

Endocrinology Update 2019

J. Matthew Neal, MD, MBA, CPE, FACP, FACE, FAAPL
Executive Medical Director, Academic Affairs
IU Health Ball Memorial Hospital
Assistant Dean and Professor of Clinical Medicine
Indiana University School of Medicine

Discussion Topics

- Management of incidentally discovered lesions
 - Adrenal
 - Thyroid
- “Adrenal Fatigue”—fact or fad?
- Diabetes therapies – focus on type 2
- Androgen replacement therapy: magic bullet or not?
- Transgender medicine update: hormone therapy
- New drugs/formulations on the horizon

Incidental Adrenal Masses

Adrenal “Incidentalomas”

- Adrenal masses found incidentally on abdominal imaging done for unrelated reasons
 - CT, MRI, rarely ultrasound
- Incidence approximately 1-4% in general population
- Up to 9% of patients have been found to have incidental adrenal masses at autopsy
- **Most are benign**
- **Some need further investigation**

Adrenal Incidentalomas

- Most are non-functioning and of no clinical consequence, however:
 - Goal is to evaluate for functioning tumors
 - If so, then removal is in order
- Nonsecretory < 4 cm – observe
- If enlarging or ≥ 4 cm – consider removal even if nonsecretory

De: 92+0

DOB: 11 Jul 1951
27 Dec 2001
512

MOV 36.0cm
STND

R

1

7

3

L

1

8

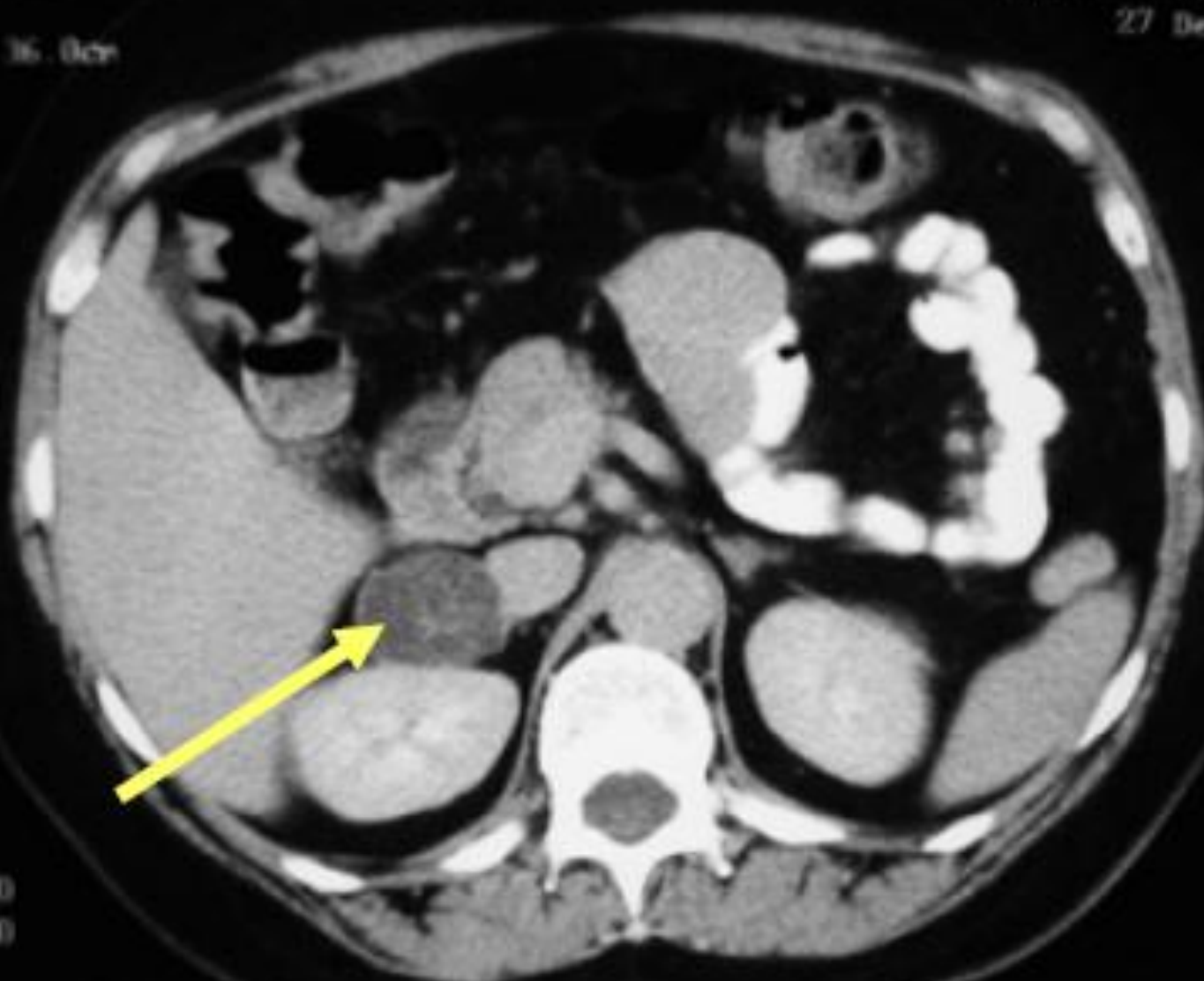
0

kV 120
mA 280

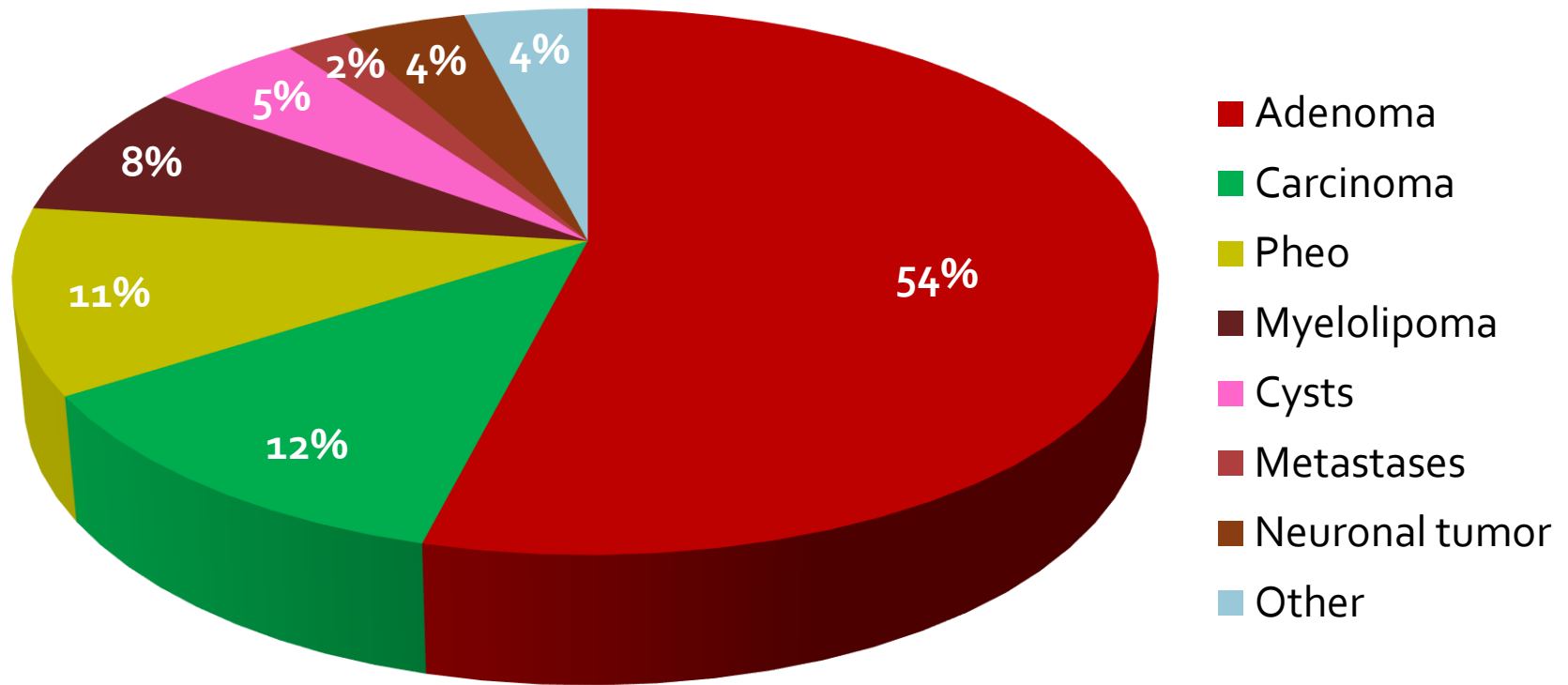
Large
5.00mm/7.50 180

1st: 0.0

0.8cm/12.5cm

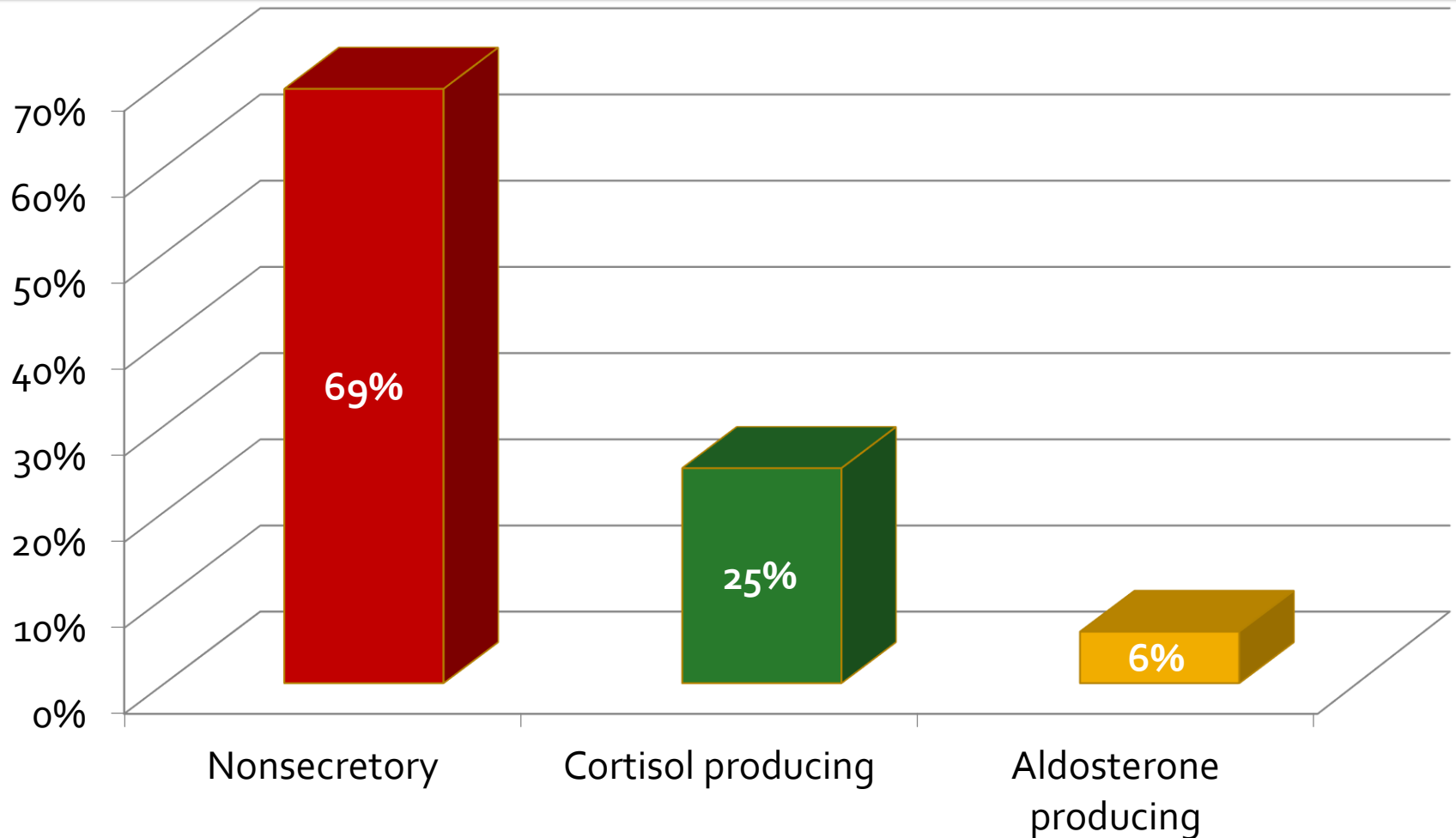


Incidental Adrenal Masses



Endo Metab Clin N Am, 2000; 1:107-125.

Adrenocortical Adenomas



Endo Metab Clin N Am, 2000; 1:107-125.

CT Imaging

