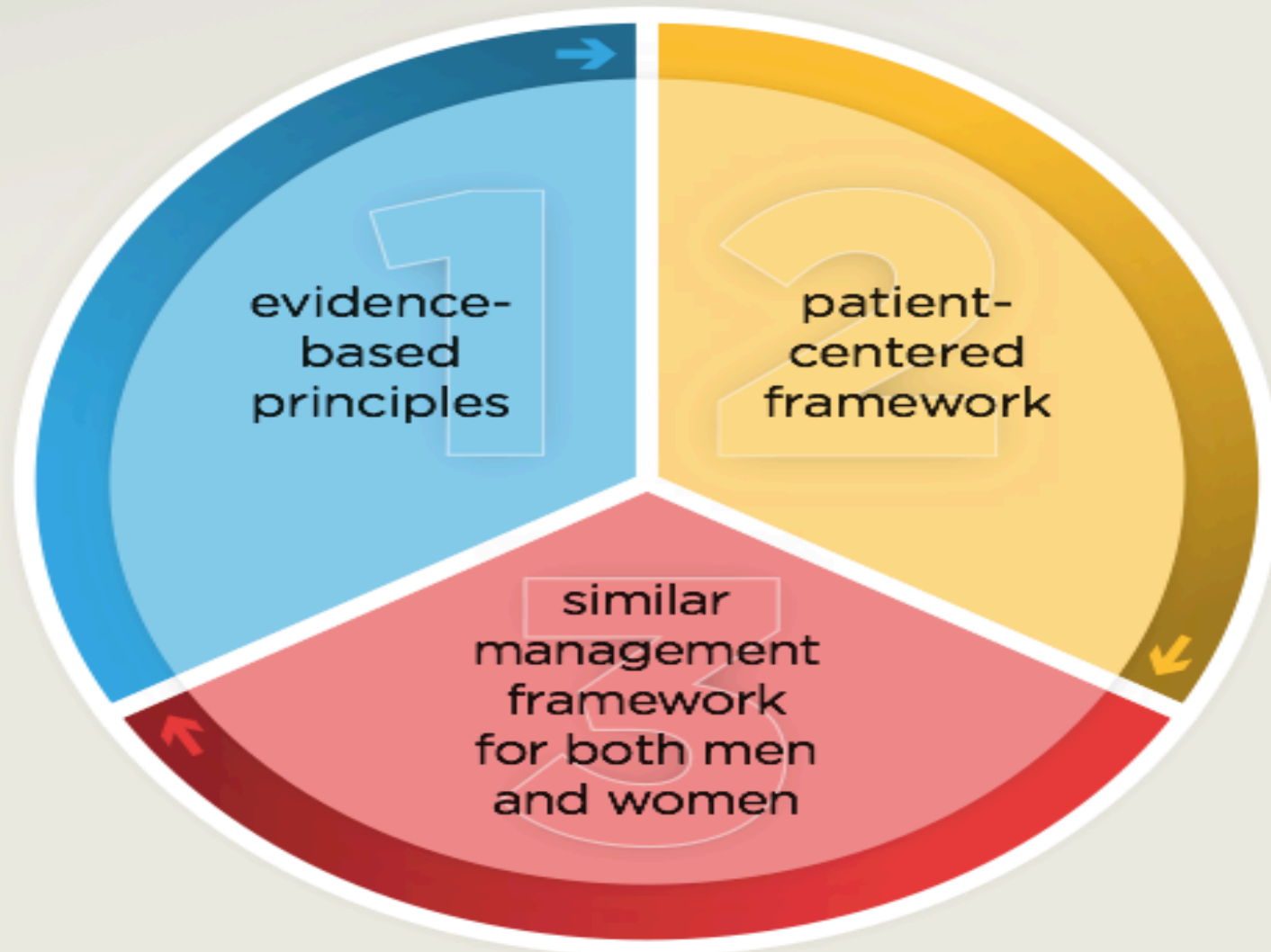


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e enough memory to
image may have
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to delete the image
l.

Γνωρίζετε καλά τα φάρμακα της στύσης; Ένα τεστ ερωτήσεων για ειδικούς

Δημήτρης Χατζηχρήστου

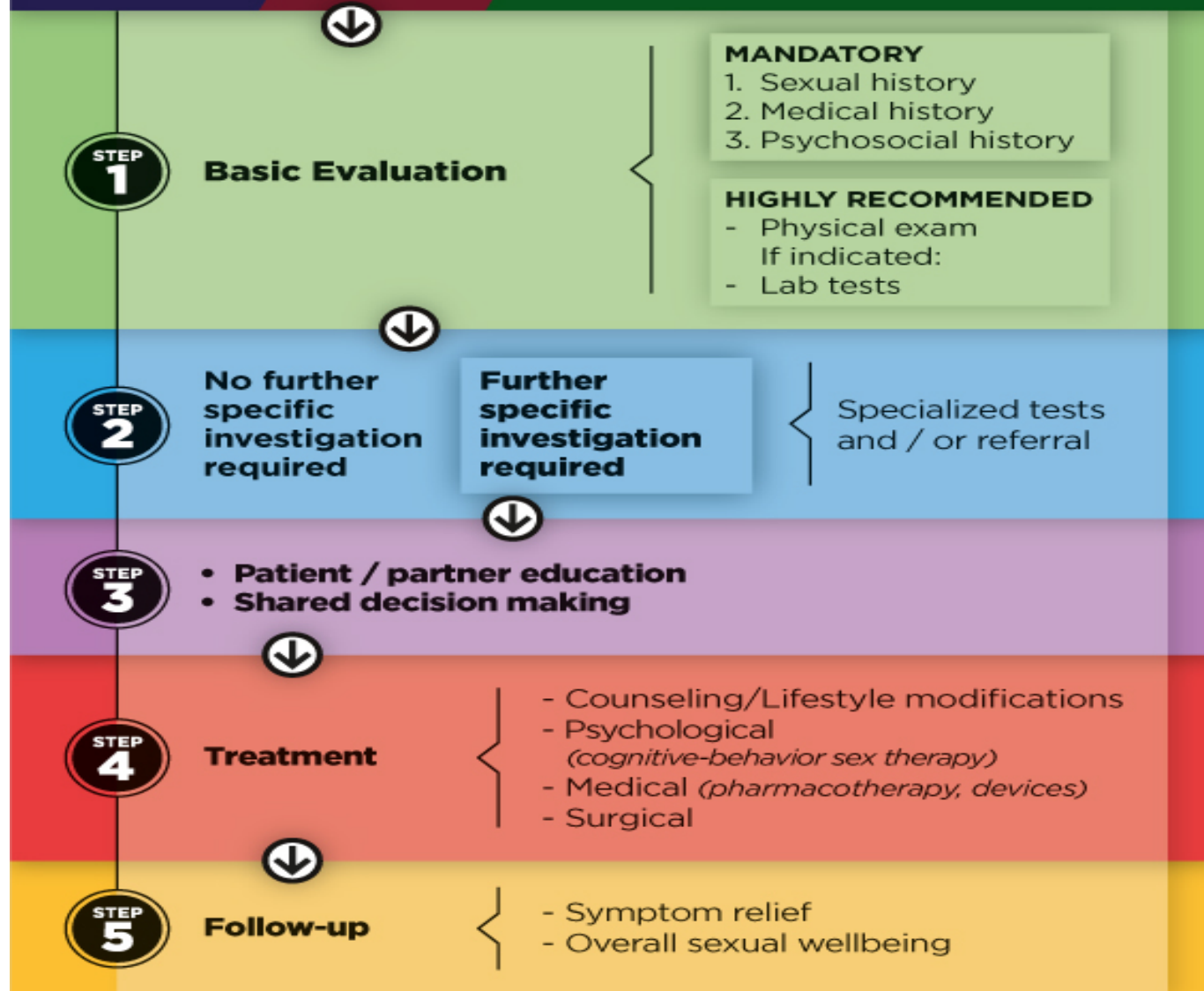
Principles of Sexual Medicine



A balanced and integrated approach to clinical evaluation and treatment of sexual dysfunctions

The ICSM-5R (5 steps-revised) Algorithm for the Management of Sexual Dysfunctions in Men and Women.

Man / Woman with sexual complaints



Summary and Recommendations: Specialized Diagnostic Tests for Erectile Dysfunction

Five diagnostic tests are recommended (grade B):

Color Duplex Doppler Penile Ultrasonography (CDDPU)

Intracavernous Injection Pharmacotesting (ICI)

Dynamic Infusion Cavernosometry Cavernosography (DICCC)

Nocturnal Penile Tumescence and Rigidity (NPTR)

Selective Internal Pudendal Arteriography (SIPA)

ΘΕΡΑΠΕΙΕΣ

ΣΤΥΤΙΚΗΣ ΔΥΣΛΕΙΤΟΥΡΓΙΑΣ

Τα κάτω...**πάνω!**



ΤΑ ΦΑΡΜΑΚΑ ΤΗΣ ΣΤΥΣΗΣ



Κανένα φυτικό σκεύασμα ή συμπλήρωμα διατροφής δεν έχει αποδείξει ότι βοηθά τη στύση!



Όλα τα αποτελεσματικά φάρμακα χορηγούνται με ιατρική συνταγή.



Η μόνη ένδειξη είναι στυτική δυσλειτουργία οργανικής και ψυχογενούς αιτιολογίας. Στη 2η περίπτωση συνδυάζεται με θεραπεία από σεξολόγο



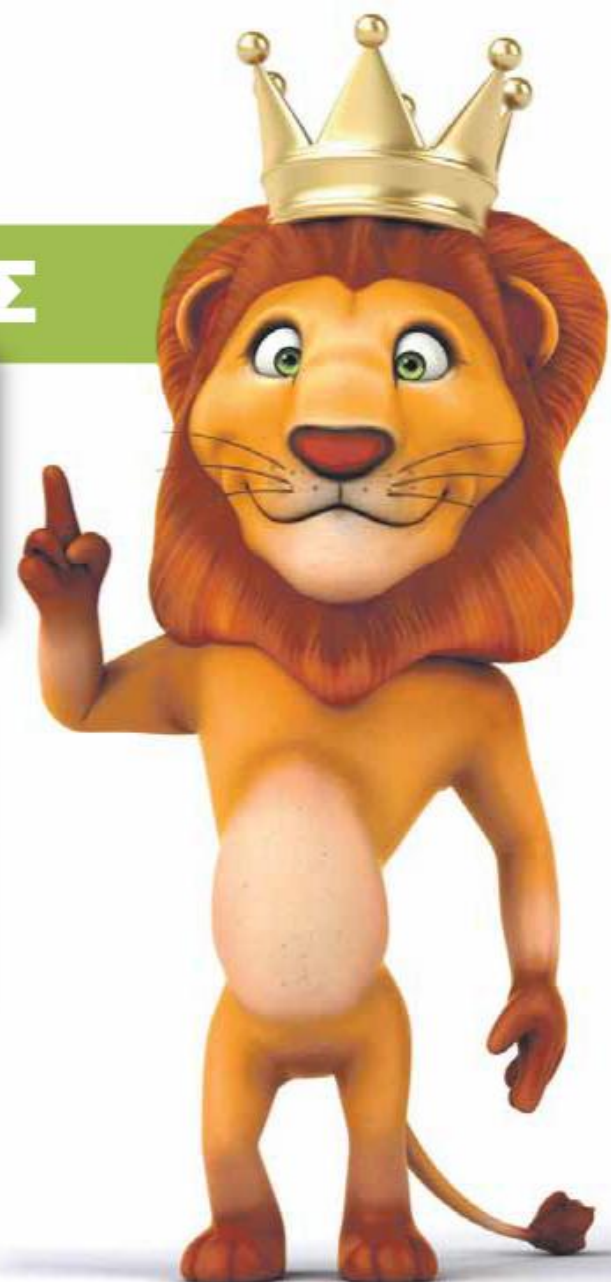
Κανένα από αυτά δεν είναι αφροδισιακό, δηλαδή δεν επηρεάζει την ερωτική διάθεση/επιθυμία



Όλα τα φάρμακα προκαλούν αγγειοδιαστολή και αύξηση της αιμάτωσης του πέους



Χωρίζονται σε 2 κατηγορίες: σε χάπια και ενέσεις



ΤΑ ΦΑΡΜΑΚΑ ΑΠΟ ΤΟ ΣΤΟΜΑ



ΔΙΑΤΙΘΕΝΤΑΙ
ΣΤΗΝ
ΕΛΛΑΔΑ

(όλα είναι σε μορφή
δισκίου για λήψη
από το στόμα)

ΑΒΑΝΑΦΙΛΗ
ΒΑΡΔΕΝΑΦΙΛΗ
ΣΙΛΔΕΝΑΦΙΛΗ
ΤΑΔΑΛΑΦΙΛΗ

κυκλοφορεί και σε μορφή
διαλυόμενου, στο στόμα, δισκίου 10mg

κυκλοφορεί και σε 5mg δόση για καθημερινή
λήψη ανεξάρτητα από την επαφή

Η ΜΟΡΦΗ ΑΥΤΗ ΕΧΕΙ 2 ΕΝΔΕΙΞΕΙΣ



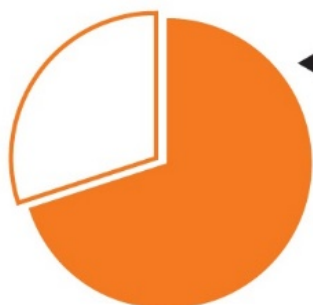
Είναι απαραίτητη
η **ΕΡΩΤΙΚΗ ΕΠΙΘΥΜΙΑ**
για να προκληθεί στύση



άντρες
με συχνές
ερωτικές
επαφές

μεγαλύτεροι άντρες που πάσχουν
και από καλοήγη υπερπλασία προστάτη
(η συχνότερη αιτία για προβλήματα
ούρησης μετά τα 50 έτη).

ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ



70%

ενώ **ΜΕΙΩΝΕΤΑΙ**
σε **50%**

σε άντρες με σοβαρό
οργανικό πρόβλημα

(σακχαρώδης διαβήτης,
νευρολογικές παθήσεις,
μετά ριζική προστατεκτομή)

ΑΠΟΛΥΤΗ
ΑΝΤΕΝΔΕΙΞΗ

Η ΛΗΨΗ
ΝΙΤΡΩΔΩΝ
ΦΑΡΜΑΚΩΝ

ΣΥΝΗΘΕΙΣ
ΠΑΡΕΝΕΡΓΕΙΕΣ
ΠΟΝΟΚΕΦΑΛΟΣ
ΔΥΣΠΕΨΙΑ
ΜΥΑΛΓΙΑ

ΠΩΣ ΕΠΗΡΕΑΖΕΙ Η ΤΡΟΦΗ...

Η τροφή καθυστερεί την απορρόφηση,
άρα και την δράση στα δισκία για λήψη
από το στόμα, εκτός της ταδαλαφίλης.

**Τα δισκία που διαλύονται στο στόμα
δεν επηρεάζονται**



Η κοινωνική
χρήση **αλκοόλ**
ΔΕΝ ΕΠΗΡΕΑΖΕΙ
τη δράση τους



ΧΑΡΑΚΤΗΡΙΣΤΙΚΑ ΤΩΝ ΦΑΡΜΑΚΩΝ ΤΗΣ ΣΤΥΣΗΣ

	ΑΒΑΝΑΦΙΛΗ	ΒΑΡΔΕΝΑΦΙΛΗ	ΣΙΛΔΕΝΑΦΙΛΗ	ΤΑΔΑΛΑΦΙΛΗ	ΑΛΠΡΟΣΤΑΔΙΛΗ
ΜΟΔΟΣ ΛΗΨΗΣ	Από το στόμα 	Από το στόμα ή διαλυόμενα δίσκιο στο στόμα	Από το στόμα 	Από το στόμα 	Ενεση στο πέος 
ΔΟΣΟΛΟΓΙΑ	mg  100 & 200	mg — 10 & = 20	mg 25 50 & 100 	mg 5 10 & 20 	μg 20 
ΕΠΙΣΤΗ συνήθης ηγούμενη δόση ηησίως (σε mg)	mg  200	mg = 20	mg  100	mg 20 	μg 40 
Επίσης χρόνος λήψη μέχρι ηράσει (σε ώρες)	ώρες  περίπου 0,5	ώρες  περίπου 1	ώρες  περίπου 1	ώρες  1-2	ώρες  0,2
Επίσης διάρκεια ησης από λήψη (σε ώρες)	 >6	 6 έως 12	 6 έως 12	 έως 36	 1 έως 2
Επίσης άζεται σεξου-ός ερεθισμός;	ΝΑΙ	ΝΑΙ	ΝΑΙ	ΝΑΙ	ΟΧΙ



ASK AN EXPERT



6+8

ερωτήσεις

ς

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 1

Γιατί μόνο 1 στους 10 ασθενείς με πρόβλημα στύσης μιλάνε σε γιατρό για το πρόβλημα;

Το πρόβλημα της περιορισμένης αναζήτησης θεραπείας για ΣΔ

- Πολλοί ασθενείς δεν αισθάνονται άνετα να αναζητήσουν θεραπεία
- Η ΣΔ δεν σχετίζεται πάντα με αυξημένη δυσαρέσκεια του ασθενή*
- **Μήνυμα προς το ασθενή (TALK)**

Talk

Εμπιστευθείτε το γιατρό σας

Ask

Ρωτήστε για το σεξουαλικό σας πρόβλημα

Learn

Μάθετε για τις θεραπευτικές επιλογές

Keep

Κρατήστε στην σύντροφο σας σύμμαχο

*Evangelia N, Kirana PS, Chiu G et al. (2010) Level of bother and treatment-seeking predictors among male and female in-patients with sexual problems: a hospital-based study. J Sex Med 7:700-711.

Training physicians to treat erectile dysfunction patients: development and evaluation of a course on communication and management strategies.

Madis L¹, Papaharitou S, Salpiggidis G, Tsimtsiou Z, Nakopoulou E, Kirana PS, Moisis K, Hatzichristou D.

Background information

Abstract

OBJECTIVE: To describe the development and assess the outcome of a workshop on erectile dysfunction (ED) management based on participants' evaluations.

DESIGN: The study involved physicians who attended a workshop offered throughout the country, during a 3-year period. The workshop included video-based dramatizations, and role-play sessions. A pilot study investigated the workshop's impact on physicians' attitudes toward illness and sexual behavior issues; Patient-Practitioner Orientation Scale (PPOS) and Cross Cultural Attitude Scale (CCAS) were administered before and after the course. New knowledge acquisition, quality of presentation, and workshop's usefulness in their clinical practice were the domains used for workshop's evaluation. Analysis used quantitative and qualitative methods.

RESULTS: A total of 194 questionnaires were administered during the pilot study and the response rate was 53.6%. A shift in attitudes toward illness and less judgmental attitude toward patients' sexual attitudes were revealed (total PPOS score and Sharing subscale: $P < 0.05$). Six hundred physicians were asked to evaluate the workshops and the response rate was 62.3%. The tutorial session for "medical history of ED" ($P < 0.001$) and the role-play on sexual history taking ($P < 0.05$) received higher evaluation scores. Qualitative analysis showed the most frequently reported category referred to the appropriateness of role-play as a teaching and awareness-raising technique (31.25%); a change in clinical practice and communication patterns was identified by 20% of the participants who stressed the necessity for multidisciplinary approach, as well as the adoption of a nonjudgmental attitude toward patients.

CONCLUSION: Training courses on ED management, using a combination of tutorial and interactive sessions, constitute an effective way of knowledge acquisition, enhancing physicians' communication skills with ED patients, and influencing attitudes toward patient-centeredness in sexual issues. Results strongly support the establishment of sexual medicine courses at continuing medical education curricula.

Συζητώντας στο ιατρείο για την Στυτική Δυσλειτουργία

- Τα σεξουαλικά προβλήματα υγείας συχνά παραμελούνται στην κλινική πράξη
- Οι ασθενείς αισθάνονται αμηχανία και ότι οι γιατροί δεν έχουν την ειδικευση για να διαχειριστούν το πρόβλημα τους
- Οι γιατροί διστάζουν να ρωτήσουν, έχουν περιορισμένο χρόνο και έτσι αυξάνεται το χάσμα μεταξύ σεξουαλικής ιατρικής και κλινικών δεξιοτήτων.

Προϋποθέσεις που πρέπει να δημιουργήσει ο γιατρός:

- Δημιουργείστε μια ατμόσφαιρα ασφάλειας και σεβασμού
- Η συζήτηση να είναι πολιτισμένη
- Σεβαστείτε τις σεξουαλικές προτιμήσεις του κάθε ατόμου
- Παρουσιάστε τεκμηριωμένα τις θεραπευτικές επιλογές
- Οργανώστε μια στενή παρακολούθηση

ΣΤΥΤΙΚΗ ΔΥΣΛΕΙΤΟΥΡΓΙΑ

Παράγοντες
κινδύνου
για στυτική
δυσλειτουργία

ΤΡΟΠΟΣ ΖΩΗΣ

Κάπνισμα
Παχυσαρκία
Χρήση
ουσιών

ΤΡΑΥΜΑ

Κάταγμα πέους
Νόσος
Peyronie

ΟΥΡΟΛΟΓΙΚΕΣ ΠΑΘΗΣΕΙΣ

Φίμωση
Καλοήθης υπερπλασία
προστάτη
Ακράτεια
Χρόνια προστατίτις
Πριαπισμός

ΝΕΥΡΟΛΟΓΙΚΕΣ ΠΑΘΗΣΕΙΣ

Σκλήρυνση
κατά πλάκες
Περιφερική
νευροπάθεια
Κακώσεις νωτιαίου
μυελού

ΚΑΡΔΙΑΓΓΕΙΑΚΕΣ ΠΑΘΗΣΕΙΣ

Υπέρταση
Στεφανιαία νόσος
Περιφερική
αγγειοπάθεια
Υπερλιπιδαιμία

Ηπατική
ανεπάρκεια

Νεφρική
ανεπάρκεια

ΕΝΔΟΚΡΙΝΟ-ΠΑΘΕΙΕΣ

Μεταβολικό σύνδρομο
Σακχαρώδης διαβήτης
Υπογοναδισμός
Υπερπρολακτιναιμία
Νόσοι
θυροειδούς

ΨΥΧΙΑΤΡΙΚΕΣ ΠΑΘΗΣΕΙΣ

Αγχώδεις
διαταραχές
Κατάθλιψη

ΙΑΤΡΟΓΕΝΕΙΣ

Χειρουργεία
πυέλου/πέους
Φάρμακα
αντιυπερτασικά
αντικαταθλιπτικά
αντιανδρογόνα
αντιψυχωσικά

ΠΝΕΥΜΟ-ΝΟΛΟΓΙΚΕΣ ΠΑΘΗΣΕΙΣ

Υπνική άπνοια
Αποφρακτική
πνευμονο-
πάθεια



ΕΡΩΤΗΣΕΙΣ

Ερώτηση 2

Τι πρέπει να καθορίσουμε;

Καθορισμός σοβαρότητας της Στυτικής Δυσλειτουργίας

Δύο βασικές ερωτήσεις:

- Είστε σε θέση να επιτύχετε μια στύση σκληρή ώστε να επιτευχθεί η διείσδυση;
- Είστε σε θέση να διατηρήσετε την στύση αυτή μέχρι της εκσπερμάτιση;

Βαρύτητα

- **Ήπια:** Υπάρχουν σεξουαλικές επαφές πάνω από τις μισές φορές, αδυναμία επίτευξης πολύ σκληρής στύσης
- **Μέτρια:** Ανεπαρκή σκληρότητα και/ή διατήρηση, διείσδυση με βοήθεια κάποιες φορές.
- **Σοβαρή:** Δεν είναι δυνατή η σεξουαλική επαφή λόγω της ποιότητας των στύσεων

1

Ψυχογενής

Απουσία
οργανικού προβλήματος

2

Οργανική

Παρουσία οργανικού αίτιου,
απουσία σημαντικής γνωστι-
κής ή/και συναισθηματικής
επιβάρυνσης / ενόχλησης

3

Μικτή

Παρουσία οργανικού αίτιου,
σημαντική γνωστική
ή/και συναισθηματική
επιβάρυνση / ενόχληση

ΤΥΠΟΙ ΣΤΥΤΙΚΗΣ ΔΥΣΛΕΙΤΟΥΡΓΙΑΣ



ΣΤΥΤΙΚΗ ΔΥΣΛΕΙΤΟΥΡΓΙΑ

Παράγοντες κινδύνου για στυτική δυσλειτουργία

ΤΡΟΠΟΣ ΖΩΗΣ

Κάπνισμα
Παχυσαρκία
Χρήση ουσιών

ΤΡΑΥΜΑ

Κάταγμα πέους
Νόσος Peyronie

ΟΥΡΟΛΟΓΙΚΕΣ ΠΑΘΗΣΕΙΣ

Φίμωση
Καλοήθης υπερπλασία προστάτη
Ακράτεια
Χρόνια προστατίτις
Πριαπισμός

ΝΕΥΡΟΛΟΓΙΚΕΣ ΠΑΘΗΣΕΙΣ

Σκλήρυνση κατά πλάκες
Περιφερική νευροπάθεια
Κακώσεις νωτιαίου μυελού

ΚΑΡΔΙΑΓΓΕΙΑΚΕΣ ΠΑΘΗΣΕΙΣ

Υπέρταση
Στεφανιαία νόσος
Περιφερική αγγειοπάθεια
Υπερλιπιδαιμία

Ηπατική ανεπάρκεια

Νεφρική ανεπάρκεια

ΕΝΔΟΚΡΙΝΟΠΑΘΕΙΕΣ

Μεταβολικό σύνδρομο
Σακχαρώδης διαβήτης
Υπογοναδισμός
Υπερπρολακτιναιμία
Νόσος θυροειδούς

ΨΥΧΙΑΤΡΙΚΕΣ ΠΑΘΗΣΕΙΣ

Αγχώδεις διαταραχές
Κατάθλιψη

ΙΑΤΡΟΓΕΝΕΙΣ

Χειρουργεία πυέλου/πέους
Φάρμακα αντιυπερτασικά
αντικαταθλιπτικά
αντιανδρογόνα
αντιψυχωσικά

ΠΝΕΥΜΟΝΟΛΟΓΙΚΕΣ ΠΑΘΗΣΕΙΣ

Υπνική άπνοια
Αποφρακτική πνευμονοπάθεια

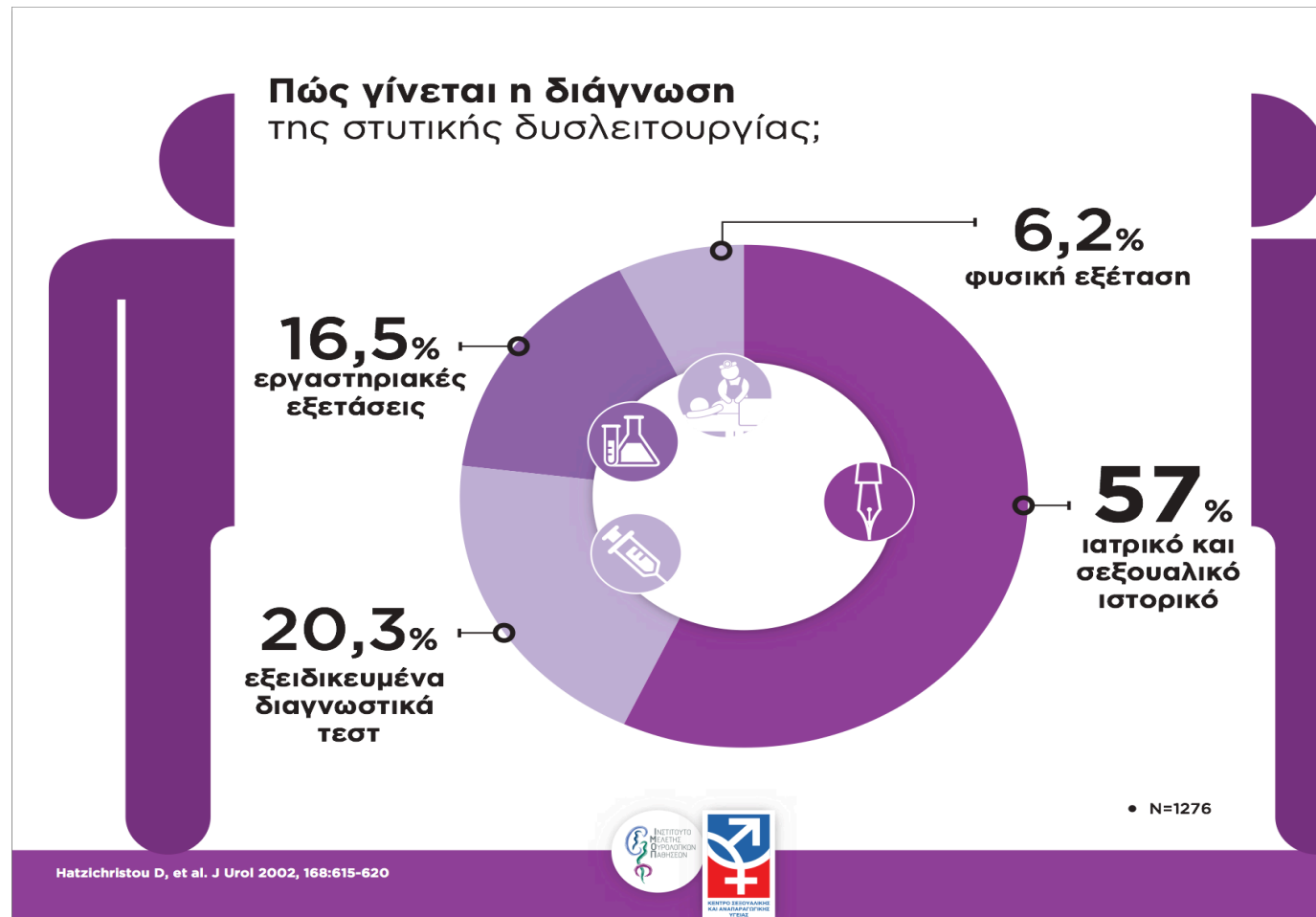




UROLOGY: Original Articles

Diagnostic Steps In The Evaluation Of Patients With Erectile Dysfunction

Hatzichristou, Konstantinos Hatzimouratidis, Michael Bekas, Apostolos Apostolidis, Vasiliios Hatzichristou, Konstantinos Yannakoyorgos



ΔΙΑΓΝΩΣΤΙΚΕΣ ΕΞΕΤΑΣΕΙΣ

ΔΙΑΓΝΩΣΤΙΚΗ ΕΞΕΤΑΣΗ

ΕΠΙΠΕΔΟ ΑΠΟΔΕΙΞΗΣ

Αγγειακές εξετάσεις

Triplex αγγείων πέους _____ 2B

Δυναμική φαρμακοσπραγγομετρία
/ σπραγγογραφία _____ 2B

Δοκιμασία ενδοσπραγγώδους ένεσης _____ 2B

Απεικονιστικές εξετάσεις

Εκλεκτική αγγειογραφία
έσω αιδοϊκών αρτηριών _____ 2C

Σεξουαλικός ερεθισμός με οπτικοακουστικό υλικό

Για εκτέλεση αγγειακών εξετάσεων _____ 3C

Με χρήση ενδοσπραγγωδών ενέσεων _____ 3C

Αξιολόγηση σκληρότητας στύσης

Καταγραφή νυκτερινών στύσεων (Rigiscan) _____ 2B

Νευροφυσιολογικές δοκιμασίες

Βολβοσπραγγώδες αντανακλαστικό _____ 2B

Βιοθεσιομετρία _____ 3C

Προκλητά δυναμικά ραχιαίου νεύρου πέους _____ 3C

Ηλεκτρομυογραφία σπραγγωδών σωμάτων _____ 3C



Η δύσκολη πρώτη επίσκεψη

1. Προσδιορίστε το σεξουαλικό πρόβλημα
2. Διάρκεια και σοβαρότητα της ΣΔ
3. Συνύπαρξη άλλων σεξουαλικών προβλημάτων
4. Καθορισμός της ποιότητας της στύσης
5. Κλινική εξέταση
6. Εργαστηριακός έλεγχος
7. Αξιολόγηση αποτελεσμάτων / Εκπαίδευση

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 3

Γνωρίζετε την
φαρμακολογία των PDE5i;

ΦΑΡΜΑΚΟΛΟΓΙΚΑ ΧΑΡΑΚΤΗΡΙΣΤΙΚΑ ΑΝΑΣΤΟΛΕΩΝ PDE5

ΠΑΡΑΜΕΤΡΟΙ	ΣΙΛΔΕΝΑΦΙΛΗ	ΤΑΔΑΛΑΦΙΛΗ	ΒΑΡΔΕΝΑΦΙΛΗ	ΑΦΑΝΑΦΙΛΗ	ΟΥΝΤΕΝΑΦΙΛΗ
	100 mg	200 mg	20 mg	200 mg	200 mg
C_{max}	560 µg/L	378 µg/L	18.7 µg/L	2920 µg/L	1139 µg/L
T_{max}	0.8-1 h	2 h	0.9 h	45 min	1 h
T_{1/2}	2.6-3.7 h	17.5 h	3.9 h	5.1 h	11 - 13 h
AUC	1685 µg.h/L	8066 µg.h/L	56.8 µg.h/L	8490 µg.h/L	7898 µg.h/L
Πρωτεϊνική δέσμευση	96%	94%	94%	99%	94%
Βιοδιαθεσιμότητα	41%	NA	15%	NA	NA



Έναρξη της δράσης

Παρόλο που κάποιοι ασθενείς θα ανταποκριθούν σε 15', χρειάζονται 30' για να ανταποκριθεί το 50% των ασθενών.

