



Service d'Urologie



ASSISTANCE
PUBLIQUE



HÔPITAUX
DE PARIS

urologie-mondor.fr

Tadalafil pour la Santé de l'Homme

Pr Alexandre de la Taille

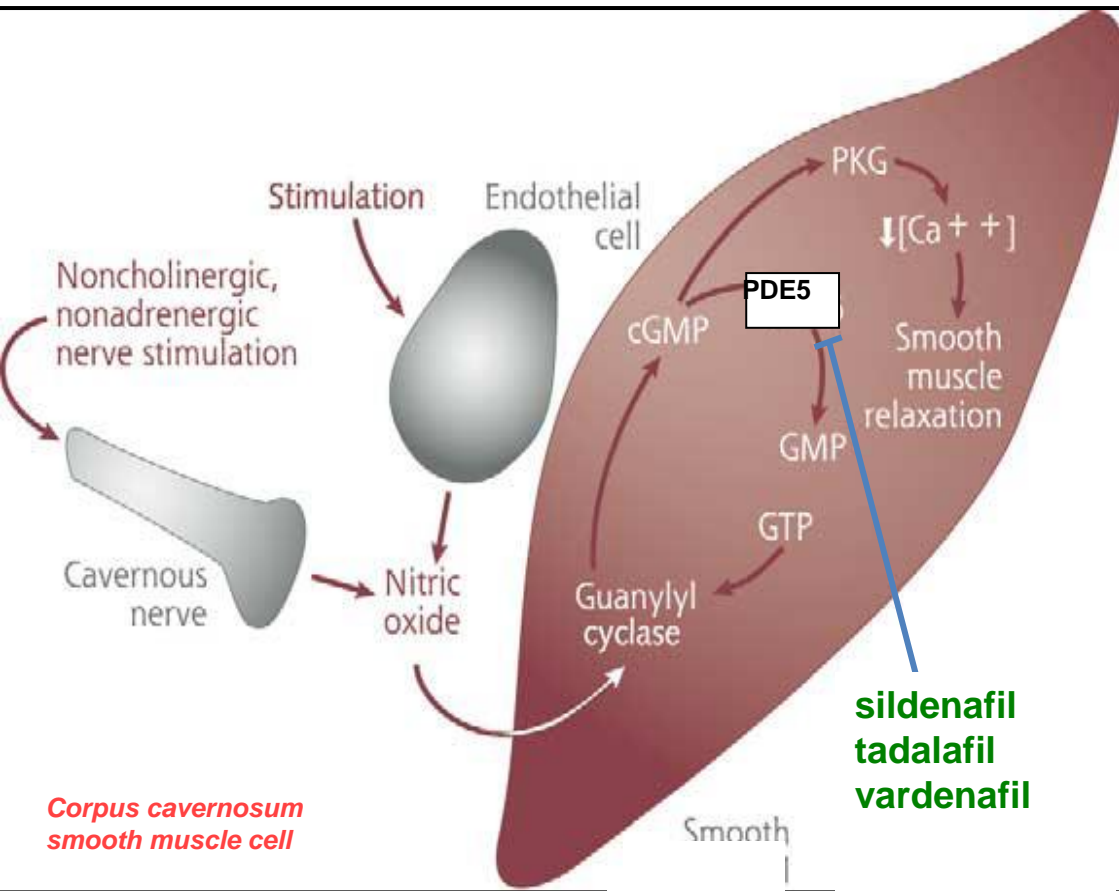


IPDE5

- 1992 : Lancement des essais des IPDE5 dans l'hypertension artérielle pulmonaire / « effet secondaire » sur la sexualité rapporté
- 1998 :
 - Le film Titanic sort sur les écrans
 - L'équipe de France de foot est championne du monde
 - Lancement du Viagra !
- 2025 :

Intérêt reconnu des IPDE5 pour : troubles de l'érection, symptômes urinaires du bas appareil liés à l'HBP, syndrome d'Eisenmenger, syndrome de Raynaud, Cystite intersticielle, douleur pelvienne et vésicale, HTAP

Tadalafil dans les troubles de l'érection



Mécanisme d'action des iPDE5 ⁽¹⁾

Stimulation sexuelle

Les iPDE5 empêchent la dégradation du GMPc en se fixant sur la PDE5. L'érection est maintenue.

Arteres contractées : Le sang n'afflue plus.

PDE5 dégrade le GMPc

ERECTION

Retour à la flaccidité

GMPc

Arteres dilatées : Le sang afflue.

Libération de GMPc

Inhibition des PDE ⁽²⁾		
PDE	Localisation	Effets des iPDE5
PDE 5	Tissu des corps caverneux Arteres péniennes	Érection
PDE 6	Rétine	Troubles visuels
PDE 1	Cerveau, cellules myocardiques et cellules musculaires lisses vasculaires	Vasodilatation Flush Tachycardie
PDE 11	Muscles squelettiques	Douleurs dorsales Myalgies

(1) Adapté de L. Fazio, G. Brock. Erectile dysfunction: management update. CMAJ 2004;170(9):1429-37.
 (2) E Bischoff. Potency, selectivity, and consequences of nonselectivity of PDE inhibition. Int J Impot Res (2004) 16, S11-S14.

