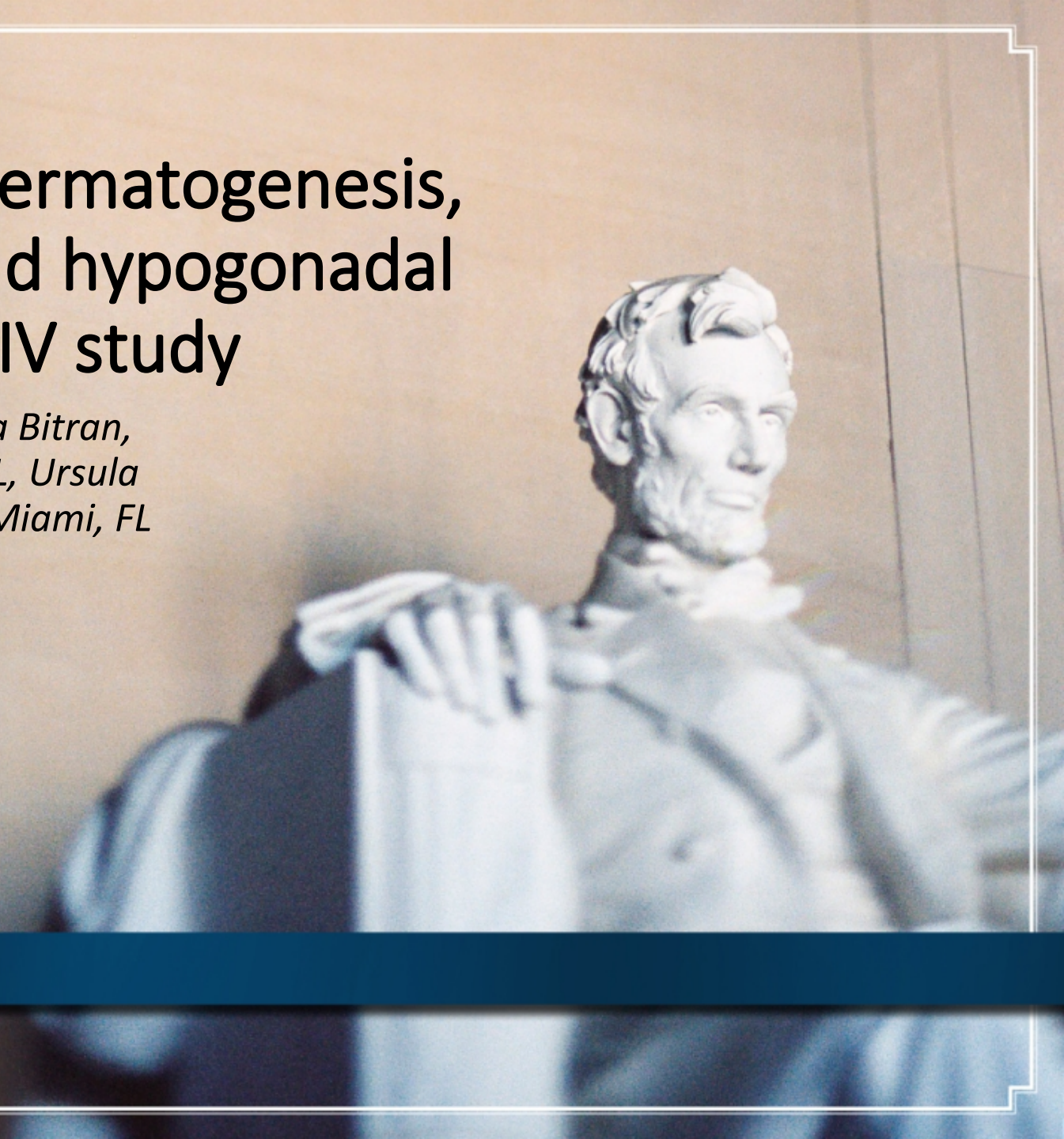


# The effect of Natesto on spermatogenesis, reproductive hormones, and hypogonadal symptoms. A phase IV study

*Thomas Masterson\**, Jordan Best, Joshua Bitran,  
Manuel Molina, Emad Ibrahim, Miami, FL, Ursula  
Kaiser, Boston, MA, Ranjith Ramasamy, Miami, FL



# Low testosterone affects men of reproductive age

- Men are fathering children at older ages
  - Approximately 25% of new Fathers are over the age of 35<sup>1</sup>
- Testosterone declines by 0.4-1.3% every year after the age of 30<sup>2</sup>
- Men receiving testosterone therapy (TTh), 12.4% were younger than 39 years old<sup>3</sup>