Διάρκεια της δράσης

- Σιλденаφίλη και βαρδεναφίλη: 6-12 h
- Αβαναφίλη: >6 h
- Ταδαναφίλη: έως 36 h

Τρόφιμα και αλκοόλ: αλληλεπιδράσεις

Σιλденаφίλη και βαρδεναφίλη: Καθυστέρηση της T και μείωση C_{max}
Ταδαναφίλη, αβαναφίλη, βαρδεναφίλη ODT: Δεν επηρεάζεται

Αποτελεσματικότητα την PDE5i

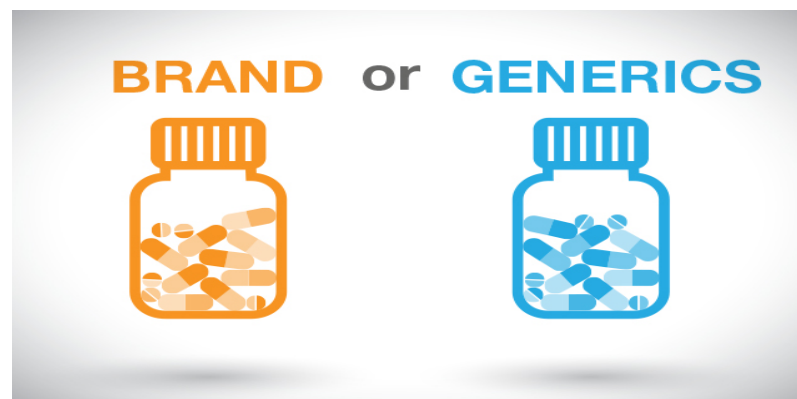
- Είναι ιδιαίτερα αποτελεσματικά φάρμακα (περίπου 75% των χρηστών απαντούν **ναι στο SEP3**)
- Η αποτελεσματικότητα είναι δοσοεξαρτώμενη
- Οι ασθενείς με μακροχρόνιο σακχαρώδη διαβήτη, μετά από ριζική και με νευρολογικές νόσου αποτελούν ειδικές κατηγορίες

Κατ' επίκληση ή καθημερινή λήψη;

- Η καθημερινή λήψη φαίνεται να έχει καλύτερα αποτελέσματα για επιτυχή συνουσία σε σύγκριση με την κατ' επίκληση λήψη ταδαναφίλης
- Η ημερήσια δοσολογία είναι καλά ανεκτή
- Σε ζευγάρια με συχνές σεξουαλικές επαφές που επιθυμούν αυθορμητισμό

- McMahon C (2005) Comparison of efficacy, safety and tolerability of on---demand tadalafil and daily dosed tadalafil for the treatment of erectile dysfunction. J Sex Med
- Rajfer J, Aliotta PJ, Steidle CP et al. (2007) Tadalafil dosed once a day in men with erectile dysfunction: a randomized, double---blind, placebo---controlled study in the US. Int J Impot Res

Τα φάρμακα για τη στύση: τελευταία νέα



Tadalafil 5mg: το τέλος των αμφισβητήσεων

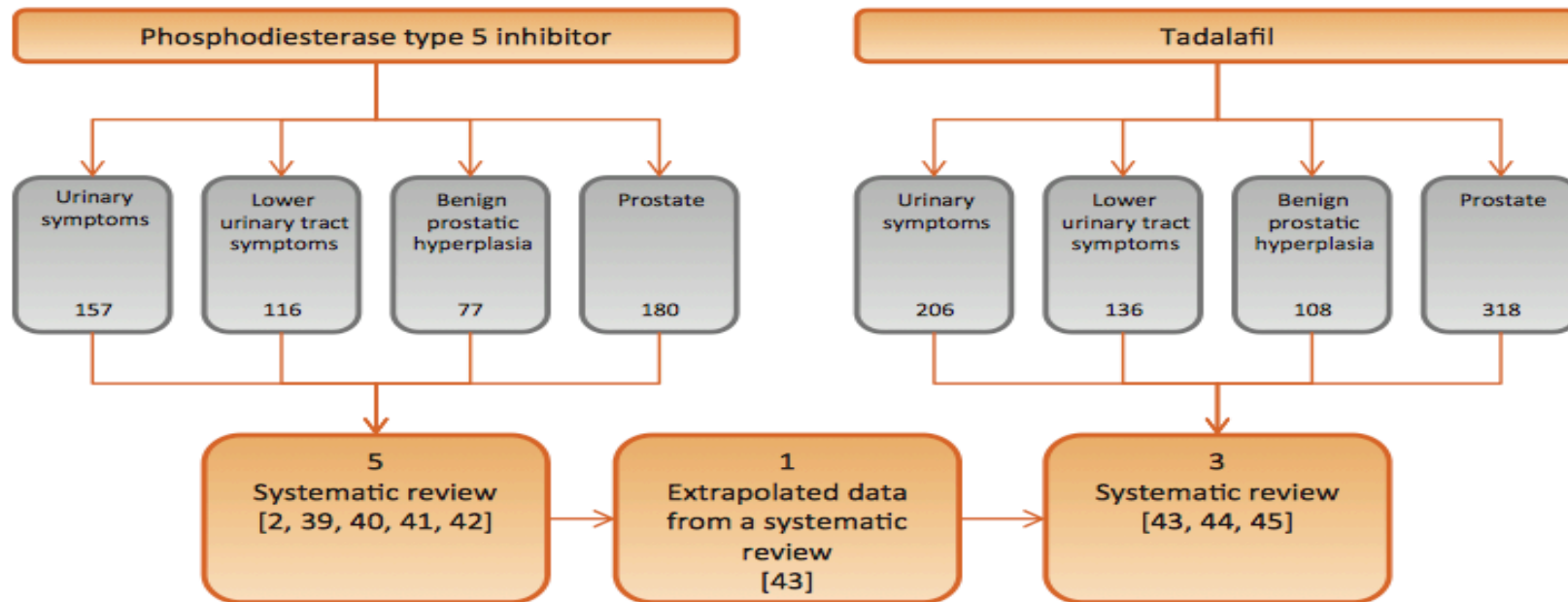
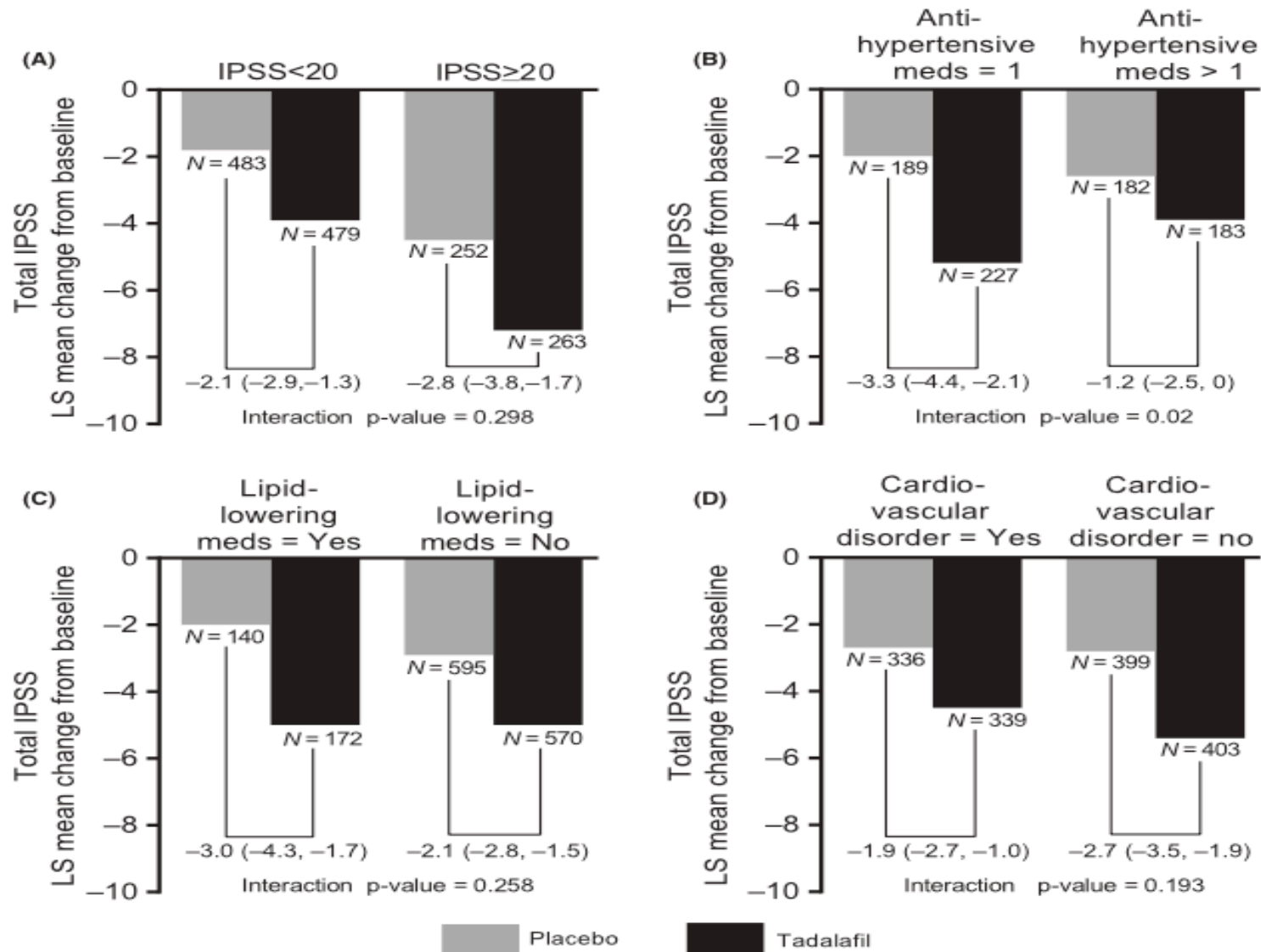


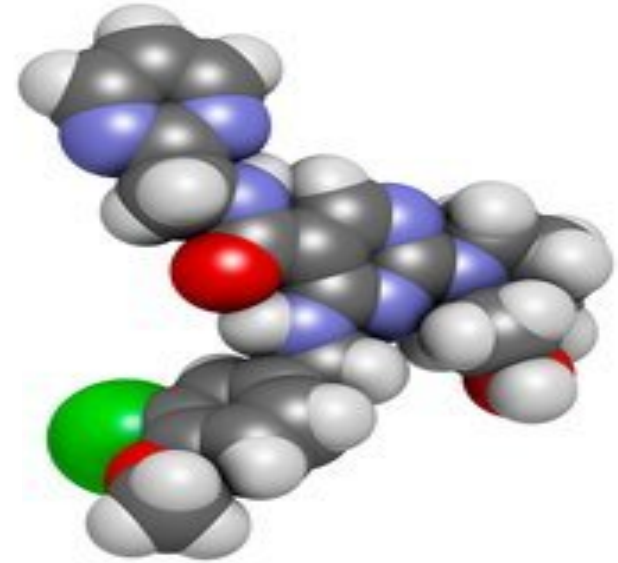
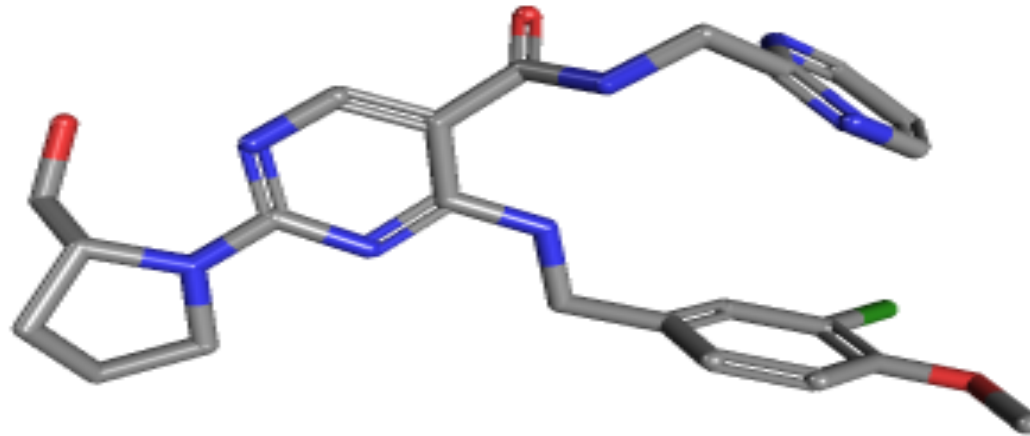
Fig. 1 – Flow diagram of literature searches in Pubmed and Scopus according to MeSH terms.

Improvement of LUT oxygenation, (2) smooth muscle relaxation, (3) negative regulation of proliferation and differentiation of LUT stroma, (4) reduction of bladder afferent nerve activity, and (5) down-regulation of prostate inflammation are the proven mechanisms of action of PDE5-Is.

Tadalafil 5mg: το τέλος των αμφισβητήσεων



Το νέο φάρμακο για τη στύση

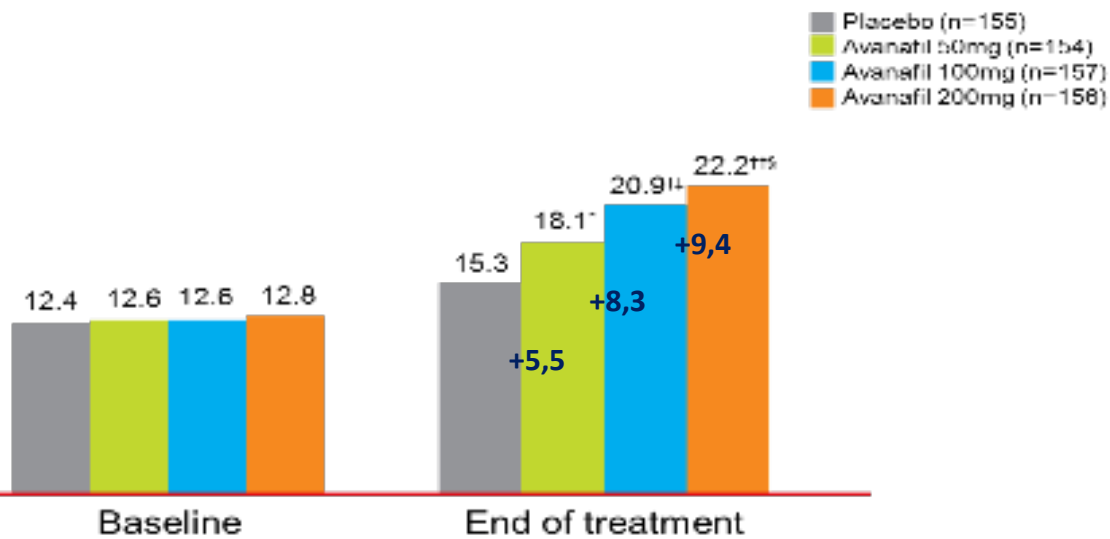


Avanafil and Vardenafil p.r.n: Historical comparison of the mean change of IIEF-EF score

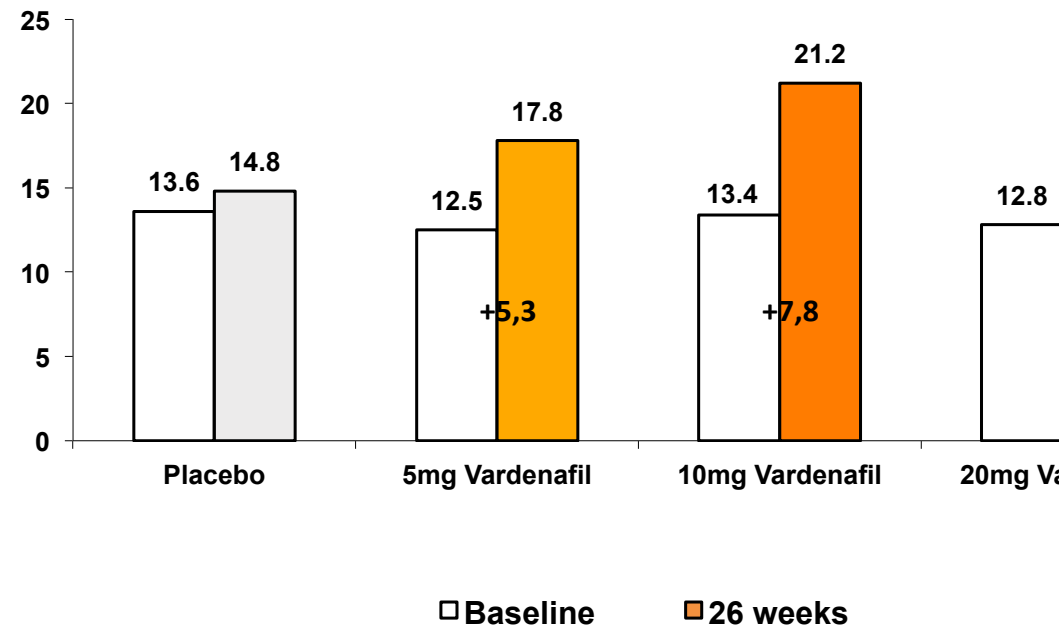
Avanafil (n = 646) (REVIVE/TA-301)
General population of men with ED

• Mean improvement from baseline:

- Placebo 2.9
- 50 mg 5.5
- 100 mg 8.3
- 200 mg 9.4



Vardenafil (n = 805) for treatment of men with erectile dysfunction: efficacy and safety in a randomized, double-blind, placebo-controlled trial.



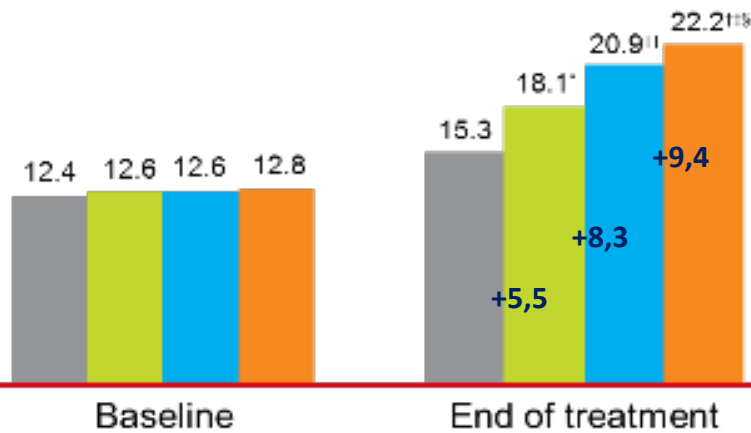
Avanafil and Tadalafil p.r.n: Historical comparison of the mean change of IIEF-EF score

Avanafil (n = 646) (REVIVE/TA-301)
General population of men with ED

Mean improvement from baseline:

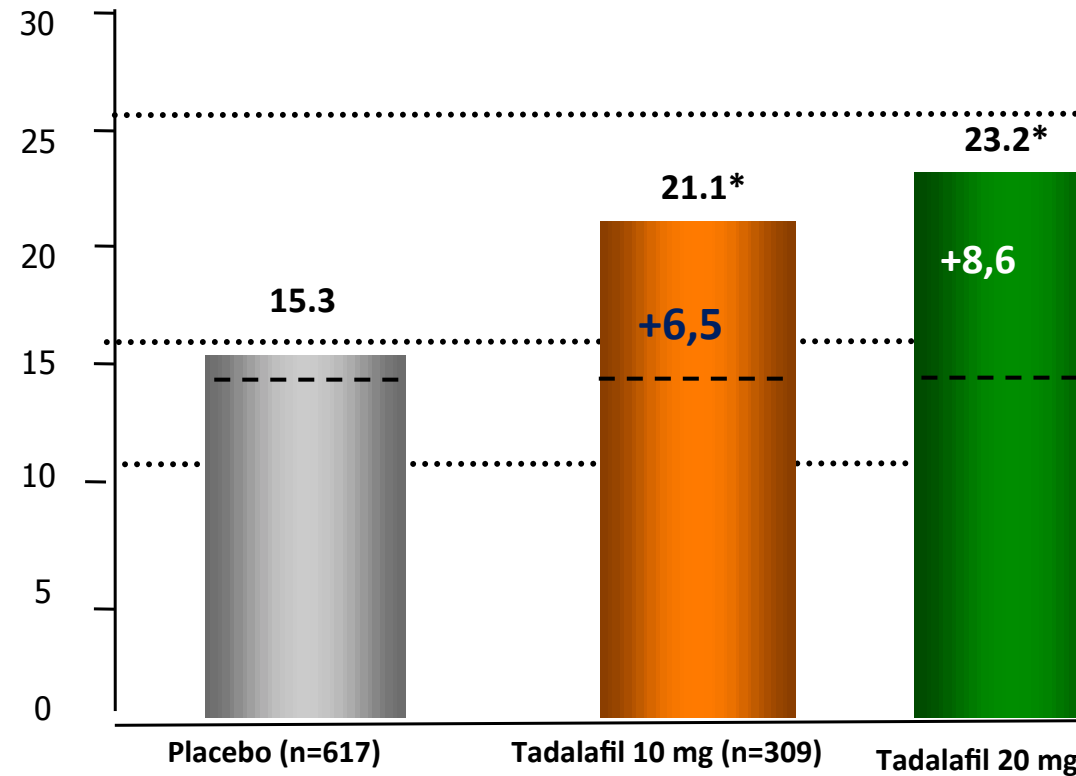
- Placebo 2.9
- 50 mg 5.5
- 100 mg 8.3
- 200 mg 9.4

■ Placebo (n=155)
■ Avanafil 50mg (n=154)
■ Avanafil 100mg (n=157)
■ Avanafil 200mg (n=158)



Tadalafil (n=2.102):

Integrated Analysis from 11 randomized, double-blind, placebo-controlled trials lasting 12 weeks in a mixed ED population



et al. J Sex Med. 2012 ;9(4):1122-33.

Carson CC, BJU Int. 2004 Jun;93(9):1276-81.

Τι λέει η φαρμακολογία;

Table 2. Pharmacokinetics of the different PDE5 inhibitors.[16,17]

	Avanafil	Sildenafil	Vardenafil	Tadalafil
Available doses (mg)	50,100, 200	25, 50, 100	5, 10, 20	10, 20
Pharmacokinetic proprieties				
Oral bioavailability	–	40%	15%	36%
t _{max} , minutes	30–45	30–120	30–120	–
C _{max} , ng/ml (fasting)	871 (100 mg)	327	20.9 (20 mg)	378 (20 mg)
Food effect (high-fat meal)	t _{max} , increased 1.25 h	t _{max} , increased 1 h	t _{max} , increased 1 h	No significant
t 1/2 (hours)	6–17	3–5	4	17.5
Renal excretion %	21	<1	1	<0.3
CYP isoenzymes	3A4 and minor contribution of 2C9	3A4 (79%), 2C9 (20%), 2C19 and 2D6 (<2%)	3A4 (major) 3A5 and 2C9 (minor)	3A4
Effect on exposure/clearance, of				
Age	None	Reduced clearance	Reduced clearance	Reduced clearance
Mild renal impairment	None	None	None	Increased exposure
Moderate renal impairment	None	None	None	Increased exposure
Severe renal impairment	No data	Increased exposure	Increased exposure	Increased exposure
Mild hepatic impairment	None	Increased exposure	Increased exposure	None
Moderate hepatic impairment	Reduced exposure	Increased exposure	Increased exposure	None
Severe hepatic impairment	Not studied	Not studied	Not studied	Limited data

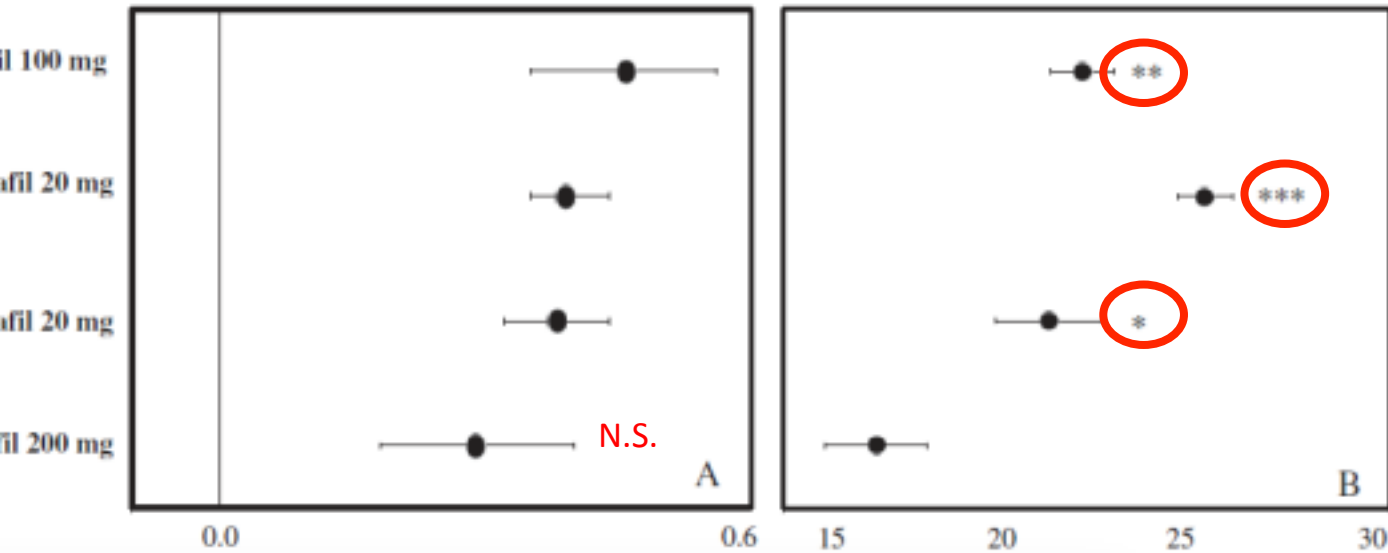
Faster

Unique pharmacokinetic profile

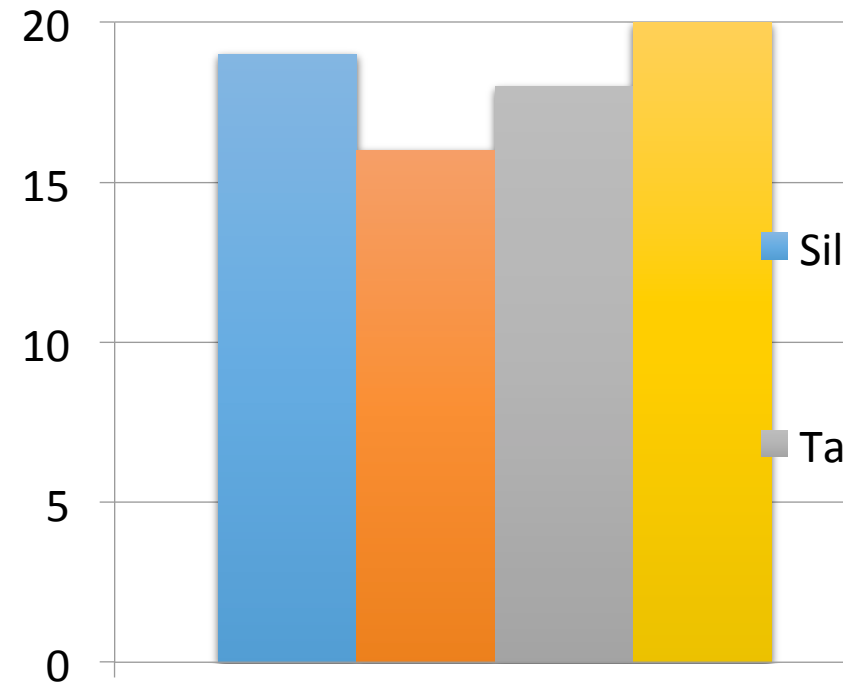
Good tolerability profile

Τι δείχνει η μετα-ανάλυση;

Πάνω από 2000 ασθενείς με Avanafil ή Placebo



EFFICACY/SAFETY RATIO



OPINION ON DRUG SAFETY, 2016
doi:10.1517/14740338.2016.1130126



SAFETY EVALUATION

safety and efficacy of Avanafil, a new 2nd generation PDE5i: comprehensive
review and meta-analysis

Corona^a, Giulia Rastrelli^b, Andrea Burri^c, Emmanuele A. Jannini^d and M Maggi^b

Ανεπιθύμητες ενέργειες PDE5i

Table 1. Incidence of drug-related side effects as derived from the first published paper dealing with them in the general population.

Side effects (%)	Sildenafil 100 mg [12]	Tadalafil 20 mg [13]	Vardenafil 20 mg [14]	Avanafil 200 mg [15]
Headache	12	21	21	9.3
Dyspepsia	5	17	6	0
Back pain		9	–	0
Nasal congestion	2	5	17	1.9
Sinusitis	–	0	5	3.7
Flushing	10	5	13	3.7
Visual disturbances	4	0	–	0
Myalgia	–	5	–	0

REGISTRATION ON DRUG SAFETY, 2016
doi:10.1517/14740338.2016.1130126



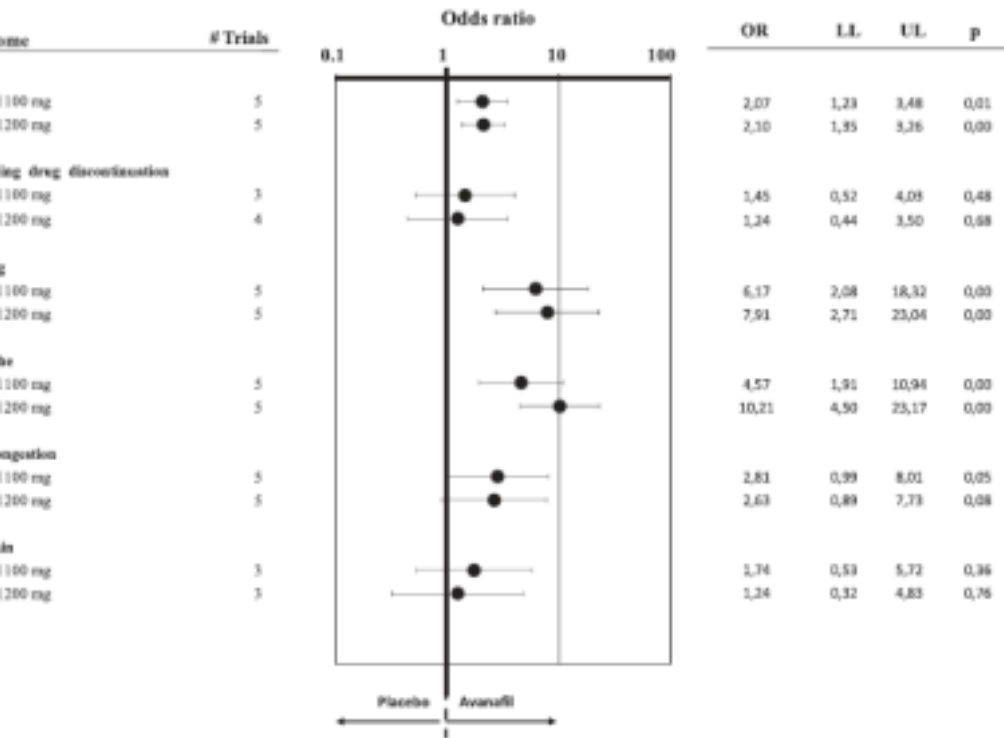
SAFETY EVALUATION

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Highest specificity for PDE5
Lowest cross-reaction with other PDEs

Ανεπιθύμητες ενέργειες στα 200mg



No differences between 100 and 200 mg of avanafil and placebo for the incidence of severe adverse events is observed:
 OR=1.99 [.67;5.93] and 1.7 [.54;5.31] for 100 and 200 mg over placebo, respectively, both p=NS

ΣΥΜΠΕΡΑΣΜΑ

Box 2. Drug summary.