Efficacité démontrée pour l'érection

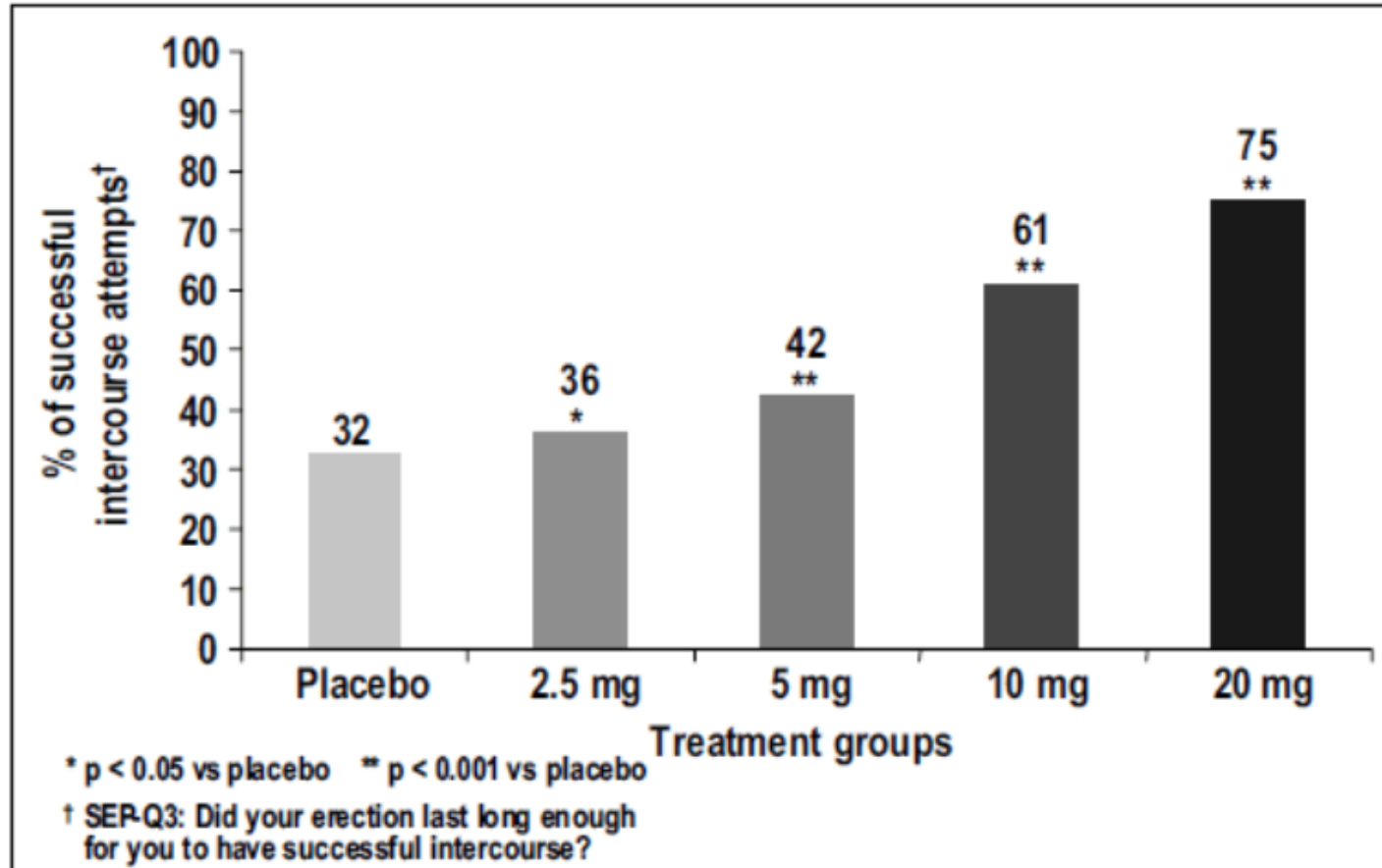


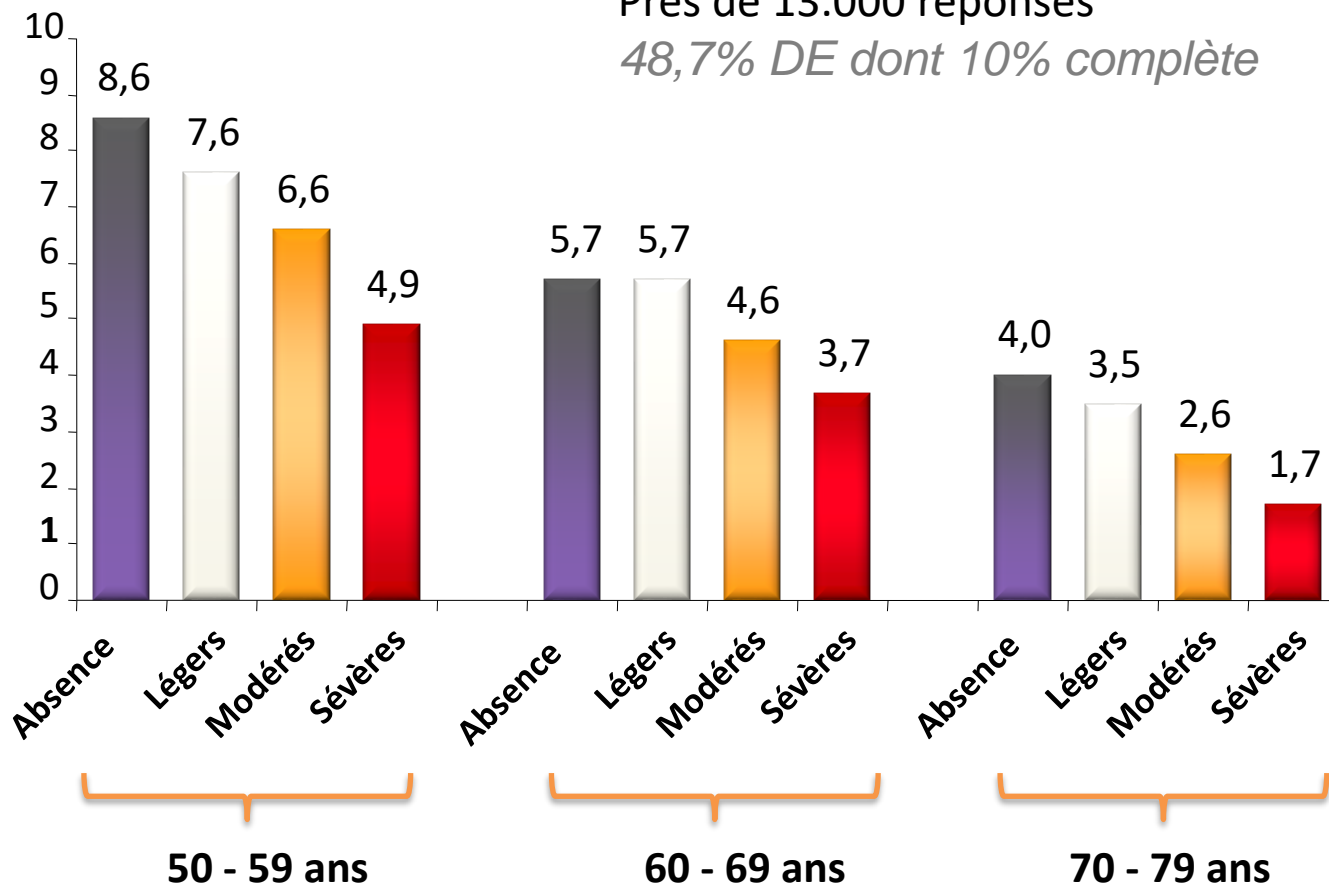
Figure 1) Effect of tadalafil on rate of successful intercourse (Sexual Encounter Profile [SEP]-Q3) (integrated analysis). Reproduced with permission from reference 8

Brock GB, McMahon CG, Chen KK, et al. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: Results of integrated analyses. J Urol 2002;168:1332-6.

SBAU et dysfonction sexuelle

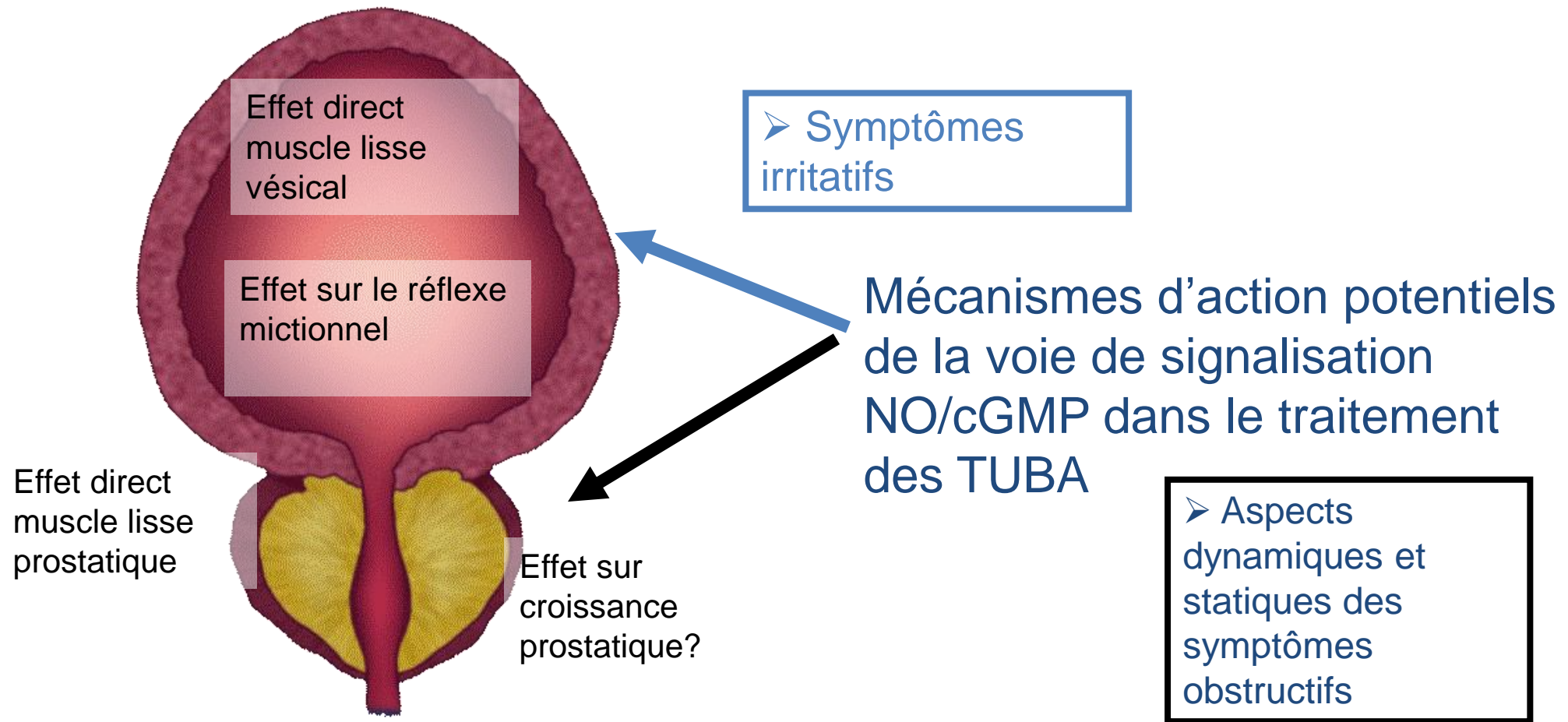
- MSAM-7
 - fort lien entre les troubles sexuels, âge et SBAU
- Simple croisement d'incidences respectives élevées chez l'homme âgé?
- Mécanismes physiopathologiques communs?
 - voie NO-cGMP
 - la voie Rho-kinase
 - système nerveux autonome
 - athérosclérose pelvienne
- Impact des traitements de l'HBP sur la sexualité

