

## TESTOSTERONE AND AGING: CLINICAL RESEARCH DIRECTIONS

Testosterone is often equated in the popular culture with youth, vitality, and strength – a perception that has fueled an increase in the use of testosterone products by men in recent years. However, there has been growing concern about the increase in the number of men using testosterone and the lack of scientific data on the benefits and risks of this therapy.

An FDA-approved treatment for male hypogonadism (a clinical condition partly defined by low testosterone levels), testosterone therapy has been found effective in ameliorating a number of symptoms in hypogonadal males and most studies have been conducted in this population. However, few studies, particularly placebo-controlled randomized trials, have been conducted in populations of middle-aged or older men who may have testosterone levels in the low range and show one or more symptoms that are common to both aging and hypogonadism, but who do not meet all the criteria for being hypogonadal.

An Institute of Medicine committee was formed to conduct a study to provide an independent assessment of clinical research on testosterone therapy in older men and make recommendations on future research directions for this field. The committee concluded that future clinical research in this area should:

- Focus on the population most likely to benefit,
- Use testosterone as a therapeutic intervention, not as a preventive measure,
- Establish clear benefit before assessing long-term risks,
- Focus on clinical outcomes in which there is preliminary suggestion of efficacy and for which safe and effective therapeutic options are not currently available, and
- Ensure the safety of research participants.

### Recommendations on Clinical Trials of Testosterone Therapy

The first and most immediate goal of studies on testosterone therapy must be to establish the nature of benefits in the population of aging males most likely to see gains from testosterone therapy. This could be accomplished by conducting a set of small-scale efficacy trials. If adequate benefits are seen in the initial trials, the next effort would involve larger scale and longer-term clinical trials. It is recommended that the initial short-term efficacy trials:

- Involve a study population of older men (65 years and older) who have clinically low testosterone levels and at least one symptom that might be related to low testosterone,
- Focus on outcomes for which safe and effective therapeutic options are not currently available,
- Examine whether testosterone therapy improves: strength/frailty/disability, cognitive function, sexual function, or vitality/well-being/quality of life, and
- Be designed as a coordinated set of trials.

There are concerns regarding the potential for adverse health outcomes associated with testosterone therapy, such as prostate cancer and benign prostatic hyperplasia. The committee believes that it is possible to ethically and safely conduct clinical trials of testosterone therapy in older men as long as thorough exclusion criteria and monitoring practices are followed.

This is an opportune time for examining the efficacy of testosterone therapy in aging men. Clearly, evidence about the efficacy and safety is critical to providing the data needed to make informed clinical decisions and to fully realize any potential health benefits of testosterone therapy.



## COMMITTEE ON ASSESSING THE NEED FOR CLINICAL TRIALS OF TESTOSTERONE REPLACEMENT THERAPY

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*Testosterone and Aging: Clinical Research Directions* is available for sale from the National Academies Press, 500 Fifth St. NW, Washington, DC 20001; call (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area), or visit the NAP's on-line bookstore at [www.nap.edu](http://www.nap.edu). For more information about the Institute of Medicine, visit the IOM home page at [www.iom.edu](http://www.iom.edu).

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