- Despite their efficacy, the discontinuation rate with first-generation phosphodiesterase type 5 inhibitors (PDE5i) is still very high.
- Avanafil is a new PDE5i approved for the treatment of ED available in several countries worldwide.
- The most important characteristic of avanafil, in comparison to the first generation of PDE5i, is its high selectivity for PDE5, which improves its adverse effect profile.
- Avanafil is up to 3-fold superior than placebo in determining a successful intercourse.
- Avanafil has similar efficacy, but the lowest incidence of drug-related side effects, when compared to the first generation of PDE5i.

Ασθενείς με Σακχαρώδη Διαβήτη

- Η παθοφυσιολογία είναι πολυπαραγοντική
- Η αποτελεσματικότητα είναι μέτρια, δεν επηρεάζονται τα επίπεδα σακχάρου
- Βελτίωση αποτελεσματικότητας: Ρύθμιση επιπέδων γλυκόζης αίματος και συνοδών νοσημάτων

Ασθενείς με ριζική προστατεκτομή

- Η παθοφυσιολογία είναι πολυπαραγοντική
- Αξιολόγηση της στυτικής ικανότητας πριν το χειρουργείο
- PDE5i μετεγχειρητικά (Tadalafil 5mg καλύτερα αποτελέσματα)
Ενημέρωση για τις δυσκολίες αποκατάστασης

Ασθενείς με νευρολογικά νοσήματα

- Περιορισμένα στοιχεία για αποτελεσματικότητα & ασφάλεια
- Sildenafil: Αποτελεσματική σε ασθενείς με Parkinson και MS
- Sildenafil: Σε ασθενείς με πολλαπλή συστηματική ατροφία παρατηρείται σοβαρή υπόταση

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 4

Ποιον PDE5i προτιμούν οι ασθενείς;

Προτίμηση PDE5i

- Διακοπή περίπου στο 50%
- Οι μεγαλύτεροι σε ηλικία άνδρες με λίγες επαφές τείνουν να προτιμούν σιλденаφίλη και βαρδεναφίλη ενώ οι νεότεροι ταδαλαφίλη καθημερινής λήψης
- Η επιλογή PDE5i θα πρέπει να είναι συνάρτηση της συχνότητας επαφών και της ανάγκης για αυθορμητισμό
- Δυνατότητα στον ασθενή να δοκιμάσει όλους τους PDE5 ώστε να επιλέξει ποιος ανταποκρίνεται στις ανάγκες του
- Ασθενείς που δοκίμασαν όλους του PDE5i: συνέχιση χρήσης στα 3 χρόνια σε ποσοστό 86%.

- Hatzimouratidis K, Hatzichristou DG (2009) Phosphodiesterase type 5 inhibitors: unmet needs. Curr Pharm Des
- Ljunggren C, Hedelin H, Salomonsson K et al. (2008) Giving patients with erectile dysfunction the opportunity to try all three available phosphodiesterase type 5 inhibitors contributes to better long-term treatment compliance. J Sex Med

Cialis®
(Tadalafil Citrate)



VIAGRA
(Sildenafil Citrate)



(Vardenafil Citrate)
LEVITRA



Continuation and effectiveness of tadalafil once daily during a 6-month observational study in erectile dysfunction: the EDATE study.

Hatzichristou D, Boess FG, Büttner H, Gehchan N, Hennes C, Porst H.

Table 4 Reasons for discontinuation of tadalafil OaD treatment

	Number (%) of patients		
	PDE5-I naïve <i>N</i> = 510	PDE5-I pretreated <i>N</i> = 267	Overall <i>N</i> = 778*
Discontinued TAD-OaD[†]	71 (100.0)	36 (100.0)	107 (100.0)
Reasons			
Lack of efficacy (hardness of erection)	18 (25.4)	15 (41.7)	33 (30.8)
Adverse event	16 (22.5)	6 (16.7)	22 (20.6)
Cost of medication	12 (16.9)	4 (11.1)	16 (15.0)
Did not want to take a pill every day	7 (9.9)	5 (13.9)	12 (11.2)
Patient discontinued study	8 (11.3)	1 (2.8)	9 (8.4)
Partner's request	3 (4.2)	2 (5.6)	5 (4.7)
Felt that medication controlled his sexual life	3 (4.2)	0	3 (2.8)
Slow onset of action	3 (4.2)	0	3 (2.8)
Lack of efficacy (duration of erection)	0	2 (5.6)	2 (1.9)
Lack of confidence in medication	0	1 (2.8)	1 (0.9)
Non-desired spontaneous erections	1 (1.4)	0	1 (0.9)

*For one patient, previous PDE5-I treatment status was unknown. [†]Includes all patients with documented end date of tadalafil OaD treatment, irrespective if the patient completed or discontinued the study. *N*, number of patients; OaD, once a day; PDE5-I, phosphodiesterase type 5 inhibitor; TAD, tadalafil.

Continuation and effectiveness of tadalafil once daily during a 6-month observational study in erectile dysfunction: the EDATE study.

Hatzichristou D, Boess FG, Büttner H, Gehchan N, Henneges C, Porst H.

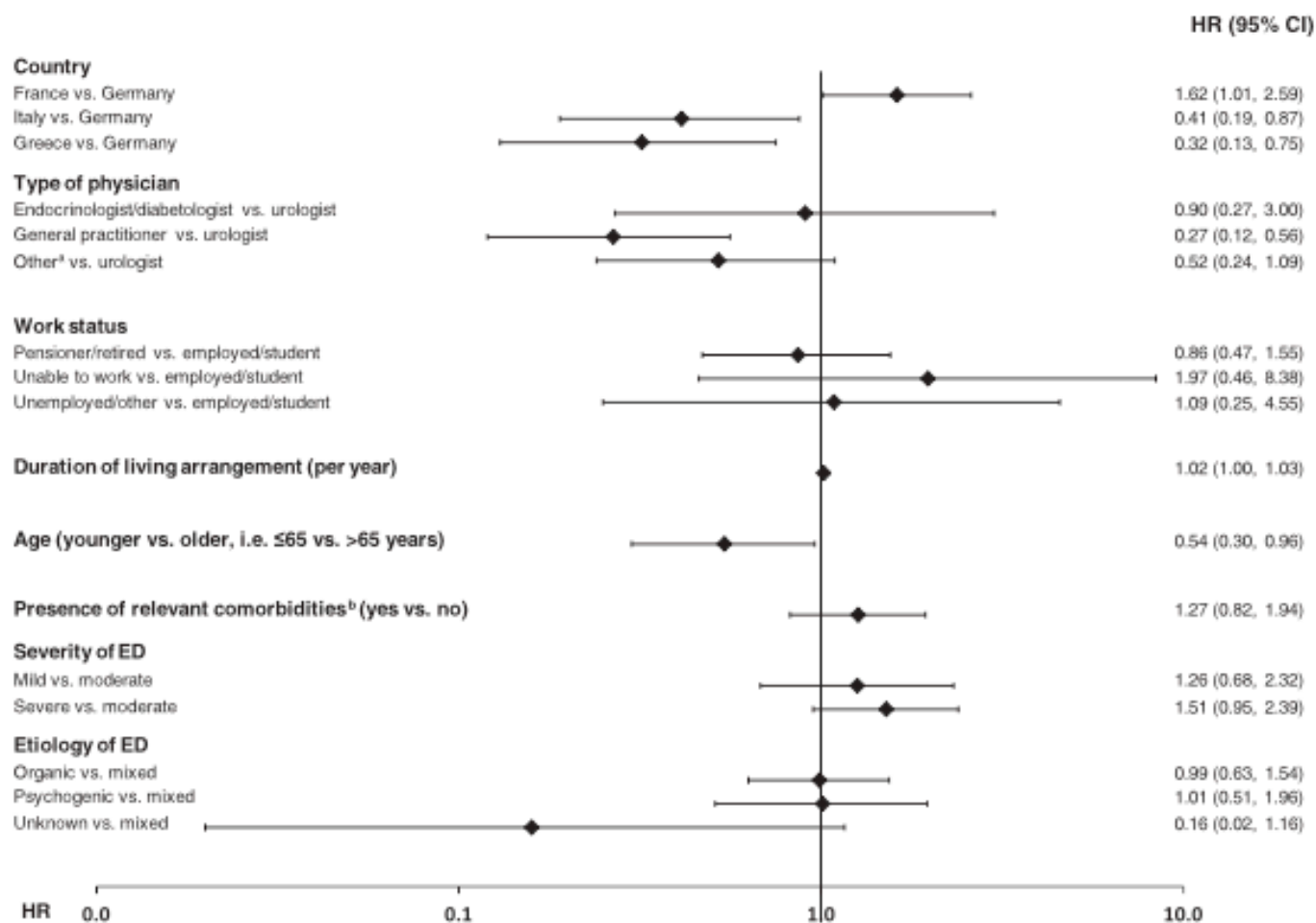


Figure 3 Factors associated with time to discontinuation of tadalafil OaD treatment (Cox proportional hazards model). Model goodness of fit (AIC): 1267.347. AIC, akaike information criterion; CI, confidence interval; ED, erectile dysfunction; HR, hazard ratio; OaD, once a day. ^a'other' includes: sexual medicine specialist, cardiologist, psychiatrist or other specialty. ^bBased on presence or absence of ≥ 1 of the following pre-existing conditions: hypertension, dyslipidaemia, diabetes, benign prostate hyperplasia, cardiovascular disease.

Continuation and effectiveness of tadalafil once daily during a 6-month observational study in erectile dysfunction: the EDATE study.

Hatzichristou D, Boess FG, Büttner H, Gehchan N, Henneges C, Porst H.

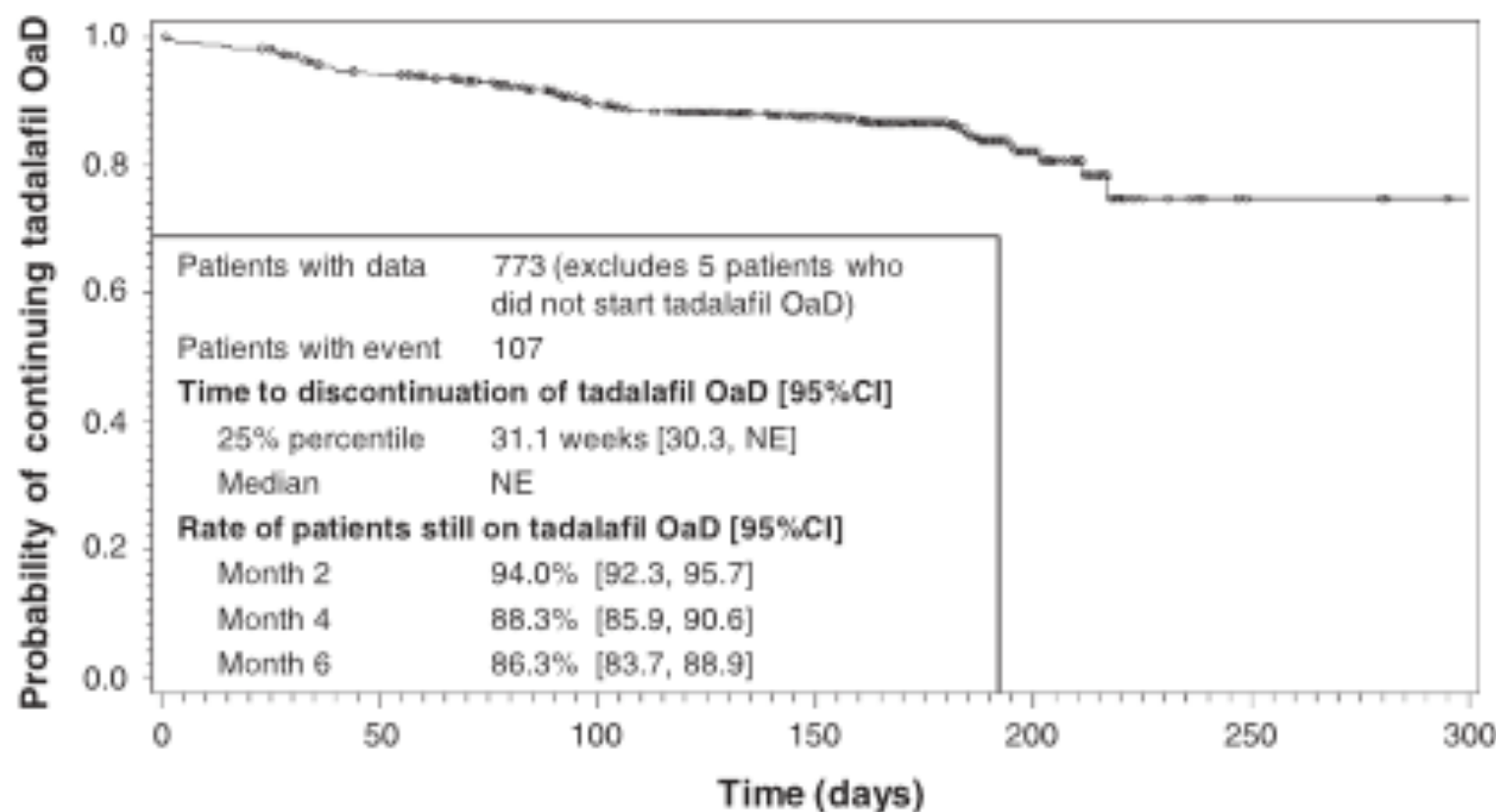


Figure 2 Kaplan–Meier estimation for time to discontinuation of tadalafil OaD treatment. CI, confidence interval; NE, estimable; OaD, once a day.

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 5

Πως χειρίζεστε ασθενείς
που δεν απαντούν στους
PDE5i;

Effectiveness' scale—therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report

F Giuliano², I Goldstein³, D Hatzichristou⁴, W Hellstrom⁵, T Lue⁶, F Montorsi⁷, R Munarriz^{3*},
H Porst⁹ and R Rosen¹⁰

Clinical trials in ED are generally characterized by:

- Motivated patients, with a high degree of compliance in treatment administration and reporting of results.
- Rigorous criteria for inclusion/exclusion, administration and evaluation.
- Narrow emphasis on measurable results from the specific treatment under study.

In contrast, clinical practice of ED is characterized by:

- Differing expectations and motivation for treatment.
- Variability among patients in medical and psychological comorbidities, degree of compliance and consistency of reported results.
- A broad range of possible approaches for managing ED (including counseling and other first- or second-line therapies).



Effectiveness' scale—therapeutic outcome of pharmacologic agents for ED: an international consensus panel report

F Giuliano², I Goldstein³, D Hatzichristou⁴, W Hellstrom⁵, T Lue⁶, F Montorsi⁷, R Munarriz^{3*},
H Porst⁹ and R Rosen¹⁰

Complete response This term describes consistent achievement and maintenance of full erection with the ability to engage and complete sexual intercourse. Such erectile response for ED patients is synonymous with 'complete or nearly complete remission of all symptoms'.

The panel agreed that complete response should include the patient's ability to tolerate side effects, without necessarily including the use of concomitant medication for side-effect relief, if any, at the clinically effective dose. Side-effect profiles in this category would not be expected to interfere significantly with the patient's functioning.



Effectiveness' scale—therapeutic outcome of pharmacologic agents for ED: an international consensus panel report

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H Porst⁹ and R Rosen¹⁰

Partial response This category is regarded as the most difficult to define, and also likely to include a large proportion of patients. As with the discussion of complete response, the possibility of basing the definition of partial response on specific scale scores was considered, although a broader definition was selected. There was general agreement that *partial response* refers to a degree of symptom improvement and/or partial remission of symptoms, as described below

1. Achievement of a degree of erection that is clearly discernible, but not adequate for intercourse or complete, or
2. Ability to achieve full erection, but not on a consistent basis over time.
3. Ability to achieve full erection, which is not maintained until completion of intercourse on a consistent basis.

The role of side effects in defining partial response was considered. The panel included in the definition of a partial responder any patient for whom treatment efficacy was adequate, but who was bothered by the side effects of treatment. Side effects were deemed in this case to be, significantly interfering with patient's use of the treatment.

Patients who had adequate efficacy with a given agent or dose, but were reluctant to use the drug due to bothersome side effects of treatment (eg, headache, dyspepsia) were defined as having a partial response to treatment.



Effectiveness' scale—therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report

F Giuliano², I Goldstein³, D Hatzichristou⁴, W Hellstrom⁵, T Lue⁶, F Montorsi⁷, R Munarriz^{3*},
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NONRESPONDERS: definition

any patient who, after four successive or closely timed trials of the maximum tolerated dose of the medication, in accordance with the regulatory agency's guidelines with respect to timing relative to meals, alcohol ingestion, use of concomitant medications and adequate sexual stimulation, is unable to achieve and sustain adequate penile rigidity until completion of sexual performance".

Effectiveness' scale—therapeutic outcome of pharmacologic options for ED: an international consensus panel report

F Giuliano², I Goldstein³, D Hatzichristou⁴, W Hellstrom⁵, T Lue⁶, F Montorsi⁷, R Munarriz^{3*},
H Porst⁹ and R Rosen¹⁰

Nonresponse This category is relatively straightforward in cases in which treatment fails to produce an ability to achieve and maintain adequate erection for sexual activity, including either slight improvement that makes no clinical difference or results in the patient's status as unchanged/worse.

The panel proposed adding to the nonresponder category patients whose burden of side effects outweighs their therapeutic gain.

Nonresponders, in general:

- Fail to respond in a clinically significant manner to the treatment,
- Experience intolerable side effects at any dosage or
- Cannot be titrated to a dose that would produce a response, due to intolerable side effects associated with treatment.

Effectiveness' scale—therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report

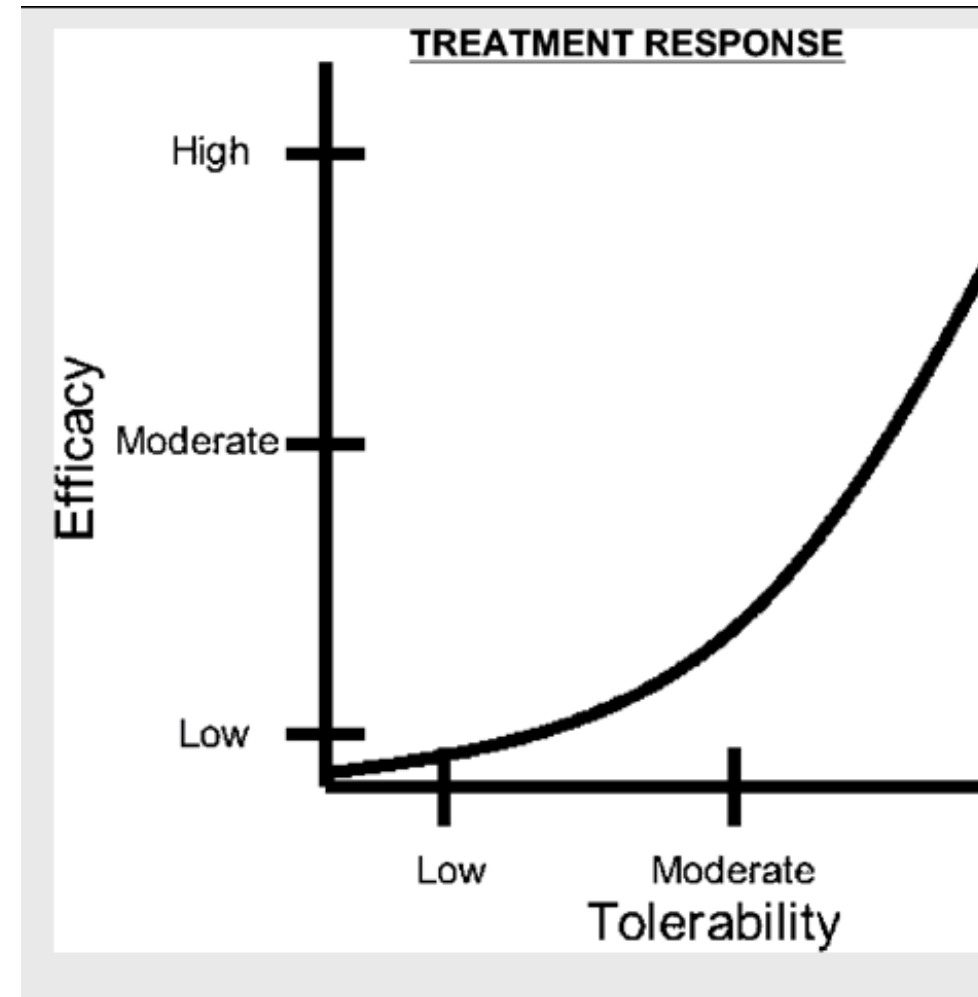
F Giuliano², I Goldstein³, D Hatzichristou⁴, W Hellstrom⁵, T Lue⁶, F Montorsi⁷, R Munarriz^{3*},
H Porst⁹ and R Rosen¹⁰

Treatment response: this dimension refers to pharmacologically based (ie, *response-based*) aspects, including both treatment efficacy and tolerability (side effects). These effects are typically self-reported by the patient and serve as surrogate end points for objective, physiological changes in penile firmness or rigidity. The 'therapeutic index' has previously been reported as a summary measure of this variable.

Treatment satisfaction: this includes both patient and partner subjective responses and overall satisfaction with treatment. Treatment satisfaction may be assessed by means of interview or self-report questionnaires.

Effectiveness' scale—therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report

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H Porst⁹ and R Rosen¹⁰



Ασθενείς που δεν ανταποκρίνονται στους PDE5i

Αίτια μη ανταπόκρισης

- Μη σωστή λήψη του φαρμάκου
- Προβλήματα ψυχολογικά και σχέσης
- Σεξουαλική δυσλειτουργία της συντρόφου
- Σοβαρή οργανική στυτική δυσλειτουργία



Intercourse treatment optimization with sildenafil citrate (Viagra®) in patients with erectile dysfunction¹

James H Barada^a, James H Barada^b, Ahmed Fawzy^c, Andre T Guay^d, Dimitrios Hatzichristou^e

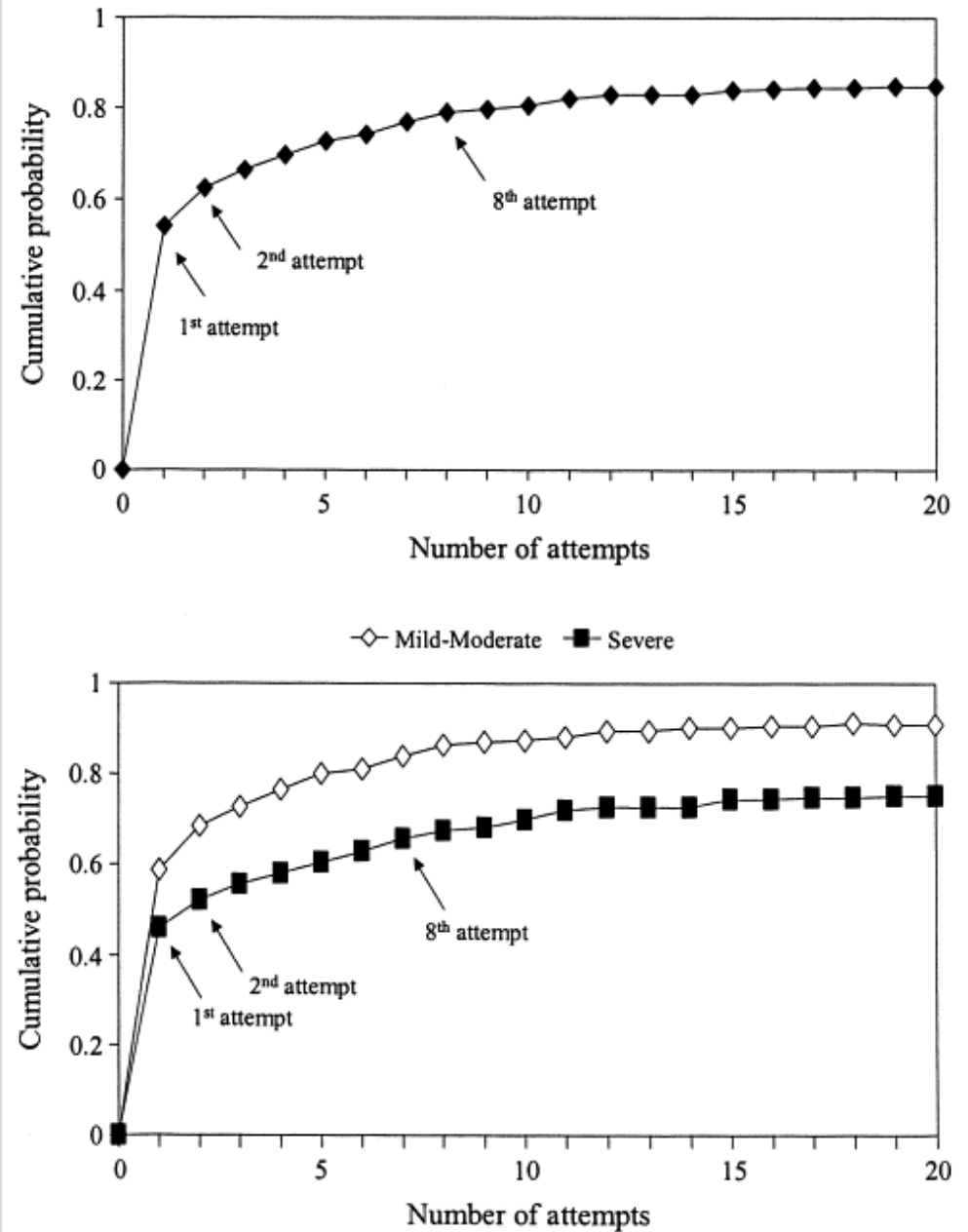


FIGURE 2. Intercourse success rates, as determined from event log data, in men with erectile dysfunction treated with sildenafil (top). Intercourse success rates in men stratified by erectile dysfunction severity (bottom).



Optimizing treatment optimization with sildenafil citrate (Viagra®) in patients with erectile dysfunction¹

James H Barada^a, James H Barada^b, Ahmed Fawzy^c, Andre T Guay^d, Dimitrios Hatzichristou^e

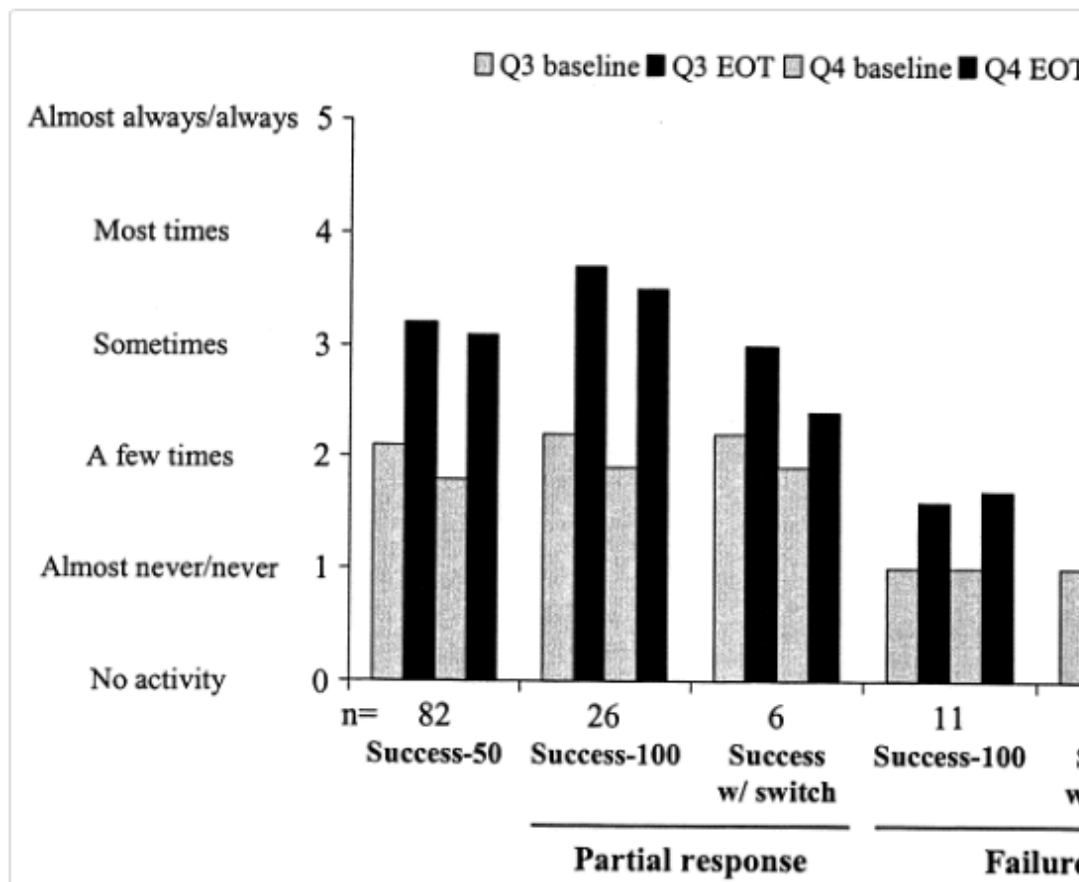


FIGURE 4. Efficacy results in a disease management program. Baseline and end-of-treatment (EOT) scores for International Index of Erectile Function question (Q)3 and Q4. EOT scores are patient response to Q4 at the stage they reached "success" (ie, 50 mg sildenafil, 100 mg sildenafil, switch to another modality).



ng treatment optimization with sildenafil citrate
 ®) in patients with erectile dysfunction¹

Cullough^a, James H Barada^b, Ahmed Fawzy^c, Andre T Guay^d, Dimitrios Hatzichristou^e

