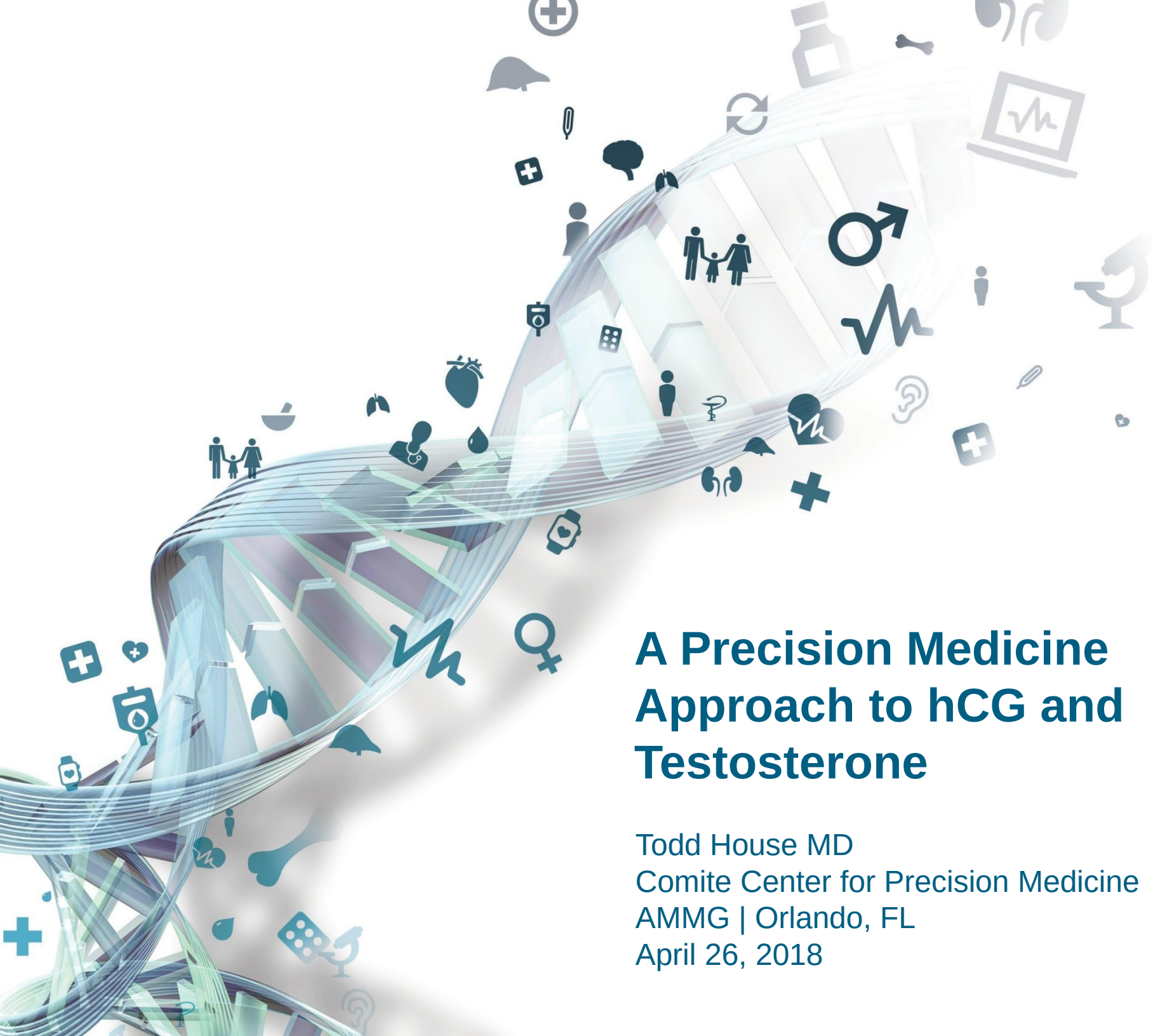
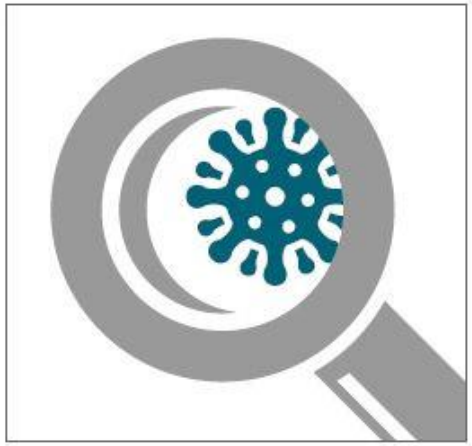


A Precision Medicine Approach to hCG and Testosterone

Todd House MD
Comite Center for Precision Medicine
AMMG | Orlando, FL
April 26, 2018

What is Precision Medicine?



Detect

Detect disease decades before symptoms.



Predict

Predict risk-prone wiring, and the genetic “switches” that control expression.



Reverse

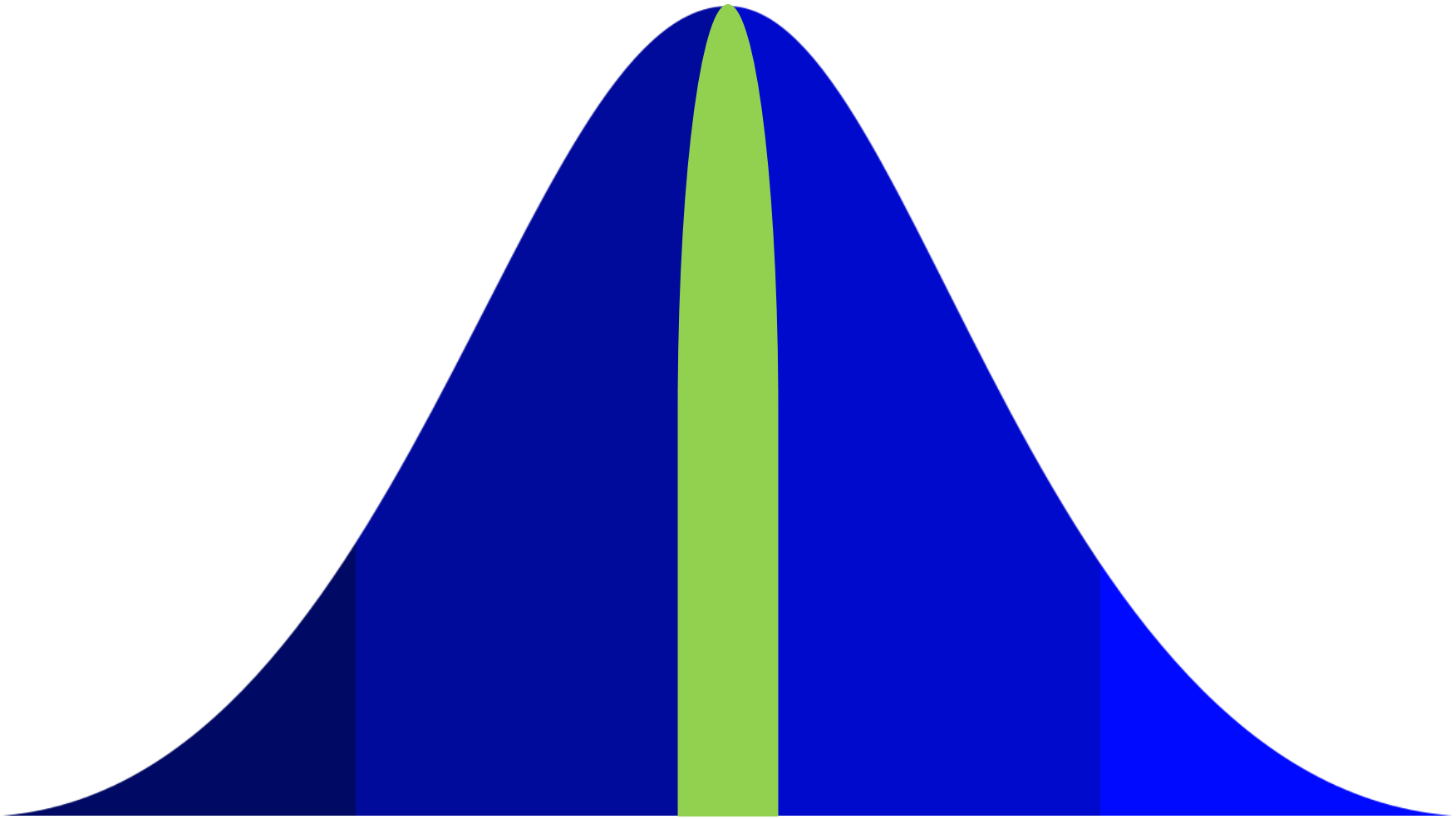
Reverse and prevent diseases of aging, with interventions personalized for you and you alone.