- Typical pre-contrast Hounsfield unit (HU) values:
 - Adipose tissue: -20 to -150 HU
- Adenoma phenotype:
 - Hypodense
 - Homogenous
 - Precontrast density < 10 Hounsfield units
 - $> 50\%$ contrast washout at 10 min

CT Imaging

- Pheochromocytoma
 - Increased attenuation (> 20 HU)
 - Delayed contrast washout ($< 10\%$)
 - High signal intensity on T2 MRI
 - Cystic – hemorrhagic
- Adrenocortical carcinoma
 - Irregular shape
 - Inhomogeneous density
 - Often > 4 cm
 - High unenhanced density (> 40 HU)
 - High to intermediate T2 on MRI

Incidentally discovered pheochromocytoma



Adrenocortical carcinoma



Fine needle aspiration of adrenal masses

- Not recommended for most incidental tumors
- Concern for “seeding” if this is a primary malignancy
- Imaging phenotype will screen out benign tumors with nearly 100% sensitivity/ specificity
- **Biochemical evaluation imperative for all lesions**
- FNA indicated for:
 - Suspected metastatic lesion
 - Infectious lesion

Screening for subclinical Cushing syndrome

- Overnight (1 mg) dexamethasone suppression test is recommended
- Suppression $< 1.8 \mu\text{g/dL}$ (50 nmol/L) is normal
- False positives may occur
- Abnormal values require further evaluation
 - Plasma ACTH (should be low if functional adrenal tumor)
 - Consider referral to endocrinology

Failure to diagnose Cushing's syndrome

- Overnight DST is not complex to perform
- Abnormalities should be evaluated by an endocrinologist
- Failure to diagnose Cushing's syndrome: #1 endocrinology malpractice claim for primary care



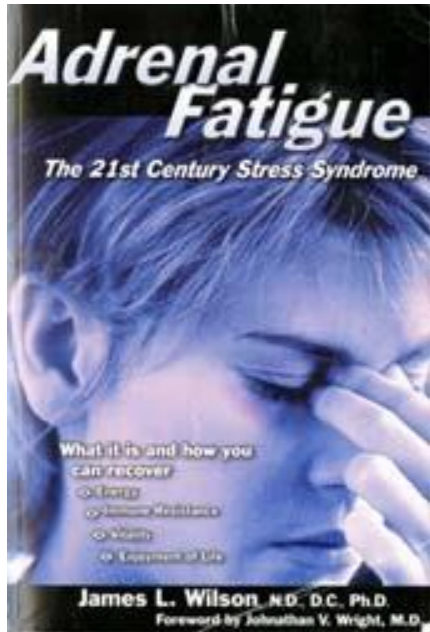
