Patient presenting with symptoms, physical conditions[1], or physical exam signs[2] consistent with testosterone deficiency

Measure morning, fasting total testosterone[3]
(Epic order: "Testosterone")

Total T > 300 ng/dL

Hypogonadism excluded
Consider other causes for symptoms

Total T < 300 ng/dL

Repeat morning, fasting total testosterone
Consider addition of free testosterone and SHBG[4]
(Epic order: "Testosterone" or
"Testosterone, bioavailable and total, SHBG, (Males 14 yrs and older or any individual on TRT)"

Total T > 300 ng/dL
Or
Normal Free T[5]

Second Total T < 300 ng/dL
Or
Low free T[5]

Hypogonadism confirmed
Determine Etiology: Measure FSH, LH

LH and FSH low or normal
(Secondary hypogonadism)

Obtain prolactin
Obtain iron saturation, ferritin
Consider Brain MRI if indicated[6]

Prolactin elevated
Total T < 150

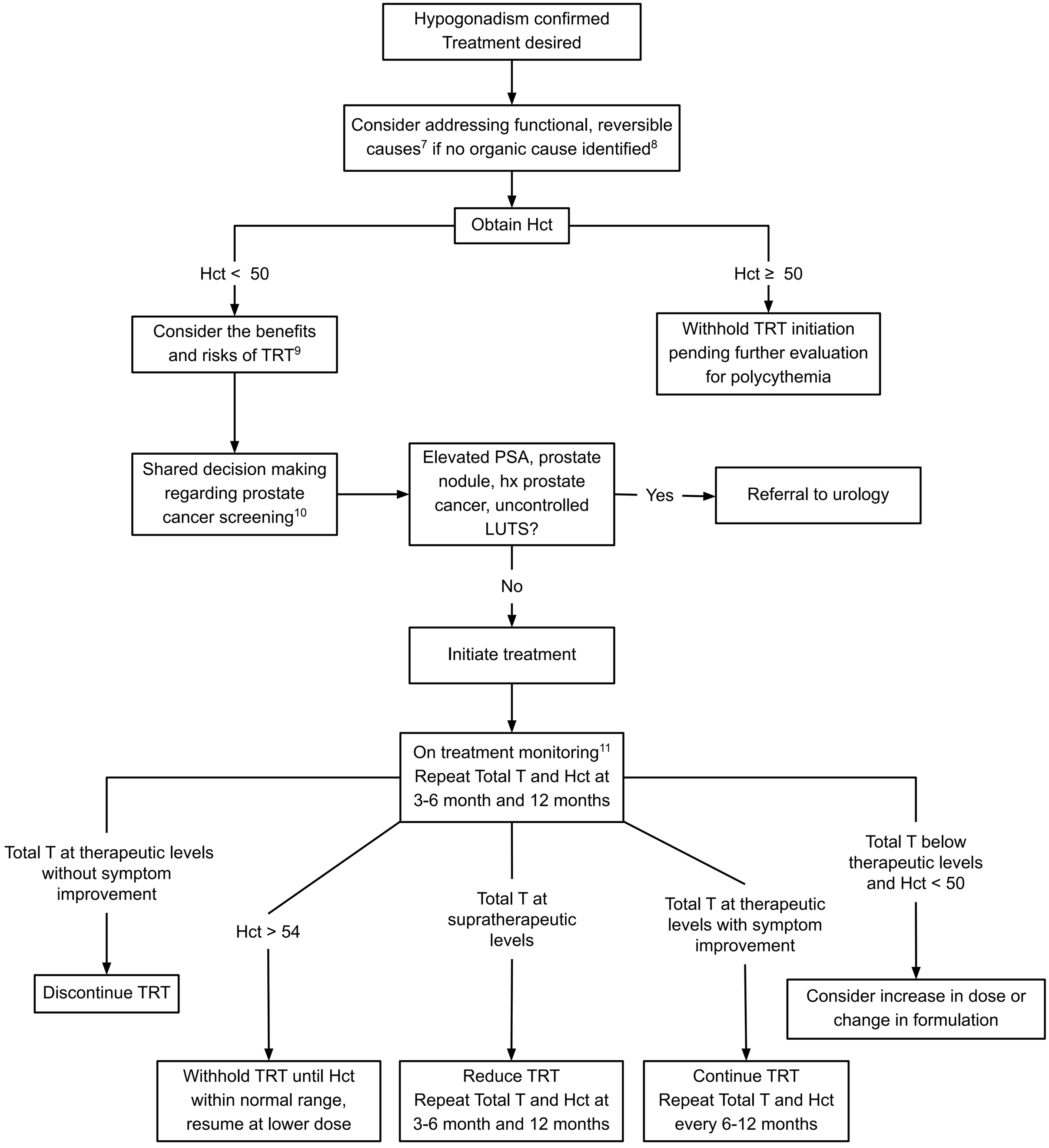
Abnormal Brain MRI

Consider endocrinology referral
Repeat prolactin

LH and FSH elevated
(Primary hypogonadism)

