11 WORKSHOP NAZIONALE CISAI

TORINO 2023

20 • 21 APRILE

CISAI FONDAZIONE ASIA

Le disfunzioni sessuali

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CISAI FONDAZIONE ASIA

I HAVE NO CONFLICTS OF INTEREST

Agenda

- Introduction to Sexual Dysfunctions (SD)
- Gender differences and Sexual Dysfunction
- SD in Women Living With HIV (WLWH)
- SD in Men Living With HIV (MLWH)
- Conclusive Remarks/Practice Points

Agenda

- **Introduction to Sexual Dysfunctions (SD)**
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YEAR 2005
THE *loneliness* OF THE HIV-PHYSICIAN

I cannot approach all these co-morbidities alone !!

How can I manage all these increasing problems ?

- ✓Obesity
- ✓Hypogonadism
- ✓Sexual dysfunction
- ✓Osteoporosis
- ✓Diabetes Mellitus

OUTCOME OF THE MULTIDISCIPLINARY APPROACH TO HIV-INFECTION in the HAART ERA

HIV physicians
+
Non-HIV physicians

One "dear doctor" letter
a single Clinical Report

Clinical Outcome

HIV physicians
+
Non-HIV physicians

Wide spectrum information

Research Outcome

Rochira V *et al.* PLoS ONE 6(12): e28512, 2011

Società Italiana di Andrologia e Medicina della Sessualità

Socio SIAMS dal 1999

- Comitato Newsletter SIAMS dal 2007 al 2011
- Commisione Studi Clinici SIAMS dal 2011 al 2012
- Commissione Scientifica SIAMS dal 2012 al 2014.
- Consiglio Direttivo SIAMS dal 2014 al 2018.
- **Coordinatore Linee Guida SIAMS dal 2018 ad oggi**
- Gruppo KING (Sindrome di Klinefelter) SIAMS

European Academy of Andrology dal 2015

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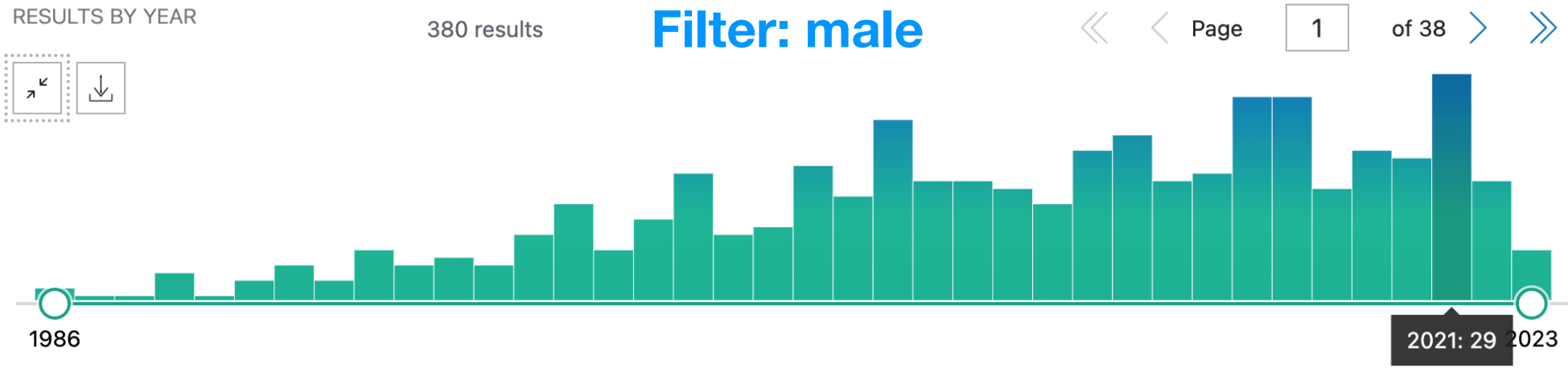
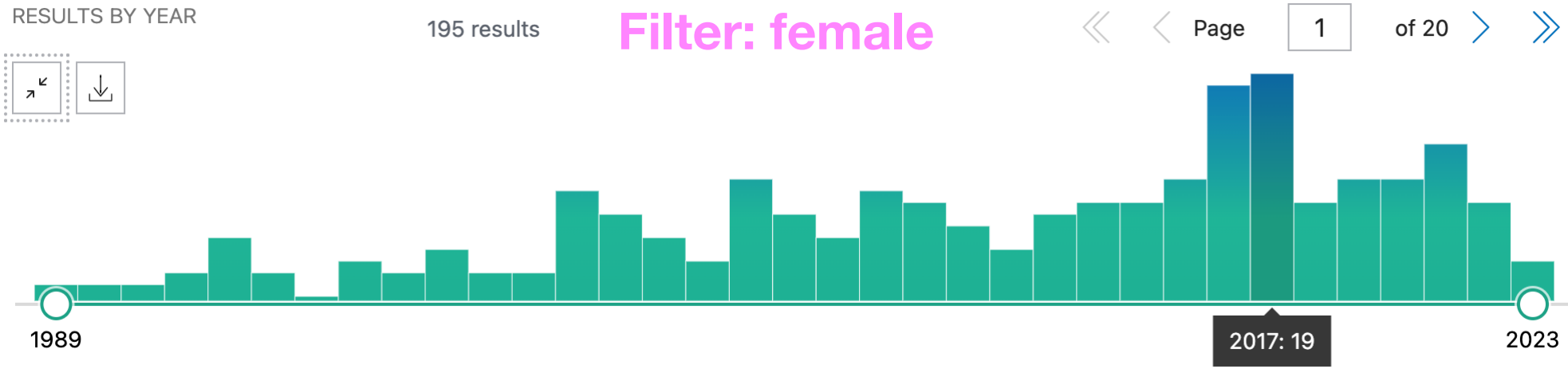
- Introduction to Sexual Dysfunctions (SD)
- **Gender differences and Sexual Dysfunction**
- SD in Women Living With HIV (WLWH)
- SD in Men Living With HIV (MLWH)
- Conclusive Remarks/Practice Points

Gender differences in Research on Sexual Dysfunction in HIV





EACS European AIDS Clinical Society

GUIDELINES

Version 8.2
January 2017

Sexual Dysfunction

When sexual complaints exist:	What is the exact nature of the problem? In which phase(s) of the sexual response cycle does the problem occur?	**1. Desire** (lack of sexual desire or libido; desire discrepancy with partner; aversion to sexual activity) **2. Arousal** (difficulties with physical and/or subjective sexual arousal; difficulties or inability to achieve or sustain an erection of sufficient rigidity for sexual intercourse (M)–i.e. erectile dysfunction; lack or impaired nocturnal erections (M); difficulties lubricating (W); difficulties sustaining arousal) **3. Orgasm** (difficulties experiencing orgasm) **4. Pain** (pain with sexual activity; difficulties with vaginal/anal penetration–anxiety, muscle tension; lack of sexual satisfaction and pleasure)	
Identify the causes:	Psychological or sociological problems?	Stigma, body image alteration, depression, fear of infecting an HIV-negative partner?	*Refer to clinical psychologist*
	Relevant co-morbidity?	CVD (note: if complete sexual response possible - e.g. with another partner, with masturbation or nocturnal - then no major somatic factors are involved)	*Refer to urologist, andrologist, cardiologist*
	Relevant medicines, drugs, lifestyle factors?	Drugs associated with sexual dysfunction: 1) psychotropics (antidepressants, antiepileptics, antipsychotics, benzodiazepines), 2) lipid-lowering drugs (statins, fibrates), 3) antihypertensives (ACE-inhibitors, betablockers, alfablockers), 4) others (omeprazole, spironolactone, metoclopramide, finasteride, cimetidine); 5) contribution from ARVs is controversial and benefit from switching studies is not proven.	*Refer to clinical pharmacologist*
	Signs of hypogonadism in men?	Signs of testosterone insufficiency (reduced sexual arousal and libido; decreased frequency of sexual thoughts and fantasies; decreased or absent nocturnal erections; decreased genital sensitivity; loss of vitality; fatigue; loss of muscle mass and muscle strength and decreased body hair)	*Refer to endocrinologist*

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GUIDELINES

Version 8.2
January 2017

Treatment of Sexual Dysfunction in HIV-positive Men

Treatment of erectile dysfunction	Treatment of premature ejaculation
Primarily oral PDE5-inhibitors (sildenafil, tadalafil, vardenafil). • All at least 30 minutes before initiation of sexual activity • Use lower dose if on PI/r — sildenafil (25 mg every 48 hours) — tadalafil 5 mg initial dose with maximum dose 10 mg in 72 hours — vardenafil 2.5 mg maximum dose in 72 hours • Tadalafil also licensed for use as an everyday ongoing therapy	Consider behavioural interventions and/or psychosexual counselling, SSRIs, tricylclic antidepressants, clomipramine and topical anaesthetics. • Use lower dose of clomipramine and other tricyclic antidepressants if on PI/r • Dapoxetine, a short-acting SSRI, is the only drug approved for on-demand treatment of premature ejaculation in Europe. • Treatment must be maintained as recurrence is highly likely following withdrawal of medicine

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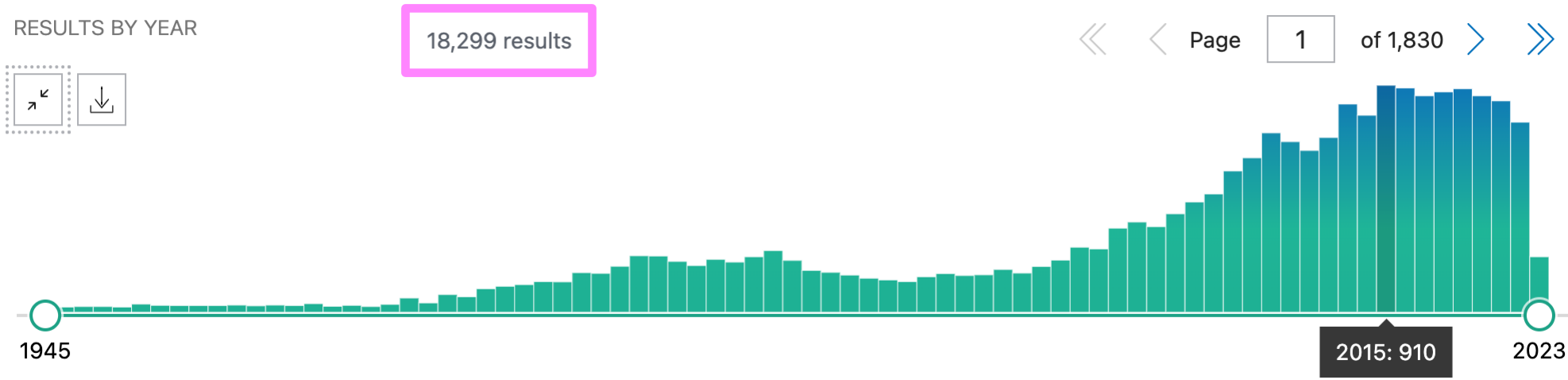
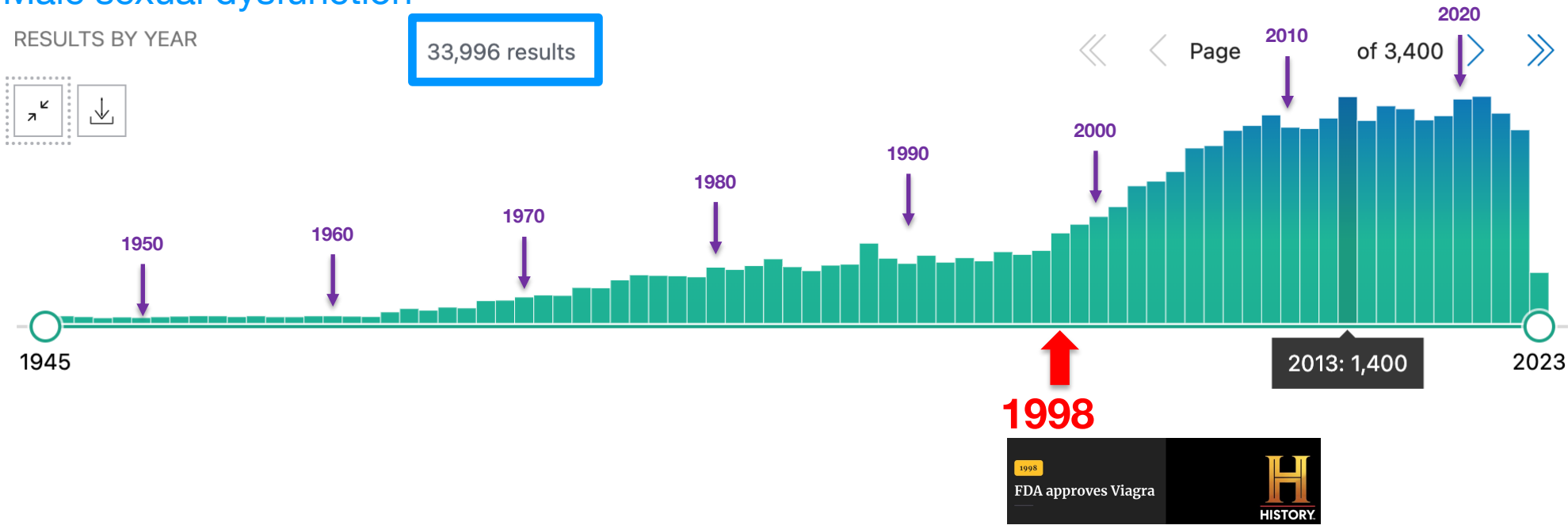
Gender differences in Sexual Dysfunction Research

Female sexual dysfunction



Male sexual dysfunction



EACS European AIDS Clinical Society

GUIDELINES

Version 10.1
October 2020

Sexual Dysfunction

When sexual complaints exist:	What is the exact nature of the problem? In which phase(s) of the sexual response cycle does the problem occur?	**1. Desire** (lack of sexual desire or libido; desire discrepancy with partner; aversion to sexual activity) **2. Arousal** (difficulties with physical and/or subjective sexual arousal; difficulties or inability to achieve or sustain an erection of sufficient rigidity for sexual intercourse MEN; i.e. erectile dysfunction; lack or impaired nocturnal erections MEN; difficulties lubricating WOMEN; difficulties sustaining arousal) **3. Orgasm** (difficulties experiencing orgasm) **4. Pain** (pain with sexual activity; difficulties with vaginal/anal penetration–anxiety, muscle tension; lack of sexual satisfaction and pleasure)	
	Self-assessment of sexual function (questionnaires):	**Men** International Index of Erectile Function, see http://files.sld.cu/urologia/files/2011/08/iief.pdf **Women** Female Sexual Function Index (FSFI), see http://www.fsfiquestionnaire.com	
Check for endocrine causes:	Signs of hypogonadism	**Men** - Look for signs of testosterone insufficiency (main: decreased or absent nocturnal erections, decrease in testes size, decreased volume of ejaculate, hot flushes, sweats, reduction of body hair and beard; others: reduced sexual arousal and libido, decreased frequency of sexual thoughts and fantasies, decreased genital sensitivity, erectile dysfunction, loss of vitality; fatigue; loss of muscle mass and muscle strength) - If signs or symptoms of hypogonadism are present ask for hormonal assessment: lutropin hormone (LH), follicle stimulating hormone (FSH), total testosterone; sex hormone-binding globulin evaluation to calculate free testosterone, see http://www.issam.ch/freetesto.htm	If hypogonadism is present (total testosterone < 300 ng/dl or calculated free testosterone below normal): refer to endocrinologist or andrologist If hypogonadism is not present: check for other causes
		Women - Look for signs of estradiol insufficiency/menopause (amenorrhoea or missed menstrual periods, vaginal dryness, hot flashes, night sweats, sleep disturbances, emotional lability, fatigue, recurrent urogenital infections) - If symptoms of menopause are present ask for hormonal assessment: LH, FSH, estradiol	If symptoms of menopause are present: refer to endocrinologist or gynaecologist If hypogonadism is not present: check for other causes
Check for other causes:	Psychological or sociological problems	Stigma, body image alteration, depression, fear of infecting an HIV-negative partner, anxiety, awareness of a chronic disease, condom use	Refer to clinical psychologist
	Infections	**Men** - Urogenital infections (note: if complete sexual response possible, e.g. with another partner, with masturbation or nocturnal erections-then no major somatic factors are involved)	Refer to urologist, andrologist, cardiologist
		Women - Urogenital infections	Refer to gynaecologist
	Relevant medicines, drugs, lifestyle factors	Drugs associated with sexual dysfunction: 1) Psychotropics – Men and Women (antidepressants, antiepileptics, antipsychotics, benzodiazepines), 2) Lipid-lowering drugs - Men (statins, fibrates), 3) Antihypertensives - Men (ACE-inhibitors, betablockers, alfablockers), 4) Others - Men and Women (omeprazole, spironolactone, metoclopramide, finasteride, cimetidine); 5) Men and Women - contribution from ART is controversial and benefit from switching studies is not proven	Consider therapy changes

from version 9.0
October 2017
gender distinction

EACS European AIDS Clinical Society

GUIDELINES

Version 10.1
October 2020

Treatment of Sexual Dysfunction in Men Living with HIV

Treatment of erectile dysfunction	Treatment of premature ejaculation
Primarily oral PDE5-inhibitors (sildenafil, tadalafil, vardenafil). • All at least 30 minutes before initiation of sexual activity • Use lower dose if on PI/b - sildenafil (25 mg every 48 hours) - tadalafil 5 mg initial dose with maximum dose 10 mg in 72 hours - vardenafil 2.5 mg maximum dose in 72 hours **Cave:** Poppers have a synergistic effect with PD5-blockers which can lead to profound hypotension thus concurrent use is not recommended • Tadalafil also licensed for use as an everyday ongoing therapy	Consider behavioural interventions and/or psychosexual counselling, SSRIs, tricylclic antidepressants, clomipramine and topical anaesthetics • Use lower dose of clomipramine and other tricyclic antidepressants if on PI/r • Dapoxetine, a short-acting SSRI, is the only drug approved for on-demand treatment of premature ejaculation in Europe • Treatment must be maintained as recurrence is highly likely following withdrawal of medicine

