

**DISFUNZIONE ERETTILE
FACE TO FACE CON I PAZIENTI**

**La terapia medica per la DE
è sicura?**

Francesco Varvello

Bra 20 Aprile 2013



vietati ai
“cardiopatici”

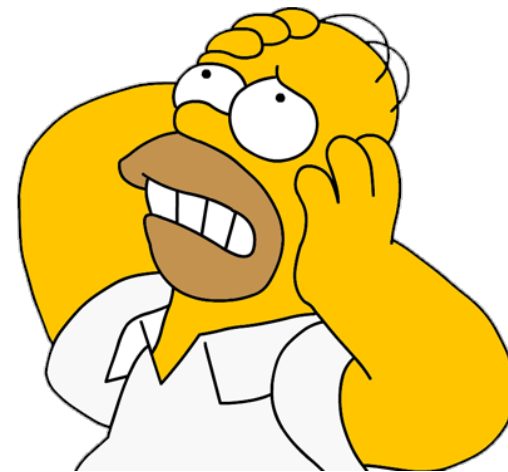
pericolosi
per il cuore

inducono
dipendenza

sostanze
dopanti

...sono stati segnalati gravi eventi cardiovascolari, inclusi infarto del miocardio, angina instabile, morte cardiaca improvvisa, aritmie ventricolari, emorragia cerebrovascolare, attacco ischemico transitorio, ipertensione ed ipotensione...è stato segnalato che molti eventi si sono verificati durante o subito dopo il rapporto sessuale e alcuni subito dopo l'assunzione del farmaco in assenza di attività sessuale...





ESISTONO DUBBI?



Comorbilità

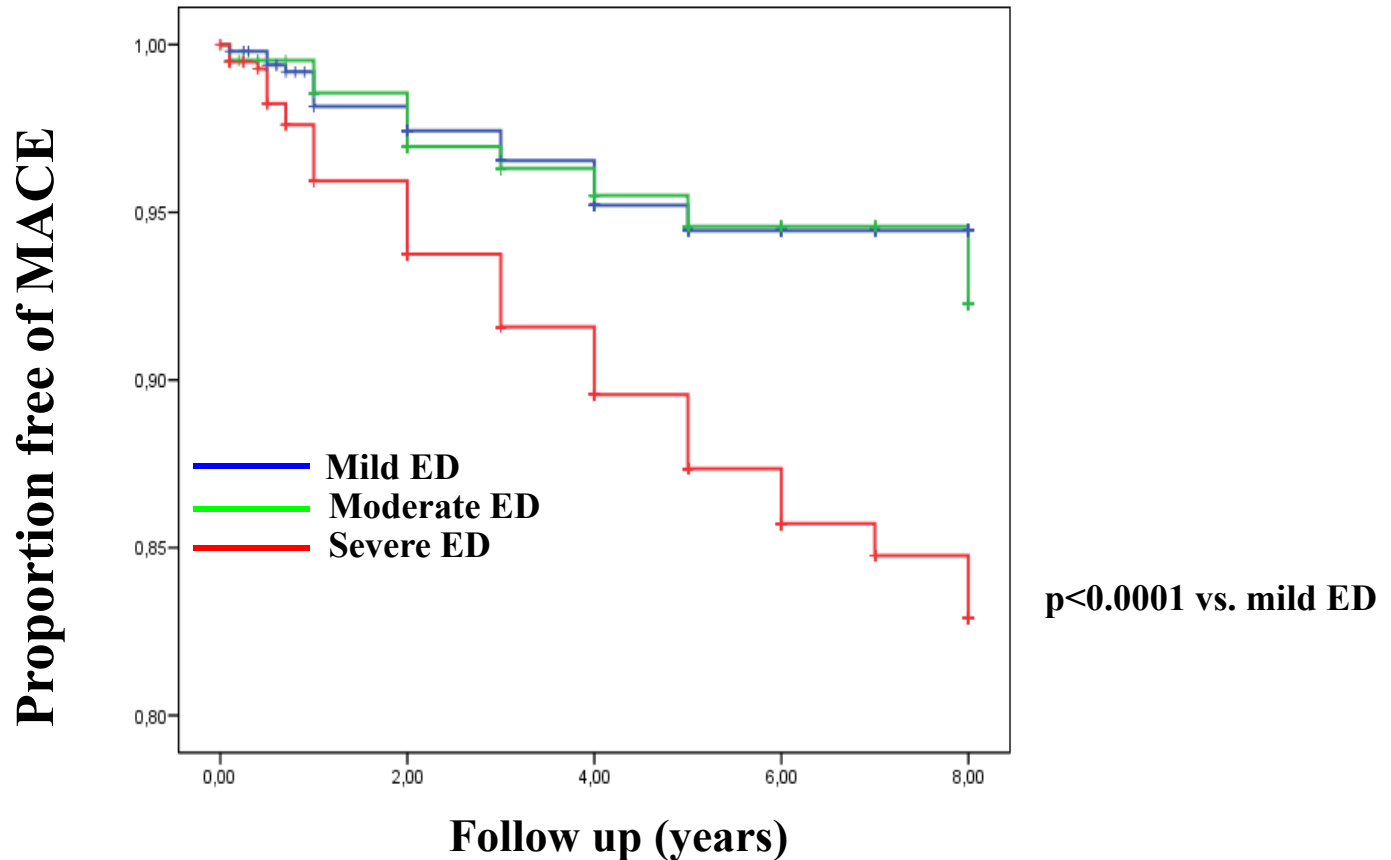
Terapie concomitanti

Effetti collaterali



La DE non solo condivide con le malattie cardiovascolari gli **stessi fattori di rischio** ma ne rappresenta **un fattore di rischio indipendente**

