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# 12º ENDO SUL

12º CONGRESSO DE ENDOCRINOLOGIA E METABOLOGIA DA REGIÃO SUL  
CONGRESSO CATARINENSE DE ENDOCRINOLOGIA E METABOLOGIA 2018

05 a 07 de julho de 2018 | Florianópolis - SC

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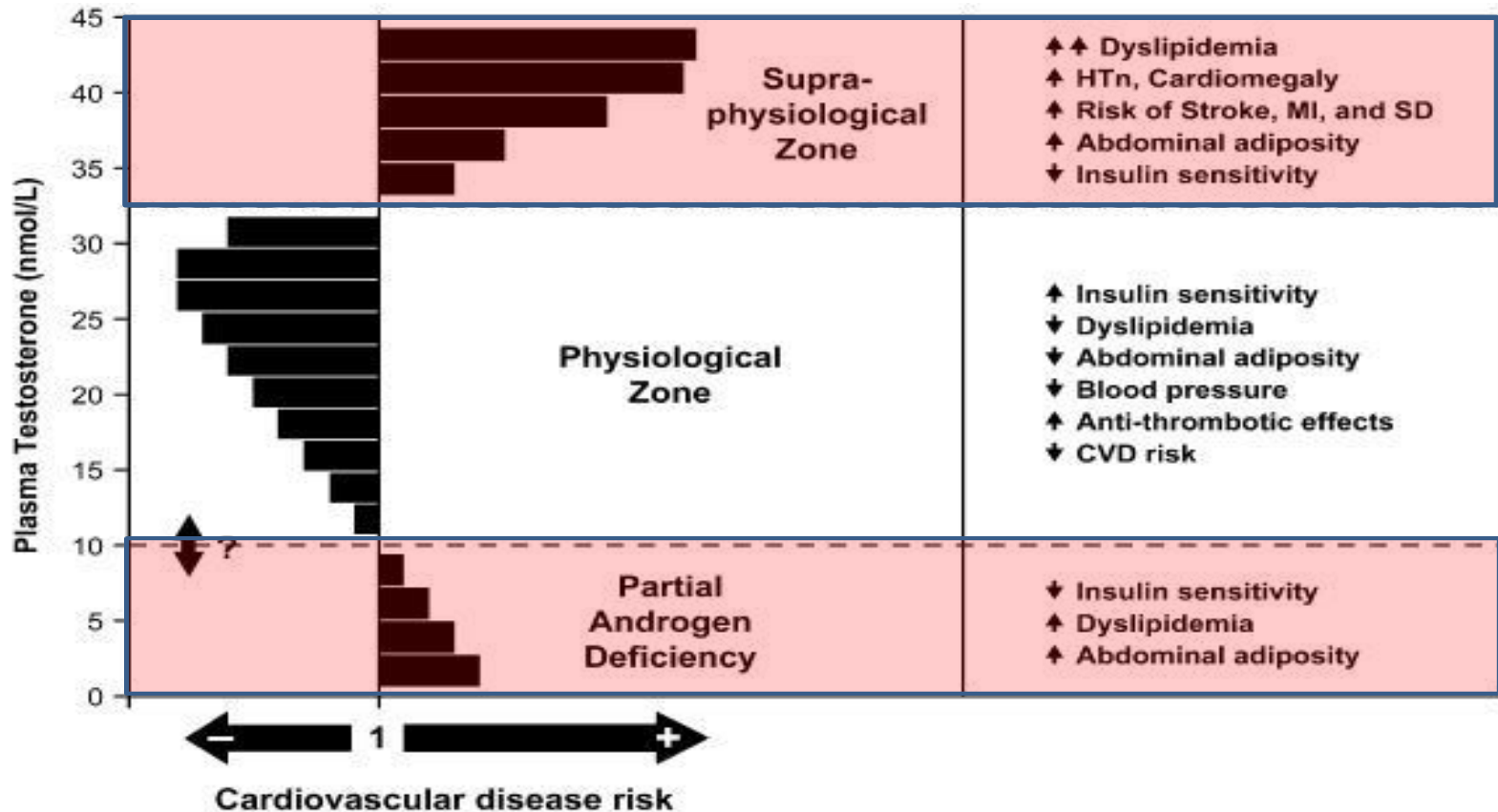
## Hot Topics - Testosterona Risco Cardiovascular