Fréquence moyenne de l'activité sexuelle
moyenne par mois



Tadalafil dans les symptômes de l'HBP

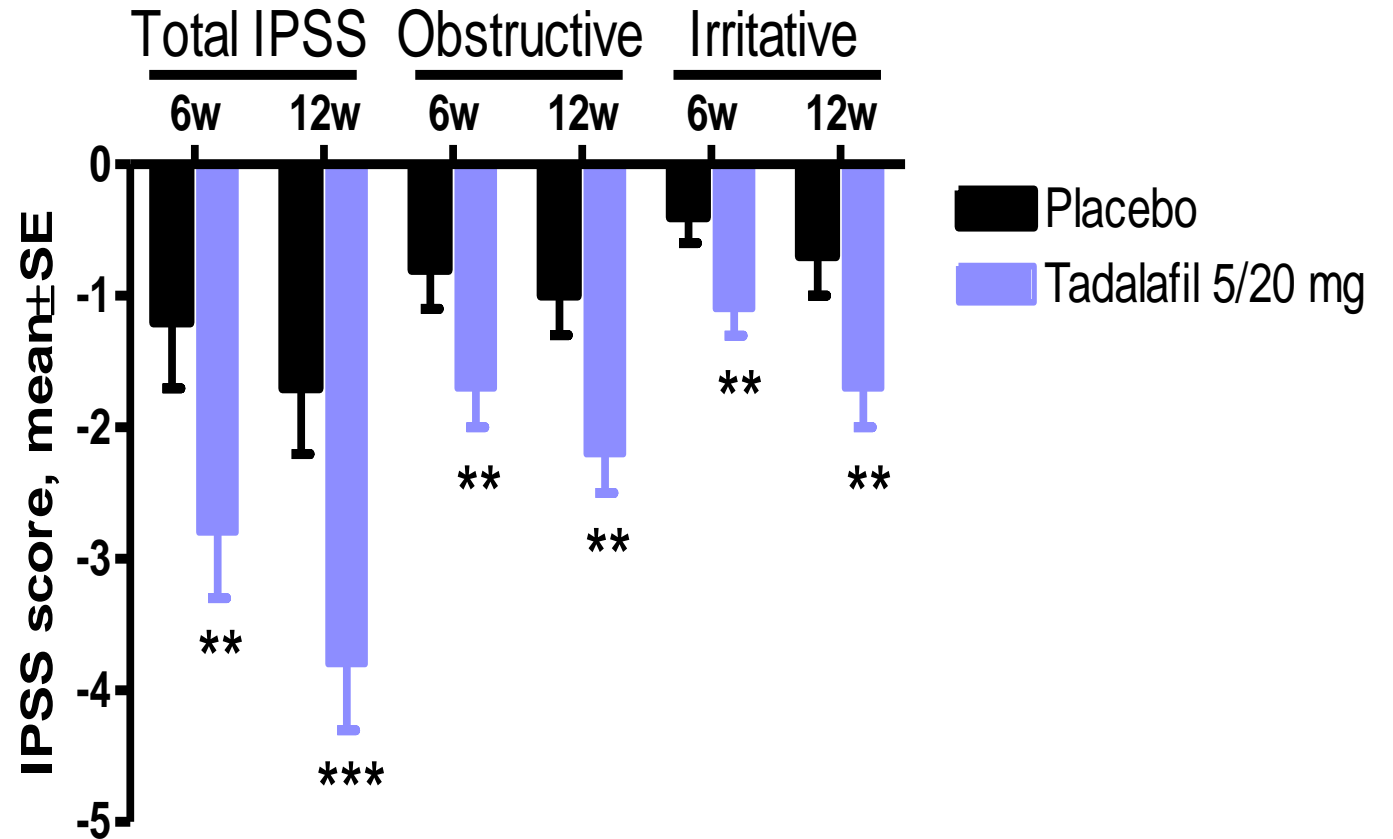
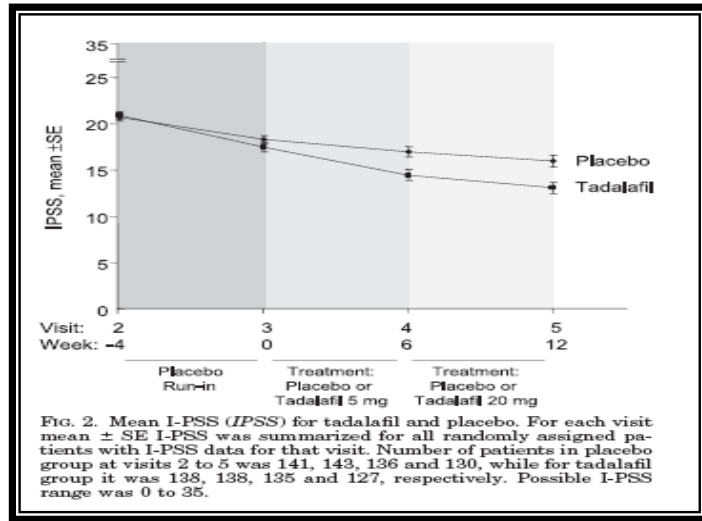
- Voie de signalisation NO/cGMP dans bas appareil urinaire : démonstrations anatomiques et pharmacologiques
- Modèles expérimentaux TUBA : rôle de NO/cGMP dans la réduction de l'hyperactivité vésicale



Etudes cliniques publiées de l'efficacité de composés ciblant la voie NO/cGMP pour le traitement de l'HBP et des TUBA

Author(s)	Nb of patients (n) (treatment interval)	Primary endpoints	Drug(s) tested
Klotz et al., Int Urol Nephrol 1999	n=32 (12 weeks)	Changes in IPSS, Qmax, PVR	Isosorbide dinitrate (60-120 mg/day)
Sairam et al., BJU Int 2002	n=112 (12 weeks)	Changes in IPSS, LUTS-specific QoL, IIEF	Sildenafil citrate
Mulhall et al., J Sex Med 2006	n=32 (12 weeks)	Changes in IPSS, QoL, IIEF	Sildenafil citrate, 100 mg
Ying et al., Zhonghua Nan Ke Xue 2004	n=32 (24 weeks)	Changes in IPSS, IIEF	Sildenafil citrate
Kaplan et al., Eur Urol 2007	n=62 (12 weeks)	Changes in IPSS, Qmax, PVR, IIEF	Alfuzosin (10 mg/day) or sildenafil citrate (25 mg/day) or both
Mc Vary et al., J Urol. 2007*	n=366 (12 weeks)	Changes in IPSS, QoL, BPH II, Qmax	Sildenafil citrate, 100 mg
McVary et al., J Urol 2007*	n=281 (12 weeks)	Changes in IPSS, QOL, BPH II, GAQ, Qmax	Tadalafil 5 and 20 mg
Stief et al., Eur Urol 2008*	n=222 (8 weeks)	Changes in IPSS, UROLIFE QoL	Vardenafil, 10 mg bid
Roehrborn et al., J Urol 2008*	n=1058 (4, 8, 12 weeks)	Changes in IPSS, IPSS-QoL, BPH II, Qmax, IIEF, GAQ, PVR	Tadalafil 2.5, 5, 10 or 20 mg
Gacci et al., J Urol 2007*	n=25 SCI patients (acute+oral oxybutinin)	Changes in MP during voiding, bladder capacity and detrusor overactivity volume	Vardenafil 20 mg

