

## Abstract

The association of metabolic syndrome or insulin resistance with low testosterone in men has led to interest in testosterone therapy to improve risk.

Cardiometabolic risk markers were tested after overnight fasting in dried blood spots (DBS), and testosterone was assayed simultaneously in either DBS or saliva. After excluding samples with insulin >15 µIU/mL (to eliminate diabetics) or high-sensitivity C-Reactive Protein (hs-CRP) >10 mg/L (indicative of inflammatory disease not cardiometabolic risk), 228 samples were available for analysis.

Samples were categorized (in tertiles) by testosterone level: low T (<300 ng/dL in DBS or <40 pg/mL in saliva); normal T (300-800 ng/dL DBS or 40-140 pg/mL saliva); and high T (>800 ng/dL DBS or >140 pg/mL saliva). Current testosterone therapy was self-reported in 1/20, 15/174, and 24/34 of the low, normal, and high T groups respectively; mean age (SD) was 54 (9.5), 50 (11), and 49 (13) respectively.

Mean insulin was significantly higher in low T than either normal or high T men; hs- CRP was significantly higher in low T than high T men; HDL-cholesterol was significantly lower in high T than normal T men; and LDL-cholesterol was significantly higher in high T than low T men. Total cholesterol, triglycerides, and HbA1c were not significantly different between groups.

Although over-supplementing with testosterone to supraphysiological levels may affect lipids adversely, normal or high testosterone levels were associated with favorable insulin and hs-CRP. Testosterone supplementation should be monitored to ensure levels remain in a physiological range for optimum cardiometabolic risk benefits.



# Cardiometabolic Risk Factors and Testosterone Levels in Men: Implications for Testosterone Supplementation [Abstract # 65]

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#### Introduction

Testosterone supplementation is being increasingly used to help reverse symptoms of metabolic syndrome and improve cardiovascular disease risk in men. Low testosterone (T) consistently correlates with insulin resistance and obesity because of the strong inverse relationship between insulin and sex hormone binding globulin (SHBG) levels and therefore a reduction in circulating T. However data is sparse regarding the direct effects of T levels on cardiometabolic risk markers.

## Methods

Blood spots (DBS) were obtained by finger stick after an overnight fast, collected on a filter paper, allowed to dry and mailed in to the lab for analysis. The DBS assay for cardiometabolic risk markers correlates highly with simultaneous serum testing in our laboratory. Testosterone was assayed in either the same blood spot collection or in a simultaneously collected saliva sample.