Screening for pheochromocytoma

- Plasma free metanephrines
- 24 hour urinary metanephrines and catecholamines
- Some patients with pheochromocytoma are normotensive or only mildly hypertensive between episodes
- Pheochromocytomas grow slowly: 0.5 to 1 cm in diameter/yr
- They are generally biochemically silent unless they are > 1.5 cm in diameter

Screening for primary aldosteronism in patients with HTN

- Plasma aldosterone concentration (PAC)
- Plasma renin activity (PRA)
- PAC/PRA ratio > 20 suspicious for primary aldosteronism
- Further evaluation needed before performing adrenalectomy
 - Adrenal vein sampling to confirm unilateral hypersecretion
 - Remember: 25% of cases are due to bilateral hyperplasia; adrenalectomy is not helpful

"Adrenal Fatigue"



- If any organ was built for stress, it's the adrenal
- At best, people waste a lot of money on a fabricated disorder
- At worst, they get very ill because someone took them off their steroids



Dr. Wilson's Adrenal Fatigue Protocol®

\$139.32 - \$188.82

Option

Adrenal Fatigue Protocol Large

Adrenal Fatigue Protocol with licorice in large size = best option

~~\$209.80~~ **\$188.82**

1

ADD TO CART

Incidental Thyroid Nodules

Incidental Thyroid Nodules

- American College of Radiology
 - Do not recommend ultrasound for incidental thyroid nodules found on CT, MRI or non-thyroid-focused neck ultrasound in low-risk patients unless the nodule meets age-based size criteria or has suspicious features:
 - < 35 years of age with normal life expectancy and nodule ≥ 1 cm.
 - ≥ 35 years of age with normal life expectancy and nodule ≥ 1.5 cm.

