TRT for Older Men - a Review of the Literature

Included are articles regarding TRT for men in general and "older" men in specific. A few also have great discussions regarding cardiac and prostate issues related to TRT for all ages. There are *no age limits* mentioned in any of the literature. The only recommendations are to treat only symptomatic patients and to provide individualized consideration of treatment for men older than 65 (after discussing risks and benefits). Several have reasonable lists of contraindications and relative contraindications. Again, none of them list age as a limiting factor for treatment. Digital rectal examination (DRE) and lab tests for prostate specific antigen (PSA) are much more important aspects for progressively older TRT patients. The text below the article titles are the important portions from the articles themselves.

SOURCES: [simple online searches of the underlined sources will yield the articles themselves]

1. Evaluation and Management of Testosterone Deficiency: AUA Guideline (2018) [by Mulhall, et al] There are a large percentage of men in need of testosterone therapy who fail to receive it due to clinician concerns, mainly surrounding prostate cancer development and cardiovascular events, although research evidence fails to support these concerns. The one research study that began these mythical concerns was debunked by dozens and dozens of experts critical of the flawed research data in the study. Further research proved the opposite; low T is worse for prostate cancer risk and cardiovascular outcomes than adequate T levels.

Clinicians should inform patients of the absence of evidence linking testosterone therapy to the development of prostate cancer, and no evidence linking TRT to higher risks of venothrombotic (clots) events. There are no definitive studies linking TRT to worsened cardiovascular outcomes, however, TRT should not be started for a period of 3-6 months following a cardiovascular event (MI, CVA - heart attack or stroke).

The Panel recognizes that in the reality of clinical practice there are men who have total testosterone levels >300 ng/dL who are symptomatic and have experienced symptoms and or signs of improvement with testosterone therapy. The Panel urges clinicians to use their clinical judgment in the management of such patients. Again, treating symptomatic men, not only focused on a level.

2. Actual FDA Insert for depo-testosterone (2023)

These guidelines include good lists of contraindications, warnings with treatment, side effects, etc No mention of age limitations for treatment.

 Diagnosis and Treatment of Testosterone Deficiency: Recommendation from the Fourth International Consultation for Sexual Medicine (ICSM 2016) Journal of Sexual Medicine 2016;13:1787 - 1804 (2016)

No age limits mentioned.

"There are no generally acceptable lower limits of normal total testosterone. Symptomatic men with total T levels lower than 350 ng/dL should be treated and **a trial of TRT in symptomatic** *men with total T levels higher than 350 ng/dL can be considered based on clinical presentation. A 3-6 month trial of empiric testosterone replacement can be considered in men with suggestive symptoms but without definitive diagnostic blood test results, because there is NO absolute T concentration that reliably distinguishes who will or will not respond to treatment because of substantial interindividual variations in testosterone physiology."* 4. <u>Recommendations on the Diagnosis, Treatment, and Monitoring of Hypogonadism in Men</u> in <u>The Aging Male</u> - Informa UK Ltd. (February 2015) - International Society for the Study of the Aging Male (ISSAM)

No mention of age limitations. General recommendations on the diagnosis, treatment, and monitoring of hypogonadism in men. It must be remembered that general recommendations can never replace clinical expertise. Treatment decisions, selection of treatment protocols, or choice of products for individual patients must also take into account patients' personal needs and wishes.

ISSAM recommends 350 ng/dL as a lower limit of normal for total testosterone level. However, due to individual differences in testosterone sensitivity some men may exhibit symptoms of hypogonadism with total T concentrations above this threshold, and they may benefit from TRT. TRT may be reasonably offered to symptomatic men with concentrations higher than 350 ng/dL based on clinical judgment......

The most widely accepted parameter to establish the presence of hypogonadism is measurement of total testosterone. Unfortunately, no consensus has ever been reached regarding the lower T threshold defining testosterone deficiency, and there are no generally accepted lower limits of normal total T. This lack of consensus follows from the fact that no studies have shown a clear threshold for total T or free T that distinguishes men who will respond to treatment from those who will not.

Androgen receptor activity varies greatly man to man, hence testosterone sensitivity may vary significantly in individual men. Again (and again), a trial of TRT for symptomatic men is safe and possibly life-changing.

5. The Journal of Sexual Medicine - <u>Testosterone Deficiency: A Review and Comparison of Current Guidelines (2019)</u> J Sex Med 2019; 16:812-820 No mentioned age limitations. Clearly addresses past concerns for prostate cancer and cardiovascular risks not being relevant to TRT. Clinical guidelines from 6 specialty organizations: Canadian Medical Association, International Society for Sexual Medicine, British Society for Sexual Medicine, American Urological Association, European Association of Urology, and the Endocrine Society. They have multiple different cut-off levels for low T; <231, <300, <264, no cutoff level from the Canadians. They have widely varying 'normal' ranges; 450-600, 433-865, 404-505, 350-600. They all have the same treatment goal of symptomatic improvement with minimal side effects. They state lab levels can support the diagnosis or clinical suspicion for low T, and they all have consensus to stop TRT if the patient has no improvement in symptoms. Other less significant parameters are also covered effectively.</p>

6. The International Society for Sexual Medicine's Process of Care for the Assessment and Management of Testosterone Deficiency in Adult Men (2015) J Sex Med 2015;12:1660-1686 Good data on possible side effects. Excellent debunking of prostate cancer and cardiovascular concerns. The concerns for prostate cancer with TRT stemmed from a 1941 article with only 3 patients in it. JAMA [Journal of the American Medical Association] published an article highly suggestive that TRT could create dangerous cardiovascular risk outcomes. It garnered enormous media attention but within one week multiple serious errors were found in the study. When the data was appropriately interpreted it showed that patients with treated lowT had ½ the number of cardiovascular events as their untreated counterparts. Powerful. A rich literature history has strongly suggested that TRT may actually be protective against prostate cancer and cardiovascular events; therefore not just not a bad thing, but instead a good thing.

- International Journal of Clinical Practice A Practical Guide to Male Hypogonadism in the Primary Care Setting (2010) Int J Clin Pract. 2010 May; 64(6):682-696 No mention of age limitations. General TRT information. Also good information on contraindications and precautions.
- 8. <u>Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice</u> <u>Guideline (2018)</u> J Clin Endocrinol Metab, May 2018;103(5): 1715-1744 They suggest against routinely prescribing testosterone therapy to all men 65 years or older with low testosterone concentrations; only treat the men with symptoms associated with low T. TRT for one year in symptomatic men >65 years resulted in moderate improvements in sexual function (sexual activity, sexual desire, and erectile function), a small improvement in walking distance, mood, and depressive symptoms, but no improvements in vitality or cognitive functions.

Basic Summary:

Older men with symptoms should be considered for TRT. Life improvements can be dramatic.

Prostate conditions should be more aggressively evaluated than for younger men.

Zero studies consider age to be a contraindication for TRT.

Men without symptoms of low testosterone don't need and won't benefit from TRT.

Does not hurt to have a specific conversation with your provider if you have symptoms that might be T-related. Show them this research and remember to ask nicely!