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Association Between Direct-to-Consumer Advertising and Testosterone Testing and Initiation in the United States, 2009–2013

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Abstract

IMPORTANCE—Testosterone initiation increased substantially in the United States from 2000 to 2013, especially among men without clear indications. Direct-to-consumer advertising (DTCA) also increased during this time.

OBJECTIVE—To investigate associations between televised DTCA and testosterone testing and initiation in the United States.

DESIGN, SETTING, AND POPULATION—Ecologic study conducted in designated market areas (DMAs) in the United States. Monthly testosterone advertising ratings were linked to DMA-

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level testosterone use data from 2009–2013 derived from commercial insurance claims. Associations between DTCA and testosterone testing, initiation, and initiation without recent baseline tests were estimated using Poisson generalized estimating equations.

EXPOSURES—Monthly Nielsen ratings for testosterone DTCA in the 75 largest DMAs.

MAIN OUTCOMES AND MEASURES—(1) Rates of new serum testosterone testing; (2) rates of testosterone initiation (in-office injection, surgical implant, or pharmacy dispensing) for all testosterone products combined and for specific brands; and (3) rates of testosterone initiation without recent serum testosterone testing.

RESULTS—Of 17 228 599 commercially insured men in the 75 DMAs, 1 007 990 (mean age, 49.6 [SD, 11.5] years) had new serum testosterone tests and 283 317 (mean age, 51.8 [SD, 11.3] years) initiated testosterone treatment. Advertising intensity varied by geographic region and time, with the highest intensity seen in the southeastern United States and with months ranging from no ad exposures to a mean of 13.6 exposures per household. Nonbranded advertisements were common prior to 2012, with branded advertisements becoming more common during and after 2012. Each household advertisement exposure was associated with a monthly increase in rates of new testosterone testing (rate ratio [RR], 1.006; 95% CI, 1.004–1.008), initiation (RR, 1.007; 95% CI, 1.004–1.010), and initiation without a recent test (RR, 1.008; 95% CI, 1.002–1.013). Mean absolute rate increases were 0.14 tests (95% CI, 0.09–0.19), 0.05 new initiations (95% CI, 0.03–0.08), and 0.02 initiations without a recent test (95% CI, 0.01–0.03) per 10 000 men for each monthly ad exposure over the entire period.

CONCLUSIONS AND RELEVANCE—Among US men residing in the 75 designated market areas, regional exposure to televised direct-to-consumer advertising was associated with greater testosterone testing, new initiation, and initiation without recent testing.

The US Food and Drug Administration (FDA) permitted televised direct-to-consumer advertising (DTCA) for prescription medications in 1997. An argument for DTCA is that it may steer consumers to beneficial treatments for high-priority illnesses,[1] but it may also contribute to escalating drug prices and reduced patient safety.[2] A growing evidence base illustrates strong associations between televised DTCA and increased product prescribing for a variety of indications,[3–5] and the American Medical Association called for a ban on such marketing in 2015, attempting to reduce prescription costs and curb consumer demand for new, expensive, and potentially inappropriate treatments.[6]

Increased awareness of and demand for a medication may be beneficial if the risk-benefit ratio of the drug is favorable. For many men taking testosterone, that assumption is questionable. Testosterone therapies were originally approved to treat hypogonadism resulting from the disruption of the pituitary-hypothalamus-gonadal axis. Now many men take or are prescribed testosterone for age-related reduced testosterone levels or nonspecific symptoms without pathological hypogonadism. Despite considerable disagreement about the necessity and safety of treatment for these findings and symptoms, testosterone prescribing has increased substantially in the absence of proven new indications,[7–9] particularly in the United States, where the testosterone initiation rate rose from 20.2 to 75.7 per 10000 person-years from 2000 to 2011.[8]

Although studies have yielded conflicting information on the risks and benefits of testosterone,[10–13] termination of a clinical trial because of excess adverse cardiovascular effects[14] and observational studies suggesting increased cardiovascular risk[11,15] led the FDA to reevaluate the risks and revise product labeling requirements in 2014, and pharmaceutical manufacturers, who had previously heavily marketed testosterone products through televised branded, product-specific promotions and unbranded, "low T" awareness advertisements, voluntarily discontinued televised DTCA for testosterone products.

Given the controversies surrounding DTCA and testosterone, we examined the association between exposure to DTCA for testosterone and testosterone testing, initiation, and initiation without a preceding testosterone test.