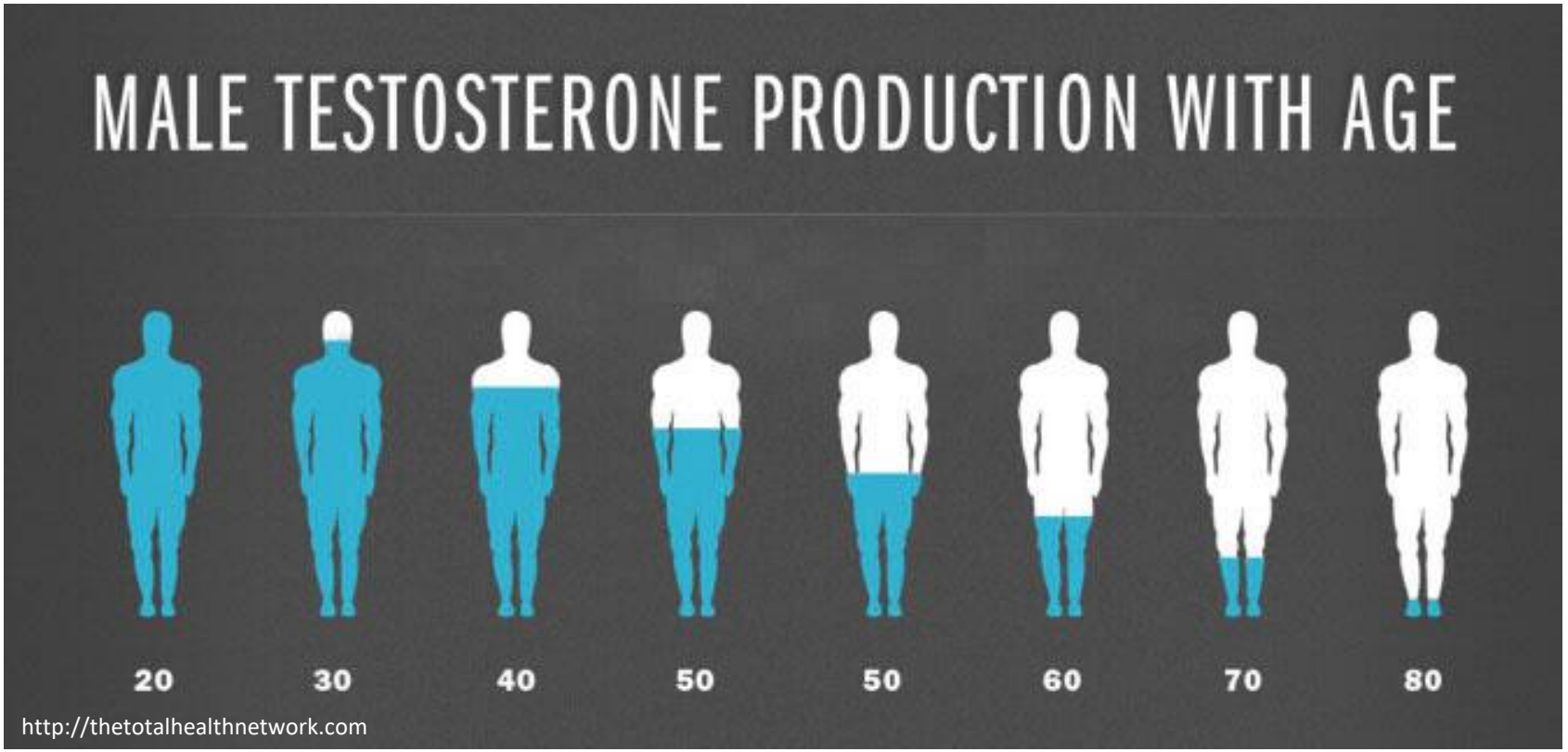
Own

Own your health destiny. Optimize your unique health trajectory and recapture health for life.

