
Methods | We used data from Clinformatics Data Mart (CDM), one of the nation’s largest commercial health insurance databases with more than 18,000,000 enrollees. Persons in the south and those aged 21 to 64 years are overrepresented in the data set. Separate cohorts were identified each year from 2002 through 2016, consisting of men 30 years and older with continuous enrollment during the index and prior year. For each year, we reported the percentage of men who were prescribed testosterone therapy and new testosterone users (no use in the prior year). We examined use over time with an interrupted time series analysis using joinpoint regression. Because testosterone use differs by age and region, we stratified by these factors. All analyses were performed using SAS (SAS Institute), version 9.4, and the Joinpoint Regression Program (National Cancer Institute), version 4.5.0.1. Statistical tests were 2-tailed and significant at an α level of .05. This study was approved by the University of Texas Medical Branch institutional review board, which waived informed consent.

Results | We examined the records of 9,962,538 men 30 years and older from 2002 through 2016, with a minimum of 1,823,000 men in any year. Over time, the median age increased (46 years in 2002 to 53 years in 2016) as did the percentage living in the south (39.5% in 2002 to 42.1% in 2016). Total testosterone use increased among men from 0.52% (95% CI, 0.51% to 0.53%) in 2002 to 3.20% (95% CI, 3.18% to 3.22%) in 2013, then decreased to 1.67% (95% CI, 1.66% to 1.69%) in 2016 (Figure 1). For new users, the rate increased from 0.28% (95% CI, 0.27% to 0.29%) in 2002 to 1.26% (95% CI, 1.25% to 1.28%) in 2013, then decreased to 0.48% (95% CI, 0.48% to 0.49%) in 2016. The relative decrease between 2013 and 2016 was 48% (95% CI, 47%-48%) in established users and 62% (95% CI, 61%-62%) in new users. Joinpoint analysis showed significant changes in the annual percentage change of total users per year over

Denominators were calculated for each calendar year. Each denominator included all men who were ≥30 years at the start of the calendar year with continuous benefits for the entire study year and prior year. The denominators range from 1,823,677 in 2002 to 2,856,954 in 2016. Error bars represent 95% CIs. Interrupted time series analysis with joinpoint regression was used to assess time-related trends in testosterone use. The analysis allowed for a maximum of 5 joinpoints (indicated by red arrows). For total testosterone users, joinpoints were located at 2007 (95% CI, 2005-2010) and 2013 (95% CI, 2012-2014). For new testosterone users, joinpoints were located at 2007 (95% CI, 2004-2012) and 2012 (95% CI, 2010-2014). The inset presents new testosterone prescription rates by month, from January 2013 through December 2016. Denominators for monthly rates included all men ≥30 years at the start of the month with continuous benefits for the entire month and the 12 previous months. The listed numbers indicate the following specific dates: (1) article by Vigen et al released online November 6, 2013; (2) article by Finkle et al released online January 29, 2014; (3) US Food and Drug Administration (FDA) safety communication on testosterone therapy, January 31, 2014; (4) FDA advisory committee meeting on possible cardiovascular risks associated with testosterone therapy, September 17, 2014; (5) FDA requires testosterone label change indicating possible increased risk of myocardial infarction and stroke, March 3, 2015.
time, from 0.10% (P = .007) for 2002-2007 to 0.34% (P = .001) for 2007-2013 and then −0.50% (P = .001) for 2013-2016. The inset in Figure 1 shows a 22% (95% CI, 19% to 26%) relative decrease in new testosterone users from October 2013 to December 2013, following a publication linking testosterone to cardiovascular adverse events and an additional 50% (95% CI, 47% to 53%) relative decrease over the next 8 months following a similar study and an FDA safety communication.

The decline in new testosterone users occurred in all age groups, ranging from 0.88% (95% CI, 0.84% to 0.91%) in 2013 to 0.41% (95% CI, 0.39% to 0.43%) in 2016 among men aged 30 to 39 years (relative decrease, 53% [95% CI, 51% to 56%]) to 0.86% (95% CI, 0.84% to 0.88%) in 2013 to 0.26% (95% CI, 0.25% to 0.27%) in 2016 among men 65 years and older (relative decrease, 69% [95% CI, 68% to 71%]) (Figure 2). The percentage of new testosterone users differed by region, but the relative decreases in the 4 regions were similar.

