.5±4.1	27.6±3.3	ns
Total testosterone (nmol/L)	10.6±4.8	11.5±4.5	ns
Current smoker (%)	23.1	22.2	ns
Hypoactive sexual desire (%)	100	41.9	0.0001
Premature ejaculation (%)	25.5	32.3	ns
Total cholesterol mg/dl	201.1±30.6	206.9±39.7	ns
LDL-cholesterol mg/dl	120.5±32.3	129.5±32.3	ns
Triglycerides mg/dl	98[78-165]	123[82-180]	ns
Glycaemia mg/dl	90 [83-99]	93[88-102]	ns
Dynamic PSV (cm/sec)	52.5±31.3	52.7±24.3	ns
MHQ-A score (free-floating anxiety symptoms)	5.3±3.4	5.8±3.1	ns

Corona et al., J Sex Med. 2009;6:1457

Comparisons between subjects with prolactin-secreting pituitary adenomas (8 micro and 5 macroadenomas) and age-BMI-smoking habit- tes[illegible]ne matched controls (1:5 ratio).

	Case patients		
Age (years)	47.8±12.2		ns
BMI (Kg/m^2)	27.5		ns
Total testosterone (nmol/L)		[illegible]±4.5	ns
Current smoker (%)		22.2	ns
Hypoactive sexual desire (%		41.9	0.0001
Premature ejacul	[illegible].3	32.3	ns
Total ch	201.1±30.6	206.9±39.7	ns
[illegible]	120.5±32.3	129.5±32.3	ns
T[illegible]	98[78-165]	123[82-180]	ns
Gly[illegible]	90 [83-99]	93[88-102]	ns
Dyna[illegible]ic PSV (cm/sec)	52.5±31.3	52.7±24.3	ns
MHQ-A score (free-floating anxiety symptoms)	5.3±3.4	5.8±3.1	ns

Low PRL does not play a direct pathogenetic role .

Corona et al., J Sex Med. 2009;6:1457

Low Prolactin Is Associated with Sexual Dysfunction and Psychological or Metabolic Disturbances in Middle-Aged and Elderly Men: The European Male Aging Study (EMAS)

Giovanni Corona, MD,[*†] Frederick C. Wu, MD,[‡] Giulia Rastrelli, MD,[*] David M. Lee, PhD,[§] Gianni Forti, MD,[¶] Daryl B. O'Connor, PhD,[**] Terence W. O'Neill, MD,[§] Neil Pendleton, MD,[††] Gyorgy Bartfai, MD,[‡‡] Steven Boonen, MD,[§§] Felipe F. Casanueva, MD,[¶¶] Joseph D. Finn, BSc,[§] Ilpo T. Huhtaniemi, MD,[***] Krzysztof Kula, MD,[†††] Margus Punab, MD,[‡‡‡] Dirk Vanderschueren, MD,[§§§] Martin Rutter, MD,[¶¶¶] Mario Maggi, MD,[*] and the EMAS Study Group[1]

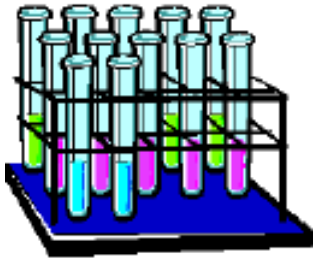
Hyposerotonergic tone:

- decreased orgasm

- anxiety & depression

- metabolic syndrome

2935 subjects mean age (60±11 years old)



PRL in the blood = 5HT in the brain?

Corona et al., J Sex Med 2013

Relationship between *orgasmic enjoyment change* and PRL levels in EMAS study

15. Compared with a year ago, has the enjoyment of your orgasmic experience changed?
    - +2. Increased a lot
    - +1. Increased moderately
    - 0. Neither increased nor decreased
    - –1. Decreased moderately
    - –2. Decreased a lot

EMAS European Male Ageing Study

Adjusted for

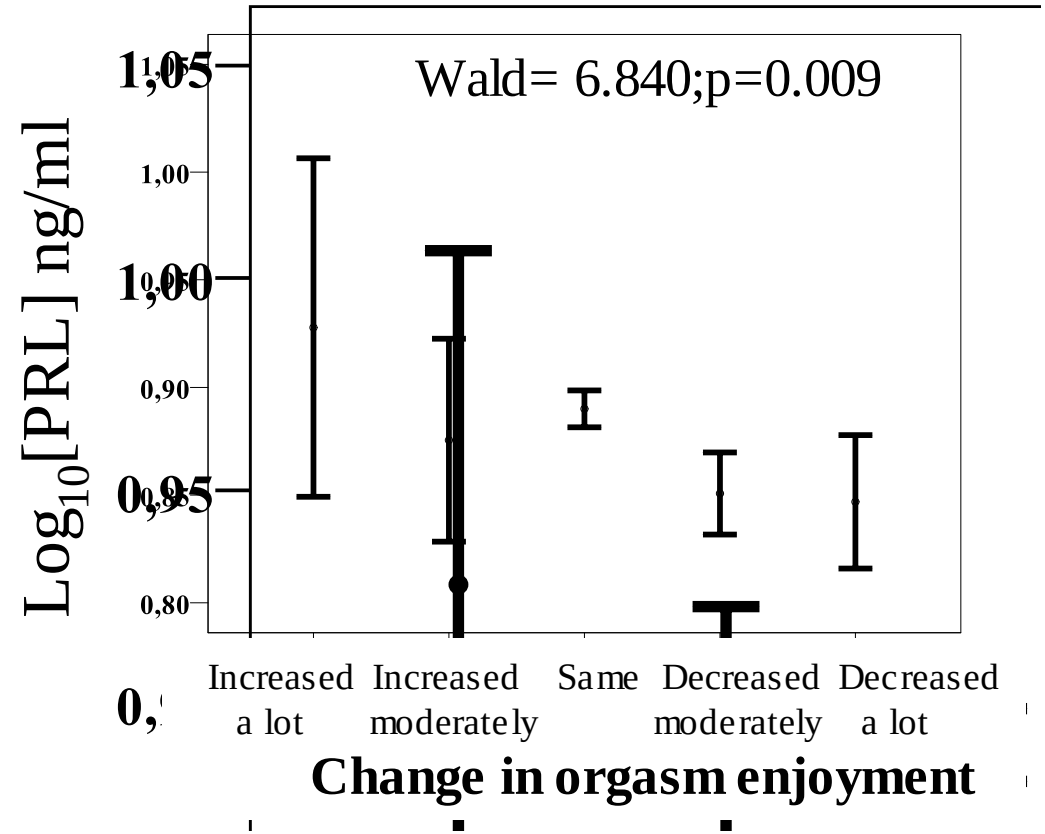
- age
- Centres
- Testosterone, estradiol, TSH
- Antidepressants
- Number of morbidities

1374

ORIGINAL RESEARCH—OUTCOMES ASSESSMENT

Assessment of Sexual Health in Aging Men in Europe: Development and Validation of the European Male Ageing Study Sexual Function Questionnaire

Daryl B. O'Connor, PhD,* Giovanni Corona,† Gianni Forti, MD,† Abdelouahid Tajar, PhD,‡ David M. Lee, PhD,‡ Joseph D. Finn, BSc,‡ Gyorgy Bartfai, MD,§ Steven Boonen, MD,¶



Corona et al., J Sex Med 2013

Hormonal control of ejaculation

1. **Thyroid hormones modulate ejaculatory reflex.**
2. **Hyperthyroidism is a cause of acquired PE**
3. **Treatment of hyperthyroidism or hypothyroidism improves ejaculatory problems**
4. **Testosterone modulates ejaculatory reflex**
5. **Low prolactin might be a marker of a reduced serotonergic tone**

ANDROLOGY

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ANDROLOGY

ORIGINAL ARTICLE

Correspondence:
Mario Maggi, Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence, Viale Pieraccini 6, Florence 50139, Italy. E-mail: m.maggi@dfc.unifi.it

Keywords:
male infertility, Premature Ejaculation Diagnostic Tool, prolactin, scrotal and transrectal colour Doppler ultrasound, seminal vesicles

Received: 6-May-2013

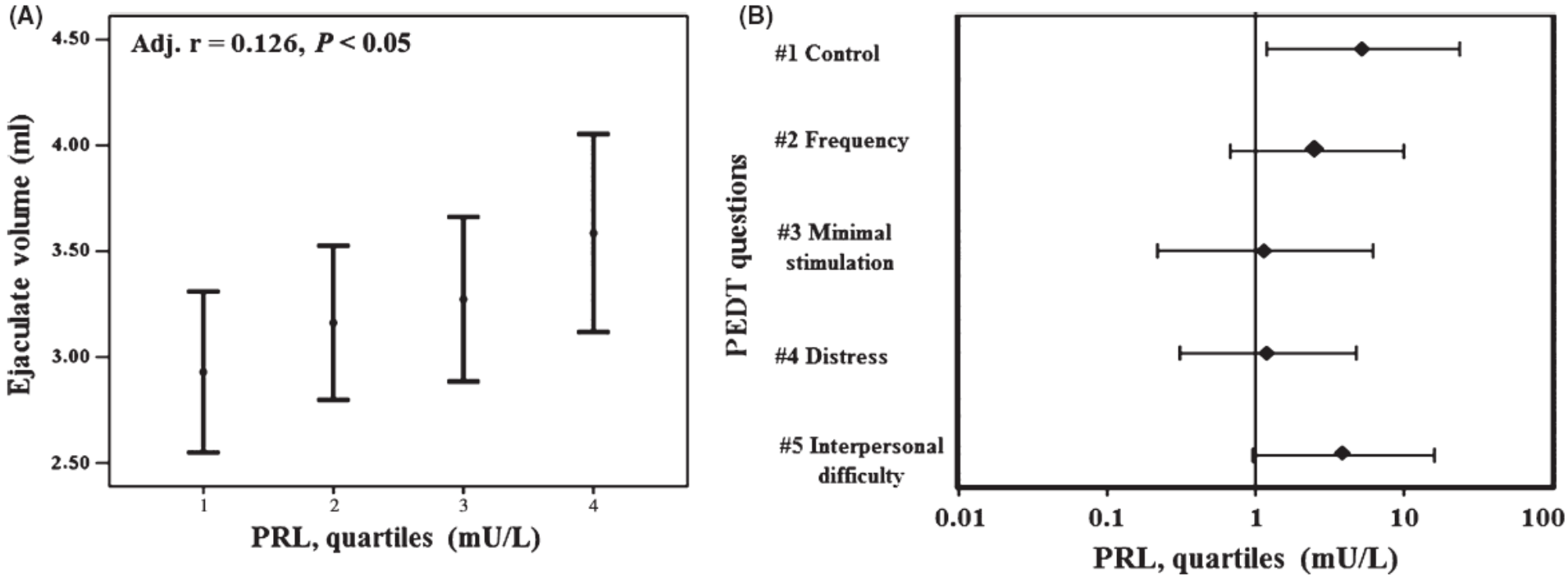
Clinical implications of measuring prolactin levels in males of infertile couples

[1]F. Lotti, [1,2]G. Corona, [1]E. Maseroli, [1]M. Rossi, [1]A. Silverii, [1]S. Degl'Innocenti, [1]G. Rastrelli, [1]G. Forti and [1]M. Maggi

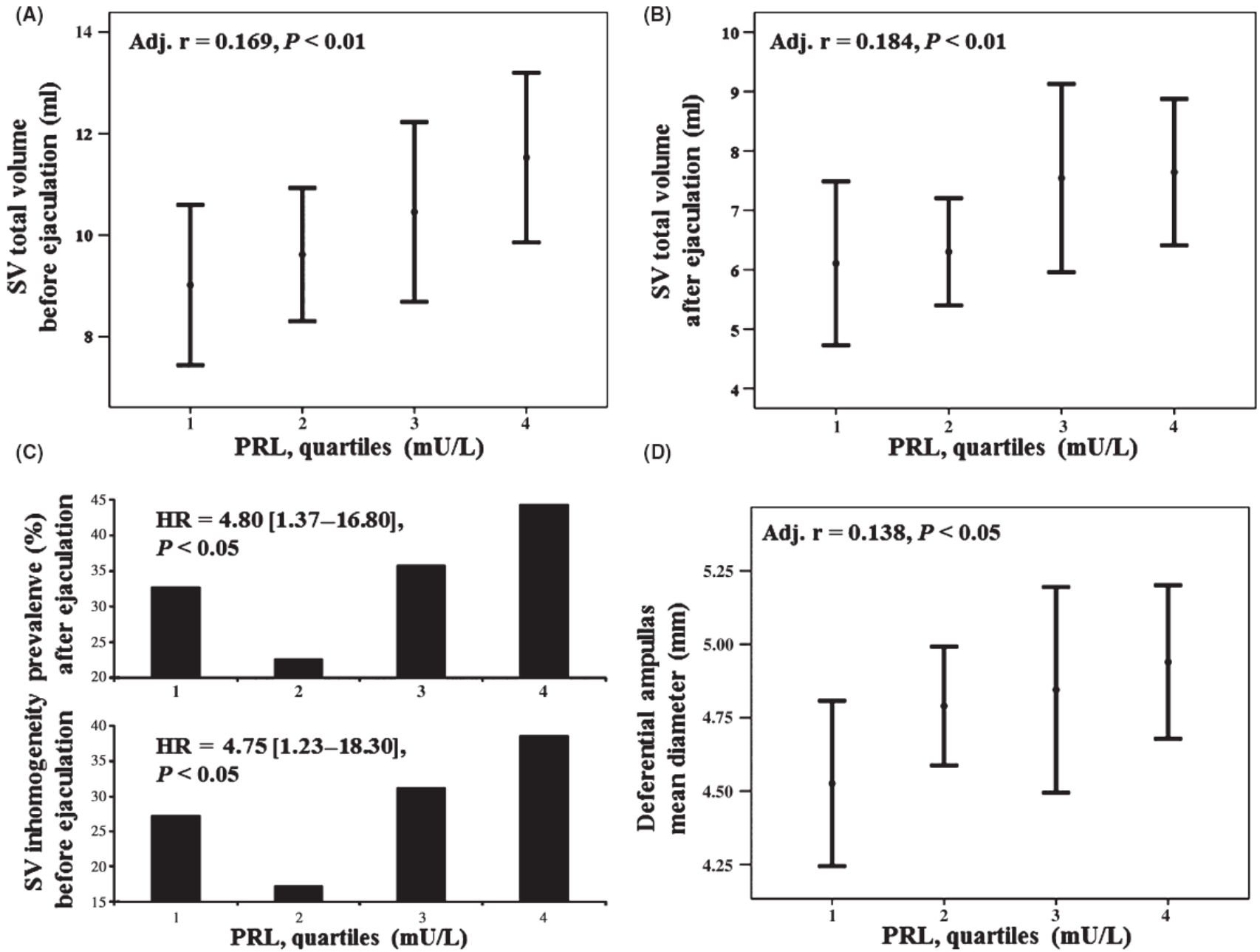
[1]Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence, Florence, and [2]Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, Italy

A consecutive series of 288 males of infertile couples, (36.6 ± 4.4 years) attending the outpatient clinic for sexual dysfunction at the University of Florence, Florence, Italy

Lotti et al., Andrology 2013



Lotti et al., Andrology 2013



Lotti et al., Andrology 2013

Comparisons between subjects with prolactin (PRL) < 140 mU/L (case patients) and age-, total testosterone-, TSH-matched controls (1:1 ratio).