Why It Matters: There is NO Normal

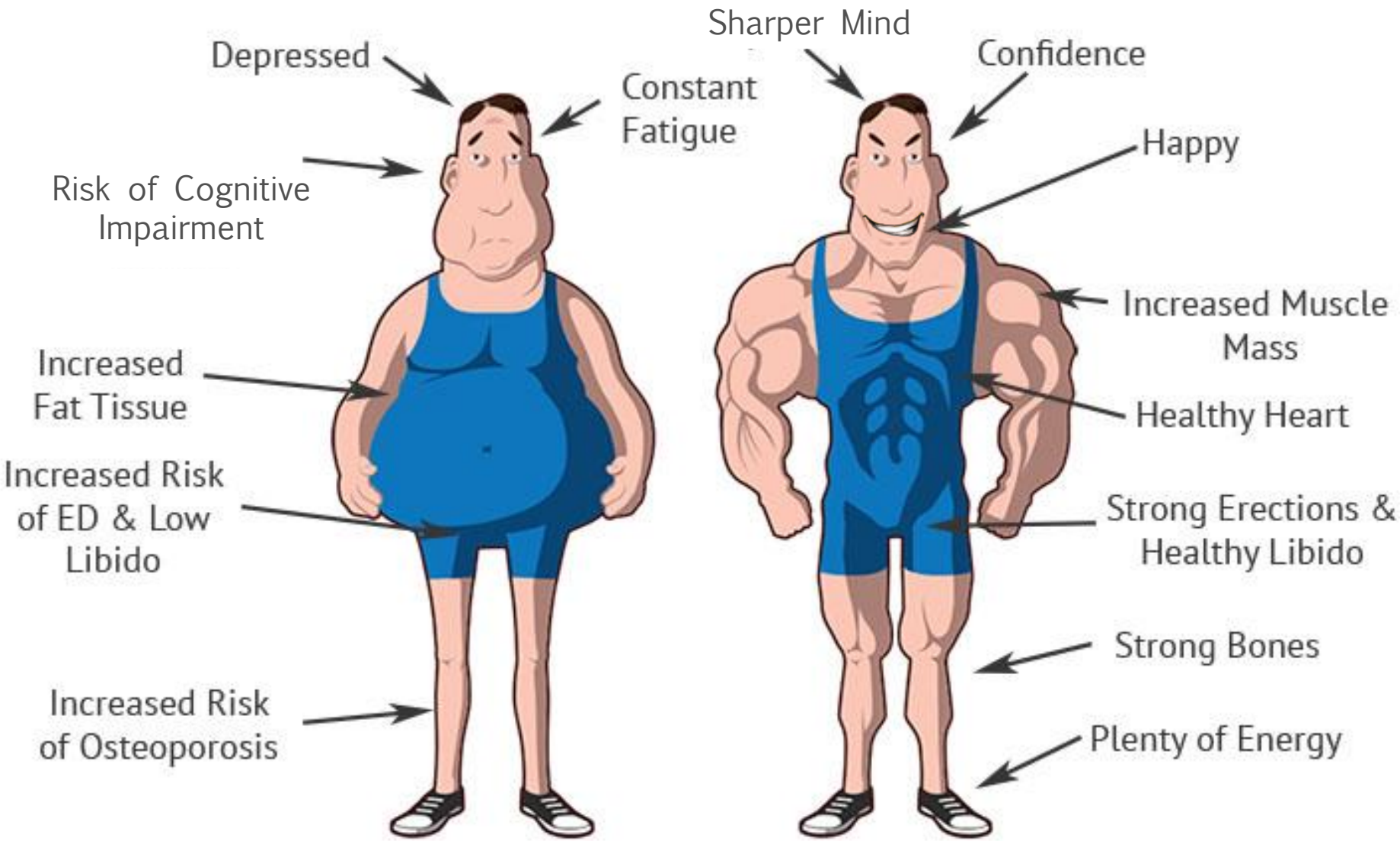


Testosterone Decline



T begins to decline by ~1-3% per year, accelerating with age.

Benefits of Optimizing Testosterone



T's Bad Reputation

European Association of Urology

Review – Andrology

Testosterone and Prostate Cancer: An Historical Perspective on a Modern Myth

Abraham Morgentaler *

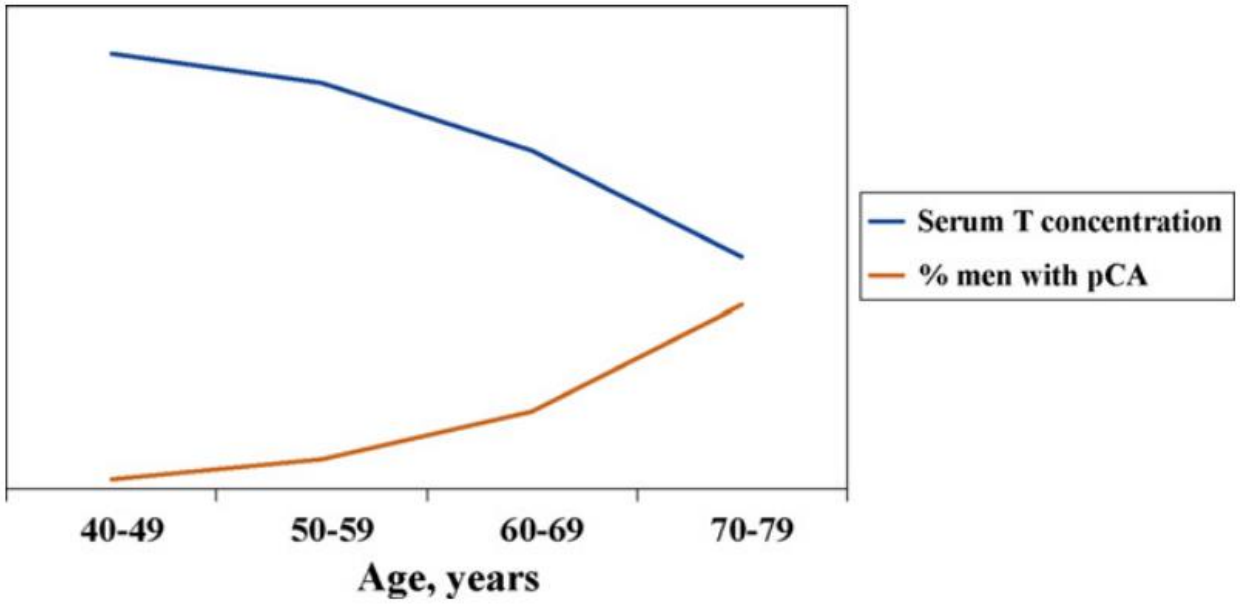


Fig. 1 – Prostate cancer prevalence and testosterone levels with ageing. pCA: prostate cancer, T: testosterone.

T's Bad Reputation

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 8, 2010 VOL. 363 NO. 2

Adverse Events Associated with Testosterone Administration

Shehzad Basaria, M.D., Andrea D. Coviello, M.D., Thomas G. Travison, Ph.D., Thomas W. Storer, Ph.D., Wildon R. Farwell, M.D., M.P.H., Alan M. Jette, Ph.D., Richard Eder, B.A., Sharon Tennstedt, Ph.D., Jagadish Ulloor, Ph.D., Anqi Zhang, Ph.D., Karen Choong, M.D., Kishore M. Lakshman, M.D., Norman A. Mazer, M.D., Ph.D., Renee Miciek, M.S., Joanne Krasnoff, Ph.D., Ayan Elmi, B.A., Philip E. Knapp, M.D., Brad Brooks, B.S., Erica Appleman, M.A., Sheetal Aggarwal, B.S., C.C.R.P., Geeta Bhasin, B.A., Leif Hede-Brierley, Ashmeet Bhatia, M.B., B.S., Lauren Collins, R.N.P., Nathan LeBrasseur, Ph.D., Louis D. Fiore, M.D., and Shalender Bhasin, M.D.

RESULTS

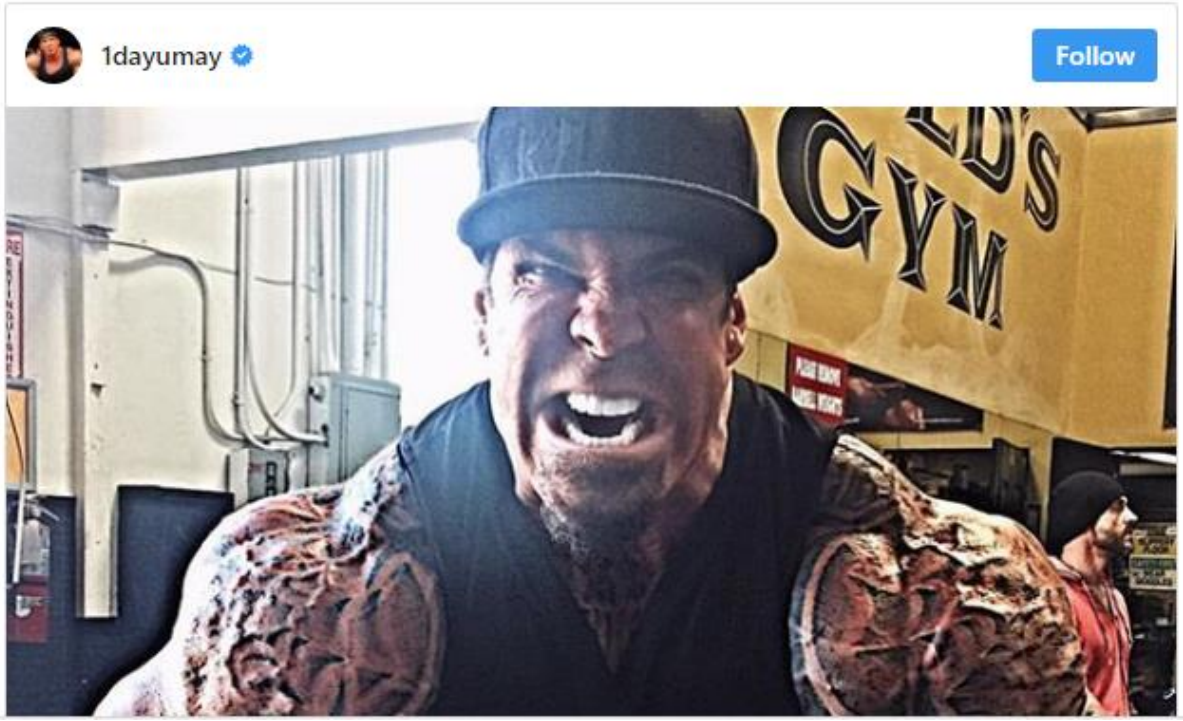
A total of 209 men (mean age, 74 years) were enrolled at the time the trial was terminated. At baseline, there was a high prevalence of hypertension, diabetes, hyperlipidemia, and obesity among the participants. During the course of the study, the testosterone group had higher rates of cardiac, respiratory, and dermatologic events than did the placebo group. A total of 23 subjects in the testosterone group, as compared with 5 in the placebo group, had cardiovascular-related adverse events. The relative risk of a cardiovascular-related adverse event remained constant throughout the 6-month treatment period. As compared with the placebo group, the testosterone group had significantly greater improvements in leg-press and chest-press strength and in stair climbing while carrying a load.

