



CONGRESSO MACROREGIONALE SIA
Sezione Lombardia-Piemonte-Valle D'Aosta



ANDROLOGIA 2022

NUOVE DOMANDE, NUOVE RISPOSTE

TORINO

18 Giugno 2022

Dalle linee guida all'attività andrologica pratica

I PDE5i da soli o in associazione
ad altre terapie?

Dr. Francesco Varvello

Ospedale Michele e Pietro Ferrero
Verduno (CN)



EAU Guidelines on Sexual and Reproductive Health

Dalle linee guida...
all'attività andrologica pratica

- Terapia di combinazione come **approccio di prima linea** per casi refrattari, complessi e difficili da trattare
- **Evidenze scientifiche limitate**
- **PDE5i + antiossidanti, LiESWT o vacuum device** migliorano i risultati senza aumentare gli effetti collaterali
- **Tadalafil giornaliero + PDE5i al bisogno** migliorano i risultati senza aumentare gli effetti collaterali



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Dal libro degli incantesimi...

...alla preparazione della
pozione magica!

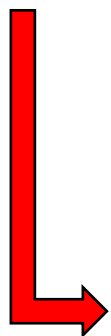
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Terapia di associazione

- da subito
- perché la monoterapia fallisce o non è sufficiente



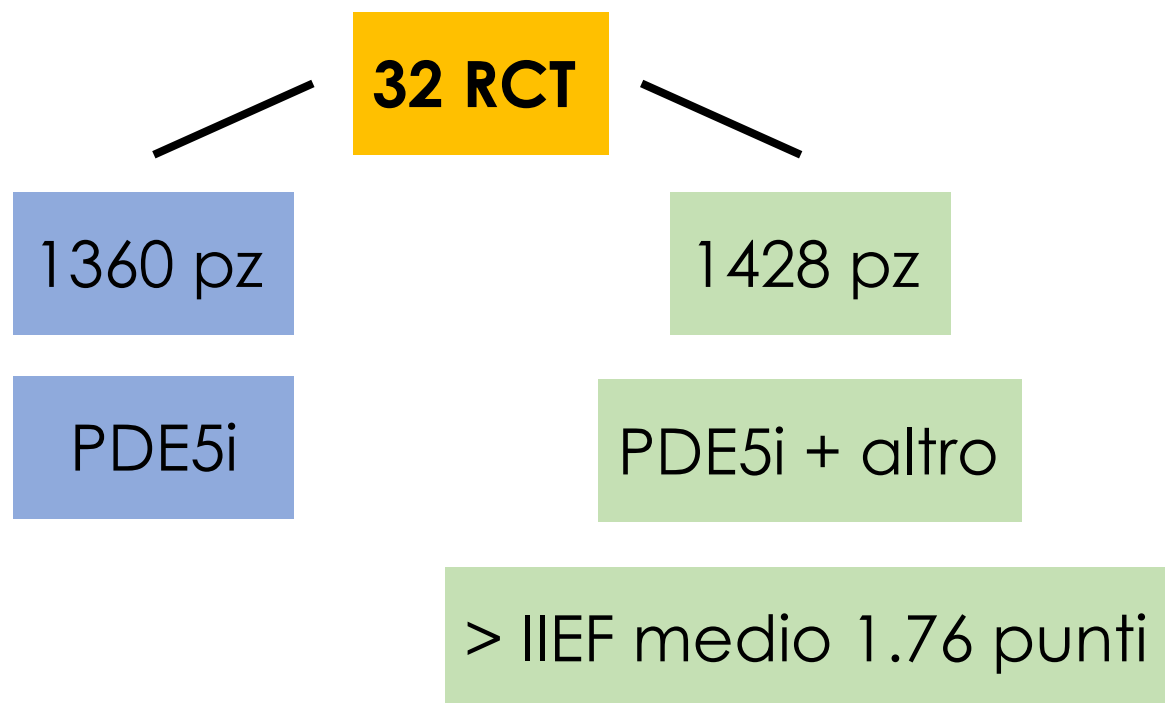
- utilizzo non corretto
- inefficacia



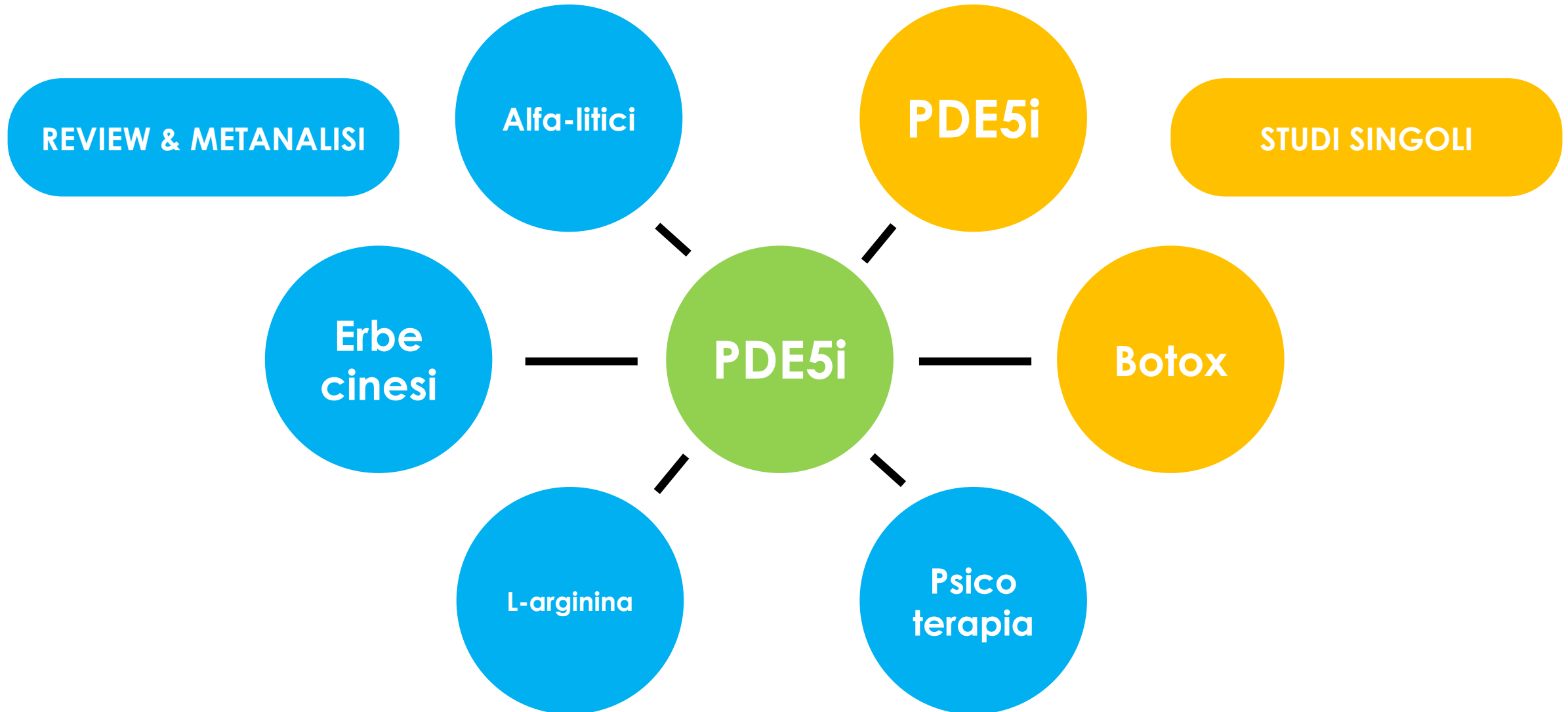
- insufficiente stimolo sessuale
- dose inadeguata
- scorretta tempistica di assunzione