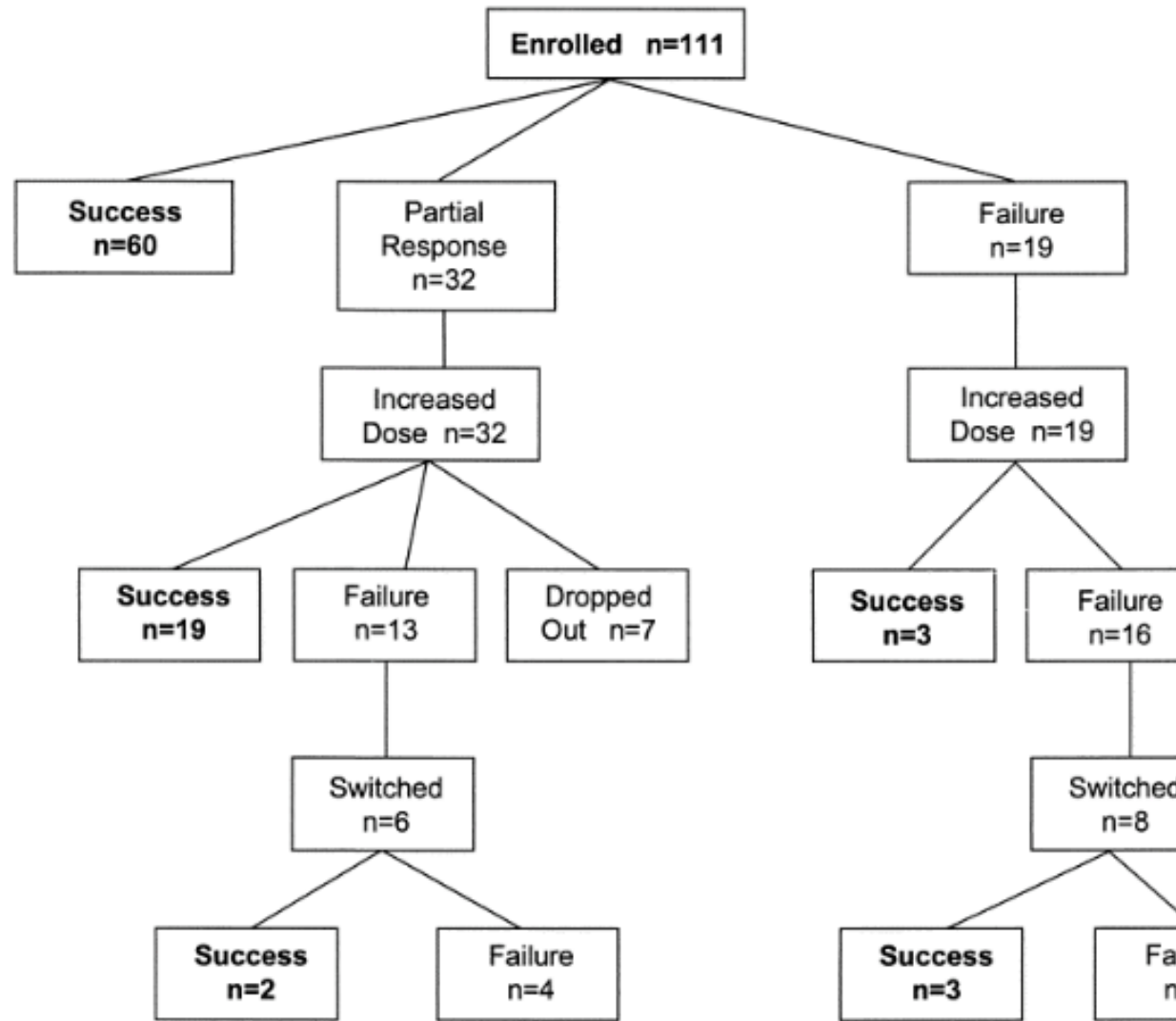


FIGURE 3.
 Patient disposition in a disease management program.

denafil citrate: lessons learned from 3 years of clinical experience

Hatzichristou^{1*}

Table 2 Essential aspects in managing patients with erectile dysfunction: the 'FAST' acronym

Follow-up of patients

Adjustment of dosing

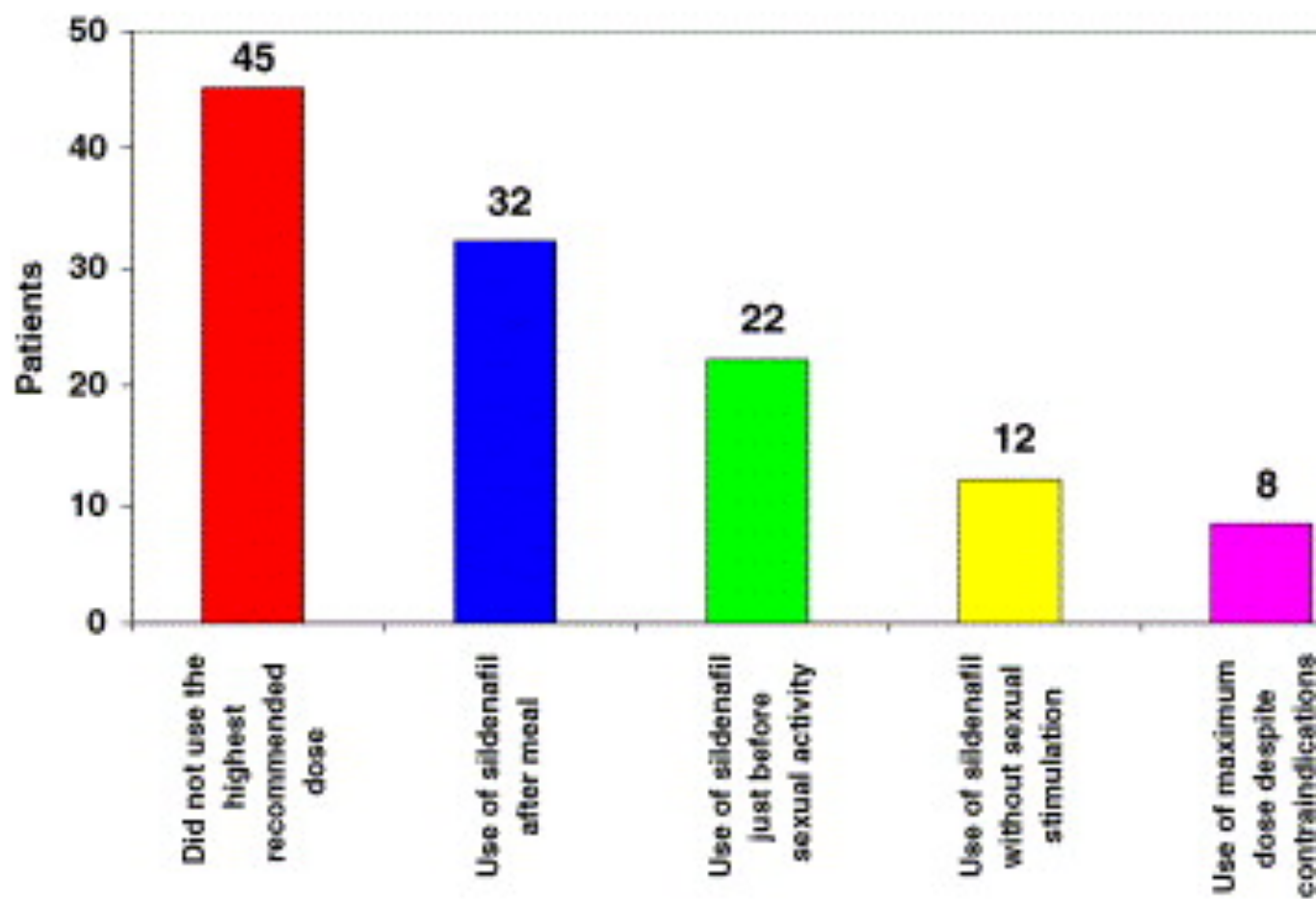
Sexual stimulation

Titration to the maximum tolerated dose



Penile Failures May Be Due to Inadequate Patient Education and Follow-Up: A Study on 100 Non-Responders

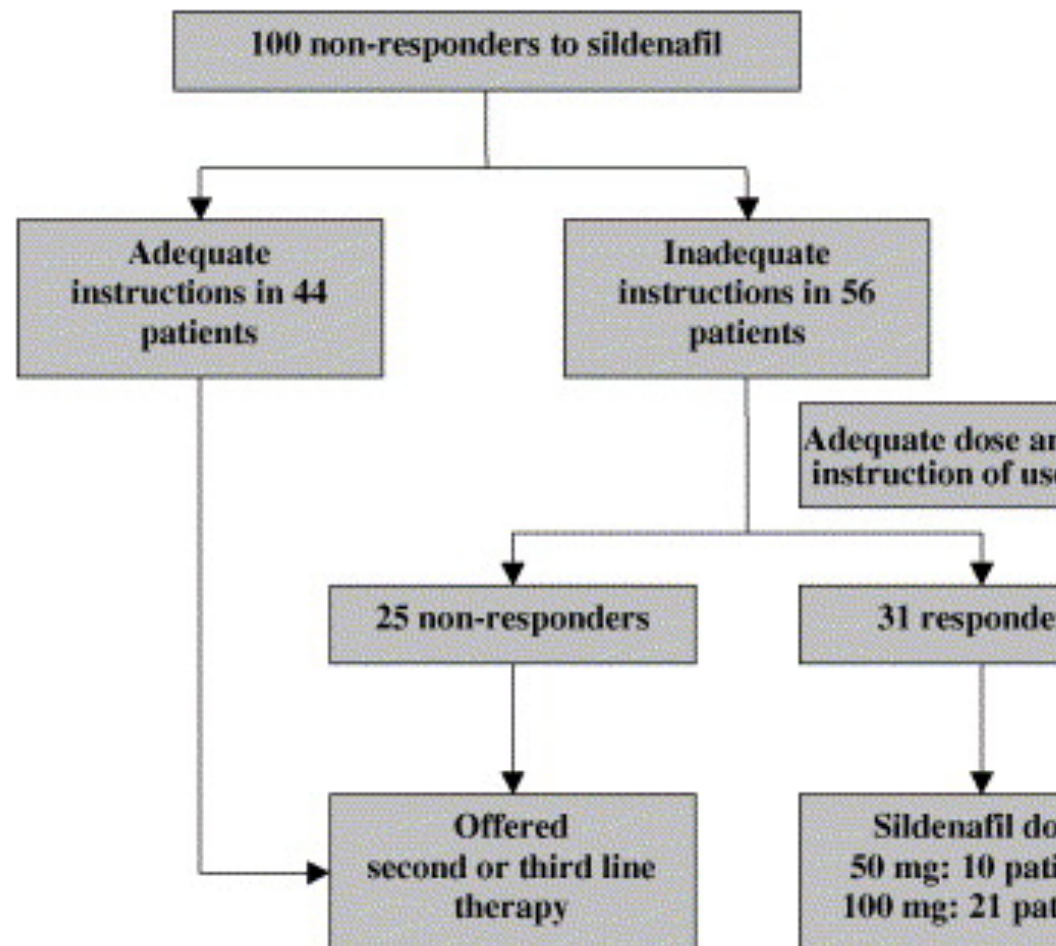
Georgios K. Katsikis, Christos K. Katsikis, Kyriakos Moysidis, Apostolos Apostolidis, Athanasios Bekos, Vasilios
Katsikis, Athanasios Katsikis, Christos Katsikis





Sildenafil Failures May Be Due to Inadequate Patient Instructions and Follow-Up: A Study on 100 Non-Responders

Georgios Christou, Kyriakos Moysidis, Apostolos Apostolidis, Athanasios Bekos, Vasilios...





al Medicine

phosphodiesterase Type 5 Inhibitors: The Day After

Hatzimouratidis, Dimitrios Hatzichristou

Table 1 – Reasons for inadequate use of PDE5-Is and treatment strategy

Study	PDE5-I used	Reasons for inadequate use	Treatment strategy	Result (response rate)
McCullough [97]	Sildenafil	<ul style="list-style-type: none"> • Only 50 mg used and <5 attempts (55%) 	<ul style="list-style-type: none"> • Re-education (proper administration and expectations) • Retrial with at least 8 attempts (100 mg if needed) 	54% complete response
Atiemo [40]	Sildenafil	<ul style="list-style-type: none"> • Use after meal (13.3%) • No sexual stimulation (33.7%) • Timing of sex (14.3%) • Too few attempts (20.4%) 	<ul style="list-style-type: none"> • Re-education (videotape, personal instructions, instruction sheets for patient and partner) • Retrial (100 mg if 50 mg after one attempt was inadequate) 	41.5% complete response
Jiann [41]	Sildenafil	<ul style="list-style-type: none"> • No sexual stimulation (30%) • <4 attempts (60%) • Maximum dose <100 mg (45%) 	<ul style="list-style-type: none"> • Adequate instructions • Retrial with 4 doses (100 mg) 	58.5% complete response
Hatzichristou [39]	Sildenafil	<ul style="list-style-type: none"> • Maximum dose <100 mg (44%) • Use after meal (32%) • Use just before sex (22%) • No sexual stimulation (12%) 	<ul style="list-style-type: none"> • Adequate instructions • Retrial with 4 doses (100 mg if needed) 	55.4% complete response
Gruenwald [43]	Sildenafil	<ul style="list-style-type: none"> • Maximum dose <100 mg (76%) • 2.5 attempts (average) 	<ul style="list-style-type: none"> • Adequate instructions (oral and written, videotape in some cases) • Retrial with 8 doses (100 mg) 	23.6% achieved normal sexual function
Hatzimouratidis [35]	Tadalafil	<ul style="list-style-type: none"> • Maximum dose <20 mg (10%) • <4 attempts (29%) 	<ul style="list-style-type: none"> • Adequate instructions • Retrial with 4 doses (100 mg if needed) 	43.75% complete response
Hatzimouratidis [35]	Vardenafil	<ul style="list-style-type: none"> • Maximum dose <20 mg (3%) • <4 attempts (38%) 	<ul style="list-style-type: none"> • Adequate instructions • Retrial with 4 doses (100 mg if needed) 	31.6% complete response

PDE5-I = phosphodiesterase type 5 inhibitor.



Urological Medicine

Phosphodiesterase Type 5 Inhibitors: The Day After

Georgios Hatzimouratidis, Dimitrios Hatzichristou

Table 3 – What can we expect in the future for PDE5-Is?

Potential indication	Rationale
Chronic administration PDE5-Is (everyday, low-dose use)	Chronic dosing may safely maximise efficacy improving endothelial dysfunction, although there are limited data on the systemic effects of the continuous inhibition of PDE5
Prevention/cure	Current evidence supports the potential of prevention/cure mainly through improving endothelial dysfunction
Treatment of LUTS due to BPH	PDE5-Is may relieve obstruction, improve LUTS, potentiate NO-mediated relaxation in prostate
Cardiovascular risk factor treatment	Beneficial effects of PDE5-Is in treating patients with cardiovascular risk factors or disease have been shown.
Combination multimodal pills	A single compound can target a number of risk factors to improve patient compliance.

PDE5-I = phosphodiesterase type 5 inhibitor; ED = erectile dysfunction; LUTS = lower urinary tract symptoms; BPH = benign prostatic hyperplasia; NO = nitric oxide.

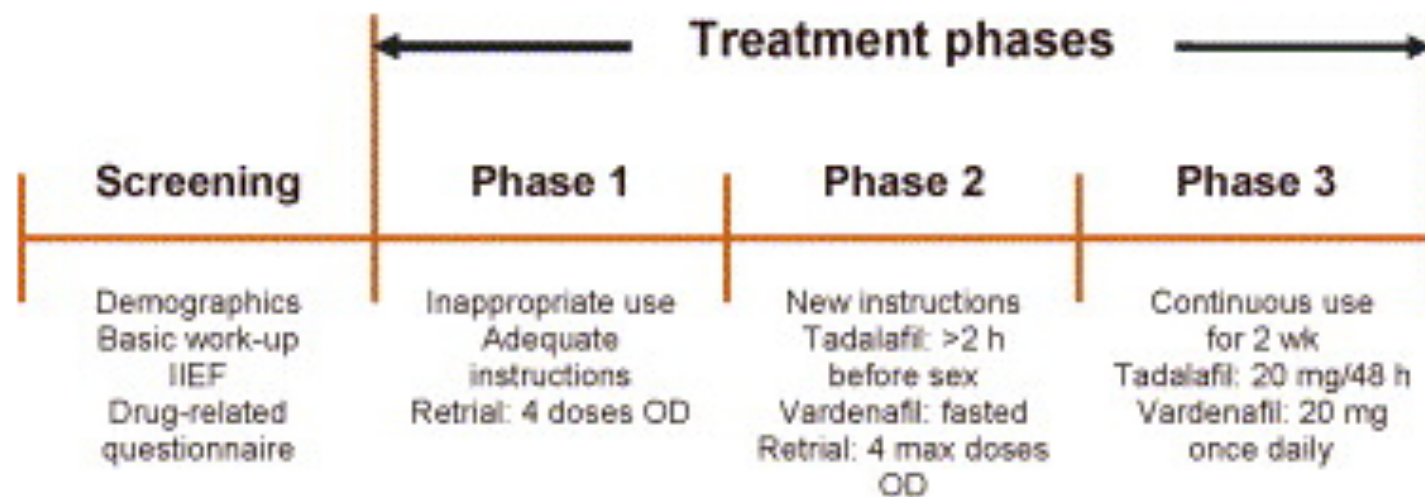


icine

Optimal Strategy for “Non-Responders” to Tadalafil and Vardenafil: A Real-Life Study ☆

Georgios Hatzimouratidis, Kyriakos Moysidis, Athanasios Bekos, Zoi Tsimtsiou, Evangelos Ioannidis, and Maria Tatzichristou

Department of Urology, Papageorgiou General Hospital, and the Center for Sexual and Reproductive Health, Aristotle University of Thessaloniki, Greece



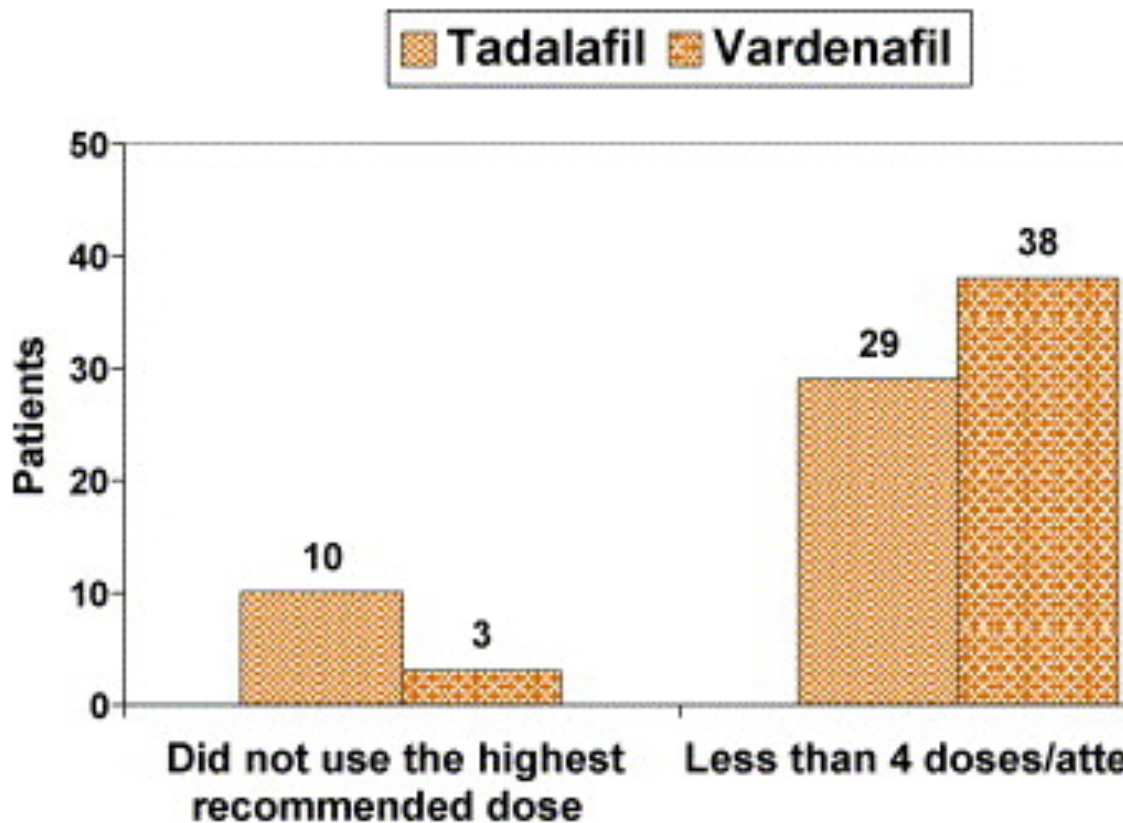


icine

Optimal Strategy for “Non-Responders” to Tadalafil and Vardenafil: A Real-Life Study ☆

Stavros Hatzimouratidis, Kyriakos Moysidis, Athanasios Bekos, Zoi Tsimtsiou, Evangelos Ioannidis, Konstantinos Tzichristou

Department of Urology, Papageorgiou General Hospital, and the Center for Sexual and Reproductive Health, Aristotle University of Thessaloniki, Greece

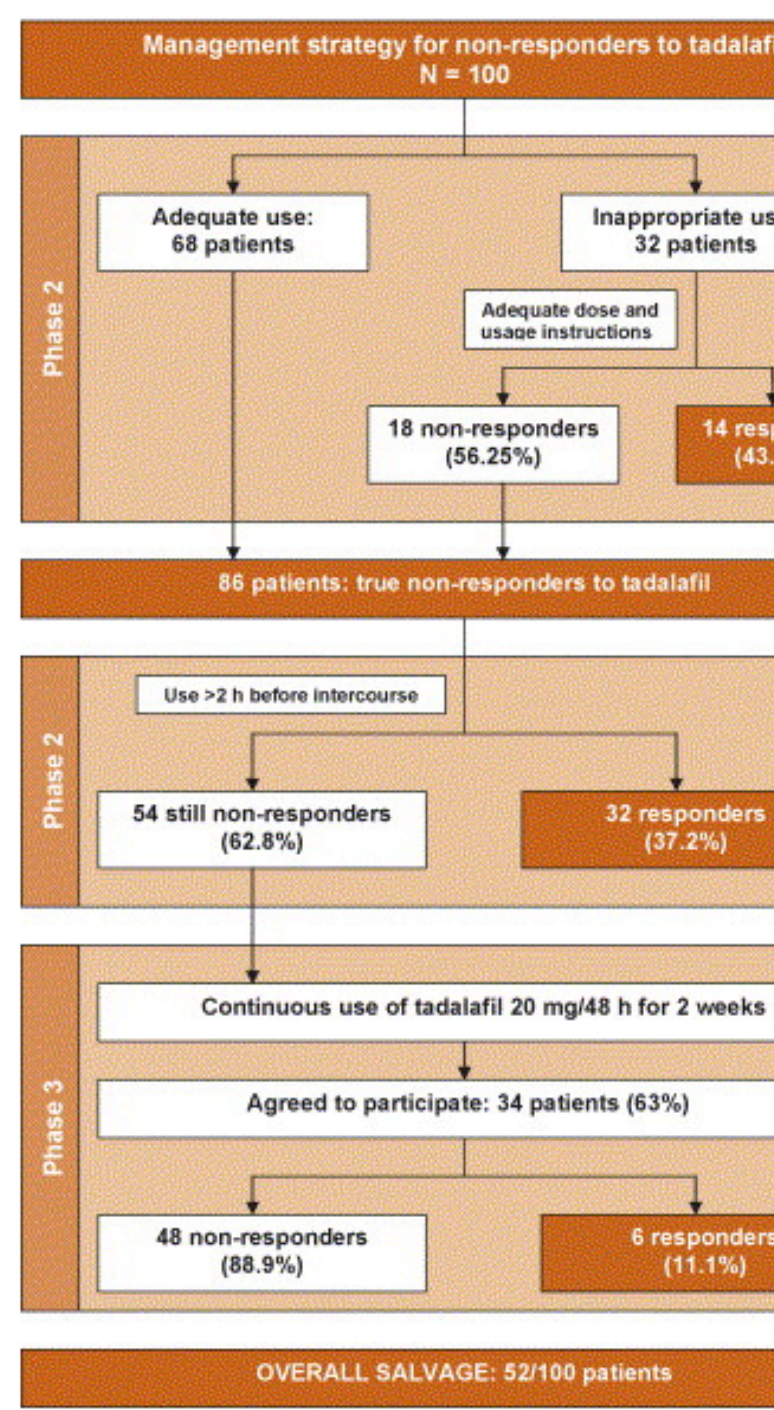
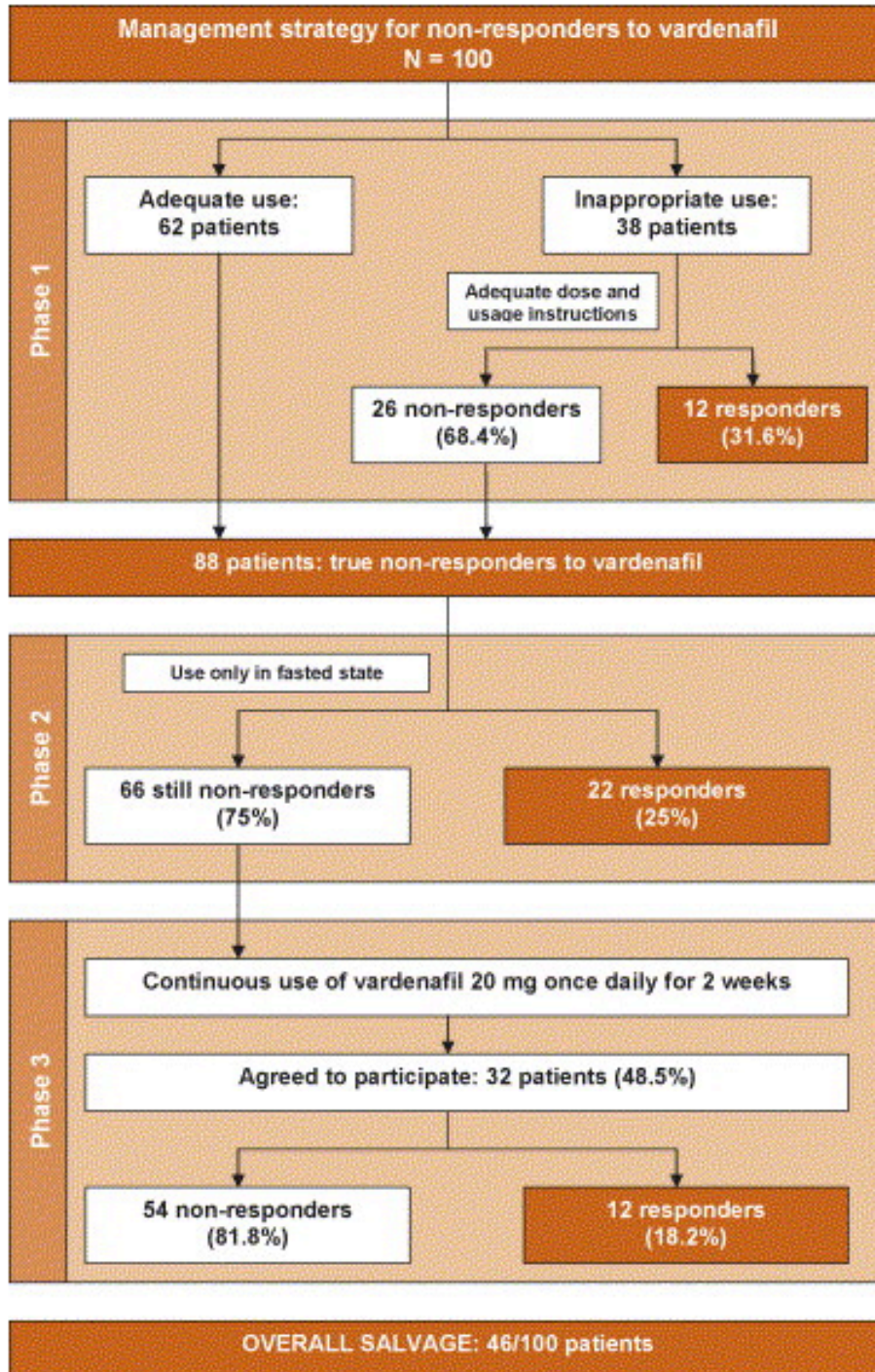




Management strategy for "Non-Responders" to Tadalafil and Vardenafil: A Real-Life Study ☆

Ioannis Kyriakos Moysidis, Athanasios Bekos, Zoi Tsimtsiou, Evangelos Ioannidis, et al.

Department of Urology, Papageorgiou General Hospital, and the Center for Sexual and Reproductive Health, Aristotle University of Thessaloniki, Greece



Positive intracavernous injection test implies normal veno-occlusive but not necessarily normal arterial function: a hemodynamic study.

Li ES¹, Hatzichristou DG, Namburi S, Goldstein I.

For information

Abstract

In impotence evaluations a positive intracavernous injection test has been presumed to signify normal erectile hemodynamics. This premise was tested by obtaining hemodynamic data in 80 patients 17 to 65 years old with positive injection tests: patients achieved maximal circumference and equilibrium intracavernous pressures of 80 mmHg or more (range 80 to 136) sustained for 30 minutes or longer. Corporeal venography revealed that flow-to-maintain (0.5 to 3 ml. per minute) and pressure decay (0 to 47 mmHg) values as well as pharmacocavernography findings (absent or minimal contrast medium in venous structures in 92% of the cases) were all consistent with low outflow erection. Arterial testing revealed right and/or left cavernous systolic arterial blood pressures always at 80 mmHg or more, consistent with a preerectile cavernous artery pressure value for a positive injection test. Systemic-cavernous systolic arterial blood pressure gradients were 0 to 24 mmHg, 25 to 34 mmHg and 35 mmHg or more in 47 (59%), 18 (22%) and 15 (19%) patients, respectively. Large systemic-cavernous pressure gradients suggest the presence of arterial occlusive disease. In 8 patients with positive injection tests and gradients of 35 mmHg or more pharmacocavernography revealed hemodynamically significant arterial occlusions. In conclusion, hemodynamic data in selected patients with positive injection tests revealed low erection states, threshold cavernous artery pressures and disparities in systemic-cavernous systolic pressure gradients that suggest the presence of arterial occlusive disease in 19% of the cases. The erectile response in a positive test is equal to or greater than a threshold response, not always the maximum as determined by the systemic blood pressure. A positive intracavernous injection test did not necessarily signify normal erectile hemodynamics.

Dynamic characterization of a functional erection. Arterial and corporeal veno-occlusive function in patients with a positive intracavernosal injection test.

Christou DG¹, Hatzimouratidis K, Apostolidis A, Ioannidis E, Yannakoyorgos K, Kalinderis A.

Key information

Object

OBJECTIVES: To characterize hemodynamically a functional/rigid erection and study the hypothesis that a positive intracavernosal injection test implies normal arterial and corporeal veno-occlusive function.

DESIGN: 33 patients (mean age 39.5 +/- 9 years), who developed rigid erection during pharmacocavernosometry, included in the present study. Presence of axial rigidity was determined at steady state equilibrium intracavernosal pressure, by absence of buckling to axial force of 1 kg applied to the erect penis and sustained for >=15 min. Arterial and veno-occlusive hemodynamic parameters were analyzed.