T’s Bad Reputation

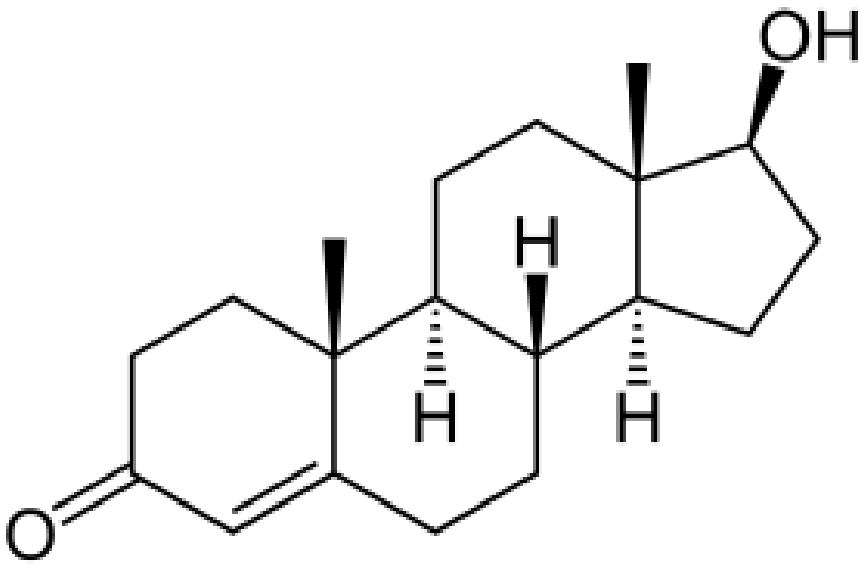
Steroid-using celeb bodybuilder dies two weeks after falling into coma

By Emma Lake, The Sun

August 25, 2017 | 11:32am | Updated



Precision Ranges for Optimal Function



	Total T	Free T
Symptomatic	< 280 ng/dL	Varies
Low	< 350 ng/dL	Varies
Optimal	**800-1200 pg/dL**	**180-300 pg/dL**

Unique Baselines Offer Critical Health Insight



GB, 49 yy
Total T 402
Free T 53.9
DHT 27
LH 5.8
FSH 11.8
E2 38



SH, 45 yy
Total T 555
Free T 86.6
DHT 56
LH 11.3
FSH --
E2 36



PW, 55 yy
Total T 975
Free T 156
DHT 53
LH 5.2
FSH 3
E2 48

Other Hormones



- Cortisol
- Testosterone, ToT, Lc/Ms/Ms
- Testosterone, Free
- Dihydrotestosterone, Lc/Ms/Ms
- LH
- FSH
- Prolactin
- Estradiol, Lc/Ms/Ms
- DHEA Sulfate Cortisol, Total, Serum LH
- PSA, Total
- IGF-I, Lc/Ms
- Z-Score
- IGF-BP Binding Protein-3
- Sex Hormone Binding Glob
- Progesterone, Lc/Ms/Ms