1. Lewis et. Al. JAMA. 2006
2. Wu et. al, European Male Aging Study Group. J Clin Endocrinol Metab. 2008.
3. Layton et al. J Clin Endocrinol Metab. 2014

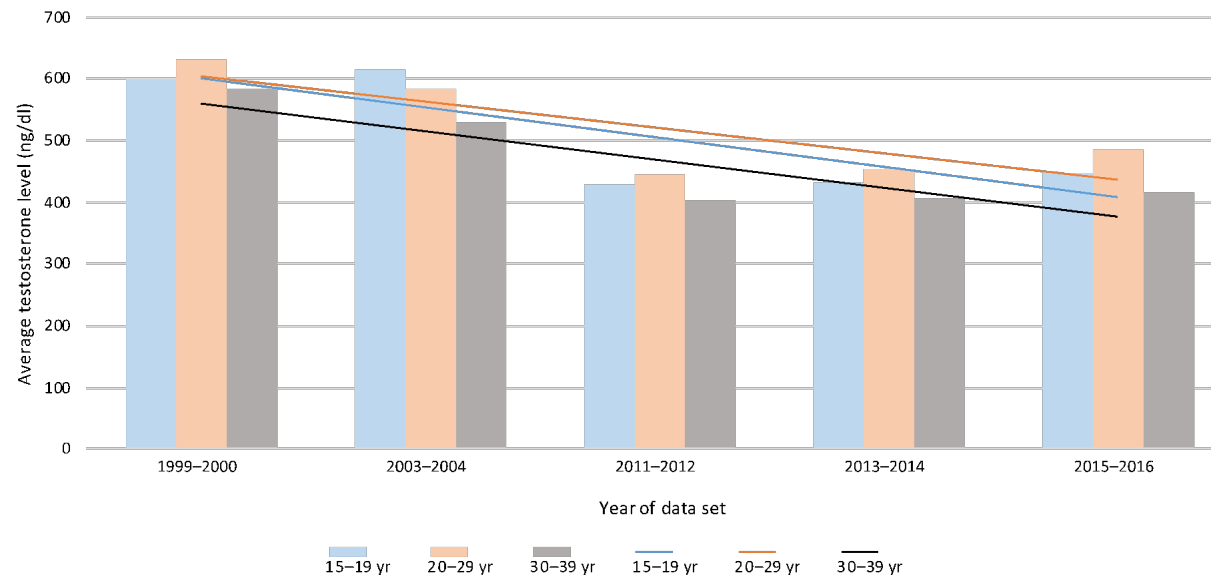
# Low Testosterone in Adolescents & Young Adults

Jordan Cohen<sup>1\*</sup>, Daniel E. Nassau<sup>2</sup>, Premal Patel<sup>1</sup> and Ranjith Ramasamy<sup>1</sup>

## Decline in Serum Testosterone Levels Among Adolescent and Young Adult Men in the USA



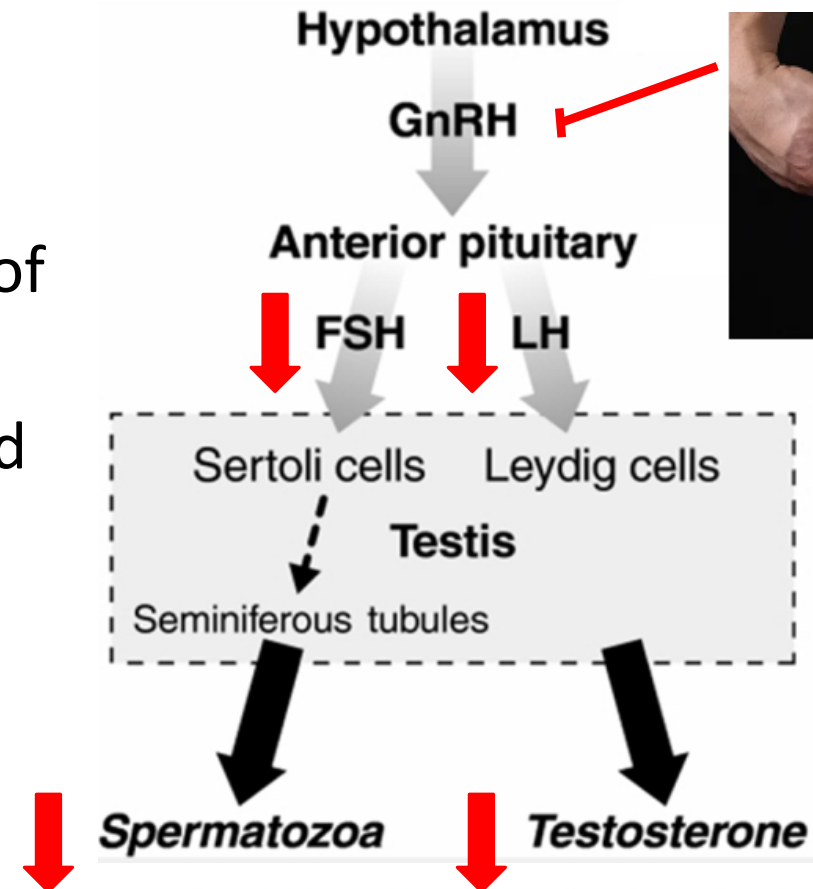
Soum D. Lokeshwar<sup>a,†</sup>, Premal Patel<sup>b,†</sup>, Richard J. Fantus<sup>c</sup>, Joshua Halpern<sup>c</sup>, Cecilia Chang<sup>d</sup>, Atil Y. Kargi<sup>a</sup>, Ranjith Ramasamy<sup>a,\*</sup>