Proportion free of MACE (Kalplan-Meier curves) as a function of baseline erectile dysfunction severity (SIEDY score) in a consecutive series of 1687 ED subjects at the University of Florence, Florence, Italy



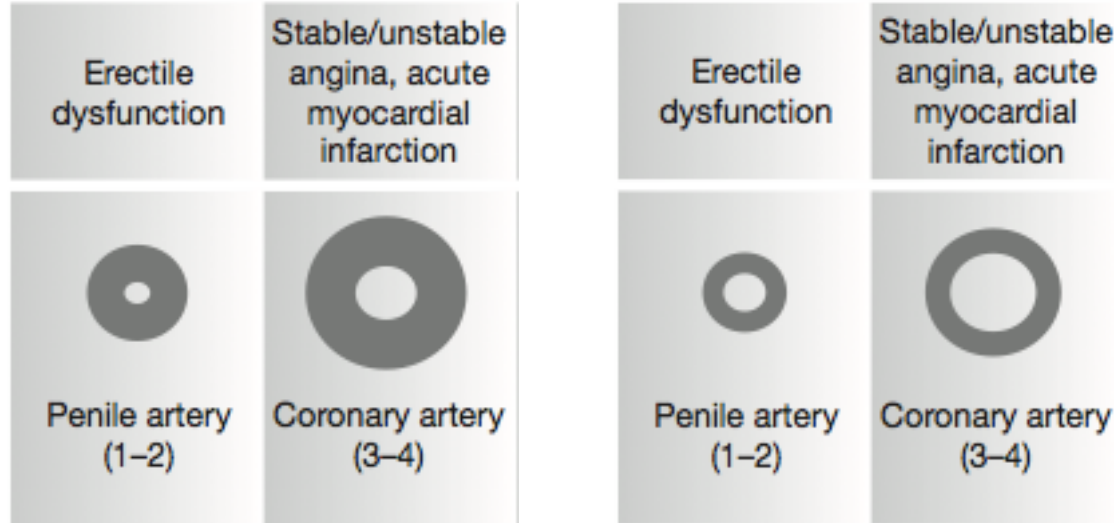
Having a severe ED is associated with an 80% increase of MACE (Cox regression HR=1.75 [1.1-2.78])

Il riscontro della DE offre
un'opportunità per la riduzione del
rischio cardiovascolare

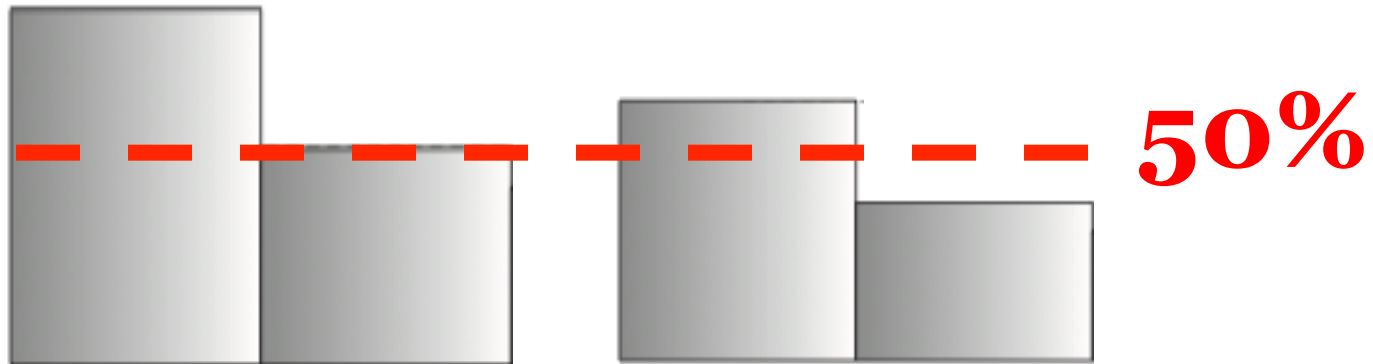
The Artery Size Hypothesis: A Macrovascular Link Between Erectile Dysfunction and Coronary Artery Disease

Piero Montorsi, MD,^{a,*} Paolo M. Ravagnani, MD,^a Stefano Galli, MD,^a
 Francesco Rotatori, MD,^a Alberto Briganti, MD,^b Andrea Salonia, MD,^b
 Patrizio Rigatti, MD,^b and Francesco Montorsi, MD^b

Sintomo



% di ostruzione



La terapia medica per la DE è sicura?