João Paulo Iazigi

**Não tenho conflito de interesses  
para esta apresentação**

# Níveis de testosterona e risco cardiovascular

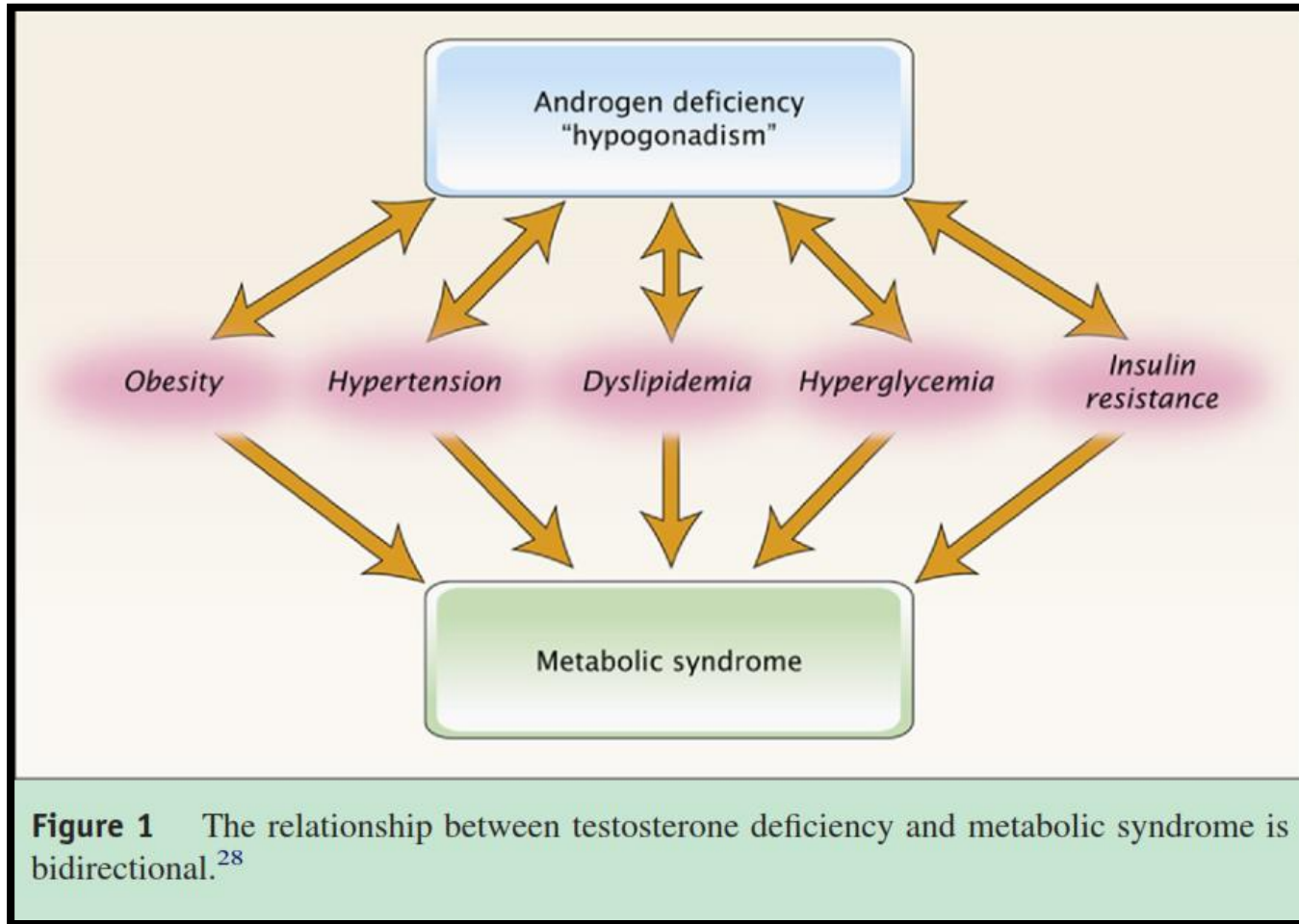
## A janela fisiológica.



