MyoSTIM ED

bioelectric treatment of erectile dysfunction

Scientific and Clinical Rationale

Although erectile dysfunction does not present risks to the individual's life, it can provoke a series of disorders, such as decreased self-esteem, increased anxiety, social relationship impairment and depression, among others. Such disorders may cause repercussions on the general health of the patient.

This is the reason why our team worked in the Complete Solution for ED.

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Souza J. Sexuality in old age: A Discussion about aids, aging and medicines for erectile dysfunction. J bras Doenças Sex Transm 2008; 20(1): 59-64.

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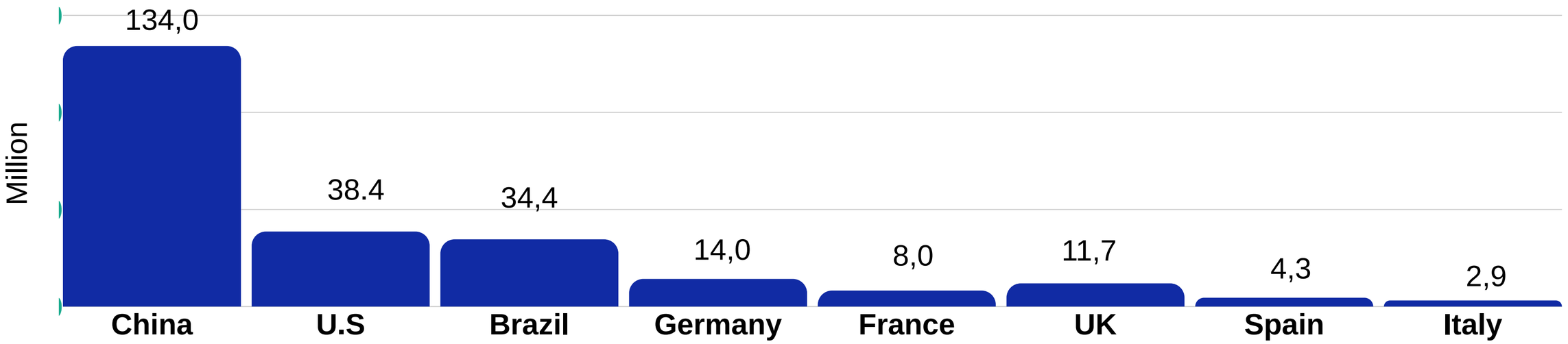
Erectile dysfunction is a global issue projected to affect 332 million people by 2025

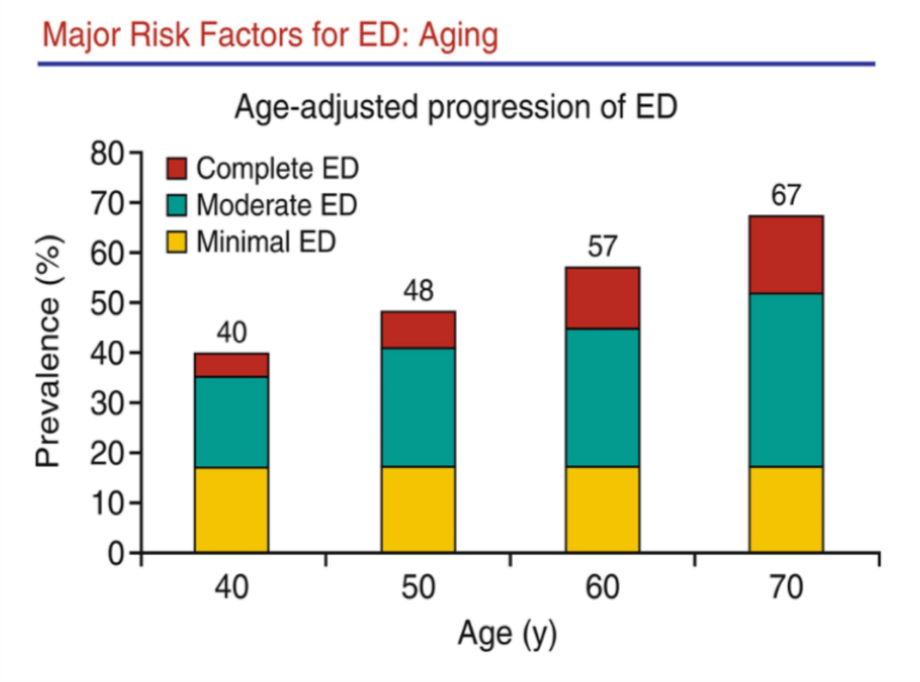


Junior, 2002; Zhag, 2017; Hallanzy,2019; Giullinano, 2002; McKinlay, 2000; Kessler, 2017

*Reporting by market may vary based on survey methodology, willingness to admit sexual issues, age distribution of population, etc.

ERECTILE DYSFUNCTION IS ASSOCIATED WITH AGING, CHRONIC DISEASES, MEDICATIONS AND BEHAVIORAL HEALTH

Erectile dysfunction is exceedingly common, affecting 35-40 million Americans.



- Hypertension (33.1 million)
- Diabetes (15.3 million)[3]
- Cardiovascular disease (14.9 million)[4]
  - Coronary artery disease, stroke
- Depression
- Chronic bronchitis & emphysema (4.8 million)[5]
- Neurological disease
  - Parkinson's Disease, Multiple Sclerosis
- Medications for hypertension, diabetes, etc.
- Psychological factors (10-20% of cases)
- Post-surgical complications
  - Radical prostatectomy, TURP

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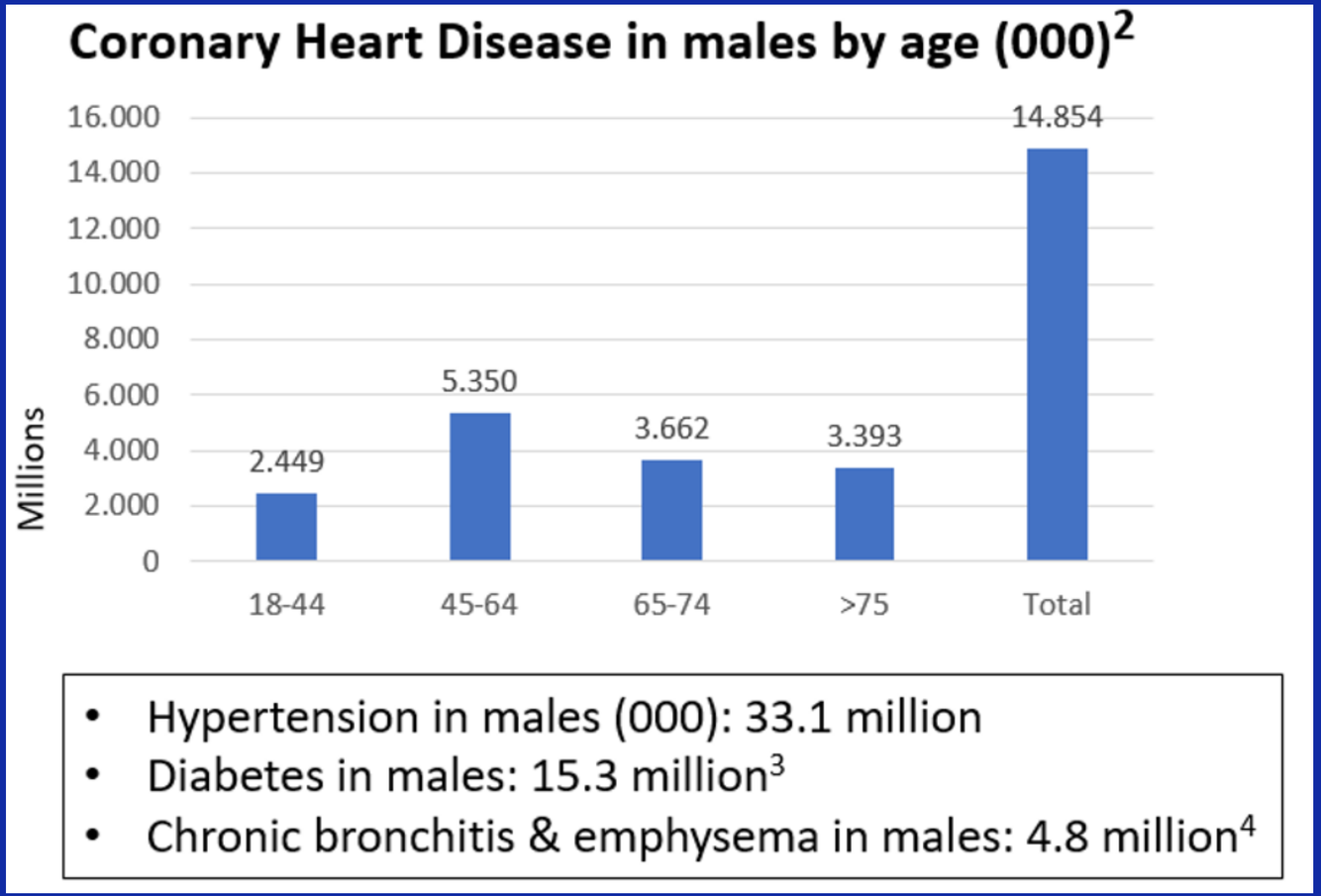
[1]Pathophysiology of Erectile Dysfunction, Penn Clinical Manual of Urology https://www.progressivemenshealth.com/age-major-risk-factor-erectile-dysfunction-2/. [2]Massachusetts Male Aging Study [3]https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf [4]CDC National Health Interview Survey https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2017_SHS_Table_A-1.pdf [5]https://www.healthline.com/health/copd/facts-statistics-infographic#1

Erectile dysfunction occurs in relatively young patients with diabetes and coronary artery disease

- **15.3 million American males have diabetes; approximately 800k million new cases per year.**
- **The occurrence of ED is 10–15 years earlier in men with diabetes; moreover, ED is more severe and less responsive to oral drugs in diabetes, leading to reduced quality of life.**
- **In the Massachusetts Male Aging Study, diabetic men showed a threefold probability of having ED when compared to men without diabetes; moreover, the age-adjusted risk of ED doubled in diabetic men when compared to those without diabetes.**