Original Investigation | Urology

Assessment of Combination Therapies vs Monotherapy for Erectile Dysfunction A Systematic Review and Meta-analysis



Testosterone	2.27 pt	5 RCT
Antiossidanti	1.99 pt	9 RCT
Alfa litico	0.80 pt	8 RCT
Tadalafil 5 mg	1.70 pt	1 RCT
Li-ESWT	3.50 pt	1 RCT
VED	8.40 pt	1 RCT
Acido folico	3.46 pt	1 RCT
Metformina	4.90 pt	1 RCT
ACE inibitore	2.07 pt	1 RCT
Pentossifillina	0.56 pt	2 RCT
Atorvastatina	-0.60 pt	1 RCT
Aspirina	-0.60 pt	1 RCT





First International Journal of Andrology

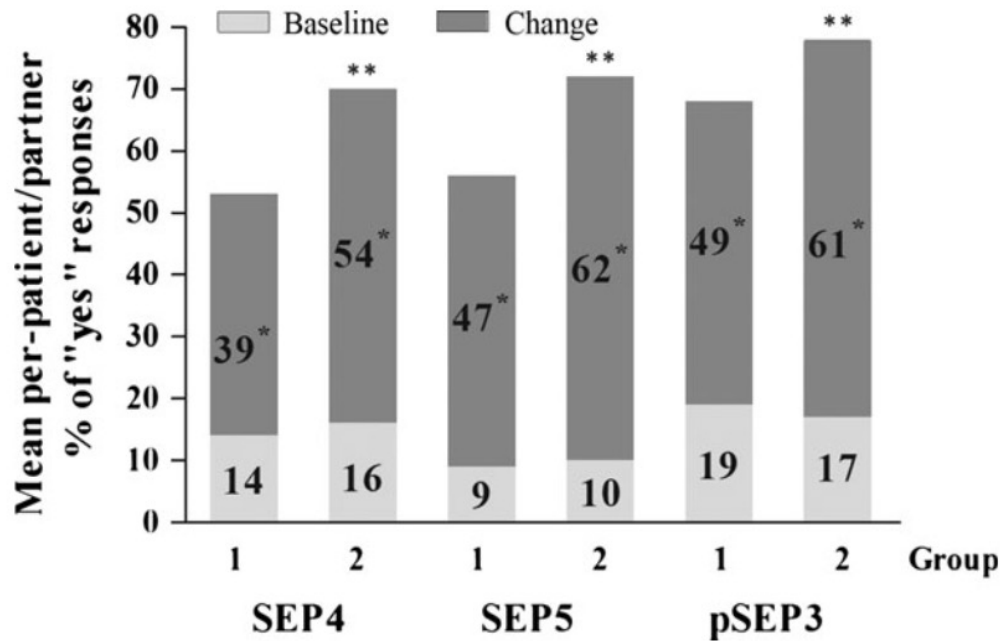
ANDROLOGIA

Andrologia 2015, **47**, 20–24

ORIGINAL ARTICLE

Efficacy and safety of long-term tadalafil 5 mg once daily combined with sildenafil 50 mg as needed at the early stage of treatment for patients with erectile dysfunction

H. Cui*, B. Liu*, Z. Song, J. Fang, Y. Deng, S. Zhang, H. Wang & Z. Wang



Adverse event	Group 1 (n = 90)		Group 2 (n = 90)	
	n	%	n	%
Flushing	6	6.7	7	7.8
Headache	5	5.6	4	4.4
Dyspepsia	3	3.3	4	4.4
Muscle pain	4	4.4	3	3.3
Nasal congestion	1	1.1	0	0.0

Non aumentano gli effetti collaterali

PDE5i

+

PDE5i + L-arginina

L-arginina

- Precursore di NO
- NO è il principale neurotrasmettitore coinvolto nel rilassamento del muscolo liscio durante la fase di erezione
- PDE5i necessitano di NO per esercitare il loro effetto
- effetto sinergico

ORIGINAL ARTICLE

First International Journal of Andrology
andrologia WILEY

Comparison of efficacy and safety of daily oral L-arginine and PDE5Is alone or combination in treating erectile dysfunction: A systematic review and meta-analysis of randomised controlled trials

Zhunan Xu MM^{1,2} | Chu Liu MD² | Shuang Liu MM³ | Zhongbao Zhou MD⁴ 

Andrologia. 2021;53:e14007.