...un passo indietro

**può il paziente riprendere l'attività
sessuale in sicurezza?**



L'equivalente di un rapporto sessuale

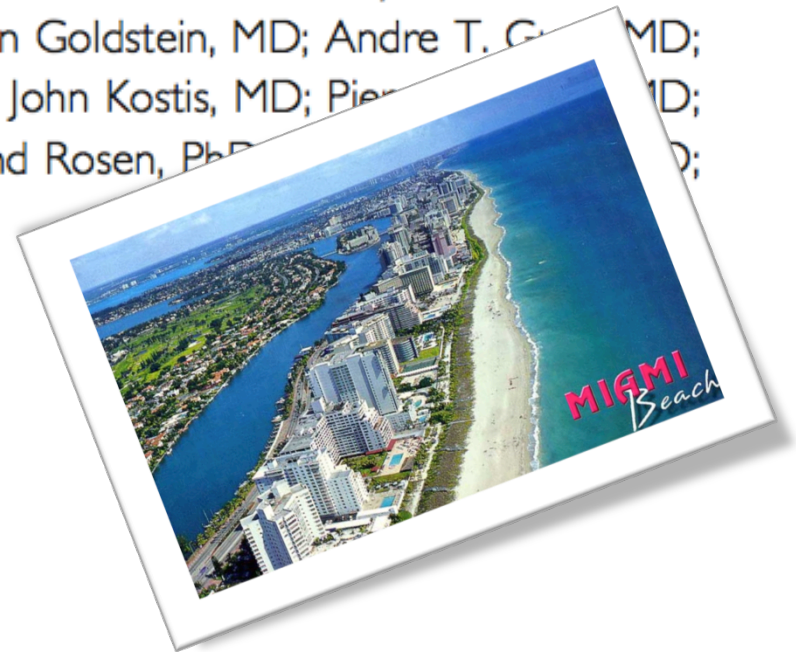


percorrere 1,5 Km
in 20 minuti

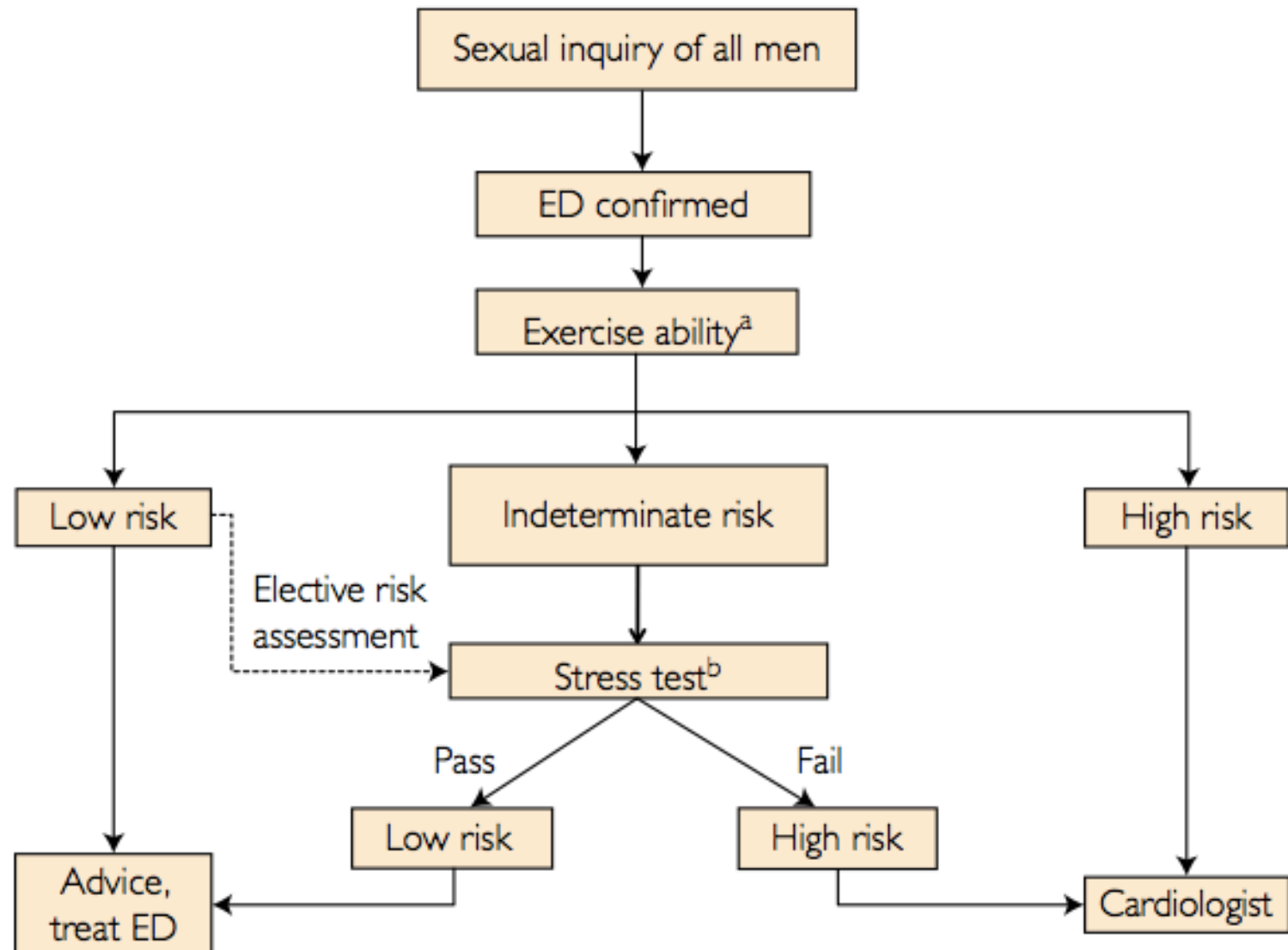
salire 2 piani di scale
in 10 secondi

The Princeton III Consensus Recommendations for the Management of Erectile Dysfunction and Cardiovascular Disease