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Sexual Dysfunction in Gender Incongruence

RESULTS BY YEAR

688 results

Page 1 of 69

1984

2019: 121

2023

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- Conclusive Remarks/Practice Points

SEXUAL MEDICINE REVIEWS REVIEW

The Evolution of the Female Sexual Disorder/Dysfunction Definitions, Nomenclature, and Classifications: A Review of DSM, ICSM, ISSWSH, and ICD

Sharon J. Parish, MD,[1,*] Sara Cottler-Casanova, MSc,[2,3,*] Anita H. Clayton, MD,[4] Marita P. McCabe, PhD,[5] Eli Coleman, PhD,[6] and Geoffrey M. Reed, PhD[7,8]

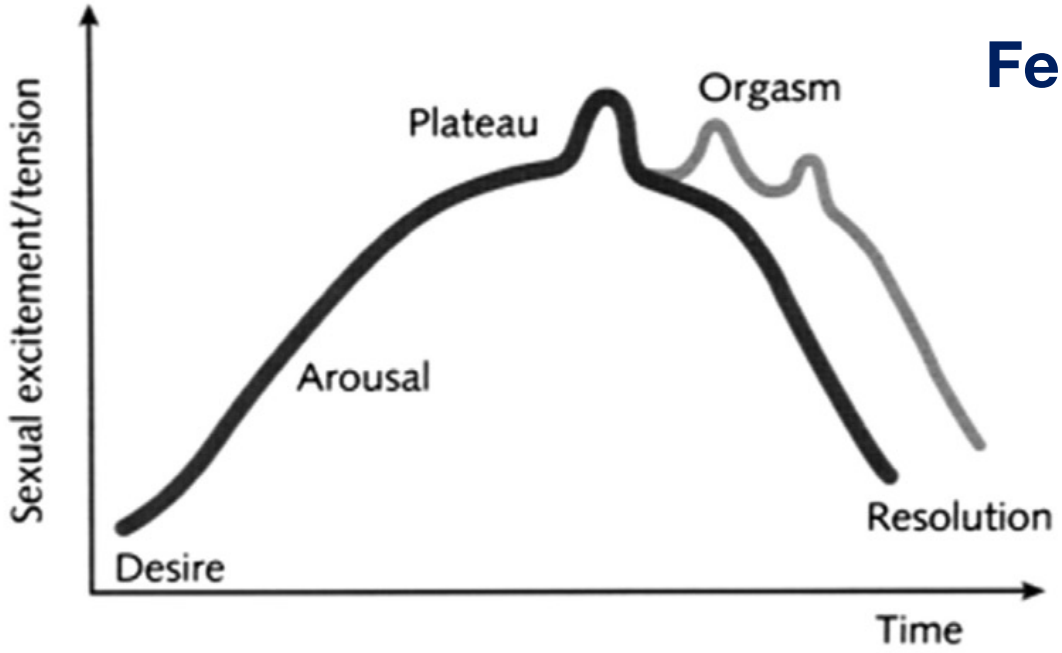

Figure 2. Traditional human sex response cycle of Masters and Johnson[13] and Kaplan[14] adapted from the study by Sand and Fisher.[15].

Female Arousal includes

- vulvovaginal lubrication
- engorgement of the genitalia
- sensitivity of the genitalia
- nongenital responses

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

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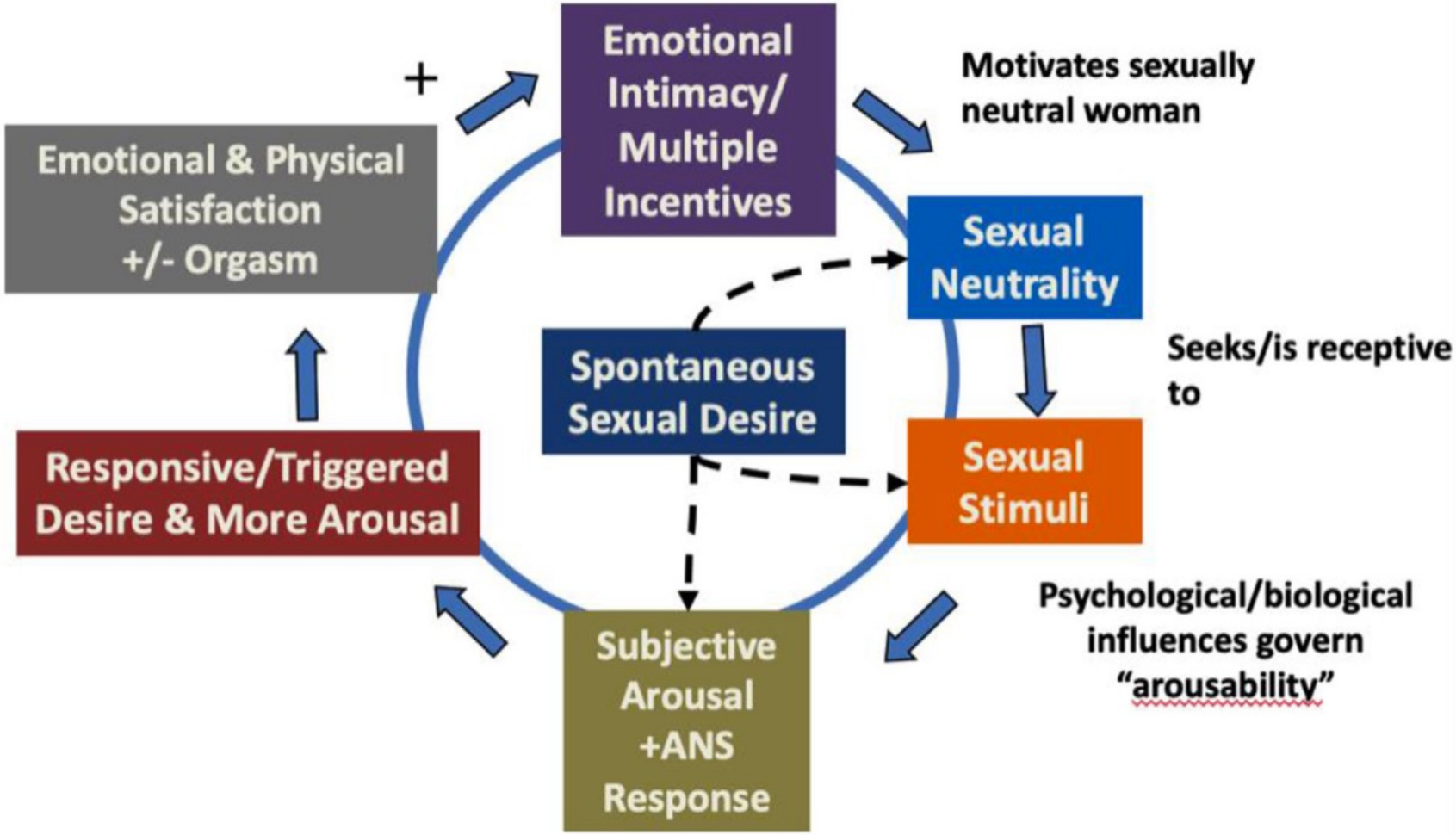

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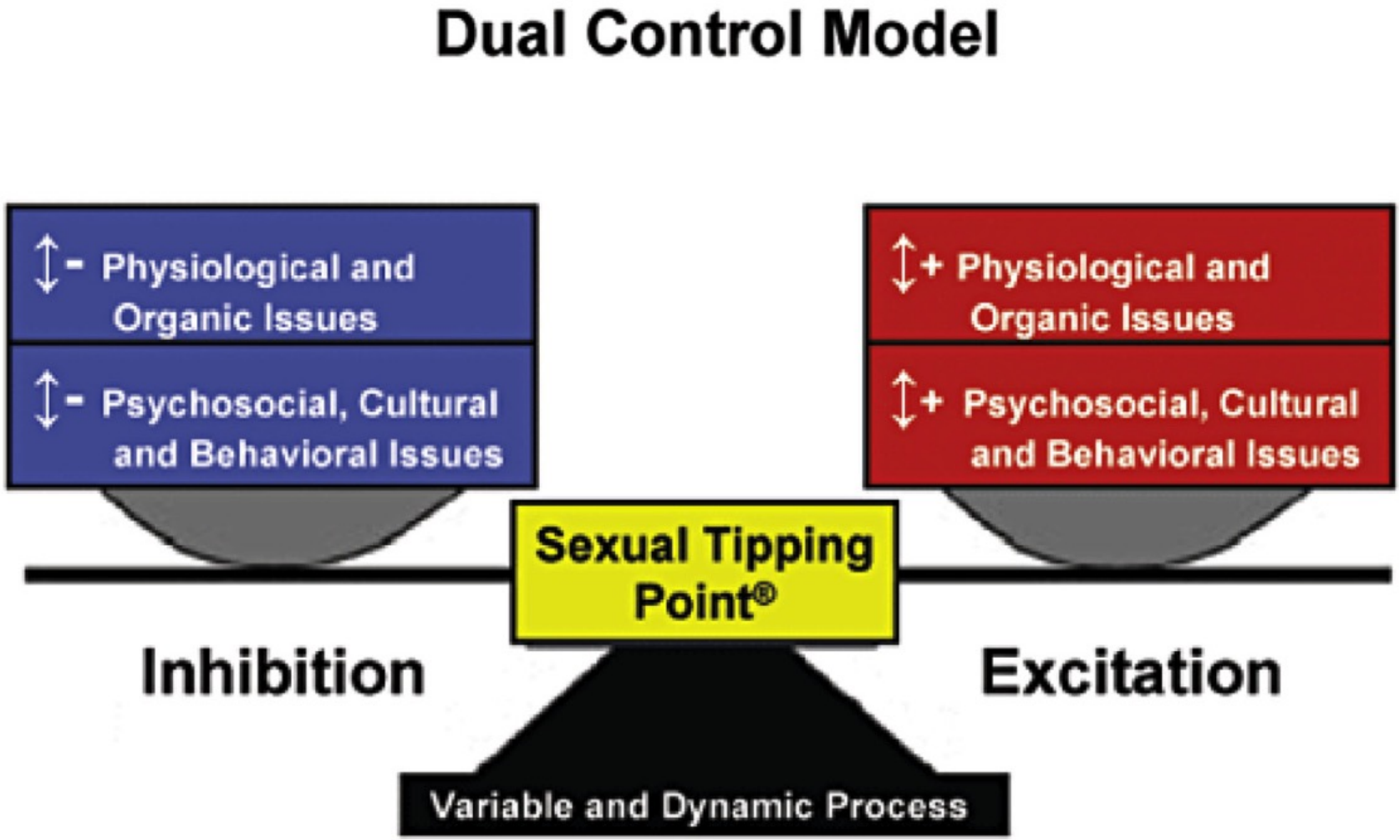

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Uncertainty on female sexual dysfunctions definition

Table 1. Comparison of DSM-IV-TR and DSM-5 female sexual dysfunctions[11,29]

DSM-IV-TR	DSM-5
Female sexual dysfunctions	Female sexual dysfunctions
Hypoactive sexual desire disorder*	Female sexual interest/arousal disorder
Female sexual arousal disorder	Female sexual interest/arousal disorder
Female orgasmic disorder	Female orgasmic disorder†
Dyspareunia (not due to a general medical condition)	Genito-pelvic pain/penetration disorder
Vaginismus (not due to a general medical condition)	Genito-pelvic pain/penetration disorder
Other sexual dysfunctions*	Other sexual dysfunctions*
Sexual aversion disorder*	Removed
Sexual dysfunction due to a general medical condition*	Removed
Substance/medication-induced sexual dysfunction*	Substance/medication-induced sexual dysfunction*,†
Sexual dysfunction not otherwise specified*	Other specified sexual dysfunction*
	Unspecified sexual dysfunction*

DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision.
*Disorders that are the same for male and female
†Unchanged from DSM-IV-TR

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

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Table 3. ISSWSH Sexual Disorders Nomenclature and definitions including level of evidence modified from the study by Parish et al[89]

ISSWSH Sexual Disorders Nomenclature and Definitions
Hypoactive sexual desire disorder (Grade B)
Manifests as any of the following for a minimum of 6 months:
Lack of motivation for sexual activity as manifested by either:
Reduced or absent spontaneous desire (sexual thoughts or fantasies)
Reduced or absent responsive desire to erotic cues and stimulation or inability to maintain desire or interest through sexual activity
Loss of desire to initiate or participate in sexual activity, including behavioral responses such as avoidance of situations that could lead to sexual activity, ie not secondary to sexual pain disorders
AND is combined with clinically significant personal distress that includes frustration, grief, incompetence, loss, sadness, sorrow, or worry
Female sexual arousal disorder
Female cognitive arousal disorder (FCAD) (expert opinion)
Characterized by the distressing difficulty or inability to attain or maintain adequate mental excitement associated with sexual activity as manifested by problems with feeling engaged, or mentally turned on or sexually aroused for a minimum of 6 months
Female genital arousal disorder (FGAD) (Grade B)
Characterized by the distressing difficulty or inability to attain or maintain adequate genital response associated with sexual activity for a minimum of 6 months, including:
Vulvovaginal lubrication
Engorgement of the genitalia
Sensitivity of the genitalia associated with sexual activity

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

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Table 3. ISSWSH Sexual Disorders Nomenclature and definitions including level of evidence modified from the study by Parish et al[89]

ISSWSH Sexual Disorders Nomenclature and Definitions
Persistent genital arousal disorder (Expert Opinion)
Characterized by persistent or recurrent, unwanted or intrusive, distressing feelings of genital arousal, or being on the verge of orgasm (genital dysesthesia), not associated with concomitant sexual interest, thoughts, or fantasies for a minimum of 6 months
May be associated with:
Limited resolution, no resolution, or aggravation of symptoms by sexual activity with or without aversive or compromised orgasm
Aggravation of genital symptoms by certain circumstances
Despair, emotional lability, catastrophizing, or suicidality
Inconsistent evidence of genital arousal during symptoms

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

SEXUAL MEDICINE REVIEWS REVIEW

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Table 3. ISSWSH Sexual Disorders Nomenclature and definitions including level of evidence modified from the study by Parish et al[89]

ISSWSH Sexual Disorders Nomenclature and Definitions
Female orgasm disorder (Grade B)
Characterized by a persistent or recurrent, distressing compromise of orgasm frequency, intensity, timing, and/or pleasure, associated with sexual activity for a minimum of 6 months:
Frequency: orgasm occurs with reduced frequency (diminished frequency of orgasm) or is absent (anorgasmia)
Intensity: orgasm occurs with reduced intensity (muted orgasm).
Timing: orgasm occurs either too late (delayed orgasm) or too early (spontaneous or premature orgasm) than desired by the woman.
Pleasure: orgasm occurs with absent or reduced pleasure (anhedonic orgasm, pleasure dissociative orgasm disorder). (Expert Opinion)
Female orgasmic illness syndrome (expert opinion)
Characterized by peripheral or central aversive symptoms that occur before, during, or after orgasm not related, per se, to a compromise of orgasm quality

This table was published in the Nomenclature III paper with the revised FGAD and new FCAD definitions.

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

Uncertainty and unmeet needs in female sexual dysfunction

- Low grade of evidence
- Unclear distinction between organic and nonorganic disorders

  (*organic vs psychogenic* obsolete)
- Psychiatric-centric view
- Lack of diagnostic tools
- Lack of effective therapies

Risk Factors for Female Sexual Dysfunction

Biological Factors

- ***Women's poor health***
- ***Total number of chronic conditions***
- Pregnancy and childbirth
- Hysterectomy
- ***Cardiovascular, endocrine, metabolic, neurological, and musculogenic diseases***
- ***Diabetes***
- ***Depression/anxiety***
- ***Genito-urinary infections***
- Pelvic surgery

Clayton AH & Valladares Juarez EM *Med Clin N Am* 103, 681–698, 2019

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

Risk Factors for Female Sexual Dysfunction

Interpersonal Factors

- ***Intimate relationship satisfaction***
- Levels of relationship satisfaction

Sociocultural Factors

- ***Past negative sexual experiences***

Role of stigma and perception of HIV as something related to sex

Clayton AH & Valladares Juarez EM *Med Clin N Am* 103, 681–698, 2019

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

Studies on Female Sexual Dysfunction in HIV

Hossein Sadeghi-Nejad, MD,* Marlene Wasserman, BA, MA, DHS,† Wolfgang Weidner, MD,‡ Daniel Richardson, BSc, MRCP,§ and David Goldmeier, MD¶

Table 2 HAART era cross-sectional studies

Design	Numbers	Findings	Reference
Cross-sectional descriptive study of women New England; wide CD4 count range; majority low income; 64% drug use; wide ethnic background	101 women	Good sexual functioning in the main; sexual dysfunction correlated to poorer mental health, less positive meaning to HIV, poorer life quality, fewer HIV symptoms, ever drug used	Bova et al. [98]
Cross sectional self-selected UK; 75% Black Africans; wide CD4 count range; HAART status unknown	82 women	35% depressed; 60% anxiety; 42% sexually dysfunctional; significant correlation between depression and sexual dysfunction; 40% had been sexually abused	Lambert et al. [99]
Cross sectional study Pan European; 83% Caucasian; CD4 > 500 in 60%; Most women using HAART	166 women	FSFI < 10 (high grade dysfunction) 25%; Low FSFI not associated with organic illness/ HAART but with anxiety/depression	Florence [95]

HAART = highly active antiretroviral therapy; FSFI = female sexual function index.