Karyotype testing if clinically indicated

Proceed to treatment algorithm (next slide)


Hypogonadism confirmed
Treatment desired
Consider addressing functional, reversible causes[7] if no organic cause identified[8]
Obtain Hct
Hct < 50
Hct ≥ 50
Consider the benefits and risks of TRT[9]
Withhold TRT initiation pending further evaluation for polycythemia
Shared decision making regarding prostate cancer screening[10]
Elevated PSA, prostate nodule, hx prostate cancer, uncontrolled LUTS?
Yes
Referral to urology
No
Initiate treatment
On treatment monitoring[11]
Repeat Total T and Hct at 3-6 month and 12 months
Total T at therapeutic levels without symptom improvement
Hct > 54
Total T at supratherapeutic levels
Total T at therapeutic levels with symptom improvement
Total T below therapeutic levels and Hct < 50
Discontinue TRT
Withhold TRT until Hct within normal range, resume at lower dose
Reduce TRT
Repeat Total T and Hct at 3-6 month and 12 months
Continue TRT
Repeat Total T and Hct every 6-12 months
Consider increase in dose or change in formulation

1. Conditions include: withdrawal from long term anabolic/androgenic steroids, HIV associated weight loss, pituitary mass, conditions or hx of radiation to sellar region, infertility, osteoporosis/low trauma fracture, unexplained anemia, low libido/erectile dysfunction, long term opioid/glucocorticoid use
2. Lack of development of secondary sex characteristics, decreased body hair, small testes, infertility, low trauma fracture
3. In patients with conditions that affect SHBG, consider using Epic order: "Testosterone, Bioavailable and Total, Sex Hormone-Binding Glob, (Males 14 yrs and older or any individuals on Testosterone Hormone Therapy)" to evaluate SHBG and bioavailable testosterone which can be used instead of measuring stand alone free testosterone
4. Conditions affecting SHBG
    a. Decreased SHBG: obesity, diabetes mellitus, use of glucocorticoids/progestins/anabolic steroids, nephrotic syndrome, hypothyroidism, acromegaly, SHBG polymorphisms
    b. Increased SHBG: Aging, HIV, cirrhosis, hyperthyroidism, hepatitis, anticonvulsants, estrogens, SHBG polymorphisms
5. Due to high interassay variability, should interpret normal ranges based on local lab parameters
6. Indications for Brain MRI: total testosterone < 150, compressive symptoms (headaches, visual field defect), persistent hyperprolactinemia, panhypopituitarism
7. Functional reversible causes include opioid use, anabolic steroid use, glucocorticoid use, alcohol use, nutritional deficiency, obesity, sleep disorders (consider treatment of reversible causes prior to initiation of TRT)
8. Organic causes include iron overload, pituitary disease, Klinefelter, cryptorchidism, orchitis, testicular trauma/irradiation/orchiectomy, advanced age, certain chemotherapies
9. Treatment should be offered on an individualized basis to those with hypogonadism and symptoms associated with low T concentrations after discussion of potential risks and benefits
    a. Absolute contraindications: active breast cancer or metastatic prostate cancer.
    b. Relative contraindications to TRT – Discussion with specialist prior to initiation recommended: planning fertility, history of breast or prostate cancer, palpable unevaluated prostate nodules, PSA >4, PSA >3 with high risk of prostate cancer, severe LUTS (AUA/IPSS >19), untreated severe OSA, uncontrolled heart failure, thrombophilia, hematocrit >48%, myocardial infarction or stroke within the last 4 months.
10. For men 55-69 y of age (40-69 y of age who are at increased risk for prostate cancer) who choose prostate monitoring after shared decision making, perform DRE and check PSA before starting the treatment, 3-12 months after initiating treatment, and then according to guidelines for age-appropriate prostate cancer screening.
11. Aim to raise total testosterone concentrations to mid-normal range, adjust dose/frequency as needed
    a. Injectable T enanthate or cypionate: measure T concentrations midway between injections
    b. Transdermal gels: measure T concentrations 2-8 hours following gel application
    c. Transdermal patches: measure T concentrations 3-12 hours after application
    d. T pellets: measure T concentration at the end of dosing interval

References:

- Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. J Urol. 2018;200(2):423-432. doi:10.1016/j.juro.2018.03.115
- Bhasin S, Brito JP, Cunningham GR, et al. Testosterone Therapy in Men With Hypogonadism: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, 2018;103 (5):1715–1744. https://doi.org/10.1210/jc.2018-00229
- Lincoff AM, Bhasin S, Flevaris P, et al; TRAVERSE Study Investigators. Cardiovascular Safety of Testosterone-Replacement Therapy. *N Engl J Med.* 2023 Jul 13;389(2):107-117. doi: 10.1056/NEJMoa2215025.