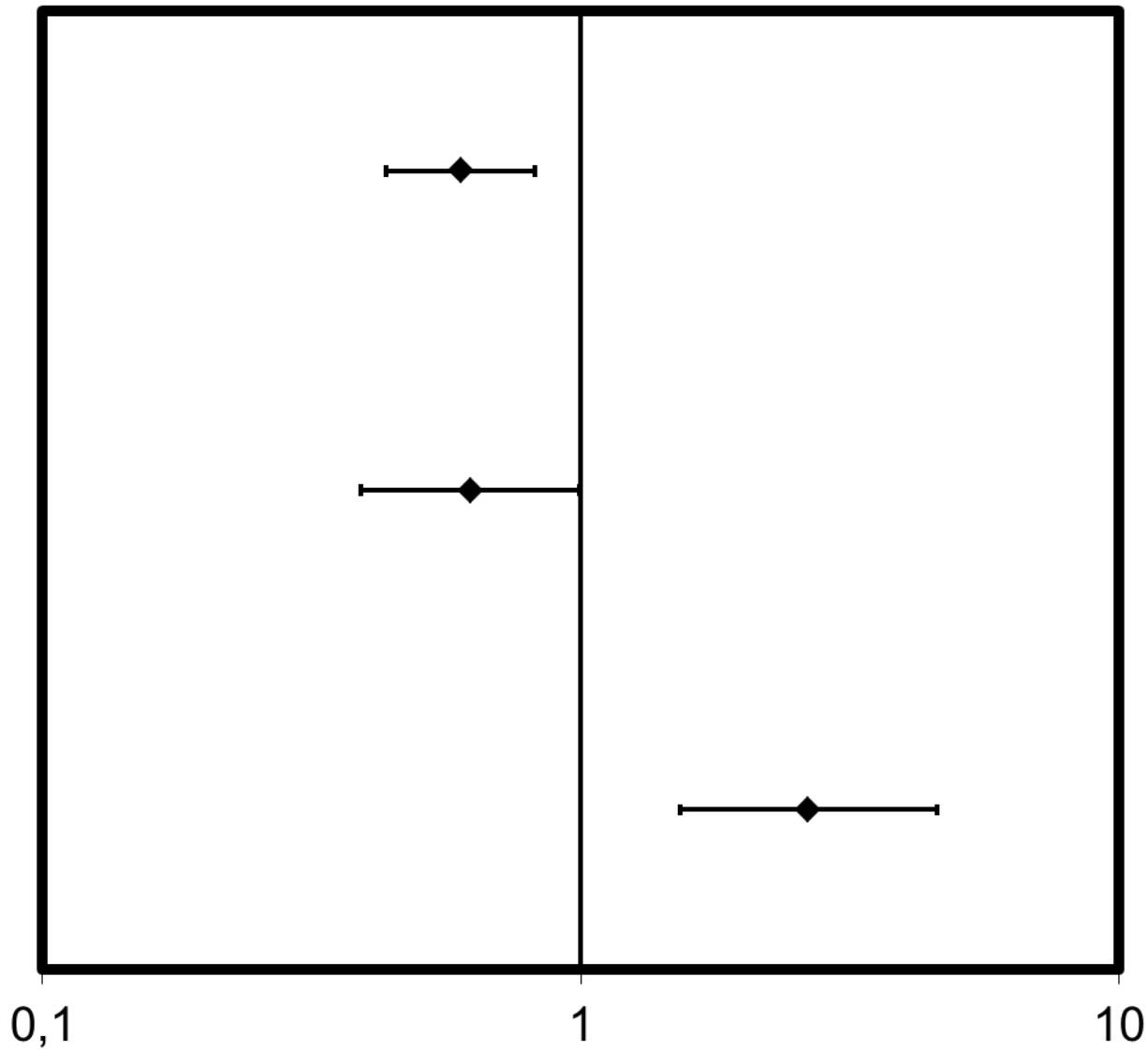
	Case patients (n = 139)	Controls (n = 139)	p
Age	37.4 ± 7.6	37.3 ± 7.6	0.968
Prolactin (mU/L)	109 [84–129]	216 [171–286]	< **0.0001**
Total testosterone (nmol/L)	16.6 ± 5.6	16.2 ± 5.7	0.587
TSH (mU/L)	1.6 ± 0.9	1.9 ± 1.5	0.108
Ejaculate volume (mL)	3.0 ± 1.7	3.5 ± 1.9	**0.022**
Sperm concentration, 10^6/mL	34.1 ± 82.4	29.0 ± 41.7	0.517
Spermatozoa per ejaculate, 10^6/mL	78.6 ± 129.6	83.1 ± 117.1	0.758
Sperm progressive motility, %	34.8 ± 20.4	32.5 ± 20.8	0.407
Sperm morphology, % normal forms	7.4 ± 7.5	6.9 ± 7.7	0.629
PEDT #1 score	1.4 ± 1.1	1.1 ± 1.0	**0.045**
PEDT #1 score ≥1 (%) (any failure in controlling ejaculation)	76.3	63.3	**0.049**
SV total volume before ejaculation at CDU	8.1 [4.7–12.8]	9.8 [6.6–14.6]	**0.008**
SV total volume after ejaculation at CDU	5.0 [3.0–7.8]	6.3 [3.7–10.8]	**0.017**
SV texture inhomogeneity before ejaculation (%) at CDU	27.3	41.7	**0.012**
SV texture inhomogeneity after ejaculation (%) at CDU	21.6	36.0	**0.009**
Deferential ampullas mean diameter (mm) at CDU	4.6 ± 1.0	4.9 ± 1.2	**0.044**

Lotti et al., Andrology 2013

Hormonal control of ejaculation

1. **Thyroid hormones modulate ejaculatory reflex.**
2. **Hyperthyroidism is a cause of acquired PE**
3. **Treatment of hyperthyroidism or hypothyroidism improves ejaculatory problems**
4. **Testosterone modulates ejaculatory reflex**
5. **Low prolactin might be a marker of a reduced serotonergic tone**
6. **Prolactin might play a direct peripheral effect in modulating ejaculatory effect**

Hazard ratio for premature ejaculation according to the hormonal milieu in 1962 subjects with sexual dysfunction (w/o hyperprolactinemia and medication) at the University of Florence, Italy



Adjusted for:

- Age
- Smooking and drinking behaviours
- ED severity
- Anxiety and depressive symptoms
- Psychiatric disease

Corona et al., Nat Rev Urol. 2012;9:508

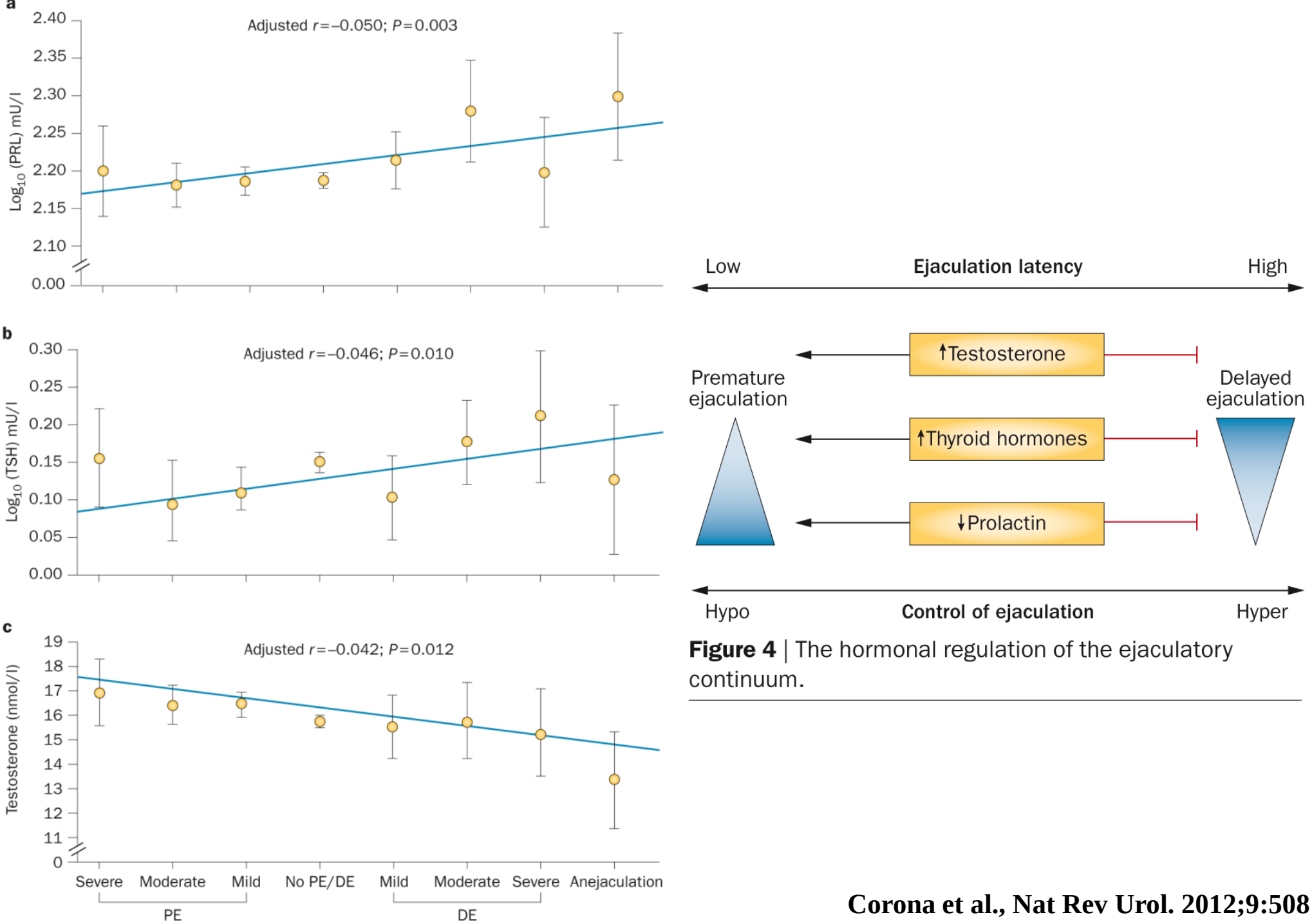


Figure 4 | The hormonal regulation of the ejaculatory continuum.

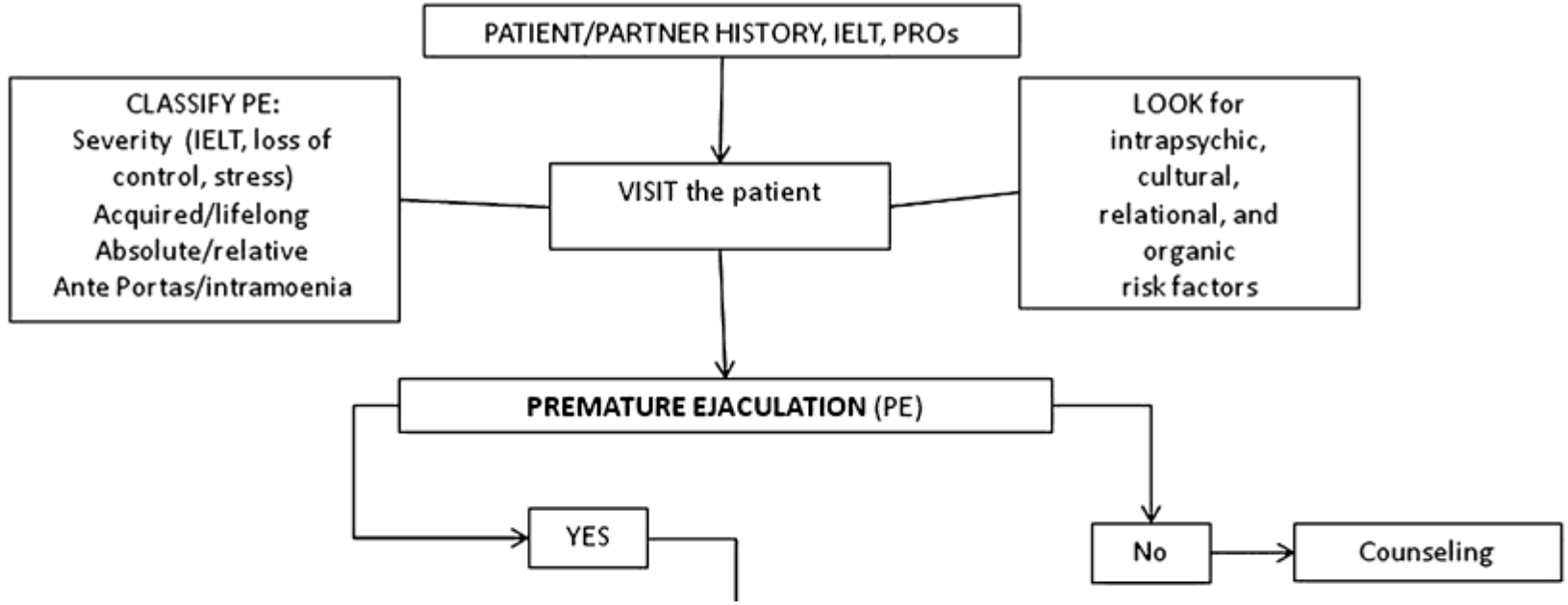
Corona et al., Nat Rev Urol. 2012;9:508

Standard Operating Procedures in the Disorders of Orgasm and Ejaculation

Chris G. McMahon, MBBS, FAChSHM,* Emmanuele Jannini, MD,† Marcel Waldinger, MD, PhD,‡ and David Rowland, PhD§

*Australian Centre for Sexual Health, Sydney, Australia; †University of L'Aquila, Endocrinology and Medical Sexology, Experimental Medicine, L'Aquila, Italy; ‡Leyenburg Hospital, Psychiatry and Neurosexology, The Hague, The Netherlands; §Valparaiso University, Psychology, Valparaiso, IN, USA

DOI: 10.1111/j.1743-6109.2012.02824.x



MCMahon et al., J Sex Med. 2013;10:204

•Reccomadation#2: Self-estimation by the patient and partner of ejaculatory latency should be used to determine IELT in clinical practice (level 1)

•Standardized assessment measures such as validated questionnaires and patient-reported outcome measures can be used as an adjunct to a full medical/sexual history and self-estimation of ejaculatory latency in the evaluation of men presenting with self-reported PE (level 1)