Sadeghi-Nejad H *et al. J Sex Med* 7:389–413, 2010

Studies on Female Sexual Dysfunction in HIV

Table 3 Qualitative studies in HAART era

Subjects	Themes	Reference
74 women in pre HAART era; 74 women in HAART era (30% on HAART); New York City; Mixed race; low income	Similar findings both eras: fear of HIV transmission; loss of sexual spontaneity and freedom; diminished participation in sex; fear of rejection; relationships a hassle; diminished sense of self-attractiveness	Siegel et al. [96]
21 women London UK; 67% Black African in HAART era; 81% currently taking HAART; No history of drug abuse	Fear of HIV transmission; fear of disclosure; relationship avoidance; reduced sense of intimacy; sex with casual partners to avoid disclosure; dislike of condoms	Keegan et al. [100]

HAART = highly active antiretroviral therapy.

Table 4 Causes of psychogenic female sexual dysfunction

Anxiety
Depression
Drug abuse
Grief reactions
Sociocultural problems
Economic problems
Sexual and physical abuse
Relationship issues
Fertility issues
Loss of partner
Lipodystrophy (change in body shape)
Fear of infecting others/stigmatization
Sex education problems

Table 5 Organic causes of female sexual dysfunction

Neurological (cortical, spinal, autonomic and sensory nerve impairments)
Endocrine (oestrogen, testosterone, thyroid problems)
Cardiovascular (atherosclerosis, hypertension, dyslipidaemia)
Iatrogenic (HAART, antidepressants, others)
Infective causes (advanced HIV disease, genital herpes, candidiasis, pelvic pain)
Others (e.g., surgery, radiotherapy)

Ieghi-Nejad H *et al. J Sex Med* 7:389–413, 2010

Bell *et al. International Journal of STD & AIDS* 17: 706–709, 2006

Diagnosis of Female Sexual Dysfunction

- **Interview including**
  - specific questions on sexuality (including partner's sexuality)
  - specific question on relationship/casual sex
  - HIV-related factors (e.g. fear of transmission, fear of disclosure)
- **Physical examination**
- Medications
- **Questionnaires**
  - Female Sexual Function Index (FSFI)
  - Others
- **Timing of sexual dysfunction:**
  - **situational/constant/ intermittent**
- **Instrumental evaluation**
  - Clitoral doppler
  - Plethysmography

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021

Hatzicristou D *et al. J Sex Med 7:337-348, 2010*

Table 9 Level of evidence for specialized tests for women

Diagnostic procedure	Recommendation
Pudendal arteriogram	B
Vaginal photoplethysmography	C
Genito-sensory analyzer	C
Laser oximetry	D
Laser Doppler perfusion imaging	D
Thermography	D
Clitoral and labial photoplethysmography	D
Duplex Doppler ultrasound	D
Vaginal and labial thermistors	D

Therapy of Female Sexual Dysfunction

Treatment of Hypoactive Sexual Desire Disorder (HSDD)

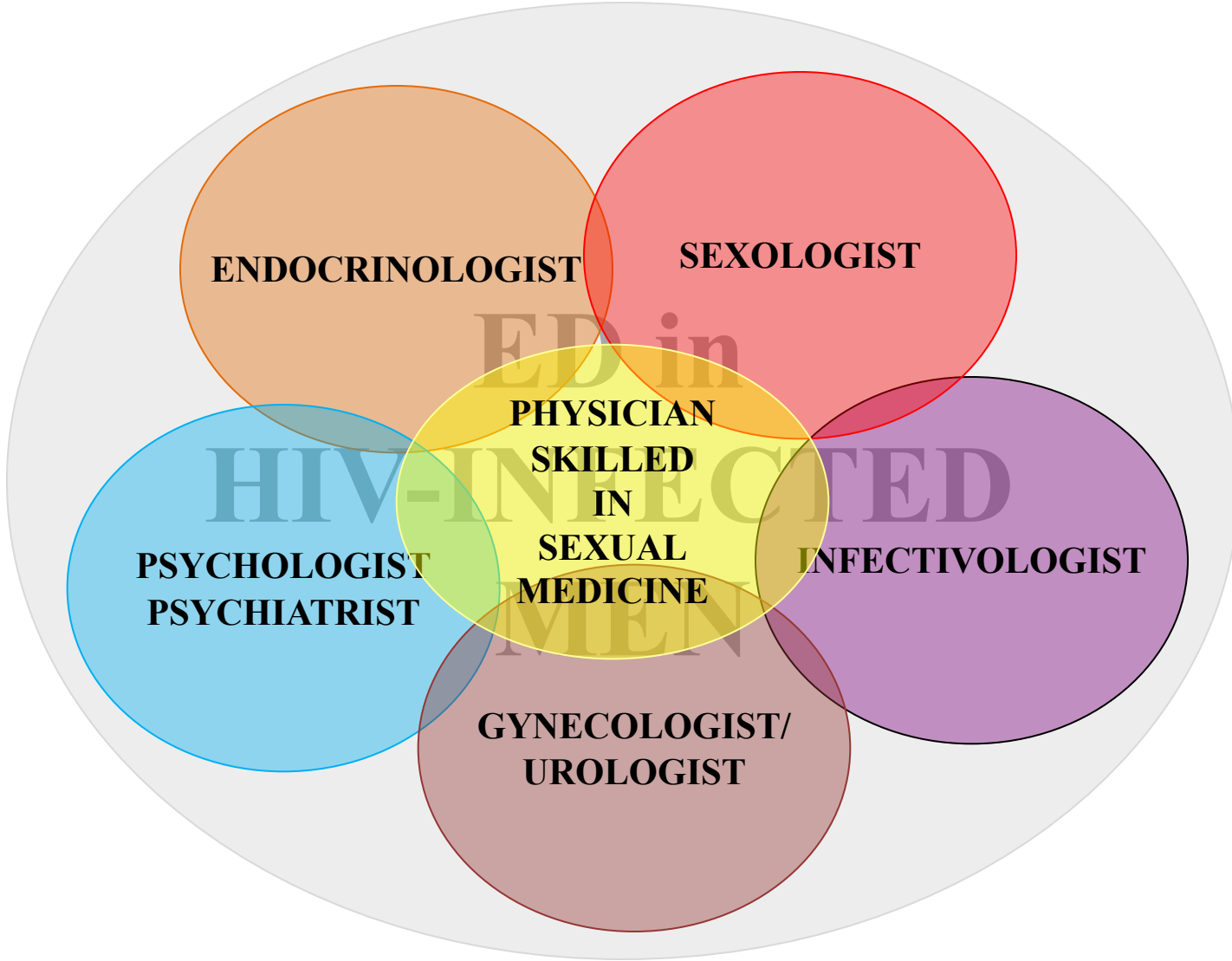
- testosterone
- Flibanserin
- investigational compounds

Treatment of Sexual Arousal Disorder (FSAD)

- Estrogen
- Sildenafil
- EROS therapy device
- Mindfulness therapies

Other therapies

- Psychotherapy



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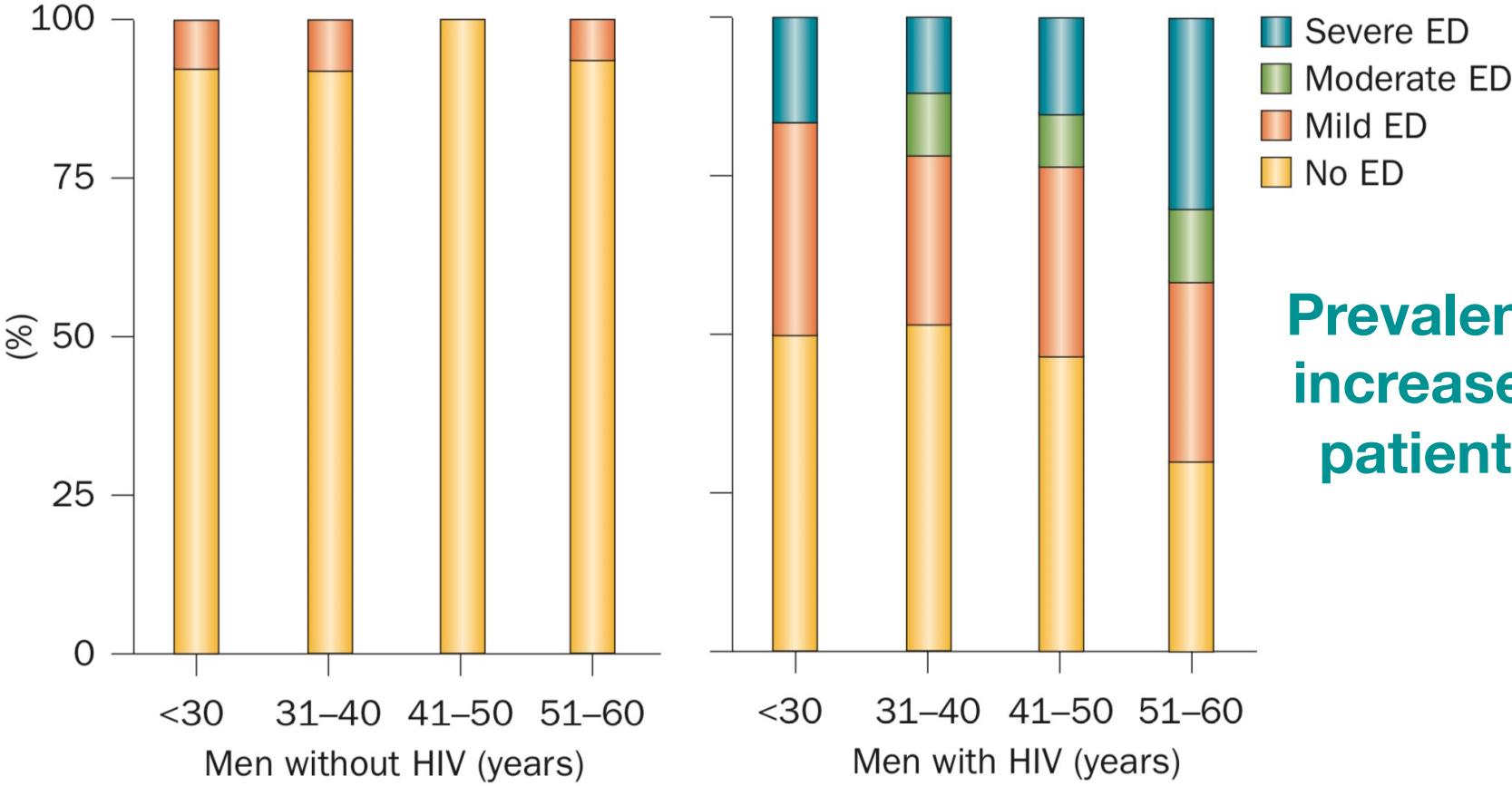
HIV INFECTION: a model of *'Androlological Premature Aging'*

REVIEWS

Male sexual dysfunction and HIV—a clinical perspective

Daniele Santi, Giulia Brigante, Stefano Zona, Giovanni Guaraldi and Vincenzo Rochira

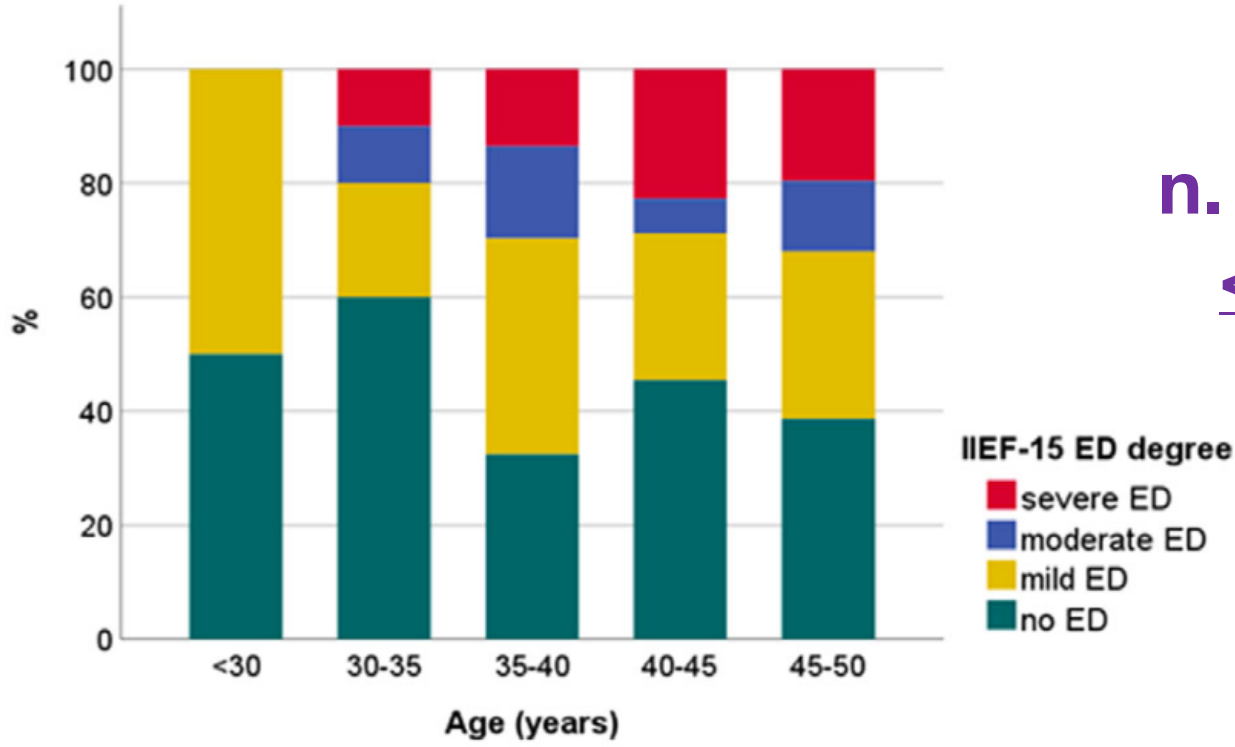


Prevalence of ED is increased in young patients with HIV

Zona *et al. J Sex Med* 9:1923-1930, 2012
Santi *et al. Nat Rev Urol* 11:99-109, 2014

Determinants of sexual function in men living with HIV younger than 50 years old: Focus on organic, relational, and psychological issues

Sara De Vincentis[1,2,3] | Maria Chiara Decaroli[1,2] | Jovana Milic[4] | Flaminia Fanelli[5] | Giulia Tartaro[1,2] | Chiara Diazzi[2] | Marco Mezzullo[5] | Maria Cristina De Santis[6] | Laura Roli[6] | Tommaso Trenti[6] | Daniele Santi[1,2] | Uberto Pagotto[5,7] | Giovanni Guaraldi[4] | Vincenzo Rochira[1,2]



n. 313 MLWH
≤50 years

FIGURE 2 Distribution of ED severity according to patients' age range. IIEF: validated International Index of Erectile Function; ED: erectile dysfunction

De Vincentis *et al. Andrology* 2023

Journal of Clinical Medicine

MDPI

Review

HIV and Sexual Dysfunction in Men

Sara De Vincentis [1,2], Giulia Tartaro [1,2], Vincenzo Rochira [1,2,*] and Daniele Santi [1,2]

Table 2. Studies that investigated erectile dysfunction (ED) and reduced libido prevalence in HIV patients.