Pathophysiology of Erectile Dysfunction, Penn Clinical Manual of Urology https://www.progressivemenshealth.com/age-major-risk-factor-erectile-dysfunction-2/. Feldman HA, Johannes CB, Derby CA, et al. Erectile dysfunction and coronary risk factors: Prospective results from the Massachusetts male aging study. PrevMed 2000; 30:328. 2CDC https://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2017_SHS_Table_A-1.pdf
3https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf 4 https://www.healthline.com/health/copd/facts-statistics-infographic#1

Erectile dysfunction is NOT always about aging; i.e., may occur for non-organic reasons

ERECTILE DYSFUNCTION IN YOUNGER MEN

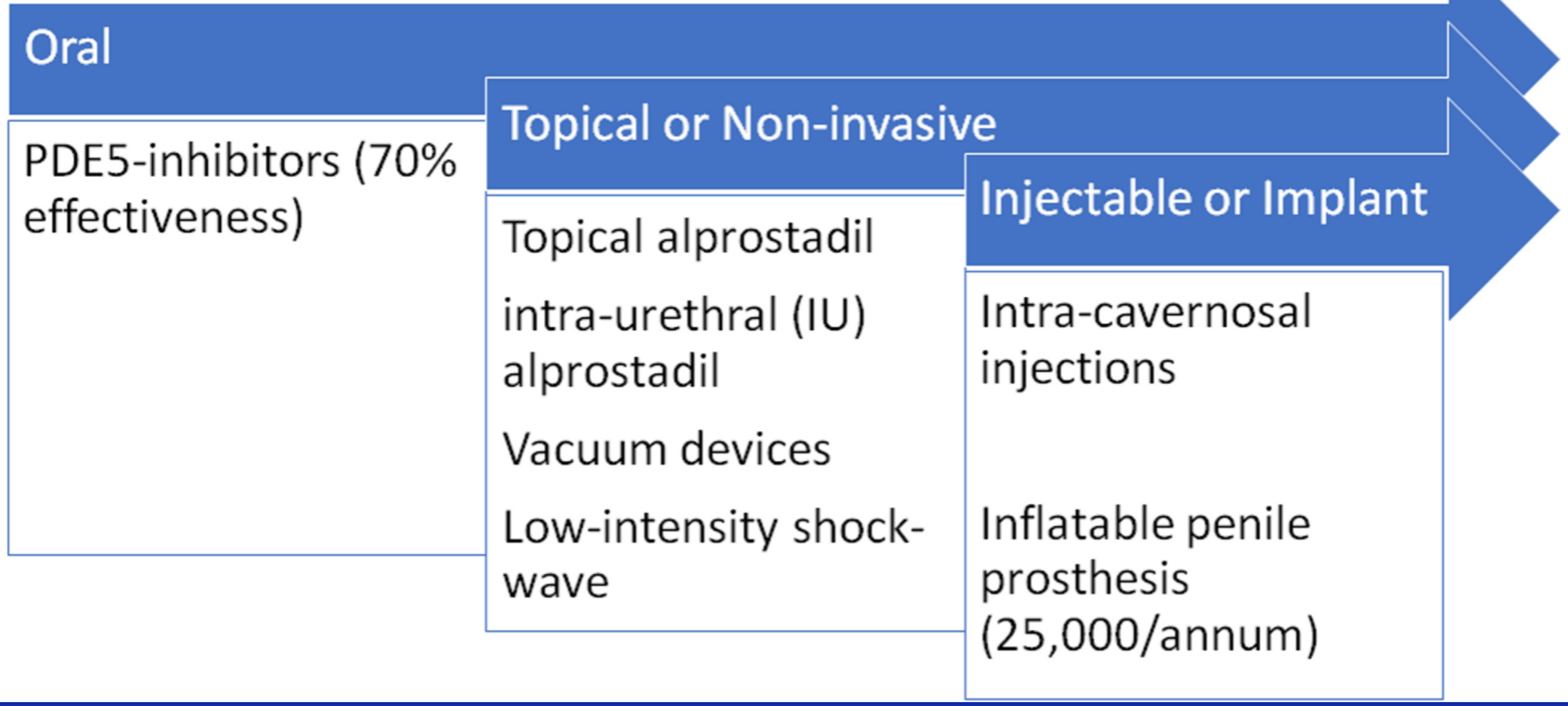
OFTEN RESULT FROM PSYCHOLOGICAL CAUSES LIKE TENSION AND ANXIETY. OTHER FACTORS INCLUDE: DEPRESSION, FATIGUE, STRESS, FEELINGS OF INADEQUACY, PERSONAL SEXUAL FEARS, REJECTION BY PARENTS OR PEERS, SEXUAL ABUSE IN CHILDHOOD

PORN ADDICTION

RESEARCHERS FOUND A STATISTICAL RELATIONSHIP BETWEEN PORN ADDICTION AND SEXUAL DYSFUNCTION, ABOUT 26 % SAID THEY VIEW PORNOGRAPHY LESS THAN ONCE A WEEK, WHILE 25 % SAID ONE TO TWO TIMES A WEEK, AND 21 % SAID THREE TO FIVE TIMES WEEKLY. AT THE OTHER EXTREME, 5 % SAID THEY USE PORNOGRAPHY SIX TO 10 TIMES A WEEK, AND 4 % MORE THAN 11 TIMES A WEEK

https://www.webmd.com/sex/news/20170512/study-sees-link-between-porn-and-sexual-dysfunction#1
https://www.webmd.com/erectile-dysfunction/qa/what-causes-erectile-dysfunction-in-younger-men

Alternative treatment modalities may be inappropriate, ineffective or associated with adverse events



Note: Intra-cavernous injections may include phentolamine, papaverine, and alprostadil. It's an invasive procedure that is associated with dropout rates as high as 40%–50% due to pain, priapism, penile fibrosis,hematoma, ecchymosis, or fear of the needle

MyoStim ED targets a large global market with unmet needs

MyoSTIM ED
bioelectric treatment of erectile dysfunction

- Erectile dysfunction is very common, especially in the rapidly aging population with co-morbid cardiovascular disease and diabetes
- Unmet needs are global and remain despite the presence of several treatments (algorithms) in the U.S. and Europe; PDE-5 inhibitors as first line therapy and a range of topicals, devices and procedures as second line therapy
- Patient preferences are integral to product selection and the trade-off between satisfaction and adverse events
- Myostim represents a potentially significant and differentiated entrant targeting the pathophysiology of erectile dysfunction with proprietary signals

MyoSTIM ED
bioelectric treatment of erectile dysfunction

Scientific Basis of Competitive Advantage

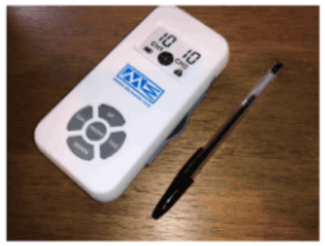
- Bioelectrical stimulation (BES) is applied clinically for treating a variety of disorders, such as wound healing
- BES is based on safely modulating various electrical signals to stimulate or inhibit the expression of specific key genes, to counteract the known molecular patho-physiology of ED and not just induce vasodilation

- Effects may potentially repair for a long-term solution: vasculature, pressure (vasoconstriction/dilation balance), nerves and penile corporal histopathology
- The first ED treatment to not just address temporary blood flow improvement but to treat muscle and nerve damage recovery

Current Electrode

Current Portable Device

Future Portable Device Look



MYOSTIM IS THE ONLY PRODUCT TARGETING THE SPECIFIC PATHOPHYSIOLOGY OF AGING AND ERECTILE DYSFUNCTION

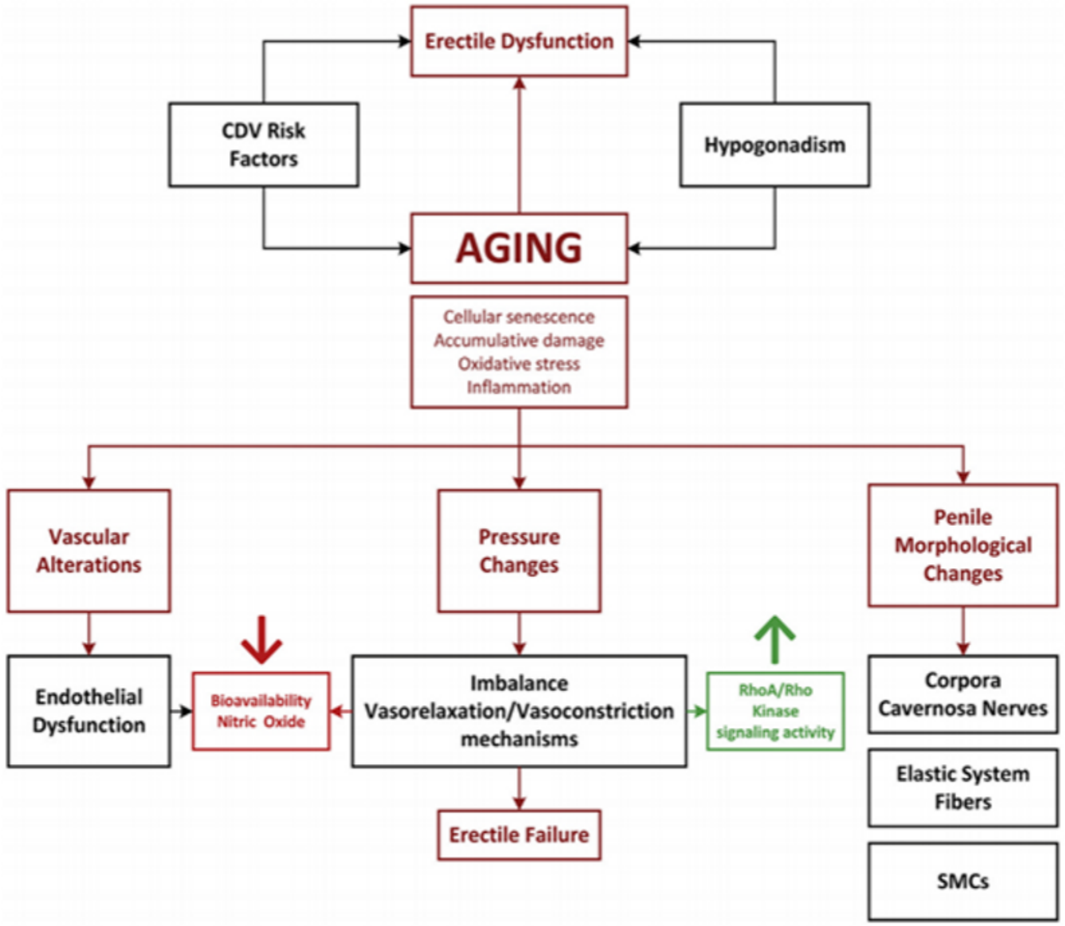


Figure 1. There are morphologic and physiologic mechanisms involved in the process of aging that play a key role in the development of sexual dysfunction. Cardiovascular risk factors and hypogonadism have a critical impact during the establishment of the aging process that could also lead to erectile dysfunction. Cellular senescence could induce oxidative stress and hence inflammation that with time leads to accumulative damage. With this overview, the main mechanisms of the aging process that drive toward erectile dysfunction include vascular and physiologic alterations and penile morphologic changes.