MCMahon et al., J Sex Med. 2013;10:204

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•**Standardized assessment measures such as validated questionnaires and patient-reported outcome measures can be used as an adjunct to a full medical/sexual history and self-estimation of ejaculatory latency in the evaluation of men presenting with self-reported PE (level 1)**

- **Premature ejaculation diagnostic tool (PEDT)**
  score > 8: PE

EUROPEAN UROLOGY 52 (2007) 565–573

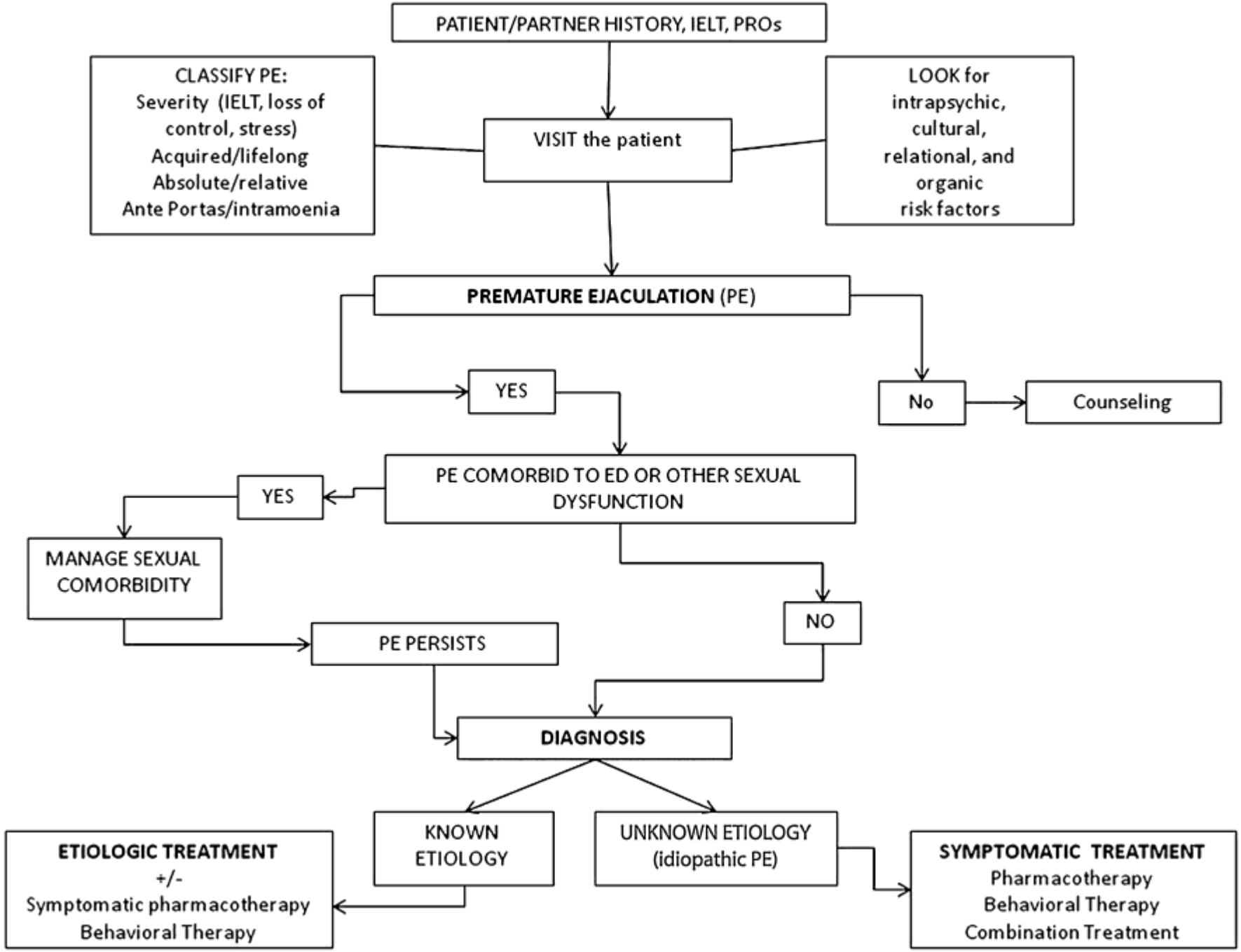
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

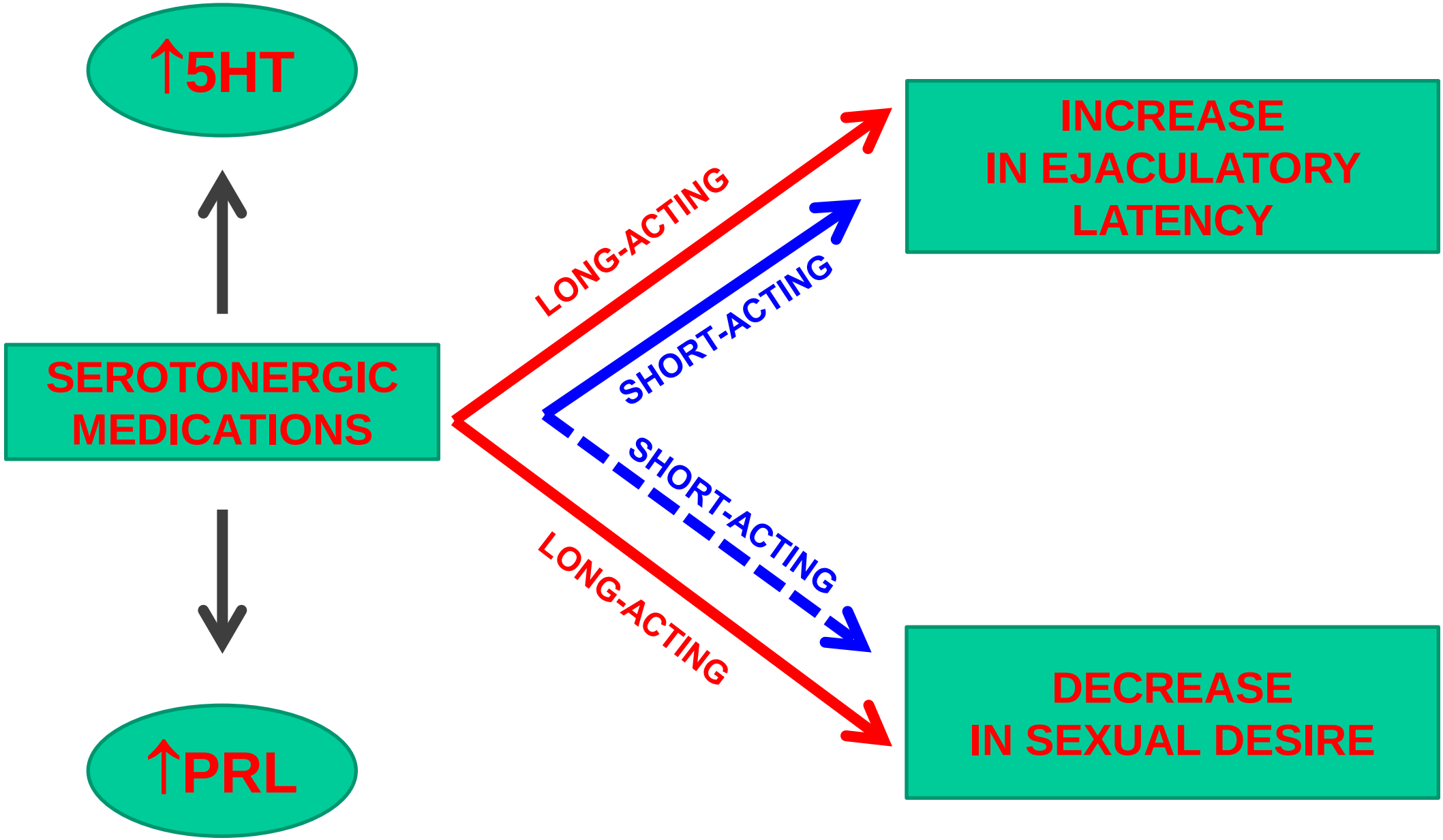
European Association of Urology

Sexual Medicine

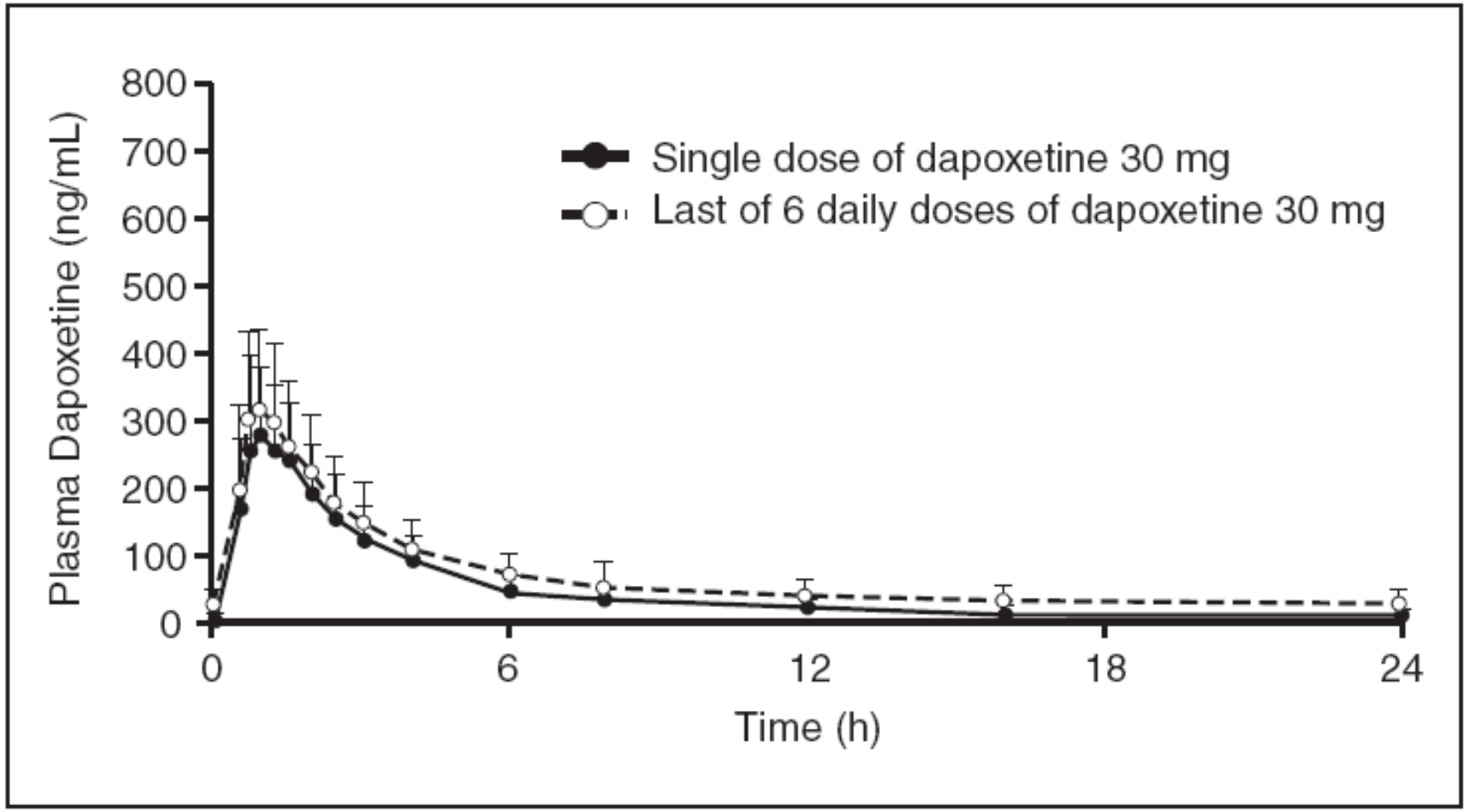
Development and Validation of a Premature Ejaculation Diagnostic Tool

Tara Symonds [a,*], *Michael A. Perelman* [b], *Stanley Althof* [c], *François Giuliano* [d], *Mona Martin* [e], *Kathryn May* [a], *Lucy Abraham* [a], *Anna Crossland* [a], *Mark Morris* [a]


PATIENT/PARTNER HISTORY, IELT, PROs
CLASSIFY PE:
Severity (IELT, loss of control, stress)
Acquired/lifelong
Absolute/relative
Ante Portas/intramoenia
VISIT the patient
LOOK for intrapsychic, cultural, relational, and organic risk factors
PREMATURE EJACULATION (PE)
YES
No
Counseling
PE COMORBID TO ED OR OTHER SEXUAL DYSFUNCTION
YES
MANAGE SEXUAL COMORBIDITY
NO
PE PERSISTS
DIAGNOSIS
KNOWN ETIOLOGY
UNKNOWN ETIOLOGY (idiopathic PE)
ETIOLOGIC TREATMENT
+/-
Symptomatic pharmacotherapy
Behavioral Therapy
SYMPTOMATIC TREATMENT
Pharmacotherapy
Behavioral Therapy
Combination Treatment