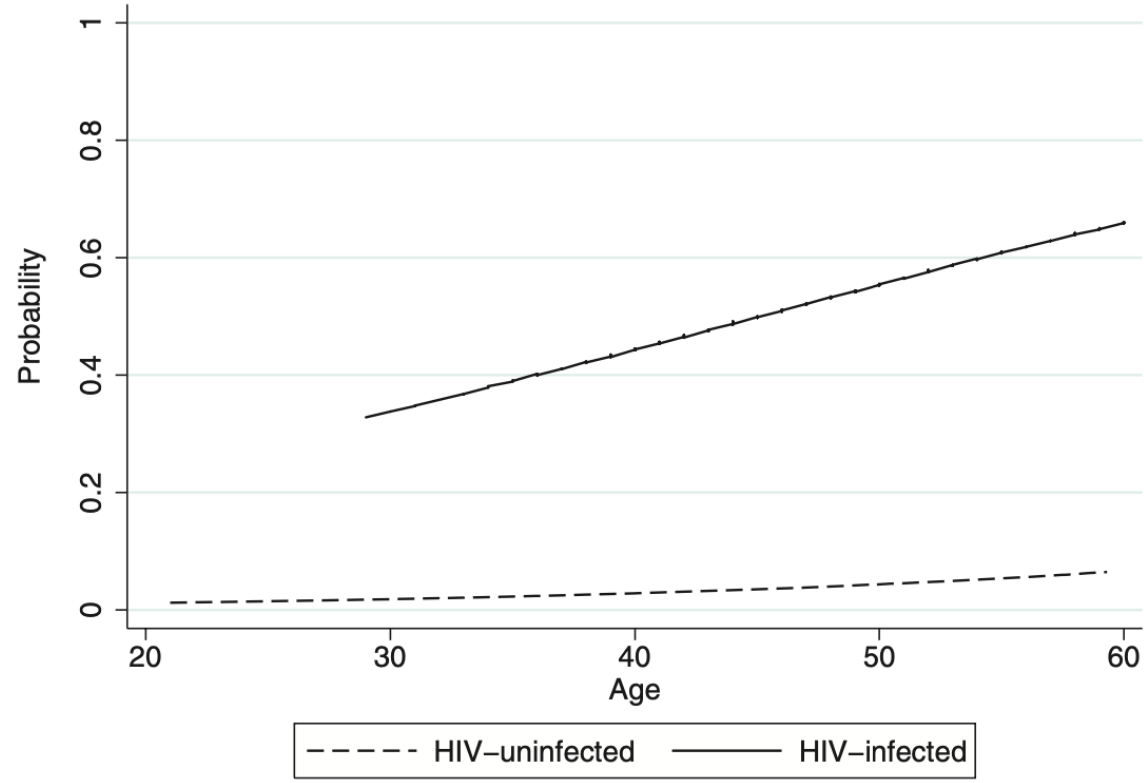
Study	*n*	Age	MSM (%)	IV Drug Use (%)	Reduced SD (%)	ED (%)	ED Diagnostic Tool
Lallemand et al. (2002) [89]	156	40.5 ± 7.7 *	100	NR	89	86	IIEF-15
Ende et al. (2006) [87]	118	41 (28–67) §	70	7	NA	74	IIEF-5
Asboe et al. (2007) [69]	668	-	73	-	24	33	IIEF-15
Crum-Cianflone et al. (2007) [90]	285	39 (19–72) *	NR	8	NR	61.4	IIEF-15
Guaraldi et al. (2007) [88]	357	45 (45–46) *	43	NR	NR	53.2	IIEF-15
Moreno-Pérez et al. (2010) [91]	90	42 ± 8.2 *	80	0	NR	53.4	IIEF-15
Rochira et al. (2011) [79]	247	45 (20–69) §	NR	NR	65.2	53.4	IIEF-15
Guaraldi et al. (2012) [45]	133	49 *	52	26	NR	59.3	IIEF-15
Zona et al. (2012) ¶ [11]	444	44.8 ± 5.9 *	43	34	NR	54.5	IIEF-15
Hart et al. (2012) ¶ [92]	1340	48 (42–54) §	100	NR	NR	21	IIEF-MSM
Vansintejan et al. (2013) [93]	72	41 ± 10 *	100	NR	15	56	IIEF-5 **
Wang et al. (2013) [95]	4064	46 §	NR	NR	NR	24	IIIEF-15 ‡‡
Perez et al. (2013) [75]	158	46 *	58.2	NR	NA	67.1	IIEF-5
Romero-Velez et al. (2014) [94]	109	39.9 ± 8.8 *	70.6	NR	NR	65	IIEF-15
Hart et al. (2015) ¶ [101]	619	47.3 ± 8.9 *	100	NR	NR	24.7	IIEF-MSM
Pinzone et al. (2015) [96]	109	47 (40–52) §	54	20.2	NR	65	IIEF-15
Fumaz et al. (2017) [97]	501	42 (35–48) §	75.8	NR	NA	58.4	IIEF-5
Aghahowa et al. (2017) [98]	217	37.9 ± 9.9 *	63.6	9.5	NR	82.3	IIEF-15
Dijkstra et al. (2018) ¶ [73]	399	53.6 (48.6–60.0) §	100	2	7	13	IIEF-15 ‡‡
Veras Gomes et al. (2019) [99]	134	44.7 ± 11.0 *	40	NR	NR	22	IIEF-15
Bernal et al. (2019) [100]	139	45.22 ± 10.47 *	55.6	3.7	NA	61.2	IIEF-5

ED and reduced sexual desire are common in MLWH ≤50 years

De Vincentis *et al. J Clin Med* 10(5):1088, 2021

Premature decline of erectile function in HIV-infected men

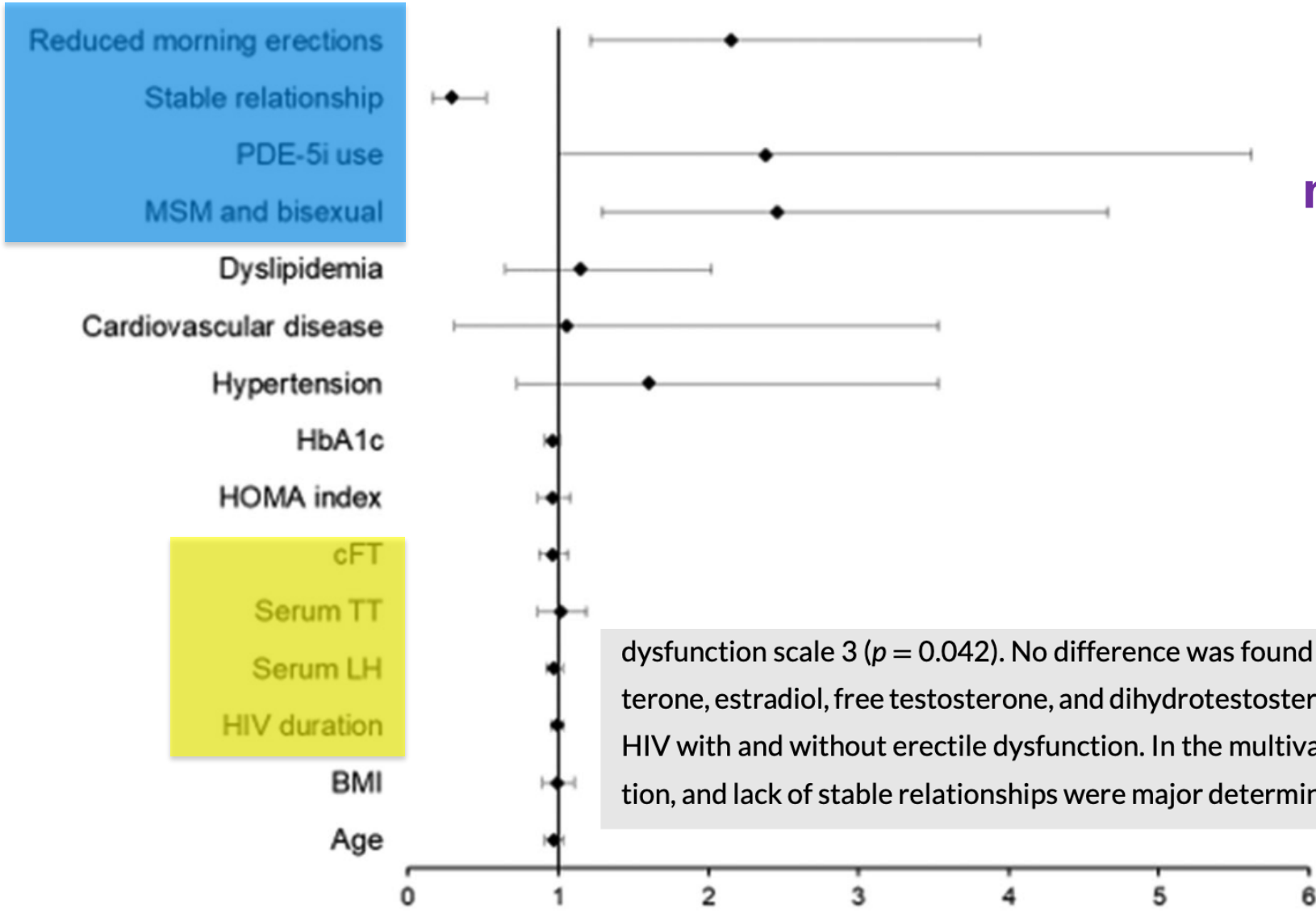
Comparative risk of ED according to age in HIV- and HIV+ patients



Predictors of ED at multiple logistic regression analysis :
HIV infection (OR=42.26, p<0.001) and hypogonadism (OR=2.63, p=0.02)

Zona et al., *J Sex Med* 2012

Determinants of ED in young to middle aged MLWH



(A)

n. 313 MLWH
≤50 years

dysfunction scale 3 ($p = 0.042$). No difference was found for sex steroids (total testosterone, estradiol, free testosterone, and dihydrotestosterone) between men living with HIV with and without erectile dysfunction. In the multivariate analysis sexual orientation, and lack of stable relationships were major determinants for erectile dysfunction.

De Vincentis *et al. Andrology* 2023

Hypogonadism in HIV

Age (years)	Entire cohort	Total T≥300 ng/dL	Total T<300 ng/dL
20–29 n (%)	12 (0.9%)	11 (91.7%)	1 (8.3%)
30–39 n (%)	207 (15.6%)	185 (89.4%)	22 (10.6%)
40–49 n (%)	800 (60.4%)	677 (84.7%)	123 (15.3%)
50–59 n (%)	245 (18.5%)	187 (76.4%)	58 (23.6%)
60–69 n (%)	61(4.6%)	53 (86.9%)	8 (13.1%)

doi:10.1371/journal.pone.0028512.t003

Prevalence of Hypogonadism is increased in young patients with HIV

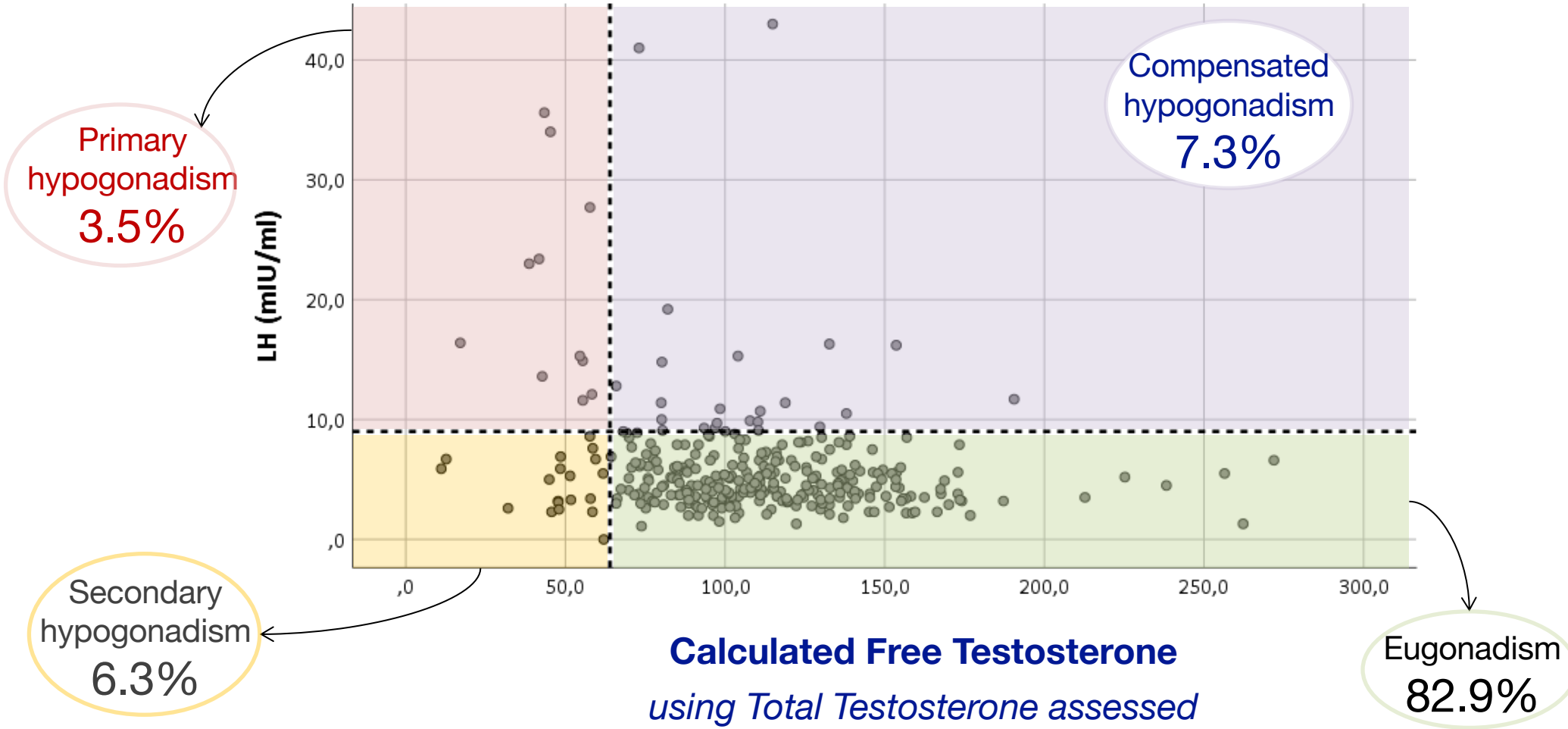
Rochira V *et al.* PLoS ONE 6(12): e28512, 2011

Hypogonadism is a rare disease before the age of 40 in HIV-uninfected men

Kaufman JM & Vermeulen A *Baillieres Clin Endocrinol Metab* 11:289-309, 1997

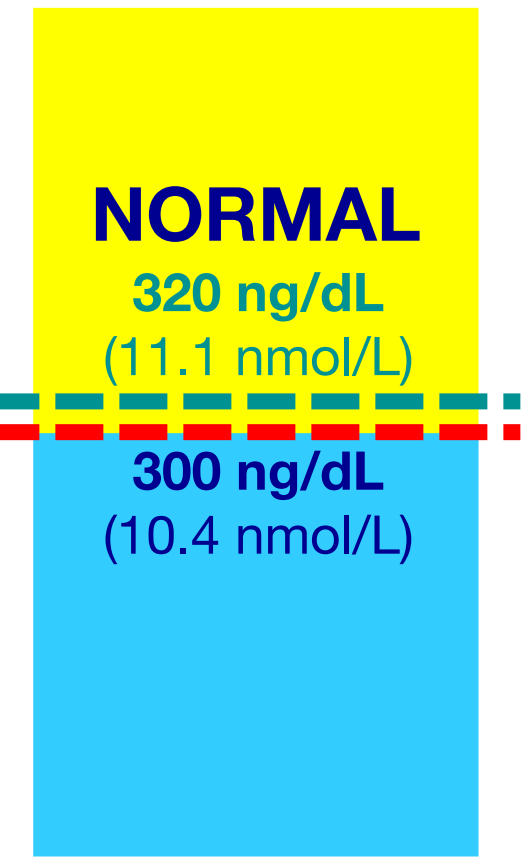
Results

n. 313 MLWH
≤50 years



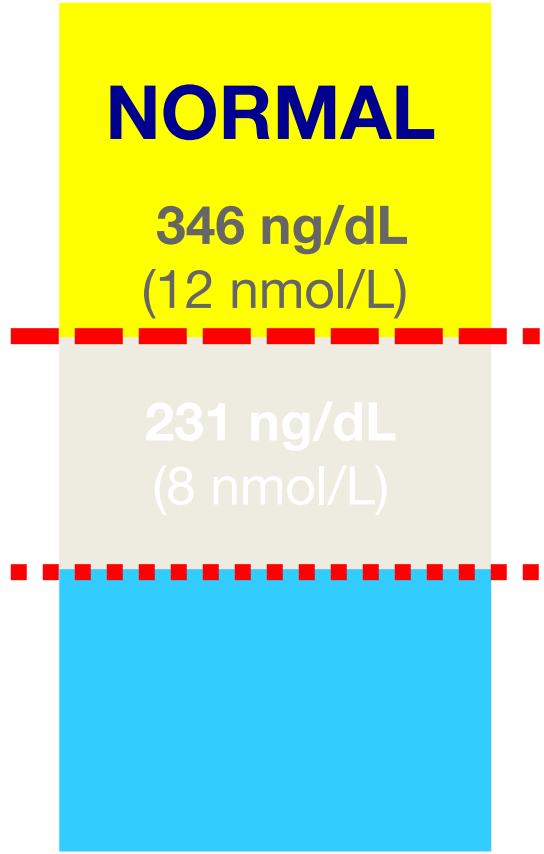
De Vincentis *et al.* Aging Male. 25(1):41-53, 2022

THRESHOLDS FOR HYPOGONADISM DIAGNOSIS



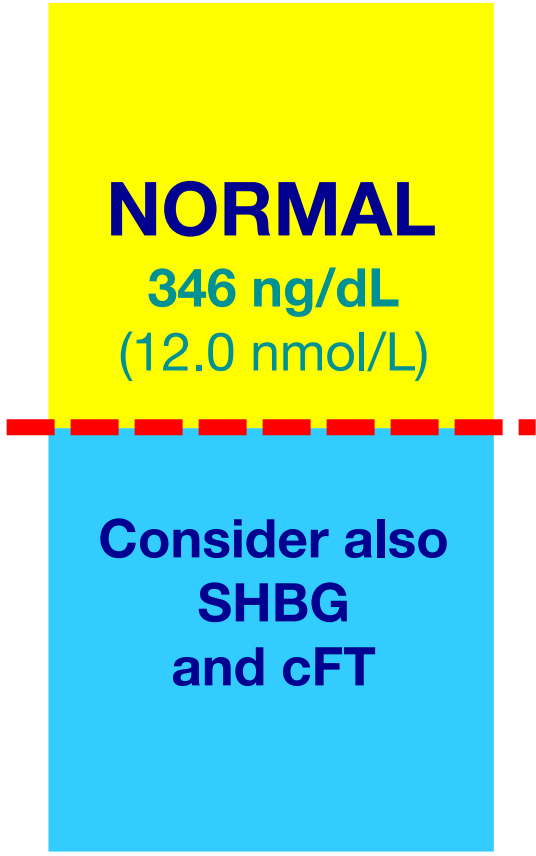
Endocrine Society

Bhasin S *et al.*. *JCE&M* 95:2536-59, 2010
Bhasin S *et al.*. *JCE&M 103*:1715-44, 2018



EAA, ISA, ISSAM and EAU

Wang C *et al. J Androl* 30:1-9, 2009
Corona et al. Andrology 2020



SIAMS

Isidori *et al.* JENI, 45:2385-2403,2022

No Universal T Threshold available

Buvat J *et al. J Sex Med*;10:245-84, 2013

Journal of Endocrinological Investigation (2022) 45:2385–2403
https://doi.org/10.1007/s40618-022-01859-7

CONSENSUS STATEMENT

Adult- and late-onset male hypogonadism: the clinical practice guidelines of the Italian Society of Andrology and Sexual Medicine (SIAMS) and the Italian Society of Endocrinology (SIE)

A. M. Isidori[1] · A. Aversa[2] · A. Calogero[3] · A. Ferlin[4] · S. Francavilla[5] · F. Lanfranco[6] · R. Pivonello[7,8] · V. Rochira[9] · G. Corona[10] · M. Maggi[11]

Diagnosis

We recommend measuring total testosterone (tT) and luteinizing hormone (LH) in all men with clinical manifestations consistent with hypogonadism and to adopt a threshold of ≤ 12.0 nmol/L to define low total testosterone (1ØØØO).