Tadalafil quotidien 5 puis 20 mg (281 pts)

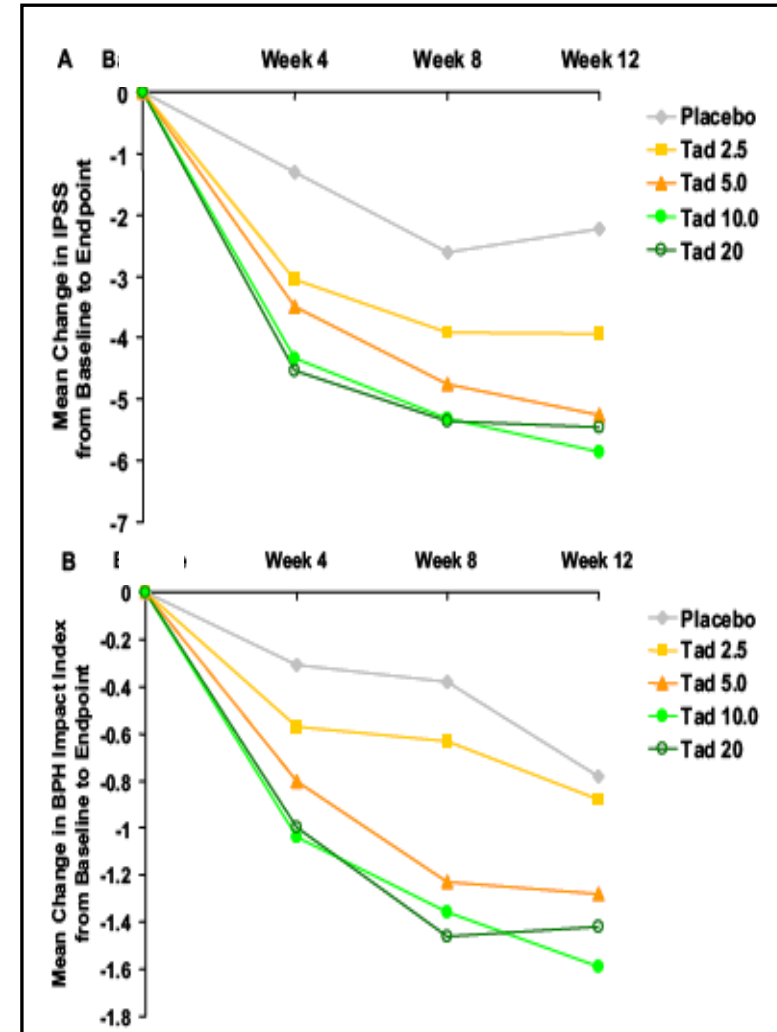
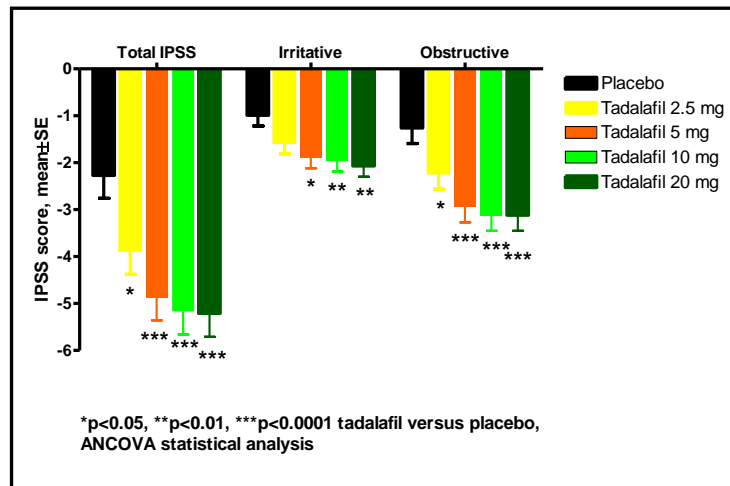
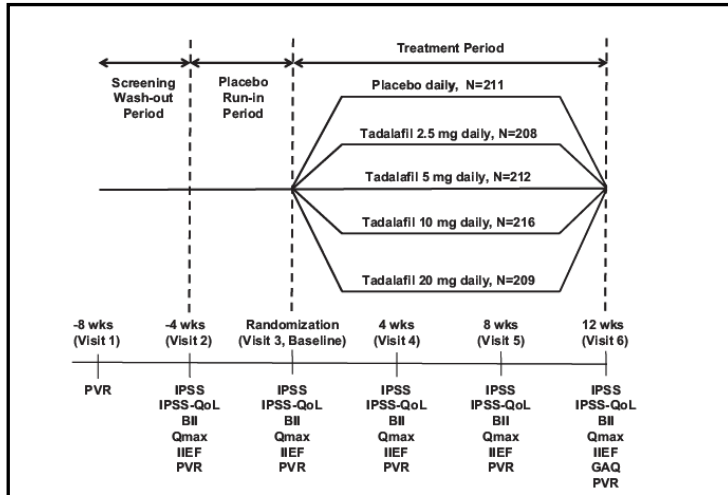


a 4-week, single-blind, placebo run-in
 281 men randomly assigned to
 5 mg tadalafil for 6 weeks,
 followed by double-blind dose
 escalation to 20 mg for 6 weeks versus
 placebo