Blouin K, et al. J Steroid Biochem Mol Biol 2008;108:272

# Testosterone Deficiency

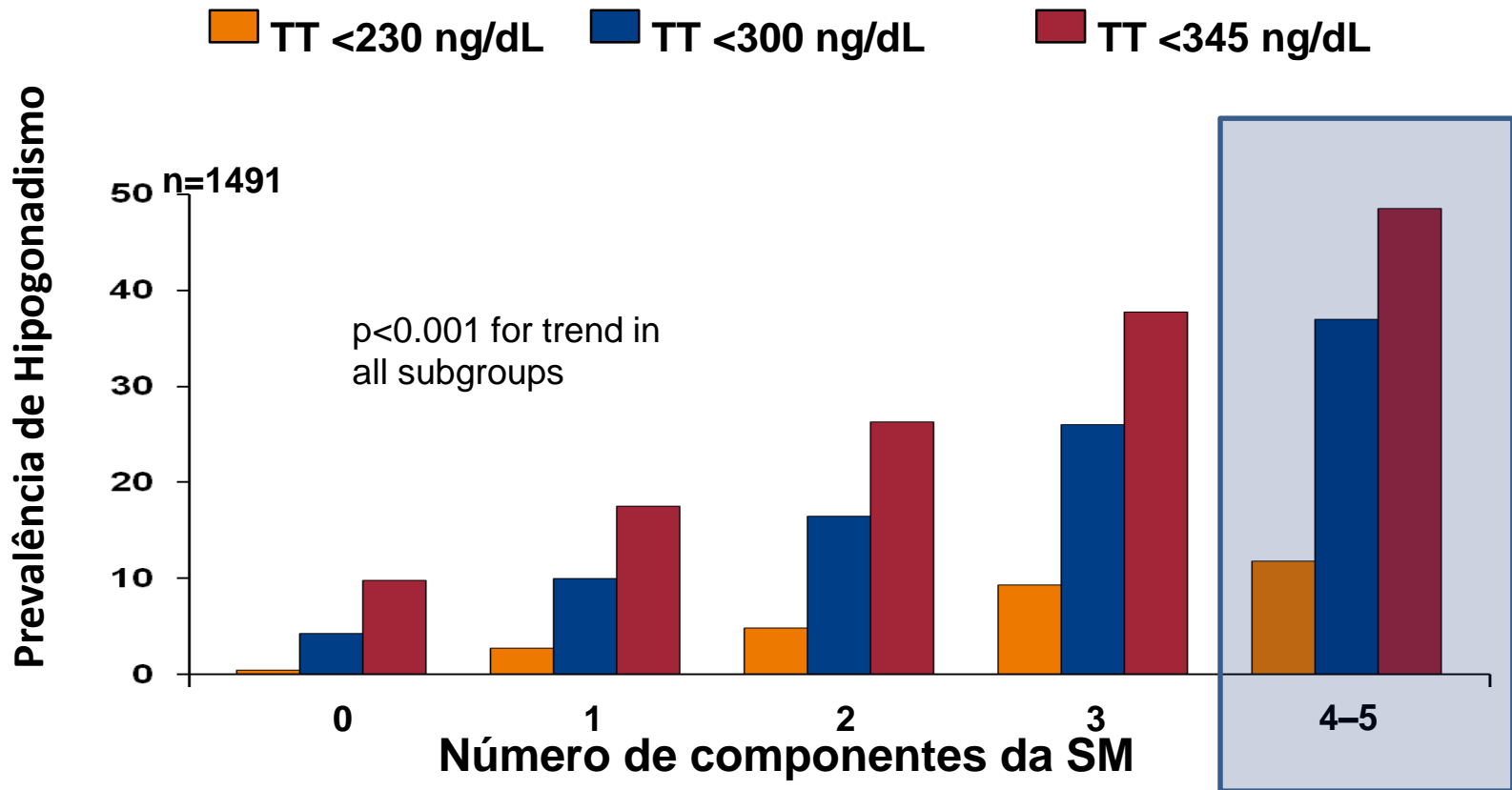
Abdulmageed M. Traish, MBA, PhD,<sup>a,b</sup> Martin M. Miner, MD,<sup>b,c</sup> Abraham Morgentaler, MD,<sup>b,d</sup> Michael Zitzmann, MD<sup>b,e</sup>  
*The American Journal of Medicine* (2011) 124, 578-587



**Figure 1** The relationship between testosterone deficiency and metabolic syndrome is bidirectional.<sup>28</sup>

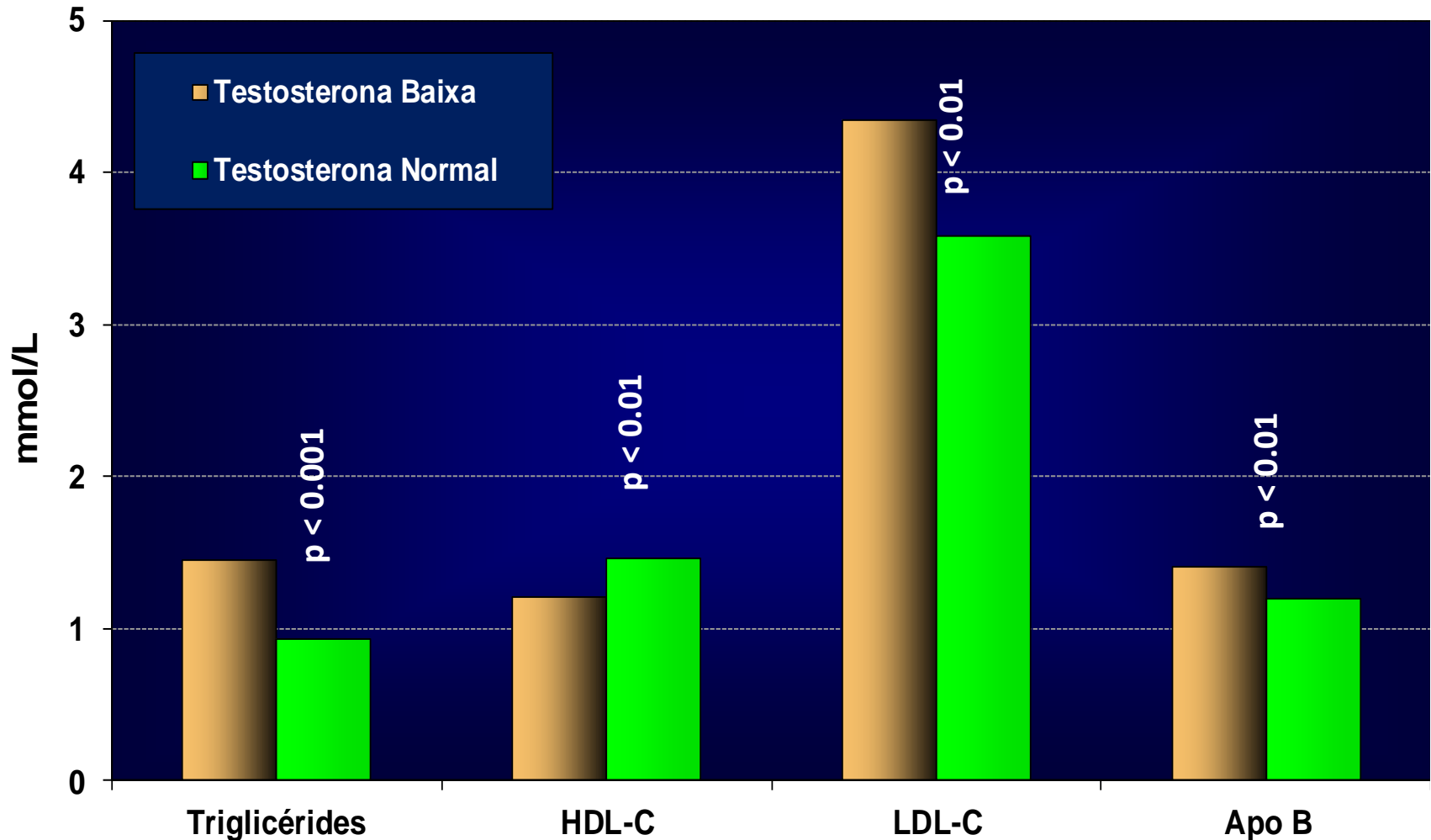
**A SÍNDROME METABÓLICA AUMENTA O RISCO  
DE HIPOGONADISMO ?**