Incidental thyroid nodules

- Suspicious features on CT, MRI or US include signs of local invasion, and the presence of abnormal lymph nodes (enlarged nodes, nodes with cystic change, calcification, or increased enhancement).
- Size criteria for enlarged lymph nodes:
 - ≥ 1.5 cm in short axis for jugulodigastric nodes
 - ≥ 1 cm for other nodes

Incidental thyroid nodules

- Clinical risk factors: Patients with history of head, neck or chest radiation, family history of thyroid cancer, or diseases that increase the risk of thyroid cancer should be further evaluated regardless of nodule size.

Type 2 Diabetes Update

Anti-hyperglycemic Therapy:

Oral agents & non-insulin injectables

- Biguanides
- Sulfonylureas
- Thiazolidinediones
- Meglitinides
- Alpha-glucosidase inhibitors
- DPP-4 inhibitors
- SGLT-2 inhibitors
- Dopamine-2 agonists
- Bile acid sequestrants
- GLP-1 receptor agonists (incretin mimetics)
- Amylinomimetics (pramlintide)

Non-insulin therapies: mean reduction in hemoglobin A_{1c}

Metformin	1.5%
Insulin secretagogues (sulfonylureas, meglitinides)	1.5-2.0%
Incretin mimetics (GLP-1 agonists—exenatide, liraglutide)	1.0 – 1.5%
DPP-IV inhibitors (sitagliptin, linagliptin, saxagliptin, alogliptin)	0.6-1.0%
α-glucosidase inhibitors (AGIs) - (acarbose, miglitol)	1.0%
Amylin agonist (pramlintide)	0.5-1.0%
Thiazolidinediones (pioglitazone, rosiglitazone)	1.0-1.4%
Bile acid sequestrants (colesevelam, colestipol)	<0.5%
SGLUT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin)	0.5-1.2%
Dopamine agonist (bromocriptine)	0.5%

Insulin pharmacokinetics

Insulin	Onset	Peak activity	Duration of action
Intermediate - human NPH (N, neutral protein Hagedorn) (U-100)	2-4 hr	4-9 hr	10-16 hr
Glargine (long acting analog) (U-100, U-300)	2-4 hr	Minimal	20-24 hr
Detemir (long acting analog) (U-100)	2-4 hr	8-10 hr	16-20 hr
Degludec (long acting analog) (U-100, U-200)	2-4 hr	Minimal	36-42 hr
Human regular* (U-100)	30-60 min	2-3 hr	5-8 hr
Human regular* (U-500)	30-60 min	4-8 hr	12-14 hr
Rapid acting analogs (lispro, aspart, glulisine) (U-100)*	5-15 min	30-90 min	4-6 hr

*lispro also available in U-200 pen

ADA and AACE Glycemic Targets

Test	ADA	AACE
HbA _{1c}	< 7%	≤ 6.5%
Fasting glucose	80-130 mg/dL	< 110 mg/dL
Postprandial glucose	< 180 mg/dL (1-2 hr)	< 140 mg/dL (2 hr)

Targets should be individualized based on factors such as age, hypoglycemia awareness, life expectancy, comorbidities

1. ADA. Diabetes Care. 2017;40(suppl 1):S1-S135.
2. Garber AJ et al. Endocr Pract. 2016;22(1):84-113.
3. Handelsman Y et al. Endocr Pract. 2015;21(suppl 1):1-8.

DM Outcomes vs. Provider Type

	NP	PA	Physician
Age, yrs	65.2	65.5	65.2
% male	96.6	96.7	96.7
% Caucasian	72.3	74.7	69.9
% with DCG < 0.5	51.8	53.1	49.6
BMI, kg/m ²	32.6	32.5	32.4
Mean HbA _{1c}	7.6	7.6	7.6
LDL-chol, mg/dL	87	87	86
% with HbA _{1c} < 7%	39.6	37.8	38.4

DM Outcomes vs. Provider Type

- No clinically significant variation found among the 3 PCP types with regard to diabetes outcomes
 - similar chronic illness outcomes may be achieved by physicians, NPs, and PAs.
- Absence of differences remained when examining only patients with high medical complexity and / or receiving insulin
- Results reaffirm recommendations for team approach to the care of patients with DM as first proposed by Eliot Joslin in 1922 following the discovery of insulin

LOW T: An Epidemic?

TREATMENT: The Magic Bullet?



Loss of Building Blocks: an Epidemic? Or Fad? Will You Turn to Dust Too?





ARE YOU:

- FATIGUED
- IRRITABLE or DEPRESSED
- LACKING ENDURANCE
- UNABLE TO BUILD MUSCLE
- TROUBLE SLEEPING
- LOW LIBIDO

LOW TESTOSTERONE LEVELS
MAY BE THE CAUSE

FIND OUT FOR FREE

START LIVING A
HIGH PERFORMANCE
LIFESTYLE TODAY

**FREE LOW
TESTOSTERONE
SCREENING**

404.303.2323
call for your appointment

 **SHAPE**
WELLNESS CENTER
Fountain Oaks Shopping Center
4920 Roswell Rd
Atlanta, GA 30342



AndroGel Extras

Model is for illustration only.



Tips from the Pro

— by Shawn Micheel —

www.golftips.micheel.com



Win a new set of Taylor Made golf clubs!

Visit golftips.micheel.com to:

- Register for a chance to win!
- Get tips from a PGA Champion



Sponsored by Auxilium Pharmaceuticals, Inc.,
makers of Testim® 1% (testosterone gel) CIII

©2007 Auxilium Pharmaceuticals, Inc. 0407-008.a

Realistic expectations or not?



Models are for illustration only.