Options for Testosterone Optimization



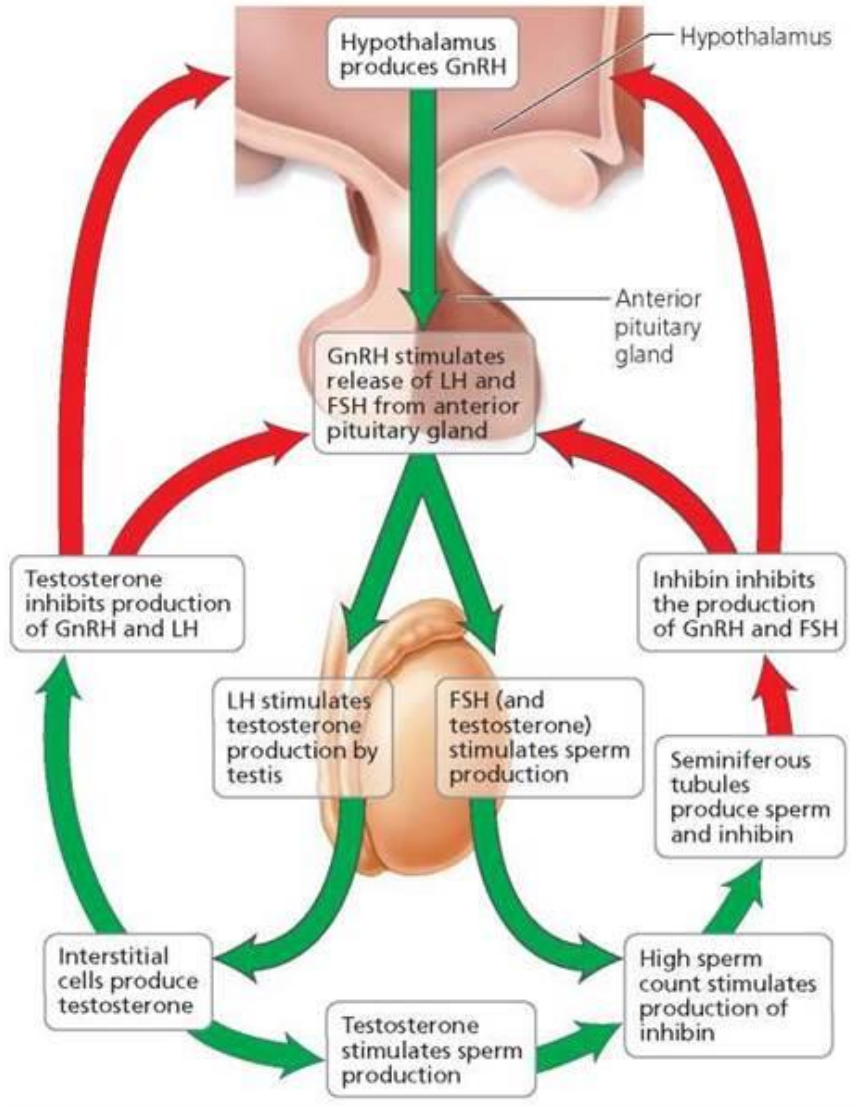




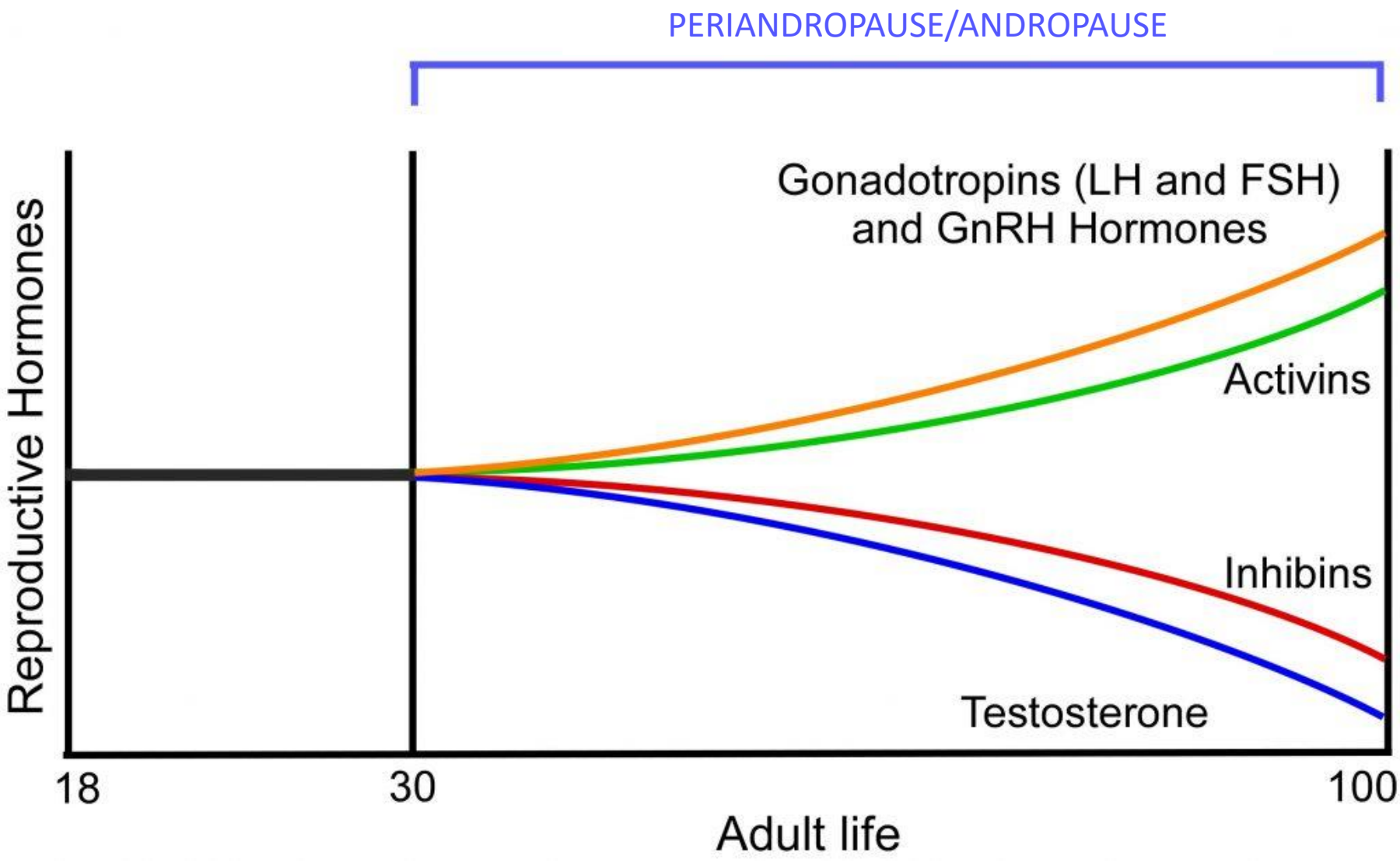




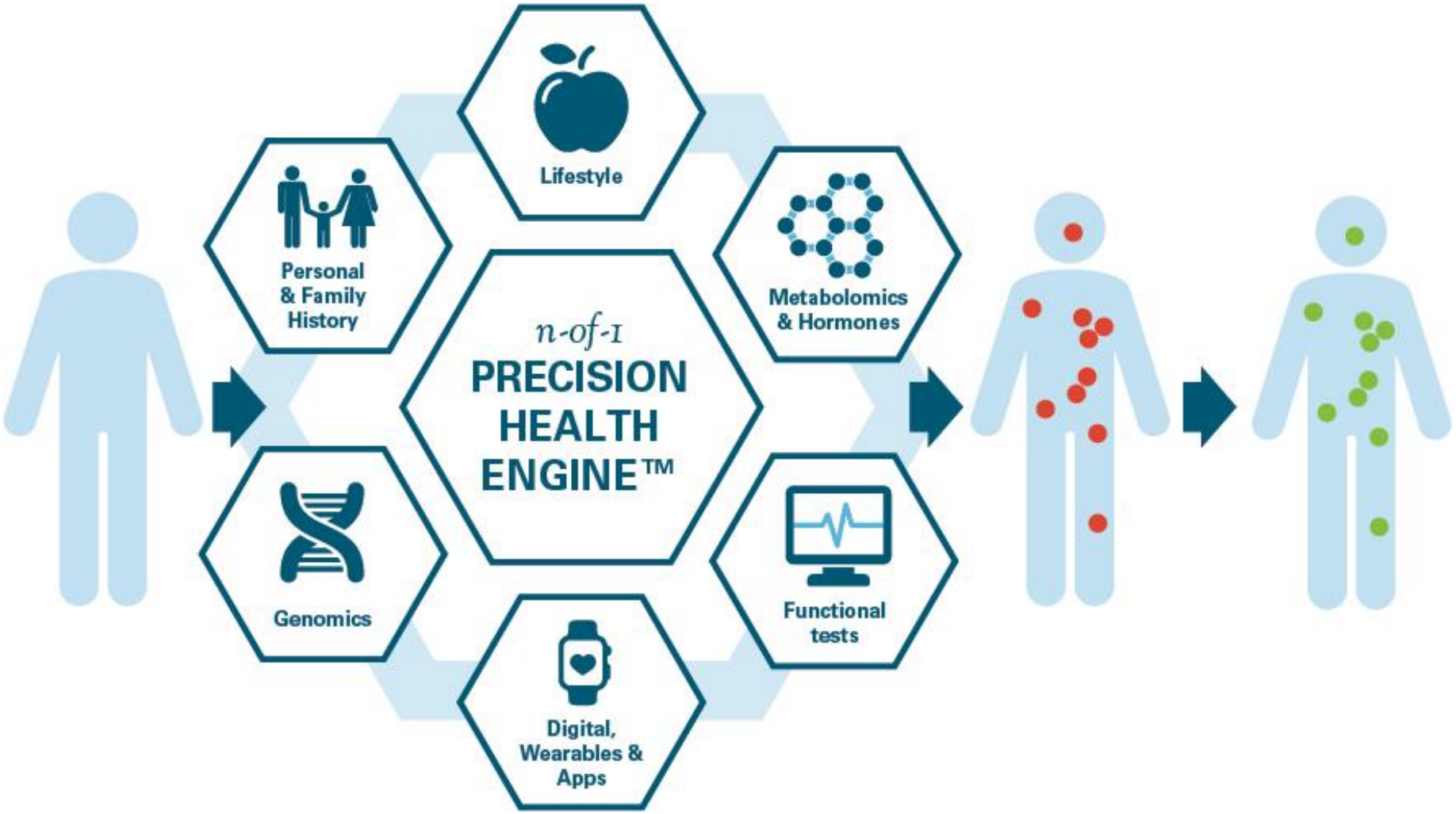
hCG: The Natural Choice for Pre-Andropause



Andropause & The Transition to Testosterone



Precision Medicine in Action: Making Omics Data Actionable



Integrate, Interpret, Intervene!