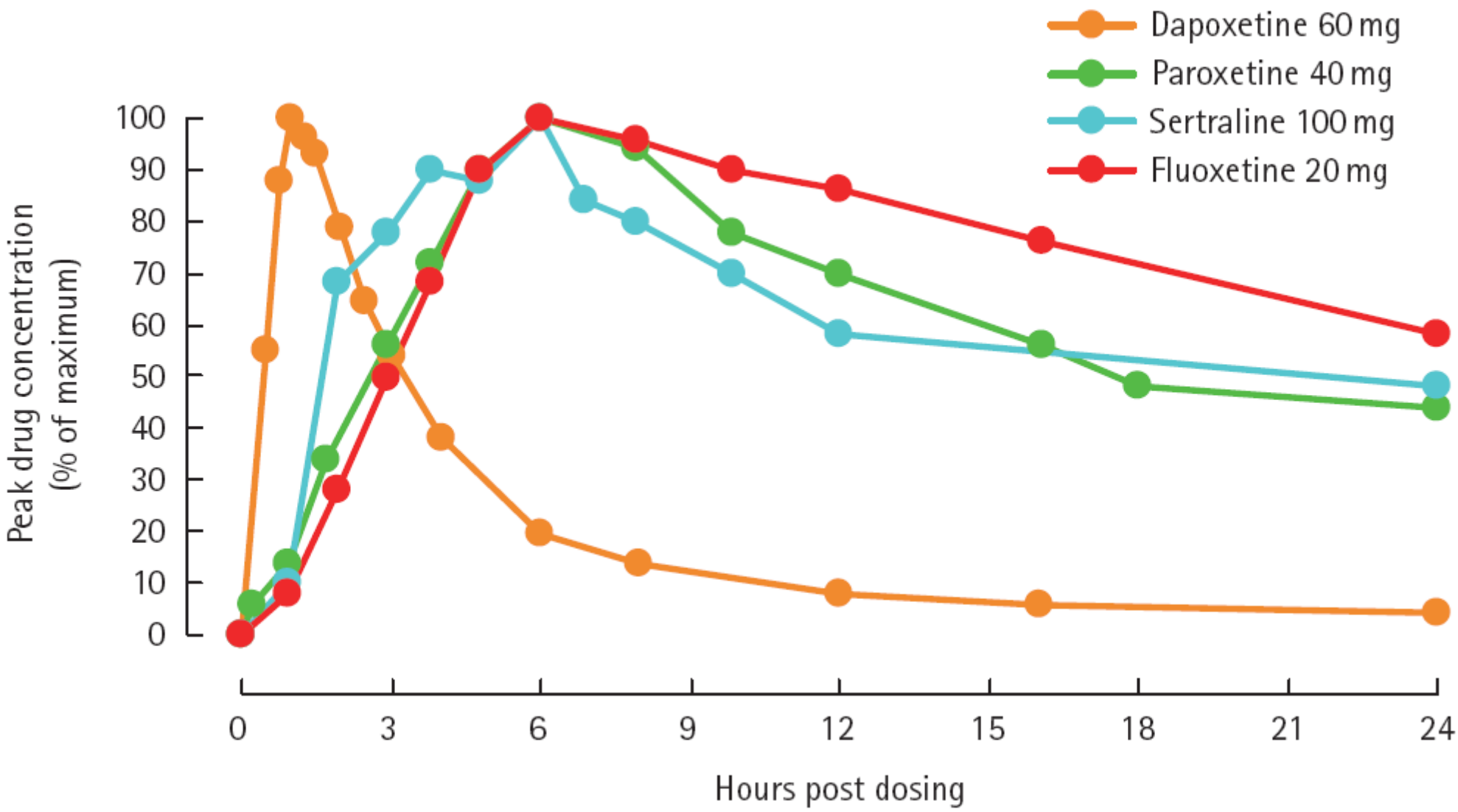

↑5HT
SEROTONERGIC MEDICATIONS
↑PRL
LONG-ACTING
SHORT-ACTING
SHORT-ACTING
LONG-ACTING
INCREASE IN EJACULATORY LATENCY
DECREASE IN SEXUAL DESIRE

Single- and multiple-dose plasma concentration profiles of dapoxetine 30 mg



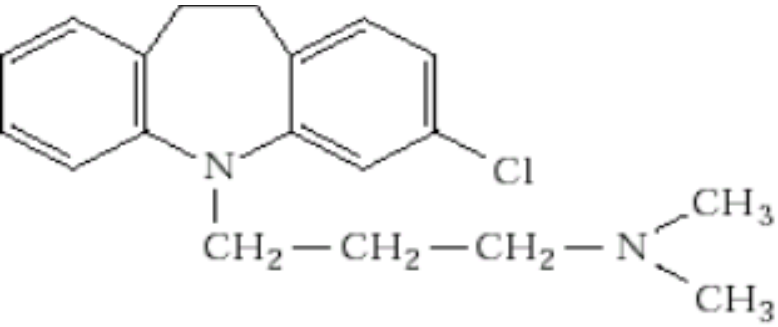
Modi et al., J Clin Pharmacol 2006;46:301

Dapoxetine has more rapid pharmacokinetics than other SSRIs.