Methods

This project was approved by the institutional review board of the University of North Carolina at Chapel Hill. Individual consent was not required for this analysis of deidentified data.

Data Sources

Direct-to-Consumer Advertising—We licensed monthly television ratings data from Nielsen Media Research for televised testosterone advertisements in the largest 75 of 210 US designated market areas (DMAs), which are whole, adjoining counties centered around large cities whose populations receive similar television programming. We collected ratings between 2008 and 2013 for both brand-specific prescription testosterone advertisements, which are regulated by the FDA, and nonbranded, condition awareness ("low T") ads, which are not FDA regulated; we measured DTCA using gross ratings points, a standard metric for quantifying advertising exposure reflecting the percentage of the target audience reached multiplied by frequency of exposures as measured by a combination of electronic metering and surveying across broadcast platforms.[16,17] We summed gross ratings points within the same DMA and month for all testosterone advertisements and for branded testosterone advertisements and condition awareness ads separately, and divided by 100 to obtain the mean number of times testosterone advertisements were viewed in television households in a given month; an ad with 100 gross ratings points per month can be interpreted as being seen 1 time per month by 100% of the audience, and each 1-unit increase in monthly exposures represented approximately 1 additional viewing of a television ad per household.[16,18]

Key Points

Question

Is there an association between televised direct-to-consumer testosterone advertising and testosterone testing and initiation in the United States?

Findings

In this ecological study of 75 US designated market areas, each exposure to a testosterone advertisement was associated with monthly relative increases in rates of new testosterone

testing of 0.6%, new initiation of 0.7%, and initiation without a recent baseline test of 0.8%.

Meaning

Regional exposure to televised direct-to-consumer advertising was associated with greater testosterone testing, new initiation, and initiation without recent serum testosterone tests.

Testosterone Testing and Initiation—We used the MarketScan Commercial Claims and Encounters databases (Truven Health Analytics) to quantify population level testosterone testing and initiation (in-office injection, surgical implant, or pharmacy dispensing) within DMAs. The MarketScan databases include individual-level clinical diagnoses, procedures, outpatient prescription dispensing (including from retail, mail-order, and specialty pharmacies), expenditures, and enrollment data paid for by employer sponsored, fee-for-service, fully capitated or partially capitated plans. Claims from employees and their dependents and those with employer-based Medicare supplemental plans also are included. Claims are fully paid and adjudicated, and the research databases are constructed after sufficient time has elapsed to allow for submission, payment, and recording of all outstanding claims. Considerable standardization and quality control activities occur during database construction.[19]

We identified men aged 18 years or older residing within defined metropolitan statistical areas (MSAs); 1 or more MSAs make up a DMA. Geographic information was not available for those residing outside MSAs or in smaller micropolitan statistical areas, so our sample focused on those in more urban population centers. Using procedure codes from submitted insurance claims, we identified men newly tested for serum testosterone levels following 6 months without testosterone receipt or testing. Initiation of testosterone gels, patches, injections, or implants was defined as pharmacy dispensing or in-office receipt identified through procedure codes of testosterone following 6 months without prior testosterone receipt. Our main analysis identified initiators of all testosterone products, while subanalyses focused on initiators of individual advertised, branded products (AndroGel [Abbvie Inc] and Axiron [Eli Lilly Inc]). The denominator for monthly rate calculations was the number of adult men enrolled in the MarketScan databases within each MSA on the 15th of each month with at least 6 months of prior continuous enrollment.

We collapsed MSA-level information into DMA levels and linked the data with advertising information.

DMA Characteristics—We collected county-level characteristics and aggregated them into DMAs to account for differences in population demographics, access to health care (measured by physician density), and socioeconomic status (median income). We derived county-level 5-year estimates of age and race/ethnicity distributions from the 2009–2013 American Community Survey, an ongoing yearly survey of US households conducted by the US Census Bureau; race/ethnicity designation was self-reported by choosing from fixed, standard categories. We derived annual estimates of county-level physician density and

median income from the Health Resources and Services Administration's Area Resource File.

Statistical Analysis

We examined the overall pattern of testosterone testing and initiation between 2009 and 2013. We estimated monthly rates of testing and initiation per 10000 menin each DMA and plotted national mean rates with their interquartile ranges. We assessed geographic variation by summing all advertising exposures throughout the study period within DMAs and divided these cumulative measures into 7 approximately equal strata using an equal-distribution (quantizing) algorithm to visualize regional variation in total DTCA; these DTCA levels were mapped across the United States by year to observe changes in geographic variation over time.