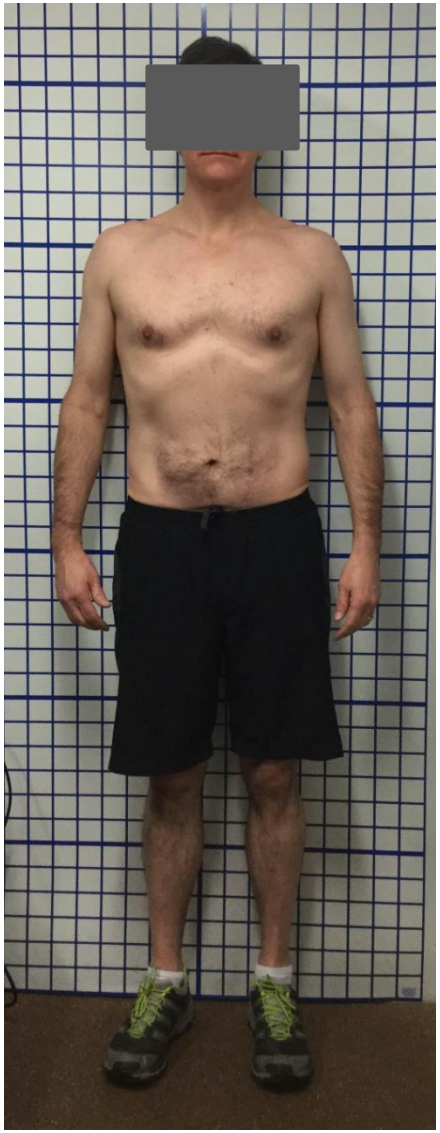


n-of-1™ Case Study, 54 yy BD: Fitter, Stronger, Leaner



	04.17.2017	**06.29.2017** hCG 5000 IU, biw DHEA 25 mg, qd Boron 2 mg, qd	**09.11.2017** hCG 5000 IU, biw DH,EA 50 mg qd Boron 2 mg, qd Arimidex 1 mg, qd	**01.18.2018** hCG 5000 IU, biw PT-141 0.2 xx prn Arimidex 1 mg, qd
Total T	377	1112	1258	1369
Free T	58.4	186.8	192.5	178.0
DHT	52	108	25	44
LH	1.8	<0.2	<0.2	<0.1
FSH	5.1	<0.7	<0.7	<0.3
E2	20	144	92	124
SSBG	58	51	43	62

n-of-1™ Case Study, 54 yy BD: Fitter, Stronger, Leaner



VO2 Max	05.24.2017	01.19.2018
	38.4 mL/kg/min	45.8 mL/kg/min

⬆ 7.4 METs

👏👏

InBody

Body Composition History

		17. 05. 24 11:22	17. 09. 28 11:05	18. 01. 19 10:37
Weight	(lbs)	175. 8	178. 5	178. 5
SMM Skeletal Muscle Mass	(lbs)	79. 8	84. 4	84. 2
PBF Percent Body Fat	(%)	18. 5	15. 8	16. 5
ECW/TBW		0. 387	0. 383	0. 378

☑ Recent ☐ Total

🔥🔥🔥

n-of-1™ Case Study, 61 yy JP: Cycling Through Andropause



	12.08.2016	**01.17.2017**	**03.06.2017** hCG 5000 IU, BIW	**05.05.2017** hCG 5000 IU, TIW Arimidex 1 mg, qd	**07.24.2017** T 200 mg, QW Arimidex 1 mg, BID	**01.22.2018** hCG 5000 IU, TIW Arimidex 1 mg, qd
Total T	458	684	1242	872	1227	846
Free T	79.7	108.8	222.3	146.5	311.7	146.4
DHT	26	42	97	18	33	28
LH	5.4	4.2	--	<0.2	<0.2	<0.2
FSH	<0.7	<0.7	<0.7	<0.7	<0.7	<0.7
E2	20	38	87	63	8	16
SHBG	32	36	40	39	27	29
HDL	64	64	61	66	64	45
LDL	124	128	100	91	101	75
RATIO	3.2	3.4	2.9	2.7	2.8	3.1

n-of-1™ Case Study, 70 yy JG: The Fog Clears



Test Name	Test Result	Interpretation	Notes
Genetic Tests by Genotyping[1,4]			
Reported Date: 03.18.16			
ApoE	E3/E3	Most common genotype.	

	06.07.2014	**10.21.2014** hcG 5000 IU, BIW	**08.18.2015** hcG 5000 IU, TIW Arimidex 1 mg, BID	**08.16.2016** T 160 mg, QW Arimidex 1 mg, BID	**03.22.2017** hcG 5000 IU, TIW T 160 mg, QW Arimidex 1 mg, BID	**01.02.2018** hcG 5000 IU, TIW T 160 mg, QW Arimidex 1 mg, qd
Total T	587	1204	836	1673	1169	1201
Free T	62.2	187.8	129.6	332.9	194.1	284.6
DHT	32	41	49	61	63	70
LH	4.9	<0.2	<0.2	<0.2	<0.2	<0.2
FSH	7.6	<.7	<.7	1.9	.07	<0.7
E2	37	108	79	7	2	19
SHBG	62	61	49	41	34	23

Poster SAT-563

Hormonal Expression of Androgen Deficiency in Aging Men (ADAM)

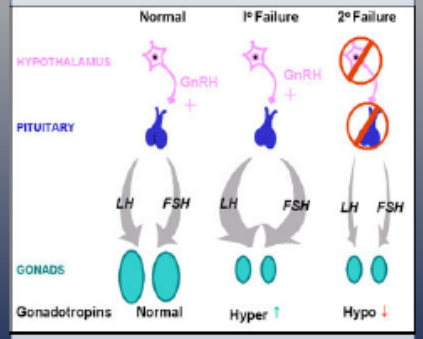
Florence Comite, MD[1,2] and Janet Baek, BS[2]
[1]North Shore-Long Island Jewish Health System, Manhasset, NY
[2]ComiteMD, New York, NY

INTRODUCTION

Aim: To explore the etiologic mechanism of androgen decrease in light of disabilities associated with the explosive aging population and surrounding low testosterone.

- Testosterone decrease is common in aging men and has been linked with multiple health risks (1,2,3).
- Low testosterone in men is most often treated singularly through testosterone gel, cream, or injections (4).
- Previous studies have suggested secondary (hypogonadotropic) hypogonadism (low or borderline Luteinizing Hormone) as etiologic, resulting in testosterone decrease (5).
- Yet currently, LH is not widely measured in clinical practice in the U.S. to diagnose ADAM.
- The importance of identifying low LH in relation to decreased testosterone, we reviewed charts and presented lab data of males at ComiteMD, a private endocrinology practice in New York City.