TABLE 3. Uroflowmetry parameters Q_{max} , Q_{ave} and V_{comp} , and PVR

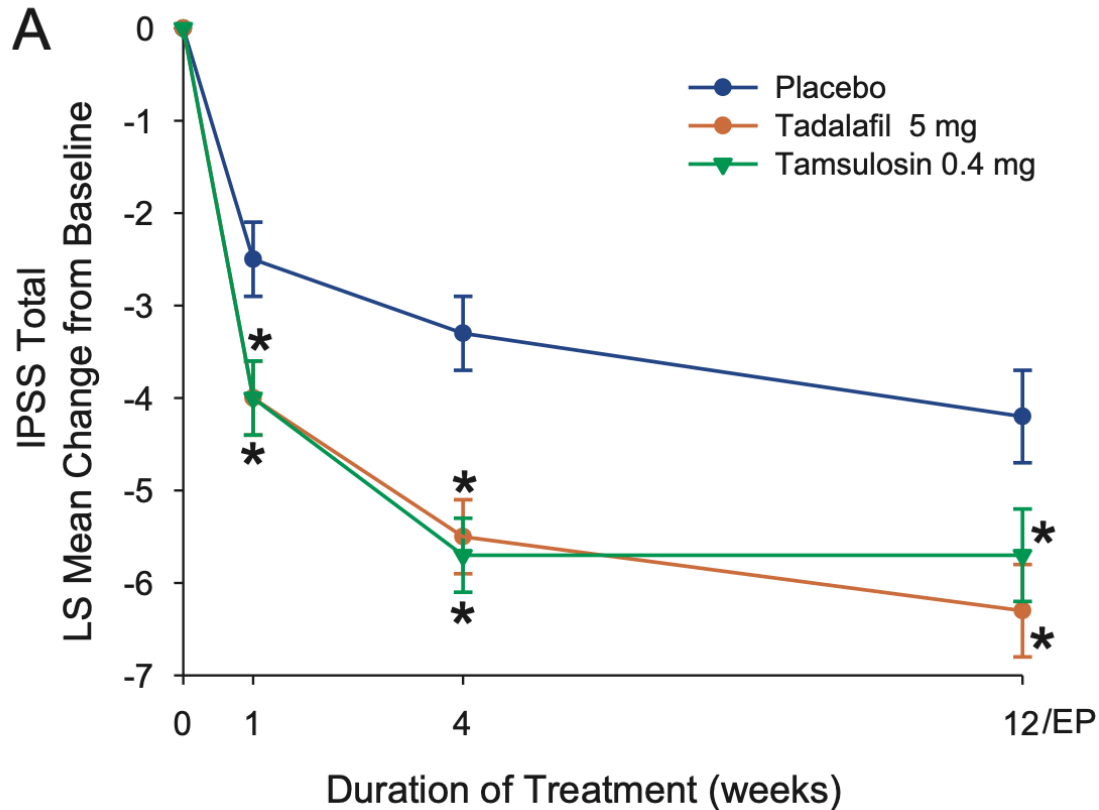
	Mean \pm SE Placebo, 6 Wks	Mean \pm SE 5 mg Tadalafil, 6 Wks	p Value (ANCOVA 1-sided)	Mean \pm SE Placebo, 12 Wks	Mean \pm SE 5/20 mg Tadalafil, 12 Wks	p Value (ANCOVA 1-sided)
Q_{max} (ml/sec):*,†						
Visit 3 (baseline)	11.2	11.7		11.1	11.8	
End point	11.8	12.2		12.1	12.3	
Change visit 3–end point (LS)	1.0 \pm 0.6	1.1 \pm 0.6	0.46	0.9 \pm 0.5	0.5 \pm 0.5	0.72
Change visit 2–end point (LS)	2.2 \pm 0.4	2.2 \pm 0.5	0.49	2.3 \pm 0.5	1.7 \pm 0.5	0.81

Tadalafil (2,5 - 5- 10 - 20 mg) (1058 pts)

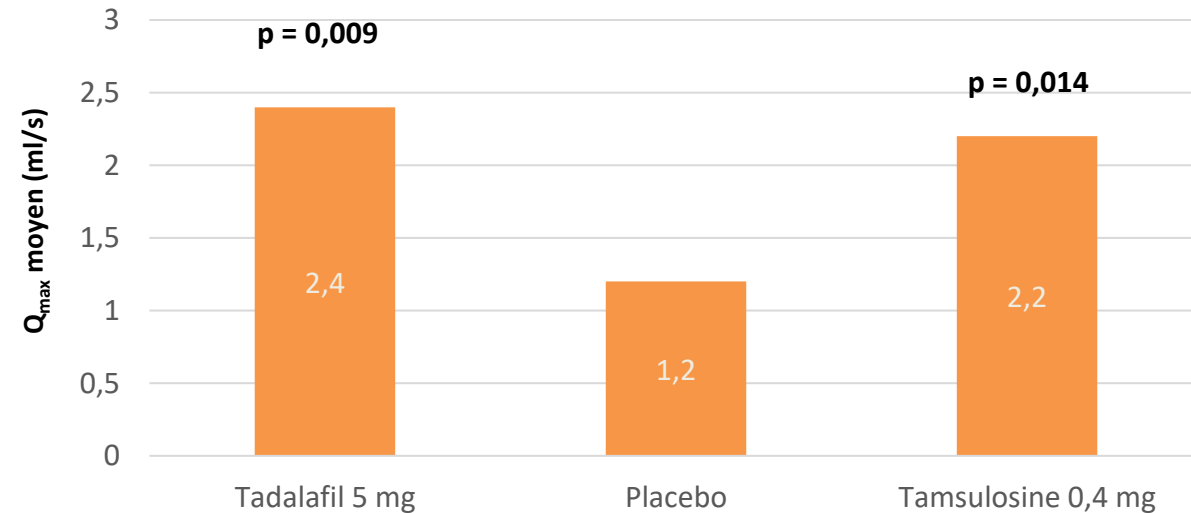


Improvements of IPSS and BPH-II scores are dose-dependent, statistically significant at 4, 8 and 12 weeks, and clinically meaningful according to the AUA guideline of a 3-point improvement in I-PSS from baseline

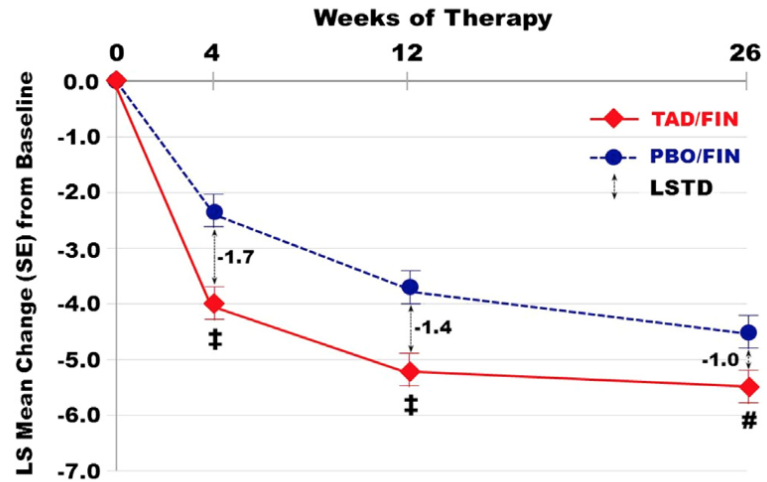
Tadalafil versus Tamsulosine



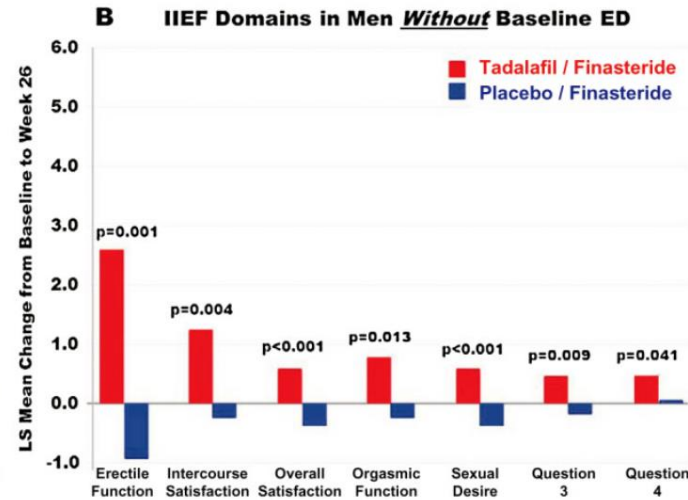
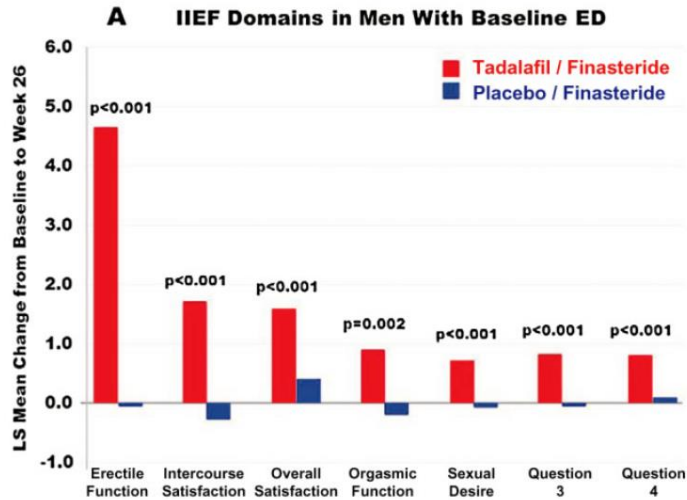
IPSS improved by 6.3 points
Qmax improved by 2.4 mL/s