We describe the association between DTCA and testosterone testing and initiation using adjusted rate ratios (RRs) and 95% confidence intervals derived from multivariable Poisson models with generalized estimating equations[20] to account for clustering within DMAs over time; we used an autoregressive (AR-1) correlation structure. Direct-to-consumer advertising exposures were included as a continuous variable; thus, the resulting RRs indicate the association between a 1-unit increase in ad exposures and testosterone rates. Monthly advertising data (November 2008 to October 2013) were linked to monthly testosterone data 2 months in the future, allowing for the passage of time between viewing an ad, seeking care, and receiving treatment. To observe the effect of varied lag times, we performed a preplanned sensitivity analyses evaluating a 1-month lag and a post hoc analysis of a 3-month lag.

We adjusted the models for age (proportion of population in age groups of 35–44, 45–54, 55–64, 65–74, and ≥75 years, included in model as 5 variables), race (proportion of white and black population, included in model as 2 variables), physician density, socioeconomic status (included in model as a quadratic trend of median income because increases in income may be more meaningful for medication use at lower income values), seasonality (modeled with 4 variables, 1 for each season, each taking a 0 or 1 value), and overall increasing usage time trend[8] to facilitate estimation of the increases in testosterone testing and initiation within a DMA not due to expected seasonal variation or overall national trends. We modeled time trends with cubic splines to allow for flexibility at nodes corresponding to key events: FDA warning of testosterone gel transfer from men to women and children[21] (May 2009); release and approval of new testosterone gel formulations[22,23] (April 2011); and National Institutes of Health funding of observational studies of the cardiovascular safety of testosterone products[24] (August 2012).

Our primary exposure variable was total monthly testosterone advertising exposures, but we additionally investigated individual branded advertisements and unbranded condition awareness advertisements from 2012 to 2013; prior to 2012, there were primarily only unbranded "low T" condition awareness advertisements. We estimated the association of advertising with(1) new serum testosterone tests; (2) all new testosterone initiations, including branded and unbranded patch, gel, injection, and implanted formulations; (3) initiation without a recent test; and(4) product-specific initiation of branded testosterone

gels. Model-based predicted rates were plotted against observed testosterone rates to evaluate model fit. As post hoc sensitivity analyses we investigated the associations in each year alone because there was substantial variation in advertising intensity by year and more diverse advertising, greater competition, and plateaued overall use during later years, and we explored nonlinear relationships by modeling DTCA with both a linear and a quadratic term.

We compared RR estimates from different periods and sensitivity analyses using ratios of RRs.[25] We considered a 2-sided threshold of $P<.05$ to be statistically significant. All analyses were conducted using SAS software, version 9.4 (SAS Institute Inc).

Results

Of 17 228 599 unique men across the 75 DMAs (mean age, 42.8 [SD, 16.0] years), 1 007 990 (mean age, 49.6 [SD, 11.5] years) had new serum testosterone tests and 283 317 (mean age, 51.8 [SD, 11.3] years) initiated testosterone treatment during the study period (59% initiated testosterone gels, 36% injections, 3% patches, and 2% implants). Baseline DMA characteristics (Table 1)and testosterone use varied widely, with DMA level testing rates ranging from 2.7 (95% CI, 0.7–7.3) to 30.5 (95% CI, 26.0–35.7) per 10000 men and initiation rates ranging from 0.6 (95% CI, 0.1–1.9) to 23.2 (95% CI, 5.9–63.0) per 10000 men (Table 1; see eTable 1 in the Supplement for DMA-level characteristics by year).

Descriptive Trends of Testosterone Testing and Initiation

Monthly testosterone testing and initiation increased between 2009 and 2012 prior to decreasing through 2013 (Figure 1, A and B); initiation without a recent baseline test decreased slightly but consistently over the period. After introduction of Axiron in 2011, Androgel initiation rates increased and then decreased in 2012–2013 (Figure 1C). Mean monthly rates per 10000 men were 24.6 (SD, 9.5) for testosterone testing, 7.6 (SD, 3.8) for testosterone initiation, and 2.4 (SD, 1.5) for testosterone initiation without prior testing.