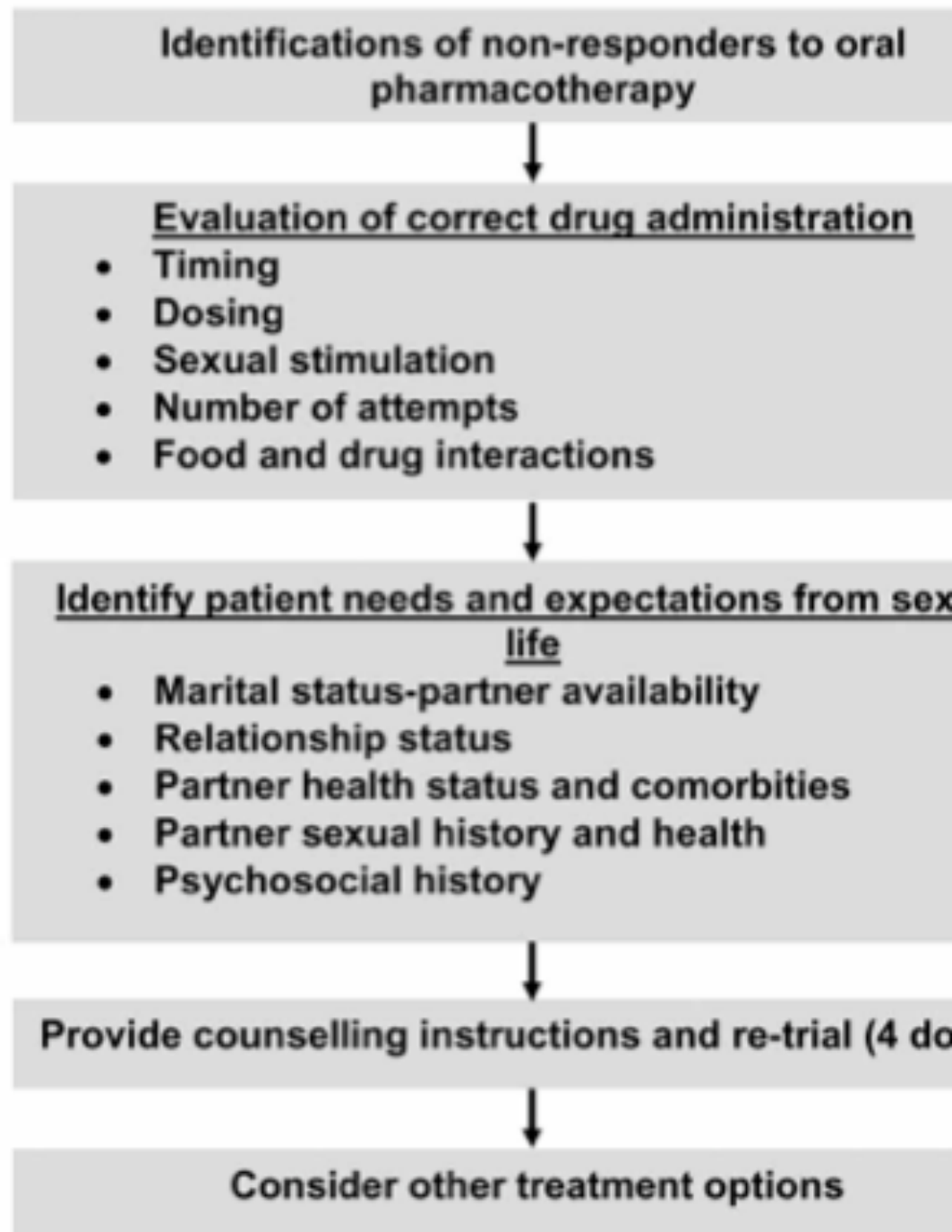
RESULTS: Flow-to-maintain at intracavernosal pressure 150 mm Hg and mean pressure decay values ranged between 0.5-13 ml/min and 5-45 mm Hg, respectively. Flow-to-maintain values >5 ml/min were noticed in 8 patients (24.24%), while pressure decay values >45 mm Hg in 13 patients (39.39%). Pharmacocavernosography revealed moderate opacification of venous structures in 7 cases (21.21%). Abnormal systemic-cavernosal arterial pressure gradients in both cavernosal arteries were noticed in 9 patients (27.27%). All patients with flow-to-maintain values >5 ml/min had normal arterial function.

CONCLUSIONS: A functional/rigid erectile response may coexist with arterial insufficiency or corporeal veno-occlusive dysfunction. Presence of normal or borderline arterial inflow may compensate minimal or moderate veno-occlusive dysfunction, resulting in a functional - but not normal erection. Such information is critical when the intracavernosal injection test is used for diagnostic purposes.

5α-reductase Type 5 Inhibitors: Unmet Needs

Chrysochouratidis and D. G. Hatzichristou*

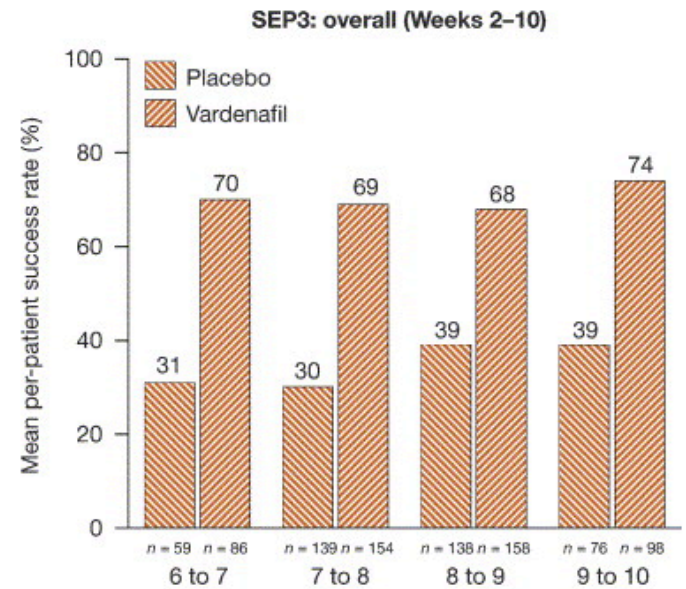
Department of Urology, Center for Sexual and Reproductive Health, 'Papageorgiou' General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece



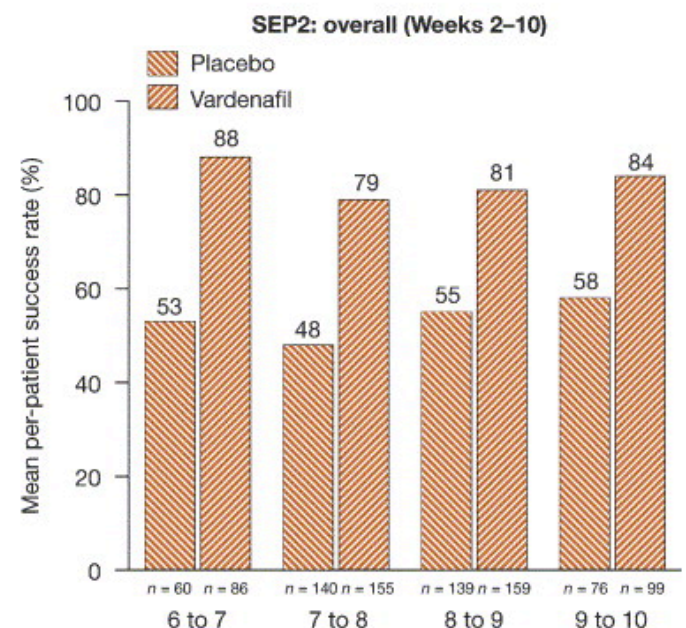


...ed Duration of Efficacy of Vardenafil When Taken 8
 ...before Intercourse: A Randomized, Double-Blind,
 ...-Controlled Study

...^a, ...^b, Ira D. Sharlip^b, Dimitris Hatzichristou^c, Eusebio Rubio-Aurioles^d, Marc Gittelman^e,
 ...^f, Peter M. Smith^f, H. Jeffrey Wilkins^g, Peter Pommerville^h, for the Vardenafil Study



(A) Time to starting sexual activity post-dose (h)
 Intent-to-treat population



(B) Time to starting sexual activity post-dose (h)

**...tolerability and satisfaction with sildenafil citrate 100-mg titration
...with continued 50-mg dose treatment in men with erectile
...tion**



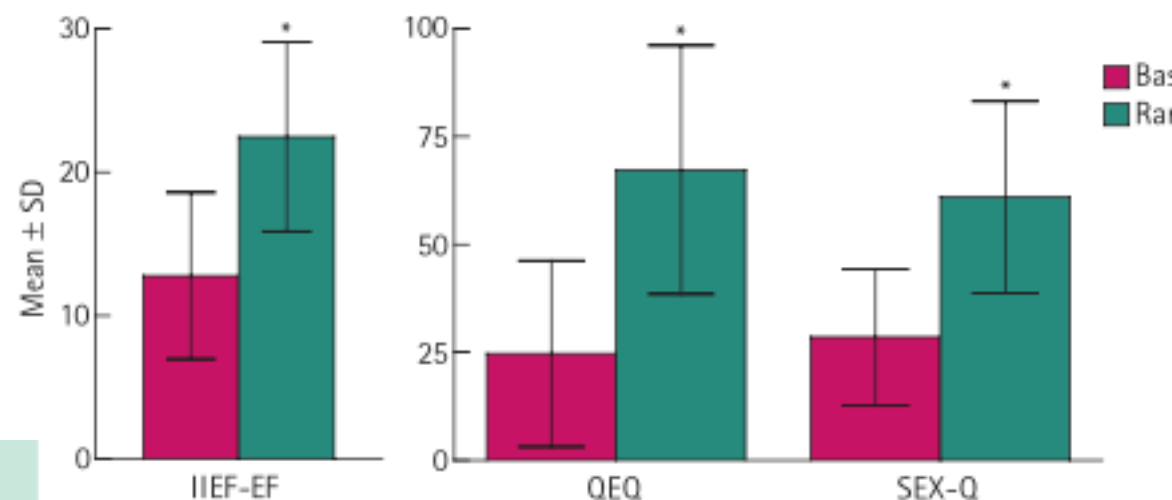
Buvat, Dimitrios Hatzichristou,
...ggi, Ian Farmer, Jose M.
...Jabaloyas, Paul J. Miller
...iel Schnetzler

Issue



BJU International
Volume 102, Issue 11, pages
1645–1650, December 2008

FIG. 1. Mean change from baseline to randomization in the IIEF-EF domain, QEQ and SEX-Q; *P



	Single-blind 50 mg	Double-blind	
		50 mg	100 mg
	492	239	236
	6.5	7.1	3.0
	3.5	4.6	3.8
	1.6	1.3	2.1
	1.2	2.1	0.8
	0.2	0	1.3
...estion	1.2	1.7	0.4
...ngitis	0	1.7	0

TABLE 2
The most frequently reported AEs (≥1% of participants; expressed as % of patients)



ive study of the beneficial effects of dose
n and customized instructions on patient satisfactio
afil citrate (Viagra®) for erectile dysfunction

ullough^{a, 1},  , Culley C. Carson^{b, 2}, Dimitrios Hatzichristou^{c, 3}

This study was conducted between September 29, 2003 and June 10, 2004.

Investigators recruited patients seeking treatment for ED for whom the investigator have prescribed sildenafil. This 8-week, multicenter, open-label, flexible-dose study of sildenafil (25, 50, or 100 mg) included 2 phases. In the first 4-week phase, patients were given sildenafil (50 mg) and were instructed to follow the dosing instructions provided in the sample package ([Table I](#)) without further verbal clarification. At the start of the first 4-week phase, patient treatment satisfaction was assessed with Question 1 (Q1) from the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS),¹³ “Overall, how satisfied are you with this treatment?” All patients who were not “very satisfied” with their treatment were interviewed to determine the reasons for their dissatisfaction; they then received customized dosing instructions in response to their specific complaints. For example, if the patient was not satisfied with how long treatment had lasted, the investigator might review the timing of the medication with respect to meals and sexual activity, and suggest increasing the sildenafil dose to 100 mg and trying the new dose at least 3 to 4 separate occasions. Conversely, a patient who experienced adverse events might be instructed to lower the sildenafil dose to 25 mg to enhance tolerability, and the investigator might additionally reassure the patient that these adverse effects are not dangerous, but are typical and provide a sign that the medication is working; the investigator might then suggest that the patient take appropriate treatment for symptomatic relief of common adverse events, such as headache, dyspepsia, and rhinitis, before taking sildenafil.



Objective study of the beneficial effects of dose titration and customized instructions on patient satisfaction with sildenafil citrate (Viagra®) for erectile dysfunction

McCullough^{a, 1},  , Culley C. Carson^{b, 2}, Dimitrios Hatzichristou^{c, 3}

TABLE I.

Information provided to patients in the Viagra® sample package

Viagra works only when you are sexually stimulated (such as kissing or touching)

For most men, Viagra works the first or second time they try it. Some men may need more attempts. So keep trying. Viagra can be taken as often as once a day

If you take any medicines that have nitrates in them (such as nitroglycerin for chest pains)—even if you take them only once in a while—you should not take Viagra

Viagra works in as quickly as 30 minutes. And it stays ready to work for at least 4 hours

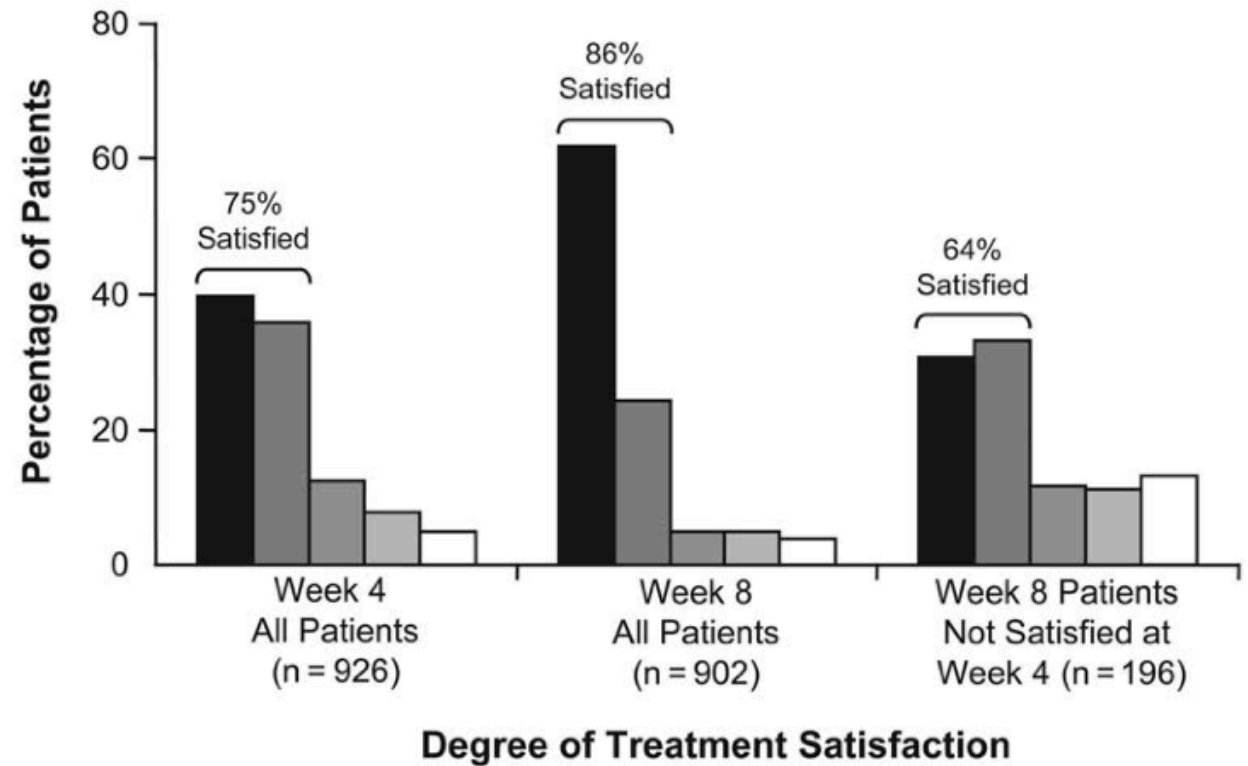
If you are not pleased with your results, talk to your doctor. Your doctor can increase your dose to 100 mg or decrease your dose to 25 mg



pective study of the beneficial effects of dose
ation and customized instructions on patient satisfaction
denafil citrate (Viagra®) for erectile dysfunction

L. McCullough^{a, 1},  , Culley C. Carson^{b, 2}, Dimitrios Hatzichristou^{c, 3}

■ Very Satisfied ■ Somewhat Satisfied ■ Neither ■ Somewhat Dissatisfied □ Very Dissatisfied



Στρατηγικές διάσωσης για ασθενείς που **ΔΕΝ ΑΠΑΝΤΟΥΝ** στη θεραπεία με αναστολείς φωσφοδιεστεράσης τύπου-5 (PDE-5)

ΨΕΥΔΟΑΠΑΝΤΗΤΕΣ

Ακολουθούν τις οδηγίες σωστά;

>4 λήψεις φαρμάκου με μικρή χρονικά απόσταση μεταξύ τους
Μέγιστη ανεκτή δόση

Λήψη δισκίου >1 ώρα πριν τη σεξουαλική δραστηριότητα

4 ώρες πριν από λιπαρό γεύμα, εφ' όσον το απαιτεί το φάρμακο που χορηγήθηκε

Χρήση συνοδών φαρμάκων, σύμφωνα με οδηγίες γιατρού

Επαρκής σεξουαλική διέγερση!

Είναι το ζευγάρι έτοιμο να επανέλθει στη σεξουαλική δραστηριότητα;

Αντιμέτωπιση σεξουαλικής δυσλειτουργίας συντρόφου, εφόσον υπάρχει

Εντοπισμός/ Επίλυση προβλημάτων στη σχέση του ζευγαριού

Συνδυασμός με ψυχοσεξουαλική θεραπεία

Αποδοχή θεραπείας από σύντροφο

ΜΗ ΑΠΑΝΤΗΤΕΣ

Επόμενα βήματα...

Συνταγογράφηση άλλου αναστολέα PDE-5

Λήψη ημερήσιας δόσης

ΛΗΨΗ ΣΥΝΔΥΑΣΤΙΚΗΣ ΘΕΡΑΠΕΙΑΣ:

1. Συμπληρωματική τεστοστερόνη, εφόσον ενδείκνυται
2. Στυτική συσκευή κενού
3. α-blockers, στατίνες ή συνεχής πίεση αεραγωγών, όταν υπάρχουν συννοσηρότητες

Ενδοσπραγγώδεις ενέσεις συν/πλην αναστολείς PDE5

Πεϊκή πρόθεση





ALPROSTADIL VERSUS INTRACAVERNOUS INJECTION ALPROSTADIL: EFFICACY AND PREFERENCE IN PATIENTS ON INTRACAVERNOUS INJECTION FOR MORE THAN 1 YEAR

ANTONIO ATZICHRISTOU, APOSTOLOS APOSTOLIDIS, VASILIOS TZORTZIS, EVANGELOS
CONSTANTINOS YANNAKOYORGOS, ATHANASIOS KALINDERIS

Table 3.

Sildenafil responder preferences at 1 month and at study end

	No. Pts.	No. Injection (%)	No. Sildenafil (%)	No. Injection + Sildenafil (%)
<i>After 1 mo.</i>				
Alprostadil (µg.):				
10 or Less	54	13 (24.1)	35 (64.8)	6 (11.1)
Greater than 10–20	28	7 (25)	17 (60.7)	4 (14.3)
Combined papaverine, phentolamine + prostaglandin E1 (ml.):				
0.05–0.3	19	5 (26.3)	12 (63.2)	2 (10.5)
0.35–0.6	12	5 (41.7)	5 (41.7)	2 (16.6)
0.7–1	3	1 (33.3)	2 (66.7)	0
<i>After 3 mos.</i>				
Alprostadil (µg.):				
10 or Less	54	13 (24.1)	39 (72.2)	2 (3.7)
Greater than 10–20	28	8 (28.6)	19 (67.8)	1 (3.6)
Combined papaverine, phentolamine + prostaglandin E1 (ml.):				
0.05–0.3	19	6 (31.6)	12 (63.1)	1 (5.3)
0.35–0.6	12	8 (66.7)	4 (33.3)	0
0.7–1	3	3 (100)	0	0



**ORAL SILDENAFIL VERSUS INTRACAVERNOUS INJECTION
OF SILDENAFIL: EFFICACY AND PREFERENCE IN PATIENTS ON
INTRACAVERNOUS INJECTION FOR MORE THAN 1 YEAR**

ANTONIO M. TZICHROSTOU, APOSTOLOS APOSTOLIDIS, VASILIOS TZORTZIS, EVANGELOS
DIMITRIOS KONSTANTINOS YANNAKOYORGOS, ATHANASIOS KALINDERIS

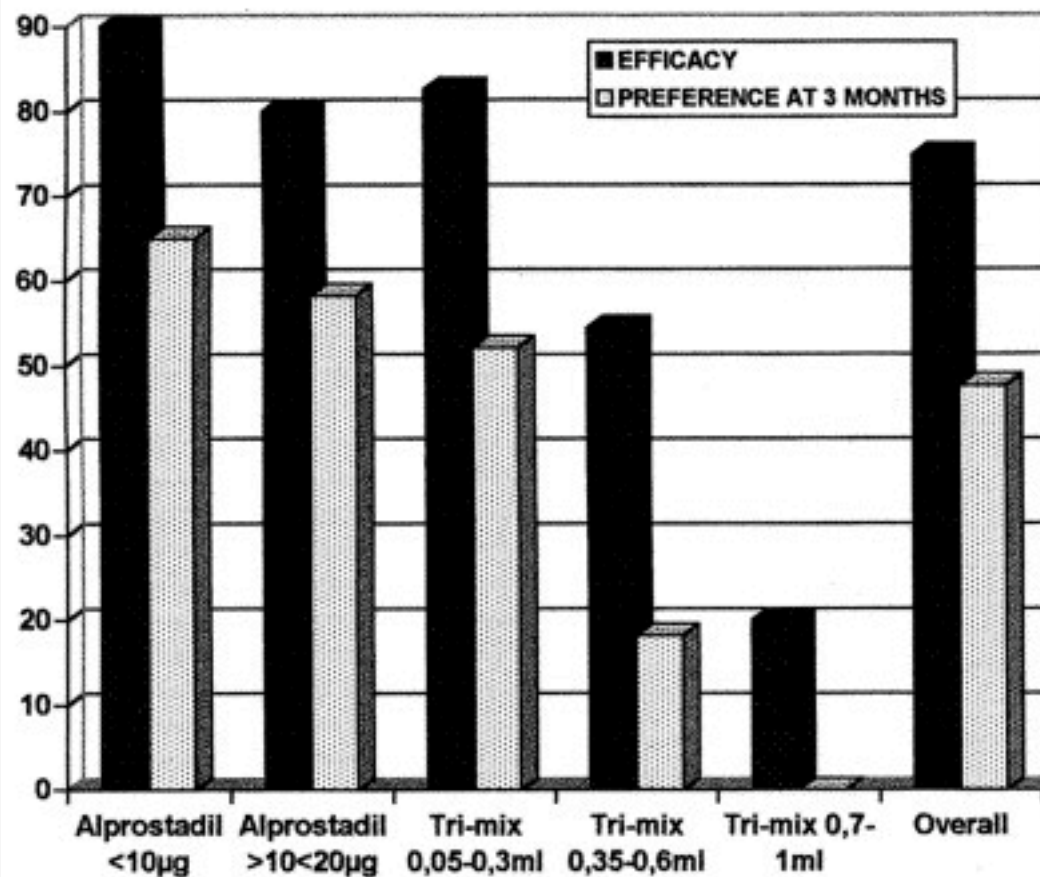
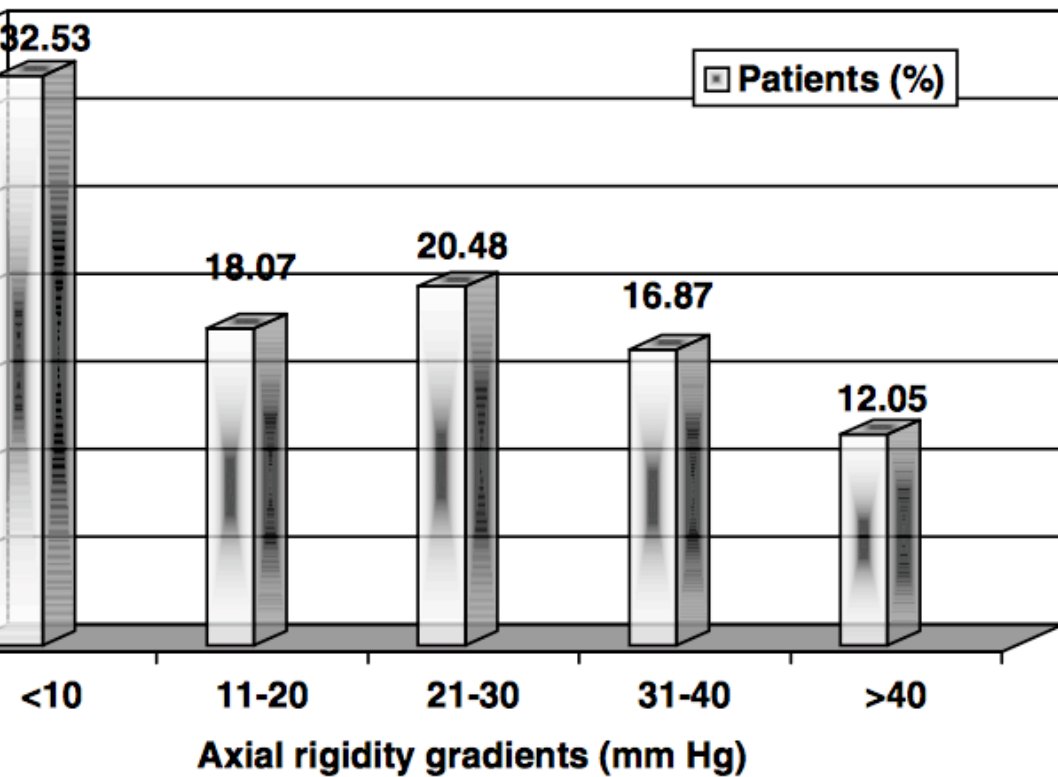


Fig. 2.

Differences in efficacy of sildenafil and preference by group in overall study sample of 155 patients combined papaverine, phentolamine and prostaglandin E1.

Normal hemodynamic parameters do not always predict the presence of a rigid erection: a quantitative assessment of functional erectile impairment

Zichristou^{1*}, K Hatzimouratidis¹, V Tzortzis¹, A Apostolidis¹, A Bekos and E Ioannidis¹



3 ARGs in the study sample.

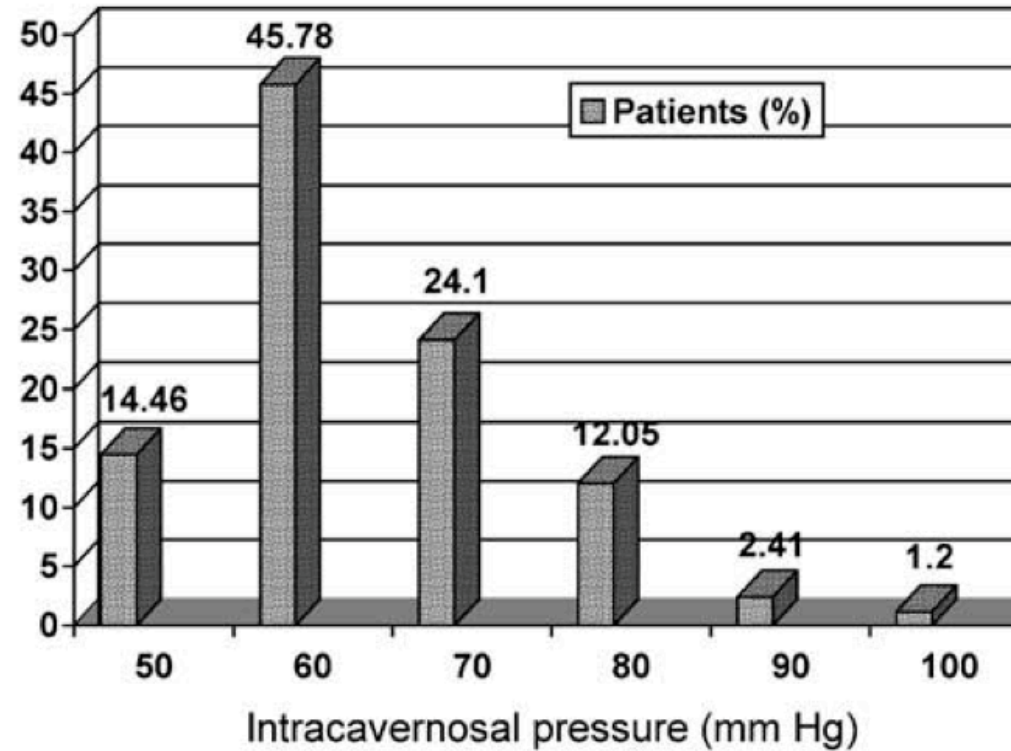


Figure 2 Intracavernosal pressure associated with presence of penile rigidity in the study sample.

Normal hemodynamic parameters do not always predict the presence of a rigid erection: a quantitative assessment of functional erectile impairment

Zichristou^{1*}, K Hatzimouratidis¹, V Tzortzis¹, A Apostolidis¹, A Bekos and E Ioannidis¹

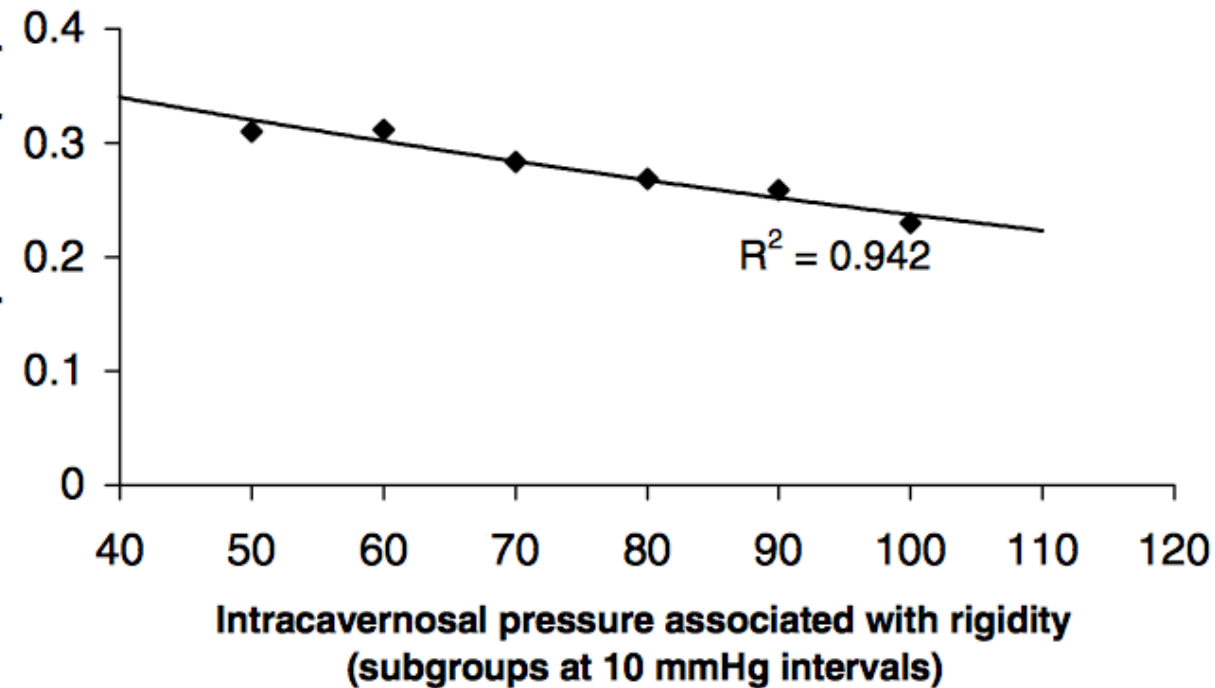


Figure 1 Relation between intracavernosal pressure associated with rigidity values and mean penile aspect ratio values (correlation coefficient 0.942).

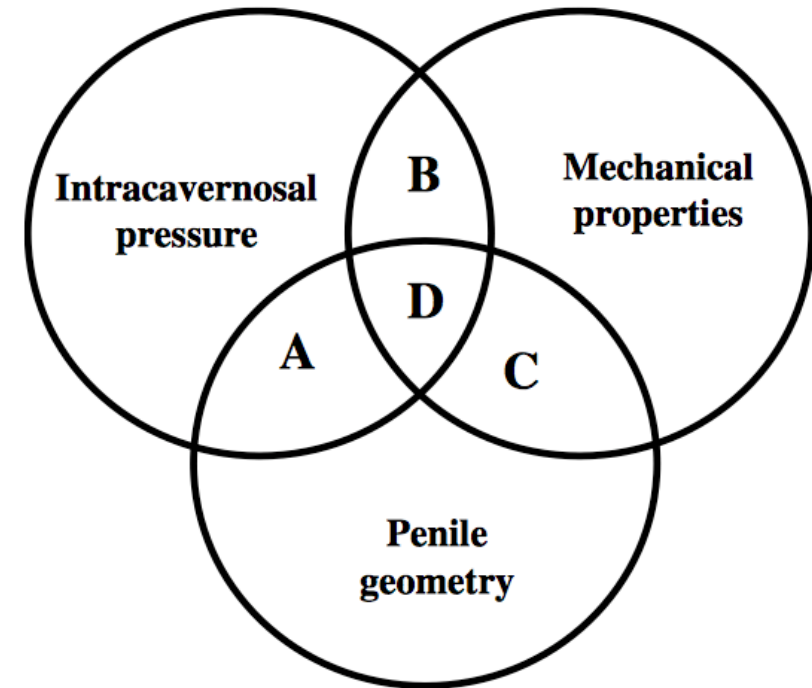


Figure 4 A conceptual model on the pathophysiology of impotence, in which impotence may be because of normal intracavernosal pressure, altered tissue mechanical properties, unfavorable penile geometry (D/L) ratio or any combination of these: (a) normal tissue expandability, low intracavernosal pressure and low D/L ratio, (b) normal penile geometry, normal intracavernosal pressure and altered tissue expandability, (c) normal intracavernosal pressure altered tissue expandability and low D/L ratio. (d) low intracavernosal pressure, altered tissue expandability and low D/L ratio.