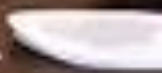


WE ARE GOING TO BRING
THE REAL YOU BACK.

TexomaWellness 
LOW-T CENTER



LowT Center



Hormonal Evaluation

- Total testosterone (AM; fasting)
- Free testosterone/SHBG in certain individuals (obesity)
- If abnormal:
 - Prolactin
 - FSH/LH
- If FSH/LH inappropriately low:
 - MRI of pituitary
 - TSH, free T₄, serum cortisol, ACTH
- When in doubt, send to endocrinology!

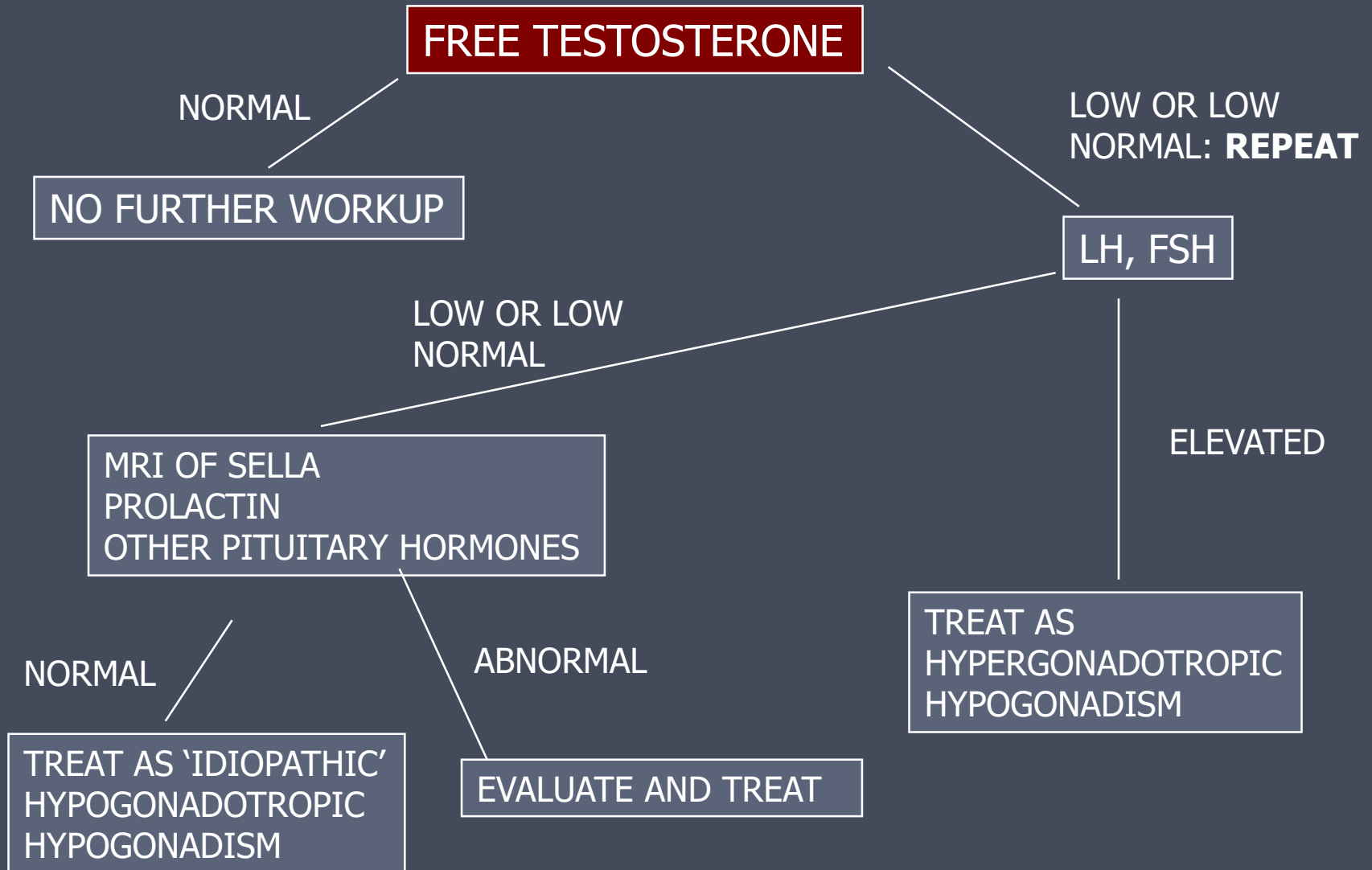
Total vs. Free Testosterone

- Testosterone circulates mostly bound to SHBG (sex hormone binding protein)
- ~3% circulates as free testosterone
- Only the free portion is biologically active
- Often patients will have slightly low total with normal free T levels
- You can't just stick the guy with "low T" on testosterone without further evaluation