Metanalisi, 4 RCT

373 pz, follow up 6-12 settimane

tadalafil 5 mg giornaliero + L-arginina 2,5-5g (3 RCT)

sildenafil 50 mg giornaliero + L-arginina 3g (1 RCT)

PDE5i

+

PDE5i + L-arginina

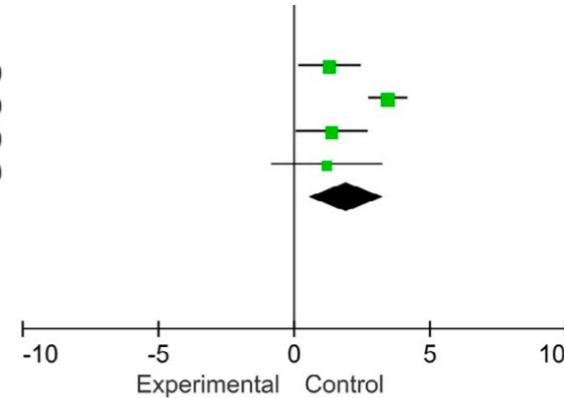
IIEF

1.1.3 PDE5 + L-arginine vs PDE5

El-Wakeel LM 2019	19.8	2.2	30	18.5	2.3	29	26.5%	1.30 [0.15, 2.45]	2019
Taieb M 2019	23.52	1.3	27	20.07	1.4	27	29.9%	3.45 [2.73, 4.17]	2019
El-Hamd MA 2020	23.15	2.91	30	21.77	2.3	30	24.9%	1.38 [0.05, 2.71]	2020
Gallo L 2020	22	7.5	100	20.8	7.3	100	18.7%	1.20 [0.85, 3.25]	2020
Subtotal (95% CI)			187			186	100.0%	1.94 [0.59, 3.30]	

Heterogeneity: $\tau^2 = 1.47$; $\chi^2 = 15.14$, $df = 3$ ($P = 0.002$); $I^2 = 80\%$

Test for overall effect: $Z = 2.81$ ($P = 0.005$)



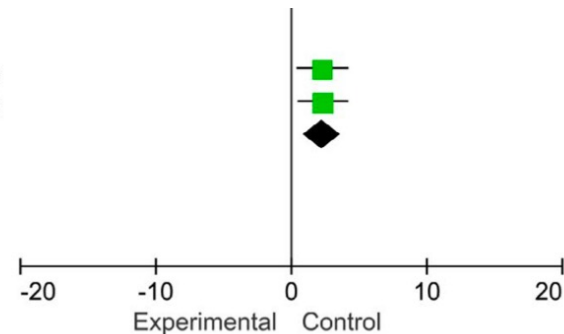
Testosterone totale

1.2.3 PDE5 + L-arginine vs PDE5

Taieb M 2019	22.48	3.6	27	20.19	3.6	27	48.7%	2.29 [0.37, 4.21]	2019
El-Hamd MA 2020	22.83	3.7	30	20.5	3.7	30	51.3%	2.33 [0.46, 4.20]	2020
Subtotal (95% CI)			57			57	100.0%	2.31 [0.97, 3.65]	

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.00$, $df = 1$ ($P = 0.98$); $I^2 = 0\%$

Test for overall effect: $Z = 3.38$ ($P = 0.0007$)



PDE5i

+

PDE5i + alfa litico

Review – Voiding Dysfunction

EUROPEAN UROLOGY FOCUS 6 (2020) 537–558

Combination Therapy with Alpha-blocker and Phosphodiesterase-5 Inhibitor for Improving Lower Urinary Tract Symptoms and Erectile Dysfunction in Comparison with Monotherapy: A Systematic Review and Meta-analysis