Ajay Nehra, MD; Graham Jackson, FRCP, FESC; Martin Miner, MD; Kevin L. Billups, MD;
Arthur L. Burnett, MD, MBA; Jacques Buvat, MD; Culley C. Carson, MD;
Glenn R. Cunningham, MD; Peter Ganz, MD; Irwin Goldstein, MD; Andre T. G... MD;
Geoff Hackett, MD; Robert A. Kloner, MD, PhD; John Kostis, MD; Pier... MD;
Melinda Ramsey, PhD; Raymond Rosen, PhD



The Princeton III Consensus Recommendations



Basso rischio

- Asintomatico, < 3 fattori di rischio
- Ipertensione controllata
- Post rivascularizzazione (bypass o PTCA) senza residua ischemia significativa
- Insufficienza ventricolare sinistra (NYHA I-II)
- FA con risposta ventricolare controllata
- Disfunzione valvolare lieve
- Prolasso mitralico
- Pericardite

Alto rischio

- Angina instabile o refrattaria
- Ipertensione non controllata
- Scompenso cardiaco (NYHA IV)
- Recente IMA (<2 settimane)
- Grave aritmia
- Cardiomiopatia ipertrofica
- Valvulopatia moderata-severa specialmente stenosi aortica



Rischio intermedio

- Asintomatico, ≥ 3 fattori di rischio (escluso il genere)
- Angina stabile, di moderata entità
- Pregresso IMA
- Scompenso cardiaco (NYHA III)
- Sequele non cardiache di malattia aterosclerotica (vasculopatia periferica, ictus, TIA)

Valutazione del rischio

NON INVASIVA

- Biomarkers
- Stress test
- Scintigrafia miocardica
- AngioTC coronarica

INVASIVA

- Coronarografia



Cardiovascular Effects of Sildenafil During Exercise in Men With Known or Probable Coronary Artery Disease

A Randomized Crossover Trial

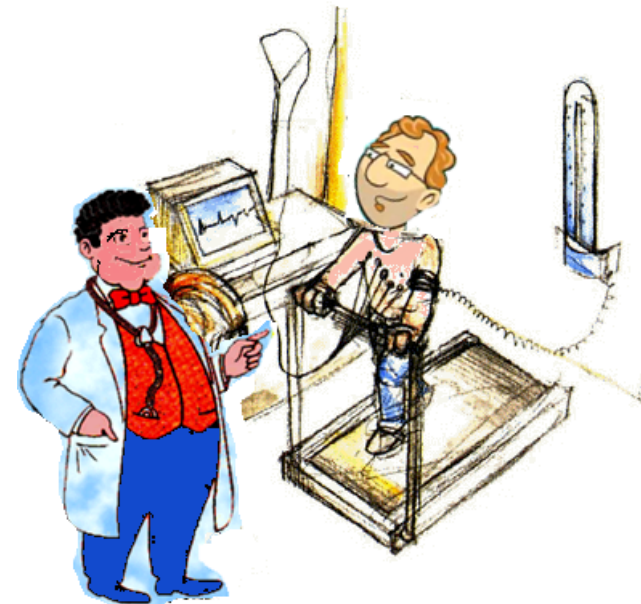
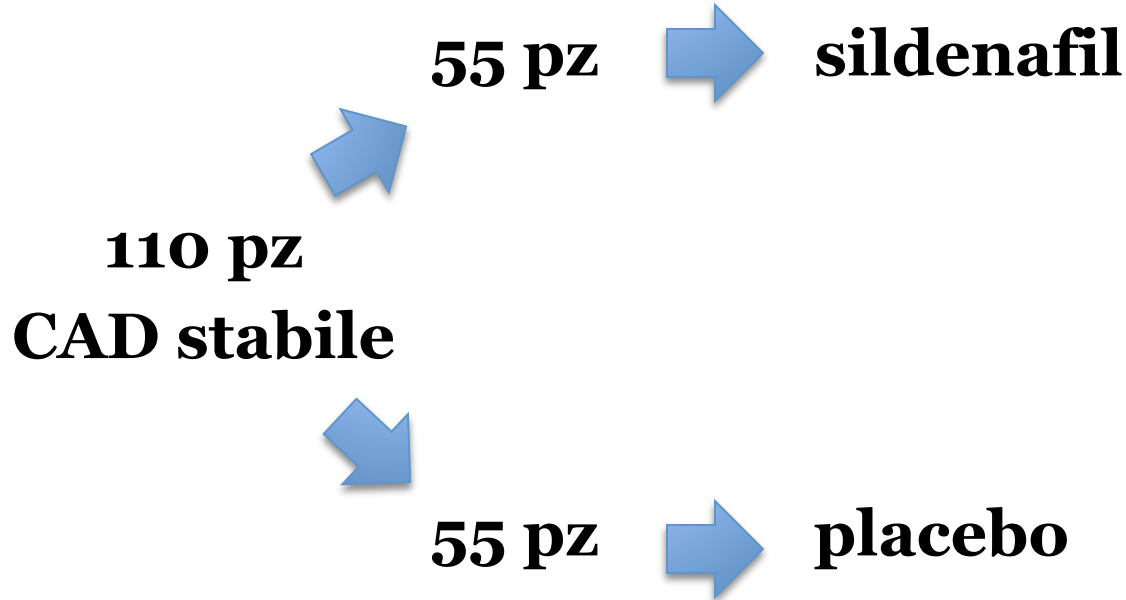
Adelaide M. Arruda-Olson, MD, PhD