Συνδυασμοί με PDE5i

PDE5i και VED

- Βελτίωση του IIEF-EF.
- Νέοι ασθενείς, μετά από ριζική.

PDE5i και ενδοπεϊκές ενέσεις

- Ανταπόκριση έως 31%
- Παρενέργειες σε ποσοστό 33%
- 20% ζάλη

PDE5i και Τεστοστερόνη

- Βελτίωση σε ασθενείς με επίπεδα T <300ng/dl

ΕΡΩΤΗΣΕΙΣ

Ερώτηση 6

Ποιος PDE5i έχει το
καλύτερο προφίλ
ασφάλειας;

ΑΝΕΠΙΘΥΜΗΤΕΣ ΕΝΕΡΓΕΙΕΣ ΤΩΝ ΑΝΑΣΤΟΛΕΩΝ ΤΗΣ PDE5

Ανεπιθύμητη ενέργεια	ΣΙΛΔΕΝΑΦΙΛΗ	ΤΑΔΑΛΑΦΙΛΗ	ΒΑΡΔΕΝΑΦΙΛΗ	ΑΦΑΝΑΦΙΛΗ	ΟΥΝΤΕΝΑΦΙΛΗ
Κεφαλαλγία	12.8%	14.5%	16%	9.3%	8.9%
Ερύθημα προσώπου	10.4%	4.1%	12%	3.7%	23.2%
Δυσπεψία	4.6%	12.3%	4%	1%	2.1%
Ρινική συμφόρηση	1.1%	4.3%	10%	1.9%	7.1%
Ζάλη	1.2%	2.3%	2%	<1%	<1%
Διαταραχές όρασης	1.9%		< 2%	1.9%	
Οσφυαλγία		6.5%			
Μυαλγία		5.7%			



Ασφάλεια των PDE5i

Καμιά
διαφορά

- Εμφάγματα μυοκαρδίου
- Τέστ κόπωσης: στον συνολικό χρόνο και τον χρόνο μέχρι τη ισχαιμία σε ασθενείς με σταθερή στηθάγχη



Συνχορήγηση

Νιτρώδη

- Αντένδειξη: σοβαρή αγγειοδιαστολή και πτώση ΑΠ

Αντιυπερτασικά - ablocker

- Κίνδυνος υπότασης – παράθυρο 4 ωρών
- Αντικατάσταση τεραζοσίνης, δοξαζοσίνης με αλφουζοσίνη ή ταμσουολσίνη
- Έναρξη με χαμηλότερη δόση PDE5i

CYP34A

- Μείωση δόσης

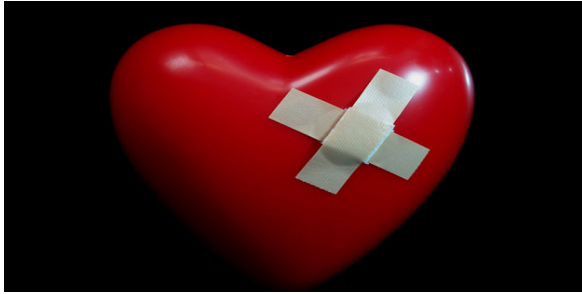
ΣΑΣ ΕΥΧΑΡΙΣΤΩ



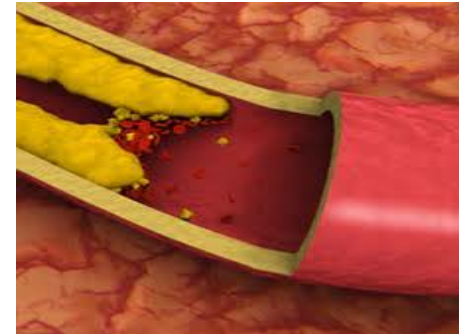
ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 1

Τι να δίνω στους
καρδιολογικούς ασθενείς;



D



- ED not only shares risk factors with CVD but also constitutes itself an independent marker of increased risk for CVD.
- The relevant CV risk is higher in men **40-49 years** with ED (Vlachopoulos et al. 2013) and those with **diabetes** (Miner et al. 2012)



The American Journal of Cardiology



Volume 96, Issue 12, Supplement 2, 26 December 2005, Pages 80–84

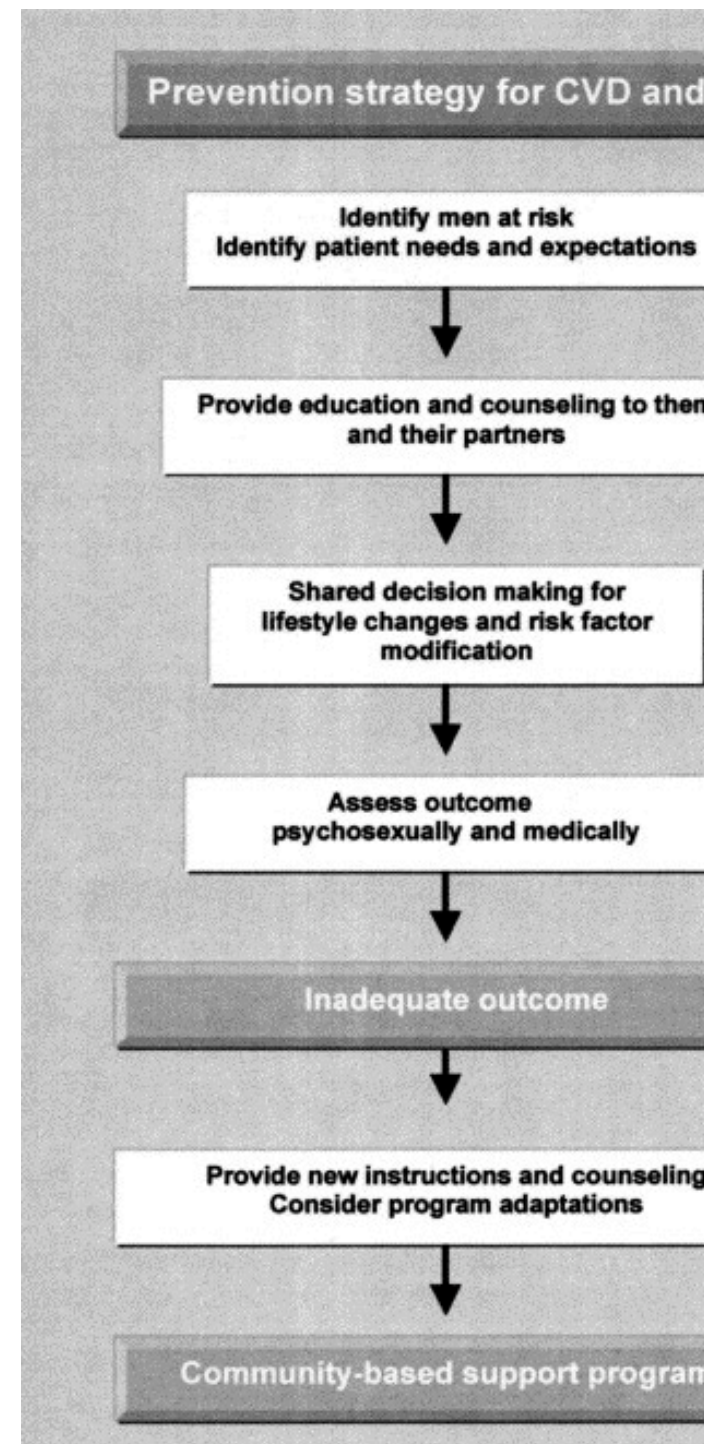
A Symposium: Sexual Dysfunction and Cardiac Risk — The Second
Princeton Consensus Conference

A Symposium: Sexual Dysfunction and Cardiac Risk



Prevention and Management of Cardiovascular Disease and Erectile Dysfunction: Toward A Common Patient-Centered, Shared Decision Model

Hatzichristou, MD  , Zoi Tsimtsiou, MD
Online 6 December 2005



ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΓΡΑΜΜΕΣ

(Princeton Consensus)
για αντιμετώπιση
στυτικής
δυσλειτουργίας
σε ασθενείς
με καρδιαγγειακή
νόσο

Σεξουαλική διερεύνηση όλων των ανδρών

ΕΠΙΒΕΒΑΙΩΜΕΝΗ ΣΔ

Ικανότητα φυσικής άσκησης (1)

Χαμηλός κίνδυνος

Απροσδιόριστος κίνδυνος

Υψηλός κίνδυνος

(1)
Σεξουαλική δραστηριότητα
ισοδυναμεί με περπάτημα
απόστασης 1 μιλίου σε επίπεδο
δρόμο 1600 μέτρα επί 20
λεπτά ή με γρήγορο ανέβασμα
2 ορόφων σε 10 δευτερόλεπτα.



(2)
Σεξουαλική δραστηριότητα
ισοδυναμεί με 4
λεπτά σε δαπεδο-
εργόμετρο (test κόπωσης
(πρωτόκολλο Bruce))



Τεστ κόπωσης (2)

Χαμηλός κίνδυνος

Υψηλός κίνδυνος

Βουλευτική, Θεραπεία στυτικής δυσλειτουργίας

Καρδιολόγος

DeBusk R, et al: Am J Cardiol. 2000; 86(2):175-81*
Kostis JB et al: Am J Cardiol. 2005; 26:96(12B):85M-93M *
Nehra A, et al: Mayo Clin Proc. 2012;87(8):766-78



DEPRESSING CONNECTION

DEPRESSION/ED
 It is unclear which comes first, but depression may interfere with normal processes of the nervous system, including erectile function.



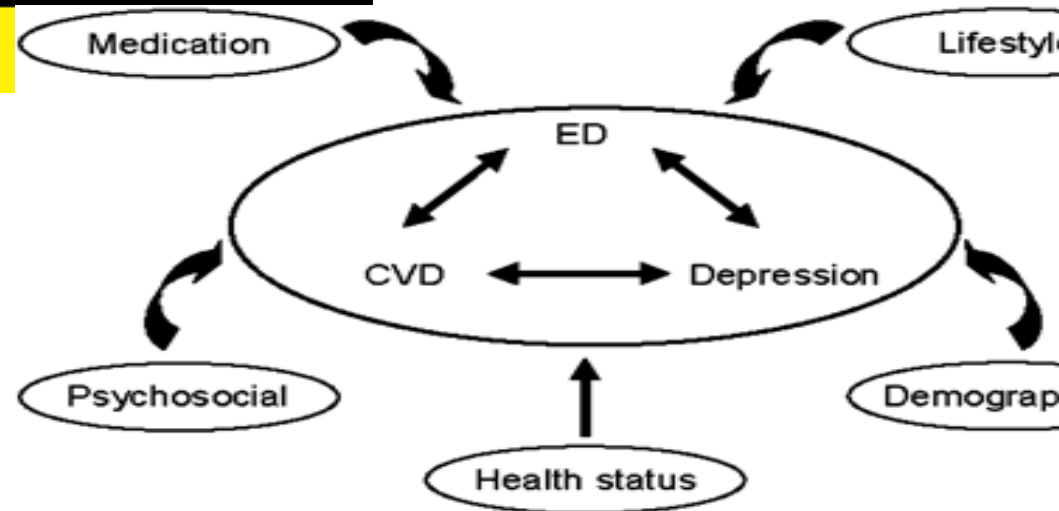
DEPRESSION/ HEART DISEASE

Depression has been linked to high levels of cortisol, which raises blood pressure and heart rate, leading to heart disease.

ED/HEART DISEASE

Obstructed blood flow may begin in the smaller arteries of the penis and affect other arteries in the future. This puts men with erectile dysfunction at a higher risk of heart problems later.

CVD, ED Depression: the fatal triad



ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

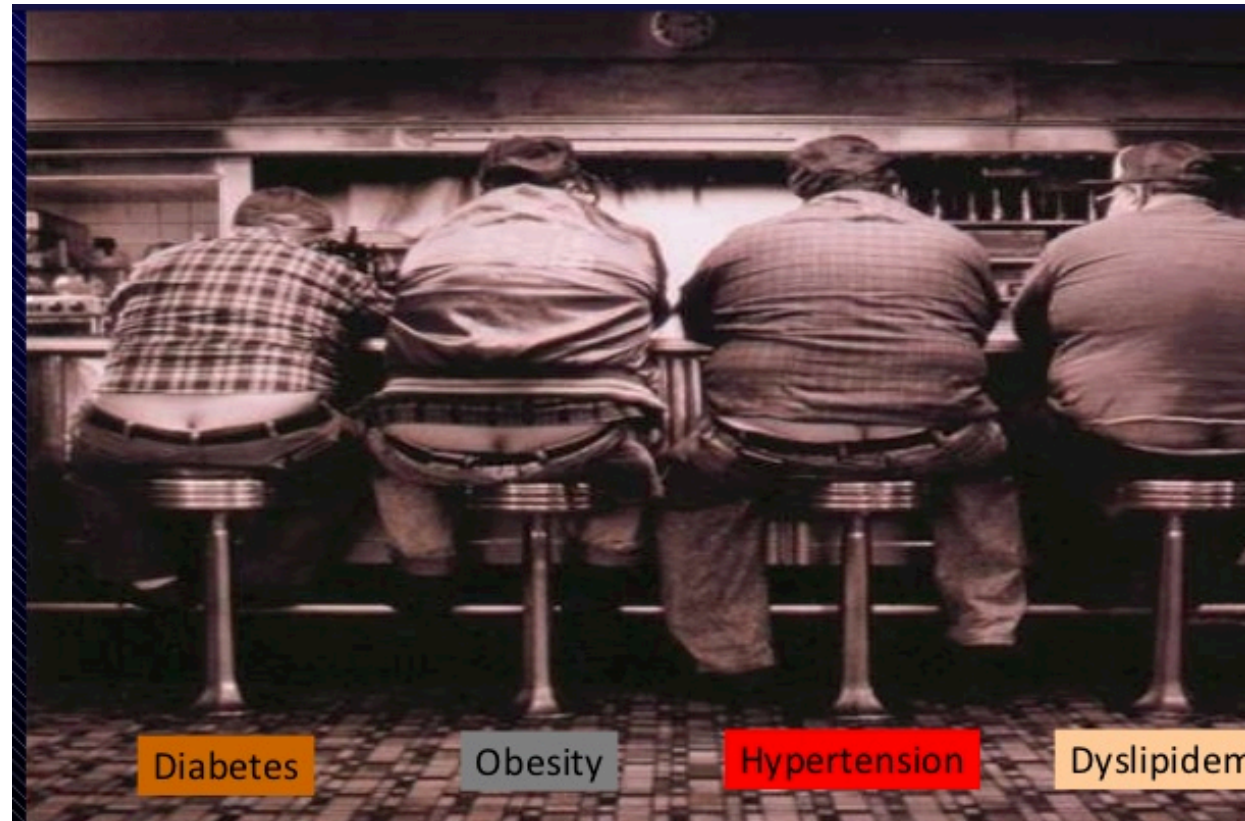
Ερώτηση 2

Πως να χειρίζομαι τους
διαβητικούς;

Metabolic Syndrome

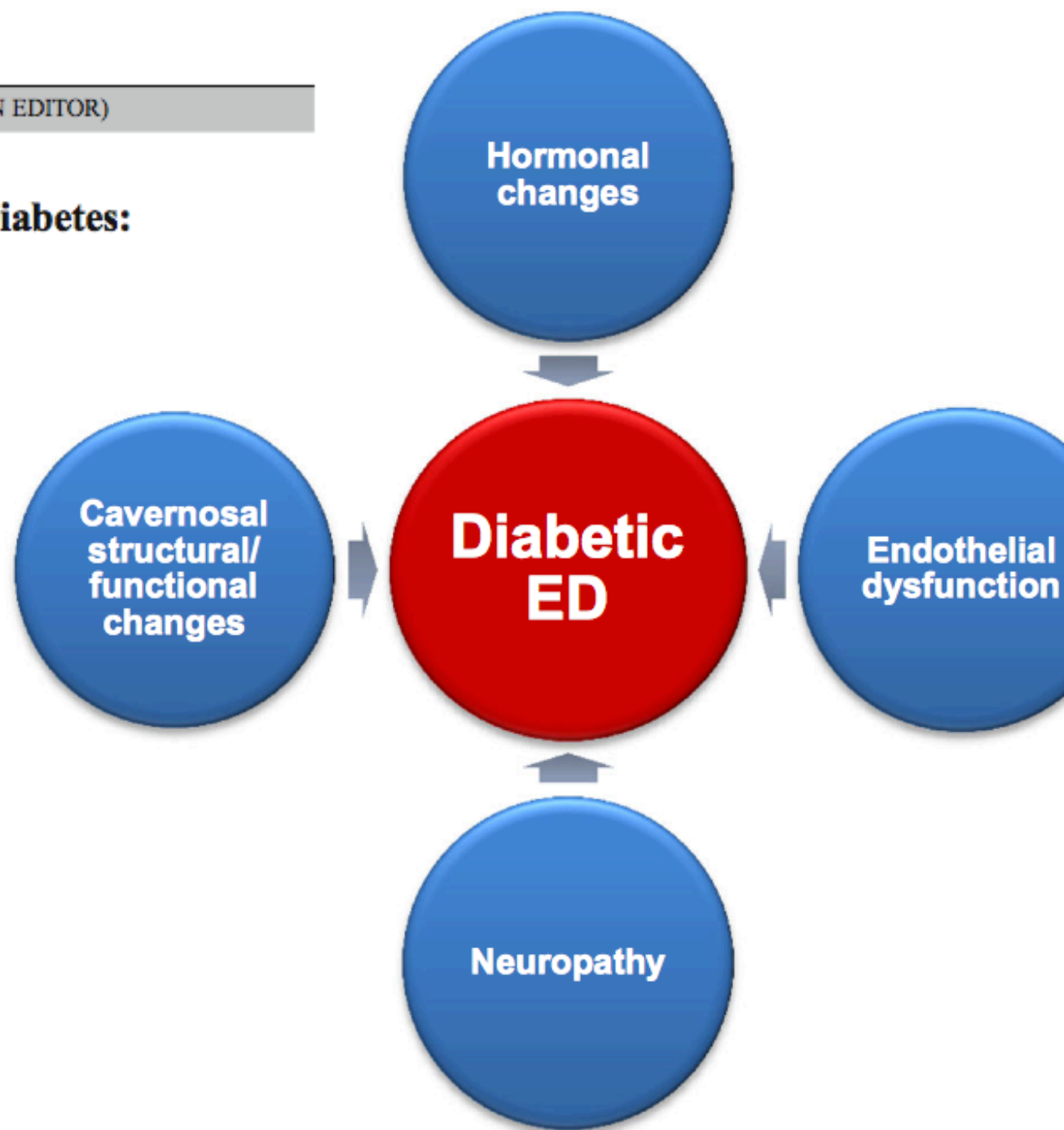
Contributing Factors

Environment – Lifestyle – Genetics – Nutrition – Diet



How to Treat Erectile Dysfunction in Men with Diabetes: Pathophysiology to Treatment

Dimitrios Hatzimouratidis · Dimitrios Hatzichristou



How to Treat Erectile Dysfunction in Men with Diabetes: From Pathophysiology to Treatment

Georgios Hatzimouratidis · Dimitrios Hatzichristou

Table 1 Efficacy of PDE5i in diabetic men (updated from [9])

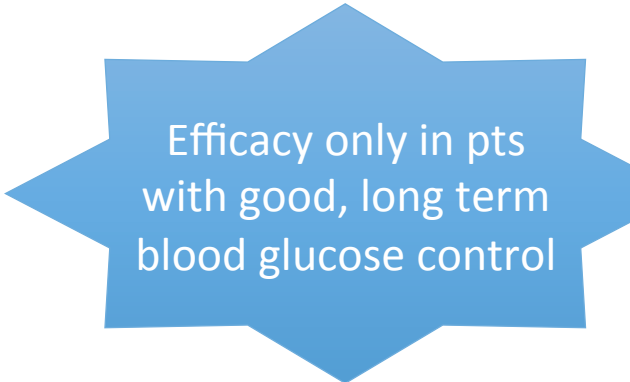
Study	Drug	Diabetes type	Outcome measure	Efficacy (%)
Rendell et al., 1999 [58]	Sildenafil (25–100 mg)	Type 1 (<i>n</i> =50) and type 2 (<i>n</i> =136)	IIEF Q4	Placebo 1.6 Sildenafil 2.7 (mean scores, <i>p</i> <0.001)
Boulton et al., 2001 [59]	Sildenafil (25–100 mg)	Type 2 (<i>n</i> =110)	IIEF Q4	Placebo 1.84 Sildenafil 3.35 (mean scores, <i>p</i> <0.001)
Stuckey et al., 2003 [60]	Sildenafil (25–100 mg)	Type 1 (<i>n</i> =188)	IIEF Q4	Placebo 2.19 Sildenafil 3.25 (mean scores, <i>p</i> <0.001)
Goldstein et al., 2003 [61]	Vardenafil (10 and 20 mg)	Type 1 (<i>n</i> =51) and type 2 (<i>n</i> =387)	SEP3	Placebo 23 % Vardenafil 10 mg 49 % Vardenafil 20 mg 54 % (<i>p</i> <0.0001 for both 10 and 20 mg)
Safarinejad, 2004 [62]	Sildenafil (100 mg)	Type 1 (<i>n</i> =48) and type 2 (<i>n</i> =234)	IIEF Q4	Placebo 2.9 Sildenafil 2 (mean scores, <i>p</i> <0.001)
Fonseca et al., 2004 [63]	Tadalafil (10 and 20 mg)	Type 1 (<i>n</i> =210) and type 2 (<i>n</i> =427)	SEP3	Placebo 21.5 % Tadalafil 10 mg 48.6 % Tadalafil 20 mg 52.8 % (<i>p</i> <0.001 for both 10 and 20 mg)
Ziegler et al., 2006 [64]	Vardenafil (5–20 mg)	Type 1 (<i>n</i> =154)	SEP3	Placebo 28 % Vardenafil 50 % (<i>p</i> <0.0001)
Hatzichristou et al., 2008 [65]	Tadalafil (2.5 and 5 mg)	Type 1 (<i>n</i> =33) and type 2 (<i>n</i> =265)	SEP3	Placebo 28.2 % Tadalafil 2.5 mg 46 % Tadalafil 5 mg 41.1 % (<i>p</i> ≤0.005 for both 2.5 and 5 mg)
Park et al., 2010 [66]	Mirodenafil 100 mg	Type 1 and type 2 (<i>n</i> =55 for both types, stratification not reported)	SEP3	Placebo 22.3 % Mirodenafil 69 % (<i>p</i> <0.0001)
Moon du et al., 2011 [67]	Udenafil (100 and 200 mg)	Type 1 and type 2 (<i>n</i> =174 for both types, stratification not reported)	SEP3	Placebo 22.6 % Udenafil 100 mg 53.13 % Udenafil 200 mg 63 % (<i>p</i> <0.0001 for both 100 and 200 mg)
Goldstein et al., 2012 [68]	Avanafil (100 and 200 mg)	Type 1 (<i>n</i> =11) and type 2 (<i>n</i> =349)	SEP3	Placebo 20 % Avanafil 100 mg 34 % Avanafil 200 mg 40 % (<i>p</i> <0.002 for 100 mg and <i>p</i> <0.001 for 200 mg)

IIEF Q4 International Index for Erectile Function Question 4 (During sexual intercourse, how often were you able to maintain completion of intercourse? Scale 0–5), **SEP3** Sexual Encounter Profile question 3 (Did your erection last long enough for you to have intercourse?)

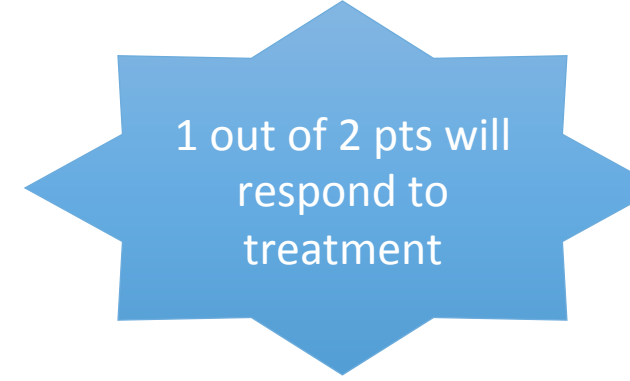
PDE5i in patients with diabetes mellitus

In a review of randomized clinical trials of PDE5i in diabetic patients, the weighted mean difference for the IIEF-EF and the percentage of successful attempts in the PDE-5 inhibitors and in the control arm was 26.7 (95% CI 23.1 to 30.3) and 6.6 (95% CI 5.2 to 7.9) respectively (Vardi and Nini 2007). This is mainly because the pathophysiology of diabetes-induced ED is multifactorial, including elevated advanced glycation endproducts, high levels of oxygen free radicals, impaired nitric oxide synthesis, increased endothelin B receptor binding sites and up-regulated RhoA/Rho-kinase pathway, neuropathic damage and impaired cyclic guanosine monophosphate (cGMP)-dependent protein kinase-1 (Thorve, Kshirsagar et al. 2011).


The only existing strategy to improve response rates include initially **management of the underlying hyperglycemia and comorbidities, as well as to start early treatment with PDE5i** (also to prevent or halt the progression of disease).



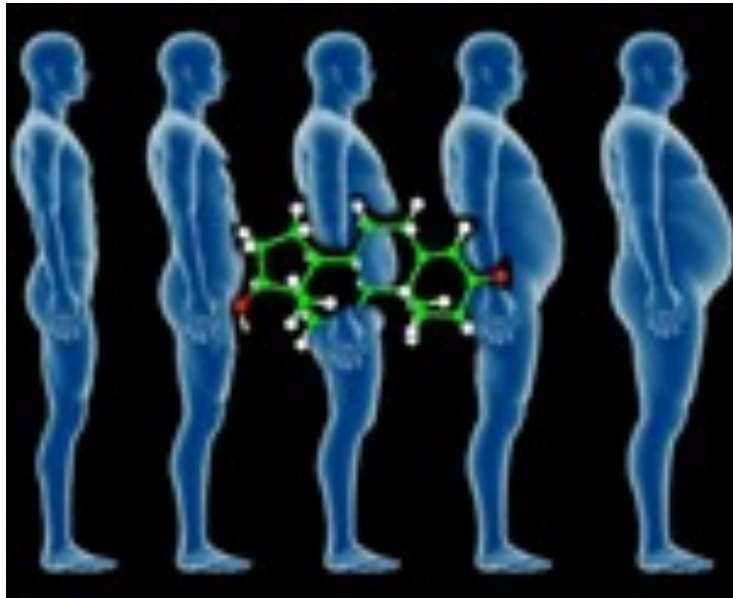
Efficacy only in pts with good, long term blood glucose control



1 out of 2 pts will respond to treatment



Treat any comorbidity



Ho JE, Arora P, Walford GA, Ghorbani A, Guanaga DP, Dhakal BP et al. Effect of phosphodiesterase inhibition on insulin resistance in obese individuals. *J Am Heart Assoc* 2014; 3

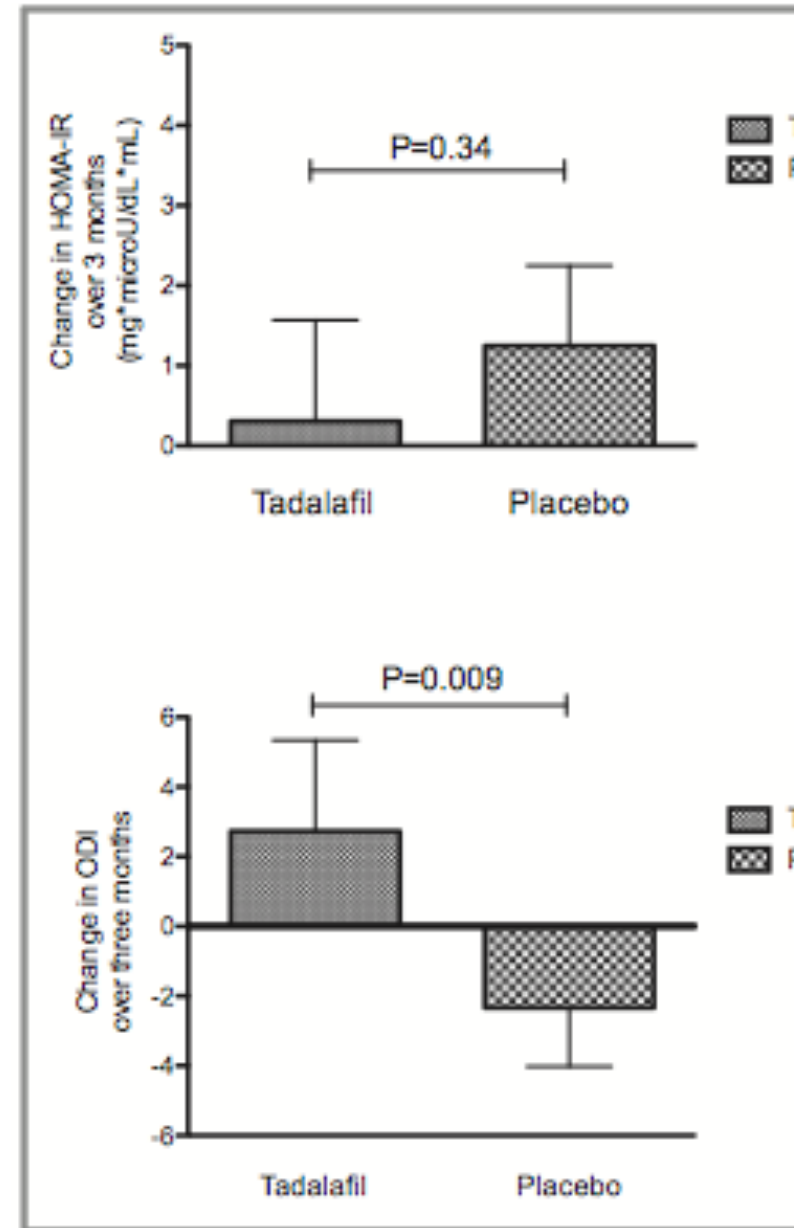
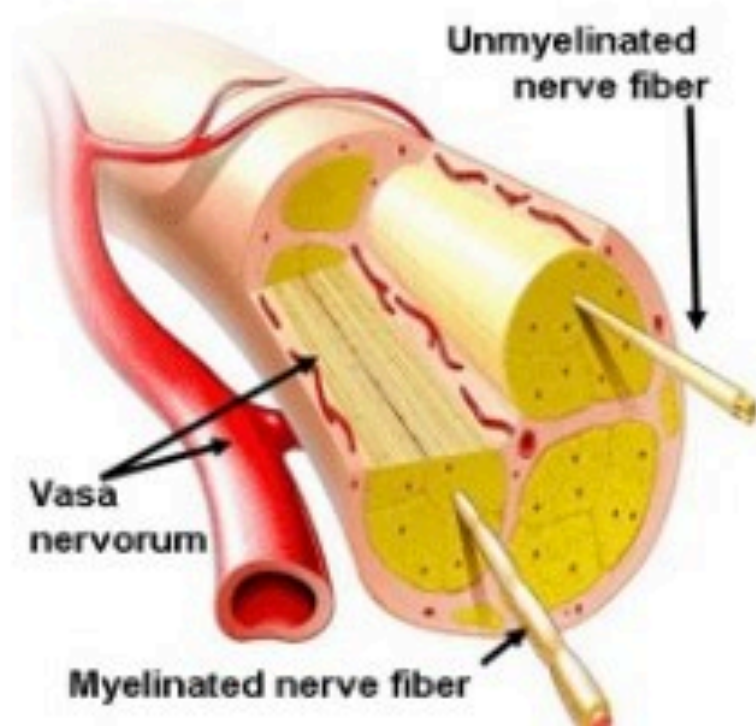


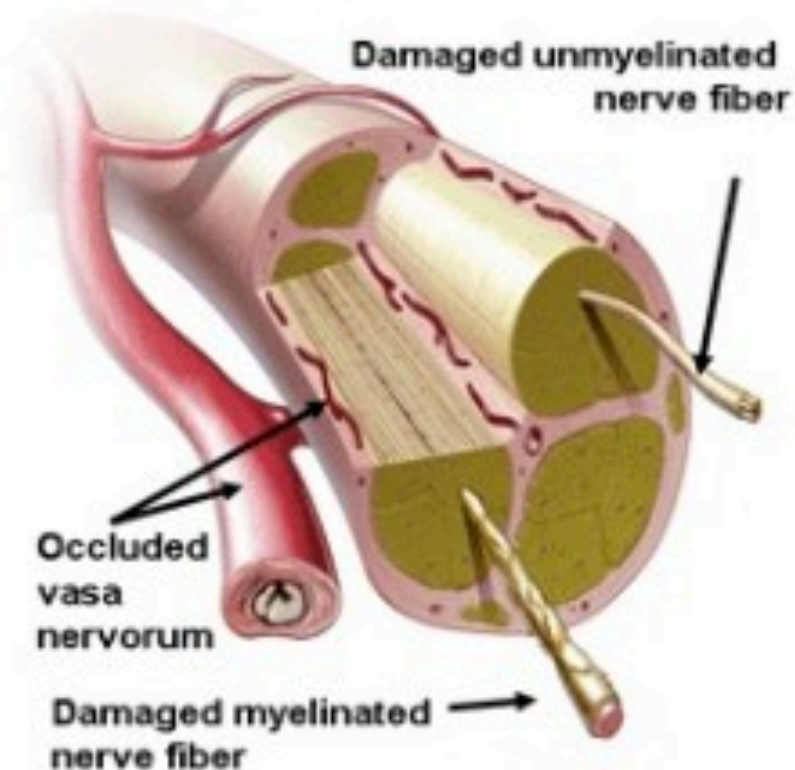
Figure 2. Change in HOMA-IR and oral disposition index over 3 months of treatment with tadalafil vs placebo groups. Values represent means \pm standard deviations. HOMA-IR indicates the static model of insulin resistance, ODI indicates oral disposition index.