Andersson et al., BJU Int 2006;97:311

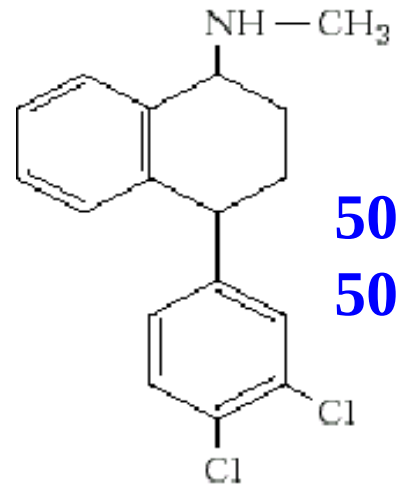
Non selective SSRI



Chlorimipramine

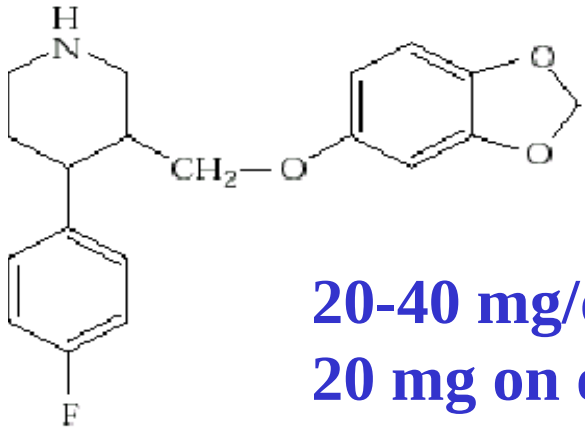
25-50 mg/daily
25 mg on demand

2) SSRI



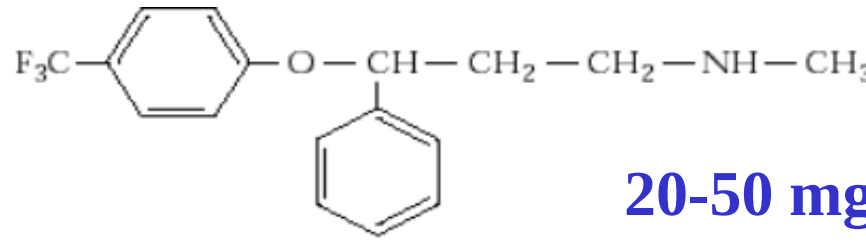
Sertraline

50-100 mg/daily
50-100 mg on demand



Paroxetine

20-40 mg/daily
20 mg on demand

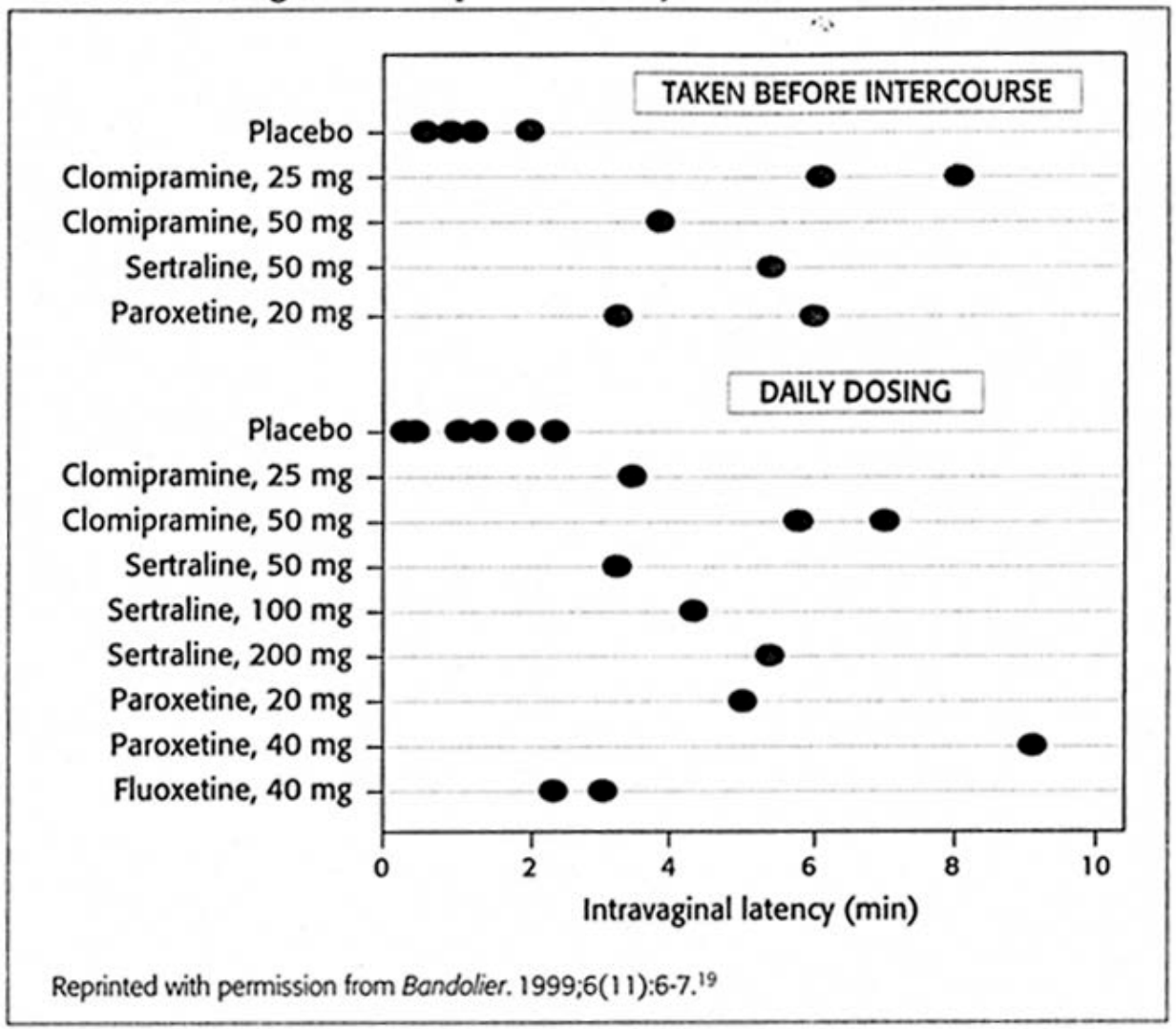


Fluoxetine

20-50 mg/daily

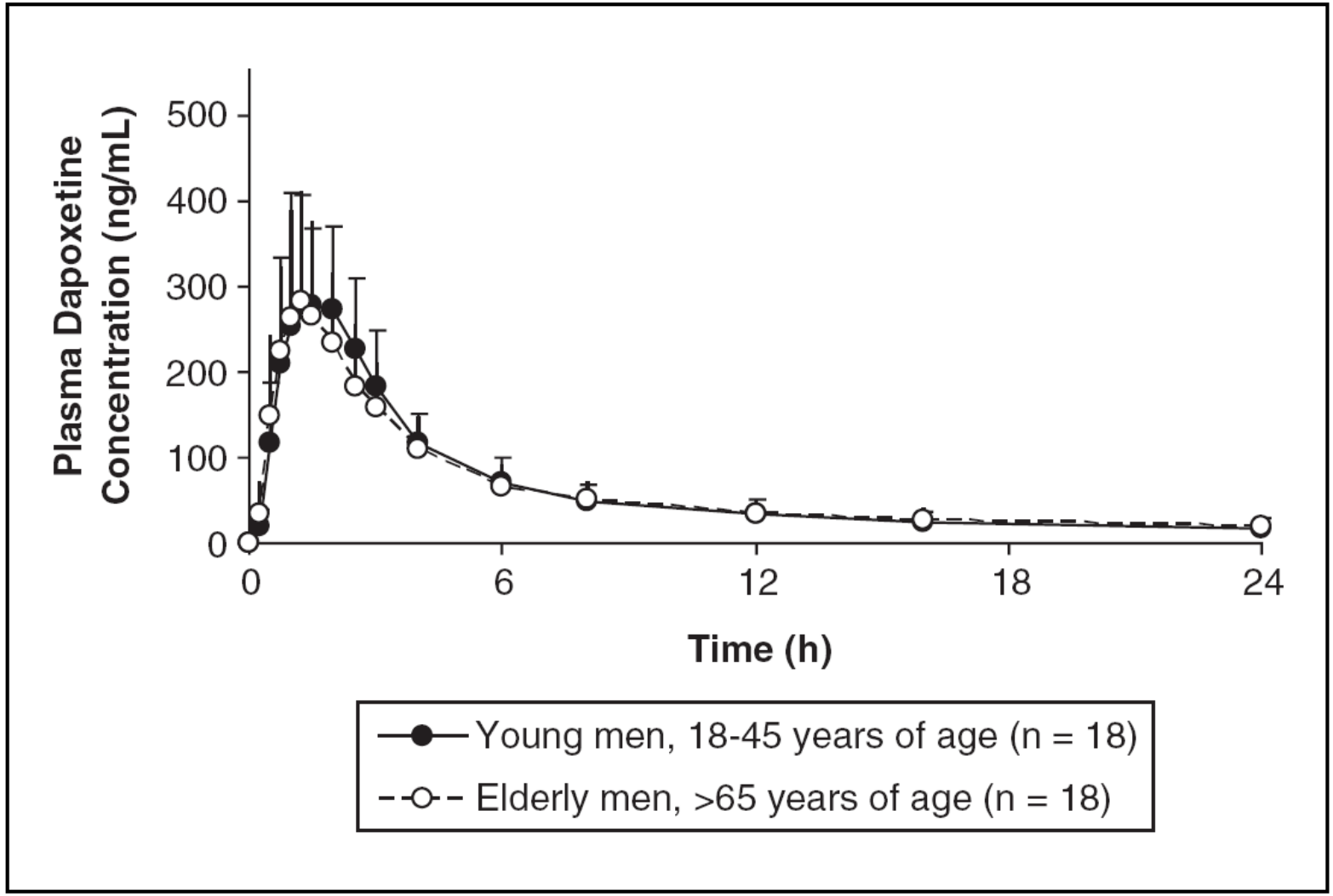
FIGURE 1

Results of drug trials for premature ejaculation



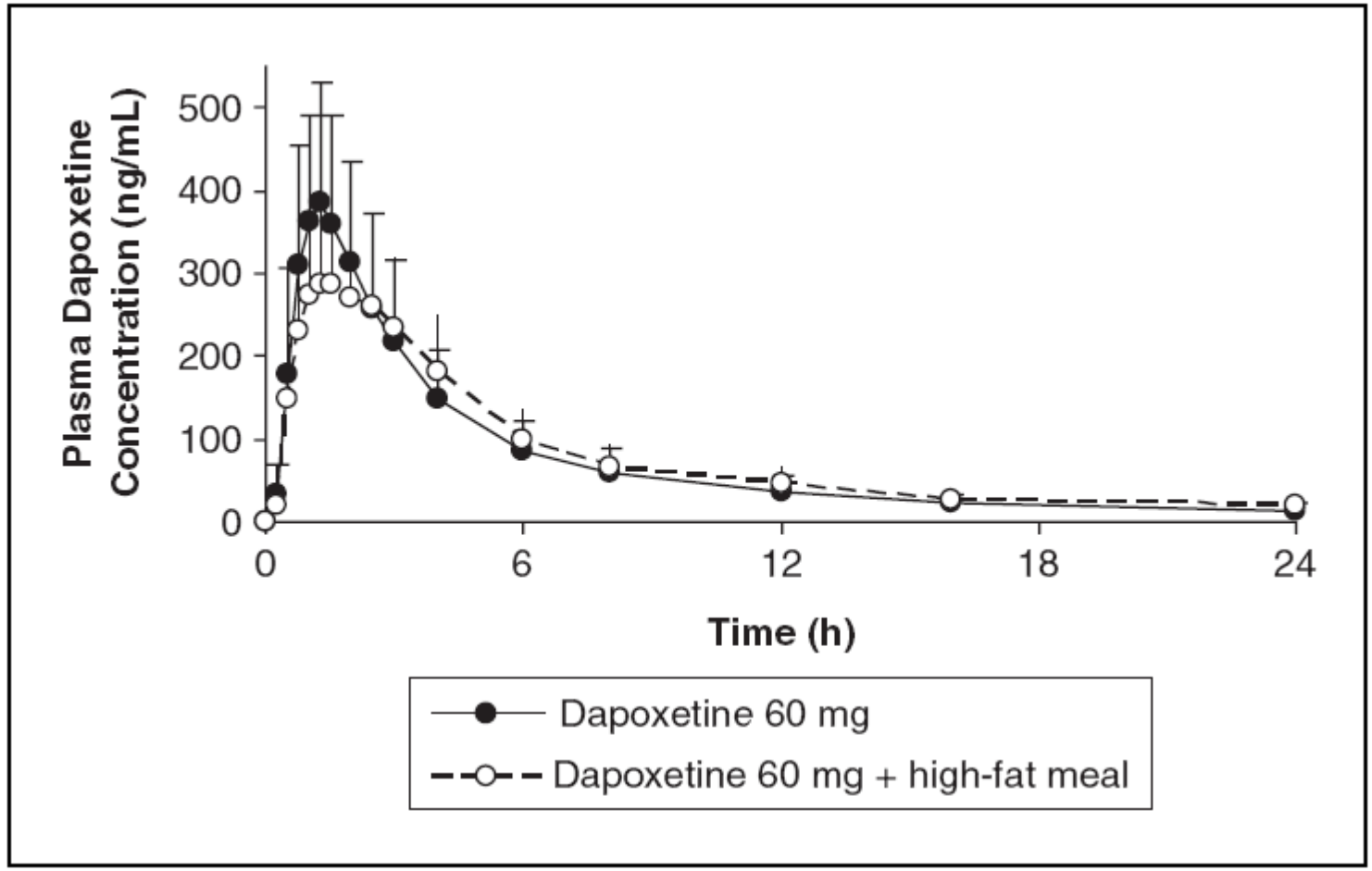
Reprinted with permission from *Bandolier*. 1999;6(11):6-7.[19]

Plasma concentrations of dapoxetine in young and elderly men



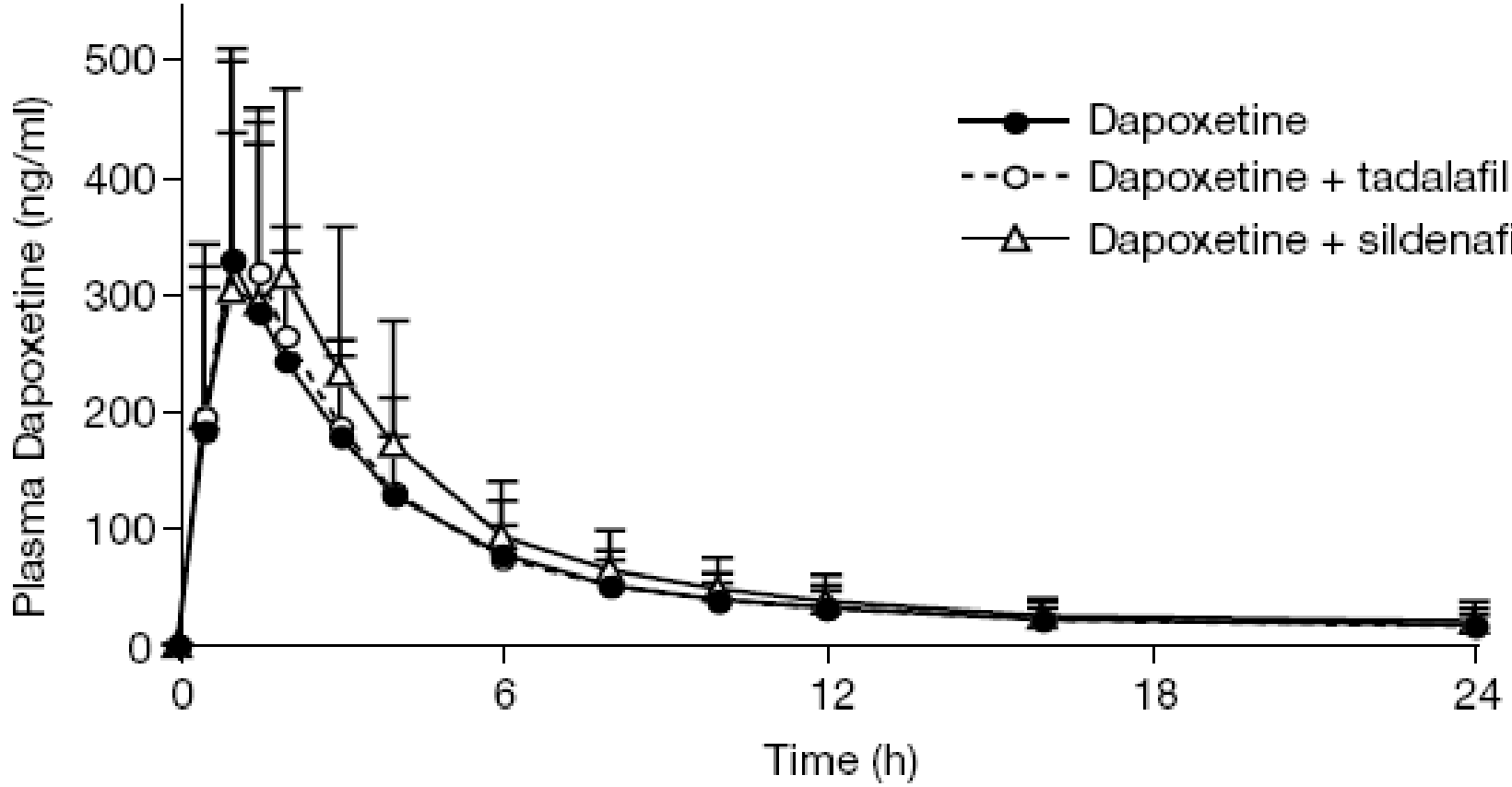
Dressers et al., J Clin Pharmacol 2006;46:1023

Plasma concentrations of dapoxetine after a high fat meal.



Dressers et al., J Clin Pharmacol 2006;46:1023

Plasma concentrations of dapoxetine after administration of dapoxetine alone or with tadalafil or sildenafil



Dressers et al., Int J Impot Res 2006;18:104

Main recommendations

- Caution in patients with moderate/severe hepatic or renal insufficiency
- No limitation with meals
- Caution with alcohol

EUROPEAN UROLOGY 55 (2009) 957–968

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

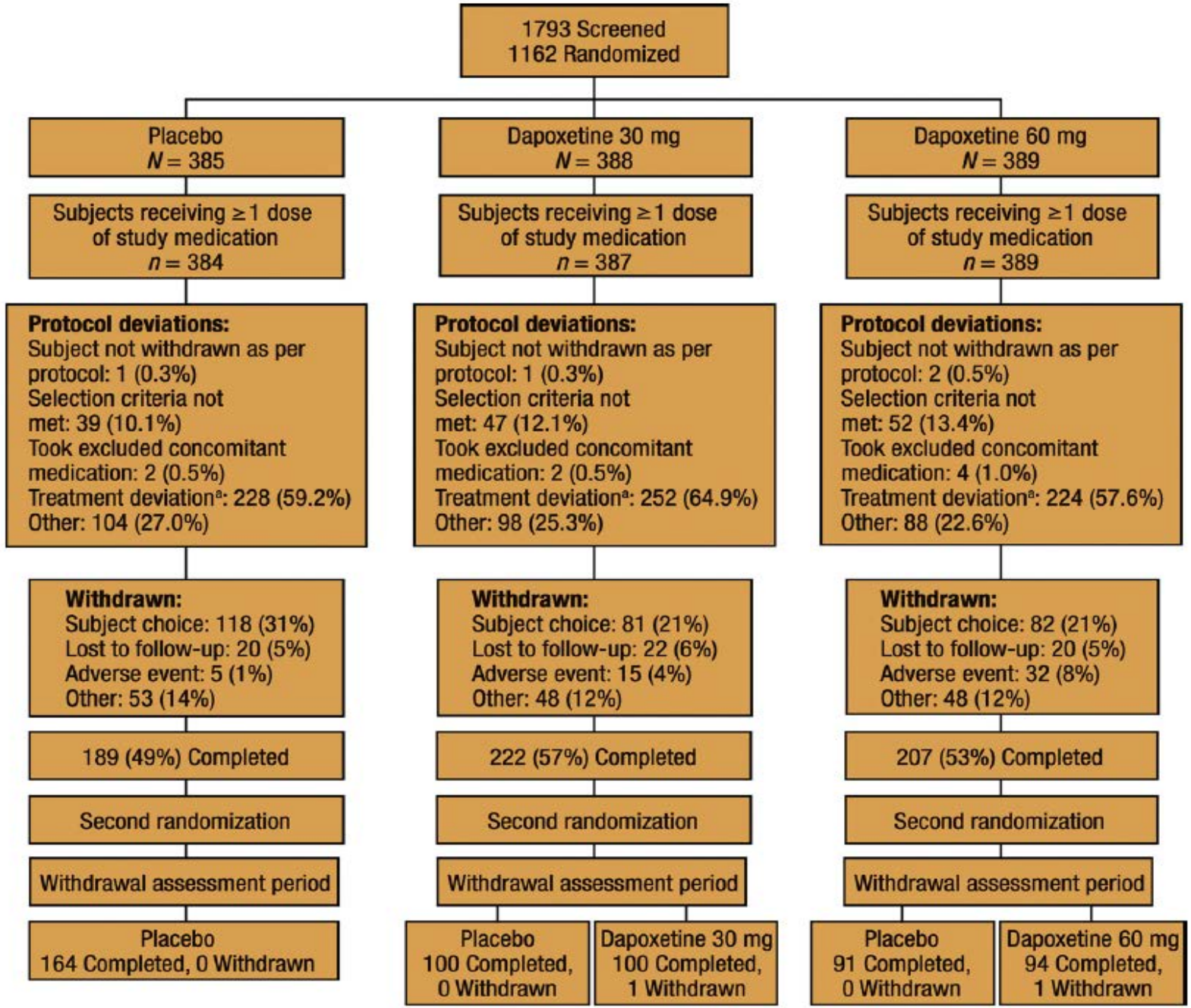
European Association of Urology

Sexual Medicine

Dapoxetine for the Treatment of Premature Ejaculation: Results from a Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial in 22 Countries

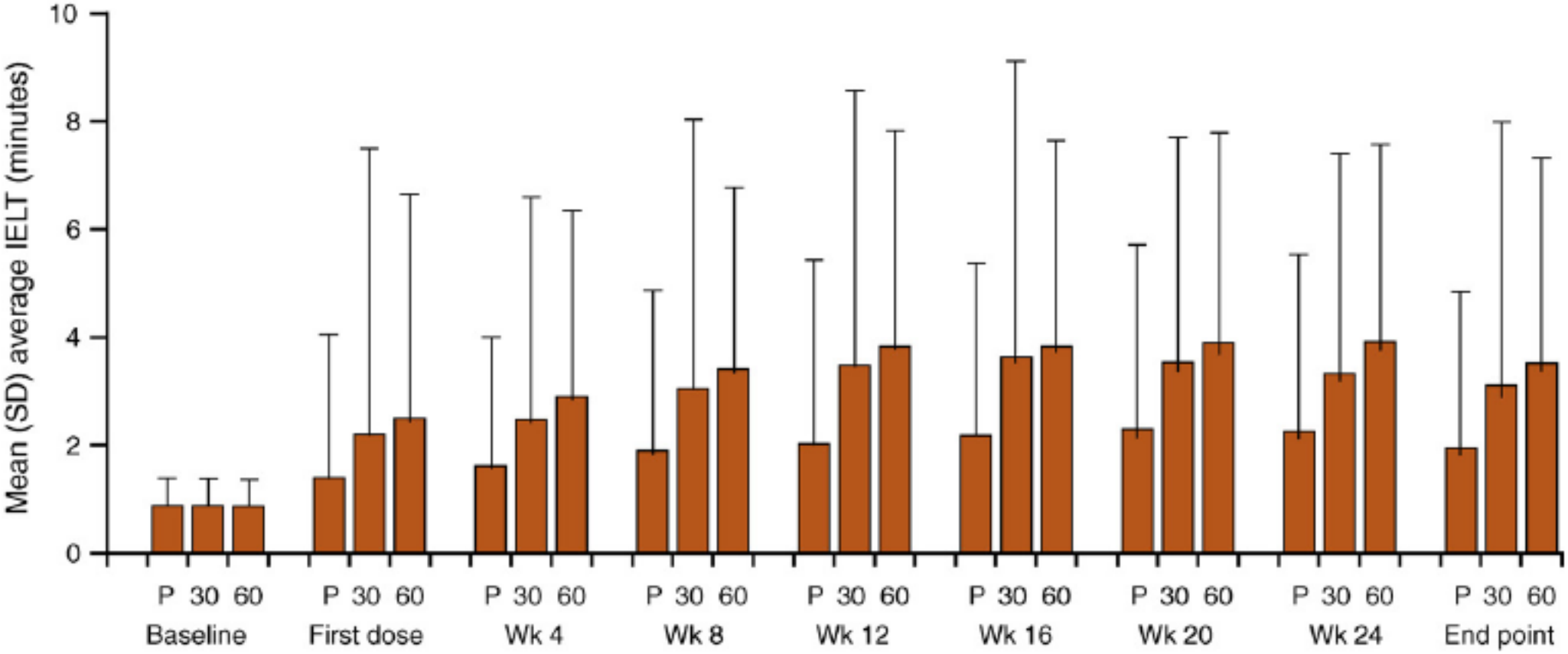
Jacques Buvat [a,*], *Fisseha Tesfaye* [b], *Margaret Rothman* [c], *David A. Rivas* [b], *François Giuliano* [d]

[a] *CETPARP/Le grand Hunier, Lille, France*
[b] *Johnson & Johnson Pharmaceutical Research & Development, L.L.C., Raritan, NJ, USA*
[c] *Johnson & Johnson Pharmaceutical Services, L.L.C., Raritan, NJ, USA*
[d] *AP-HP, Neuro-Urology-Andrology, Raymond Poincaré Hospital, Garches, France*