MyoSTIM ED

bioelectric treatment of erectile dysfunction

Proprietary precise bioelectric signaling affects local physiology

SDF-1 for stem cell homing

IGF-1 for DNA repair

Follistatin for muscle repair

eNOS for dilating blood vessels

VEGF, PDGF, EGF, HIF1a, CXCL5 and SDF1

DNA REPAIR AND ANTI AGING

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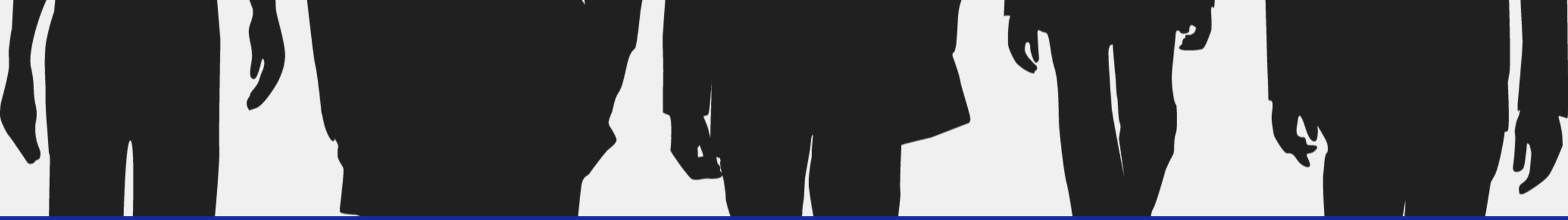
bioelectric treatment of erectile dysfunction

The regeneration of smooth muscle cavernosa by BES should result in the *spontaneous return* of erectile[1] in contrast to the oral, injection therapy and the use of a vacuum pump where the patient is treatment dependent[2]

1. Stief CG. Wolrd J Urol (1995) 13:243-247.
2. Feys H. PHYS THER. 2003; 83:536-543.

- **Klotho:** the secretory Klotho results in the reduction in TNFα and IFNγ, which can show anti-inflammatory properties. Klotho can interact with Wnt, which results in the inhibition of Wnt pathway activity, thus inhibiting the aging process[3].
- **IGF-1:** improve nerve regeneration and neuromuscular recovery[4].
- **Follistatin:** promotes muscle regeneration and recovery. Follistatin is able to accomplish accelerated muscle restoration not only by leveraging the regenerative effects of myostatin inhibition but potentially through modulating inflammation[5].

3. Neurological Sciences (2018) 39:1677–1682 https://doi.org/10.1007/s10072-018-3496-x
4. Muscle Nerve. 2010 March ; 41(3): 335–341. doi:10.1002/mus.21485.
5. Journal of Pharmacology and Experimental Therapeutics · March 2014 DOI: 10.1124/jpet.113.211169



BES FOR ED HAS BEEN STUDIED FOR MANY YEARS

Vol. 170, No. 2, 1990 BIOCHEMICAL AND BIOPHYSICAL

July 31, 1990 Pages 843-850

NITRIC OXIDE AND CYCLIC GMP FORMATION UPON ELECTRICAL FIELD STIMULATION CAUSE RELAXATION OF CORPUS CAVERNOSUM SMOOTH MUSCLE

Loui s 0 . Ignarro, Peggy A. Bush, Georgette M. Buga, Kei th S. Wood
Jon M. Fukuto and Jacob Rajfer*

Department of Pharmacology and Divi sion of Urology, *Department of Surgery University of Cal iforni a, Los Angeles, Cal iforni a 90024

Received June 18, 1990

SUMMARY : In the presence of functional adrenergic and chol inergi c blockade, el ectrical fiel d stimulation relaxes corpus cavernosum smooth muscle by unknown mechanisms . We report here that el ectrical field stimulation of i sol ated stri ps of rabbit corpus cavernosum promotes the endogenous formation and rel ease of ni tric oxide (NO) , ni trite, and cycl ic GMP. Corporal smooth muscle relaxation in response to el ectrical field stimul ation, in the presence of

대한남성과학회지 : 제 18권 제 2호 2000년 8월
Kor J Androl. Vol 18, No. 2, August 2000

발기부전 환자에서 전기자극치료효과

동아대학교 의과대학 비뇨기과학교실
길명철 · 옥윤철 · 강태우 · 정경우

=Abstract=

The Effect of Treatment of Erectile Dysfunction with Electrical Stimulation

Myung-Cheol Gil, Yun-Chul Ok, Tae-Woo Kang and Gyung-Woo Jung

From the Department of Urology and the Institute of Andrology, Dong-A university, Pusan, Korea

World J Urol (1995) 13:243–247

Free paper

World Journal of *Urology*

Functional electromyostimulation of the corpus cavernosum penis – preliminary results of a novel therapeutic option for erectile dysfunction*

C. G. Stief[1], E. Weller[2], T. Noack[3], M. Djamilian[1], M. Meschi[1], M. Truss[1], and U. Jonas[1]

[1] Department of Urology, Medizinische Hochschule Hannover, D-30623 Hannover, Germany
[2] Department of Physical Medicine and Rehabilitation, Medizinische Hochschule Hannover, D-30623 Hannover, Germany
[3] Department of Physiology, University of Marburg, Marburg, Germany

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MYOSTIM ED CLINICAL TRIALS

Preliminary data suggestive of MyoStim ED safety and efficacy
Statistical significance obtained in 22-patient trial!

UIR: Your Sexual Medicine Journal (2018) 30:97–101
https://doi.org/10.1038/s41443-018-0024-8

ARTICLE

Check for updates

An initial study on the effect of functional electrical stimulation in erectile dysfunction: a randomized controlled trial

Cristiane Carboni[1] · Alexandre Fornari[1] · Karoline C. Bragante[1] · Marcio A. Averbeck[1] · Patrícia Vianna da Rosa[1] · Rodrigo Della Mea Plentz[1]

Received: 7 April 2015 / Revised: 27 December 2017 / Accepted: 12 February 2018 / Published online: 22 May 2018

Abstract

Erectile dysfunction (ED) affects approximately 150 million men worldwide. Functional electrical stimulation (FES) therapy has shown a high regenerative capacity for smooth muscle cells and, therefore, is being increasingly adopted. FES can be a beneficial treatment option when the cause of ED is related to degeneration of cavernous smooth muscle. To evaluate the

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MYOSTIM ED CLINICAL TRIALS

COLLECTION | 10 MAY 2019

IJIR: Your Sexual Medicine 30th Anniversary Collection

IJIR: Your Sexual Medicine Journal is one of the leading journals in the field of sexual medicine and it has been a privilege to serve as Editor-in-Chief since 2018. I would like to express my sincere gratitude to our readers, authors, reviewers and editorial board members for their ongoing support to our journal.

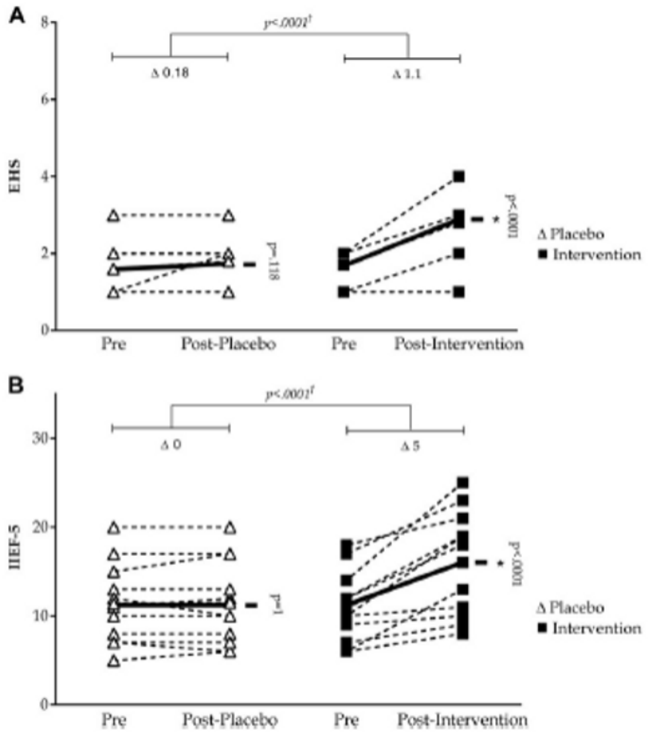

Fig. 2 Individual changes in the EHS score (**a**) and IIEF-5 score (**b**)

Table 2 Comparison between groups and intra groups regarding EHS and IIEF-5 questionnaire

	Placebo			Intervention		
Variable	Pre	Post	Diff	Pre	Post	Diff
EHS	1.64 ± 0.19	1.82 ± 0.17	.18	1.73 ± 0.13	2.82 ± 0.3*	1.1†
IIEF-5	11.4 ± 1.3	11.4 ± 1.4	0	11 ± 1.2	16 ± 1.7*	5†

Value are Mean ± SEM

Generalized Estimating Equations Model was used to test for significant differences at different visits and time points according to each treatment

EHS erection hardness score, *IIEF-5* International index of erectile function-5, *Diff* mean difference post-treatment

*$p < .0001$ from Pre in each questionnaire, †$p < 0.05$ Comparison between questionnaire changes

An initial study on the effect of functional electrical stimulation in erectile dysfunction: a randomized controlled trial. IJIR: Your Sexual Medicine Journal (2018) 30:97–101

ELECTROSTIMULATION APPEARS SAFE AND EFFECTIVE FOR POST-PROSTATECTOMY ED

PD28-03

EFFECTS OF FUNCTIONAL ELECTROSTIMULATION ON ERECTILE FUNCTION RECOVERY FOLLOWING BILATERAL NERVE-SPARING RADICAL PROSTATECTOMY: A RANDOMIZED SHAM-CONTROLLED STUDY

Ana Paula Bispo, Scheila Nascimento, Roberto Soler, Sao Paulo, Brazil*

INTRODUCTION AND OBJECTIVES: To evaluate the effect of functional electrostimulation (FES) as a penile rehabilitation procedure on the erectile function (EF) of patients following nerve sparing radical prostatectomy (NSRP).