346 ng/dL

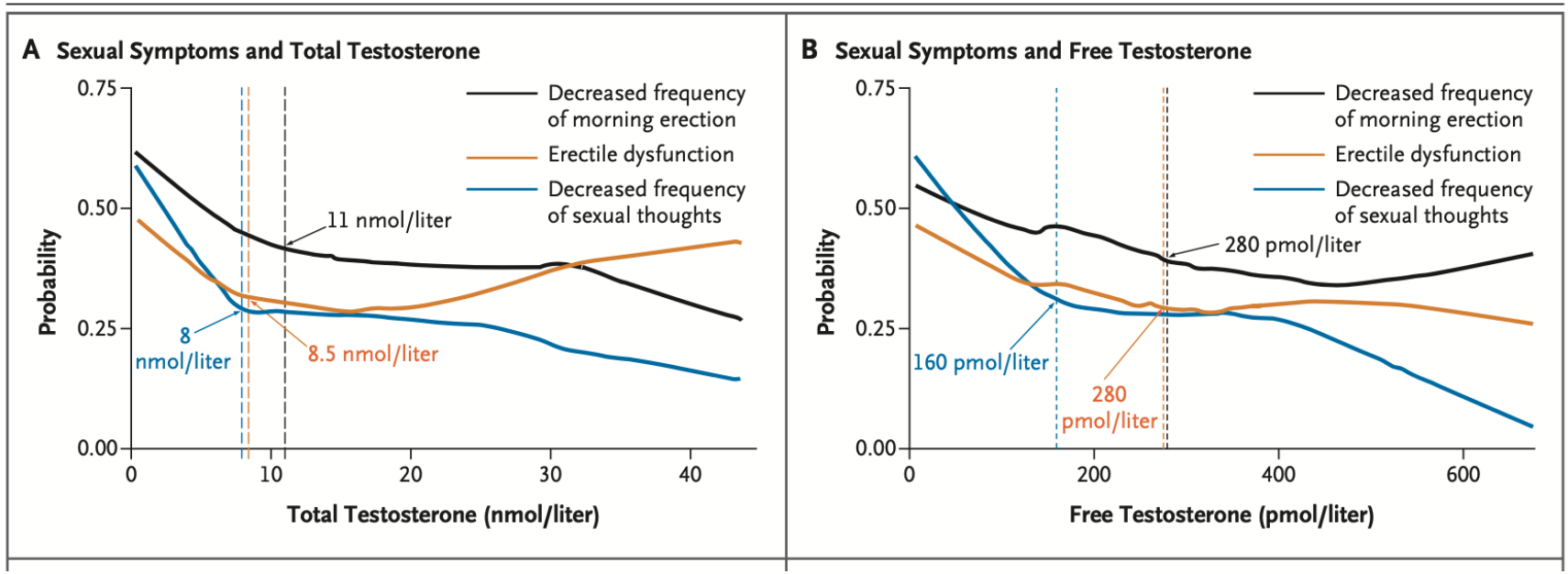
Isidori *et al.* JENI, 45:2385-2403,2022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Identification of Late-Onset Hypogonadism in Middle-Aged and Elderly Men

Frederick C.W. Wu, M.D., Abdelouahid Tajar, Ph.D., Jennifer M. Beynon, M.B., Stephen R. Pye, M.Phil., Alan J. Silman, M.D., Joseph D. Finn, B.Sc., Terence W. O'Neill, M.D., Gyorgy Bartfai, M.D., Felipe F. Casanueva, M.D., Ph.D., Gianni Forti, M.D., Aleksander Giwercman, M.D., Ph.D., Thang S. Han, M.D., Ph.D., Krzysztof Kula, M.D., Ph.D., Michael E.J. Lean, M.D., Neil Pendleton, M.D., Margus Punab, M.D., Ph.D., Steven Boonen, M.D., Ph.D., Dirk Vanderschueren, M.D., Ph.D., Fernand Labrie, M.D., Ph.D., and Ilpo T. Huhtaniemi, M.D., Ph.D., for the EMAS Group*



Wu *et al. NEJM*, 363:123-135, 2020

Circulating Testosterone

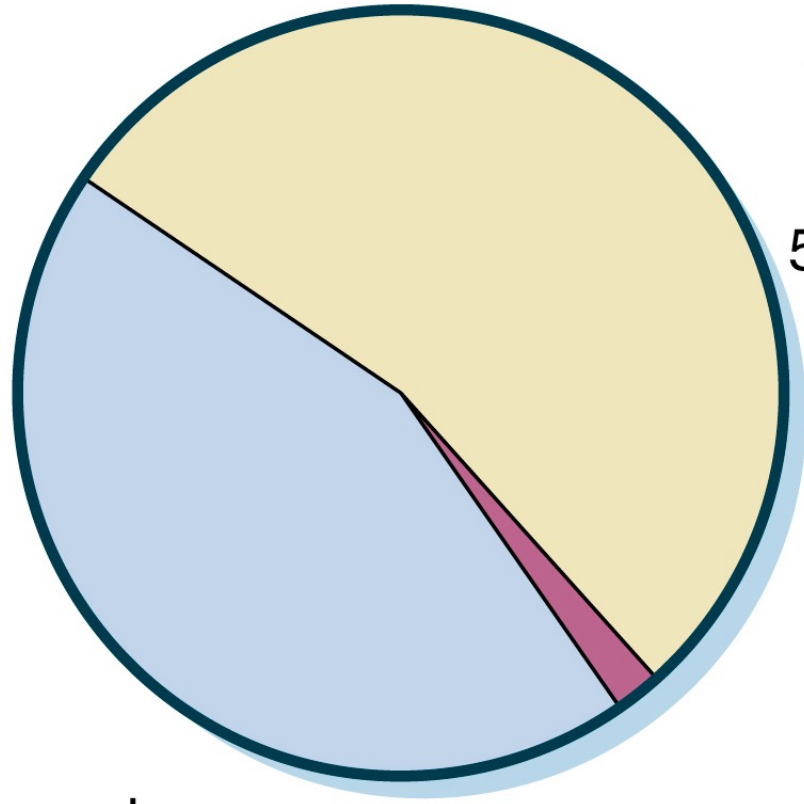


FIG. 19.10 Fractions of circulating testosterone in blood. The majority of circulating testosterone (T) is bound to serum proteins: approximately 54% is weakly bound to albumin, and 44% is tightly bound to sex hormone–binding protein (SHBG). Only about 2% of circulating T is free of protein binding. The combination of free and weakly bound (albumin-bound) T is referred to as bioavailable testosterone.

from Melmed S, Koenig, RJ, Auchus, RJ, Rosen CJ, Goldfine AB
Williams Textbook of Endocrinology 14th edition 2019

Journal of Endocrinological Investigation (2022) 45:2385–2403
https://doi.org/10.1007/s40618-022-01859-7

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Table 1 Main factors associated with an increase or with a reduction of Sex hormone binding globulin (SHBG) circulating levels

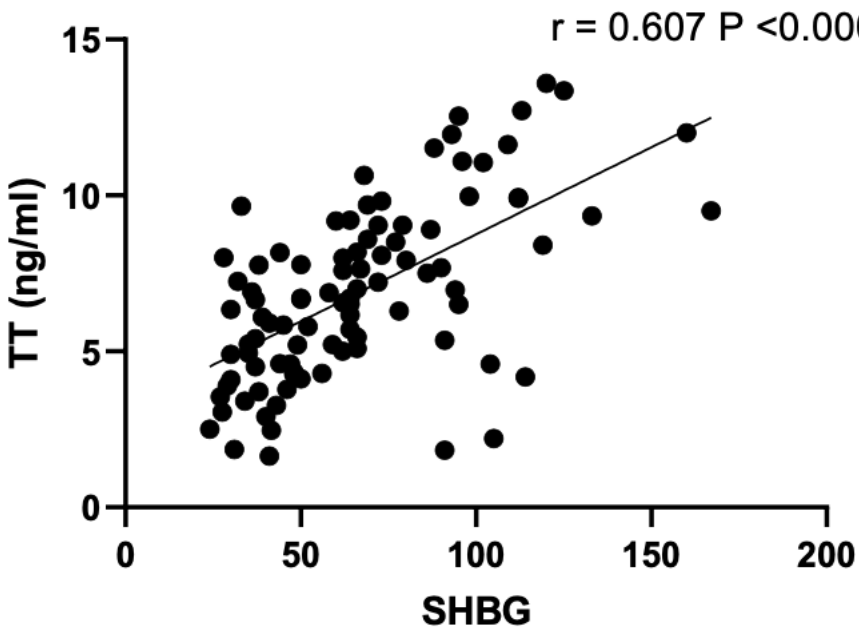
SHBG increase	- Drugs: anticonvulsant, estrogens, thyroid hormone, antiretroviral drugs - Hyperthyroidism - HIV disease - Cirrhosis and hepatitis - Aging
SHBG decrease	-Drugs: GH, glucocorticoids, testosterone, Anabolic androgenic steroids -Hypothyroidism -Obesity -Acromegaly -Cushing Disease -Insulin resistance -Nephrotic syndrome

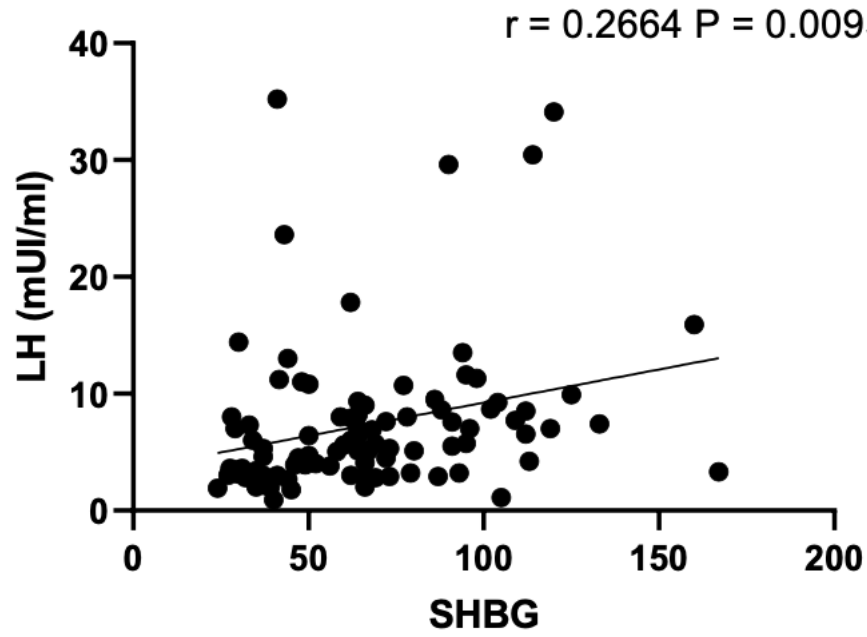
Infection (2021) 49:295–303
https://doi.org/10.1007/s15010-020-01558-6

ORIGINAL PAPER

The importance of SHBG and calculated free testosterone for the diagnosis of symptomatic hypogonadism in HIV-infected men: a single-centre real-life experience

Letizia Chiara Pezzaioli[1] · Eugenia Quiros-Roldan[2] · Simone Paghera[3] · Teresa Porcelli[4] · Filippo Maffezzoni[5] · Andrea Delbarba[5] · Melania Degli Antoni[2] · Carlo Cappelli[1] · Francesco Castelli[2] · Alberto Ferlin[1]





Results

	Total testosterone Number of patients (%)		Free testosterone Number of patients (%)	
	Chemiluminescent immunoassay	LC-MS/MS	Chemiluminescent immunoassay	LC-MS/MS
Eugonadal	275 (87.0%)	268 (84.8%)	267 (84.8%)	262 (82.9%)
Compensated Hypogonadism	31 (9.8%)	31 (9.8%)	18 (5.7%)	23 (7.3%)
Primary Hypogonadism	3.2%	5.3%	6.9%	9.8%
Secondary Hypogonadism	7 (2.2%)	14 (4.4%)	14 (4.4%)	20 (6.3%)

Prevalence of hypogonadism considering total testosterone and free testosterone are significantly different (p<0.0001)

De Vincentis *et al.* Aging Male. 25(1):41-53, 2022

Free & Bioavailable Testosterone calculator

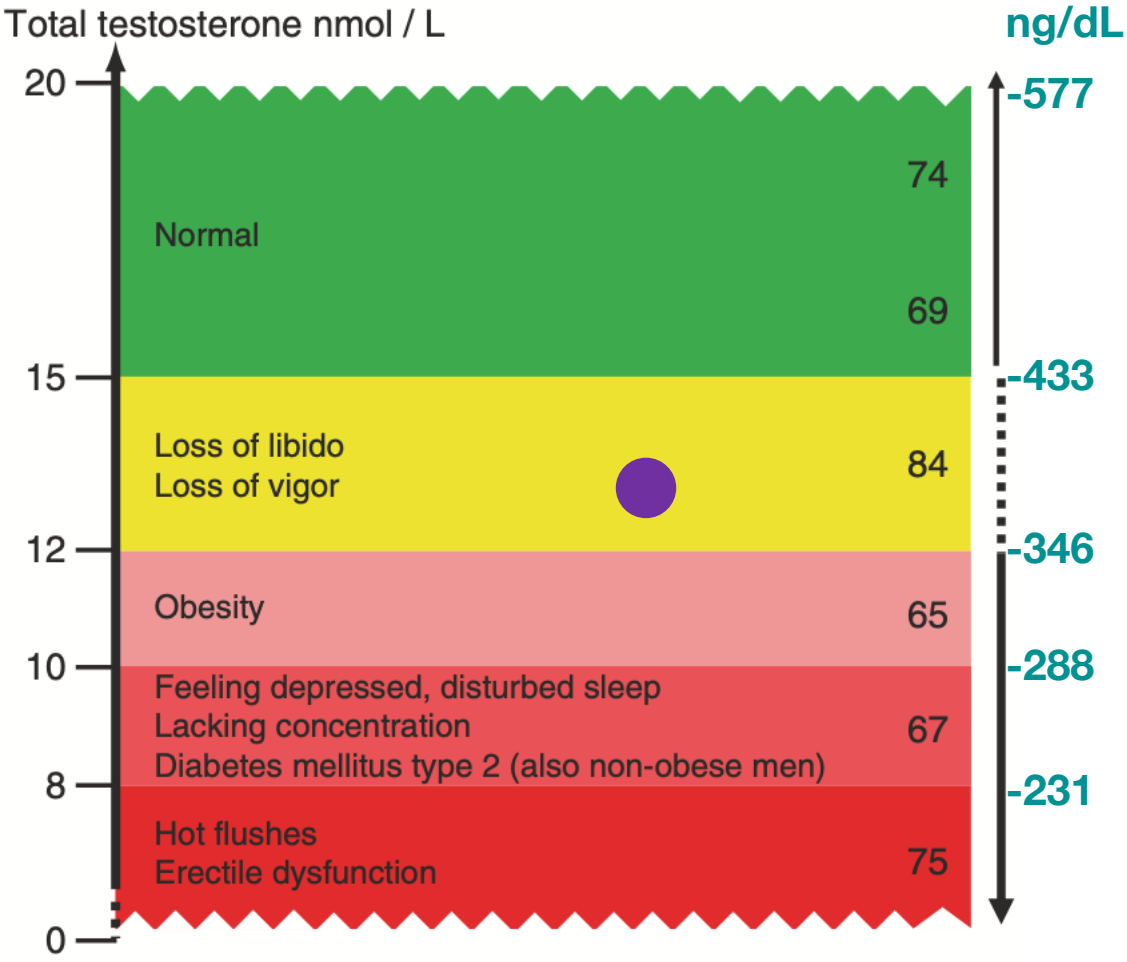
These calculated parameters more accurately reflect the level of bioactive testosterone than does the sole measurement of total serum testosterone. Testosterone and dihydrotestosterone (DHT) circulate in plasma unbound (free approximately 2 - 3%) ,bound to specific plasma proteins (sex hormone-binding globulin SHBG) and weakly bound to nonspecific proteins such as albumin. The SHBG-bound fraction is biologically inactive because of the high binding affinity of SHBG for testosterone. Free testosterone measures the free fraction, bioavailable testosterone includes free plus weakly bound to albumin.