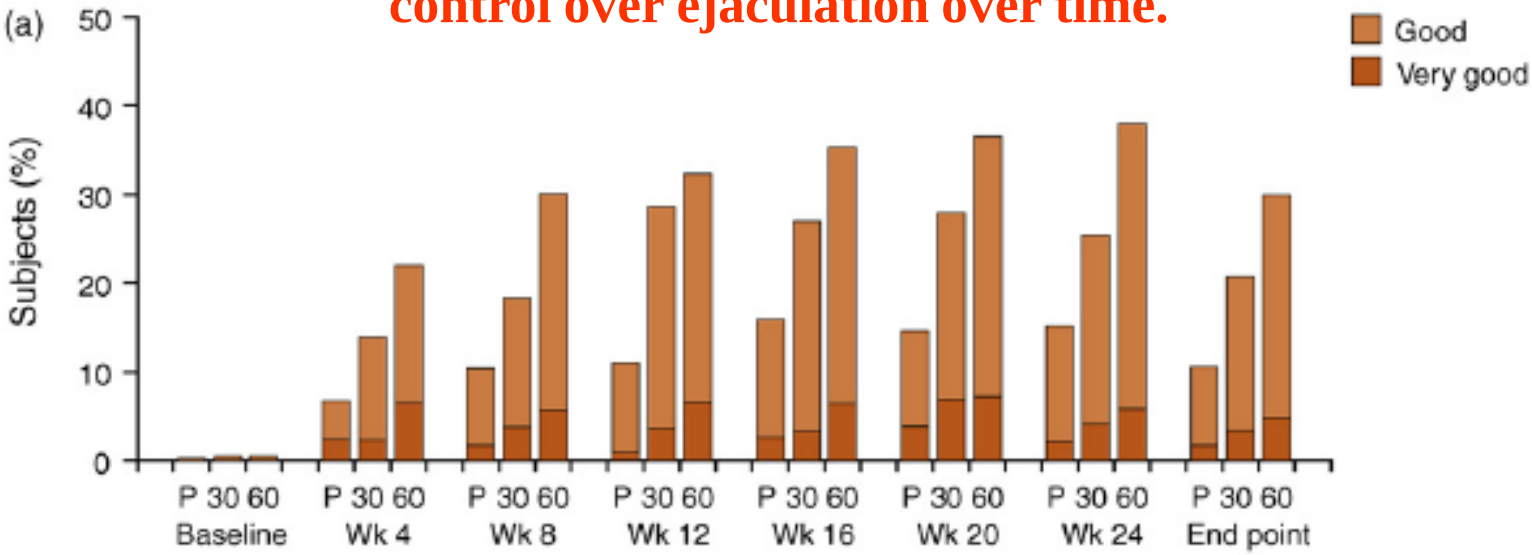
Buvat et al., Eur Urol 2009;55:957

Mean average intravaginal ejaculatory latency time (IELT) over time.

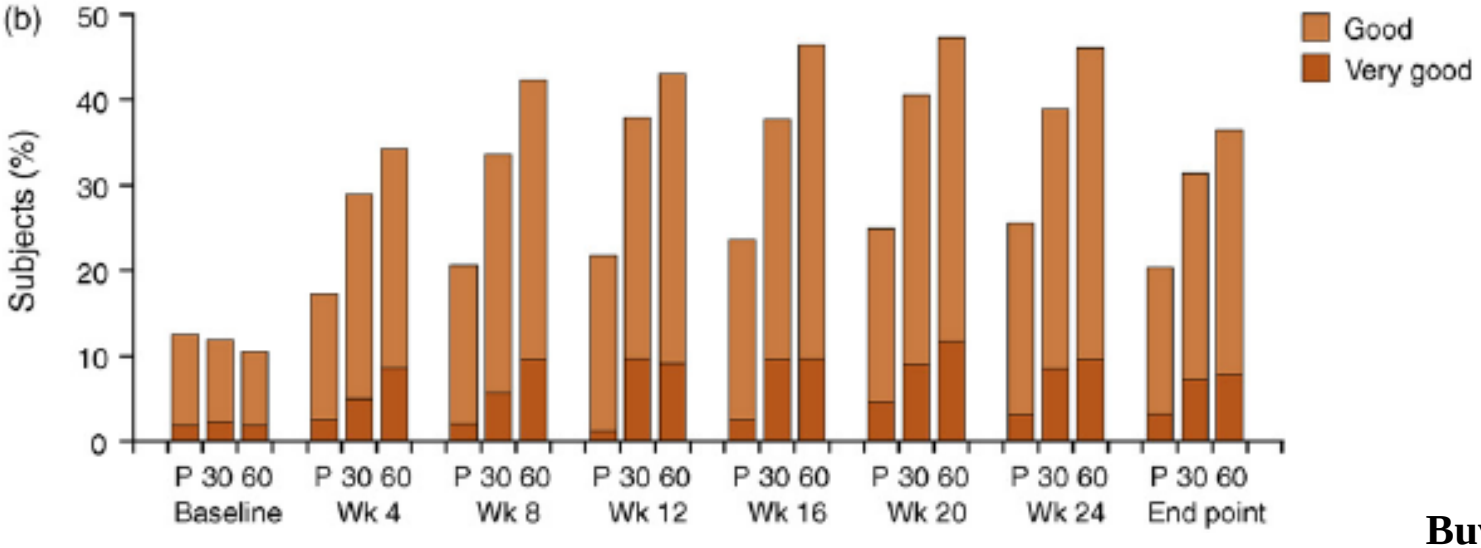


Buvat et al., Eur Urol 2009;55:957

Percentages of subjects reporting "good" or "very good" control over ejaculation over time.

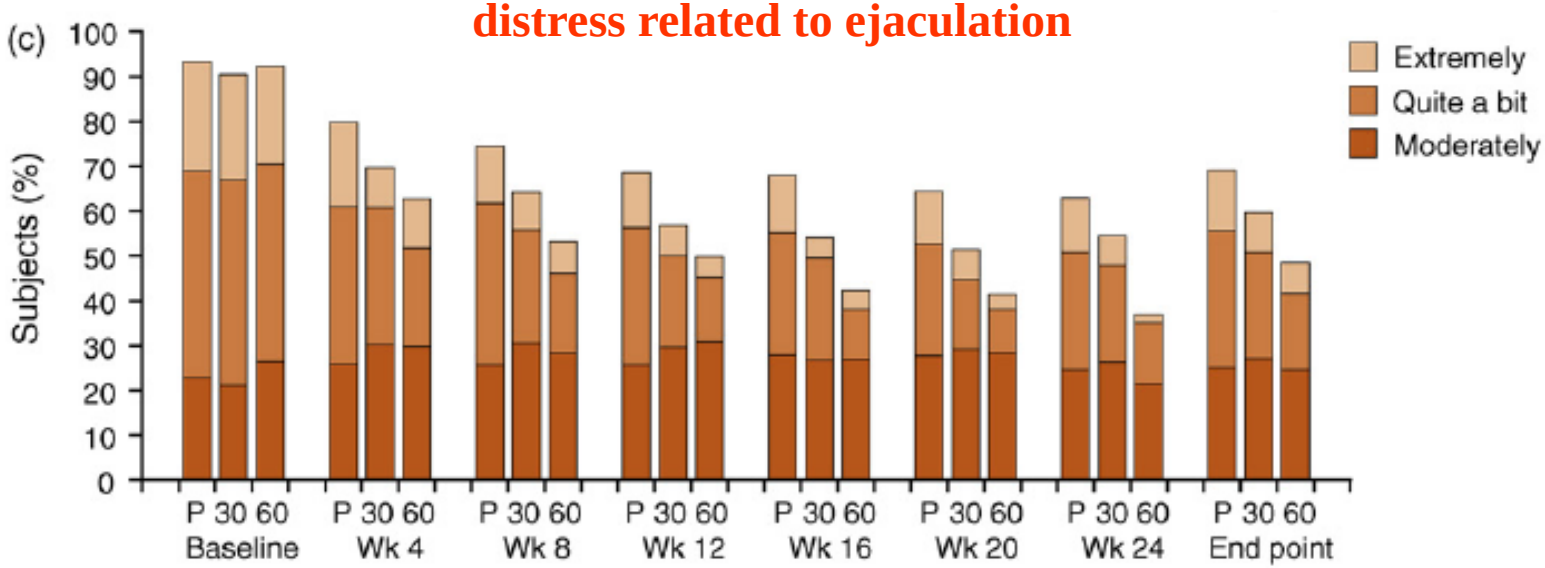


Percentages of subjects reporting "good" or "very good" satisfaction with sexual intercourse over time.

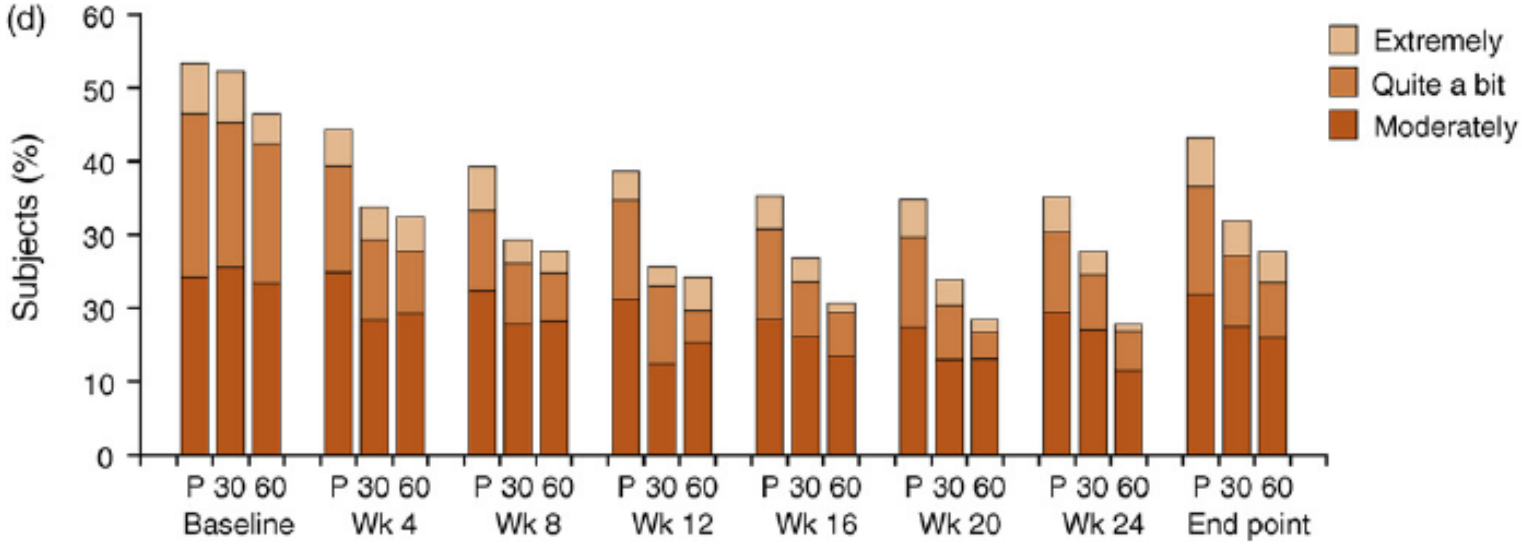


Buvat et al., Eur Urol 2009;55:957

Percentages of subjects reporting "moderately," "quite a bit," or "extremely" distress related to ejaculation



Percentages of subjects reporting "moderately," "quite a bit," or "extremely" interpersonal difficulty related to ejaculation



Buvat et al., Eur Urol 2009;55:957

Treatment-emergent adverse events occurring in ≥2% of subjects

Adverse event	Subjects, *n* (%)		
	Placebo (*n* = 385)	Dapoxetine 30 mg (*n* = 388)	Dapoxetine 60 mg (*n* = 389)
Total	148 (38.4)	218 (56.2)	265 (68.1)
Nausea	11 (2.9)	64 (16.5)	119 (30.6)
Headache	32 (8.3)	25 (6.4)	53 (13.6)
Dizziness	10 (2.6)	30 (7.7)	52 (13.4)
Diarrhoea	6 (1.6)	15 (3.9)	44 (11.3)
Somnolence	4 (1.0)	15 (3.9)	28 (7.2)
Insomnia	12 (3.1)	10 (2.6)	27 (6.9)
Fatigue	8 (2.1)	22 (5.7)	26 (6.7)
Nasopharyngitis	13 (3.4)	21 (5.4)	24 (6.2)
Dry mouth	2 (0.5)	9 (2.3)	17 (4.4)
Influenza	10 (2.6)	18 (4.6)	16 (4.1)
Anxiety	2 (0.5)	11 (2.8)	12 (3.1)
Blood pressure increased	1 (0.3)	2 (0.5)	12 (3.1)
Erectile dysfunction	8 (2.1)	8 (2.1)	12 (3.1)
Vomiting	2 (0.5)	5 (1.3)	12 (3.1)
Dyspepsia	5 (1.3)	6 (1.5)	10 (2.6)
Hyperhidrosis	2 (0.5)	7 (1.8)	10 (2.6)
Abdominal pain	1 (0.3)	3 (0.8)	9 (2.3)
Asthenia	1 (0.3)	9 (2.3)	4 (1.0)
Back pain	6 (1.6)	8 (2.1)	4 (1.0)

Buvat et al., Eur Urol 2009;55:957

Efficacy and Safety of Dapoxetine for the Treatment of Premature Ejaculation: Integrated Analysis of Results from Five Phase 3 Trials