Descriptive Trends of Testosterone DTCA

Direct-to-consumer advertising exposure increased over the period with substantial variation, ranging from months without any advertising to a mean 13.6 (SD, 0.8) monthly household exposures in December 2012 (Figure 2A). Prior to 2012, Abbvie-funded, unbranded “low T” advertisements were the primary form of advertising. Following the introduction of Axiron and a more concentrated Androgel formulation in 2011, more branded, product-specific advertising emerged and unbranded condition awareness advertisements decreased (Figure 2B).

Television advertising intensity varied by DMA region, with cumulative exposures ranging from 154.9 to 203.5 advertisement exposures per DMA over the study period (mean, 179.1; SD, 10.0). The most concentrated advertising occurred in the Southeast and the southern Great Lakes regions (Figure 3), a geographic focus consistent through most of the study period (eFigure 1 in the Supplement).

Association of DTCA and Testosterone Testing and Initiation

Increases in advertisement exposure were associated with higher rates of testosterone testing, initiation, and initiation without testing (Table 2), except Axiron initiation, which was introduced later in the period and had lower overall use (Table 2; see eTable 2 and eFigure 2 in the Supplement for model goodness-of-fit estimates). Each additional ad exposure was associated with a relative 0.6%(95% CI, 0.4%–0.8%) increase in testing, 0.7%(95% CI, 0.4%–0.10%) increase in initiation, and 0.8%(95% CI, 0.2%–0.13%) increase in initiation of testosterone without baseline testing, corresponding to absolute monthly increases of 0.14 new tests (95% CI, 0.09–0.19), 0.05 initiations (95% CI, 0.03–0.08), and 0.02 initiations without baseline testing (95% CI, 0.01–0.03) per 10 000 men across the study period.

Prior to 2012, advertising—almost all of which was unbranded “low T” advertising—was associated with testosterone testing (RR, 1.012; 95% CI, 1.009–1.014) and initiation (RR, 1.012; 95% CI, 1.007–1.017); after 2012, the advertising was primarily branded, but associations with testing (RR, 0.998; 95% CI, 0.995–1.001) or initiation (RR, 0.998; 95% CI, 0.994–1.003)were no longer statistically significant (ratios of RRs in 2012–2013 vs 2009–2011, 0.986 [95% CI, 0.982–0.990]; $P < .001$ for testing and 0.986 [95% CI, 0.980–0.993]; $P < .001$ for initiation, suggesting a statistically significant difference in association between the periods). Androgel was the most widely used branded product during the entire study period and the most widely advertised branded product after 2012; its advertising was associated with increased rates of testing and initiation across all domains (Table 2). However, other advertising types showed a more attenuated or no association in 2012 and 2013.

When exploring nonlinear relationships between DTCA and testosterone by modeling with a quadratic term, we observed a “saturation effect” wherein the association between a 1-unit increase in DTCA exposure and testosterone became weaker at higher levels of DTCA (eTable 4 in the Supplement). For example, when a DMA’s monthly exposure increased from 1 to 2, the association between the increase in DTCA with new testing was an RR of 1.015 (95% CI, 1.012–1.019); from 5 to 6, an RR of 1.012 (95% CI, 1.009–1.014); and from 10 to 11, an RR of 1.007 (95% CI, 1.005–1.009).

There were no statistically significant associations between DTCA and testosterone testing and initiation in sensitivity analyses testing 1- and 3-month lag periods (eTable 5 in the Supplement).

Discussion

Increasing televised DTCA for testosterone therapies was observed across US metropolitan areas between 2009 and 2013, and both branded and condition awareness ads were associated with increased testosterone testing and initiation. Although the average increase in testosterone rates associated with a single ad exposure was less than 1%, advertisements were widespread and frequent during the study period; with cumulative ad exposures of close to 200 in some DMAs, DTCA was associated with substantial overall increases in testosterone testing and initiation.