# Níveis de T total diminuem com o aumento do número de componentes da Síndrome Metabólica



**O HIPOGONADISMO AUMENTA O RISCO DE  
SÍNDROME METABÓLICA ?**

# Associação entre Testosterona e Fatores de Risco Cardiovascular em Homens Adultos Saudáveis: **Estudo Telecom**





## **Testosterone Therapy in Men With Hypogonadism: An Endocrine Society\* Clinical Practice Guideline**

Shalender Bhasin,<sup>1</sup> Juan P. Brito,<sup>2</sup> Glenn R. Cunningham,<sup>3</sup> Frances J. Hayes,<sup>4</sup>  
Howard N. Hodis,<sup>5</sup> Alvin M. Matsumoto,<sup>6</sup> Peter J. Snyder,<sup>7</sup> Ronald S. Swerdloff,<sup>8</sup>  
Frederick C. Wu,<sup>9</sup> and Maria A. Yialamas<sup>10</sup>

<sup>1</sup>Brigham and Women's Hospital, Boston, Massachusetts 02115; <sup>2</sup>Mayo Clinic, Rochester, Minnesota 55905; <sup>3</sup>Baylor College of Medicine, Houston, Texas 77030; <sup>4</sup>Massachusetts General Hospital, Boston, Massachusetts 02114; <sup>5</sup>Keck School of Medicine, University of Southern California, Los Angeles, California 90033; <sup>6</sup>Veterans Affairs Puget Sound Health Care System, Seattle, Washington 98108; <sup>7</sup>Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104; <sup>8</sup>Harbor-UCLA Medical Center, Torrance, California 90502; <sup>9</sup>University of Manchester, Manchester M13 9PL, United Kingdom; and <sup>10</sup>Brigham and Women's Hospital, Boston, Massachusetts 02115

# Hipogonadismo

Sintomas

+

Texto baixa  
< 264 ng/dL

Avaliar  
contra-indicações

## Diagnosis

### Diagnosis of Hypogonadism in Men

#### Diagnosis of Men with Suspected Hypogonadism

- Endocrine Society (ES) recommends diagnosing hypogonadism in men with symptoms and signs of testosterone deficiency and unequivocally and consistently low serum total testosterone (TT) and/or free testosterone (FT) concentrations (when indicated). (1|⊕⊕⊕○)

#### Screening and Case Detection for Hypogonadism

- ES recommends against routine screening of men in the general population for hypogonadism. (1|⊕⊕○○)

#### Distinguishing Between Primary or Secondary Hypogonadism

- In men who have hypogonadism, ES recommends distinguishing between primary (testicular) and secondary (pituitary-hypothalamic) hypogonadism by measuring serum luteinizing hormone and follicle-stimulating hormone concentrations. (1|⊕⊕⊕○)

# Hipogonadismo e Sintomas

**Table 3. Symptoms and Signs Suggestive of T Deficiency in Men**

**Specific symptoms and signs**

Incomplete or delayed sexual development  
Loss of body (axillary and pubic) hair  
Very small testes (<6 mL)

**Suggestive symptoms and signs**

Reduced sexual desire (libido) and activity  
Decreased spontaneous erections, erectile dysfunction  
Breast discomfort, gynecomastia  
Eunuchoidal body proportions  
Inability to father children, low sperm count  
Height loss, low-trauma fracture, low BMD  
Hot flushes, sweats

**Nonspecific symptoms and signs associated with testosterone deficiency**

Decreased energy, motivation, initiative, and self-confidence  
Feeling sad or blue, depressed mood, persistent low-grade depressive disorder  
Poor concentration and memory  
Sleep disturbance, increased sleepiness  
Mild unexplained anemia (normochromic, normocytic)  
Reduced muscle bulk and strength  
Increased body fat, body mass index

Adapted with permission from Bhasin *et al.* (7).