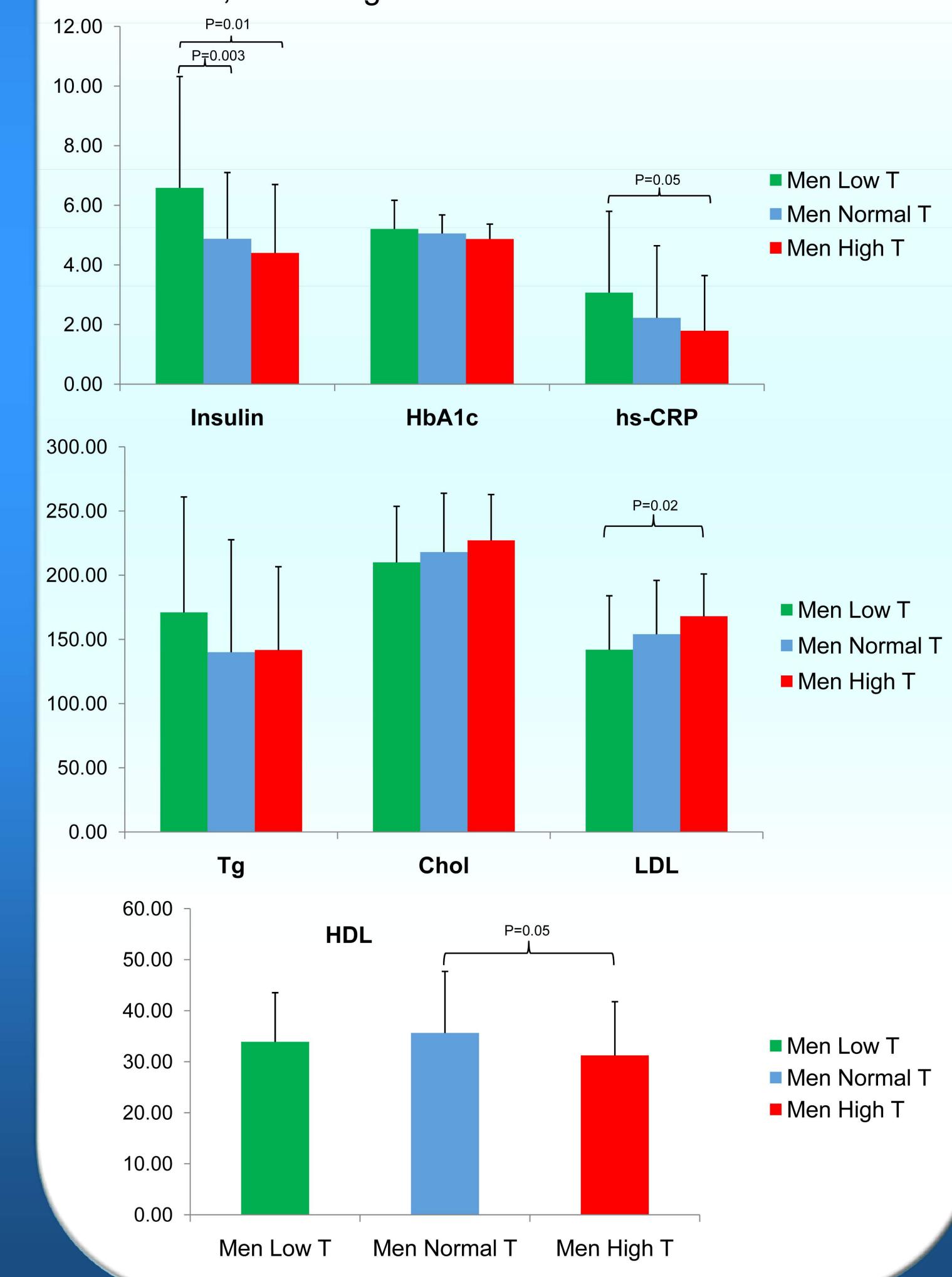
Samples with hs-CRP values >10 mg/L (an indication of acute inflammatory disease rather than cardiometabolic risk) and fasting insulin values >15 µIU/mL (probability of diabetes) were excluded, leaving a total of 228 samples for analysis.

Samples were then categorized by testosterone level as low, normal, or high, according to reference ranges established in our laboratory. The T values used to define each category, the number of samples in each group for which testosterone usage was reported, and the mean age in each group, are shown in the table below.

Category	T values	Self-reported T therapy	Age (mean ± SD)
Low T	<300 ng/dL in DBS <40 pg/mL in saliva	1/20 (5%)	54 ± 9.5
Normal T	300-800 ng/dL in DBS 40-140 pg/mL in saliva	15/174 (8.6%)	50 ± 11
High T	>800 ng/dL in DBS >140 pg/mL in saliva	24/34 (70.6%)	49 ± 13

## Results

The graphs show the mean/SD values for insulin (µIU/mL), HbA1c (%), hs-CRP (mg/L), triglycerides (mg/dL), total cholesterol (mg/dL), LDL cholesterol (mg/dL), and HDL cholesterol (mg/dL) in the low T, normal T, and high T groups. The only significant between-group differences (p<0.05) were: insulin in low T vs high T; insulin in low T vs normal T; hs-CRP in low T vs high T; HDL in high T vs normal T; LDL in high T vs low T.



#### Discussion

Our data show significantly higher fasting insulin levels in men with lower than normal T, confirming the evidence in the literature of a strong link between insulin resistance and low T. SHBG levels are known to correlate inversely with insulin resistance; recent data indicates that SHBG synthesis is suppressed by the action of monosaccharide-induced lipogenesis in hepatic cells. The reduction in SHBG reduces circulating T, which is largely bound to SHBG. However, low could indirectly affect cardiometabolic risk through reductions in muscle mass leading to reduced benefits from exercise, increased inflammation, etc. Studies have shown significant benefits of testosterone supplementation to improve parameters of metabolic syndrome, possibly attributable to increased muscle strength improving exercise and visceral fat-burning, as well as antiinflammatory effects, beneficial effects on blood vessel walls, and improved quality of life.

T supplementation has also been associated with adverse effects on blood lipids and our data confirm this, yet only at supraphysiological T levels. Our lab uses saliva or DBS testing, which better reflect tissue levels of steroid hormones administered transdermally than serum testing.

## Summary & Conclusions

Supplementing with T may improve cardiometabolic risk in men with T deficiency, but dosing to supraphysiological levels may affect blood lipids adversely. Appropriate monitoring with saliva or DBS can ensure levels remain in a physiological range for optimum cardiometabolic risk benefits.

#### References

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