METHODS: This was a prospective, blind, randomized, sham-controlled trial. The study included men $\leq$ 70 yr undergoing radical prostatectomy with bilateral preservation of the neurovascular bundle, with previous unassisted normal EF (International Index of Erectile Function, Erectile Function domain [IIEF-EF] score $\geq$ 26); total PSA $<$ 10 ng/mL and Gleason score $\leq$ 7. Patients were randomly assigned, in a 1:1 ratio, to undergo FES or sham procedure. Penile rehabilitation was performed for 6 months, twice a week, during 30 minutes. Patients were evaluated at 1, 3, 6, 9 and 12 months after the start of the procedures. The primary endpoint was proportion of patients with IIEF-EF score $\geq$ 22 after 12 months of the start of treatment. Secondary endpoints included rate of positive responses to Sexual Encounter Profile (SEP) questions 2 and 3 and to Global Assessment Question (GAQ) questions 1 and 2.

RESULTS: Twenty and three patients were randomized to FES and 26 to sham. After 12 months of the start of the study procedures 52.2% and 19.2% of patients reached IIEF-EF score $\geq$ 22 in FES and sham groups, respectively ($p = 0.016$). This effect was also observed in other endpoints (table 1). A significantly higher proportion of patients in FES group compared to sham group had positive responses to SEP2 and GAQ1 from the 6th month to the end of the study. There was numerical, but no statistical, difference in the rate of SEP3 and GAQ2 positive responses between the groups. No adverse events related to FES were reported by patients.

CONCLUSIONS: Functional electrostimulation was efficacious and safe as a penile rehabilitation procedure in improving recovery of unassisted EF in patients undergoing NSRP. The effect of FES was maintained after cessation of active therapy.

Table 1 – Proportion of patients with IIEF-EF ≥ 22 according to treatment group

	Treatment		
Month	FES (n=23)	SHAM (n=26)	P
1	16.7%	11.8%	1.000
3	26.1%	4.0%	0.044
6	45.5%	15.4%	0.022
9	47.8%	19.2%	0.033
12	52.2%	19.2%	0.016

Source of Funding: Coordination for the Improvement of Higher Education Personnel (CAPES)

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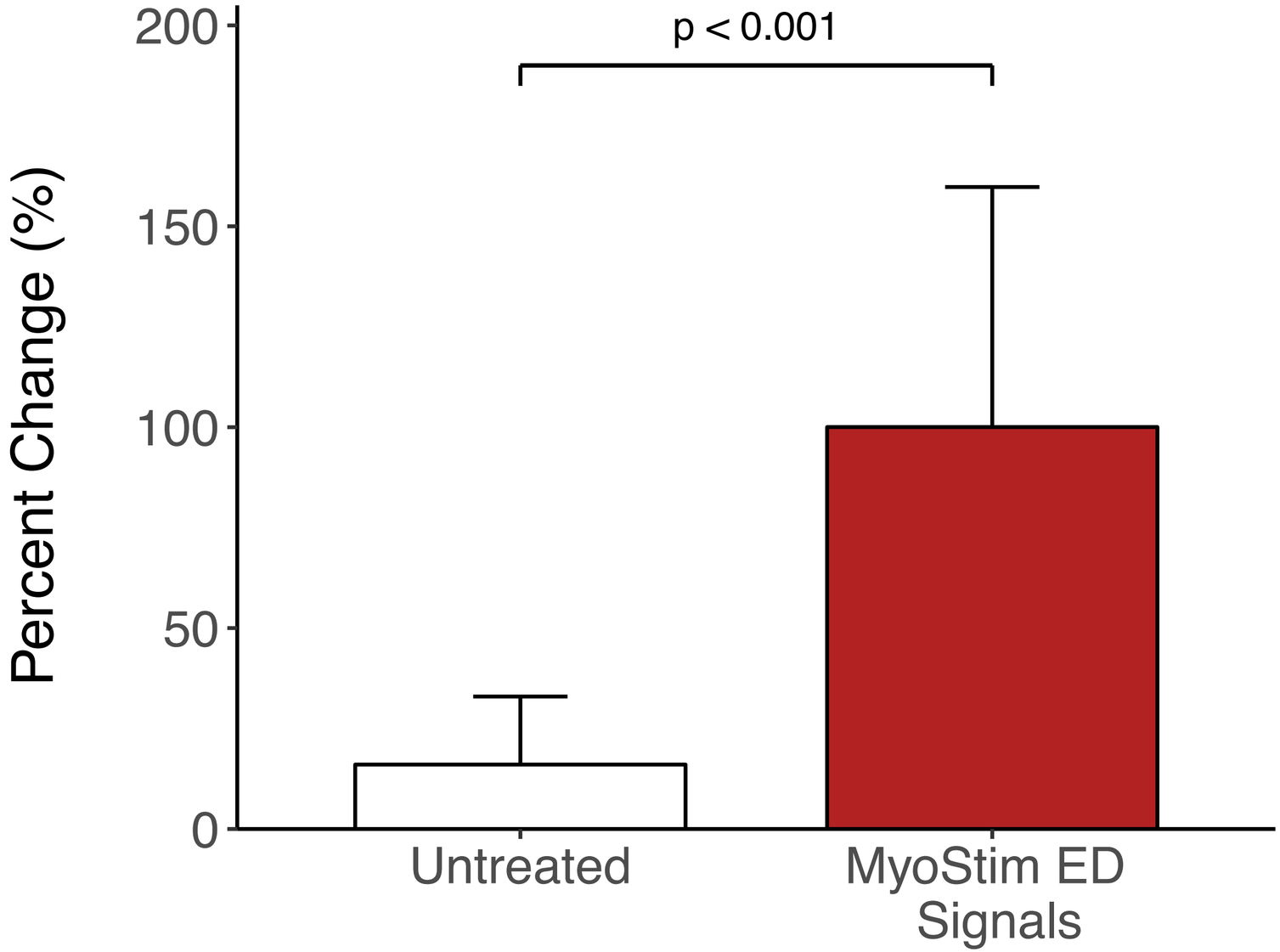
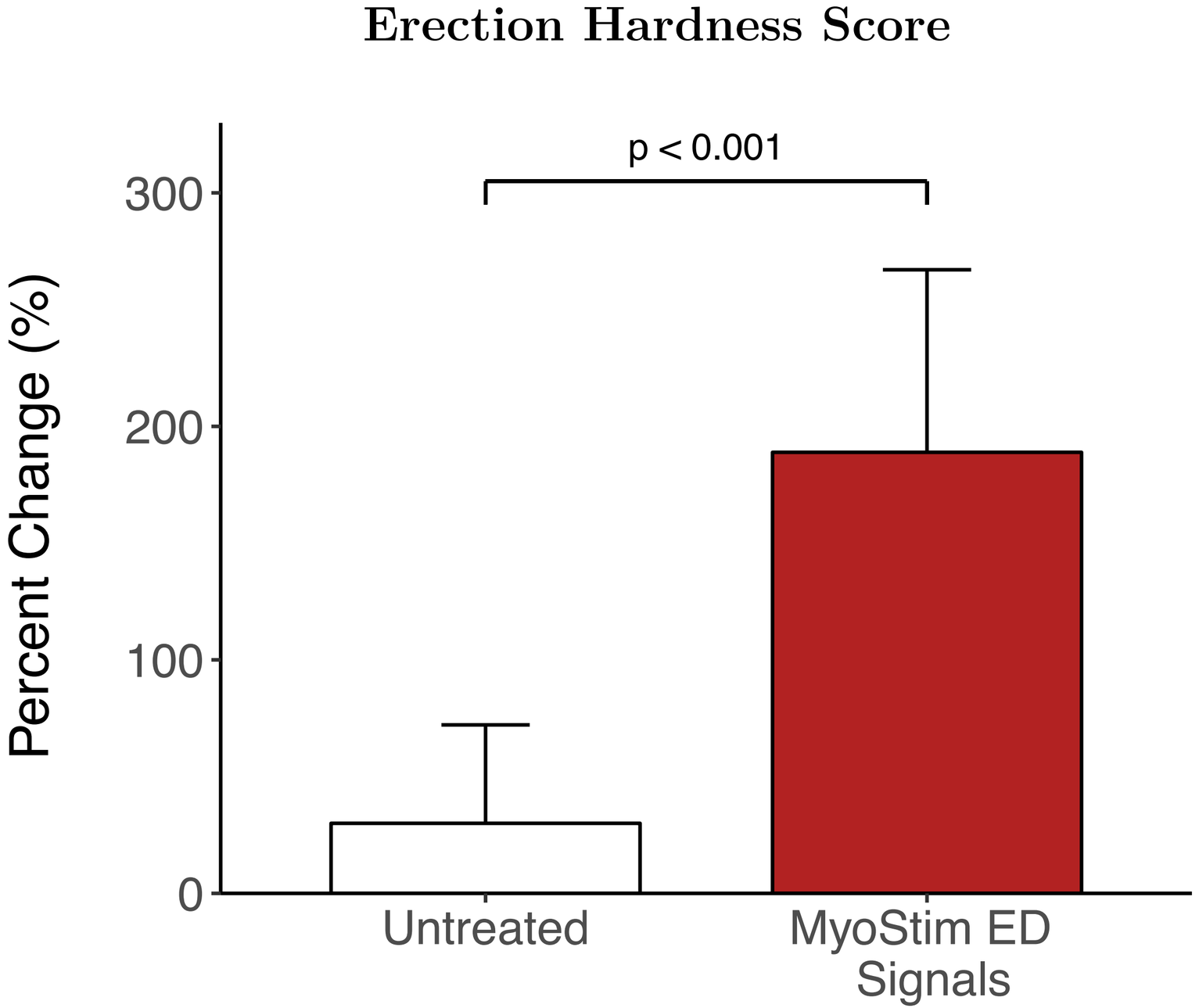
MYOSTIM ED II CLINICAL TRIALS UNPUBLISHED DATA (n=?)