These associations were strongest when only a single brand was being advertised, and there may have been a saturation effect, as DTCA was more prevalent during 2012 and 2013 than earlier periods, yet with increasing safety concerns, introduction of new formulations, and competing advertising campaigns, testosterone use decreased somewhat and the associations of DTCA with testing or initiation became attenuated (eTable 3 and eTable 4 in the Supplement). Additionally, DTCA was associated with more initiation of test osterone without recent serum testing, contrary to treatment guidelines.[26]

These findings illustrate the association between mass marketing efforts and demand for a prescription drug in a context in which it has been widely overused.[7,8] Ultimately, prescribing decisions rest with physicians, but patient preferences and requests for specific medications influence prescribing decisions,[27–29] and DTCA may be associated with increased patient demand. While other studies have demonstrated associations between DTCA and increasing medication use, this study demonstrates increases in potentially inappropriate use and increasing initiation during a time when most testosterone use was of questionable value for age-related testosterone decreases without strong evidence of benefit. Characterizing the role of DTCA in promoting testosterone initiation among a large segment of middle-aged and older men for nonspecific symptoms and age-related declines in testosterone levels is relevant to ongoing policy debates regarding DTCA. This study complements many others that suggest the contribution that DTCA may make in the early adoption of recently approved treatments whose risk-benefit profile may be quite unclear.[2]

Furthermore, concerns remain regarding the safety and benefit of using testosterone to treat age-related declines in testosterone levels. Original FDA approval of testosterone formulations was based on trials demonstrating increased testosterone blood levels among men with specific disorders of the testes or pituitary, not amelioration of any clinical symptoms.[30] A recent study on the benefits of raising testosterone levels among older men with low testosterone but without pathological hypogonadism found moderate improvements in sexual function and mood but no benefit in vitality or walking distance[31]; this may reignite the cost-benefit discussion, yet the trials were too small to evaluate safety, and they offer little support for widespread use of testosterone outside the narrow approved indications. Although the current study lacks individual-level information on patients' indications for treatment, much of the increase in testosterone use in the United States has been among men being treated for age related decreases in testosterone or nonspecific symptoms.[8]

This study has limitations. As an ecologic study, it lacks information on individual-level DTCA exposures. Some individuals residing near DMA boundaries may view televised ads outside their assigned DMA. For pharmacy-dispensed products, the study assessed receipt from the pharmacy, not actual use by patients. Although there were no explicitly missing data from any data source, the findings may under estimate true testosterone testing and initiation if tests or prescriptions were not submitted to insurers for reimbursement. Additionally, the Market Scan data bases contain information only on those with employer-sponsored health insurance in the United States; these results may not be generalizable to men covered by public insurance plans or uninsured men. This analysis was limited to investigating geographic variation in televised pharmaceutical advertising; there may be

additional forms of influential promotion, such as physician-targeted promotion, internet advertising (including branded ads and unbranded disease awareness symptom quizzes), or advertisements by men's health specialty clinics, thus potentially over attributing some testosterone use to televised DTCA. While televised DTCA is the most common and influential type of direct-to-consumer advertising medium,[32,33] internet advertising was also widespread throughout most of the study period, although it likely lacks the geographic variation of televised DTCA. However, televised DTCA was consistently associated with multiple dimensions of testosterone use. Finally, the statistically significant associations between DTCA and testosterone testing and initiation we report at 2 months were not apparent in sensitivity analyses testing of 1- and 3-month lag periods; the reasons for the dependence of the association on the 2-month lag period are not knowable from our data.

Conclusions

Among US men residing in 75 US DMAs, regional exposure to televised DTCA was associated with greater testosterone testing, new initiation, and initiation without recent testing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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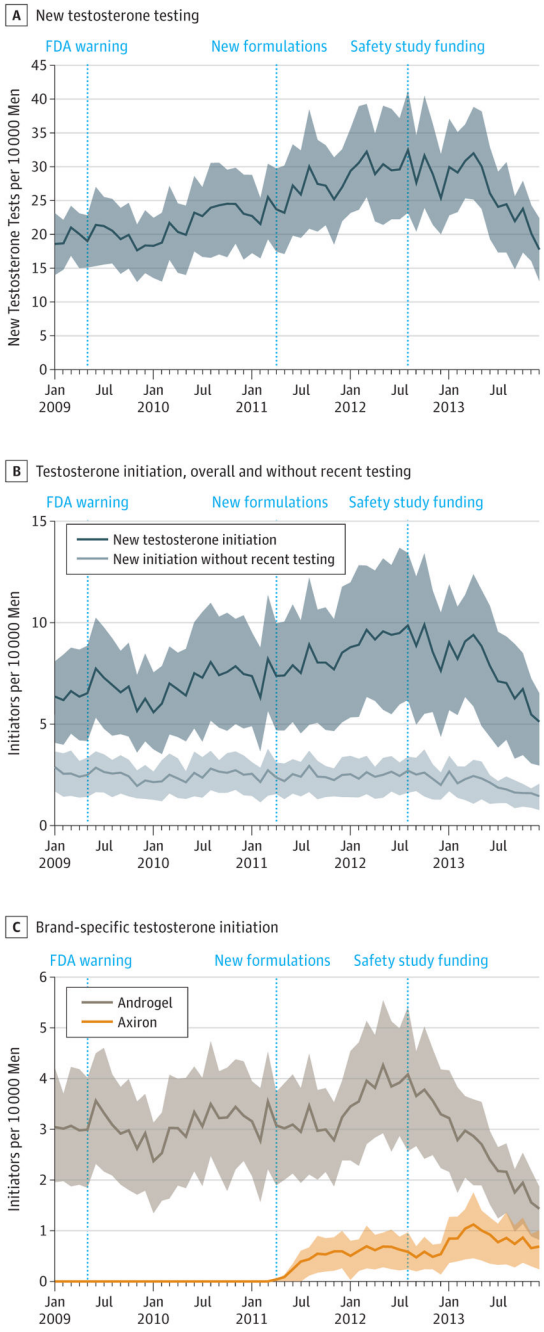