Albumin	4.3	g/dL	Calculate	Explanation and examples
SHBG	73	nmol/L		
Testosterone	355	ng/dL		

Free Testosterone	4.07 ng/dL = 1.15 %
Bioavailable Testosterone	95.5 ng/dL = 26.9 %

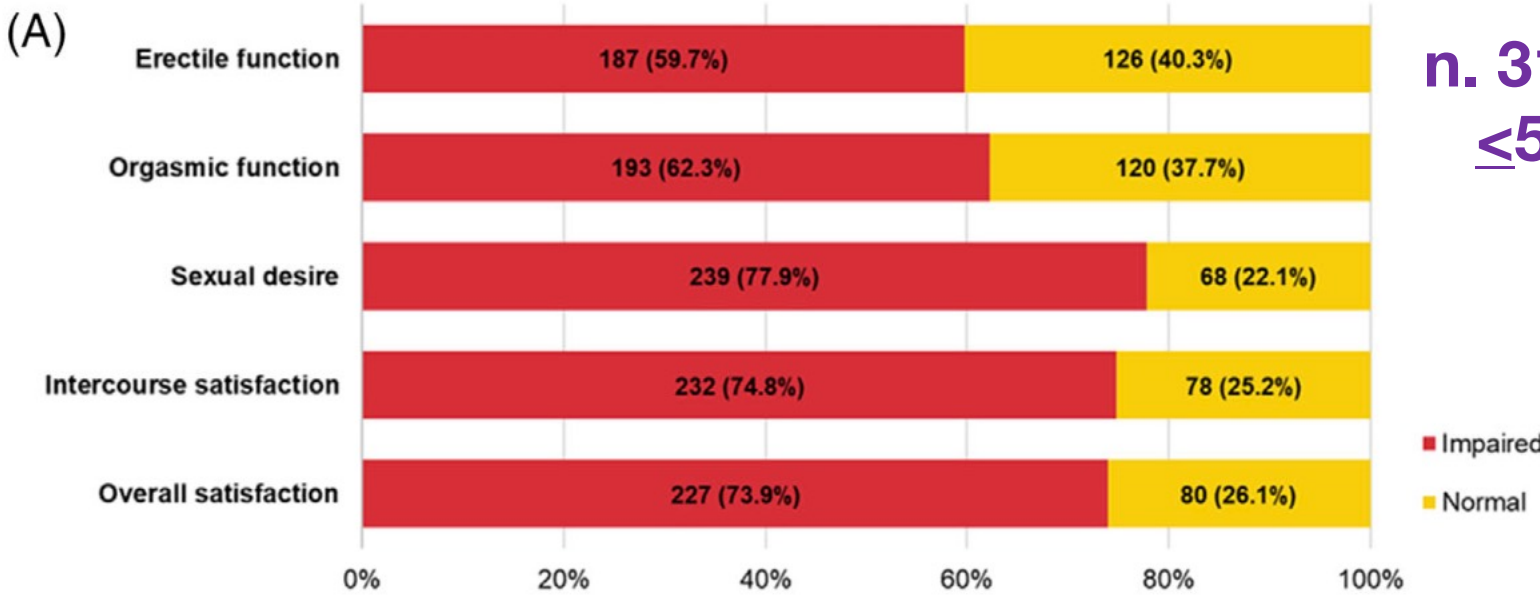
http://www.issam.ch/freetesto.htm

To treat or not to treat?



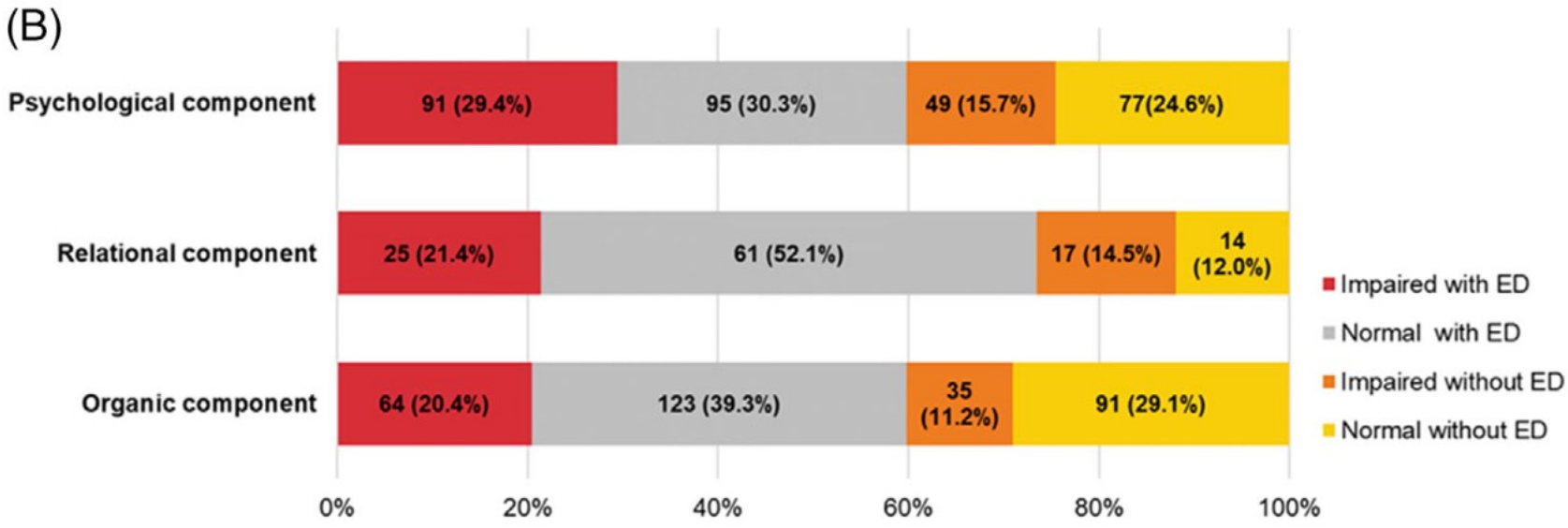
- Male patient 30 years
- Living with HIV
- HAART therapy since 6 years
- Low sexual desire, slightly impaired erectile function, overweight.
- No important comorbidities
- Serum TT: 355 ng/dL (12.3 nmol/L)
- LH and FSH in the normal range
- PRL: normal
- SHBG: 73 nmol/L (13.5-71.4)
- cFT: 4.07 ng/dL (100 pmol/L)

Determinants of ED in young to middle aged MLWH



n. 313 MLWH
≤50 years

IIEF-15



SIEDY

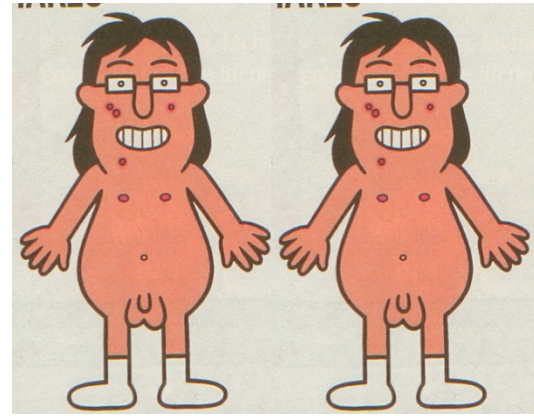
De Vincentis *et al. Andrology* 2023

Erectile Dysfunction and HIV infection
OTHER PSYCHOSEXOLOGICAL CORRELATES

FEAR OF VIRUS TRANSMISSION

LONG PERIODS OF SEXUAL ABSTINENCE

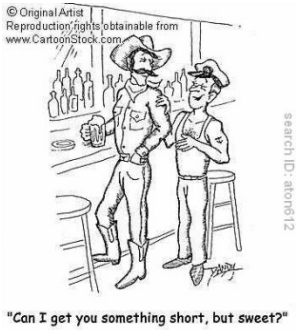
HIGH % OF GAY MEN – NEED OF A BETTER RIGIDITY FOR ANAL INTERCOURSES



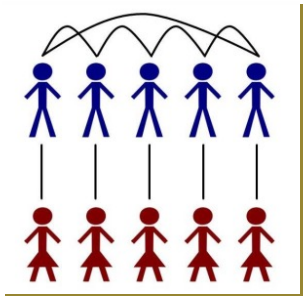
Guaraldi *et al.* Antiviral Therapy 2007
Shindel *et al.* AIDS Patient Care STD 2011

Erectile Dysfunction and HIV infection
OTHER PSYCHOSEXOLOGICAL CORRELATES

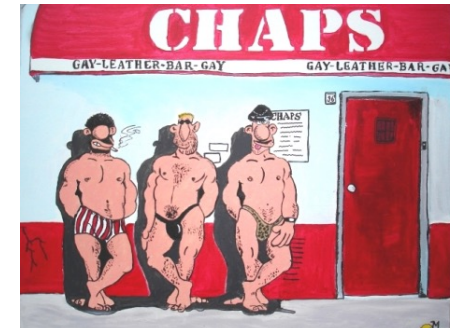
Consider some aspects of “Gay culture” in Homosexual HIV-infected men



IMPORTANCE OF PERFORMANCE



PECULIAR BEHAVIORS: ATTITUDE TOWARDS PROMISCUITY



PECULIAR BEHAVIORS: ATTITUDE TOWARDS SEXUAL MARATHONS

(Request for prolonged erection in the context of many repeated sexual intercourses, group sex, sex workers' activities)

Richardson et al. 2007, Nettles et al.2009, Shindel *et al. AIDS Patient Care STD* 2011

Erectile Dysfunction in HIV-infected Men Predisposes to High Risk Sexual Behaviour

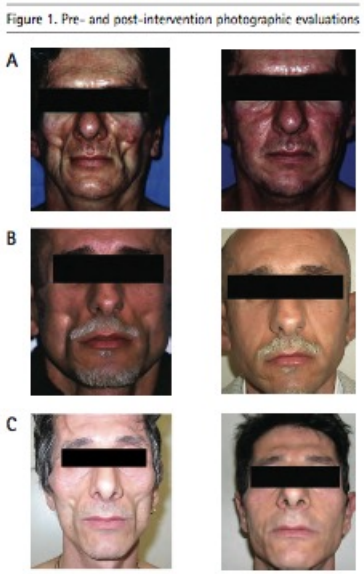
REINFORCE COUNSELING FOR STD AT EACH VISIT ESPECIALLY WHEN PROVIDING A TREATMENT FOR ED

Condom removal due to ED to increase penile sensitivity

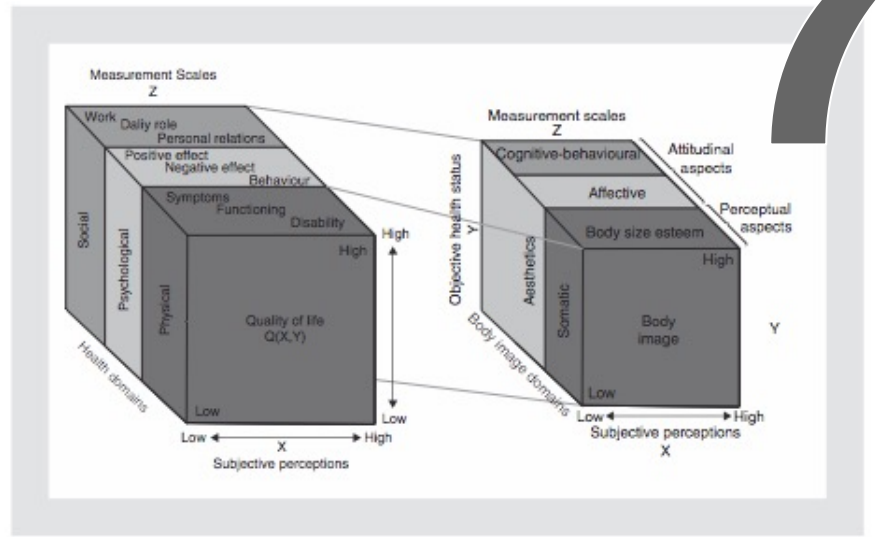
Santi *et al. Nat Rev Urol* 11:99-109, 2014

Body Changes, Body Images, Quality of Life and ED in HIV-infected men

Body changes



Perception of Body Image



Low self-esteem
Stigma of a stigmatized disease

METABOLIC & HORMONAL CORRELATES → ED ← OTHER PSYCHOLOGICAL CORRELATES

Santi *et al. Nat Rev Urol* 11:99-109, 2014
De Vincentis *et al. J Clin Med* 10(5):1088, 2021

Journal of
Clinical Medicine

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Review

HIV and Sexual Dysfunction in Men

Sara De Vincentis [1,2], Giulia Tartaro [1,2], Vincenzo Rochira [1,2,*] and Daniele Santi [1,2]

Table 1. Specific factors that influence sexuality in human immunodeficiency virus (HIV)-infected men.

HIV-Related Organic Factors
Effect of HIV-related comorbidities (e.g., hypertension, diabetes mellitus, dyslipidemia) on cardiovascular function
HIV-Related Psychosexological Issues
Fear of virus transmission
Disclosure of HIV status to the partner
Stigma
Body image changes (i.e., lipodystrophy)
MSM Related Psychosexological Issues
Gay Culture
Self-perceived body image
Body image importance in gay culture
Importance of sexual performance
Anal sex
Casual sex and group sex
Recreational drugs abuse
HIV-Related Sexual Behavioral Issues
Obligatory condom use

PECULIAR ASPECTS TO BE CONSIDERED IN HIV-INFECTED MEN WITH ED AT INTERVIEW

Andrological interview peculiar for HIV positive men:

- **Fear of transmission**

effects of the use of condom on the quality of the erection

- **Altered perception of body image**

effects on the whole sex function

- **Sexual orientation**
- **Sexual behavior**

quality of erection to ensure anal penetration etc.

- **Psycho-sexological background**
- **Drug therapy**
- **Comorbidity**

Santi *et al. Nat Rev Urol* 11:99-109, 2014

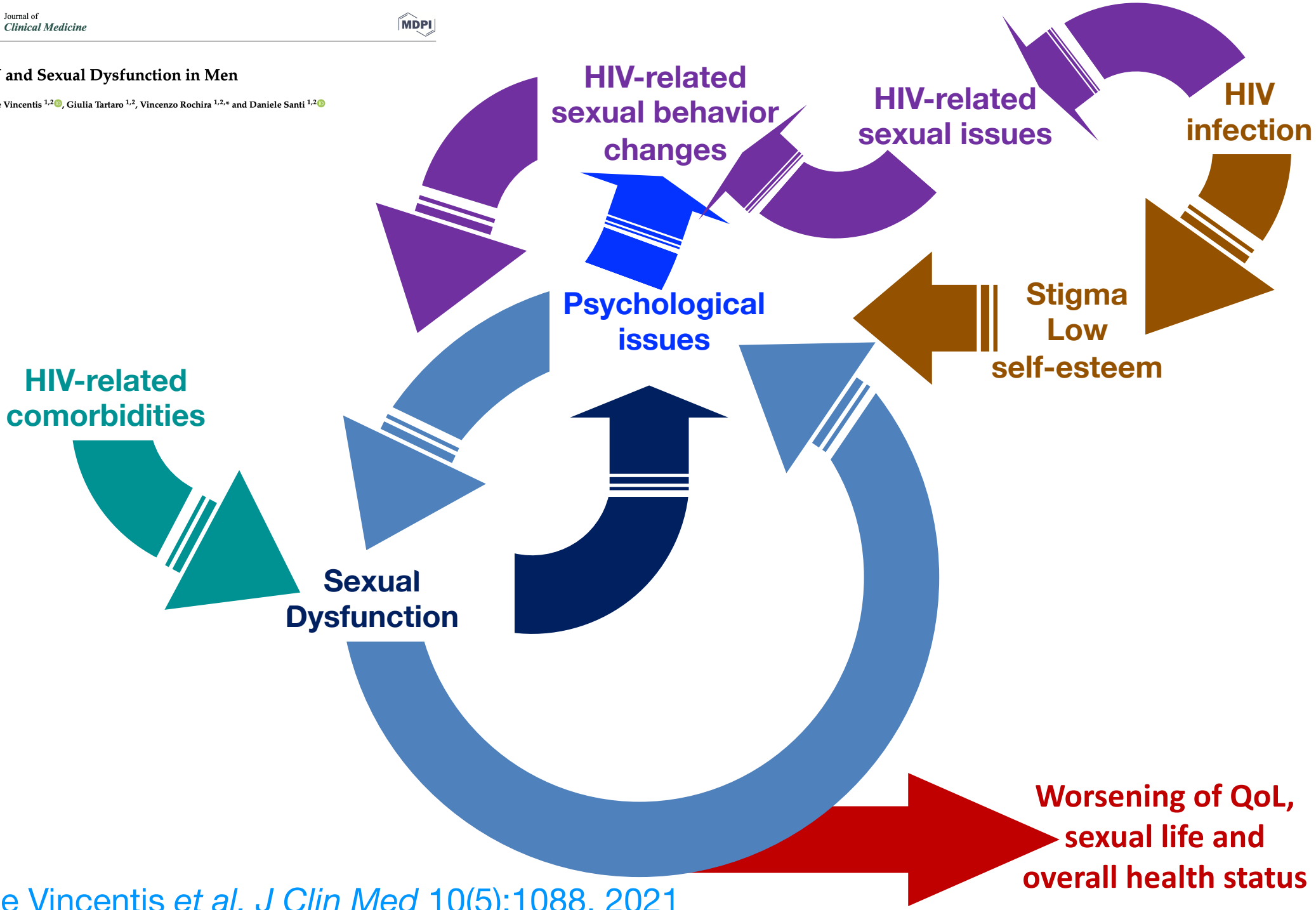
Journal of *Clinical Medicine*

MDPI

Review

HIV and Sexual Dysfunction in Men

Sara De Vincentis [1,2], Giulia Tartaro [1,2], Vincenzo Rochira [1,2,*] and Daniele Santi [1,2]