Finasteride + Tadalafil



Sexual side effects perfectly balanced by IPDE5 association



Tadalafil + Tamsulosine

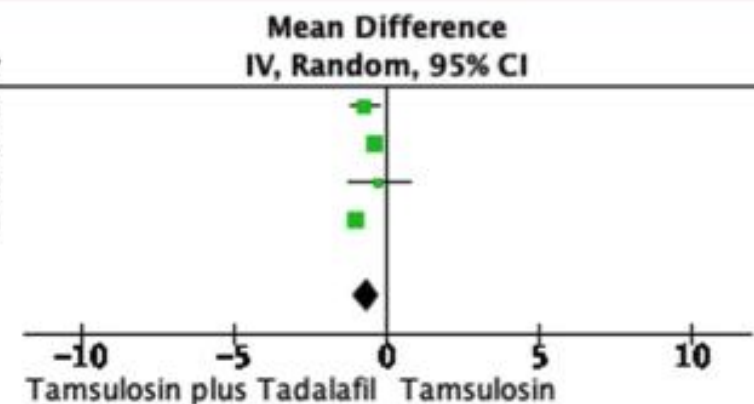
Rui Zhou^{1*}, Xuanyan Che^{2*}, Zhongbao Zhou², and Yue Ma¹

A. QoL

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95% CI	Year
	Mean	SD	Total	Mean	SD	Total			
Bechara, A. 2008	-2.5	0.69	15	-1.8	0.72	15	23.4%	-0.70 [-1.20, -0.20]	2008
Singh, D. V. 2014	-4.5	0.368	44	-4.11	0.509	44	32.8%	-0.39 [-0.58, -0.20]	2014
Negoro, H. 2019	-0.76	1.2	13	-0.52	1.4	13	11.8%	-0.24 [-1.24, 0.76]	2019
Nagasubramanian, S. 2020	-2.15	0.65	69	-1.13	0.7	71	31.9%	-1.02 [-1.24, -0.80]	2020
Total (95% CI)			141			143	100.0%	-0.65 [-1.07, -0.22]	

Heterogeneity: $\tau^2 = 0.13$; $\chi^2 = 18.72$, $df = 3$ ($P = 0.0003$); $I^2 = 84\%$

Test for overall effect: $Z = 2.98$ ($P = 0.003$)

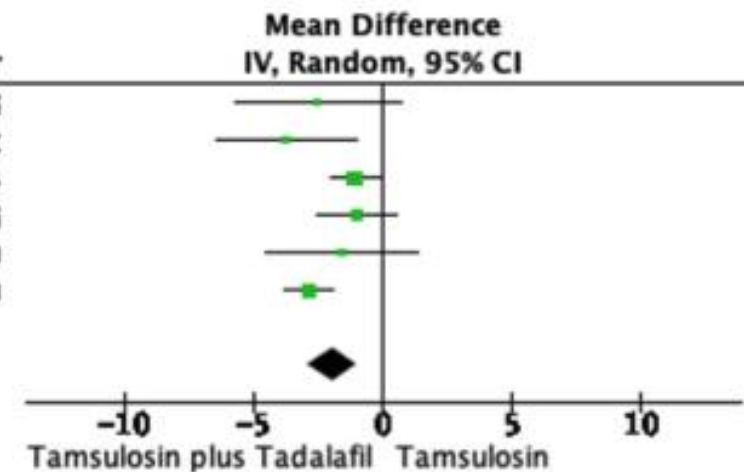


B. Total IPSS

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95% CI	Year
	Mean	SD	Total	Mean	SD	Total			
Bechara, A. 2008	-9.2	5.08	15	-6.7	3.87	15	7.2%	-2.50 [-5.73, 0.73]	2008
Regadas, P. R. 2012	-9.75	5.1	20	-6	3.6	20	9.4%	-3.75 [-6.49, -1.01]	2012
Singh, D. V. 2014	-11.73	2.978	44	-10.67	1.389	44	27.3%	-1.06 [-2.03, -0.09]	2014
Karami, H. 2016	-11.1	4.4	58	-10.1	3.9	59	19.7%	-1.00 [-2.51, 0.51]	2016
Negoro, H. 2019	-3.42	4.2	13	-1.85	3.4	13	8.4%	-1.57 [-4.51, 1.37]	2019
Nagasubramanian, S. 2020	-6.42	2.52	69	-3.57	3.06	71	28.0%	-2.85 [-3.78, -1.92]	2020
Total (95% CI)			219			222	100.0%	-1.95 [-2.91, -0.98]	

Heterogeneity: $\tau^2 = 0.64$; $\chi^2 = 10.20$, $df = 5$ ($P = 0.07$); $I^2 = 51\%$

Test for overall effect: $Z = 3.95$ ($P < 0.0001$)



IPDE5 + Alpha bloquant

Study or Subgroup	AB plus PDE-5I			AB plus placebo			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
2.1.1 International Prostate Symptom Score (IPSS)								
Bechara 2008	9.2	4.5	27	6.7	4.5	27	23.1%	2.50 [0.10, 4.90]
Gacci 2012	5.8	0.95	30	3.7	11.01	29	8.9%	2.10 [-1.92, 6.12]
Regadas 2013	9.75	5.1	20	6	3.6	20	18.2%	3.75 [1.01, 6.49]
Tuncel 2010	6.35	2.43	20	5.35	2.43	20	49.9%	1.00 [-0.51, 2.51]
Subtotal (95% CI)			97			96	100.0%	1.94 [0.72, 3.17]

Heterogeneity: $\text{Tau}^2 = 0.19$; $\text{Chi}^2 = 3.37$, $\text{df} = 3$ ($P = 0.34$); $I^2 = 11\%$

Test for overall effect: $Z = 3.11$ ($P = 0.002$)

2.1.2 Urinary peak flow rate (Qmax, mL/sec)

Bechara 2008	3	2.1	27	2.1	2.1	27	26.7%	0.90 [-0.22, 2.02]
Gacci 2012	2.6	0.95	30	0.1	0.8	29	31.0%	2.50 [2.05, 2.95]
Regadas 2013	1	2.4	20	1.4	2.4	20	23.7%	-0.40 [-1.89, 1.09]
Tuncel 2010	5.7	3.41	20	3.2	3.45	20	18.6%	2.50 [0.37, 4.63]
Subtotal (95% CI)			97			96	100.0%	1.39 [-0.03, 2.80]

Heterogeneity: $\text{Tau}^2 = 1.63$; $\text{Chi}^2 = 18.46$, $\text{df} = 3$ ($P = 0.0004$); $I^2 = 84\%$

Test for overall effect: $Z = 1.92$ ($P = 0.06$)

2.1.3 Post-void residual volume (PVR, mL)

Bechara 2008	38.7	6.7	27	35.2	6.7	27	58.0%	3.50 [-0.07, 7.07]
Gacci 2012	10.2	7.15	30	4.9	10.92	29	33.2%	5.30 [0.57, 10.03]
Tuncel 2010	33.3	15.39	20	26.2	14.11	20	8.8%	7.10 [-2.05, 16.25]
Subtotal (95% CI)			77			76	100.0%	4.42 [1.69, 7.14]

Heterogeneity: $\text{Tau}^2 = 0.00$; $\text{Chi}^2 = 0.72$, $\text{df} = 2$ ($P = 0.70$); $I^2 = 0\%$

Test for overall effect: $Z = 3.18$ ($P = 0.001$)