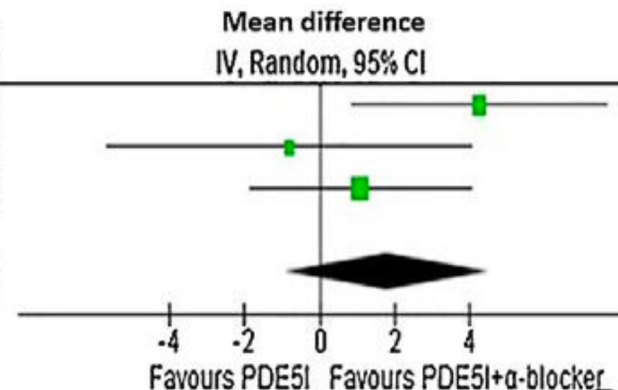
Panagiotis Kallidonis^{a,*}, Constantinos Adamou^a, Dimitrios Kotsiris^a, Panteleimon Ntasiotis^a, Paolo Verze^b, Anastasios Athanasopoulos^a,

IIEF-ED

Study or subgroup	PDE5i + α -blocker			PDE5i			Weight	Mean difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Kaplan 2007	25.7	4.9	18	21.4	5.7	19	35.9%	4.30 [0.88, 7.72]
Kumar 2013	22	9.1	25	22.8	8.5	25	22.6%	-0.80 [-5.68, 4.08]
Liguori 2009	19.9	4.8	21	18.8	4.8	19	41.5%	1.10 [-1.88, 4.08]
Total (95% CI)			64			63	100.0%	1.82 [-0.91, 4.54]

Heterogeneity: $\tau^2 = 2.34$; $\chi^2 = 3.34$, $df = 2$ ($P = 0.19$); $I^2 = 40\%$

Test for overall effect: $Z = 1.31$ ($P = 0.19$)

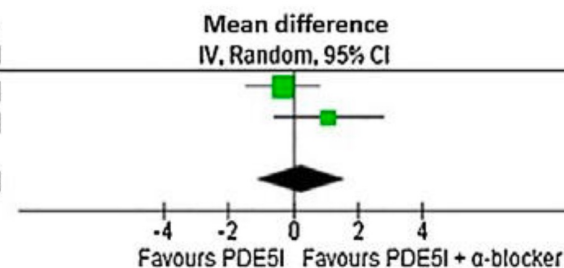


IIEF-ED mean change

Study or subgroup	PDE5i + α -blocker			PDE5i			Weight	Mean difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Kim S. W. 2017	9.17	4.9776	134	9.49	4.9315	152	59.6%	-0.32 [-1.47, 0.83]
Kumar 2013	4.3	3.4	25	3.2	2.6	25	40.4%	1.10 [-0.58, 2.78]
Total (95% CI)			159			177	100.0%	0.25 [-1.11, 1.62]

Heterogeneity: $\tau^2 = 0.47$; $\chi^2 = 1.87$, $df = 1$ ($P = 0.17$); $I^2 = 47\%$

Test for overall effect: $Z = 0.36$ ($P = 0.72$)



PDE5i

+

BTX-A

BTX-A

- Riduce l'attività simpatica dei nervi cavernosi
- Determina un blocco parziale del rilascio di noradrenalina nella giunzione neuromuscolare
- Aumenta espressione di VEGF e CD31 coinvolti nella vasodilatazione e proliferazione endoteliale

THE JOURNAL OF
SEXUAL MEDICINE

ORIGINAL

ERECTILE DYSFUNCTION

Long Term Effectiveness and Safety of Intracavernosal Botulinum Toxin A as an Add-on Therapy to Phosphodiesterase Type 5 Inhibitors or Prostaglandin E1 Injections for Erectile Dysfunction

Francois Giuliano, MD, PhD,^{1,2} Charles Jousain, MD, PhD,^{1,2} and Pierre Denys, MD, PhD^{1,2}