Figure 1.

Mean Testosterone Testing and Initiation Rates Among Adult Men in the 75 Largest Designated Market Areas in the United States, January 2009–December 2013

Shaded areas are interquartile ranges. Vertical dotted lines in all panels indicate 3 key events that may be associated with overall use: (1) May 2009, US Food and Drug Administration warning of transfer of testosterone gel from men to women and children; (2) April 2011, release of new testosterone gel formulations; and (3) August 2012, increased concern about

cardiovascular safety of testosterone products as evidenced by the National Institutes of Health funding safety studies of testosterone in older men.

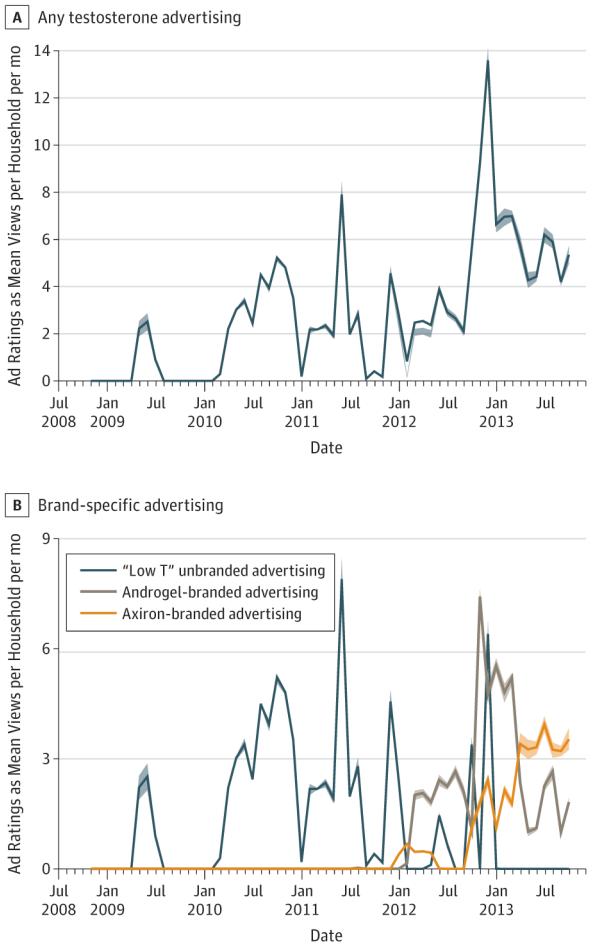

Figure 2.

Mean Household Testosterone Advertisement Exposures From Nielsen Television Ratings Across the 75 Largest Designated Market Areas in the United States, November 2008–October 2013

Shaded areas are interquartile ranges.