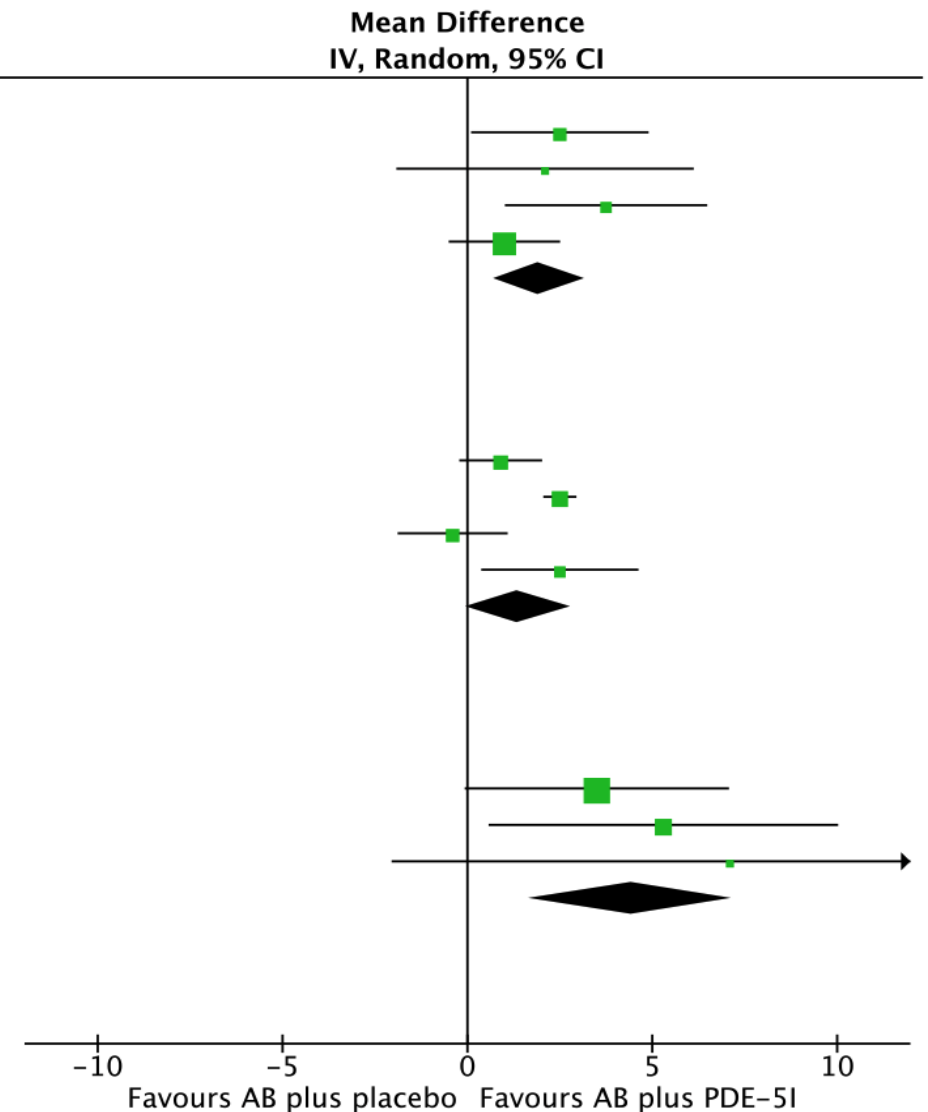
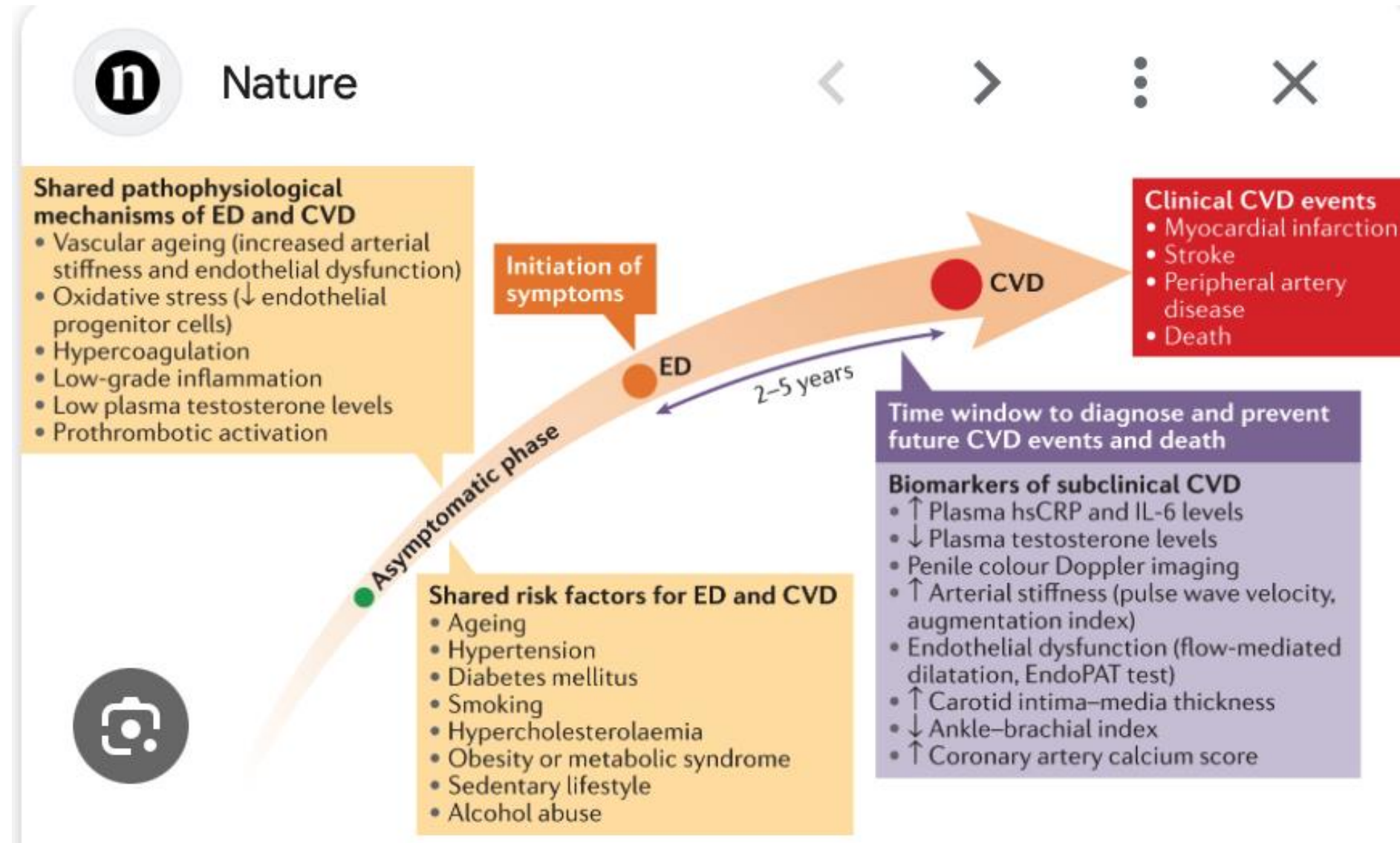


Tableau 2 : Options thérapeutiques médicamenteuses et chirurgicales dans l'hyperplasie bénigne de prostate.

Option thérapeutique	Indication préférentielle	
Traitement médicamenteux	Volume prostatique	Remarque
Alpha-bloquant	Tout volume	SBAU gênants Rétention aiguë d'urine
I5AR	> 40 mL	SBAU gênants
Alpha-bloquants et I5AR	> 40 mL	SBAU gênants
Alpha-bloquant et anticholinergiques	Tout volume	SBAU de la phase de remplissage prédominants ou persistants après alpha-bloquant seul
IPDE5 ± alpha-bloquant	Tout volume	Dysfonction érectile et SBAU
Phytothérapie	Tout volume	SBAU peu gênants et effets indésirables des autres classes thérapeutiques non acceptés

Dysfonction érectile et risque cardiovasculaire



Tadalafil et réduction du risque cardio-vasculaire

TriNetX Research Network

821,592 men that did not use an alpha blocker or tadalafil,
5,004 men using tadalafil but no alpha blocker,
327,482 men that used an alpha blocker but no tadalafil,
6,603 men that used both an alpha blocker and tadalafil.