Douglas W. Mahoney, MS

Ajay Nehra, MD

Marilyn Leckel, RN

Patricia A. Pellikka, MD



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NESSUNA DIFFERENZA

- Incremento di pressione arteriosa e frequenza cardiaca
- Sviluppo di dispnea o angina (69 vs 70)
- Modificazioni ischemiche ECG (11% sildenafil vs 16% placebo)

Cardiovascular Safety Update of *Tadalafil*: Retrospective Analysis of Data from Placebo-Controlled and Open-Label Clinical Trials of *Tadalafil* With As Needed, Three Times-per-Week or Once-a-Day Dosing

Robert A. Kloner, MD, PhD^{a,*}, Graham Jackson, MD^b, Adolph M. Hutter, MD^c,
 Murray A. Mittleman, MD^d, Melanie Chan, MS^e, Margaret R. Warner, PhD, DVM^f,
 Timothy M. Costigan, PhD^f, and G. Matthew Vail, MD^f



Days on Tadalafil	Patients (n)	Patient Exposure (PYs)	No. Pts With Serious CVTEA	Rate (95% CI)
≥0-30	4,601	373	2 [†]	0.54 (0.06–1.94)
31-60	4,389	337	2	0.59 (0.07–2.14)
61-90	3,677	273	1	0.37 (0.01–2.04)
91-180	2,245	100	0	0 (0–3.69)
Total	4,601	1,082	5 [†]	0.46 (0.15–1.08)
≥0-30	2,047	164	1	0.61 (0.02–3.40)
31-60	1,911	142	1	0.71 (0.02–3.92)
61-90	1,495	109	0	0 (0–3.38)
91-180	850	45	0	0 (0–8.20)
Total	2,047	460	1	0.43 (0.05–1.57)

Safety of sildenafil citrate: review of 67 double-blind placebo-controlled trials and the postmarketing safety database

F. Giuliano,¹ G. Jackson,² F. Montorsi,³ A. Martin-Morales,⁴ P. Raillard⁵

Adverse events†	Fixed-dose trials			Flexible-dose trials		
	Sildenafil dose			Modal sildenafil dose*		
	50 mg (N = 804)	100 mg (N = 1373)	Placebo (N = 1623)	50 mg (N = 2060)	100 mg (N = 3479)	Placebo (N = 4979)
AE, number of events						
All causality	1101	1419	769	1807	2768	2491
Treatment-related	501	781	181	1077	1421	668
AE, number (%) of patients						
All causality	498 (61.9)	655 (47.7)	489 (30.1)	951 (46.2)	1549 (44.5)	1572 (31.6)
Severe	51 (6.3)	56 (4.1)	41 (2.5)	87 (4.2)	102 (2.9)	127 (2.6)
Serious	17 (2.1)	19 (1.4)	23 (1.4)	37 (1.8)	55 (2.6)	67 (1.3)
DC	14 (1.7)	20 (1.5)	19 (1.2)	50 (2.4)	27 (0.8)	49 (1.0)

Serious	17 (2.1)	19 (1.4)	23 (1.4)	37 (1.8)	55 (2.6)	67 (1.3)
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Acknowledgment: The authors thank Yi Xia, MS, Lingling Xie, MS, and Shuhuan Zhang, MS, Lilly Research Laboratories, Eli Lilly and Company, for their assistance with statistical analyses.

REVIEW ARTICLE

THE INTERNATIONAL JOURNAL OF
CLINICAL PRACTICE

Safety of sildenafil citrate: review of 67 double-blind placebo-controlled trials and the postmarketing safety database

F. Giuliano,¹ G. Jackson,² F. Montorsi,³ A. Martin-Morales,⁴ P. Raillard⁵

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ORIGINAL RESEARCH—ED PHARMACOTHERAPY

10-Year Analysis of Adverse Event Reports to the Food and Drug Administration for Phosphodiesterase Type-5 Inhibitors