Combine slides 18-19

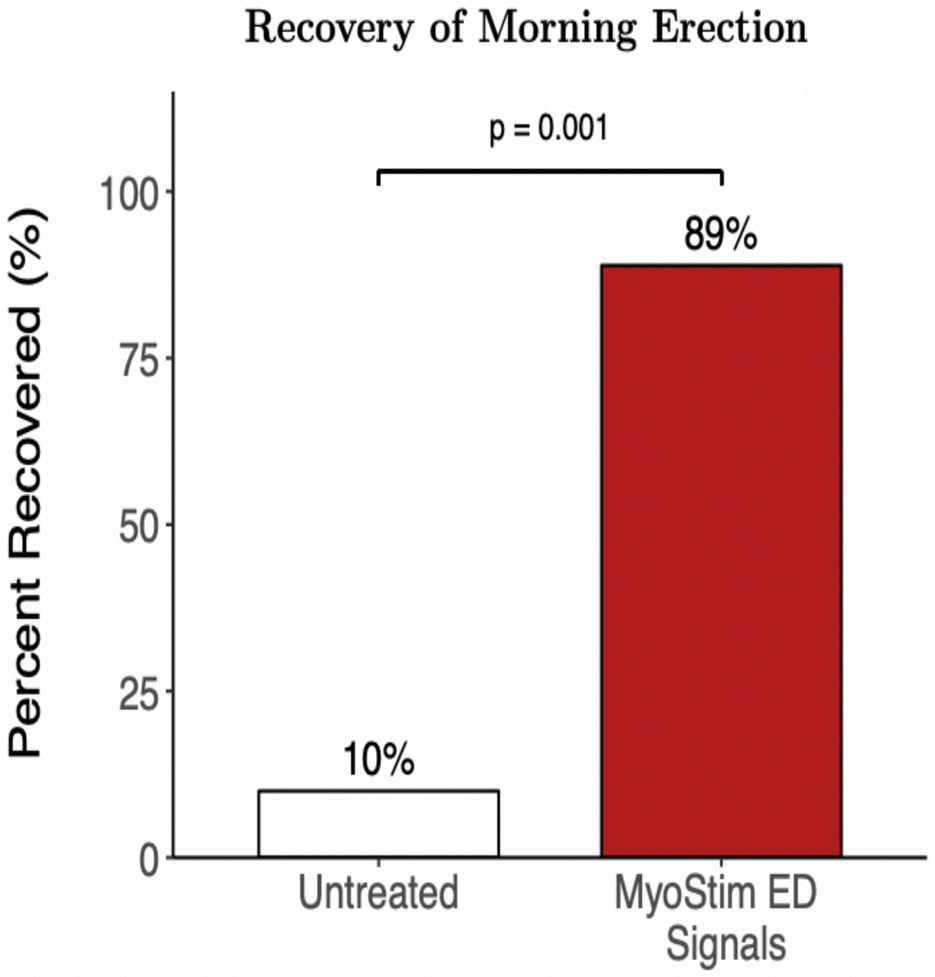
International Index of Erectile Function Questionnaire

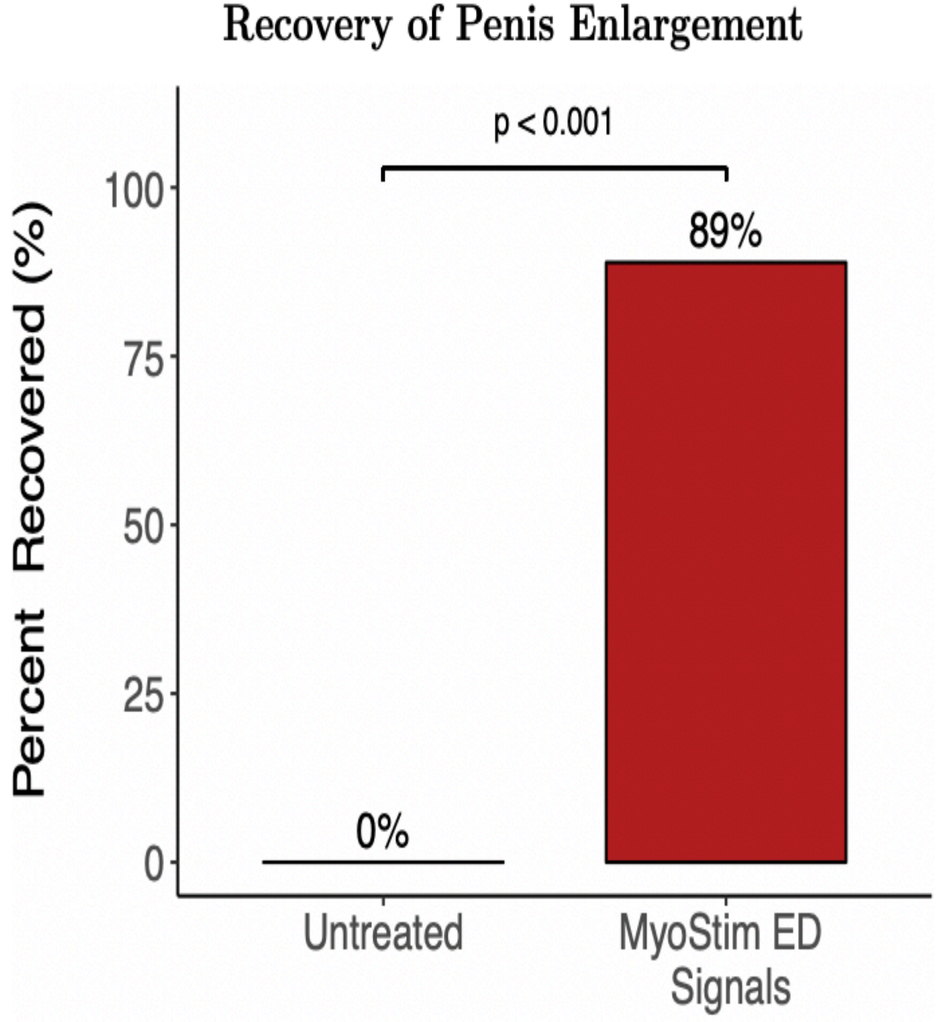



Erection Hardness Score
p < 0.001
300
200
100
0
Percent Change (%)
Untreated
MyoStim ED Signals

Significance re: ED?

MyoStim ED II study results





MyoSTIM ED
bioelectric treatment of erectile dysfunction

Blood Flow + Muscle + Nerve Regeneration. We have the Only Complete ED Solution addressing ALL Causes

HOWARD LEONHARDT, CEO

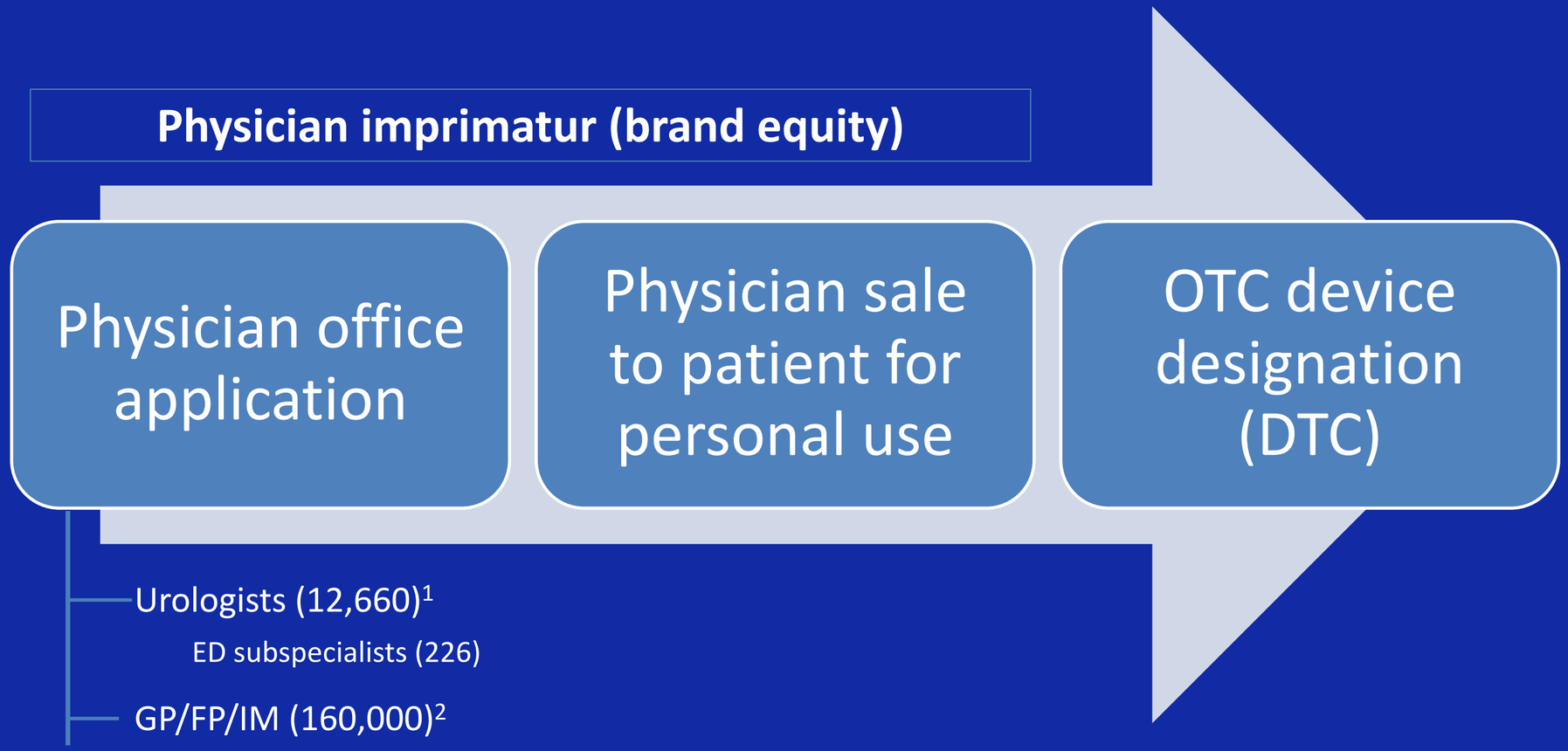
Future MyoStim ED ErectiStim portable device design