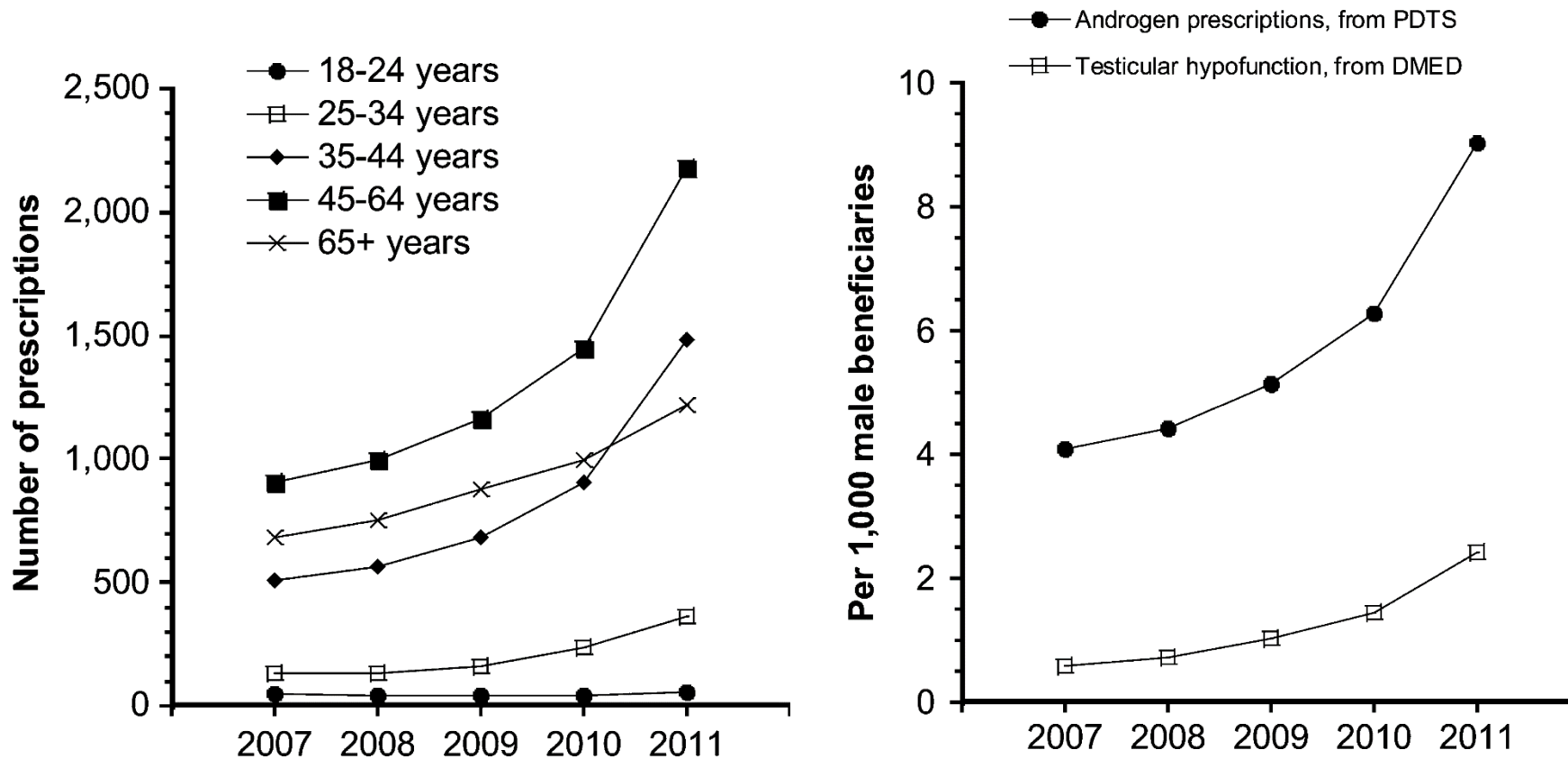
Measuring Testosterone

- Always check T level in the morning (levels are lowest in the afternoon)
- Always fasting (levels are affected by food)
- If low, confirm with free T, SHBG (sex hormone binding globulin)
 - Most cases of “low T” are due to (a) levels being checked in the afternoon or (b) low SHBG (almost always due to obesity).

EVALUATION OF HYPOGONADISM

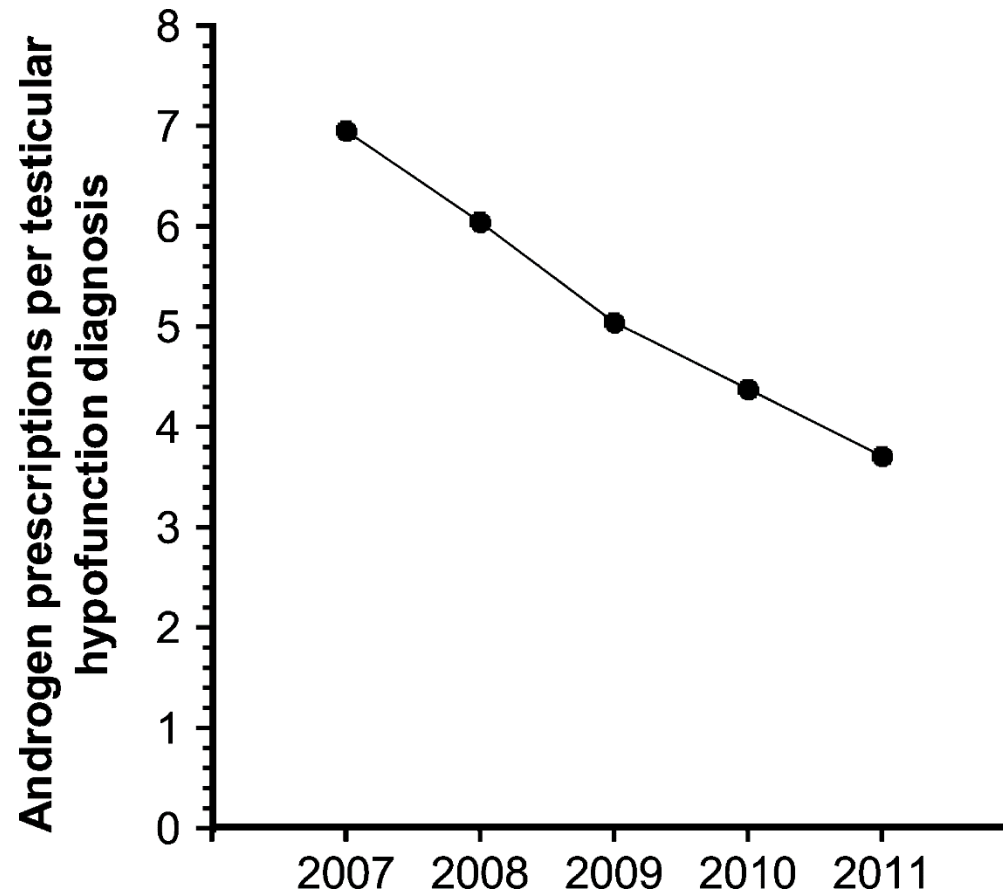


Prescription Trends



Canup et al. Trends in Androgen Prescriptions From Military Treatment Facilities: 2007 to 2011. Military Medicine 2015; 7:728.