J Sex Med 2022;19:83–89

Retrospettivo, singolo centro

131 pz, valutati a circa 1 mese

AbobotulinumtoxinA 250-500 unità

OnabotulinumtoxinA 100 unità

74 non responders a PDE5i

57% aumento IIEF clinicamente rilevante

PDE5i

+

Erbe medicinali cinesi

Medicina tradizionale cinese

- I pz con DE presentano problemi emozionali, di desiderio sessuale, depressione e altre patologie sistemiche
- MTC agisce a livello multisistemico, multilivello e multitarget

Andrology, 2020, 8, 268–276

ANDROLOGY

Chinese herbal medicine combined with tadalafil for erectile dysfunction: a systematic review and meta-analysis

¹Y. L. Wang , ^{2,3}L. G. Geng, ³C. B. He and ³S. Y. Yuan

Metanalisi, 8 RCT

452 pz tadalafil 5-10 mg

451 pz tadalafil 5-10 mg + erbe cinesi

Erdibiejia decoction

Shisanwei ziyinzhuangyang capsule

Baji capsule

Compound xuanju capsule

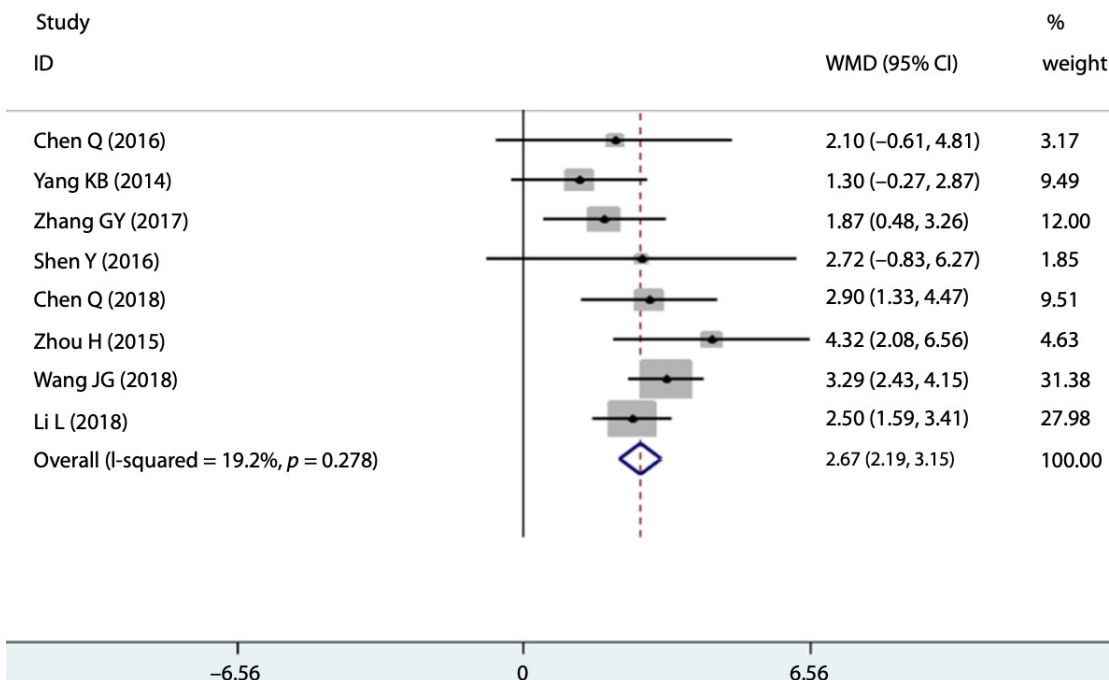
Congrong yishen capsule

PDE5i

+

Erbe medicinali cinesi

IIEF



Andrology, 2020, 8, 268–276

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PDE5i

+

Psicoterapia

Combination of Psychological Intervention and Phosphodiesterase-5 Inhibitors for Erectile Dysfunction: A Narrative Review and Meta-Analysis