Diabetic Peripheral Neuropathy

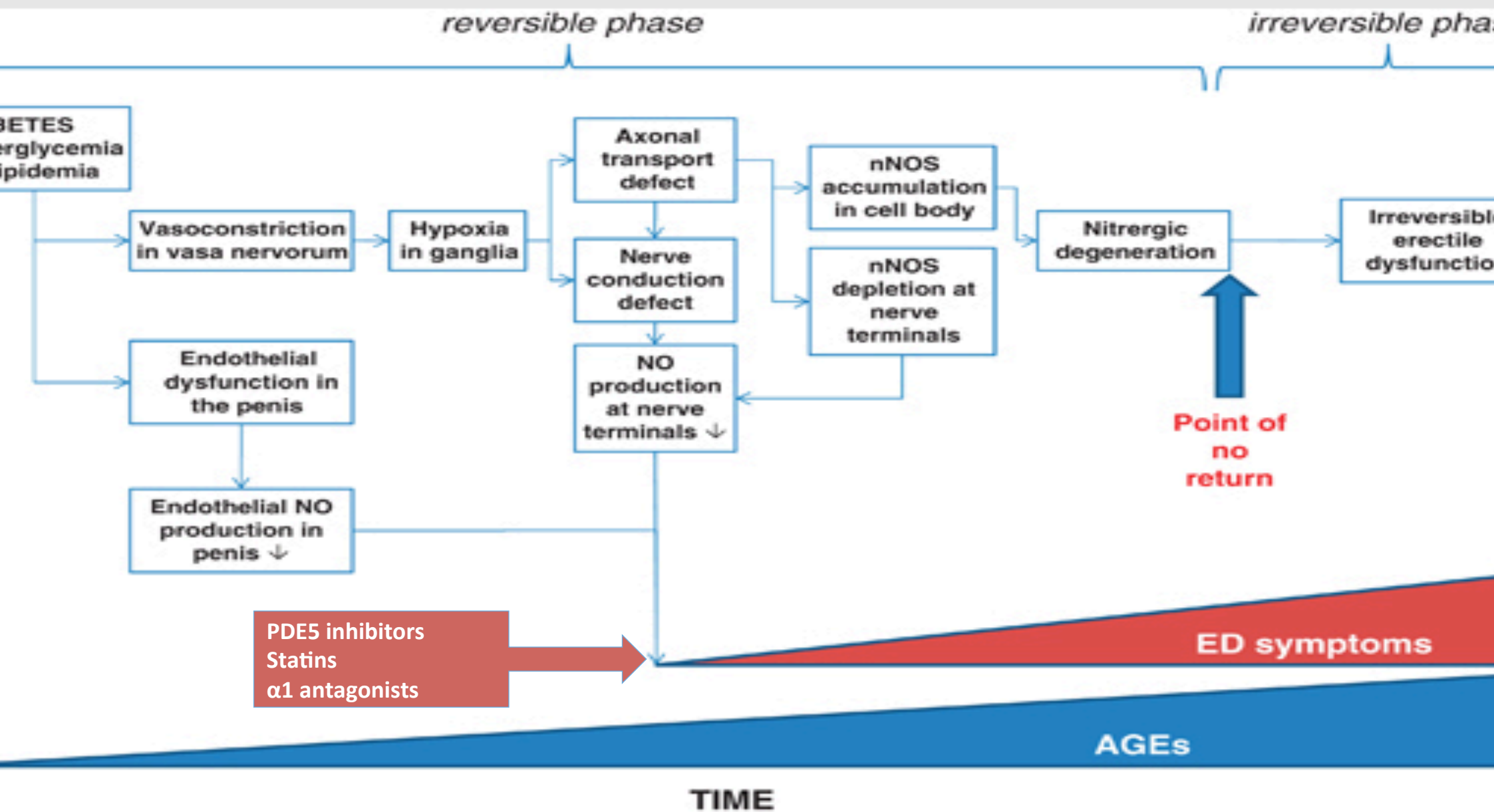
Healthy Nerves and Blood Vessels



Nerves and Blood Vessels Damaged by DPN



Diabetes mellitus and ED



ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 3

Πως να χειρίζομαι τους
ασθενείς με ΚΥΠ;

Common pathophysiologic mechanisms of **Erectile dysfunction** and **Benign Prostatic Hyperplasia**



LIFESTYLE Vascular risk factors

1.

Alteration of the nitric oxide (NO)-cyclic guanosine monophosphate (GMP) pathway

Decreased smooth muscle relaxation

2.

Increased Rho-kinase (ROCK) contractile signalling

Increased smooth muscle tone

3.

Autonomic adrenergic hyperactivity

Adrenergic receptor imbalance /dysregulation

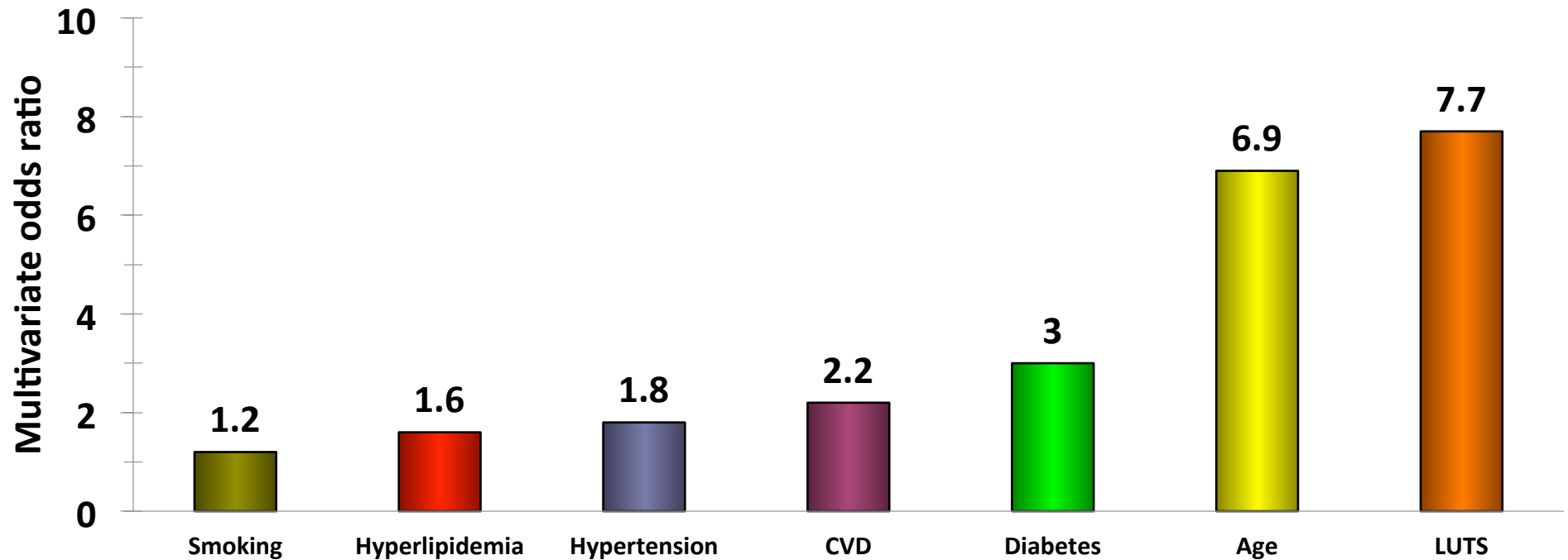
4.

Pelvic atherosclerosis

Structural and functional impairment

Erectile dysfunction + Lower urinary tract symptoms (BPH-associated)

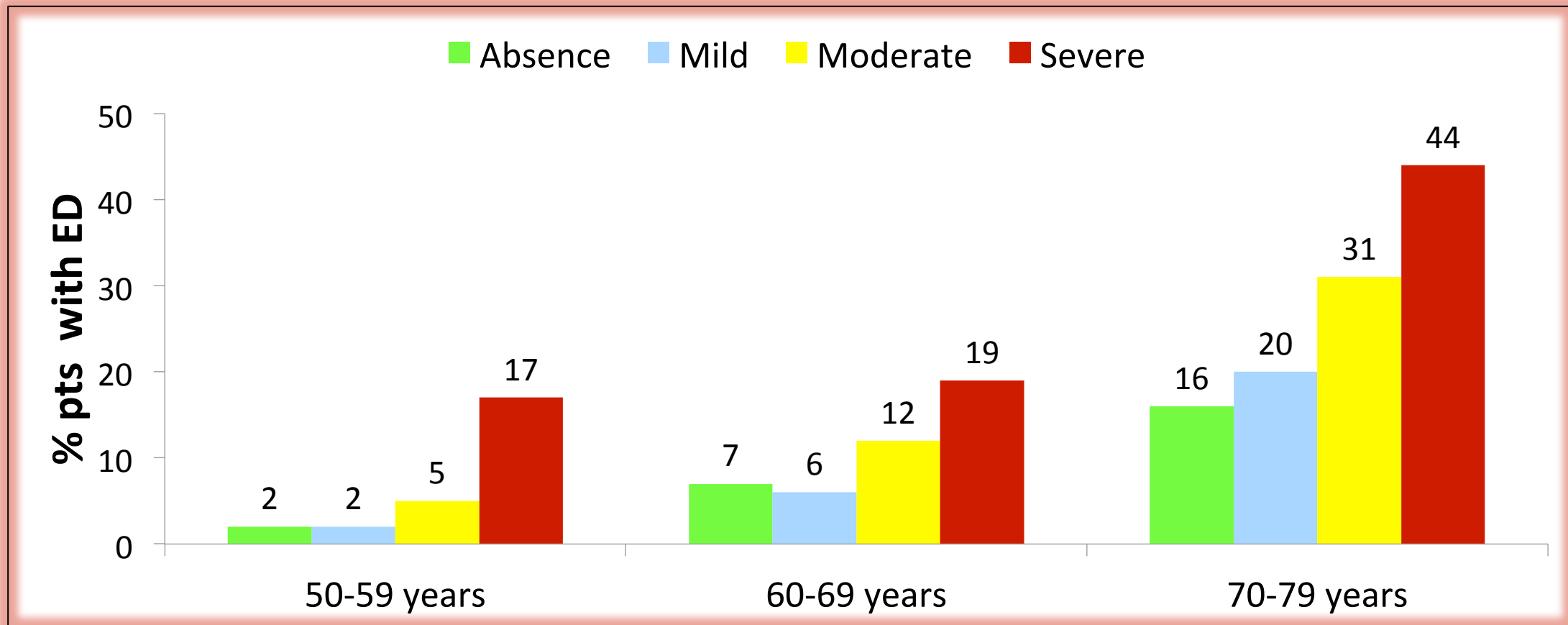
BPH-associated LUTS is strong predictor of ED



Rosen R et al. Eur Urol 2003, 44:637-649

- 24.8% had reduced or no sexual activity because of LUTS (Wein, Coyne et al. 2009)
- 31.1% of those with ED+BPH are treated for ED; 51.7% of men with BPH were under treatment (Foster, Annunziata et al. 2013).

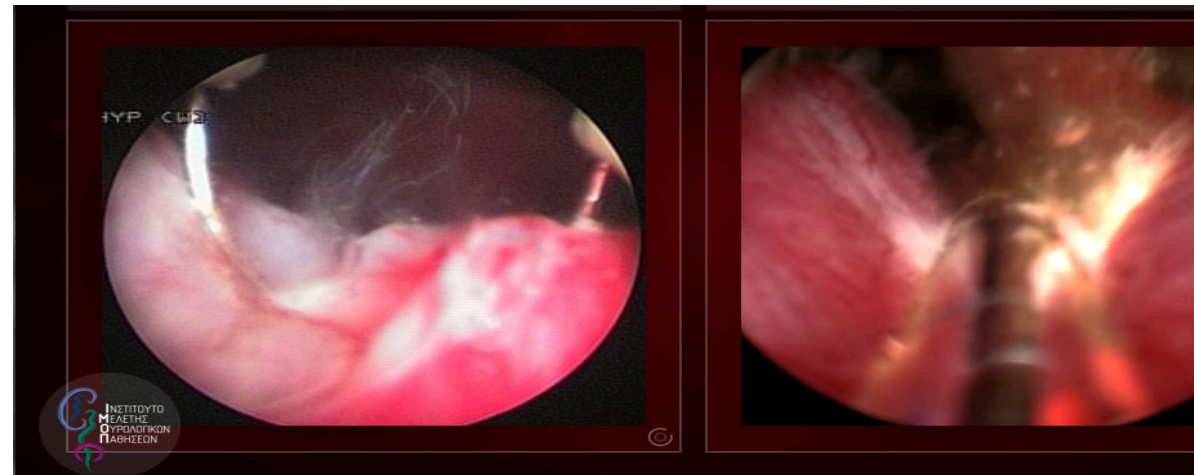
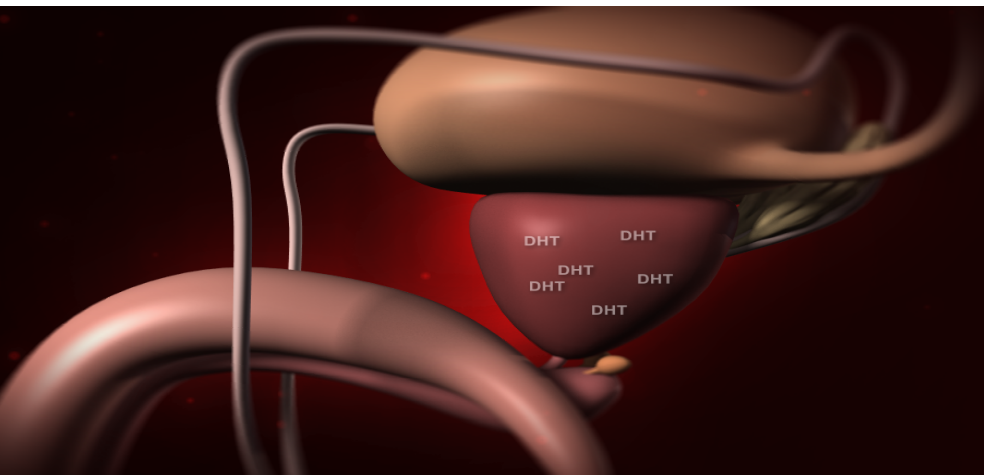
Severity of LUTS predicts severity of ED



Rosen et al. Eur Urol 2003, 44:637-649

BPH-therapies and ED

- Clinical trials with 5ARI report prevalence rates of de novo erectile dysfunction of 5 - 9%, while decreased circulating dihydrotestosterone (DHT) in diminished sexual desire and/or orgasm (Gur et al. 2013).
- Prolonged adverse effects on sexual function are reported by a subset of men, raising the possibility of a causal relationship (Traish et al. 2011)
- A systematic review of 33 randomized controlled trials and cohort studies showed that minimally invasive surgeries for BPH have comparable effects to those of TURP on erectile function (Friebe, Lin et al. 2010).
- Bipolar and monopolar TURP have no difference on overall sexual function (Mamoulakis et al. 2013).



ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 4

Πως να χειρίζομαι ασθενείς
που λαμβάνουν φάρμακα
που βλάπτουν την στύση;

Drug-induced ED

- Antihypertensives, antidepressants and antiandrogens are the 3 most harmful drug categories for EF (Simonsen 2010)
- From a clinical practice point of view, the only way to identify the effect of a drug is to order a drug holiday, if indicated (Taylor et al. 2013).

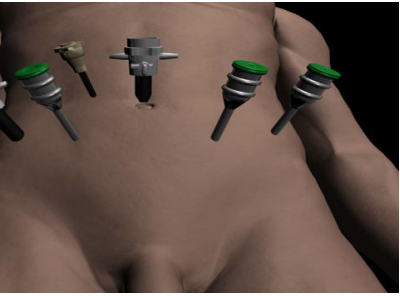
Clinical strategies to restore drug-induced ED:

- Dose reduction, if indicated;
- Dose schedule after sexual activity;
- Scheduling a drug holiday periodically, e.g. a two-day drug holiday (weekends) of an antidepressant may restore sexual function without the drug losing its efficacy.

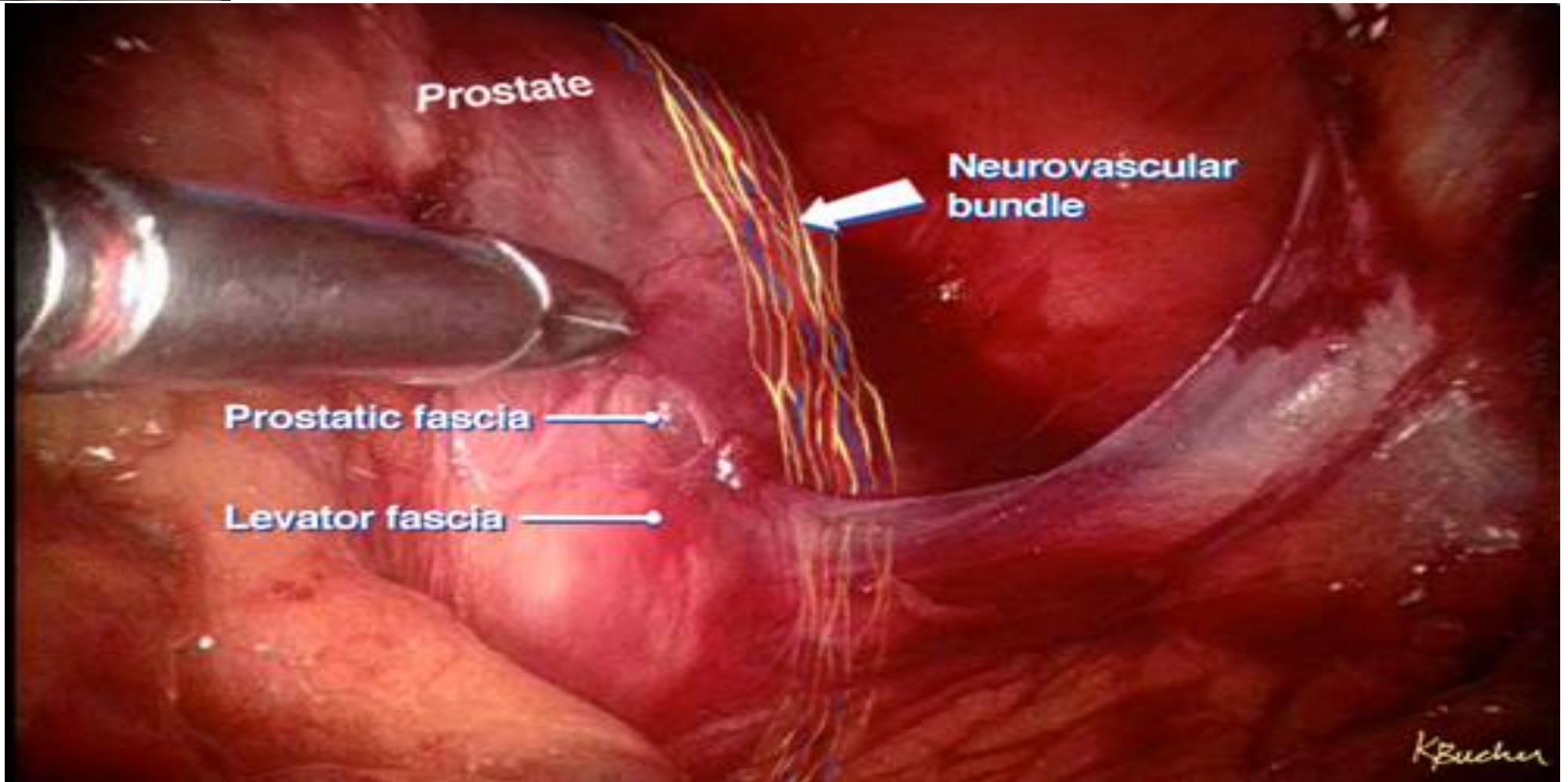
ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

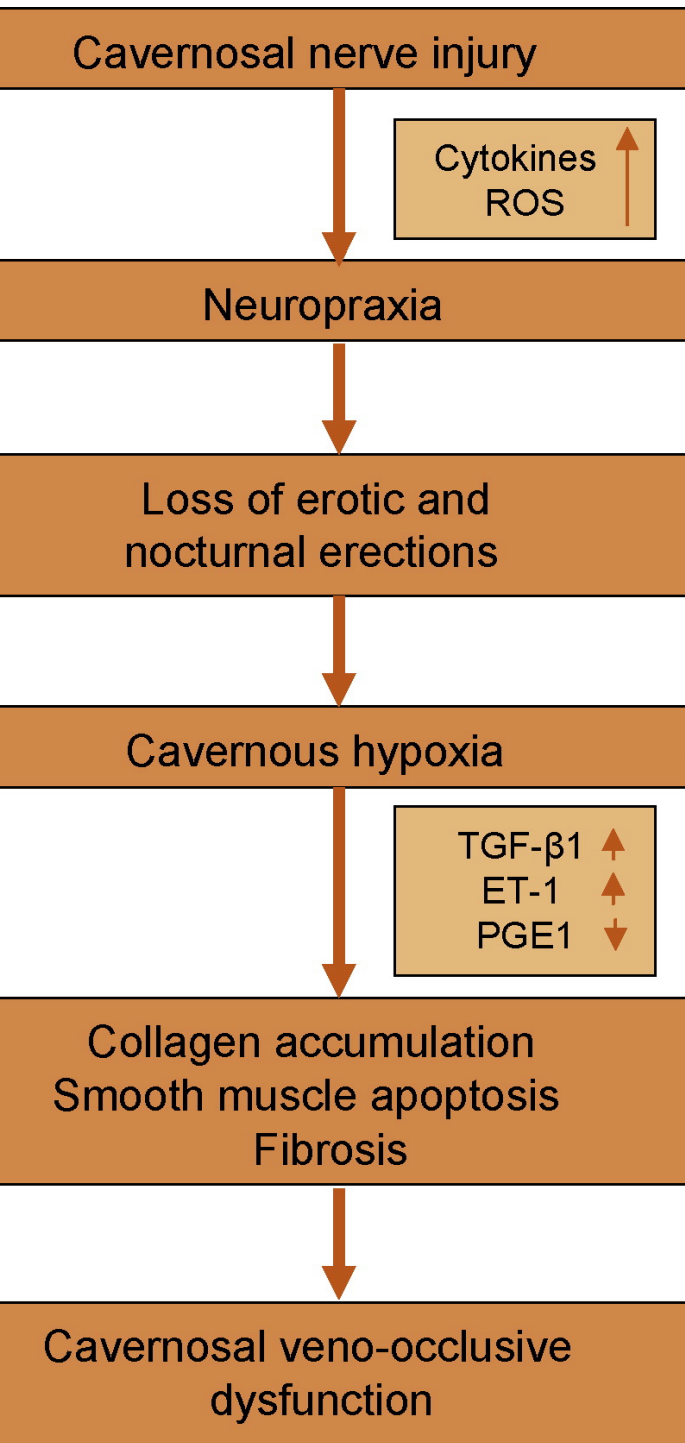
Ερώτηση 5

Τελικά η προστασία των
νεύρων στη ριζική
προστατεκτομή σώζει τη
στύση;



The incredible nerve-sparing surgery





Collaborative Review – Prostate Cancer

Phosphodiesterase Type 5 Inhibitors in Postprostatectomy Erectile Dysfunction: A Critical Analysis of the Basic Science Rationale and Clinical Application

Konstantinos Hatzimouratidis^a, Arthur L. Burnett^b, Dimitrios Hatzichristou^a, Andrew R. Morrison^c, Francesco Montorsi^d, John P. Mulhall^e

Nerve-sparing Radical Prostatectomy: myth or fact?

- Post-radical prostatectomy ED prevalence varies in different studies between 25-75% (Sanda et al. 2008)
- Such discrepancy in success rates allows clinicians to bypass the lack of well-designed head-to-head, comparative studies on different surgical techniques and eventually provide patients with unrealistic expectations (Hatzichristou 2012).
- The primary parameters contributing to EF recovery (Salonia, Burnett et al. 2012):
 - ✓ Patient factors, including age, baseline EF and comorbid conditions),
 - ✓ Cancer location (unilateral vs bilateral nerve-sparing),
 - ✓ Technical aspects (i.e. intra- vs inter- vs extrafascial technique), surgical approach (i.e. open, laparoscopic and robot-assisted RP), as well as
 - ✓ Surgeon factors (i.e. surgical volume and surgical skill)




Radical prostatectomy and erectile function: the end of the miracle

A randomized, double-blind, double-dummy, multicentre, parallel group study conducted at 87 centres worldwide, included 628 patients scheduled to undergo bilateral NSRP within 1 month of screening and having a normal IIEF-EF score of >26 at screening.

Three significant observations are of particular interest:

In 87 centers of excellence worldwide, 9 months postoperatively, only **16.8% of the patients in the placebo group had normal erectile function**, as they had preoperatively;



Most pts will have ED postop

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 6

Να χορηγώ PDE5i μετά τη
ριζική προστατεκτομή;

Rehabilitation Program: is it time to forget about it?

- Two double-blind studies have found no difference between nightly vs on-demand use of vardenafil or sildenafil after nerve-sparing radical prostatectomy (Montorsi et al. 2008; Pavlovich et al. 2013)
- A goal-oriented treatment paradigm has been recently proposed, where any chosen treatment may actually induce erections that allow sexual intercourse (Fode, Ohl et al. 2013)



One must be very careful not to repeat the statement that penile rehabilitation regimens improve erectile function after radical prostatectomy many times that it becomes a truth, even without the proper scientific backing”

Fode, Ohl et al. 2013

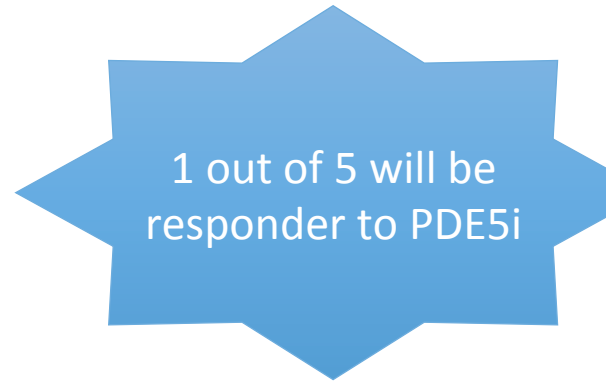
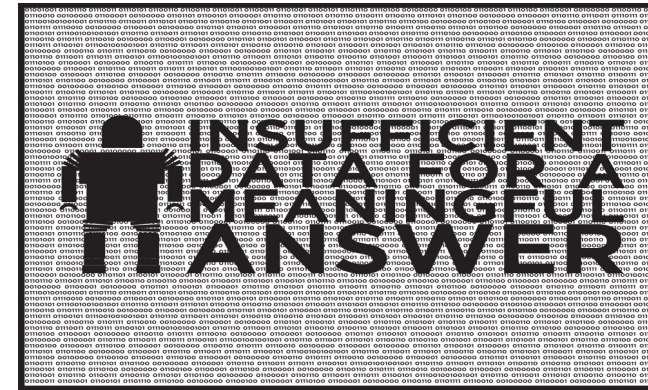
**YOU
ALWAYS
BELIEVE**

Radical prostatectomy and erectile function: the end of the miracle

A randomized, double-blind, double-dummy, multicentre, parallel group study conducted at 87 centres worldwide, included 628 patients scheduled to undergo bilateral NSRP within 1 month of screening and having a normal IIEF-EF score of >26 at screening.