Prescription Trends



Canup et al. Trends in Androgen Prescriptions From Military Treatment Facilities: 2007 to 2011. *Military Medicine* 2015; 7:728.

MONITORING

- Clinical symptoms
 - reliability varies with patient
- Testosterone levels
 - peak vs. trough levels with esters?
 - simpler with transdermal preparations
- Monitor hemoglobin/hematocrit yearly
 - Concern when Hgb > 18 g/dL
- Monitor for signs of OSA (or worsening of OSA if already on CPAP)

MONITORING

- Baseline digital rectal examination and PSA before starting TRT
- PSA should be checked 6–12 weeks after initiation of androgen therapy
- Check PSA and digital rectal examination annually as long as patient remains on TRT
- PSA velocity > 0.75 ng/mL/y, regardless of baseline PSA, or a nodule on digital rectal examination while on TRT requires referral to urology.

CV Risk of Androgen Therapy

- Current literature examining the relationship between TRT and CVD outcomes is conflicting
- Two meta-analyses showed no statistically significant differences in cardiovascular events between patients receiving TRT and patients receiving placebo

CV Risk of Androgen Therapy

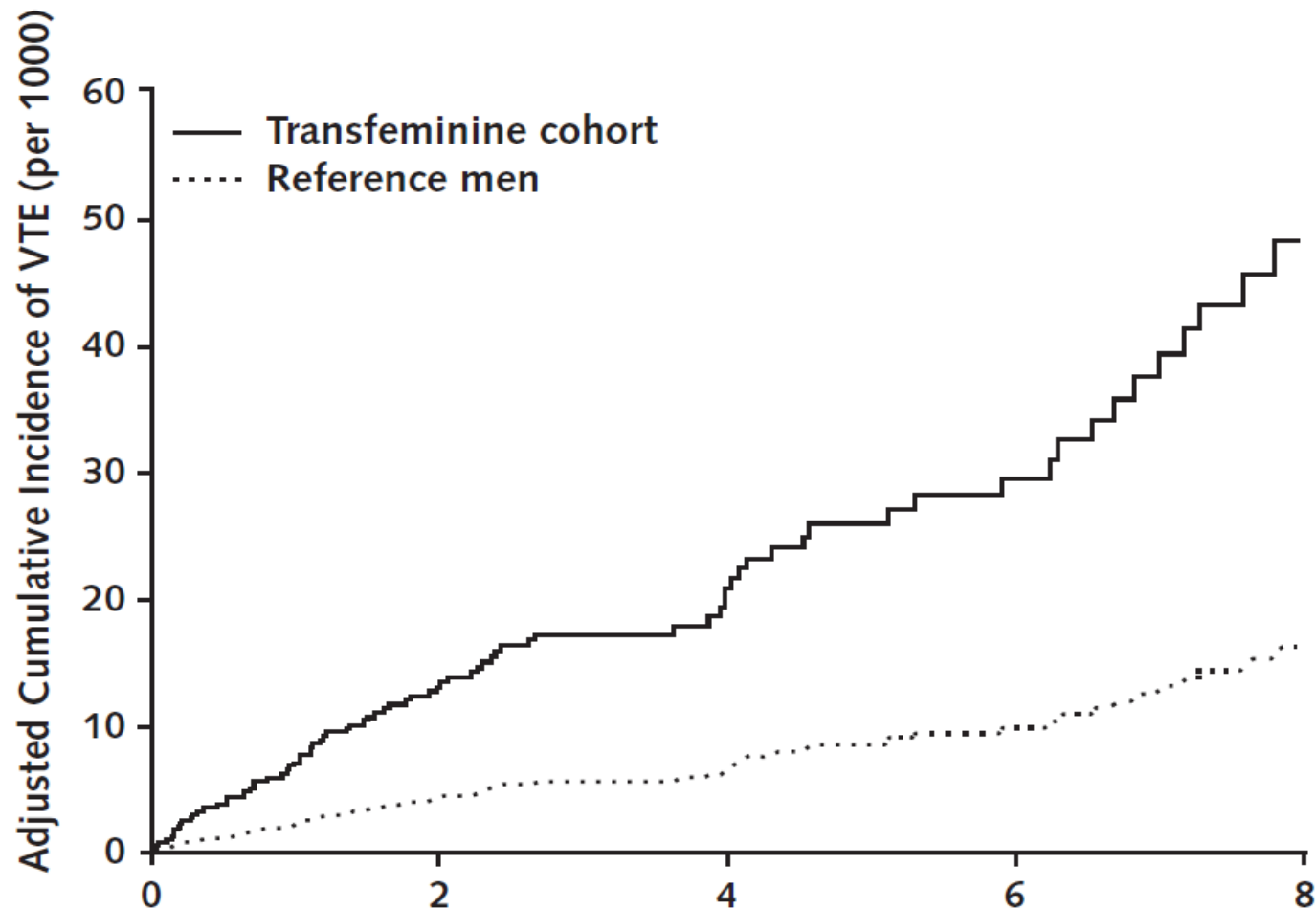
- Epidemiologic studies have innate problems of confounding and bias
- Dependent on underlying prevalence of the condition in the population
- Men with lower testosterone are less healthy (obesity, chronic disease)
 - Testosterone is a marker of good health