# Traditional long acting testosterone is a male contraceptive

- Exogenous long acting testosterone injections cause azoospermia in >60% of men after 6 months through suppression of gonadotropins (LH and FSH)<sup>1</sup>
- Once discontinued, recovery is not assured
  - Longer duration of TRT requires a longer time to recovery<sup>2</sup>
  - Post TRT sperm concentration 85% of pre treatment<sup>3</sup>



1. World Health Organization Task Force on methods for the regulation of male fertility. Lancet. 1990
2. Liu et al. Lancet. 2006
3. Ly et al. Hum Reprod. 2005

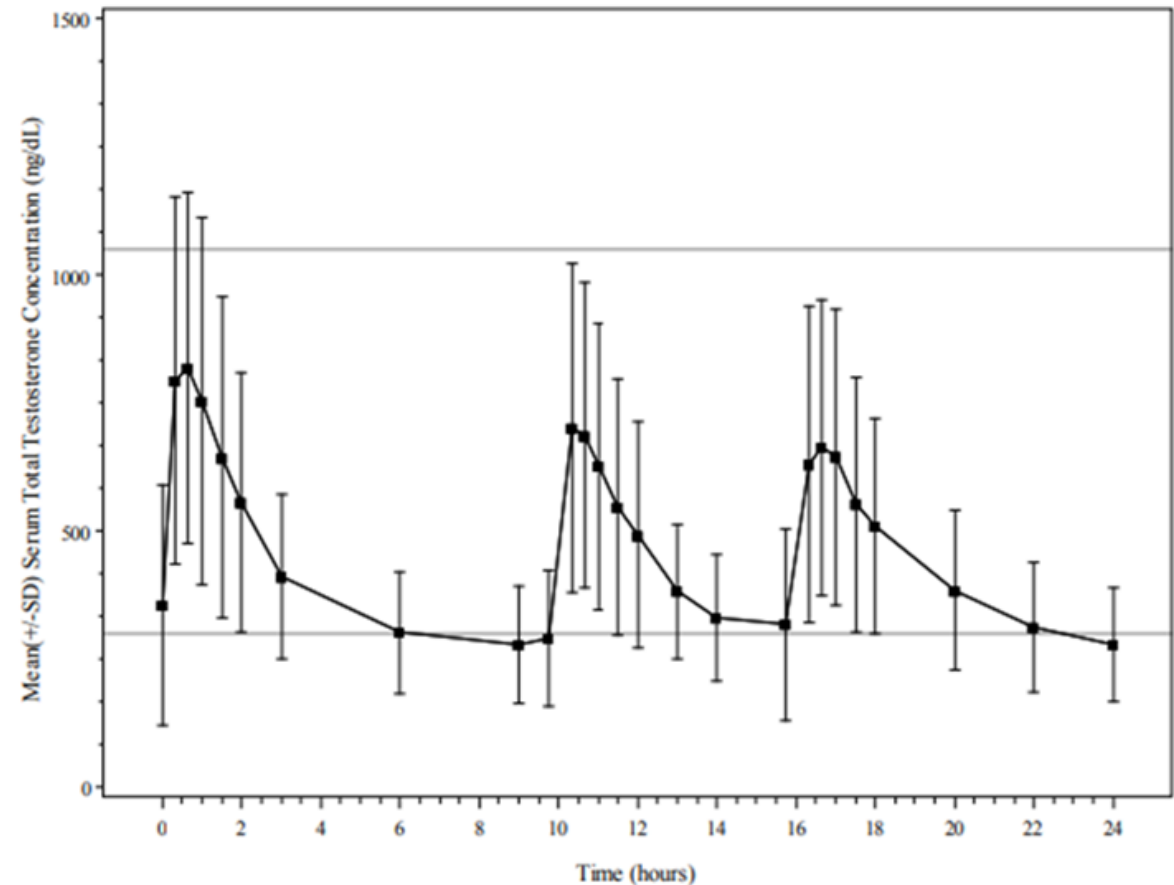
# Medications to increase and preserve spermatogenesis