Hypothalamic-Pituitary-Gonadal Axis



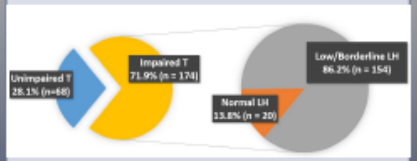
METHODS

- Subjects included a cohort of men aged 30 to 80 years old (n=242) who voluntarily visited a private endocrinology practice specializing in age management in New York City.
- Measurements taken from blood sample in a fasting state included total testosterone (TT), free testosterone (FT), Luteinizing Hormone (LH), fasting blood glucose (FBG), Hemoglobin A1c (HbA1c), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and Estradiol (E2).
- Statistical analysis included essential descriptive profiles of all measured values, correlation coefficient between biomarkers and total testosterone datasets, and determination of significance of ρ within the 95% confidence interval.

RESULTS

- 71.9% of the subjects (n=174) had low testosterone, defined in this study as having low FT (< 90 pg/ml) and/or low TT (< 240 ng/dl).
- Of those, 86.2% showed low (< 3 MIU/ml) or borderline (3-7 MIU/ml) LH.

Testosterone and Luteinizing Hormone Levels

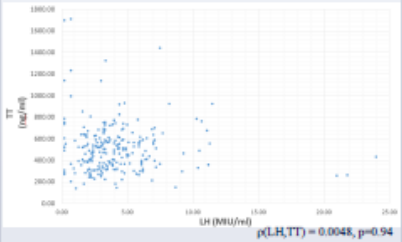


Age Group (yr)	n	% Low T	% Low T Low LH	% Low T Borderline LH	% Low T Elevated LH
30-39	11	81.82%	45.45%	36.36%	0.00%
40-49	82	75.61%	26.83%	41.46%	7.32%
50-59	83	66.27%	20.48%	37.35%	8.43%
60-69	60	70.00%	18.57%	32.86%	8.57%
70-79	6	100.00%	50.00%	33.33%	16.67%

RESULTS CONTINUED

- Neither TT nor FT was significantly correlated with LH.

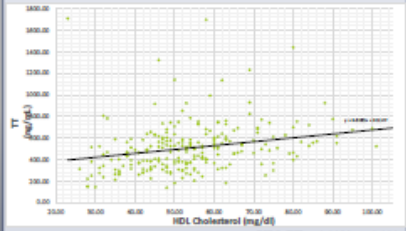
Total Testosterone (ng/dl) v. LH (MIU/ml)



ρ(LH,TT) = 0.0048, p=0.94

- Of the seven biomarkers evaluated, only HDL was found to be significantly less in the low testosterone subjects when compared to those with testosterone within the reference range (p < 0.001).

Total Testosterone (ng/dl) v. HDL (mg/dl)



ρ(HDL,TT) = 0.0039, p<0.001

CONCLUSIONS

- Our research suggests a compromised negative feedback loop in men with ADAM where the pituitary is desensitized to lower levels of testosterone.
- Human Chorionic Gonadotropin (hCG) is a viable option for men with hypogonadotropic hypogonadism, allowing for Leydig cell stimulation to increase testosterone physiologically.

FUTURE RESEARCH

- A longitudinal study with multiple LH readings
- Randomized sample group to hCG and placebo
- Biomarkers beyond blood levels, such as performance as measured by VO2 Max test and Body Composition

ACKNOWLEDGEMENTS

We would like to thank Matthew Vinson, Moazah Ahmed, Tim Coyle, Brent Halsey, and Steven Villagomez.

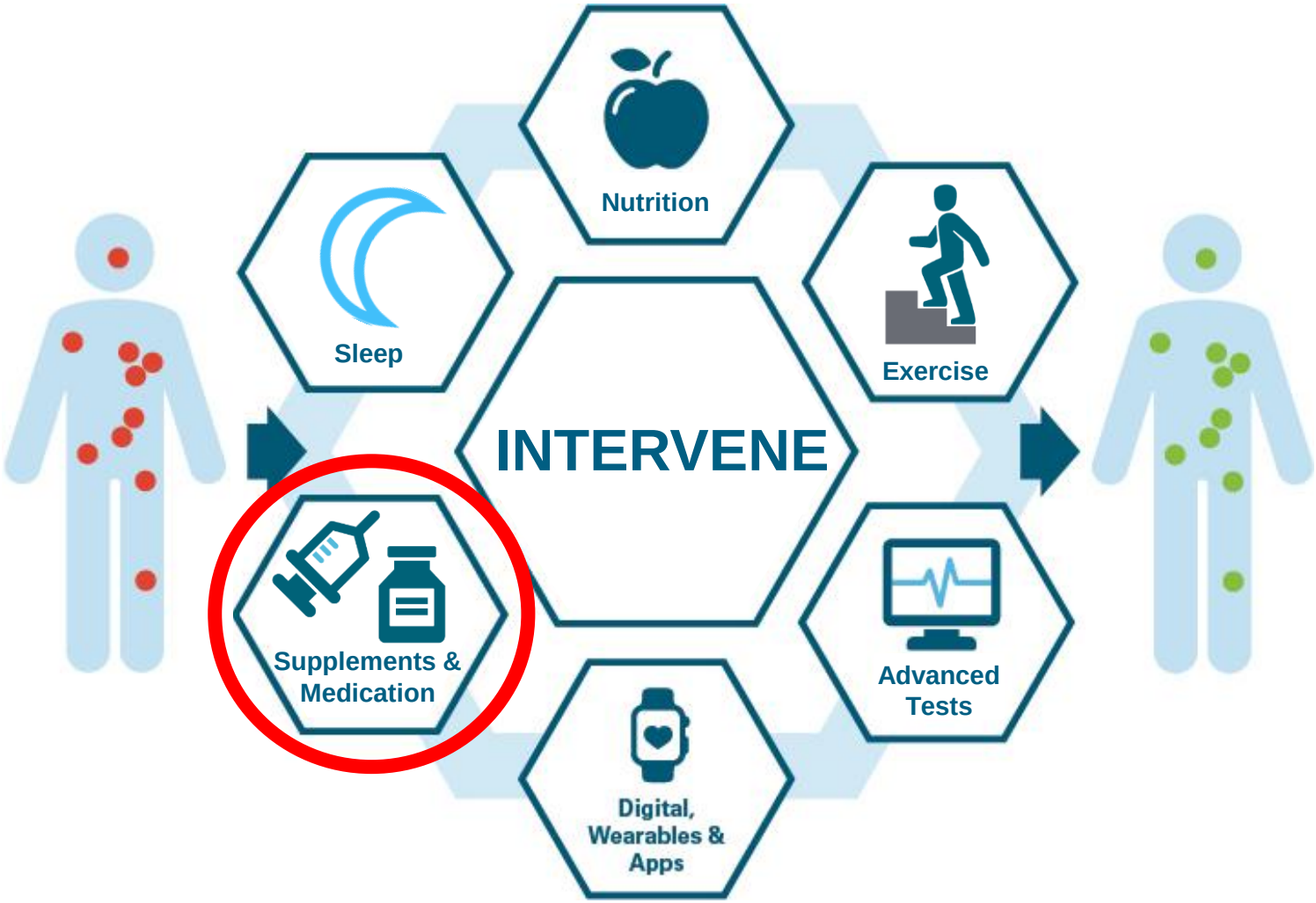
REFERENCES

1. Kratzik CW, Schatzl G, Lunglmayr G, Rucklinger E, Huber J. The impact of age, body mass index and testosterone on erectile dysfunction. The Journal of urology. 2005; 174(1): 240-243.
2. Matsumoto AM. Andropause: Clinical implications of the decline in serum testosterone levels with aging in men. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2002; 57(2): M76-M99.
3. Chin KY, Ima-Nirwana S, Mohamed IS, Shahar S, Teng NI, Ramli ES, Ahmad F, Aminuddin A, Ngah WZ. Testosterone is associated with age-related changes in bone health status, muscle strength and body composition in men. The Aging Male. 2012; 15(4): 240-245.
4. Bhasin S, Buckwalter JG. Testosterone supplementation in older men: a rational idea whose time has not yet come. Journal of Andrology. 2001; 22(5): 718.
5. Mulligan TA, Iranmanesh A, Veldhuis JD. Pulsatile iv infusion of recombinant human LH in leuprolide-suppressed men unmasks impoverished Leydig-cell secretory responsiveness to midphysiological LH drive in the aging male. Journal of Clinical Endocrinology & Metabolism. 2001; 86(11): 5547-53.