MyoSTIM ED

bioelectric treatment of erectile dysfunction

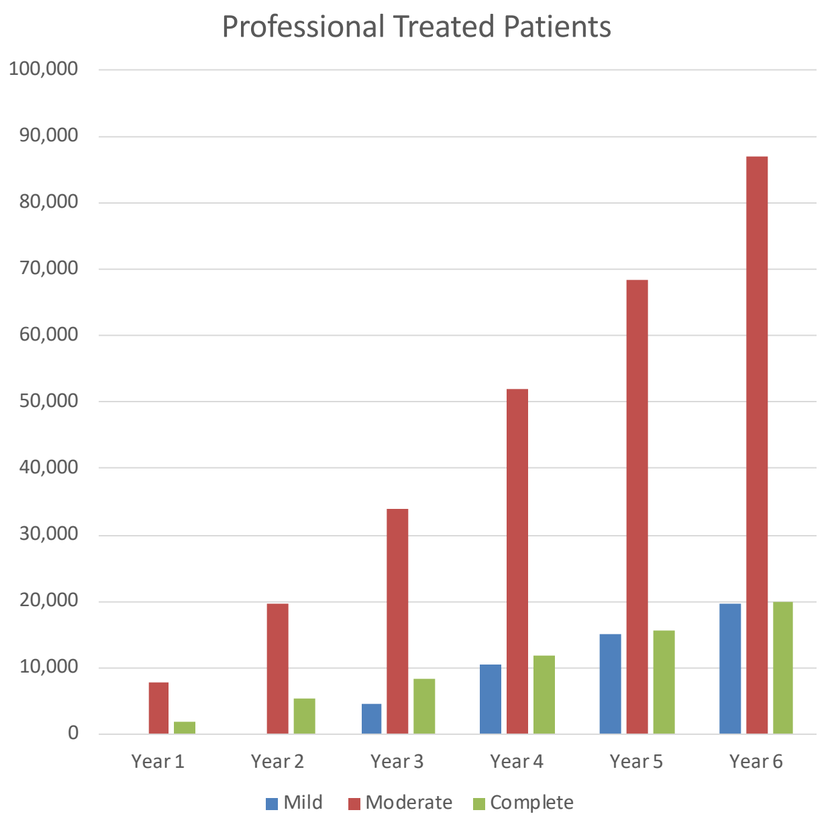
MyoSTIM ED
bioelectric treatment of erectile dysfunction

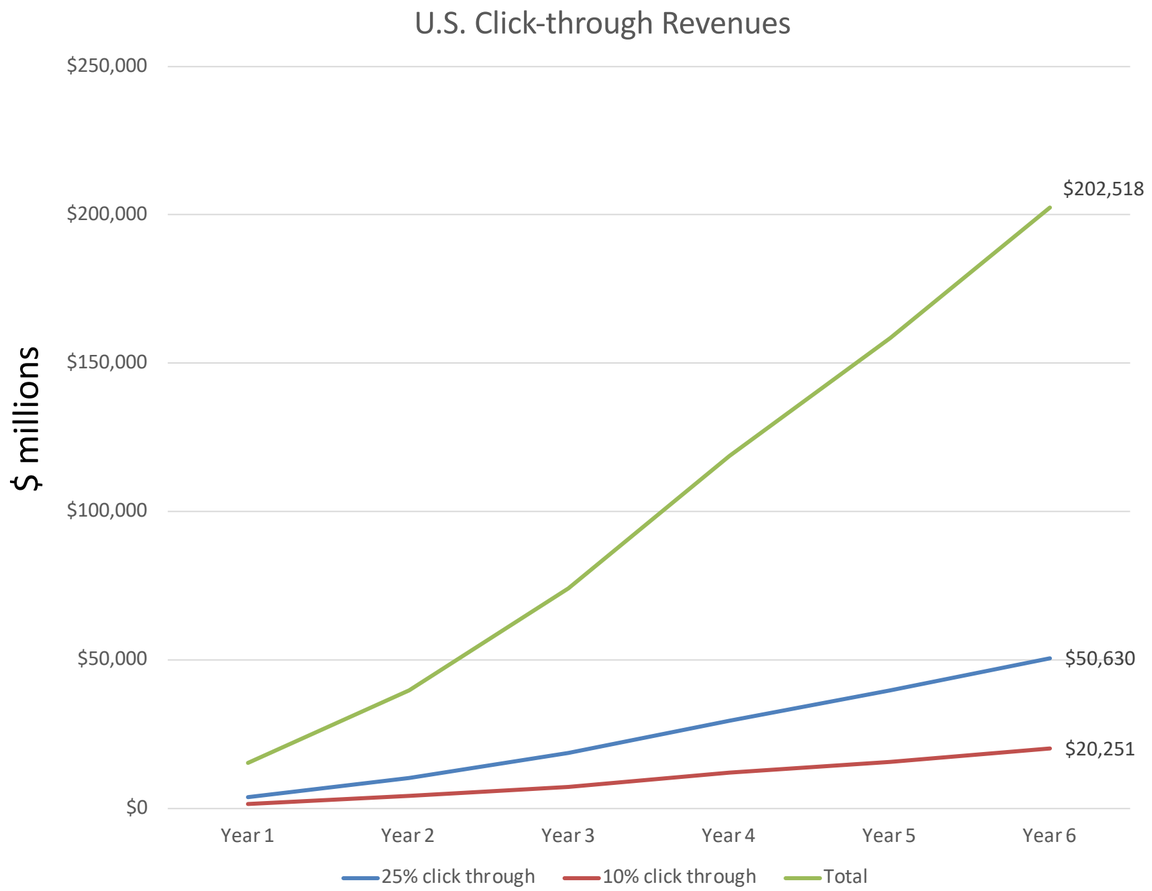
U.S. Business Model



file:///C:/Users/grube/Downloads/2018%20The%20State%20of%20the%20Urology%20Workforce%20Census%20Book.pdf
https://www.ahrq.gov/research/findings/factsheets/primary/pcwork1/index.html#targetText=Of%20the%20624%2C434%20physicians%20in,%2C%20general%20pediatricians%2C%20and%20geriatricians.

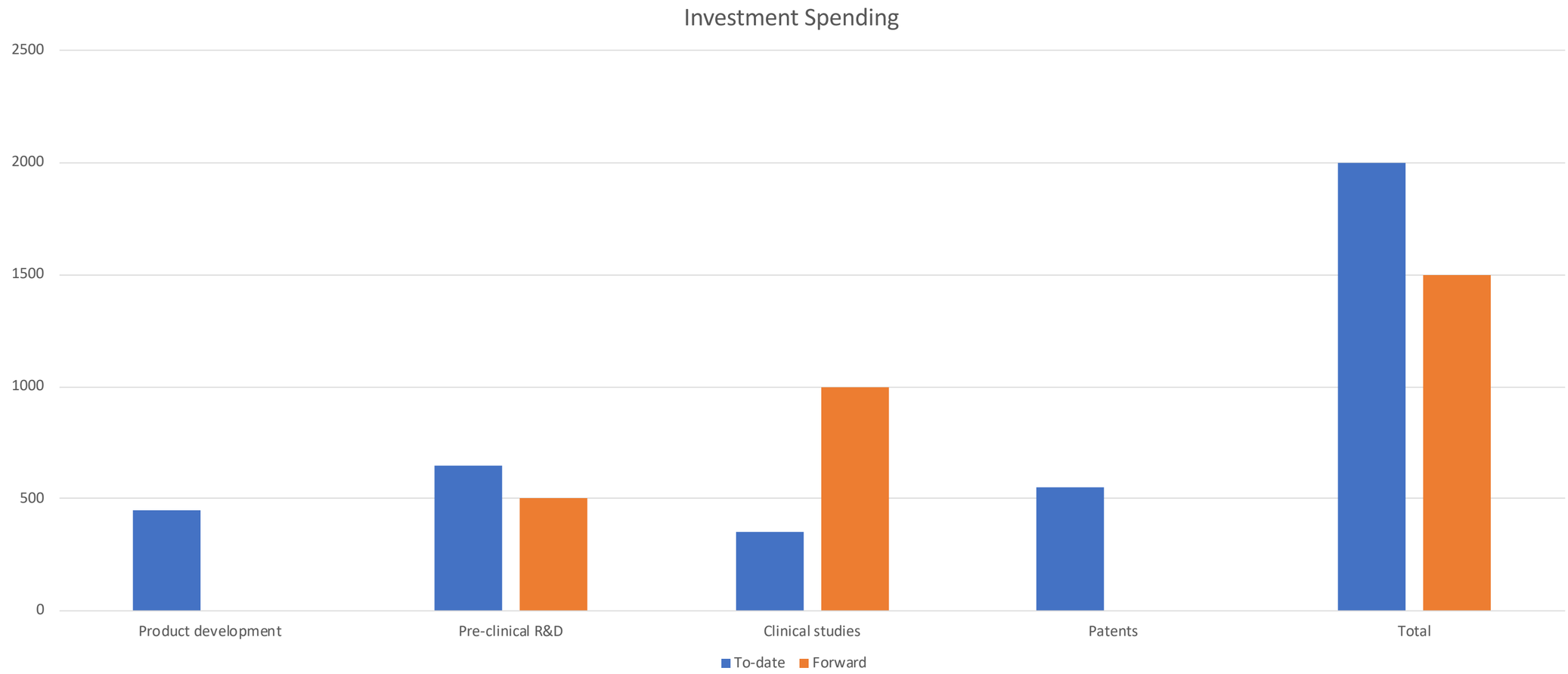
127k Myostim patients – 4.2% of the referral population - at $1,600 per patient ($200 per treatment) generates >$200m in U.S. high margin practice revenues.





