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# EDITORIAL

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## Boosting Free Testosterone With OTC Natural Supplements: Be Careful What You Wish For

There has been a significant surge in interest in testosterone supplementation. Many new products approved by the FDA over the last 10 years have provided both safer and more convenient ways to administer testosterone supplements. Direct to consumer advertising of over the counter (OTC) natural testosterone supplements has reportedly tripled over the same time period. Most direct to consumer advertising is focused on men over 40 years of age since above this age there is a gradual and natural decline in testosterone. OTC sponsors tout that their product is always “all natural, safe and side effect free” and it will make men “feel stronger and more energetic”. This advertising is often accompanied with a wink by the product endorser suggesting the product will also improve sexual performance.

Most non-FDA approved supplements cite validation of their product in clinical studies. One heavily advertised supplement that is “supported by clinical studies” has just one Pub Med clinical paper written by a group outside the US studying a naturally occurring plant product. This plant extract now has been given an impressive and official sounding name with heavy marketing. These natural male enhancement supplements often stress the ability to increase free testosterone subtly suggesting this is a more desirable effect than just increasing total testosterone.

If this increase in free testosterone is proven to be valid, here is where we may have a problem. Although it is generally agreed that testosterone replacement in hypogonadal men does not cause prostate cancer, several recent studies have suggested that there is a relationship in free testosterone and prostate cancer. Free testosterone is considered the bioactive form of testosterone. Men with low levels of circulating free testosterone may have a lower risk of prostate cancer compared with men with higher concentrations of free testosterone. Recent clinical studies have demonstrated that for every increase of just 50 pmol/L of free testosterone there is a 10% increase in prostate cancer risk.<sup>1</sup> Men with the highest free testosterone levels had a 18% greater risk of prostate cancer, compared to those with the lowest levels. Assuming these OTC supplements do actually increase free testosterone, this could be concerning.

There is ample level evidence and guideline endorsement that FDA approved testosterone supplementation in men who have laboratory and clinically documented hypogonadism derive benefits in terms of sexual function, bone mineral density and metabolic syndrome without evidence of increased prostate cancer risk. Although controversial, cardiovascular health may also be improved. The unknown is the impact of these OTC testosterone supplements potentially increasing free testosterone in men with normal testosterone levels.

Guidelines from the American Urological Association and the American College of Physicians conclude that testosterone supplementation should not be routinely used in the aging male unless clinically significant decreased laboratory measured blood levels are demonstrated and there are significant troubling symptoms.

Is it wise to be promoting a free testosterone boost without scientific data? The free testosterone impact on health and disease is just coming into focus and more studies are needed. Men should be aware that we have no data concerning these OTC testosterone supplements and how they may impact prostate cancer risk.

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### References

1. Watts EL, Appleby PN, Perez-Cornago A et al. Low free testosterone and prostate cancer risk: a collaborative analysis of 20 prospective studies. *Eur Urol* 2018;74(5):585-594.