# Testosterona baixa e mortalidade CV

SPECIAL FEATURE

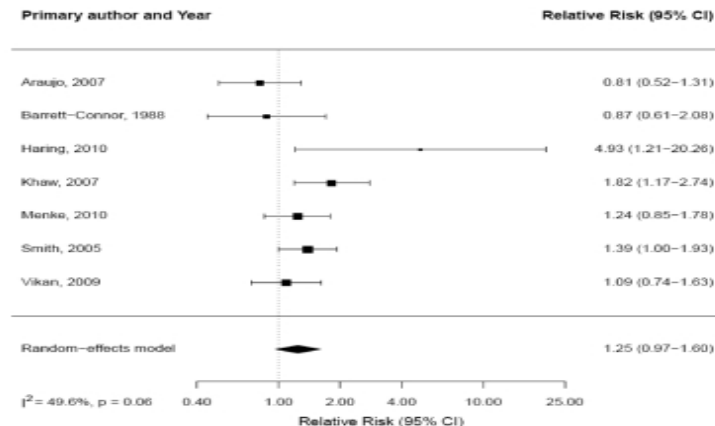
Clinical Review

## Endogenous Testosterone and Mortality in Men: A Systematic Review and Meta-Analysis

Andre B. Araujo, Julia M. Dixon, Elizabeth A. Suarez, M. Hassan Murad,  
Lin T. Guey, and Gary A. Wittert

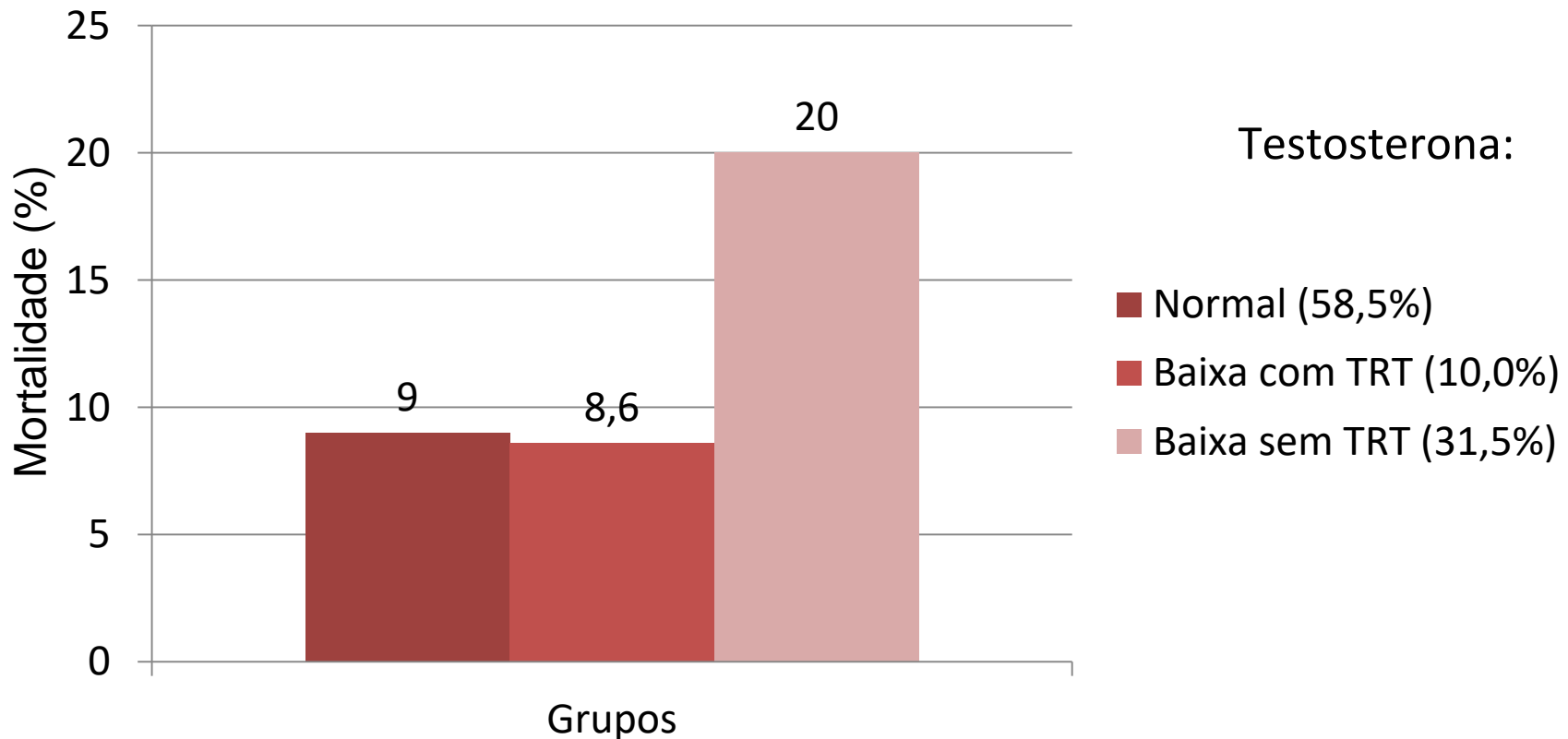
Department of Epidemiology (A.B.A., J.M.D., E.A.S., L.T.G.), New England Research Institutes, Inc., Watertown, Massachusetts 02472; Division of Preventative Medicine (M.H.M.), Mayo Clinic, Rochester, Minnesota 55905; and Department of Medicine (G.A.W.), University of Adelaide, Adelaide, South Australia 5005, Australia