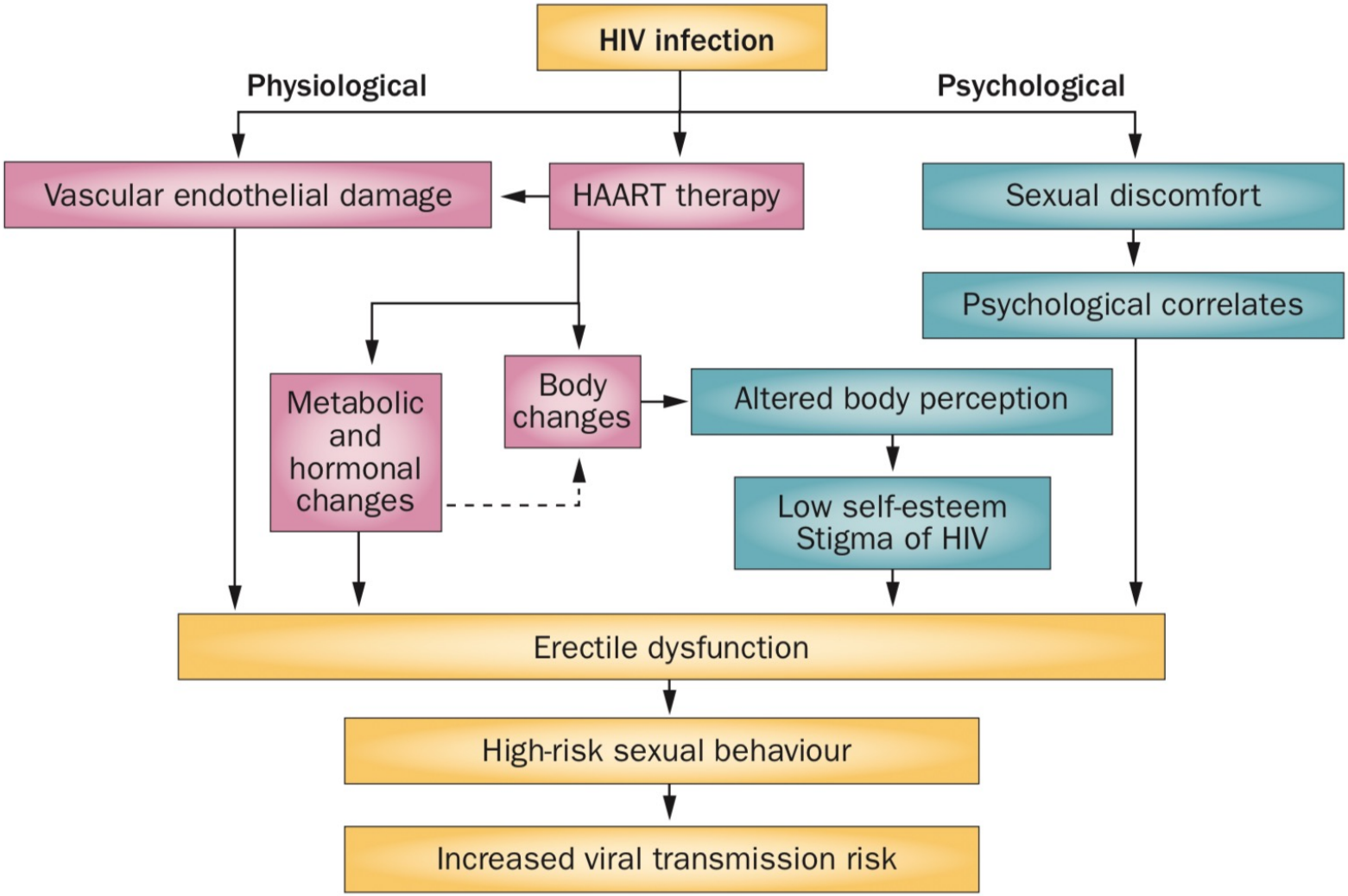


De Vincentis *et al. J Clin Med* 10(5):1088, 2021

Male sexual dysfunction and HIV—a clinical perspective

Daniele Santi, Giulia Brigante, Stefano Zona, Giovanni Guaraldi and Vincenzo Rochira

cians owing to many factors, including



Santi D, Brigante G, Zona S, Guaraldi G, Rochira V
Nature Rev Urol 2014

Journal of
Clinical Medicine

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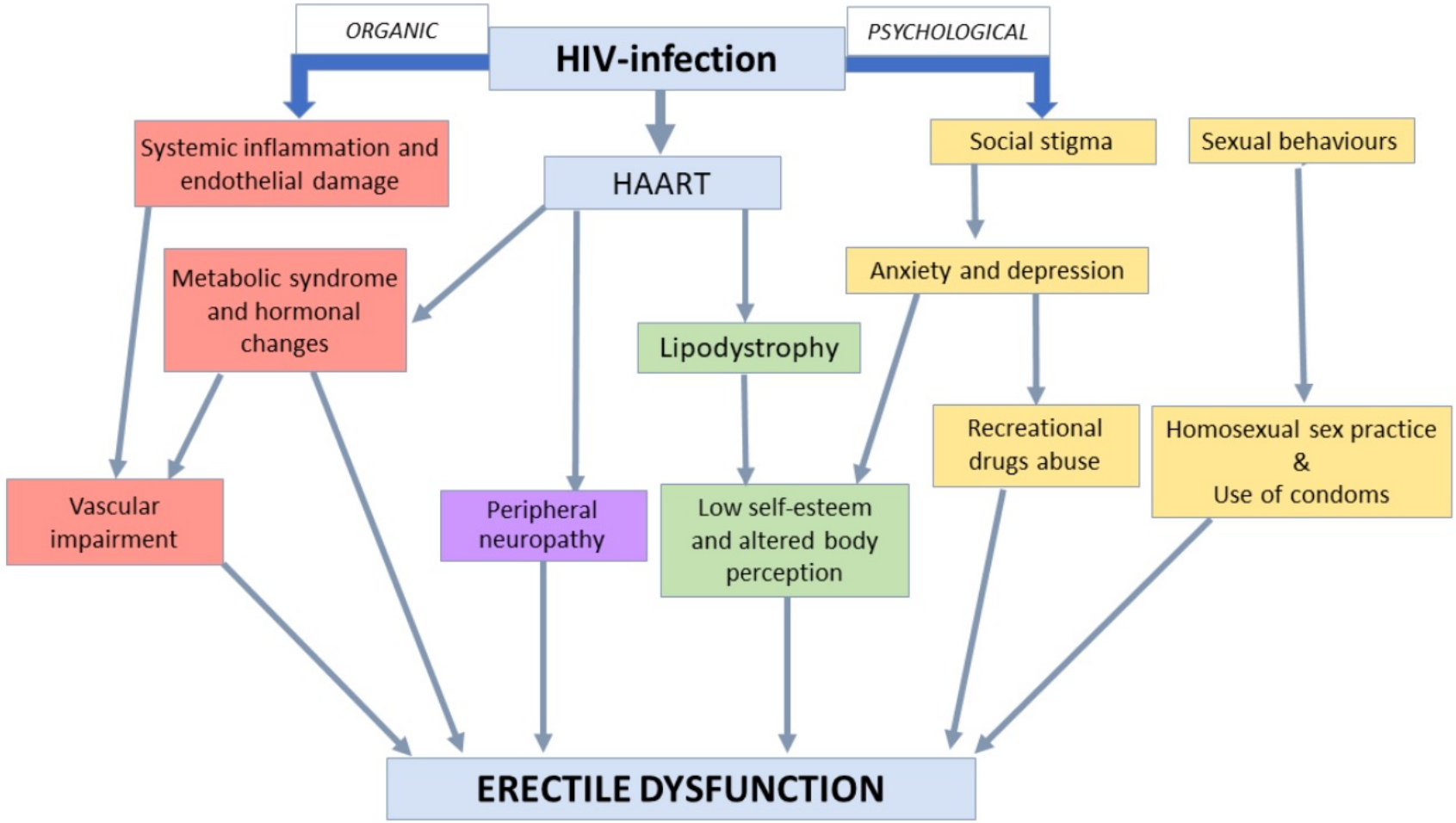
Review

HIV and Sexual Dysfunction in Men

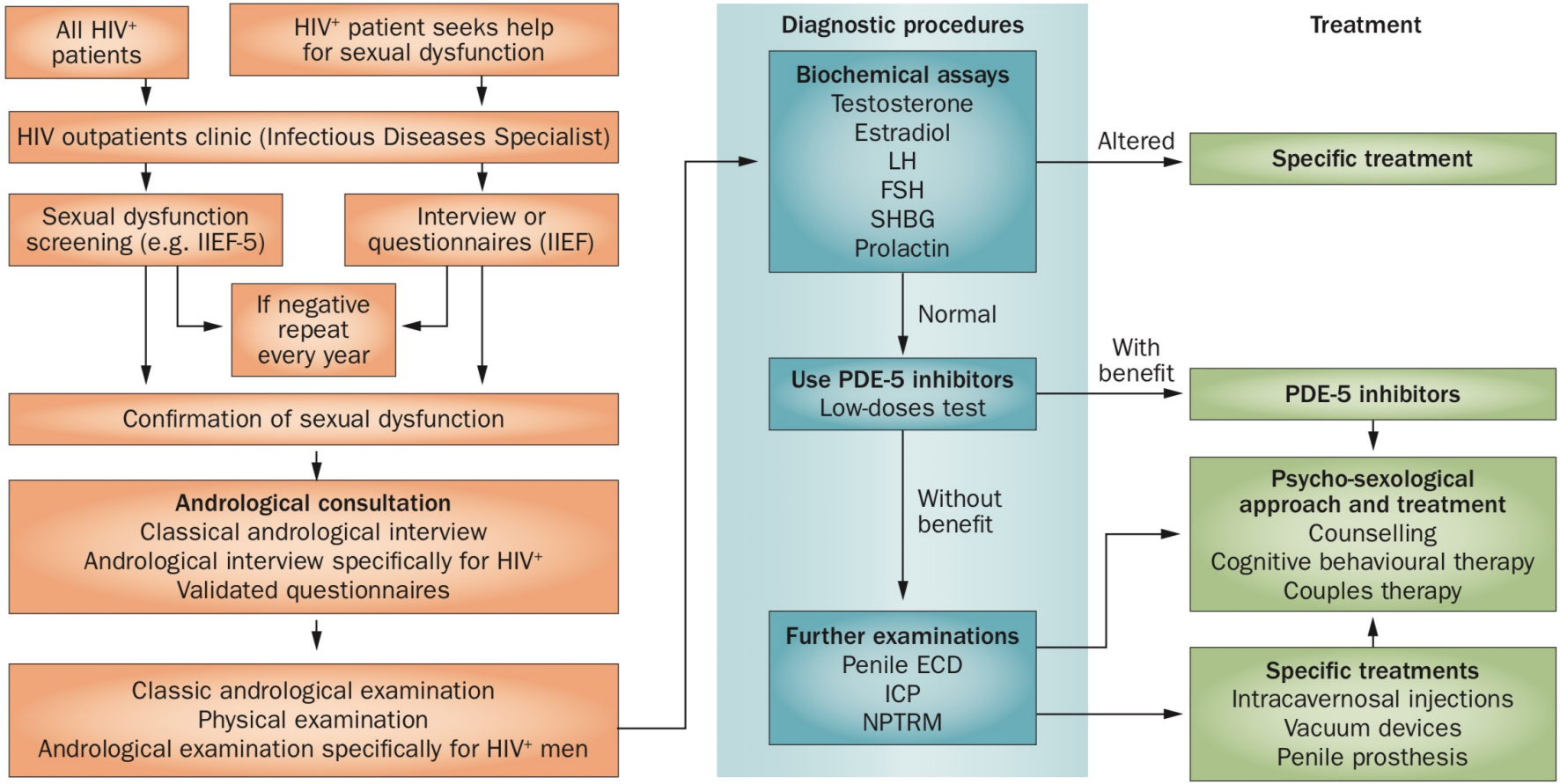
Sara De Vincentis [1,2], Giulia Tartaro [1,2], Vincenzo Rochira [1,2,*] and Daniele Santi [1,2]



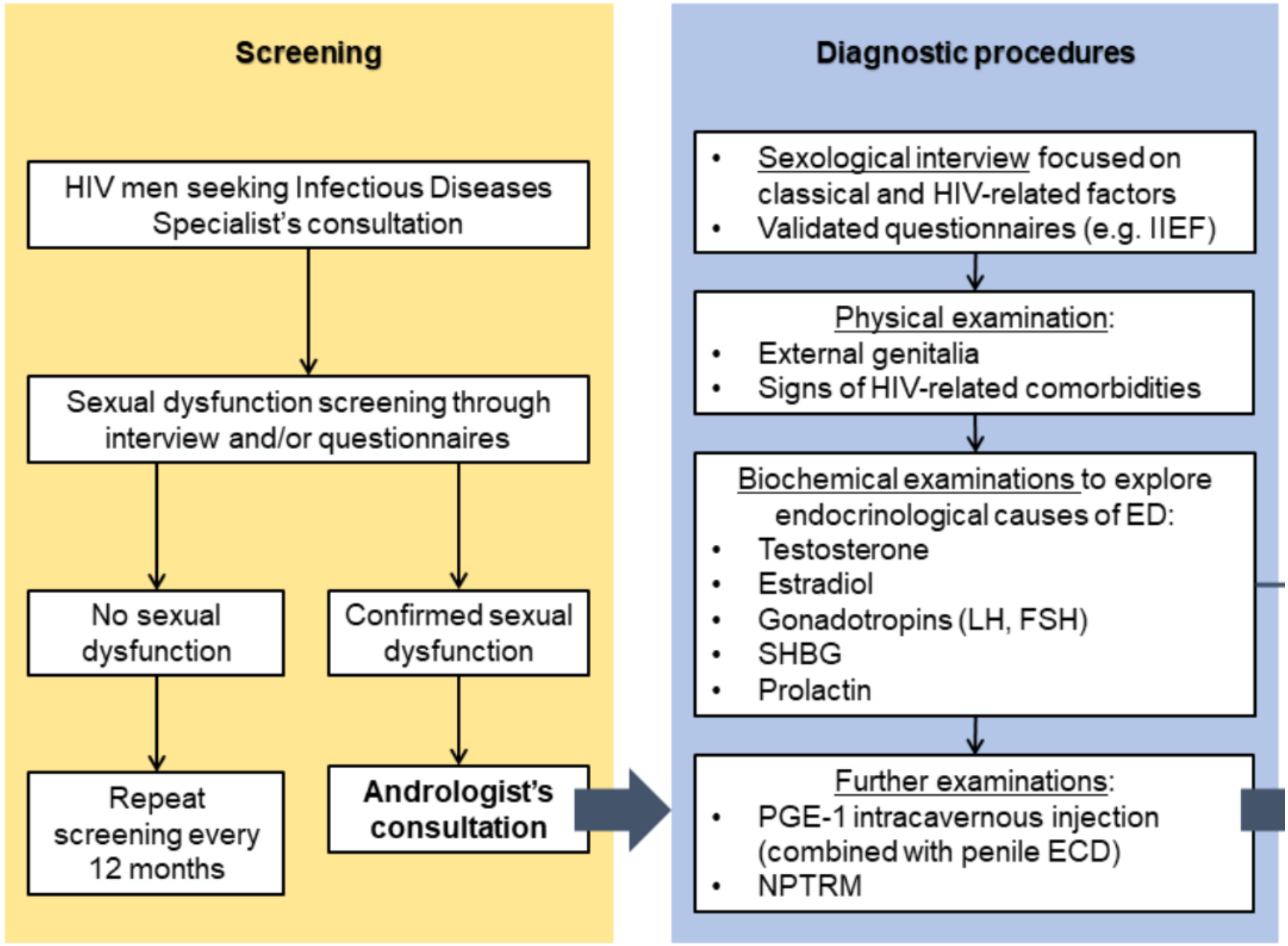
Male sexual dysfunction and HIV—a clinical perspective

Daniele Santi, Giulia Brigante, Stefano Zona, Giovanni Guaraldi and Vincenzo Rochira

Abstract | Sexual dysfunction in men with HIV is often overlooked by clinicians owing to many factors, including



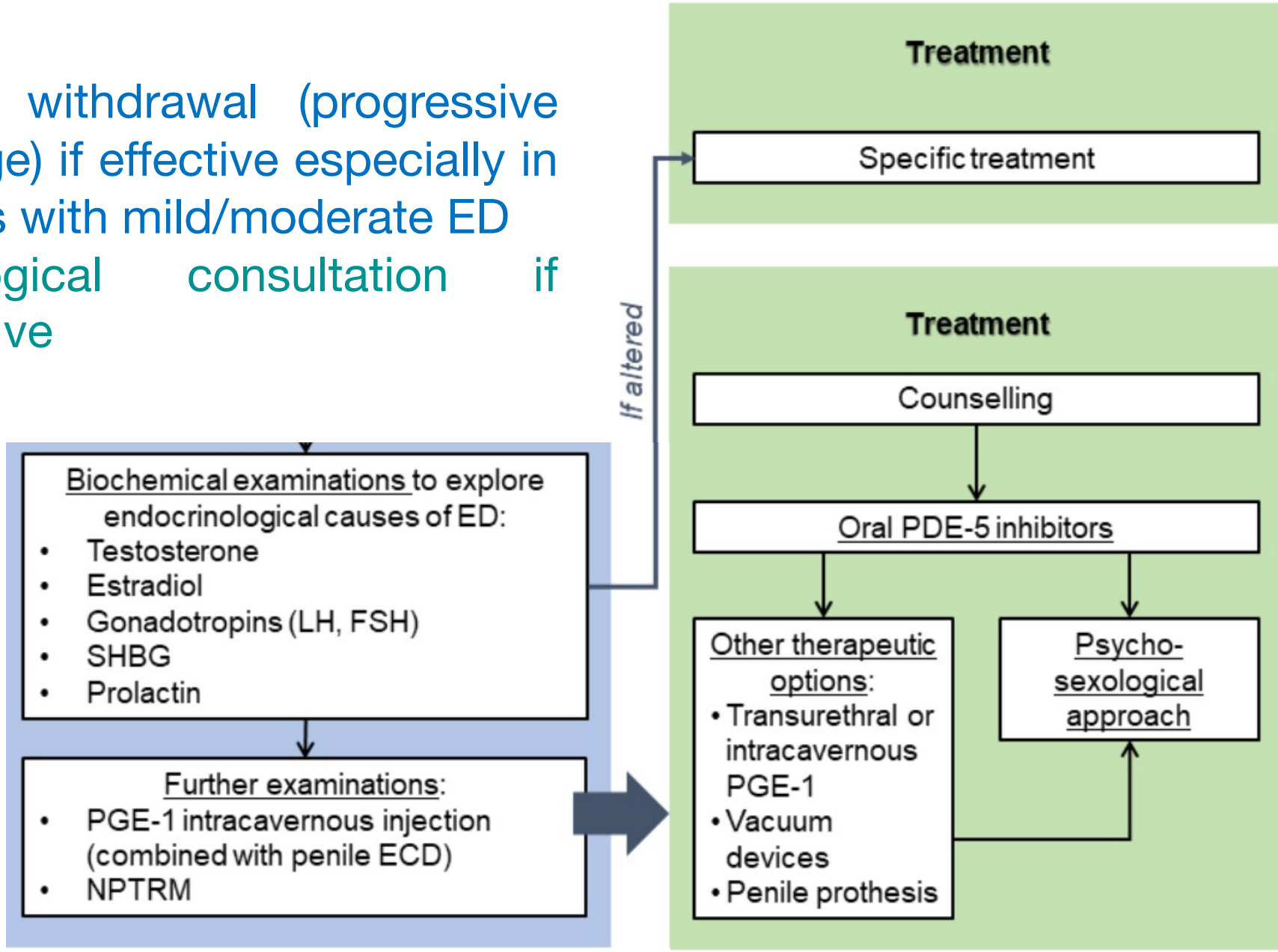
Santi D, Brigante G, Zona S, Guaraldi G, Rochira V *Nature Rev Urol 2014*



De Vincentis *et al. J Clin Med* 10(5):1088, 2021

Consider

1. PDE5-I withdrawal (progressive decalage) if effective especially in patients with mild/moderate ED
2. Andrological consultation if ineffective



De Vincentis *et al. J Clin Med* 10(5):1088, 2021

ED remains an undertreated and undermanaged condition in MLWH.