- Aromatase Inhibitors (Anastrozole)
  - Hot flashes, hypertension, nausea, back pain, dyspnea, peripheral edema
  - Not FDA approved in males
- Selective estrogen receptor modulators (Clomiphene Citrate)
  - Visual symptoms, flushing, headache, abdominal pain
  - Not FDA approved in males
- LH analogue (HCG)
  - Headache, irritability, depression, fatigue, gynecomastia
  - Only approved in hypogonadotropic hypogonadism (Low LH, Low T)



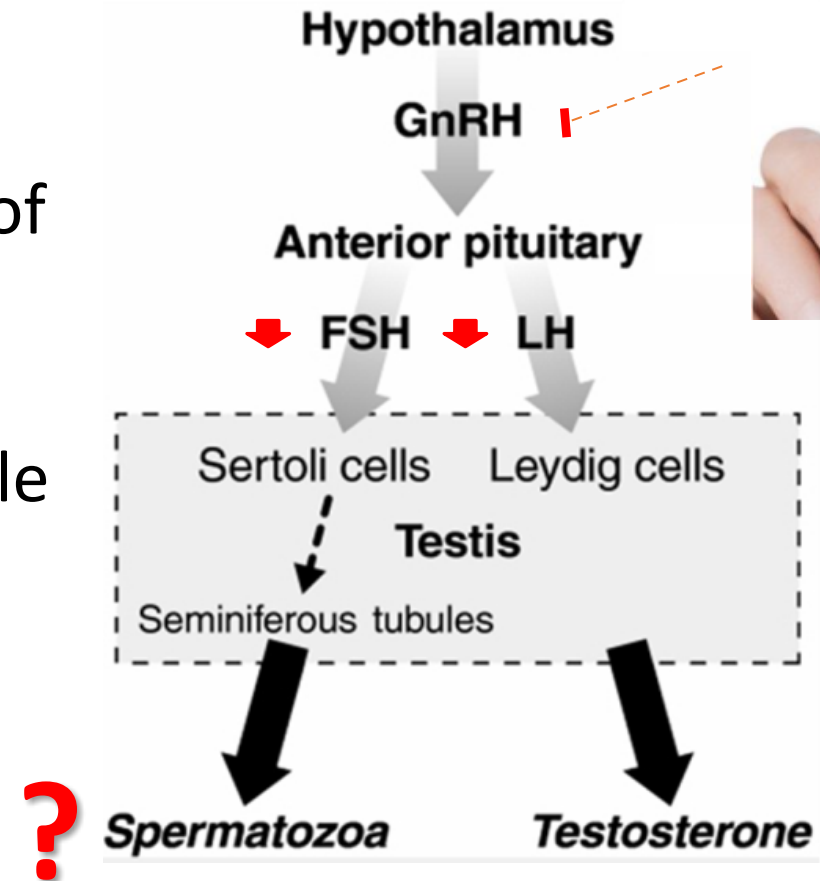
# Natesto is a short acting testosterone

- Half life is approximately 100 minutes
- FDA approved TID dosing



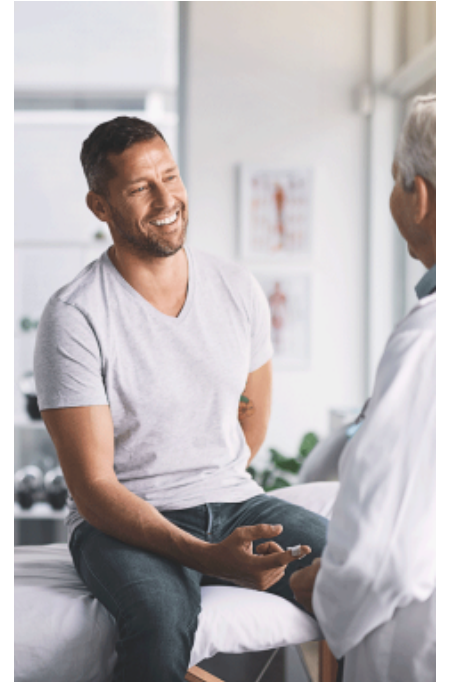
# Short acting testosterone preserves gonadotropins

- Short acting Natesto (intranasal testosterone) preserves normal levels of LH and FSH<sup>1</sup>
- Can Natesto increase testosterone while preserving spermatogenesis?