*Revenues also generated from premium device sales to urologists and professional sale of “basic” device to patients. *Excludes use of Myostim as commercially available consumer product*. European ED market (patients) > U.S. > Brazil. China has 3-4x number of ED patients as compared to the U.S.

To-date investment spending reflects leverage of technology platform and effective resource use; additional $1.5 million requested



HOWARD LEONHARDT

Executive Chairman and CEO

NESTOR GONZALEZ-CADAVID

Chief Scientific Advisor

CRISTIANE CARBONI

Chief Scientific Officer

LESLIE MILLER

Chief Medical Officer

ALEX RICHARDSON

Vice President

JORGE GENOVESE

Vice President

STUART WILLIAMS

Vice President

PROJECT TEAM

LEADING THE WAY TO CHANGE

LEONHARDT'S LAUNCHPADS
BY CAL-X STARS

12655 W Jefferson Blvd, Los Angeles, CA 90066

LEONHARDT'S
LAUNCHPADS UTAH, INC

370 S, 300 E, Salt Lake City, UT 84111

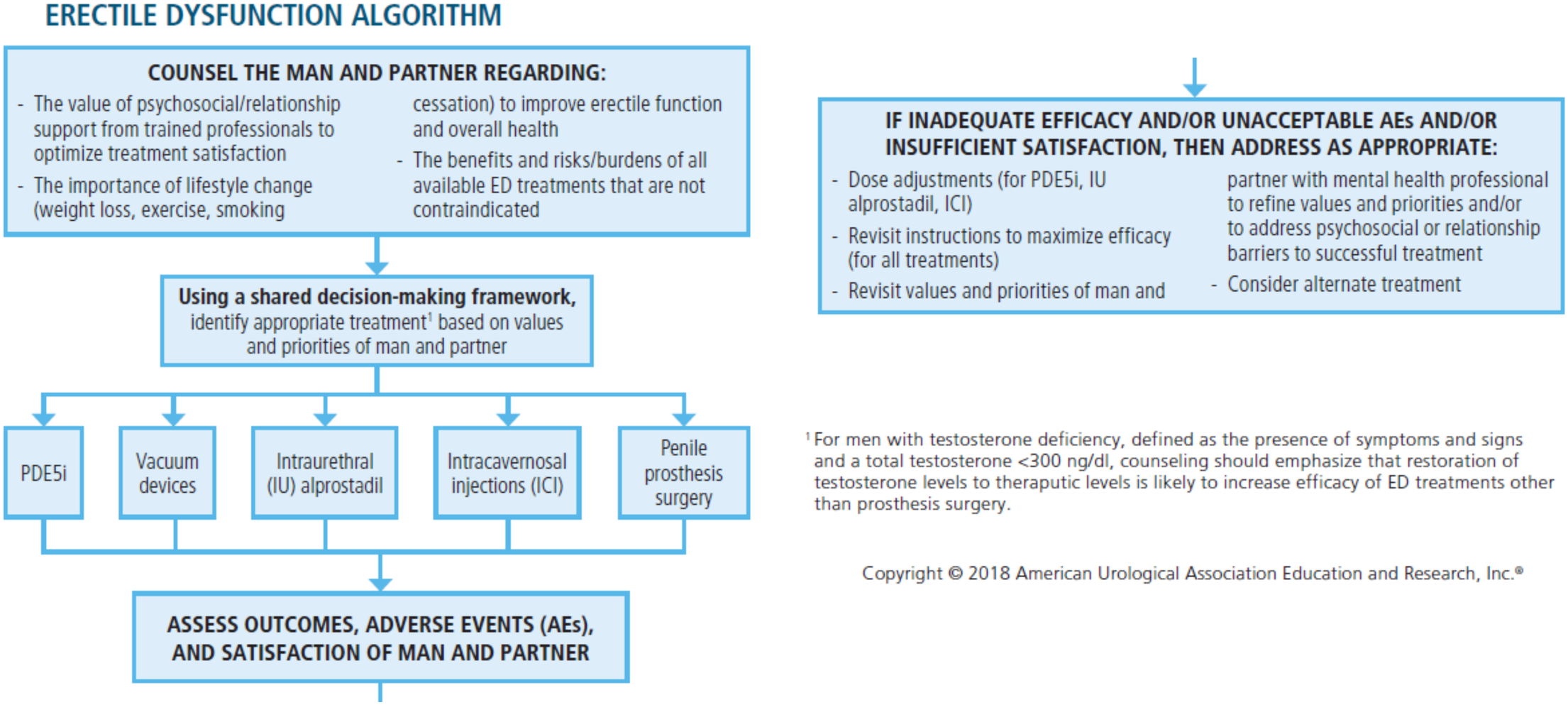
EMAIL ADDRESS

hleonhardt@aol.com

CONTACT INFORMATION

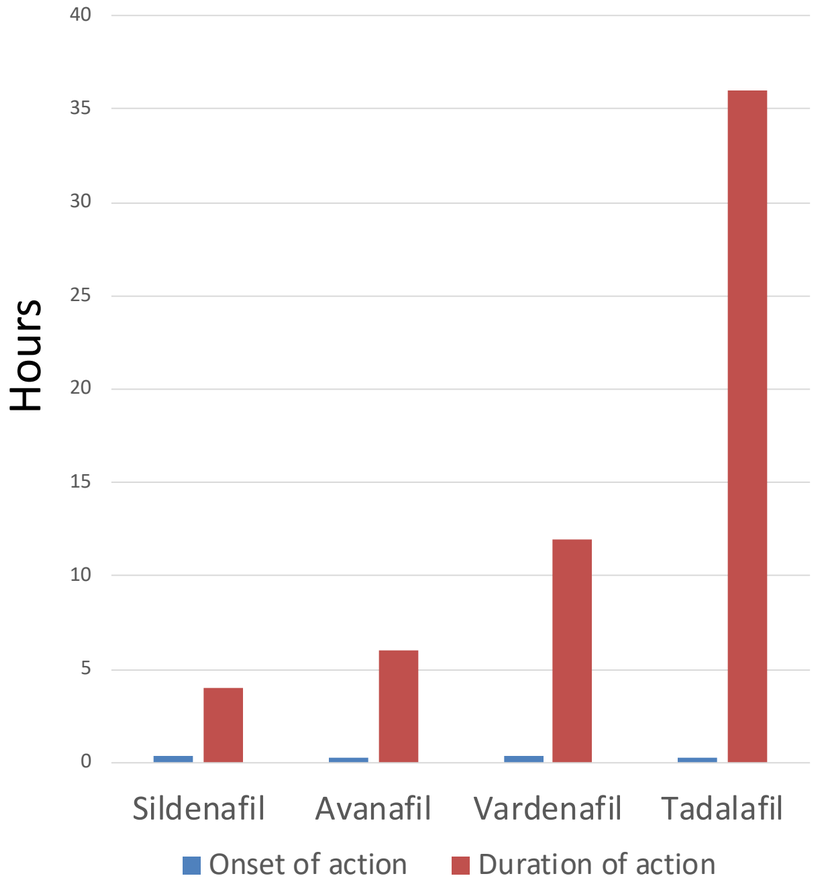
Appendix
Alternative Treatments

Treatment algorithms established by AUA and European Associated of Urology based on severity of ED, outcomes, adverse events and satisfaction. Patient preferences noted



[1] For men with testosterone deficiency, defined as the presence of symptoms and signs and a total testosterone <300 ng/dl, counseling should emphasize that restoration of testosterone levels to theraputic levels is likely to increase efficacy of ED treatments other than prosthesis surgery.