Discussion | After a decade of growth, the percentage of US men receiving testosterone prescriptions decreased from 2013 through 2016. The steepest decrease coincided with 2 published reports of testosterone-associated adverse cardiovascular events and an FDA communication.

This study has limitations. First, commercial insurance data selected for employed males; the results for men 65 years and older are not generalizable to most older men who are retired and on Medicare. Second, men may obtain testosterone from clinicians not reimbursed by their insurance. Third, indications for testosterone use could not be determined. Fourth, the demographic composition of the CDM population changed over time. Fifth, the reasons for the decrease in testosterone prescriptions cannot be determined. A recent study within the Veterans Administration system reported a 40% decrease in testosterone prescriptions from 2013 to 2016. Given the debate that has surrounded this issue, continued monitoring of testosterone prescribing trends will be important.

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Denominators were calculated for each calendar year. Each denominator included men with continuous benefits for the entire study year and prior year. Regions were based on US census regions. Error bars reflect the 95% CIs.

A, The denominators for any age category in any year ranged from 284,602 to 1,109,387.
B, The denominators for any region category in any year ranged from 11,999 to 1,106,148.
COMMENT & RESPONSE

Low-Fat vs Low-Carbohydrate Diets and Weight Loss

To the Editor In the Diet Intervention Examining The Factors Interacting with Treatment Success (DietFITS) randomized clinical trial, the investigators concluded that there was no significant difference in weight change between a healthy low-fat diet vs a healthy low-carbohydrate diet. At baseline, both groups consumed a comparable percentage of daily calories from fat: 34.8% for the low-fat group and 36.0% for the low-carbohydrate group. At the conclusion of the 12-month study period, the percentage of daily calories from fat was 28.7% in the low-fat group and 44.6% in the low-carbohydrate group. Although the percentage of daily calories from fat was reduced from 34.8% to 28.7% in the low-fat group, a diet composed of 28.7% of the daily calories from fat is a high-fat diet.

In the Lifestyle Heart Trial, participants with angiographically documented coronary artery disease were randomized to an experimental group or a control group. The experimental group was asked to eat a low-fat vegetarian diet, quit smoking, practice stress management techniques, and engage in moderate physical exercise for 12 months. The percentage of daily calories from fat decreased from 31.5% to 6.8%, and the average weight decreased from 91.1 to 81.0 kg. In the control group receiving usual care, the percentage of daily calories from fat changed minimally from 30.1% to 29.5%, and the average weight increased from 80.4 to 81.8 kg.

The DIETSFITS randomized clinical trial compared a high-fat diet with a very high-fat diet; therefore, it is not surprising that both groups showed comparable weight loss results. Is it possible that comparing a low-carbohydrate diet vs a low-fat diet in which less than 10% of the daily calories are from fat would have yielded different results?

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported authoring 2 books on plant-based nutrition; serving as a consultant to the Physicians Committee for Responsible Medicine; running a plant-based weight-loss program at Kaiser-Permanente; and offering nutrition counseling in her private practice.


To the Editor In a 12-month, behavior modification diet intervention study, Dr Gardner and colleagues compared the effects of a healthy low-fat diet with a healthy low-carbohydrate diet on weight loss among 609 overweight adults. The authors did not find a significant difference in weight loss between the 2 diet intervention groups, in line with results from several previous studies. Different from traditional diet intervention trials, 1 of the primary aims of the DIETSFITS study was to test diet × genotype pattern interactions on weight loss in response to the diet intervention. The authors did not observe significant diet × genotype pattern interactions and concluded that there was no significant difference in genotype pattern associated with the dietary effects on weight loss.

Even though the rationale to test diet × genotype pattern interaction on weight loss in response to interventions was sound, the strategy in the selection and analysis of the genetic