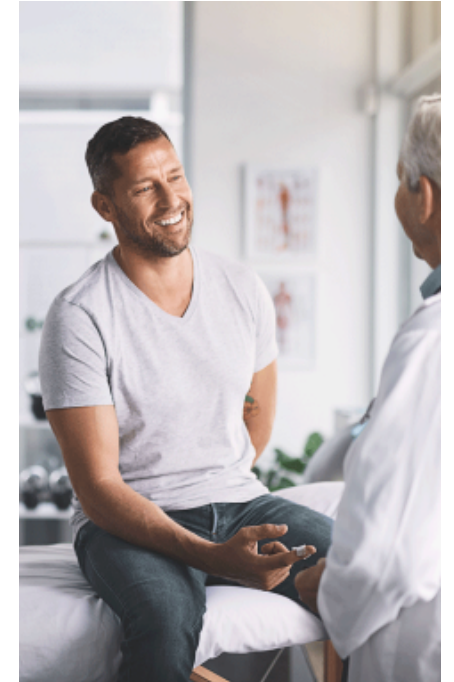
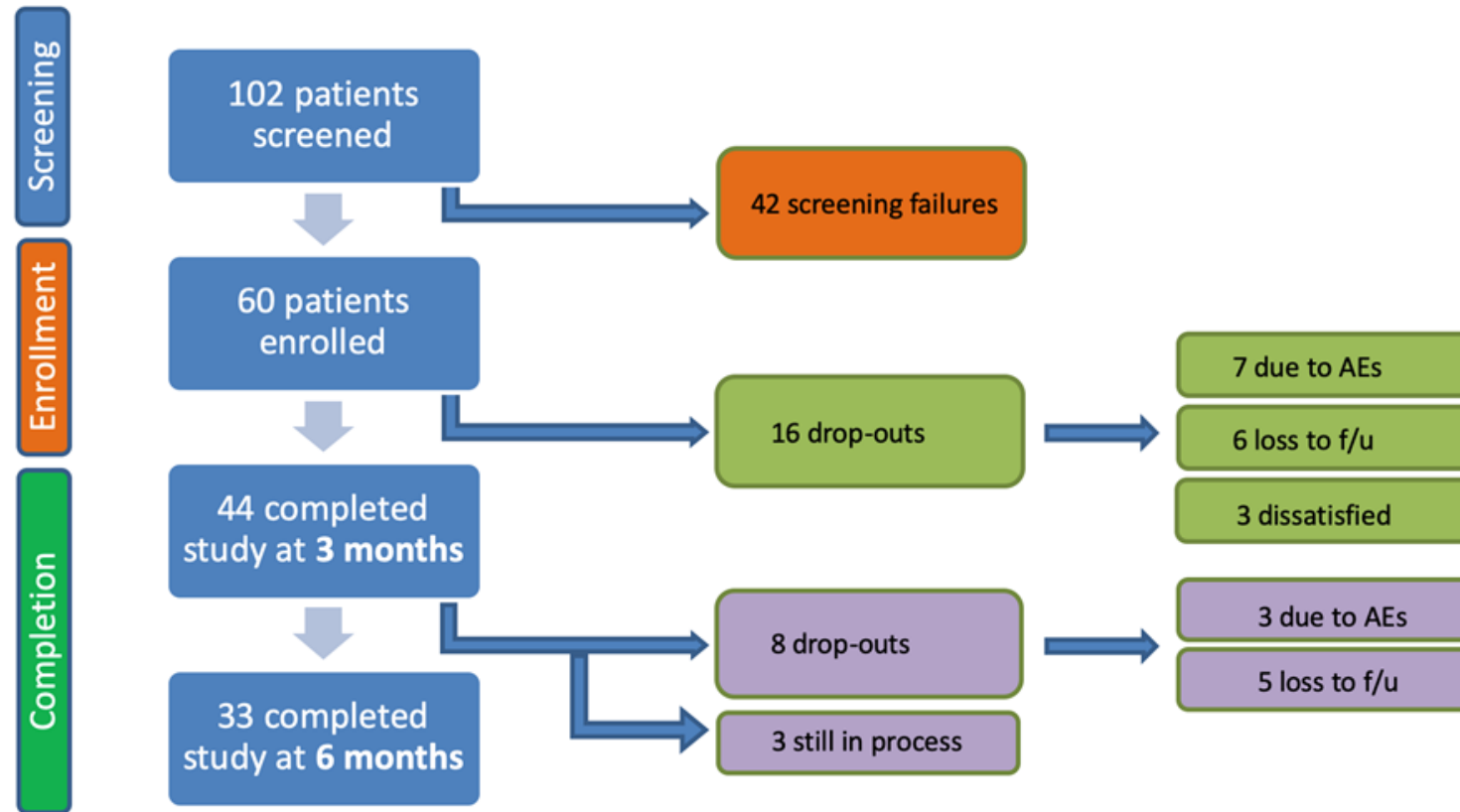
# Trial design