Tadalafil was independently associated with a decreased risk of MACE/VTE within a 3-year time period (OR=0.59, 95%CI 0.49–0.70, $p < 0.0001$).

Among men with a history of alpha blocker use, tadalafil use was also independently associated with a decreased risk of MACE or VTE, both before and after controlling for potentially confounding variables (OR=0.57, 95%CI: 0.50–0.66; $p < 0.0001$).

World Journal of Urology (2022) 40:1799–1803
<https://doi.org/10.1007/s00345-022-04005-3>

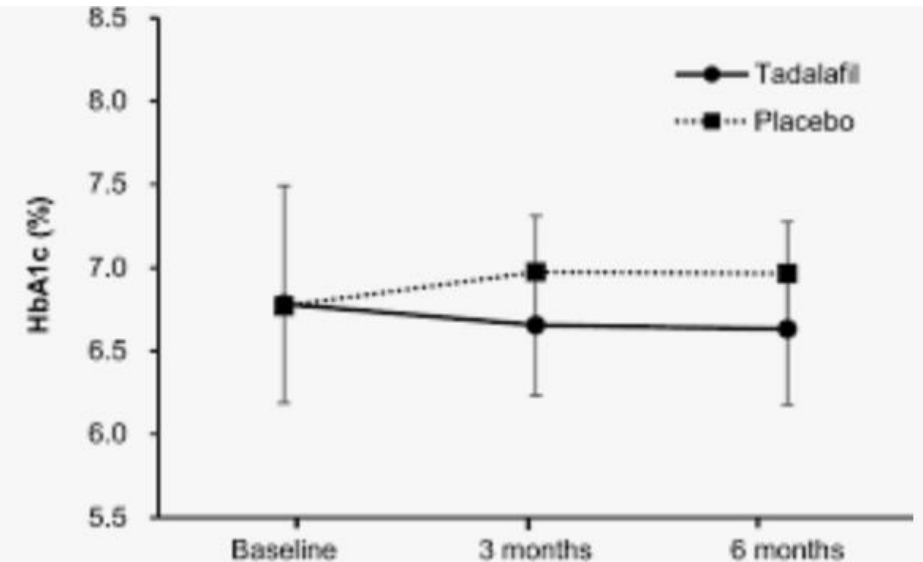
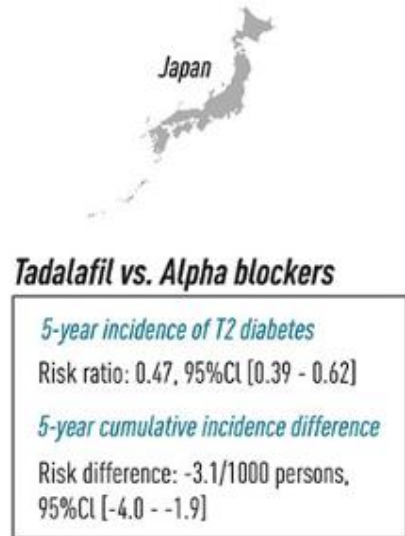
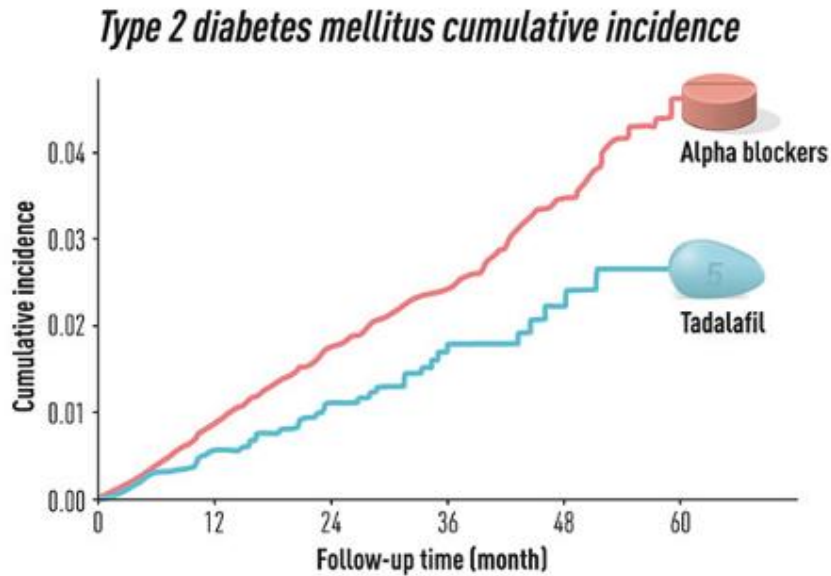
ORIGINAL ARTICLE

Is tadalafil associated with decreased risk of major adverse cardiac events or venous thromboembolism in men with lower urinary tract symptoms?

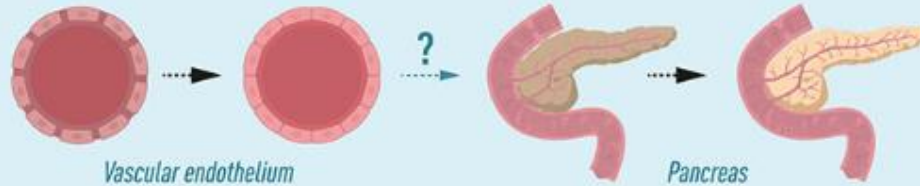
Sankalp Goberdhan¹ · Ruben Blachman-Braun² · Sirpi Nackeeran² · Thomas A. Masterson 3rd²  · Ranjith Ramasamy²

Tadalafil et risque de diabète

Tadalafil use is associated with a lower incidence of type 2 diabetes in men with benign prostatic hyperplasia: A population-based cohort study



Improving endothelial dysfunction could be associated with a lower incidence of T2 diabetes



Tadalafil et Alzheimer

les hommes à qui l'on a prescrit des médicaments contre la dysfonction érectile tels que le Viagra et le Cialis ont 18 % de risques en moins de développer la maladie d'Alzheimer.

La nouvelle étude britannique porte sur près de 270 000 hommes à qui on avait diagnostiqué des troubles de l'érection et qui n'avaient pas de problèmes cognitifs au début de l'étude.

Cleveland Clinic

Sildenafil users were 69% less likely to develop Alzheimer's disease than non-sildenafil users after 6 years of follow-up. Specifically, sildenafil had a 55% reduced risk of the disease compared to losartan, 63% compared to metformin, 65% compared to diltiazem and 64% compared to glimepiride.



Cleveland Clinic researchers find **sildenafil, a therapy for erectile dysfunction and pulmonary hypertension, is associated with a **69% reduction in developing Alzheimer's.****

Published in Nature Aging



IPDE5 et démence

- Longitudinal study analyzed data from 50 million US men using the TriNetX database.
- Men at least 40 years of age prescribed tadalafil or sildenafil after an erectile dysfunction diagnosis, or tadalafil after lower urinary tract symptom diagnoses, from 2004 to 2021 were included. The final cohort included 509,788 men with erectile dysfunction and 1,075,908 with lower urinary tract symptoms.
- Three-year outcomes assessed included all-cause mortality, cardiovascular disease, and dementia, comparing men on PDE-5 inhibitors to those not on these medications.
- Tadalafil and sildenafil were associated with (in ED patients and in lower urinary tract symptom patients)
 - significantly reduced risks of all-cause mortality (RR 0.66/0.76),
 - myocardial infarction (0.73/0.83), stroke (0.66/0.78),
 - venous thromboembolism (0.79/0.80),
 - dementia (0.68/0.75)

Conclusion

IPDE5 pour tous ?

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Hôpital Henri Mondor - V1.1 - FS9

Merci de votre attention
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