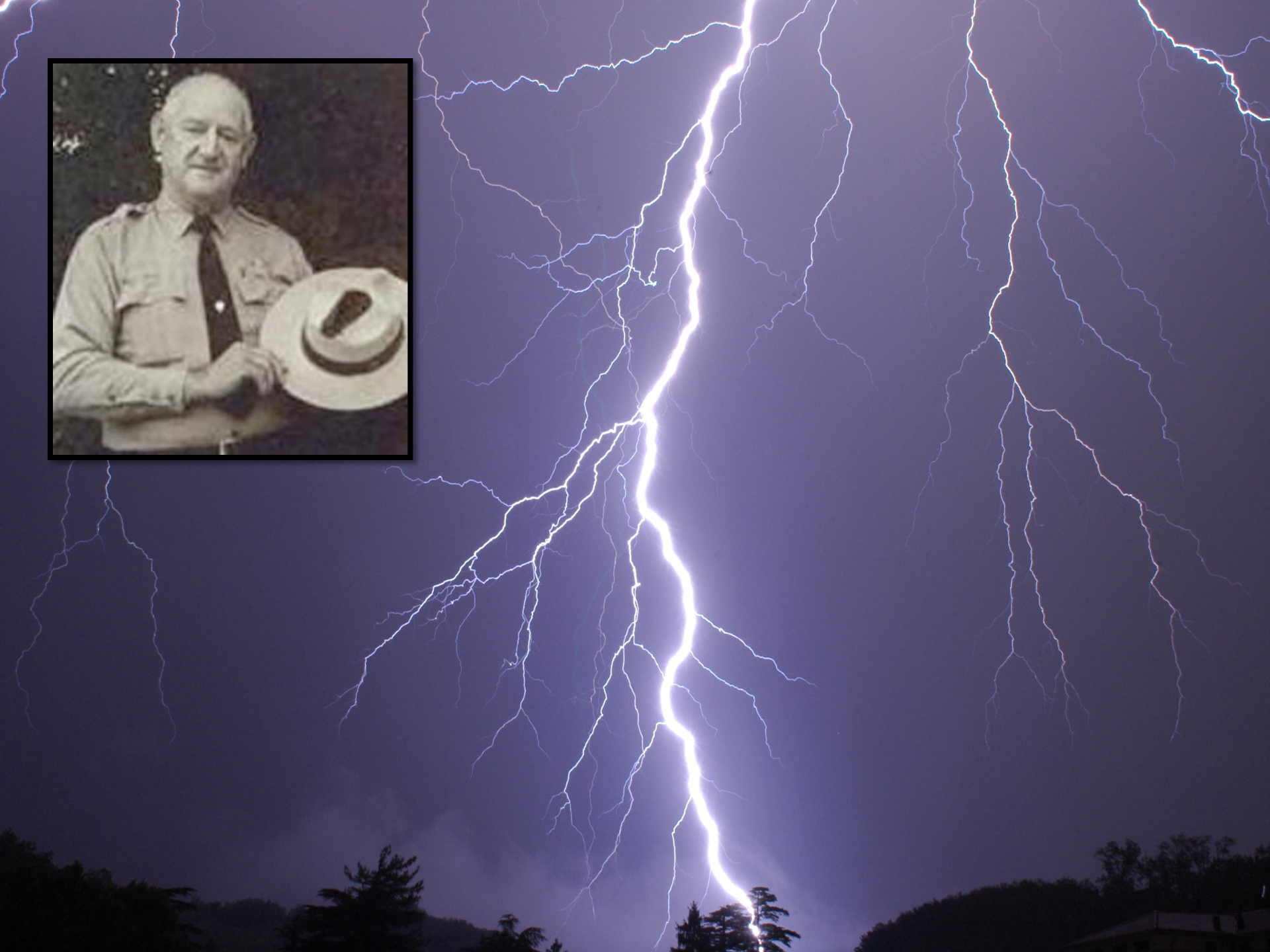
Gregory Lowe, MD*† and Raymond A. Costabile, MD†

*Department of Urology, Ohio State University Medical Center, Columbus, OH, USA
†Department of Urology, University of Virginia Health System, Charlottesville, VA, USA

Conflict of Interest: None.

0,00006%

Probabilità di incorrere in un evento avverso cardiovascolare



Controindicazioni rare

- Retinite pigmentosa
- Pregressa NAION
- Atrofia multisistemica
- Predisposizione al priapismo
- Intolleranza al lattosio