Take-Away Points

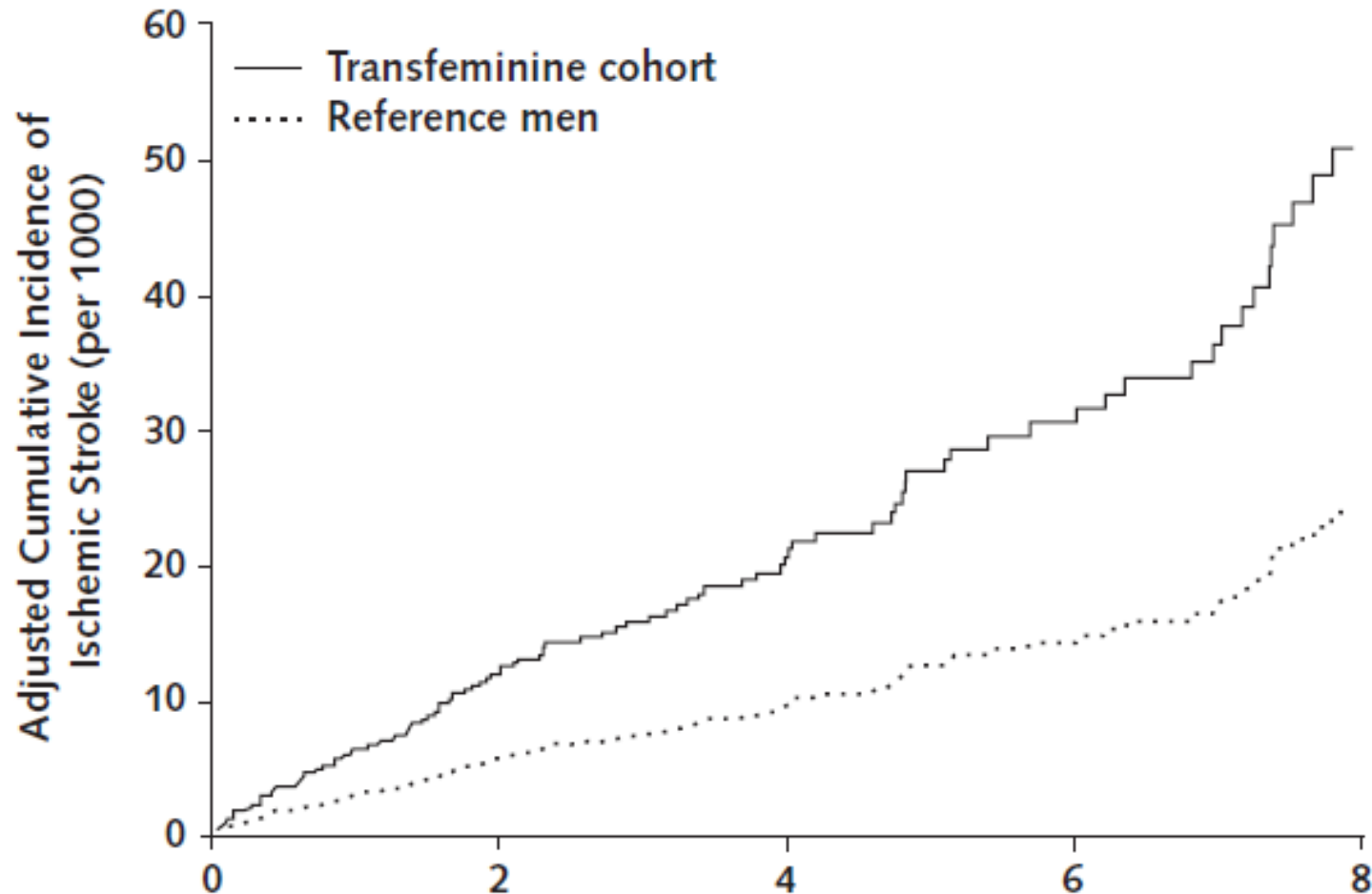
- Male hypogonadism exists, but is not nearly as prevalent as the popular media suggests
- In select patients it may offer benefits but is rarely a “magic bullet”
- Evaluate properly before considering treatment
- Treatment is not without risks/side effects
- Rare patients have serious underlying conditions which require expert management
- Treat cautiously in older individuals with comorbid conditions

Transgender Medicine

Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons



Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons



Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons

- Study strengths:
 - Represents largest cohort of transgender persons in US
 - Transgender status verified
- Study limitations
 - This not a placebo controlled RCT
 - Data regarding hormonal agent and dosing were minimal
 - Information not available re: comorbidities and use of other medications (e.g. statins)

Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons

- MTF participants have higher rates of VTE, ischemic stroke, and MI; FTM to lesser extent
- This increase in acute CV events was most pronounced in those initiating estrogen therapy
- These results indicate need for increased vigilance for adverse vascular events in transgender persons receiving hormonal therapy

New Drugs & Quick Updates

- SGLT2 inhibitors and necrotizing fasciitis (Fournier gangrene) of the perineum (May 2019)
- Investigational oral semaglutide (GLP-1 agonist) for the treatment of type 2 diabetes (May 2019)
- Canagliflozin in patients with diabetes and proteinuria (April 2019) – reduced incidence of ESRD and hospitalization for heart failure

New Drugs & Quick Updates

- Primary care-led intensive lifestyle interventions and remission of type 2 diabetes (March 2019)
- SGLT2 inhibitors (dapagliflozin) and improved cardiovascular and renal outcomes in type 2 diabetes (November 2018)
- Testosterone therapy in men: new bioavailable oral preparation (May 2019) – only for patients with specific forms of hypogonadism, not age-related

Thank you!

Questions?