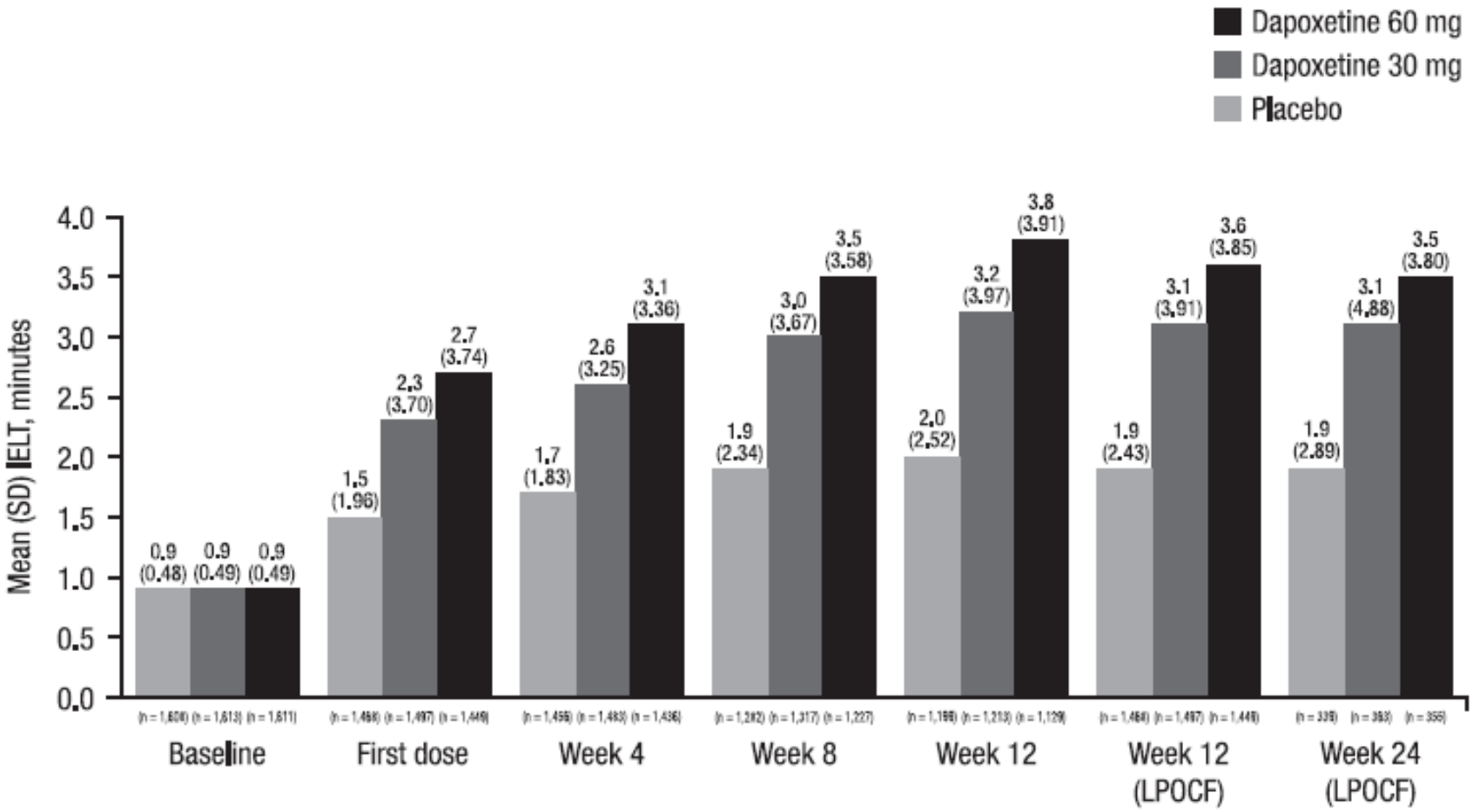
Chris G. McMahon, MD,* Stanley E. Althof, PhD,† Joel M. Kaufman, MD,‡ Jacques Buvat, MD,§ Stephen B. Levine, MD,¶ Joseph W. Aquilina, MD,** Fisseha Tesfaye, PhD,** Margaret Rothman, PhD,†† David A. Rivas, MD,†† and Hartmut Porst, MD‡‡

*Australian Centre for Sexual Health, St Leonards, New South Wales, Australia; †University of Miami Miller School of Medicine, West Palm Beach, FL, USA; ‡Advanced Urology, PC, Urology Research Options, Aurora, CO, USA; §CETPARP/Le grand Hunier, Lille, France; ¶Case Western Reserve University School of Medicine, Center for Marital and Sexual Health and Department of Psychiatry, Beachwood, OH, USA; **Johnson & Johnson Pharmaceutical Research & Development, Raritan, NJ, USA; ††Johnson & Johnson Pharmaceutical Services, Raritan, NJ, USA; ‡‡Private Urological Practice, Hamburg, Germany

DOI: 10.1111/j.1743-6109.2010.02097.x

Study (clinical registration number)	Study description	Treatment duration	Randomized subjects	Inclusion criteria
U.S. study (NCT00211094) [23]	Multicenter, double-blind, randomized, placebo-controlled, parallel-group	12 weeks	1,294	• ≥18 years of age • In a monogamous, heterosexual relationship for ≥6 months • Met DSM-IV-TR criteria for PE for ≥6 months • IELT ≤ 2 minutes in ≥75% of intercourse episodes during a 2-week baseline period; • PE severity rated as at least "moderate"
U.S. study (NCT00211107) [23]	Multicenter, double-blind, randomized, placebo-controlled, parallel-group	12 weeks	1,320	• Same as above
International study (NCT00229073) [21]	Multi-center, double-blind, randomized, placebo-controlled, parallel-group study conducted in 22 countries, primarily in Europe and South America	24 weeks	1,162	• Same as above except: • IELT of ≤2 minutes in ≥75% of intercourse episodes during a 4-week baseline period • At least "moderate" PE-related distress or interpersonal difficulty
Asia-Pacific study (NCT00210704) [22]	Multicenter, double-blind, randomized, placebo-controlled, parallel-group	12 weeks	1,067	• Same as International study
North American study (NCT00210613) [24]	Multicenter, double-blind, randomized, placebo-controlled, parallel-group	9 weeks	1,238	• Same as International study except no IELT criterion

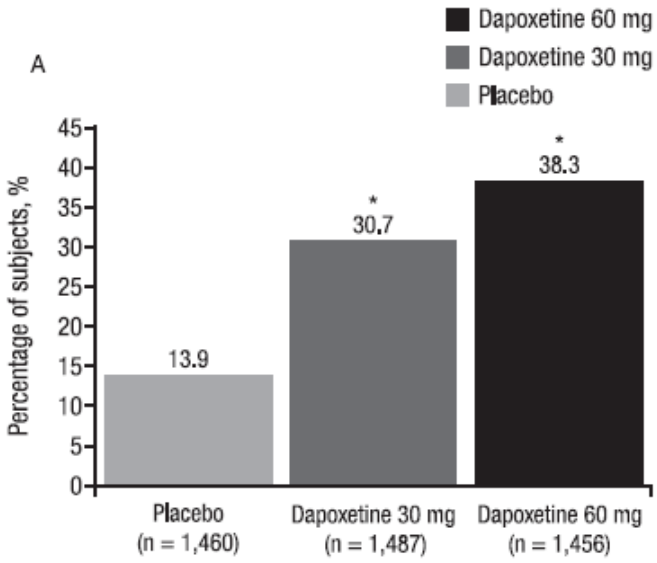
Changes in IELT over time



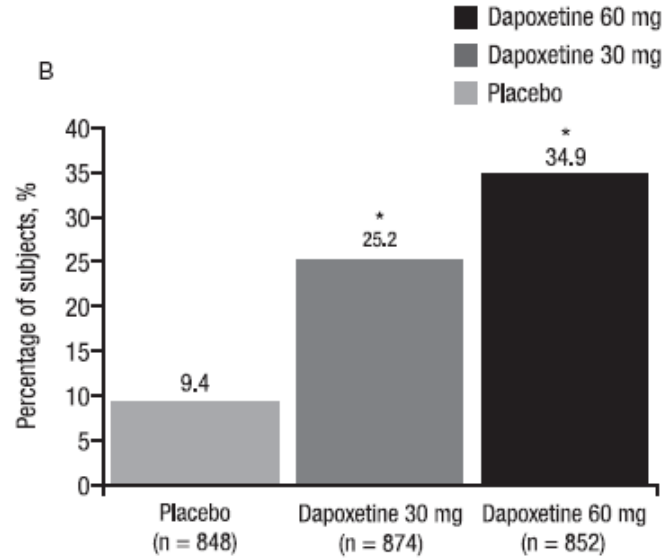
McMahon et al., J Sex Med 2011;8:524

Percentages of subjects reporting that their PE was “better” or “much better” at week 12

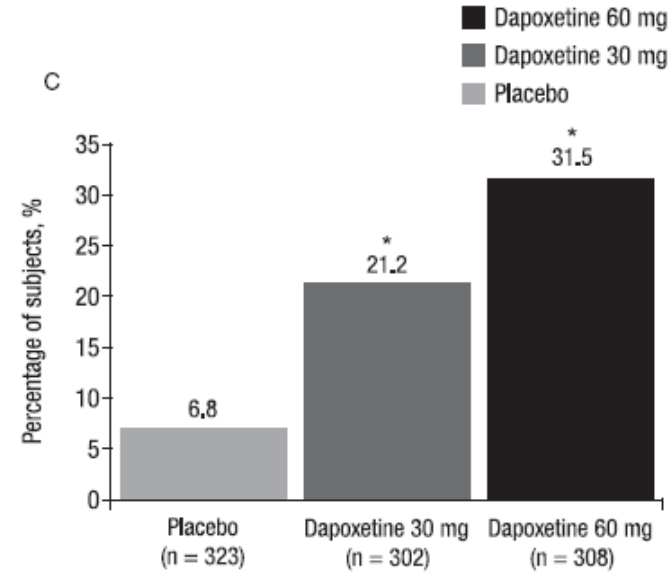
Overall



Baseline IELT ≤ 60 sec



Baseline IELT ≤ 30 sec



McMahon et al., J Sex Med 2011;8:524

Treatment-emergent adverse events occurring in at least 2% of subjects

Adverse event, N (%)	Placebo (N = 1,857)	Total dapoxetine (N = 4,224)	Dapoxetine 30 mg prn (N = 1,616)	Dapoxetine 60 mg prn (N = 2,106)	Dapoxetine 60 mg qd (N = 502)
Nausea	41 (2.2)	731 (17.3)	178 (11.0)	467 (22.2)	86 (17.1)
Dizziness	40 (2.2)	399 (9.4)	94 (5.8)	230 (10.9)	75 (14.9)
Headache	89 (4.8)	332 (7.9)	91 (5.6)	185 (8.8)	56 (11.2)
Diarrhea	32 (1.7)	248 (5.9)	56 (3.5)	145 (6.9)	47 (9.4)
Somnolence	10 (0.5)	166 (3.9)	50 (3.1)	98 (4.7)	18 (3.6)
Fatigue	23 (1.2)	164 (3.9)	32 (2.0)	86 (4.1)	46 (9.2)
Insomnia	28 (1.5)	161 (3.8)	34 (2.1)	83 (3.9)	44 (8.8)
Nasopharyngitis	43 (2.3)	129 (3.1)	51 (3.2)	61 (2.9)	17 (3.4)

prn = on demand; qd = daily.

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Studies of SSRIs in patients with major psychiatric disorders, such as depression or obsessive compulsive disorder, have suggested that SSRIs are potentially associated with certain safety risks, including anxiety, akathisia, changes in mood, and suicidality (in adolescents)

Coupland et al.; J Clin Psychopharmacol 1996;16:356–62.
Tamam & Ozpoyraz Adv Ther 2002;19:17–26.
Zajecka et al., J Clin Psychiatry 1997;58:291–7.

Mean (SD) scores for BDI-II, MADRS, HAM-A, and BARS at baseline and end point

	International study			North American study		
	Placebo	Dapoxetine 30 mg prn	Dapoxetine 60 mg prn	Placebo	Dapoxetine 60 mg prn	Dapoxetine 60 mg qd
n						
Baseline	384	387	388	245	491	502
End point	356	368	363	218	436	445
BDI-II (possible score range 0–63)*						
Baseline	2.6 (4.27) [N = 375]	2.4 (4.35) [N = 377]	2.3 (3.72) [N = 380]	2.7 (3.66) [N = 241]	2.9 (4.01) [N = 485]	3.3 (4.61) [N = 491]
End point	1.8 (4.04) [N = 345]	1.8 (4.52) [N = 356]	1.6 (3.40) [N = 352]	1.6 (3.61) [N = 221]	1.6 (3.30) [N = 431]	1.6 (3.05) [N = 443]
MADRS (possible score range 0–60)†						
Baseline	1.0 (2.08)	0.9 (2.25)	1.0 (1.93)	1.0 (2.00)	0.9 (1.80)	1.1 (2.14)
End point	0.8 (2.38)	0.9 (2.57)	0.7 (2.20)	0.9 (2.55)	0.9 (2.53)	0.9 (2.33)
HAM-A (possible score range 0–56)‡						
Baseline	2.2 (2.41)	2.3 (2.64)	2.2 (2.36)	2.3 (2.33)	2.2 (2.31)	2.3 (2.36)
End point	1.6 (2.36)	1.6 (2.68)	1.5 (2.25)	1.9 (2.60)	1.6 (2.42)	1.8 (2.50)
BARS (total score; possible score range 0–18)						
Baseline	0.1 (0.05)	0.1 (0.53)	0.1 (0.45)	0.1 (0.39)	0.0 (0.28) [N = 490]	0.1 (0.40) [N = 500]
End point	0.2 (0.05)	0.1 (0.44)	0.0 (0.32)	0.1 (0.38)	0.0 (0.29)	0.1 (0.38)

BDI-II = Beck Depression Inventory-II
MADRS = Montgomery-Åsberg Depression Rating Scale
HAM-A = Hamilton Anxiety Scale;
BARS = Barnes Akathisia Rating Scale

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Evaluation of suicidality: responses to BDI-II (Item 9) and MADRS (Item 10), n (%)

	International study			North American study		
	Placebo	Dapoxetine 30 mg prn	Dapoxetine 60 mg prn	Placebo	Dapoxetine 60 mg prn	Dapoxetine 60 mg qd
BDI-II (item 9) score						
Baseline	384	386	388	244	490	501
0	376 (97.9)	380 (98.4)	383 (98.7)	243 (99.6)	489 (99.8)	498 (99.4)
1	8 (2.1)	6 (1.6)	5 (1.3)	1 (0.4)	1 (0.2)	3 (0.6)
2	0	0	0	0	0	0
3	0	0	0	0	0	0
End point	346	359	353	222	434	447
0	338 (97.7)	357 (99.4)	351 (99.4)	221 (99.5)	432 (99.5)	447 (100)
1	8 (2.3)	2 (0.6)	2 (0.6)	1 (0.5)	2 (0.5)	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
MADRS (item 10) score						
Baseline	384	387	388	245	491	502
0	382 (99.5)	383 (99.0)	388 (100)	245 (100)	490 (99.8)	498 (99.2)
1	1 (0.3)	2 (0.5)	0	0	1 (0.2)	4 (0.8)
2	1 (0.3)	2 (0.5)	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
End point	356	368	363	218	436	445
0	354 (99.4)	366 (99.5)	363 (100)	218 (100)	433 (99.3)	444 (99.8)
1	1 (0.3)	1 (0.3)	0	0	3 (0.7)	1 (0.2)
2	1 (0.3)	1 (0.3)	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0