FURTHER INFORMATION

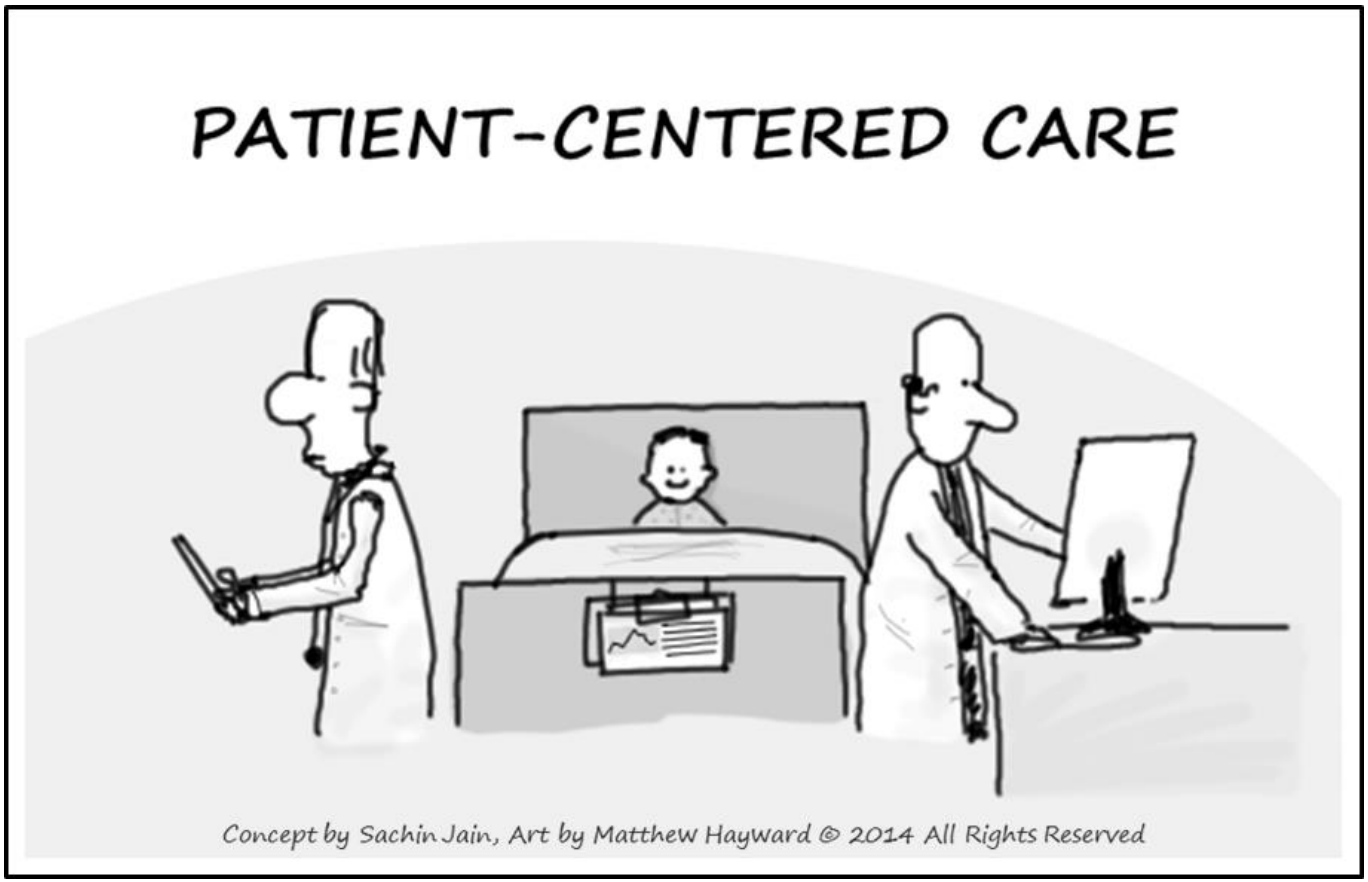
Florence Comite: Fcomite@ComiteMD.com
(212) 288-8123

Optimal T: Critical, Integral to *n-of-1*™ Intervention



Thank you

Barbara Blum
Suzanne Dudgeon
Anita Emly
Marylynn Fisch
Janine Forrestal
Erin Gress
Andi Hanken
Amanpreet Kaur
Sarah Lehman
Christie Leinbach
Daniel Lenzo
Nina Luban
Matthew Porter
Talat Rubin
Umbar Sattar
Cecelia Smith
Michael Tucci



Sources

Basaria S, Coviello AD, Travison TG, Storer TW, Farwell WR, Jette AM, Eder R, Tennstedt S, Ulloor J, Zhang A, Choong K, Lakshman KM, Mazer NA, Miciek R, Krasnoff J, Elmi A, Knapp PE, Brooks B, Appleman E, Aggarwal S, Bhasin G, Hede-Brierley L, Bhatia A, Collins L, LeBrasseur N, Fiore LD, Bhasin S. Adverse events associated with testosterone administration. N Engl J Med. 2010

Comite F, Baek, J. Hormonal Expression of Androgen Decline in Aging Men (ADAM). Endocr Rev June 2013; 34 [Abstract]: SAT-563.

Comite, F. Keep It Up: The Power of Precision Medicine to Conquer Low T and Revitalize Your Life! 2013

Dunkel, T. “Vigor Quest.” New York Times Magazine. January 15, 2010.

Glina S, Rivero MA, Morales A, Morgentaler A. Studies on prostatic cancer I. The effect of castration, of estrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate by Charles Huggins and Clarence V. Hodges. J Sex Med. 2010

Liu PY, Wishart SM, Handelsman DJ. A double-blind, placebo-controlled, randomized clinical trial of recombinant human chorionic gonadotropin on muscle strength and physical function and activity in older men with partial age-related androgen deficiency. J Clin Endocrinol Metab. 2002

Morgentaler A. Testosterone and prostate cancer: an historical perspective on a modern myth. Eur Urol. 2006 Nov;50(5):935-9. Epub 2006

Rhoden EL, Morgentaler A. Risks of testosterone-replacement therapy and recommendations for monitoring. N Engl J Med. 2004

Traish AM, Vance JC, Morgentaler A. Overselling hysteria: The role of the media and medical journals in promoting questionable risks-a case study of the testosterone controversy. EMBO Rep. 2017

Tsujimura, A, K Matsumiya, T Takao, Y Miyagawa, S Takada, M Koga, M Koga, et al. “Treatment with Human Chorionic Gonadotropin for PADAM: A preliminary report.” Aging Male: The Official Journal of the International Society for the Study of the Aging Male 3.4 (2005): 175–79.