- Prospective 6 months trial
- Natesto for 6 months TID(11mg/dose, 33mg/day)
  - Men 18-55 y/o M with low testosterone
  - 2 semen parameters with TMSC >5 million
- Outcomes:
  - Hormones: T, LH, FSH
  - Semen parameters: concentration, motility, total motile count
  - Symptoms: IIEF





# Patient enrolment

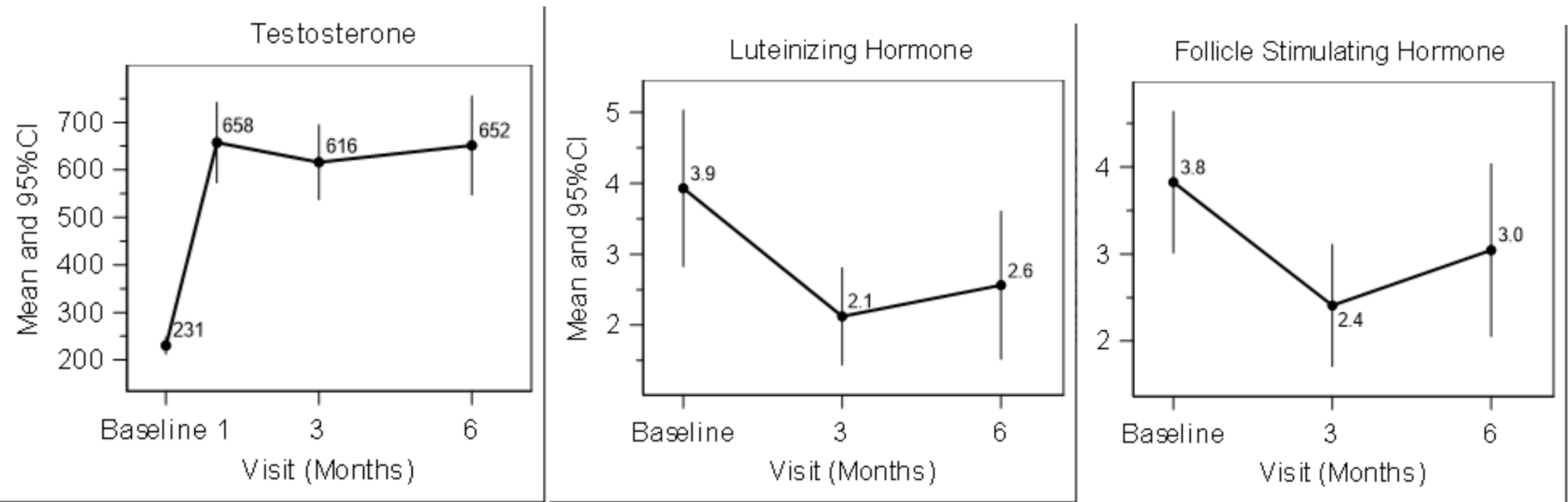


# Patient characteristics

<u>Patients</u>	<u>60 (100%)</u>
<u>Race</u>	-
Caucasian	12 (20%)
African American	2 (3.3%)
Hispanic	34 (56.7%)
Asian	1 (1.7%)
Other	11 (18.3%)
<u>Age , years</u>	
Mean (SD)	37.5 (7.2)
Median (Range)	37.5 (19, 55 <del>6</del> )
<u>Body Mass Index (BMI), kg/m<sup>2</sup> (n=58)</u>	
Mean (SD)	30.6 (5.6)
Median (Range)	30.0 (21.7, 47.1)
BMI > 30	29 (50%)