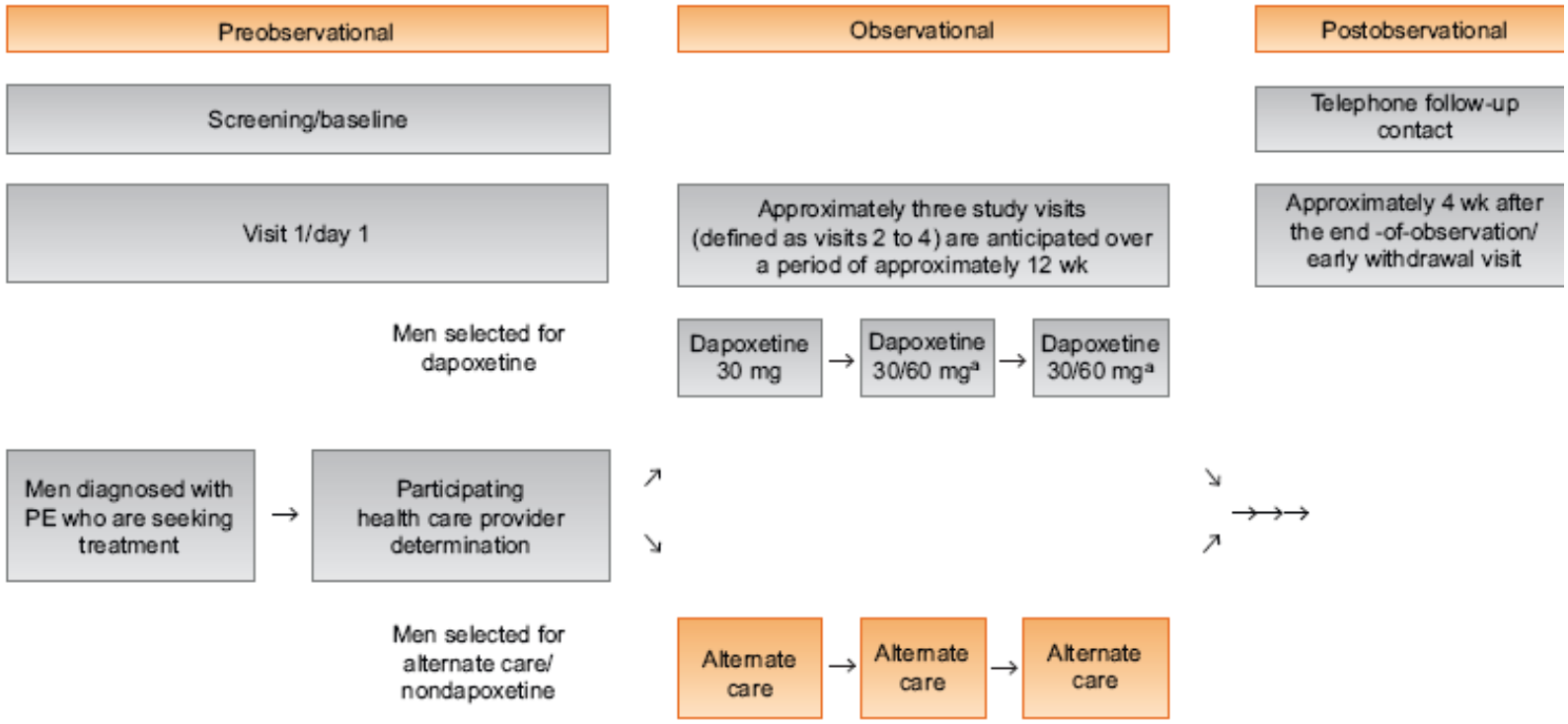
BDI-II = Beck Depression Inventory-II
MADRS = Montgomery-Åsberg Depression Rating Scale

McMahon et al., J Sex Med 2011;8:524

Results from a Prospective Observational Study of Men with Premature Ejaculation Treated with Dapoxetine or Alternative Care: The PAUSE Study

Vincenzo Mirone [a,*], *Davide Arcaniolo* [a], *David Rivas* [b], *Scott Bull* [b], *Joseph W. Aquilina* [b], *Paolo Verze* [a], *on behalf of the PAUSE study team*

[a] *Department of Urology, University of Naples Federico II, Naples, Italy;* [b] *Janssen Research & Development, LLC, Raritan, NJ, USA*



Mirone et al., Eur Urol. 2014;65:733

	Dapoxetine	Alternative care/nondapoxetine	Total
No. of patients	6712	3316	10 028
Age, yr			
Mean (SD)	40.6 (11.78)	40.2 (12.35)	40.5 (11.97)
Median	40.0	39.0	40.0
Range	17–79	17–81	17–81
Race, no. (%)			
White	6437 (95.9)	3189 (96.2)	9626 (96.0)
Black	79 (1.2)	41 (1.2)	120 (1.2)
Asian	62 (0.9)	51 (1.5)	113 (1.1)
Unknown	6 (0.1)	6 (0.2)	12 (0.1)
Multiple	2 (<0.1)	2 (0.1)	4 (<0.1)
Not reported	1 (<0.1)	1 (<0.1)	2 (<0.1)
Other	125 (1.9)	26 (0.8)	151 (1.5)
PE diagnosis, no. (%)			
Lifelong	3133 (46.7)	1292 (39.0)	4425 (44.1)
Acquired	2951 (44.0)	1596 (48.1)	4547 (45.3)
Unsure	628 (9.4)	426 (12.8)	1054 (10.5)
Missing	0	2 (0.1)	2 (<0.1)

SD = standard deviation; PE = premature ejaculation.
For continuous variables, mean and median are rounded to one decimal point, and standard deviations are rounded to two decimal points.

Mirone et al., Eur Urol. 2014;65:733

Study visit	Total (*N* = 9443)				
	Dapoxetine	Nondapoxetine			Total
		Total	Nonoral	Oral drug	
Dapoxetine dose, mg					
No. of patients*	6128	3315	1898	1417	**9443**
Patients with at least one AE, no. (%)	737 (12.0)	294 (8.9)	66 (3.5)	228 (16.1)	**1031** (10.9)
Nausea, no. (%)	192 (3.1)	34 (1.0)	1 (0.1)	33 (2.3)	**226** (2.4)
Headache, no. (%)	157 (2.6)	24 (0.7)	5 (0.3)	19 (1.3)	**181** (1.9)
Vertigo, no. (%)	64 (1.0)	13 (0.4)	0	13 (0.9)	**77** (0.8)
Fatigue, no. (%)	22 (0.4)	40 (1.2)	0	40 (2.8)	**62** (0.7)
Diarrhea, no. (%)	34 (0.6)	24 (0.7)	1 (0.1)	23 (1.6)	**58** (0.6)

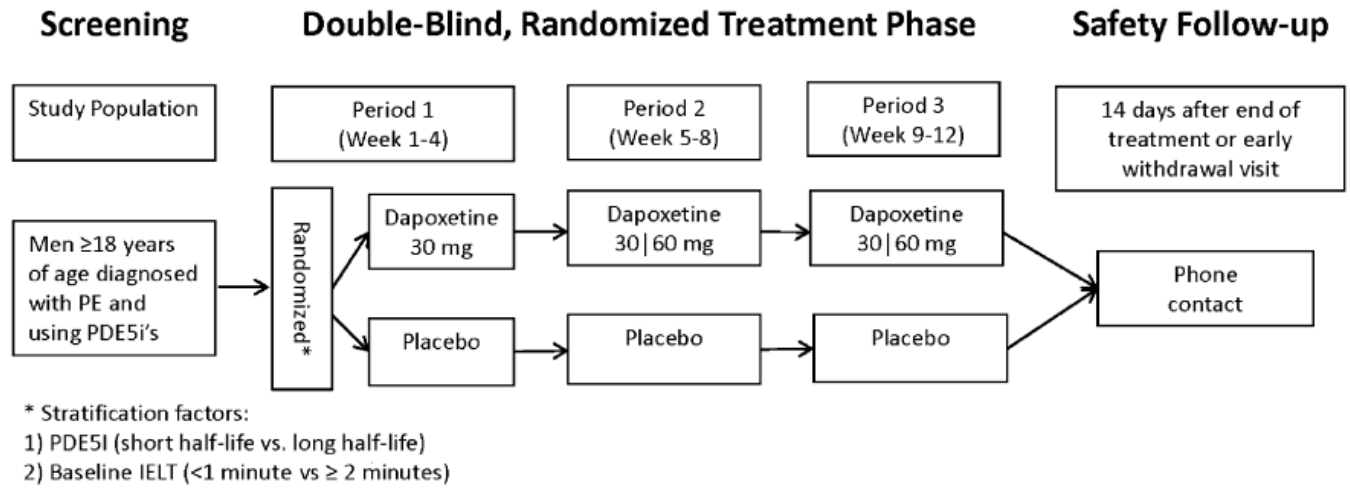
Mirone et al., Eur Urol. 2014;65:733

Main recommendations

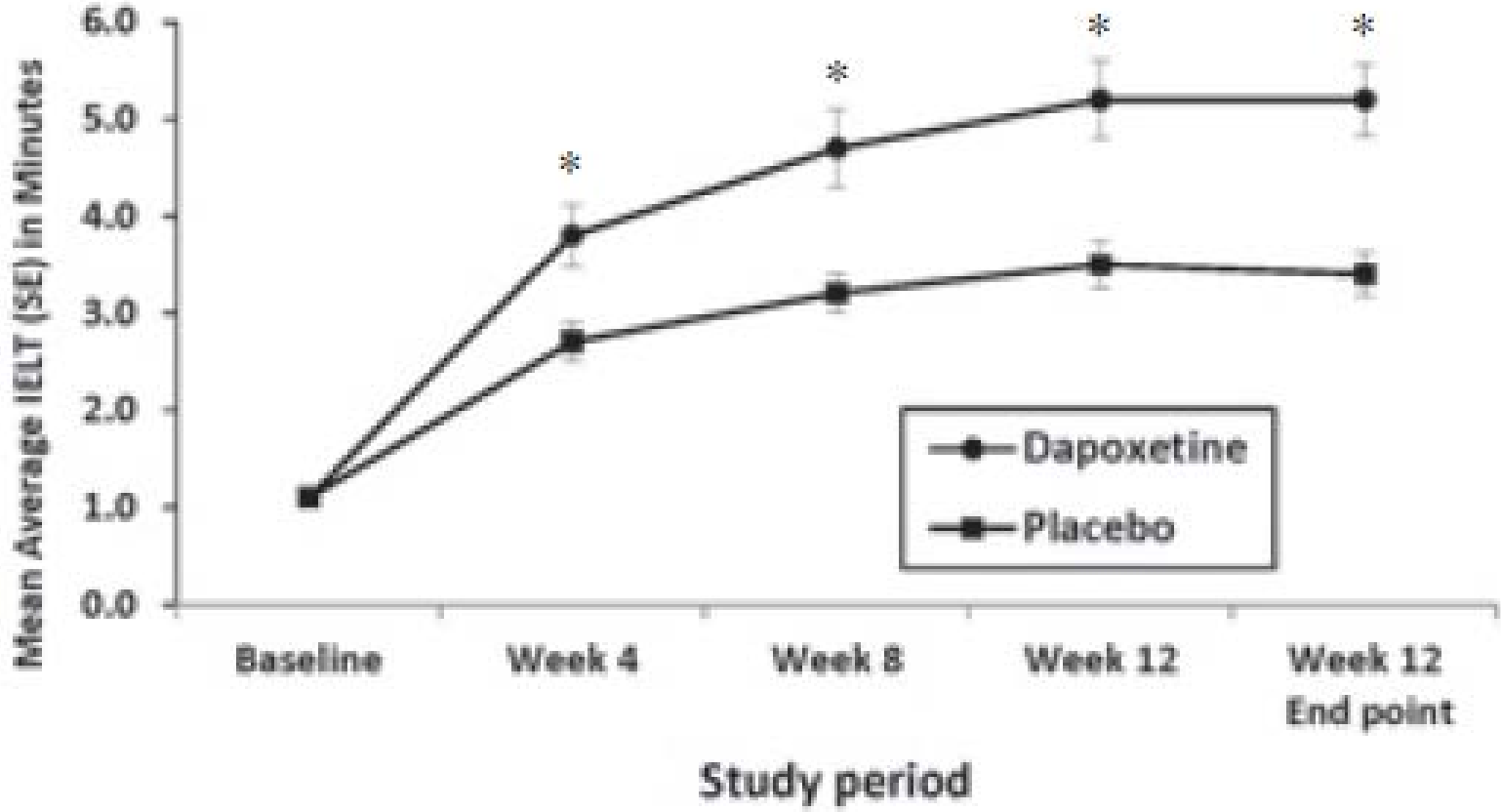
- Caution in patients with moderate/severe hepatic or renal insufficiency
- No limitation with meals
- Caution with alcohol
- Concomitant use of Priligy with PDE5 inhibitors may result in orthostatic hypotension. The efficacy and safety of Priligy in patients with both premature ejaculation and erectile dysfunction concomitantly treated with Priligy and PDE5 inhibitors have not been established

Efficacy and Safety of Dapoxetine in Men with Premature Ejaculation and Concomitant Erectile Dysfunction Treated with a Phosphodiesterase Type 5 Inhibitor: Randomized, Placebo-Controlled, Phase III Study

Chris G. McMahon, MBBS, FAChSHM,* Francois Giuliano, MD, PhD,†
John Dean, MBBS, MRCGP, FRCGP,‡ Wayne J.G. Hellstrom, MD, FACS,§ Scott Bull, PharmD,¶
Fisseha Tesfaye, PhD,¶ Om Sharma, PhD,¶ David A. Rivas, MD,¶ and Joseph W. Aquilina, MD¶



McMahon et al., J Sex Med 2013;10:2312



McMahon et al., J Sex Med 2013;10:2312

TEAE	Placebo (n = 245)	Dapoxetine (n = 250)	*P* value*
Total subjects with TEAE, n (%)	49 (20.0)	74 (29.6)	0.0135
Nausea	3 (1.2)	23 (9.2)	<0.0001
Headache	12 (4.9)	11 (4.4)	0.7924
Diarrhea	2 (0.8)	9 (3.6)	0.0357
Dizziness	2 (0.8)	6 (2.4)	0.1624
Dizziness postural	1 (0.4)	6 (2.4)	0.0606
Upper respiratory tract infection	1 (0.4)	4 (1.6)	0.1849
Vertigo	1 (0.4)	4 (1.6)	0.1849
Dyspepsia	1 (0.4)	3 (1.2)	0.3252
Hyperhidrosis	0	3 (1.2)	0.0855
Insomnia	1 (0.4)	3 (1.2)	0.3252
Nasopharyngitis	4 (1.6)	3 (1.2)	0.6836
Flushing	3 (1.2)	0	0.0793
Nasal congestion	3 (1.2)	0	0.0793

McMahon et al., J Sex Med 2013;10:2312

Efficacy and Safety of Dapoxetine in Men with Premature Ejaculation and Concomitant Erectile Dysfunction Treated with a Phosphodiesterase Type 5 Inhibitor: Randomized, Placebo-Controlled, Phase III Study

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Fisseha Tesfaye, PhD,¶ Om Sharma, PhD,¶ David A. Rivas, MD,¶ and Joseph W. Aquilina, MD¶

Conclusions. In men with PE and comorbid ED on a stable regimen of PDE5 inhibitor, dapoxetine provided meaningful treatment benefit and was generally well tolerated.

McMahon et al., J Sex Med 2013;10:2312

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PROF MARIO MAGGI
CHIEF OF
Sexual Medicine & Andrology
Unit, University of Florence,
Florence, Italy

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