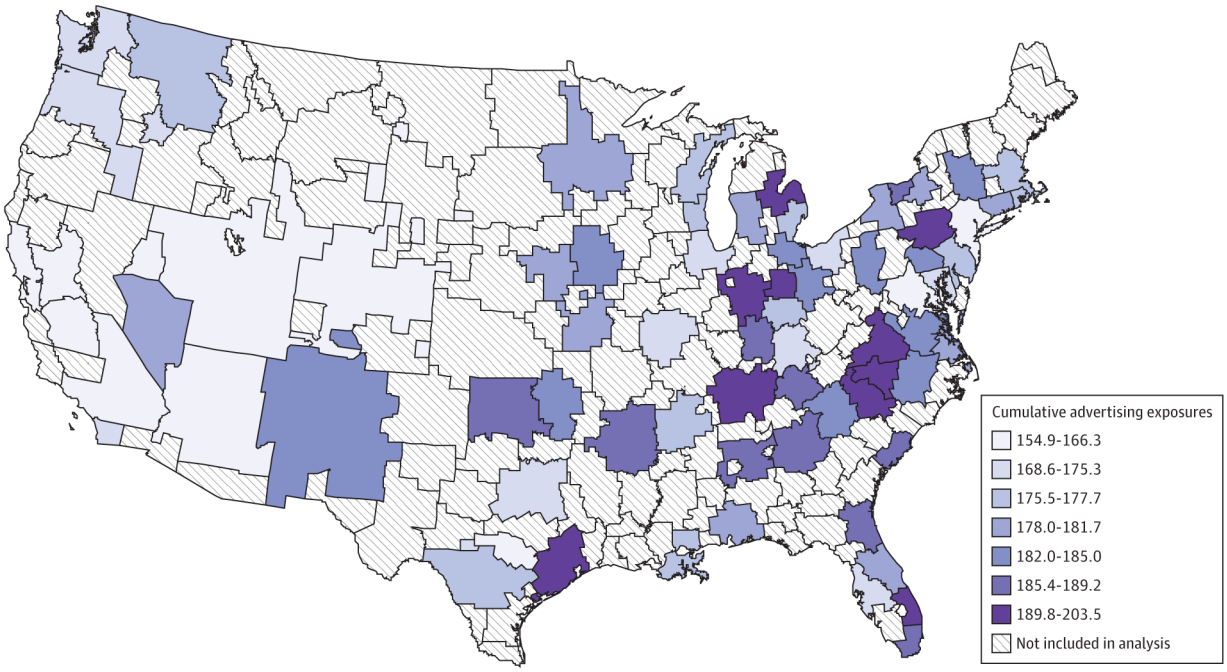

Figure 3.

Geographic Distribution of Cumulative Testosterone Advertisement Exposures From Nielsen Television Ratings (Total Summed Ratings, November 2008–October 2013) in the 75 Largest US DMAs

Monthly advertisement exposures were summed across the entire study period within designated market areas (DMAs), and DMAs were stratified into 7 strata of cumulative advertising exposures containing approximately equal numbers of DMAs. The borders between exposure strata were defined empirically; thus, there are gaps between strata where no DMA had measures in that range.

Table 1

Characteristics of 75 DMAs, January 2009

DMA Characteristics	Estimate
Enrolles per DMA, median (IQR)[a]	45 501 (23 311–74 815)
Age, mean (SD) % in category, y[b]	
35–39	6.30 (0.51)
40–44	6.71 (0.41)
45–49	7.13 (0.39)
50–54	7.26 (0.44)
55–59	6.46 (0.48)
60–64	5.58 (0.53)
65–69	4.14 (0.55)
70–74	3.11 (0.51)
≥75	6.21 (1.30)
Race, mean (SD) % in category[b]	
White	77.2 (11.6)
Black	12.2 (8.7)
Physician density/10 000 men, mean (SD)[c]	22.7 (5.1)
Mean (SD) of median household income, $[c]	45 757 (8401)

Abbreviations: DMA, designated market area; IQR, interquartile range.

[a]Data on adult male enrollees are from Truven Health Analytics MarketScan databases, defined as adult men enrolled in the MarketScan database residing in the DMA on the 15th of the month with 6 months of previous enrollment.

[b]Data on age and race distributions are from the US Census American Communities Survey.

[c]Data on income and physician density are from the Health Resources and Services Administration's Area Resource File.