First line of treatment, PDE-5 Inhibitors, do NOT meet the needs of all patients (and are contra-indicated in angina, heart attack and uncontrolled hypertension)



Sildenafil

Viagra

EFFICACY: **69%**

- **Recommended dose:** 50mg, 1 hour before sexual activity, may be adjusted to 100mg or 25mg
- **Bioavailability:** 41%
- **Time to peak plasma levels:** 60 minutes
- **Half-life:** 3–5 hours
- **Onset of action:** 25 minutes
- **Duration of action:** up to 4 hours
- **Food:** high-fat meals delay the time to peak plasma concentration by 60 mins and reduce peak plasma levels by 29%
- **Common side effects:** headache, dizziness, flushing, nasal congestion, nausea, dyspepsia, visual abnormalities

Tadalafil

Cialis

EFFICACY: **75%**

- **Recommended dose:** 10mg, 30 minutes before sexual activity, may be adjusted to 20mg; or 2.5–5.0mg daily
- **Bioavailability:** not determined
- **Time to peak plasma levels:** 120 minutes
- **Half-life:** 17.5 hours
- **Onset of action:** 15–30 minutes
- **Duration of action:** up to 36 hours
- **Food:** rate and extent of absorption are not influenced by food
- **Common side effects:** headache, flushing, nasal congestion, dyspepsia, myalgia and back pain

Vardenafil

Levitra

EFFICACY: **71–80%**

- **Recommended dose:** 10mg, 25–60 minutes before sexual activity. May be adjusted to 20mg or 5mg (film-coated only)
- **Bioavailability:** 15%, (film-coated), 19% (orodispersible)
- **Time to peak plasma levels:** 60 minutes (film-coated), 45–90 minutes (orodispersible)
- **Half-life:** 4-5 hours
- **Onset of action:** 25 minutes
- **Duration of action:** up to 12 hours
- **Food:** high-fat meals delay the time to peak plasma concentration by 60 mins (film-coated) and reduce peak plasma levels by 20% (film-coated) or 35% (orodispersible)
- **Common side effects:** headache, dizziness, flushing, nasal congestion, dyspepsia. Inhibits PDE6, which can cause transient visual abnormalities. Can prolong QTc interval

Avanafil

EFFICACY: **47–59%**

- **Recommended dose:** 100mg, 15 to 30 minutes before sexual activity, may be adjusted to 200mg or 50mg
- **Bioavailability:** not determined
- **Time to peak plasma levels:** 30–45 mins
- **Half-life:** 6–17 hours
- **Onset of action:** 15-30 minutes
- **Duration of action:** up to 6 hours
- **Food:** high-fat meals delay the time to peak plasma concentration by 75 mins and reduce peak plasma levels by 39%
- **Common side effects:** headache, flushing, nasal congestion

Efficacy: Successful intercourse for general ED population
https://www.pharmaceutical-journal.com/download?ac=1072931

Second- and third-line product offerings may impact intimacy, result in local adverse events or be invasive

	Efficacy[1]	Impact on intimacy	Functional recovery period	Immediacy of effect	Sustainability of effect	Adherence	Safety	Cost
First-line								
PDE5 inhibitors	70%	Low	NA	15-30 minutes	4-36 hours	NA	systemic side effects; drug interactions. Contra-indicated CV disease	$25-60/pill x 40 pills/year =$1,000-2,400/annum
Second-line								
Topical alprostadil[2]	39-75%	Moderate	NA	5-30 minutes	1 hour	Dose titration often required	Local burning, pain erythema; resolve 2 hours	
intra-urethral (IU) alprostadil (suppository)	68%	Moderate	NA	5-20 minutes	1 hour	Dose titration may be required	Penile pain (36%), urethral burning and pain (13%), erythema, bleeding	$66/suppository
Vacuum devices	50-80%	High	NA	2-3 minutes	30 minutes	Difficult in obese men; need coordination	Numbness, pain, bruising, painful ejaculation; unnatural feeling	$300-500/unit
Low-intensity shock-wave[3]	60-65% in patient subsets	None	4-16 weeks?	Spontaneous		No standard protocol (6-12 applications x 1-2/week) +/- break	+/- painful during administration	$2,500-6,000; platelet rich plasma extra
MyoStim ED	70-80%	None	4-8 weeks	Spontaneous	>6 months	Two 45 minute office visits per week x 4-8 weeks	No side effects	$1,600
Third-line								
Intra-cavernosal injections	94%	High	2 session injection training	5-15 minutes	<2-4 hours	Penile injection required	wrong injection site, trauma, fibrosis, priapism	$3-6/dose, syringes
Inflatable penile prosthesis (IPP)[1]	80-90%	Moderate	2-4 weeks	NA	Manual controls	Permanent	Infection, bleeding, scar tissue	$20-30,000
[1] Based on patient selection criteria; [2] Pending FDA approval; [3]FDA status unclear								

SHOCK WAVE THERAPY: “INVESTIGATIONAL” AND “EXPERUMENTAL”

- American Urological Association: “investigational” (2018); Sexual Medicine Society of North America “experimental, for use under research protocols” (March 2019)
- Expensive $3-6,000 for treatment; use in “packages” with platelet rich plasma and other adjunctive technologies (e.g., vacuum pumps)
- Use by unscrupulous clinics or spas without evidence-based treatment protocols

- Targets vasculogenic source of ED i.e., atheromatous plaque destruction and not neovascularization, tissue regrowth, etc.
- Poorly designed clinical studies precludes generalizability of results:
  - different treatment protocols (application frequency and duration, therapy duration),
  - patient inclusion/exclusion criteria,
  - types of devices (# shock waves, energy level),
  - Clinical end-points, etc.*
- Pooling of data (n-873) suggests improvement in vasculogenic patients.
- Registry trial planned by GAINSWave

Urology Times; August 6, 2019; 2Int J Impot Res 2019 May;31(3):177-194

ORAL AND TOPICAL ED THERAPIES HAVE LIMITATIONS

Limitations and adverse events of erectile dysfunction (ED) treatment with phosphodiesterase type 5 (PDE5) inhibitors

Limitation	Adverse event
Systemic side effects	• Headache • Visual disturbance • Priapism • Flushing • Muscular pain • Dyspepsia • Sinus congestion
Drug interactions • Inhibitors/inducers of P-450* • Antihypertensive agents • Alpha-blockers** • Nitrates	• Variable efficacy as a result of increased/decreased PDE5 inhibitor plasma concentration • Enhanced variable efficacy • Severe hypotension
Decreased absorption with fatty meals	• Decreased efficacy • Loss of spontaneity

Notes:

*Cytochrome P-450 inhibitors;
**alpha-blockers are used for the treatment of hypertension and benign prostatic hyperplasia.

Study	Design	Patient population	Topical alprostadil dosage	Efficacy	Treatment-related adverse events[a]	
Goldstein et al[37]	Phase I: RCT [1:1]	n=60 31, alprostadil 29, placebo	1% alprostadil + 5% SEPA	Improvement in vaginal penetration: 12/31 (39%) in alprostadil vs 2/29 (7%) in placebo, *P*<0.005	30% - placebo 50% - alprostadil	
Padma-Nathan et al[38]	Phase II: multicenter, double-blind, placebo-controlled RCT [3:1]	n=303 161 (study 1) - mild-to-moderate ED[b] 121, alprostadil 40, placebo 142 (study 2) - severe ED[c] 107, alprostadil 35, placebo	Study 1 - 50, 100, or 200 µg Study 2 - 100, 200, or 300 µg	Change in EF domain of IIEF from baseline: Study 1: 3.7±1.2 in alprostadil vs. −0.8±1.1 in placebo, *P*<0.01 Study 2: 9.4±1.5 in alprostadil vs. 2.7±1.3 in placebo, *P*<0.01	Study 1: 53% - placebo 67% - 50 µg 67% - 100 µg 78% - 200 µg Discontinuation due to AE: 14%	Study 2: 11% - placebo 30% -100 µg 60% - 200 µg 51% -300 µg Discontinuation due to AE: 11%
Padma-Nathan et al[40]	Phase III: multicenter, double-blind, placebo-controlled, long-term[d] RCT [3:1]	n=1,732 1,298, alprostadil 434, placebo	100, 200, or 300 µg	Change in EF domain of IIEF from baseline (*P*<0.001): 1.6 for 100 µg 2.5 for 200 µg 2.4 for 300 µg −0.7 for placebo	12% - placebo 46% - 100 µg 62% - 200 µg 67% - 300 µg Discontinuation due to AE: 2.7%	
Rooney et al[44]	Open label: multicenter, long-term[e] study	n=1,101	Before titration: 1,101, 200 µg After titration: 25, 100 µg	Change in EF domain of IIEF from baseline (*P*<0.001): 13.0 for 100 µg 13.2 for 200 µg 10.1 for 300 µg	Before titration: 23% - 200 µg After titration: 36% - 100 µg 42% - 200 µg 34% - 300 µg Discontinuation due to AE: 4.3%	

Notes:

[a]Treatment-related adverse events (AEs) usually included penile burning, genital pain, and erythema, which resolved within 2 hours;
[b]mild-to-moderate ED defined as IIEF 14-21;
[c]severe EF defined as IIEF <14;
[d]long term defined as 3 months in this study;

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4977016/

VALIDATED SURVEY INSTRUMENTS

IIEF Questionnaire

In a recent study[1],the IIEF Questionnaire was tested in a series of 111 men with sexual dysfunction and 109 age-matched, normal volunteers. The following mean scores were recorded:

FUNCTION DOMAIN	MAX SCORE	CONTROLS	PATIENTS
A. Erectile Function (Q1,2,3,4,5,15)	30	25.8	10.7
B. Orgasmic Function (Q9,10)	10	9.8	5.3
C. Sexual Desire (Q11,12)	10	7.0	6.3
D. Intercourse Satisfaction (Q6,7,8)	15	10.6	5.5
E. Overall Satisfaction (Q13,14)	10	8.6	4.4

Clinical Application

IIEF assessment is limited by the superficial assessment of psychosexual background and the very limited assessment of partner relationship, both important factors in the presentation of male sexual dysfunction. Analysis of the questionnaire should, therefore, be viewed as an adjunct to, rather than a substitute for, a detailed sexual history and examination. The following guide-lines may be applied:

1. Patients with low IEEF scores (<14 out of 30) in Domain A (Erectile Function) may be considered for a trial course of therapy with Sildenafil unless contraindicated. Specialist referral is indicated if this is unsuccessful.

2. Patients demonstrating primary orgasmic or ejaculatory dysfunction (Domain B) should be referred for specialist investigation.

3. Patients with reduced sexual desire (Domain C) require testing of blood levels of androgen and prolactin.

4. Psychosexual counselling should be considered if low scores are recorded in Domains D and E but there is only a moderately lowered score (14 to 25) in Domain A.

IIEF-5 Questionnaire

Over the past six months:

1	How do you rate your **confidence** that you could get and keep an erection?	Very low	Low	Moderate	High	Very high
		1	2	3	4	5
2	When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
		1	2	3	4	5
3	During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most time (much more than half the time)	Almost always/always
		1	2	3	4	5
4	During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
		1	2	3	4	5
5	When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
		1	2	3	4	5

Erection Hardness Score (EHS)

0 – Penis does not enlarge.

- 1 – Penis is larger, but not hard.
- 2 – Penis is hard, but not hard enough for penetration.
- 3 – Penis is hard enough for penetration, but not completely hard.
- 4 – Penis is completely hard and fully rigid.