Comorbidità



Terapie concomitanti

Effetti collaterali



Nitrati

Table 3 Contraindications and dose adjustments for PDE5 inhibitors^{15,42}

Pharmacodynamic interactions

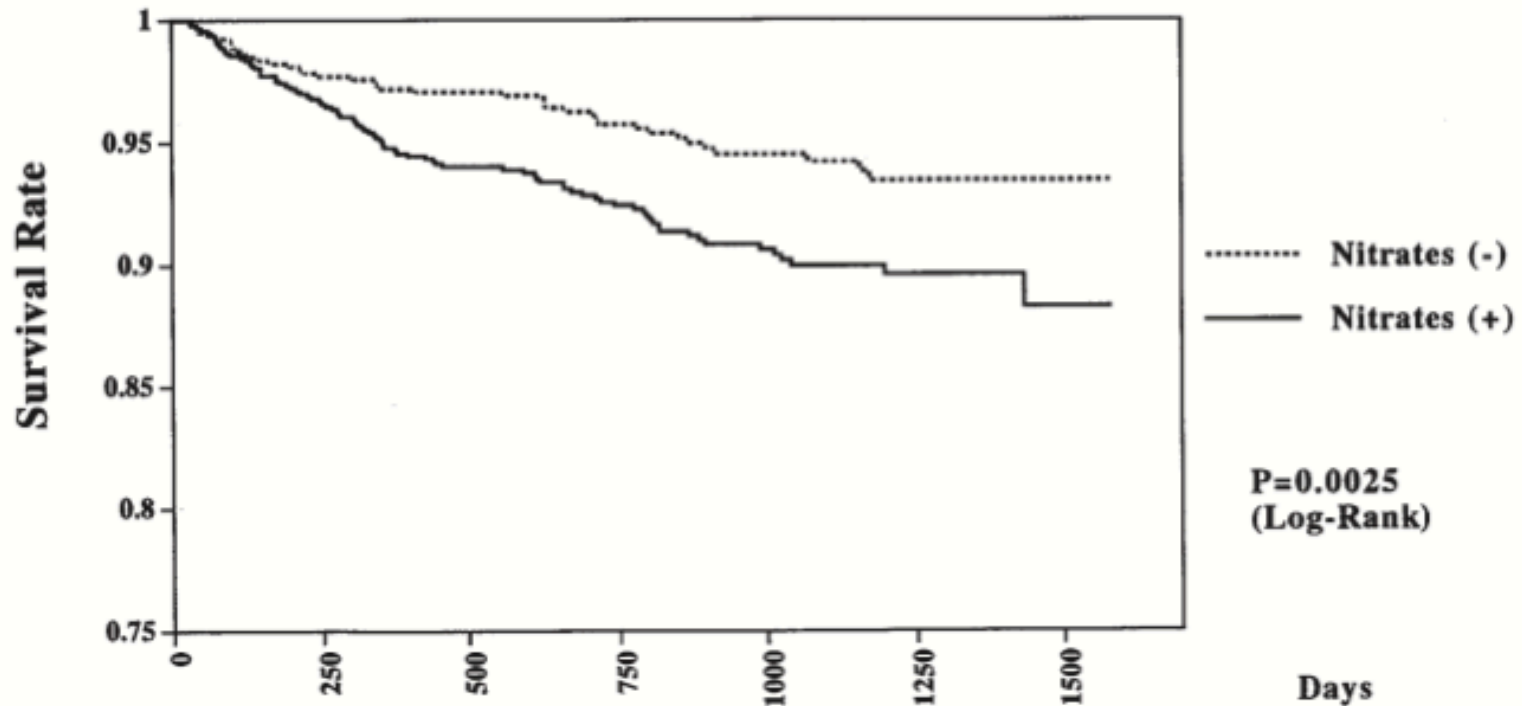
Contraindications

- *Nitrates*: concomitant use of PDE5 inhibitors with nitrates is absolutely contraindicated as they potentiate the hypotensive effects of nitrates



Long-term nitrate use may be deleterious in ischemic heart disease: A study using the databases from two large-scale postinfarction studies

Yasuyuki Nakamura, MD,^a Arthur J Moss, MD,^c Mary W. Brown, RN, MS,^c Masahiko Kinoshita, MD,^a and Chuichi Kawai, MD,^b for the Multicenter Myocardial Ischemia Research Group *Sbiga and Kyoto, Japan; and Rochester, NY*

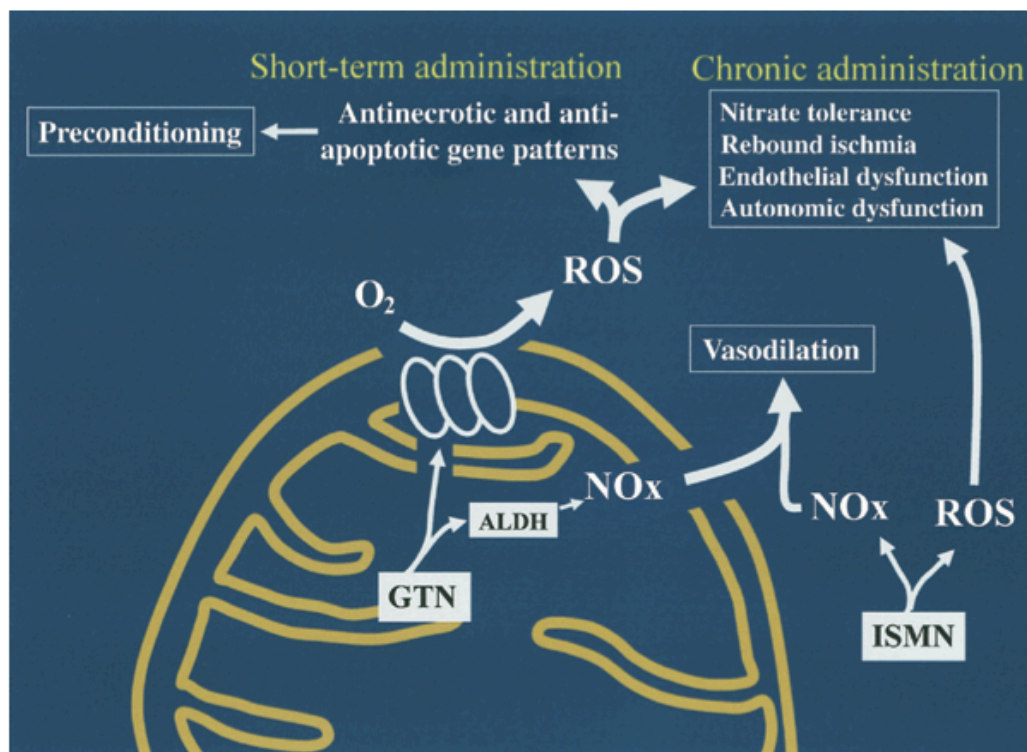


VIEWPOINT

Nitrate-Induced Toxicity and Preconditioning

A Rationale for Reconsidering the Use of These Drugs

Tommaso Gori, MD, PhD,*† John D. Parker, MD, FACC‡
Siena, Italy; Mainz, Germany; and Toronto, Ontario, Canada



2007 Chronic Angina Focused Update of the ACC/AHA 2002 Guidelines for the Management of Patients With Chronic Stable Angina

J Am Coll Card 2007



EUROPEAN
SOCIETY OF
CARDIOLOGY®

European Heart Journal (2006) 27, 1341–1381
doi:10.1093/eurheartj/ehl001

ESC guidelines

Guidelines on the management of stable angina pectoris: executive summary

The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology

J Am Coll Card 2007

POPPERS



(nitrito di amile)

Antipertensivi

- Alfa bloccanti *iniziare con basse dosi*
- Beta bloccanti *labetalolo, carvedilolo*

Antiarritmici

SOLO PER IL VARDENAFIL

- Tipo 1A *chinidina, procainamide*
- Tipo 3 *sotalolo, amiodarone*
- Sindrome QT lungo, ipokaliemia

Antiaggreganti e anticoagulanti

Precauzione in pazienti ad elevato rischio cardiovascolare e in terapia multipla antiaggregante e anticoagulante