### B CVD Mortality



# Níveis baixos de testosterona são preditivos de aumento de mortalidade e TRT melhora a sobrevida em homens com DM2

581 homens DM2; Idade:  $59,5 \pm 10,8$  anos; Acompanhamento:  $5,8 \pm 1,7$  anos  
TT normal  $> 10,4$  nmol/L (300 ng/dL)



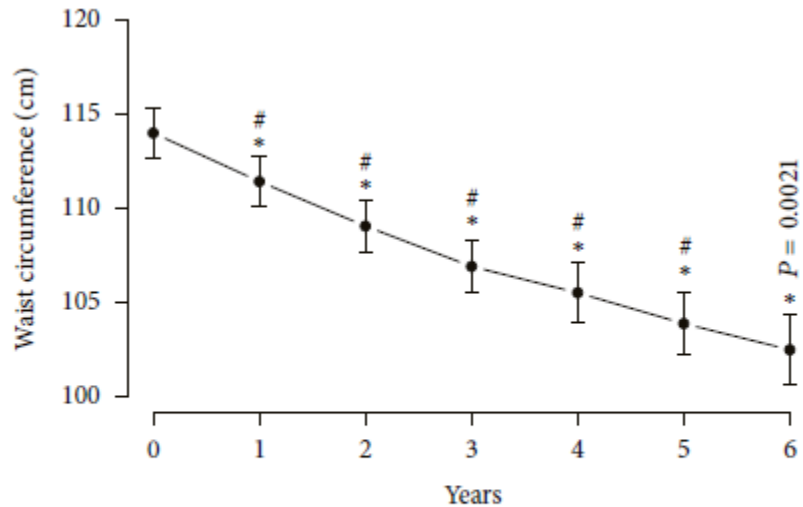
*Clinical Study*

**Effects of Long-Term Testosterone Therapy on Patients with “Diabesity”: Results of Observational Studies of Pooled Analyses in Obese Hypogonadal Men with Type 2 Diabetes**

**156 patients with T2D With Low Testosterone**

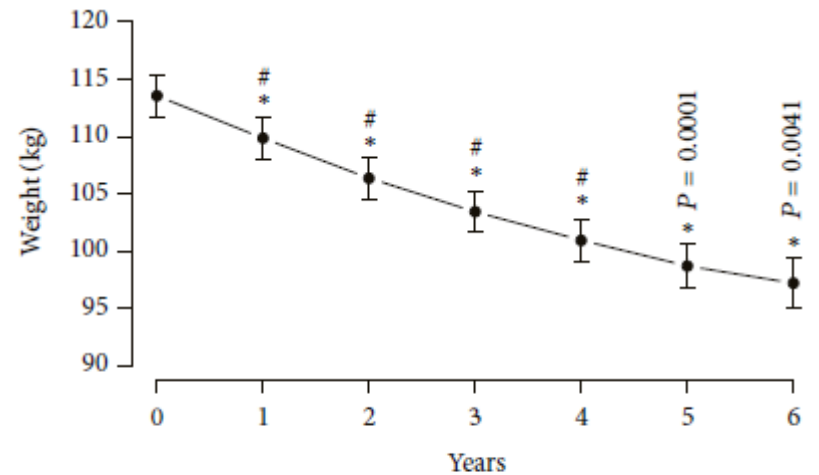
*Haider A, Int. Journal of Urology , 2014*