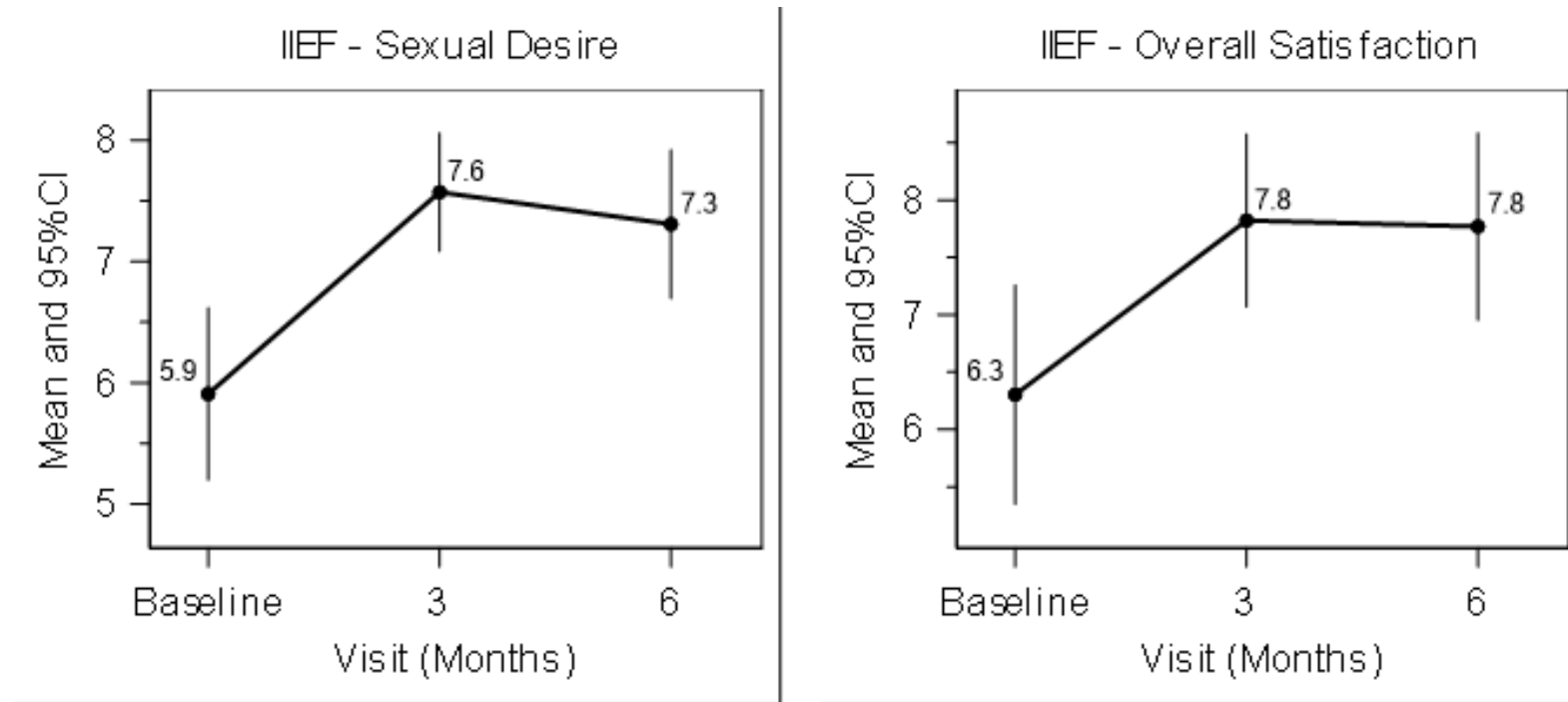


# Natesto improved testosterone, maintained LH and FSH



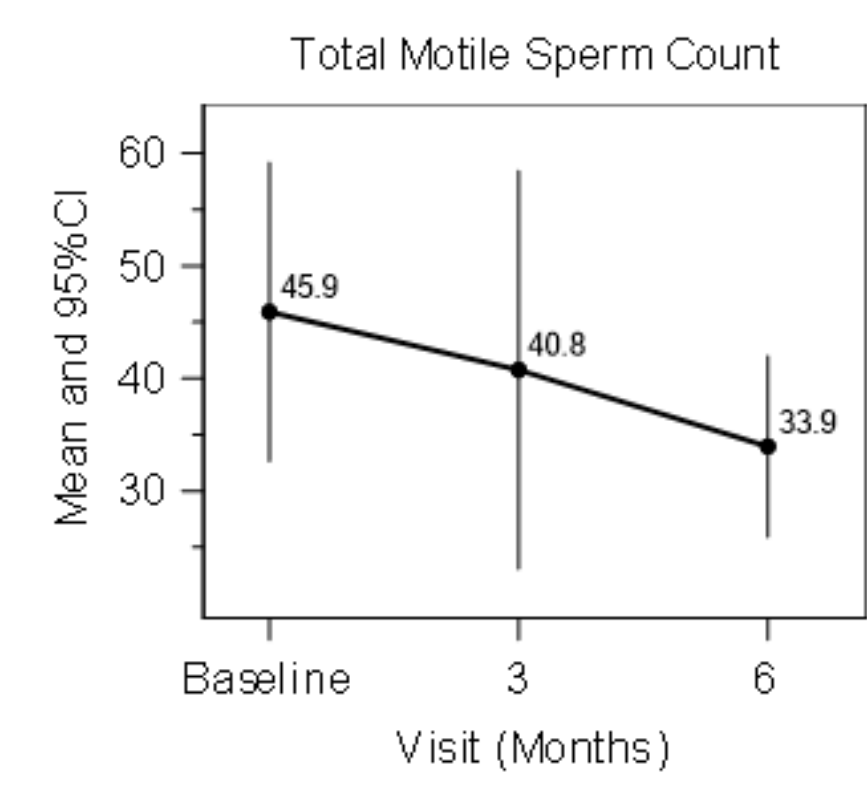
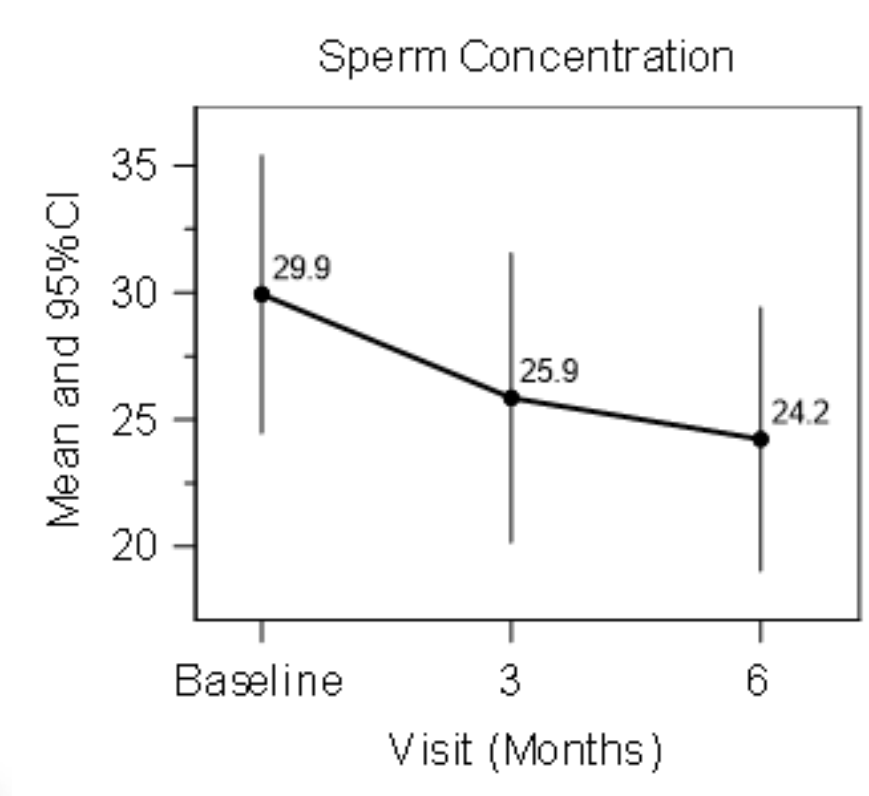
Ramasamy R, et al. Effect of Natesto on Reproductive Hormones, Semen Parameters and Hypogonadal Symptoms: A Single-Center, Open-Label, Single-Arm Trial [published online ahead of print, 2020 Apr 14]. J Urol

# Natesto improved hypogonadal symptoms



Ramasamy R, et al. Effect of Natesto on Reproductive Hormones, Semen Parameters and Hypogonadal Symptoms: A Single-Center, Open-Label, Single-Arm Trial [published online ahead of print, 2020 Apr 14]. J Urol

# Natesto maintained semen parameters



Ramasamy R, et al. Effect of Natesto on Reproductive Hormones, Semen Parameters and Hypogonadal Symptoms: A Single-Center, Open-Label, Single-Arm Trial [published online ahead of print, 2020 Apr 14]. J Urol



# Strengths and limitations

- Strengths: This is the first and only prospective study evaluating Nateso's effect on semen parameters
- Limitations: Relatively high dropout rate, arguably short study duration



# Conclusion

- After 6 months:
  - Natesto improved hypogonadal symptoms
  - Increased Testosterone levels
  - Maintained semen parameters
- Therefore, Natesto could be an ideal treatment for men with low testosterone concerned with future fertility.



# Thank you!



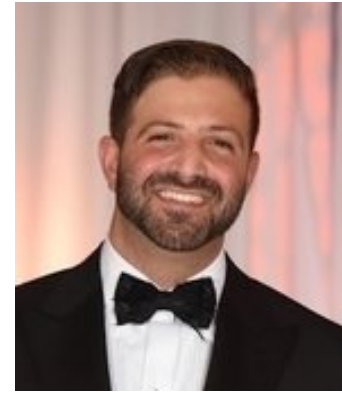
Ranjith  
Ramasamy MD



Emad  
Ibrahim MD



Manuel  
Molina MD



Joshua  
Bitran MD



Jordan Best