SOPRATTUTTO PER SILDENAFIL

Altri

- Inibitori CYP450
ritonavir, saquinavir, indinavir
- Inibitori del CYP3A4
ketoconazolo, eritromicina, cimetidina



Comorbilità

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Effetti collaterali

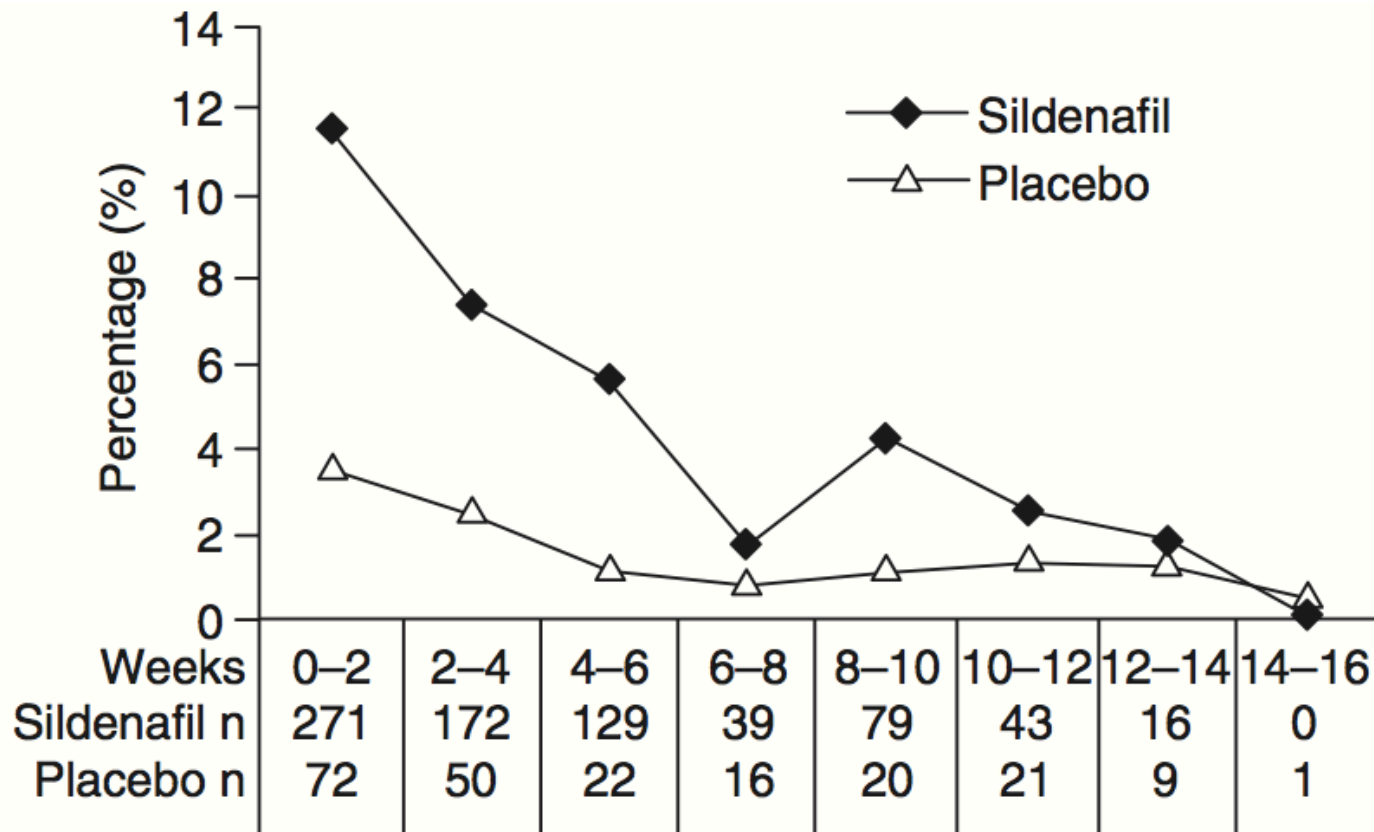


Effetti collaterali comuni



- cefalea **10%**
- vampate di calore **10%**
- dispepsia
- disturbi della vista
- congestione nasale **<3%**
- capogiri
- alterata percezione dei colori **<3%**

Durata degli effetti collaterali



Tadalafil 5 mg: terapia cronica

Benign Prostatic Hyperplasia

Efficacy and Safety of Tadalafil Once Daily in the Treatment of Men With Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia: Results of an International Randomized, Double-Blind, Placebo-Controlled Trial

Hartmut Porst^{a,}, Edward D. Kim^b, Adolfo R. Casabé^c, Vincenzo Mirone^d, Roberta J. Secrest^e, Lei Xu^e, David P. Sundin^e, Lars Viktrup^e, for the LVHJ study team*

	Placebo (N = 164), n (%)	Tadalafil 5 mg (N = 161), n (%)
Subjects with ≥ 1 TEAE	36 (22.0)	42 (26.1)
TEAEs [*] :		
Headache	1 (0.6)	6 (3.7)
Back pain	4 (2.4)	5 (3.1)
Subjects discontinuing because of an AE [†]	1 (0.6)	3 (1.9)**
Subjects with ≥ 1 SAE [‡]	0 (0)	2 (1.2)**
Subjects with ≥ 1 treatment-emergent positive orthostatic test ¹	38 (23.2)	31 (19.3)









La terapia medica per la DE è sicura?

<http://goo.gl/YBm3E>