# Tratamento do Hipogonadismo: Circunferência da cintura e Peso corporal



Patients, *n* 156 156 146 136 114 105 69

\*  $P < 0.0001$  versus baseline  
#  $P < 0.0001$  versus previous year

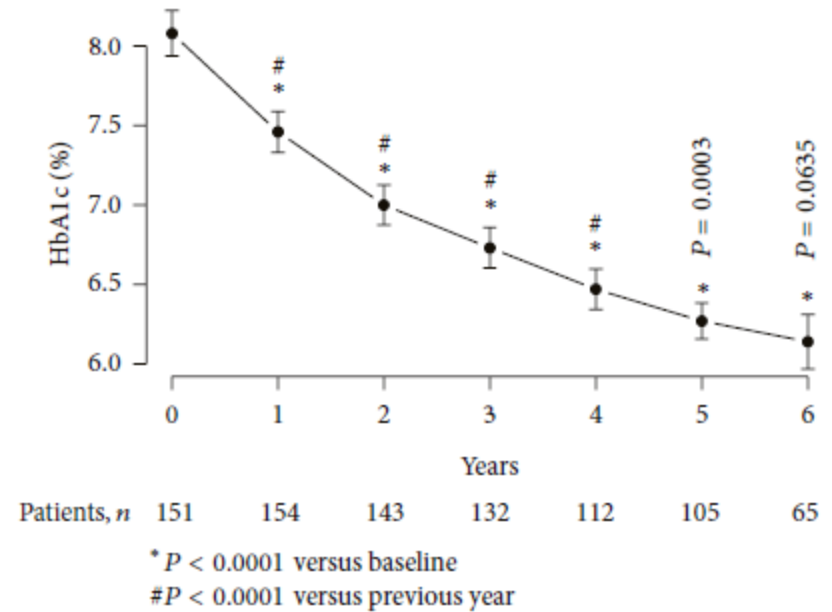
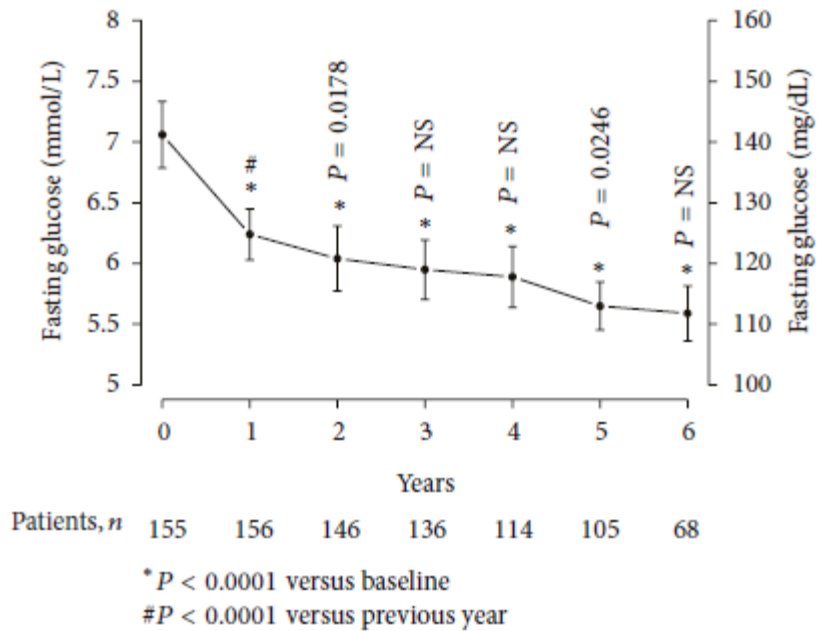


Patients, *n* 156 151 146 135 114 105 68

\*  $P < 0.0001$  versus baseline  
#  $P < 0.0001$  versus previous year

**Haider A, Int. Journal of Urology, 2014**

# Tratamento do Hipogonadismo: Glicemia de jejum e A1c



**Haider A, Int. Journal of Urology, 2014**



# Hipogonadismo e Diabetes

## ***Men with type 2 diabetes mellitus***

2.6 In men with type 2 diabetes mellitus who have low testosterone concentrations, we recommend against testosterone therapy as a means of improving glycemic control. (1|⊕⊕OO)

## ***Technical remark***

- Testosterone therapy in hypogonadal men who have T2DM should follow the same treatment and monitoring plan as hypogonadal men without T2DM.

International Journal of  
Andrology



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ORIGINAL ARTICLE

## **Type 2 diabetes mellitus and testosterone: a meta-analysis study**

G. Corona,<sup>\*§1</sup> M. Monami,<sup>†1</sup> G. Rastrelli,<sup>\*</sup> A. Aversa,<sup>‡</sup> A. Sforza,<sup>§</sup> A. Lenzi,<sup>‡</sup> G. Forti,<sup>\*</sup> E. Mannucci<sup>‡</sup> and M. Maggi<sup>\*</sup>

<sup>\*</sup>Andrology Unit and Endocrinology, Department of Clinical Physiopathology, University of Florence, Florence; <sup>†</sup>Diabetes Section Geriatric Unit, Department of Critical Care, University of Florence, Florence; <sup>‡</sup>Department of Medical Pathophysiology (DFM-Fisiopatologia Medica), Sapienza University, Rome; and <sup>§</sup>Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, Italy