Determinants of sexual function in men living with HIV younger than 50 years old: Focus on organic, relational, and psychological issues

Sara De Vincentis[1,2,3] | Maria Chiara Decaroli[1,2] | Jovana Milic[4] | Flaminia Fanelli[5] | Giulia Tartaro[1,2] | Chiara Diazzi[2] | Marco Mezzullo[5] | Maria Cristina De Santis[6] | Laura Roli[6] | Tommaso Trenti[6] | Daniele Santi[1,2] | Uberto Pagotto[5,7] | Giovanni Guaraldi[4] | Vincenzo Rochira[1,2]

n. 313 MLWH
≤50 years

Only 35 of 187 patients with ED (18.7%) reported the use of ED medications.

The high prevalence of sexual dysfunctions in our cohort clashes with the low reported use of PDE5-i (14.4%).

De Vincentis *et al. Andrology* 2023

Journal of
Clinical Medicine

MDPI

Review

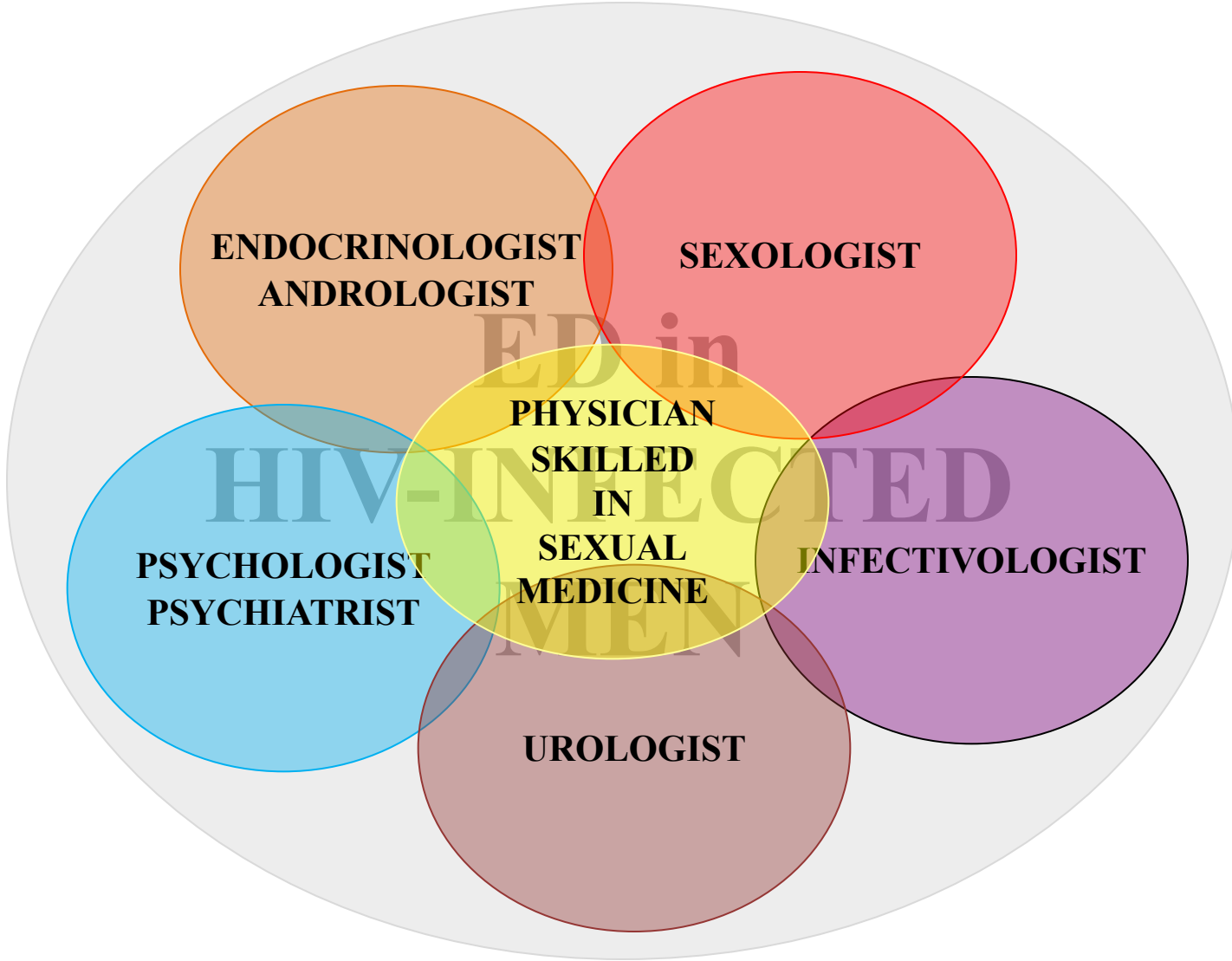
HIV and Sexual Dysfunction in Men

Sara De Vincentis [1,2], Giulia Tartaro [1,2], Vincenzo Rochira [1,2,*] and Daniele Santi [1,2]

- **Disorders of Ejaculation**
- **Infertility**
- **Diseases of the Seminal Tract**

less studied

De Vincentis *et al. J Clin Med* 10(5):1088, 2021



Agenda

- Introduction to Sexual Dysfunctions (SD)
- Gender differences and Sexual Dysfunction
- SD in Women Living With HIV (WLWH)
- SD in Men Living With HIV (MLWH)
- **Conclusive Remarks/Practice Points**

Società Italiana di Andrologia e Medicina della Sessualità

Centri accreditati SIAMS

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- PADOVA | UOC ANDROLOGIA E MEDICINA DELLA RIPRODUZIONE
- MILANO | IRCCS ISTITUTO AUXOLOGICO ITALIANO – OSPEDALE SAN LUCA
- TORINO | S.S. ANDROLOGIA, SEMINOLOGIA, CRIOCONSERVAZIONE E DISFORIA DI GENERE
- MODENA | UOC ENDOCRINOLOGIA
- FIRENZE | UOC MEDICINA DELLA SESSUALITÀ E ANDROLOGIA
- ANCONA | SOD ENDOCRINOLOGIA E MALATTIE METABOLICHE
- L'AQUILA | UOC ANDROLOGIA MEDICA
- ROMA | UOC ENDOCRINOLOGIA, MALATTIE DEL METABOLISMO ED ANDI SEMINOLOGIA E BANCA DEL SEME
- NAPOLI | SOD CENTRO DI ANDROLOGIA E MEDICINA DELLA RIPRODUZI FEMMINILE
- CATANIA | UOC ANDROLOGIA ED ENDOCRINOLOGIA

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- CATANZARO | U.O.C. di Endocrinologia
- LATINA| FISIOPATOLOGIA DELLA RIPRODUZIONE E ANDROLOGIA – S. MARIA GORETTI
- ROMA | OSPEDALE SANT'ANDREA – UNITÀ DI ANDROLOGIA CLINICA, LABORATORISTICA ED ECOGRAFICA
- ROMA | OSPEDALE PERTINI – UOC FISIOPATOLOGIA DELLA RIPRODUZIONE E ANDROLOGIA
- ROMA | CENTRO SANT'ANNA
- ROMA | OSPEDALE SAN GIOVANNI CALIBITA FATEBENEFRATELLI ISOLA TIBERINA
- PADOVA | STUDIO MEDICO GAROLLA
- BARI | CENTRO POLISPECIALISTICO DI ENDOCRINOLOGIA E MALATTIE METABOLICHE
- CAGLIARI | CENTRO MEDICO I MULINI – SU PLANU – CAGLIARI
- TORINO | S.S. ANDROLOGIA, SEMINOLOGIA, CRIOCONSERVAZIONE E DISFORIA DI GENERE
- ROZZANO (MI) | ISTITUTO CLINICO HUMANITAS
- ROMA| FONDAZIONE POLICLINICO A. GEMELLI

Conclusive Remarks/Practice Points

- Sexual dysfunction are common in PLWH
- Gender gap of knowledge as in non HIV population (gender incongruence<<<women<<<men)
- Check hypogonadism in MLWH (common)
- HIV-related factors related to sexual dysfunction shared by gender
- Therapy available in men with ED
- Unmeet needs in women or other sexual dysfunctions in men
- Counselling on STDs in presence of SD
- Physician expert in sexual medicine for consultation
- Multidisciplinary approach

REFLECTIONS

Jazz and the 'Art' of Medicine: Improvisation in the Medical Encounter

Paul Haidet, MD, MPH

Medicine is progressively reaching the status of a SCIENCE…..
but in some conditions still remains an ART

Rather than an expert it is important to be experienced

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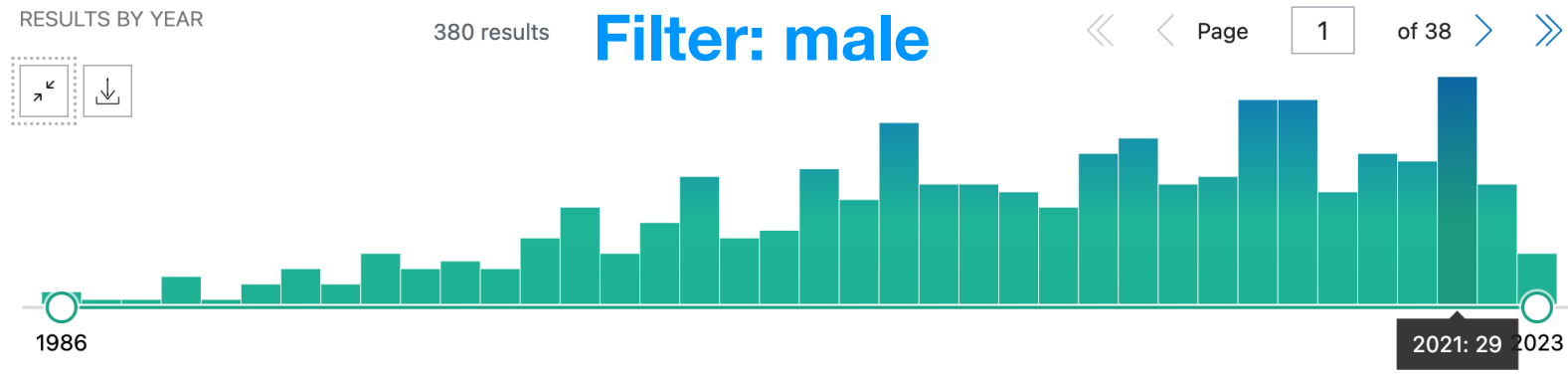
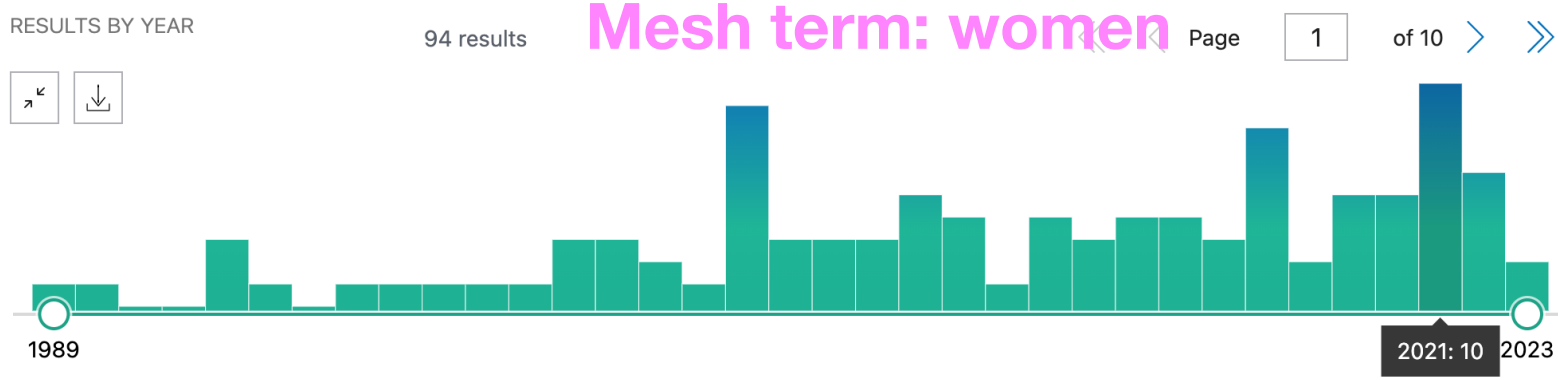
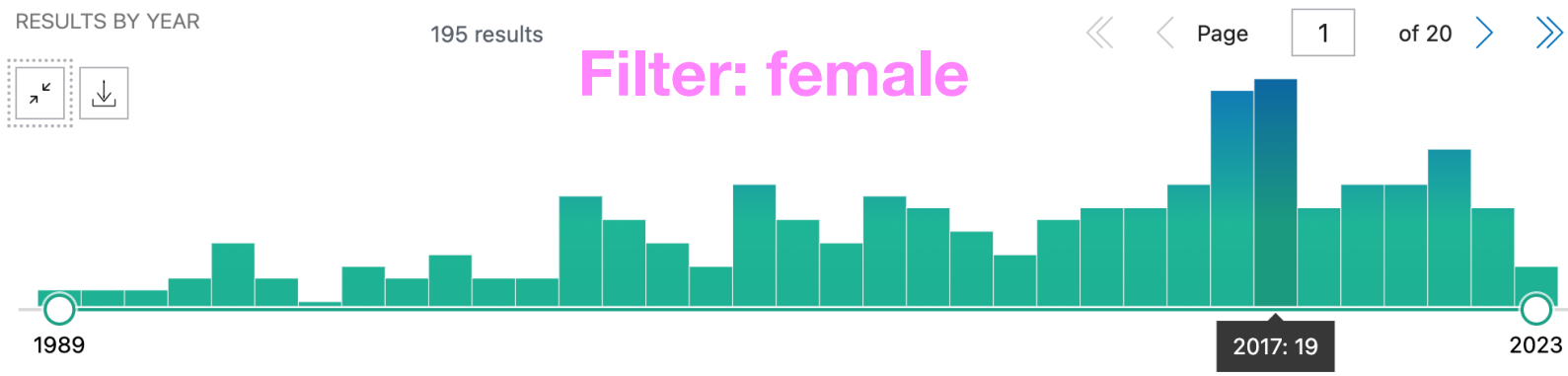
European Reference Network

Gender differences in Research on Sexual Dysfunction in HIV







The Evolution of the Female Sexual Disorder/Dysfunction Definitions, Nomenclature, and Classifications: A Review of DSM, ICSM, ISSWSH, and ICD

Sharon J. Parish, MD,[1]* Sara Cottler-Casanova, MSc,[2,3]* Anita H. Clayton, MD,[4] Marita P. McCabe, PhD,[5] Eli Coleman, PhD,[6] and Geoffrey M. Reed, PhD[7,8]

Table 2. International Consultation in Sexual Medicine (ICSM) female sexual sysfunction definitions from the article by McCabe et al[35]

ICSM female sexual dysfunctions	Definition
Hypoactive sexual desire dysfunction (clinical principle)	Persistent or recurrent deficiency or absence of sexual or erotic thoughts or fantasies and desire for sexual activity
Female sexual arousal dysfunction (clinical principle)	Persistent or recurrent inability to attain or maintain arousal until completion of the sexual activity, an adequate subjective assessment of her genital response
Female orgasmic dysfunction (Grade B)	(i) Marked delay in, marked frequency of, or absence of orgasm and/or (ii) markedly decreased intensity of orgasmic sensation
Female genital-pelvic pain dysfunction (Grade C)	Persistent or recurrent difficulties with at least one of the following: (i) vaginal penetration during intercourse; (ii) marked vulvovaginal or pelvic pain during genital contact; (iii) marked fear or anxiety about vulvovaginal or pelvic pain in anticipation of, during, or as a result of genital contact; or (iv) marked hypertonicity or overactivity of pelvic floor muscles with or without genital contact
Persistent genital arousal disorder (expert opinion)	Spontaneous, intrusive, and unwanted genital arousal (ie, tingling, throbbing, pulsating) in the absence of sexual interest and desire. Awareness of subjective arousal is typically, but not invariably, unpleasant. The arousal is unrelieved by at least one orgasm and the feeling of arousal persists for hours or days.
Postcoital syndrome (postorgasmic illness syndrome) (expert opinion)	Negative feelings, experiences, and/or physical symptoms such as headache, malaise, fatigue, and other symptoms after sexual activity
Hypohedonic orgasm (expert opinion)	Lifelong or acquired decreased or low level of sexual pleasure with orgasm
Painful orgasm (expert opinion)	The occurrence of genital and/or pelvic pain during or shortly after orgasm

Parish SJ *et al. Sex Med Rev* 9:36-56, 2021