Hannah M. Schmidt, MA, Thomas Munder, PhD, Heike Gerger, PhD, Sarah Frühauf, MA, and Jürgen Barth, PhD

Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland

J Sex Med 2014;11:1376–1391

Psicoterapia

La terapia farmacologica non interviene su fattori

- Psicologici
- Relazionali
- Culturali

Metanalisi, 8 studi clinici

562 pz (USA, Brasile, AUS, Cina, Egitto)

Sildenafil vs sildenafil + psicoterapia

Scarsa qualità metodologica

Cieco non possibile

PDE5i

+

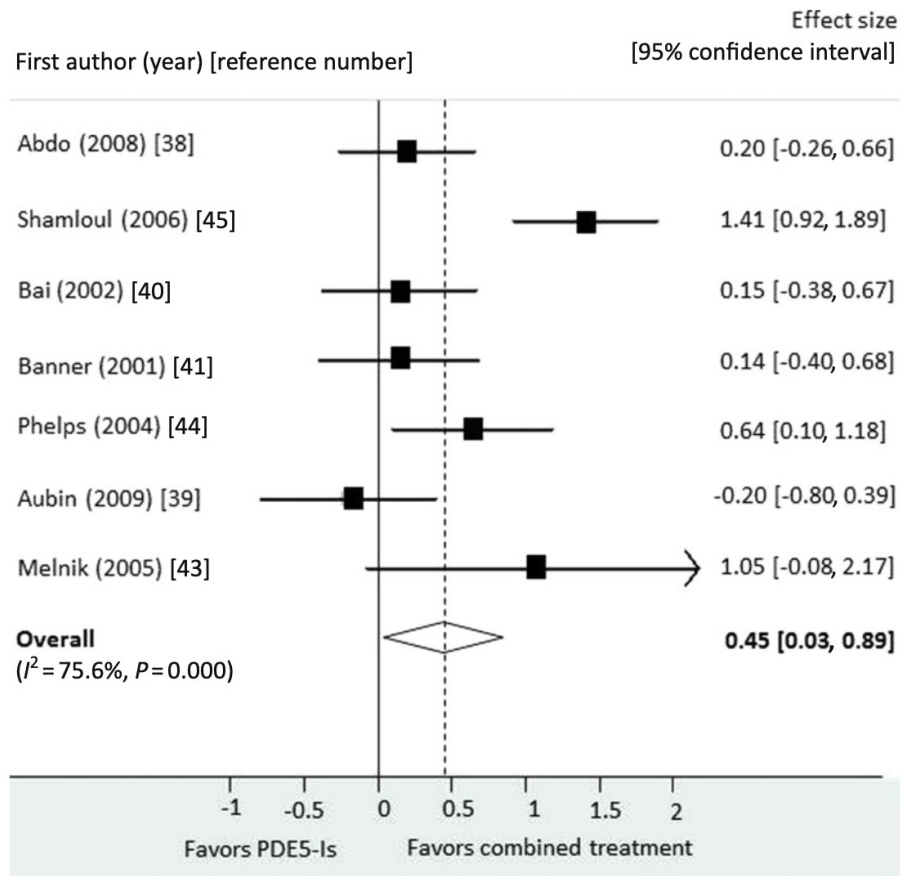
Psicoterapia

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Sildenafil vs sildenafil + psicoterapia

Scarsa qualità metodologica

Cieco non possibile

Conclusioni

- Terapia di associazione raccomandata per i casi più difficili ma sostenuta da deboli evidenze
- Testosterone utile se accertato ipogonadismo
- PDE5i in cronico + PDE5i al bisogno non aumentano effetti collaterali
- L-arginina 3-5 g/die aumenta % responders a PDE5i
- PDE5i + Li-ESWT migliorano i risultati in pz con DE vasculogenica lieve-moderata
- Psicoterapia può aumentare la risposta dei pz ai PDE5i