A statistically significant difference compared to placebo was noticed only at the on-demand administration of PDE5i (p = 0.0003);

On-demand administration of PDE5i **one year postoperatively reached mean IIEF-EF3 success rates of approximately 60%**

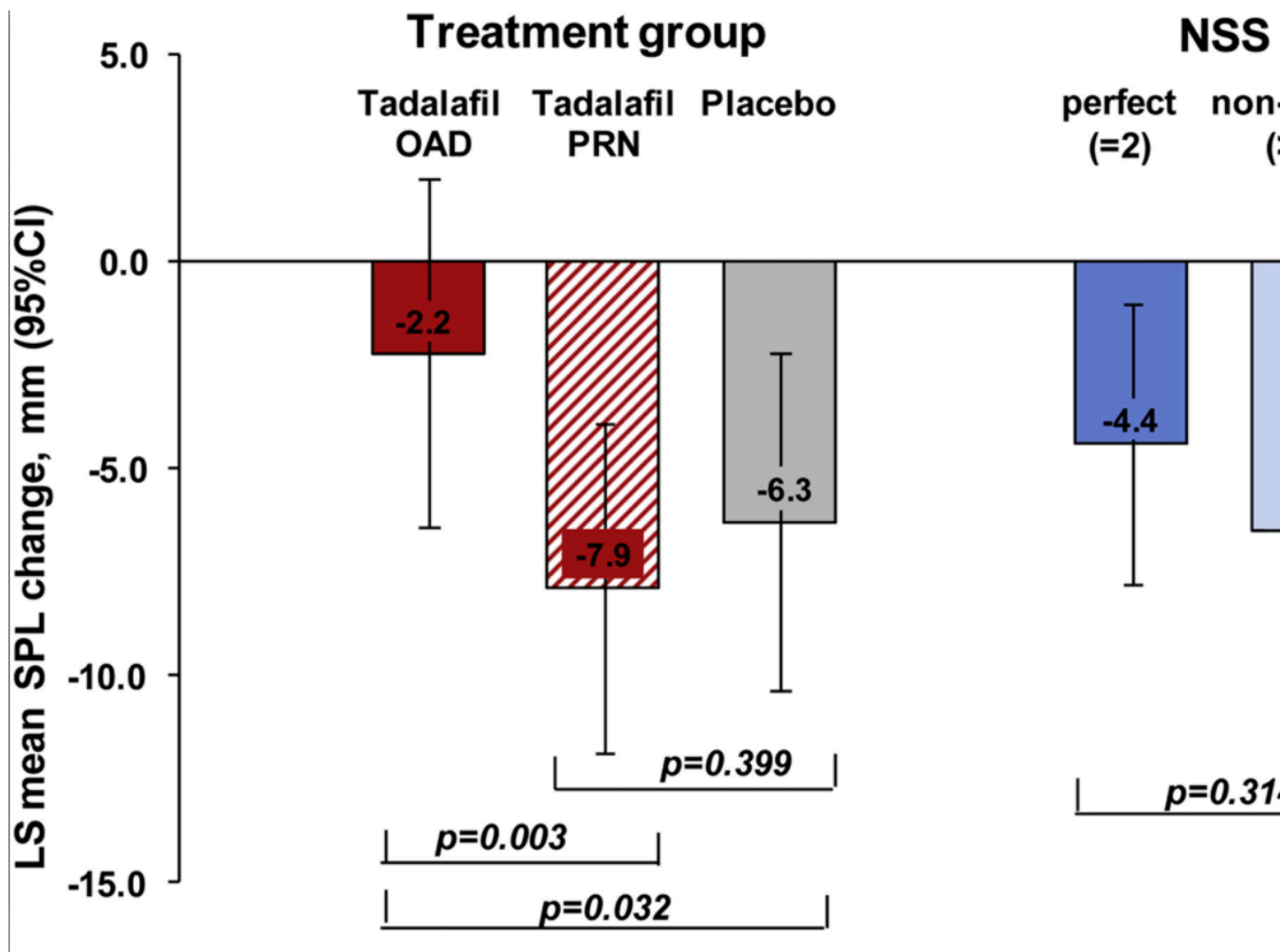




Dysfunction

Effect of Tadalafil Once Daily on Penile Length Loss and Morning Erections in Patients After Bilateral Nerve-sparing Prostatectomy: Results From a Randomized Controlled Trial

Authors: Francesco Montorsi^b, Pierre Costa^c, Nimish Shah^d, Jose Maria Martinez-Jabaloyas^e, ...





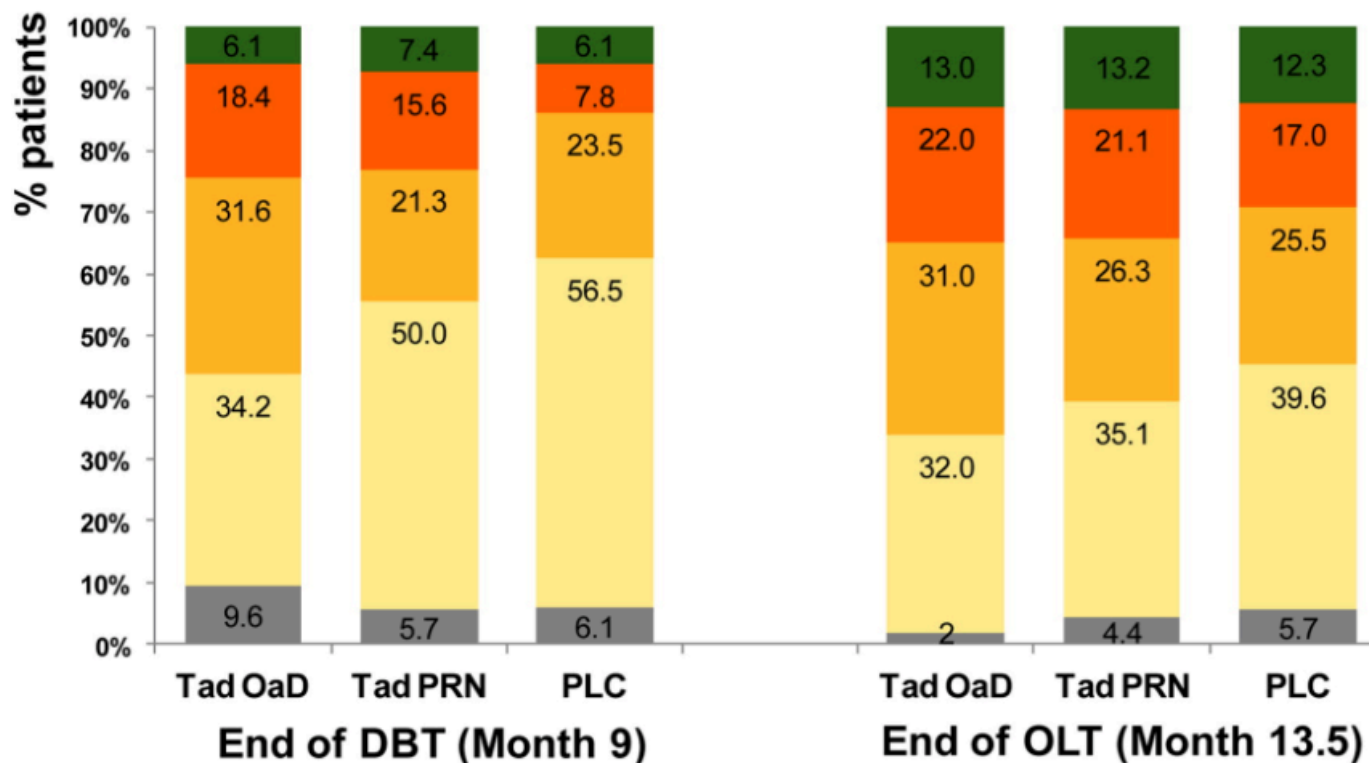
Dysfunction

Effect of Tadalafil Once Daily on Penile Length Loss and Morning Erections in Patients After Bilateral Nerve-sparing Radical Prostatectomy: Results From a Randomized Controlled Trial

Authors: ^a, ^b, ^c, ^d, ^e, ^f, ^g, ^h, ⁱ, ^j, ^k, ^l, ^m, ⁿ, ^o, ^p, ^q, ^r, ^s, ^t, ^u, ^v, ^w, ^x, ^y, ^z, ^{aa}, ^{ab}, ^{ac}, ^{ad}, ^{ae}, ^{af}, ^{ag}, ^{ah}, ^{ai}, ^{aj}, ^{ak}, ^{al}, ^{am}, ^{an}, ^{ao}, ^{ap}, ^{aq}, ^{ar}, ^{as}, ^{at}, ^{au}, ^{av}, ^{aw}, ^{ax}, ^{ay}, ^{az}, ^{ba}, ^{bb}, ^{bc}, ^{bd}, ^{be}, ^{bf}, ^{bg}, ^{bh}, ^{bi}, ^{bj}, ^{bk}, ^{bl}, ^{bm}, ^{bn}, ^{bo}, ^{bp}, ^{bq}, ^{br}, ^{bs}, ^{bt}, ^{bu}, ^{bv}, ^{bw}, ^{bx}, ^{by}, ^{bz}, ^{ca}, ^{cb}, ^{cc}, ^{cd}, ^{ce}, ^{cf}, ^{cg}, ^{ch}, ^{ci}, ^{cj}, ^{ck}, ^{cl}, ^{cm}, ^{cn}, ^{co}, ^{cp}, ^{cq}, ^{cr}, ^{cs}, ^{ct}, ^{cu}, ^{cv}, ^{cw}, ^{cx}, ^{cy}, ^{cz}, ^{da}, ^{db}, ^{dc}, ^{dd}, ^{de}, ^{df}, ^{dg}, ^{dh}, ^{di}, ^{dj}, ^{dk}, ^{dl}, ^{dm}, ^{dn}, ^{do}, ^{dp}, ^{dq}, ^{dr}, ^{ds}, ^{dt}, ^{du}, ^{dv}, ^{dw}, ^{dx}, ^{dy}, ^{dz}, ^{ea}, ^{eb}, ^{ec}, ^{ed}, ^{ee}, ^{ef}, ^{eg}, ^{eh}, ^{ei}, ^{ej}, ^{ek}, ^{el}, ^{em}, ^{en}, ^{eo}, ^{ep}, ^{eq}, ^{er}, ^{es}, ^{et}, ^{eu}, ^{ev}, ^{ew}, ^{ex}, ^{ey}, ^{ez}, ^{fa}, ^{fb}, ^{fc}, ^{fd}, ^{fe}, ^{ff}, ^{fg}, ^{fh}, ^{fi}, ^{fj}, ^{fk}, ^{fl}, ^{fm}, ^{fn}, ^{fo}, ^{fp}, ^{fq}, ^{fr}, ^{fs}, ^{ft}, ^{fu}, ^{fv}, ^{fw}, ^{fx}, ^{fy}, ^{fz}, ^{ga}, ^{gb}, ^{gc}, ^{gd}, ^{ge}, ^{gf}, ^{gg}, ^{gh}, ^{gi}, ^{gj}, ^{gk}, ^{gl}, ^{gm}, ^{gn}, ^{go}, ^{gp}, ^{gq}, ^{gr}, ^{gs}, ^{gt}, ^{gu}, ^{gv}, ^{gw}, ^{gx}, ^{gy}, ^{gz}, ^{ha}, ^{hb}, ^{hc}, ^{hd}, ^{he}, ^{hf}, ^{hg}, ^{hh}, ^{hi}, ^{hj}, ^{hk}, ^{hl}, ^{hm}, ^{hn}, ^{ho}, ^{hp}, ^{hq}, ^{hr}, ^{hs}, ^{ht}, ^{hu}, ^{hv}, ^{hw}, ^{hx}, ^{hy}, ^{hz}, ^{ia}, ^{ib}, ^{ic}, ^{id}, ^{ie}, ^{if}, ^{ig}, ^{ih}, ⁱⁱ, ^{ij}, ^{ik}, ^{il}, ^{im}, ⁱⁿ, ^{io}, ^{ip}, ^{iq}, ^{ir}, ^{is}, ^{it}, ^{iu}, ^{iv}, ^{iw}, ^{ix}, ^{iy}, ^{iz}, ^{ja}, ^{jb}, ^{jc}, ^{jd}, ^{je}, ^{jf}, ^{jj}, ^{jk}, ^{jl}, ^{jm}, ^{jn}, ^{jo}, ^{jp}, ^{jq}, ^{jr}, ^{js}, ^{jt}, ^{ju}, ^{jv}, ^{jw}, ^{jx}, ^{ky}, ^{kz}, ^{la}, ^{lb}, ^{lc}, ^{ld}, ^{le}, ^{lf}, ^{lg}, ^{lh}, ^{li}, ^{lj}, ^{lk}, ^{ll}, ^{lm}, ^{ln}, ^{lo}, ^{lp}, ^{lq}, ^{lr}, ^{ls}, ^{lt}, ^{lu}, ^{lv}, ^{lw}, ^{lx}, ^{ly}, ^{lz}, ^{ma}, ^{mb}, ^{mc}, ^{md}, ^{me}, ^{mf}, ^{mg}, ^{mh}, ^{mi}, ^{mj}, ^{mk}, ^{ml}, ^{mn}, ^{mo}, ^{mp}, ^{mq}, ^{mr}, ^{ms}, ^{mt}, ^{mu}, ^{mv}, ^{mw}, ^{mx}, ^{my}, ^{mz}, ^{na}, ^{nb}, ^{nc}, nd, ^{ne}, ^{nf}, ^{ng}, ^{nh}, ⁿⁱ, ^{nj}, ^{nk}, ^{nl}, ^{nm}, ⁿⁿ, ^{no}, ^{np}, ^{nq}, ^{nr}, ^{ns}, ^{nt}, ^{nu}, ^{nv}, ^{nw}, ^{nx}, ^{ny}, ^{nz}, ^{oa}, ^{ob}, ^{oc}, ^{od}, ^{oe}, ^{of}, ^{og}, ^{oh}, ^{oi}, ^{oj}, ^{ok}, ^{ol}, ^{om}, ^{on}, ^{oo}, ^{op}, ^{oq}, ^{or}, ^{os}, ^{ot}, ^{ou}, ^{ov}, ^{ow}, ^{ox}, ^{oy}, ^{oz}, ^{pa}, ^{pb}, ^{pc}, ^{pd}, ^{pe}, ^{pf}, ^{pg}, ^{ph}, ^{pi}, ^{pj}, ^{pk}, ^{pl}, ^{pm}, ^{pn}, ^{po}, ^{pp}, ^{pq}, ^{pr}, ^{ps}, ^{pt}, ^{pu}, ^{pv}, ^{pw}, ^{px}, ^{py}, ^{pz}, ^{qa}, ^{qb}, ^{qc}, ^{qd}, ^{qe}, ^{qf}, ^{qg}, ^{qh}, ^{qi}, ^{qj}, ^{qk}, ^{ql}, ^{qm}, ^{qn}, ^{qo}, ^{qp}, ^{qq}, ^{qr}, ^{qs}, ^{qt}, ^{qu}, ^{qv}, ^{qw}, ^{qx}, ^{qy}, ^{qz}, ^{ra}, ^{rb}, ^{rc}, rd, ^{re}, ^{rf}, ^{rg}, ^{rh}, ^{ri}, ^{rj}, ^{rk}, ^{rl}, ^{rm}, ^{rn}, ^{ro}, ^{rp}, ^{rq}, ^{rr}, ^{rs}, ^{rt}, ^{ru}, ^{rv}, ^{rw}, ^{rx}, ^{ry}, ^{rz}, ^{sa}, ^{sb}, ^{sc}, ^{sd}, ^{se}, ^{sf}, ^{sg}, ^{sh}, ^{si}, ^{sj}, ^{sk}, ^{sl}, sm, ^{sn}, ^{so}, ^{sp}, ^{sq}, ^{sr}, ^{ss}, st, ^{su}, ^{sv}, ^{sw}, ^{sx}, ^{sy}, ^{sz}, ^{ta}, ^{tb}, ^{tc}, ^{td}, ^{te}, ^{tf}, ^{tg}, th, ^{ti}, ^{tj}, ^{tk}, ^{tl}, tm, ^{tn}, ^{to}, ^{tp}, ^{tq}, ^{tr}, ^{ts}, ^{tt}, ^{tu}, ^{tv}, ^{tw}, ^{tx}, ^{ty}, ^{tz}, ^{ua}, ^{ub}, ^{uc}, ^{ud}, ^{ue}, ^{uf}, ^{ug}, ^{uh}, ^{ui}, ^{uj}, ^{uk}, ^{ul}, ^{um}, ^{un}, ^{uo}, ^{up}, ^{uq}, ^{ur}, ^{us}, ^{ut}, ^{uu}, ^{uv}, ^{uw}, ^{ux}, ^{uy}, ^{uz}, ^{va}, ^{vb}, ^{vc}, ^{vd}, ^{ve}, ^{vf}, ^{vg}, ^{vh}, ^{vi}, ^{vj}, ^{vk}, ^{vl}, ^{vm}, ^{vn}, ^{vo}, ^{vp}, ^{vq}, ^{vr}, ^{vs}, ^{vt}, ^{vu}, ^{vv}, ^{vw}, ^{vx}, ^{vy}, ^{vz}, ^{wa}, ^{wb}, ^{wc}, ^{wd}, ^{we}, ^{wf}, ^{wg}, ^{wh}, ^{wi}, ^{wj}, ^{wk}, ^{wl}, ^{wm}, ^{wn}, ^{wo}, ^{wp}, ^{wq}, ^{wr}, ^{ws}, ^{wt}, ^{wu}, ^{wv}, ^{ww}, ^{wx}, ^{wy}, ^{wz}, ^{xa}, ^{xb}, ^{xc}, ^{xd}, ^{xe}, ^{xf}, ^{xg}, ^{xh}, ^{xi}, ^{xj}, ^{xk}, ^{xl}, ^{xm}, ^{xn}, ^{xo}, ^{xp}, ^{xq}, ^{xr}, ^{xs}, ^{xt}, ^{xu}, ^{xv}, ^{xw}, ^{xx}, ^{xy}, ^{xz}, ^{ya}, ^{yb}, ^{yc}, ^{yd}, ^{ye}, ^{yf}, ^{yg}, ^{yh}, ^{yi}, ^{yj}, ^{yk}, ^{yl}, ^{ym}, ^{yn}, ^{yo}, ^{yp}, ^{yq}, ^{yr}, ^{ys}, ^{yt}, ^{yu}, ^{yv}, ^{yw}, ^{yx}, ^{yy}, ^{yz}, ^{za}, ^{zb}, ^{zc}, ^{zd}, ^{ze}, ^{zf}, ^{zg}, ^{zh}, ^{zi}, ^{zj}, ^{zk}, ^{zl}, ^{zm}, ^{zn}, ^{zo}, ^{zp}, ^{zq}, ^{zr}, ^{zs}, ^{zt}, ^{zu}, ^{zv}, ^{zw}, ^{zx}, ^{zy}, ^{zz}

Overall p=0.045

Overall p=0.873



"Do you ever wake up with an erection?" Response:

- yes, regularly
- less frequently than before
- only occasionally
- never
- missing

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

Ερώτηση 7

Να χορηγώ PDE5i στην
Peyronie;



Peyronie's disease: grafting procedures are not friendly to erectile function

3.1% reported preoperative ED (vascular disease in 76.8%) (Kadioglu et al. 2011).

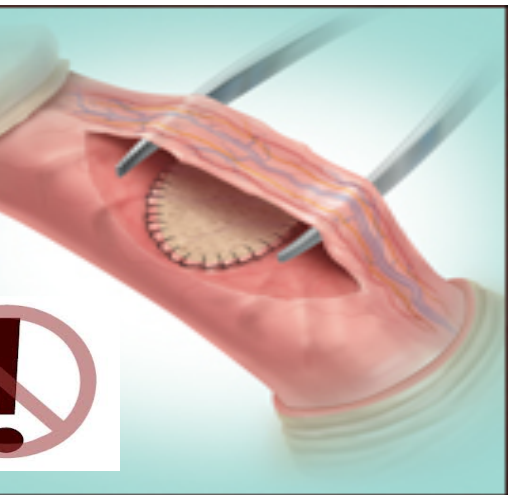
The risk of new ED with plication/tunica excision techniques is 0–13%, compared to 5–53% for grafting techniques

(Hatzimouratidis et al. 2012)

5% of patients were dissatisfied with the outcome of graft surgery at 5-years (Chung et al. 2011)

Diminished sensation is reported in 4–21% for plication / tunica excision, with limited data for grafting procedures (Levine 2013).

Patients should be aware of grafting major drawbacks before surgery.

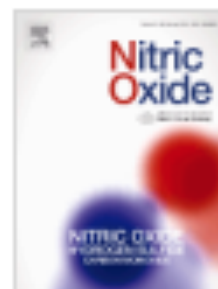


Based on the above, all proposed guidelines recommend tunica plication procedures for curvature $<60^\circ$ and absence of extreme deformities (hourglass, hinge). (Hatzimouratidis, Eardley et al. 2012; Levine and Burnett 2013).



Nitric Oxide

Volume 9, Issue 4, December 2003, Pages 229–244

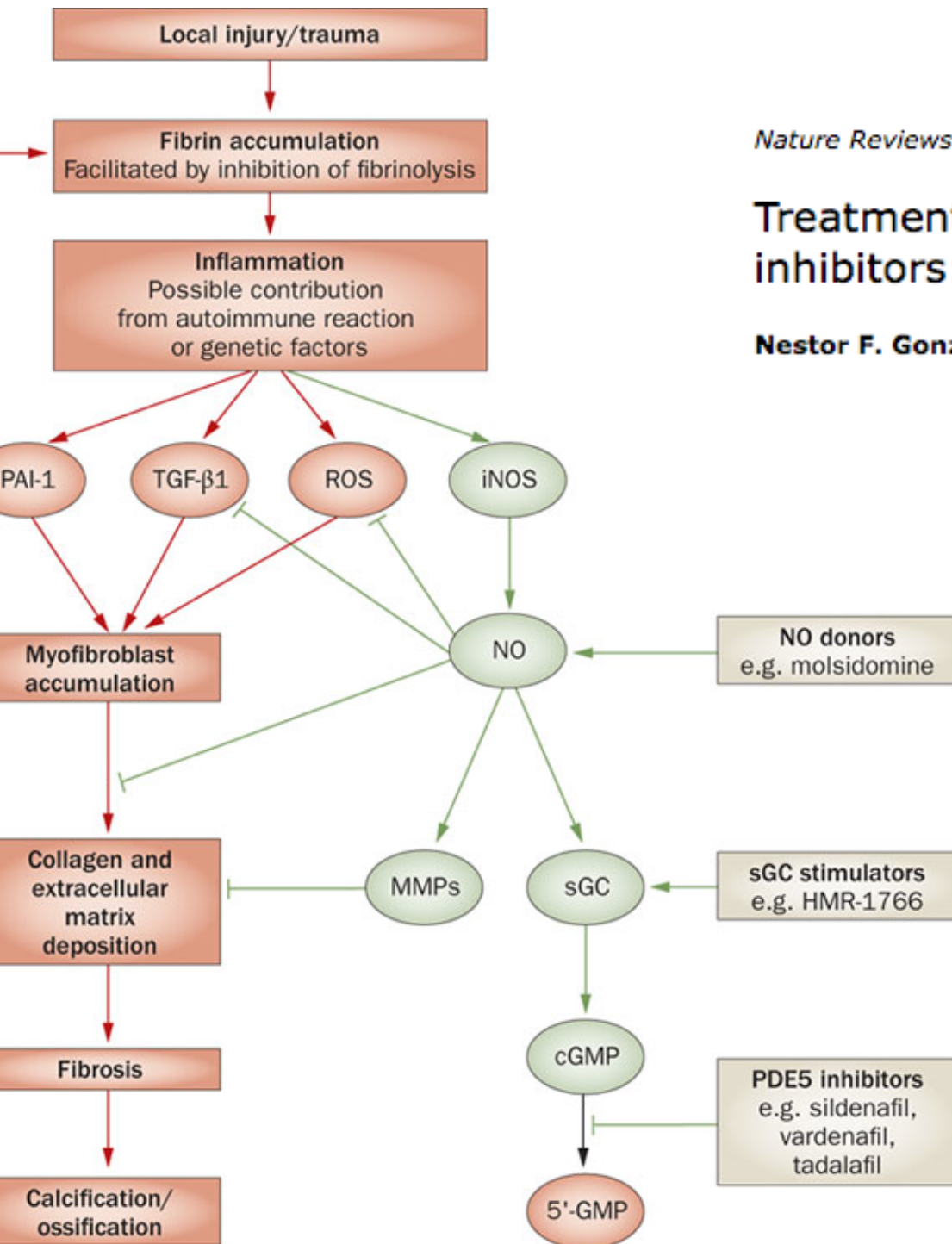


L-Arginine and phosphodiesterase (PDE) inhibitors counteract fibrosis in the Peyronie's fibrotic plaque and related fibroblast cultures

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Treatment of Peyronie's disease with PDE5 inhibitors: an antifibrotic strategy

Nestor F. Gonzalez-Cadavid & Jacob Rajfer



Prevention of Peyronie's disease with PDE5 inhibitors: an antifibrotic strategy

J. Gonzalez-Cadavid & Jacob Rajfer

Peyronie's disease (PD) is a localized fibrotic condition of the tunica albuginea that is associated with risk factors for corpora cavernosa fibrosis (such as advanced age and diabetes) and Dupuytren contracture, another localized fibrotic process.

Most of the current pharmacological treatments for PD are not based on antifibrotic approaches that have shown promising results in animal models and clinical efficacy in other fibrotic conditions, which may explain why they are generally unsuccessful.

Evidence gathered in human specimens and animal models of PD have elucidated aspects of its etiology and histopathology, showing that overexpression of transforming growth factor β 1, plasminogen activator inhibitor 1, reactive oxygen species and other profibrotic factors, which are, in most cases, assumed to be induced by trauma to the tunica albuginea, leads to myofibroblast accumulation and excessive deposition of collagen.

At the same time, a steady overexpression of inducible nitric oxide synthase, leading to increased nitric oxide and cGMP levels, seems to act as an endogenous antifibrotic mechanism.

This process has also been reported in corporal and cardiovascular fibrosis, and has led to the demonstration that long-term continuous administration of phosphodiesterase type 5 inhibitors counteracts the development of a PD-like fibrotic plaque in a rat model, and later extended to the prevention of corporal fibrosis in animal models of erectile dysfunction.

ΟΙ ΚΟΚΚΙΝΕΣ ΕΡΩΤΗΣΕΙΣ

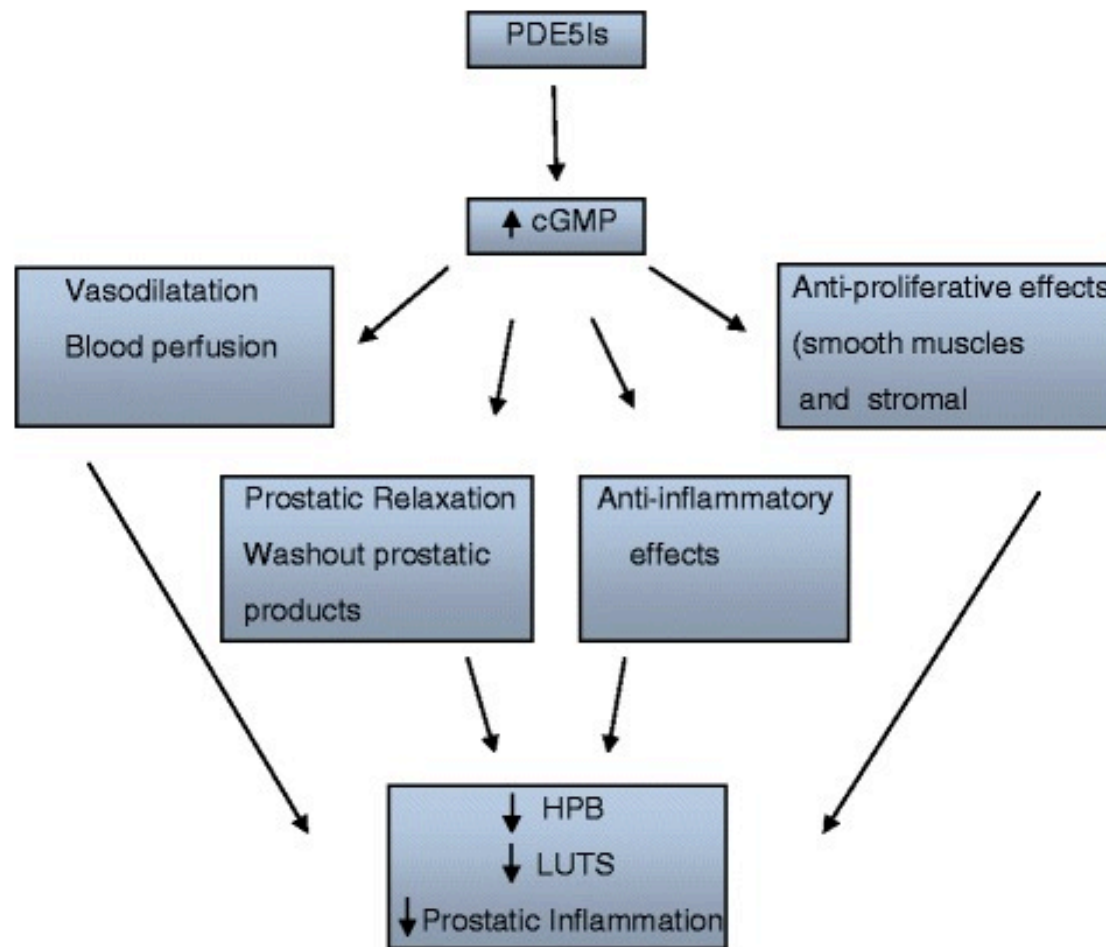
Ερώτηση 8

Να χορηγώ PDE5i στην
χρόνια προστατίτιδα;

koto CA, Gomes FO dos S. The role of phosphodiesterase-5 inhibitors in prostatic inflammation: a review. *Journal of Inflammation (London, England)*. 2015;12:54.

1. PDE5Is are therapeutical tools used for several urological and non-urological disorders, and experimental evidence suggest that their chronic use does not induce cellular and molecular prostatic alterations.
2. The mechanisms involved in improvements observed in BPH/LUTS possibly include relaxation of the smooth muscles of the bladder and prostate by NO/cGMPc signaling or via improving RhoA/Rho-kinase (ROCK), and by reduction of the hyperactivity of the autonomic nervous system.
3. PDE5Is can also direct and indirectly down-regulate prostatic inflammation/BPH/LUTS by inducing high levels of cGMP.
4. In conclusion, since inflammation is a major factor in benign prostatic hyperplasia (BPH) progression, PDE5Is could also restore prostatic function, as they act as potent anti-inflammatory drugs.

Fig. 1



Schematic diagram showing the hypothetical mechanism of Phosphodiesterase 5 Inhibitors (PDE5Is) on prostatic inflammation. PDE5Is directly and indirectly down-regulate prostatic inflammation/BPH/LUTS by inducing high levels of cGMP

5-phosphodiesterase type 5 inhibitor tadalafil: a new treatment option for chronic abacterial prostatitis/prostatodynia?

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The University of North Carolina, Chapel Hill, NC, USA*

In addition to the symptom of pelvic pain, men with chronic abacterial prostatitis/prostatodynia also frequently complain of associated LUTS and ejaculatory discomfort. Consequently treatment with tadalafil at a dose of 5 mg/day for a period of time would seem logical. It could be surmised that many of its beneficial effects might stem from an improvement of blood flow to pelvic organs as a consequence of its anti-inflammatory and vasodilatory activity, as well as a relaxant effect on smooth muscle, as has been previously suggested in the case of LUTS by Andersson and others [6–8]

Daily phosphodiesterase type 5 inhibitor therapy: a new treatment option for prostatitis/prostatodynia?

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Clearly the hypothesis that daily treatment with a PDE5 inhibitor might be beneficial in men with the prevalent condition of chronic abacterial prostatitis/prostatodynia will need to be formally tested in the context of a randomised controlled trial. If the results of such a study were to prove positive, the quality of life of very many sufferers of this disorder might be significantly improved. One might also speculate that it could provide a concomitant benefit to the partners of these often very unhappy men.

Α ΦΑΡΜΑΚΑ ΤΗΣ ΣΤΥΣΗΣ

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80%
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- Αρνητική στάση στα φάρμακα



Η ΣΥΝΔΥΑΣΤΙΚΗ ΘΕΡΑΠΕΙΑ

(ΨΥΧΟΣΕΞΟΥΑΛΙΚΗ
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ΠΡΟΣΦΕΡΕΙ:



ΠΗΓΗ: Melnik T: J. Sex. Medicine; 5(1), (2008)

ΠΕΪΚΕΣ ΠΡΟΘΕΣΕΙΣ

Αποτελούν την πιο παλιά μέθοδο αντιμετώπισης

Έχει ένδειξη σε κάθε άντρα που έχει δοκιμάσει
ΑΝΕΠΙΤΥΧΩΣ τις άλλες θεραπείες.

Υπάρχουν **2** τύποι προθέσεων:

ΟΙ **ΣΤΑΘΕΡΕΣ**] →
ΚΑΙ ΟΙ **ΔΙΟΓΚΟΥΜΕΝΕΣ**

Οι σταθερές αποτελούνται από 2 κυλίνδρους από ειδικό βιο-υλικό που τοποθετούνται μέσα στα 2 σπραγγώδη σώματα.



Στις διογκούμενες, οι κύλινδροι είναι συνδεδεμένοι με σύστημα αντλίας που δίνει τη δυνατότητα πλήρωσης των κυλίνδρων με φυσιολογικό ορό. Δίνουν άριστο αισθητικό αποτέλεσμα, αλλά έχουν υψηλό κόστος.

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