Table 2

Association of Monthly Testosterone Direct-to-Consumer Advertising With Testosterone Testing and Initiation Among US Men Living in the 75 Largest Designated Market Areas[a]

Testosterone Measure	Years	Base Testosterone Rate Per 10 000 Men, Mean (SD)[b]	Advertising Type	Association of 1-Unit Increase in Advertising Exposures With Testosterone Testing or Initiation, Rate Ratio (95% CI)
Testing	2009–2013	18.6 (6.2)	Total, any ads	1.006 (1.004–1.008)
	2009–2011	18.6 (6.2)	Total, any ads[c]	1.012 (1.009–1.014)
	2012–2013	29.4 (9.4)	Total, any ads	0.998 (0.995–1.001)
	2012–2013	29.4 (9.4)	“Low T” disease awareness	1.046 (1.038–1.054)
	2012–2013	29.4 (9.4)	Androgel, branded	1.001 (0.997–1.006)
	2012–2013	29.4 (9.4)	Axiron, branded[d]	0.995 (0.983–1.007)
Initiation	2009–2013	6.4 (3.4)	Total, any ads	1.007 (1.004–1.010)
	2009–2011	6.4 (3.4)	Total, any ads[c]	1.012 (1.007–1.017)
	2012–2013	8.8 (4.3)	Total, any ads	0.998 (0.994–1.003)
	2012–2013	8.8 (4.3)	“Low T” disease awareness	1.055 (1.043–1.066)
	2012–2013	8.8 (4.3)	Androgel, branded	1.001 (0.996–1.007)
	2012–2013	8.8 (4.3)	Axiron, branded[d]	0.999 (0.985–1.012)
Initiation without testing	2009–2013	2.9 (2.7)	Total, any ads	1.008 (1.002–1.013)
	2009–2011	2.9 (2.7)	Total, any ads[c]	1.013 (1.004–1.022)
	2012–2013	2.5 (1.5)	Total, any ads	0.995 (0.986–1.004)
	2012–2013	2.5 (1.5)	“Low T” disease awareness	1.055 (1.035–1.076)
	2012–2013	2.5 (1.5)	Androgel, branded	0.996 (0.987–1.006)
	2012–2013	2.5 (1.5)	Axiron, branded[d]	1.006 (0.989–1.024)
Androgel initiation	2009–2013	3.0 (1.4)	Total, any ads	1.008 (1.003–1.013)
	2009–2011	3.0 (1.4)	Total, any ads[c]	1.017 (1.009–1.025)
	2012–2013	3.5 (1.6)	Total, any ads	0.995 (0.989–1.001)
	2012–2013	3.5 (1.6)	“Low T” disease awareness	1.034 (1.017–1.052)
	2012–2013	3.5 (1.6)	Androgel, branded	1.001 (0.994–1.008)
	2012–2013	3.5 (1.6)	Axiron, branded[d]	0.977 (0.962–0.992)
Axiron initiation	2009–2013	0.0 (0.0)	Total, any ads	0.998 (0.992–1.004)
	2012–2013	0.5 (0.5)	Total, any ads	1.011 (0.994–1.027)
	2012–2013	0.5 (0.5)	“Low T” disease awareness	1.074 (1.046–1.103)
	2012–2013	0.5 (0.5)	Androgel, branded	1.004 (0.987–1.022)
	2012–2013	0.5 (0.5)	Axiron, branded[d]	1.035 (0.964–1.111)

[a]Source: Truven Health Analytics MarketScan databases, Nielsen television ratings, 2009–2013. The rate ratio and 95% confidence interval (95% CI) of mean rates was derived from rate ratio estimates from Poisson generalized estimating equation regression adjusting for income, race/ethnicity, age, physician density, overall time trend, and seasonality. Testosterone ad exposures was included as a continuous variable, and the rate ratios estimate the association between a 1-unit increase in ad exposure and the testosterone rate; for example, across the entire study period, 1 exposure to a testosterone advertisement was associated with a 0.7% higher subsequent initiation rate (rate ratio, 1.007; 95% CI, 1.004–1.010),

corresponding to a mean absolute increase of 0.05 initiations (95% CI, 0.03–0.07) per 10 000 men per ad. However, the mean number of ad exposures per month was 2.9 (SD, 2.8), which was associated with a 2.0% higher subsequent initiation rate (rate ratio, 1.020; 95% CI, 1.011–1.029) and a mean absolute increase of 0.15 initiations (95% CI, 0.09–0.22) per 10 000 men.

[b] Rate during the first month of the considered period.

[c] Prior to 2012, almost all recorded advertisements were unbranded disease awareness ads.

[d] Models restricted to the months following the beginning of Axiron-branded advertising (December 2011).