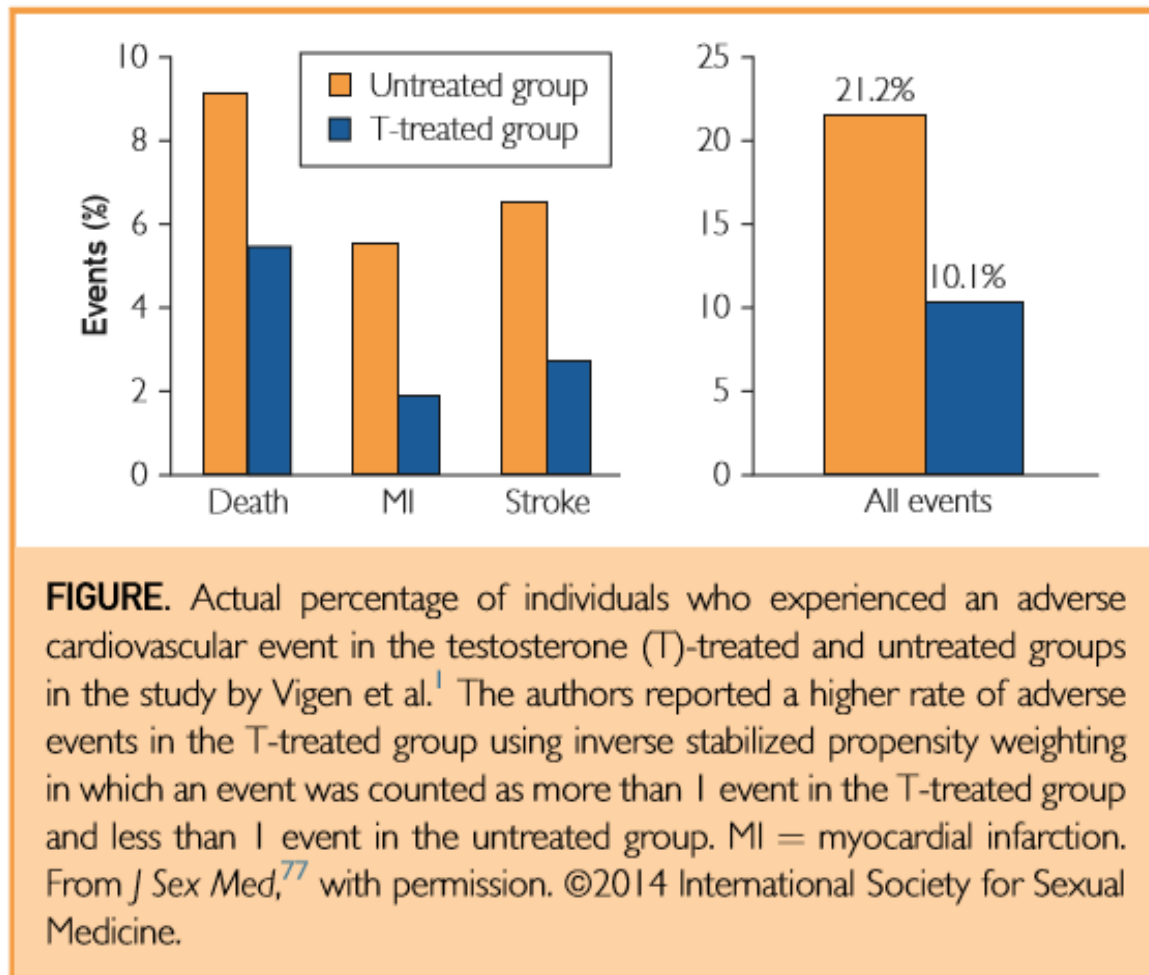
# Testosterone Therapy and Cardiovascular Risk: Advances and Controversies

Abraham Morgentaler, MD; Martin M. Miner, MD; Monica Caliber, MSc;  
Andre T. Guay, MD<sup>†</sup>; Mohit Khera, MD; and Abdulmaged M. Traish, PhD

## Abstract

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Two recent studies raised new concerns regarding cardiovascular (CV) risks with testosterone (T) therapy. This article reviews those studies as well as the extensive literature on T and CV risks. A MEDLINE search was performed for the years 1940 to August 2014 using the following key words: *testosterone, androgens, human, male, cardiovascular, stroke, cerebrovascular accident, myocardial infarction, heart attack, death, and mortality*. The weight and direction of evidence was evaluated and level of evidence (LOE) assigned. Only 4 articles were identified that suggested increased CV risks with T prescriptions: 2 retrospective analyses with serious methodological limitations, 1 placebo-controlled trial with few major adverse cardiac events, and 1 meta-analysis that included questionable studies and events. In contrast, several dozen studies have reported a beneficial effect of normal T levels on CV risks and mortality. Mortality and incident coronary artery disease are inversely associated with serum T concentrations (LOE IIa), as is severity of coronary artery disease (LOE IIa). Testosterone therapy is associated with reduced obesity, fat mass, and waist circumference (LOE Ib) and also improves glycemic control (LOE IIa). Mortality was reduced with T therapy in 2 retrospective studies. Several RCTs in men with coronary artery disease or heart failure reported improved function in men who received T compared with placebo. The largest meta-analysis to date revealed no increase in CV risks in men who received T and reduced CV risk among those with metabolic disease. In summary, there is no convincing evidence of increased CV risks with T therapy. On the contrary, there appears to be a strong beneficial relationship between normal T and CV health that has not yet been widely appreciated.



# Endocrine Society 2018

## Testosterona e Risco CV

- Não existem RCT grandes e longos o suficiente para determinar os efeitos da reposição de TESTO sobre MACE. Os que existem são limitados pelo tamanho pequeno e curta duração
- Apesar das evidências da associação de TESTO baixa com maior risco de mortalidade CV, estes resultados podem apenas mostrar associação, mas não causalidade.
- As metanálises não mostraram associação estatisticamente significativa entre reposição de TESTO com MACE, eventos CV ou morte.
- A reposição de TESTO deve ser individualizada, para aqueles com TESTO baixa associada a sintomatologia
- Hábitos de vida saudáveis