

# FDA Safety Warnings and Trends in Testosterone Marketing to Physicians

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In response to study findings showing the risk of cardiovascular adverse events associated with testosterone therapy, the FDA issued safety warnings in 2014 and modified testosterone labeling in March 2015 to indicate the increased risk of stroke and heart attack.<sup>1</sup> It is unknown whether testosterone marketing practices by pharmaceutical companies changed after the label warning. Both primary care physicians (PCPs) and non-PCPs prescribe testosterone and are targeted by pharmaceutical marketing representatives to encourage prescribing. Likewise, such marketing occurs in both urban and rural areas. Our study is the first to examine testosterone marketing practices around the time of the label warning by physician specialty and rural vs urban primary care service area (PCSA).

## METHODS

We identified physicians who received testosterone marketing spending from the CMS Open Payment Database between August 2013 and December 2017 and constructed 3 outcome measures for testosterone marketing for each physician–quarter-year observation: number of marketing encounters, marketing spending per encounter, and total marketing spending per physician.

We estimated linear regressions for each of the outcome variables, adjusting for indicators of quarter-year, physician Census region, physician location in a rural PCSA (vs urban), and physician specialty (PCP or not). To examine whether the marketing outcome variables were different by PCPs vs non-PCPs in any given quarter-year, we also included interactions of the PCP indicator with each quarter-year. In separate models, to examine differential adjusted outcomes by physician rural/urban status, we included interactions of the physician rural location indicator with each quarter-year. We then presented adjusted outcome variables by physician specialty and rural/urban status with CI bands over each quarter in the study period.

## RESULTS

The open payment sample contained 54,365 unique physicians, of whom 38.97% were PCPs and 90.32% were located in urban

## ABSTRACT

In response to study findings showing the risk of cardiovascular adverse events associated with testosterone therapy, the FDA issued safety warnings in 2014 and modified testosterone labeling in March 2015 to indicate the increased risk of stroke and heart attack. It is unknown whether there were changes in testosterone marketing practices by pharmaceutical companies following the FDA label warning. Both primary care physicians (PCPs) and non-PCPs prescribe testosterone and are targeted by pharmaceutical marketing representatives to encourage testosterone prescribing. Likewise, pharmaceutical marketing occurs in both urban and rural areas. Our study is the first to examine testosterone marketing practices around the period of the testosterone label warning by physician specialty and rural vs urban primary care service area.

In this study, we found that testosterone marketing efforts such as marketing spending per encounter, quarterly marketing spending per physician, and quarterly number of encounters per physician increased among non-PCPs and urban physicians for 4 quarters following an FDA boxed warning in 2015 on testosterone prescriptions. After the black box warning, off-label testosterone advertisements stopped. This reduction in advertising could have made it more attractive for pharmaceutical companies to increase their marketing spending targeting non-PCPs and physicians in urban areas. Understanding responses of pharmaceutical companies to FDA guidelines is important and can help inform future guideline initiatives.

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PCsAs. By Census region, 43.03% were from the South; 19.44%, Midwest; 18.95%, Northeast; and 18.58%, West.

Throughout the study period, non-PCPs received more marketing encounters per physician than PCPs, as did urban physicians compared with rural physicians (eAppendix Figures 1 and 2 [eAppendix available at [ajmc.com](http://ajmc.com)]). For non-PCPs and urban physicians, all marketing outcome variables increased following the FDA warning in quarter 1 of 2015 and stayed higher for an additional 3 quarters before returning to levels similar to those prior to the FDA warning (Figure and eAppendix Figures 1-5). For example, in quarter 1 of 2015—the quarter of the FDA warning—total marketing spending per non-PCP was \$278.26 more than per PCP (95% CI, \$240.88–\$315.65;  $P < .001$ ) (Figure), marketing spending per encounter was \$40.36 more than per PCP (95% CI, \$29.41–\$51.30;  $P < .001$ ) (eAppendix Figure 3), and number of encounters per non-PCP was 0.15 more than per PCP (95% CI, 0.08–0.22;  $P < .001$ ) (eAppendix Figure 1). For periods outside the immediate 4 quarters following the FDA label warning, total marketing spending per physician and spending per encounter for non-PCPs were not significantly different from those for PCPs (Figure and eAppendix Figure 1).

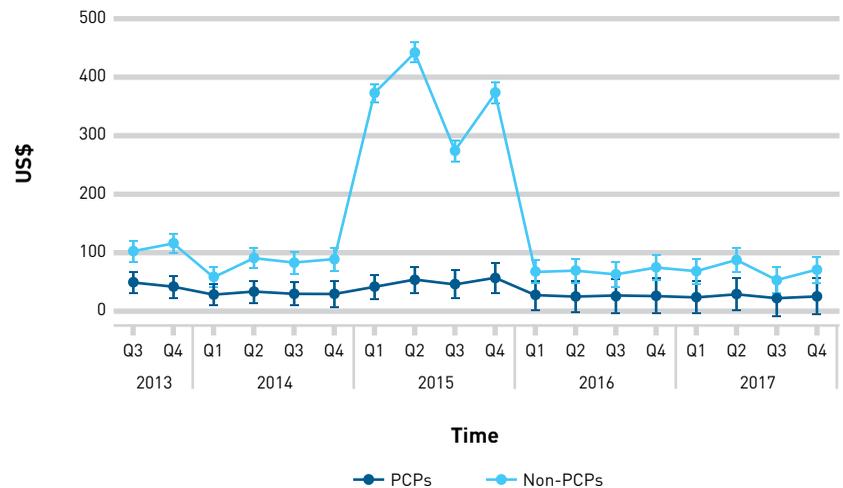
## DISCUSSION

Pharmaceutical companies spend money on marketing to influence and increase physician drug prescriptions and boost sales.<sup>2</sup> In this study, we found that testosterone marketing efforts such as marketing spending per encounter, quarterly marketing spending per physician, and quarterly number of encounters per physician increased among non-PCPs and urban physicians for 4 quarters following an FDA boxed warning in 2015 on testosterone prescriptions. After the black box warning, off-label testosterone advertisements stopped.<sup>3</sup> This reduction in advertising could have made it more attractive for pharmaceutical companies to increase their marketing spending<sup>4</sup> targeting non-PCPs and physicians in urban areas. Other studies' findings have showed that non-PCPs prescribe testosterone more than PCPs<sup>5</sup> and that men in urban areas are more likely to choose testosterone replacement therapy than their counterparts in rural areas,<sup>6</sup> making non-PCPs and urban areas a more suitable target for pharmaceutical marketing. ■

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**FIGURE.** Total Quarterly Testosterone Marketing Spending per Physician by Physician Specialty, Adjusted Predictive Margins With 95% CIs<sup>a</sup>



PCP, primary care physician; Q, quarter.

<sup>a</sup>Trends adjusted for physician type (PCP vs non-PCP), physician Census region, and physician location in urban or rural primary care service areas. Quarters are interacted with physician type and 95% CI bars for the adjusted trends are shown extending from each data point.

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**Authorship Information:** Concept and design (AT, AS, PK-M); acquisition of data (PK-M); analysis and interpretation of data (AT, AS, PK-M); drafting of the manuscript (AT, AS, PK-M); critical revision of the manuscript for important intellectual content (AT, AS, PK-M); statistical analysis (AT, AS, PK-M); provision of patients or study materials (AT, AS); obtaining funding (PK-M); and supervision (AT, AS, PK-M).

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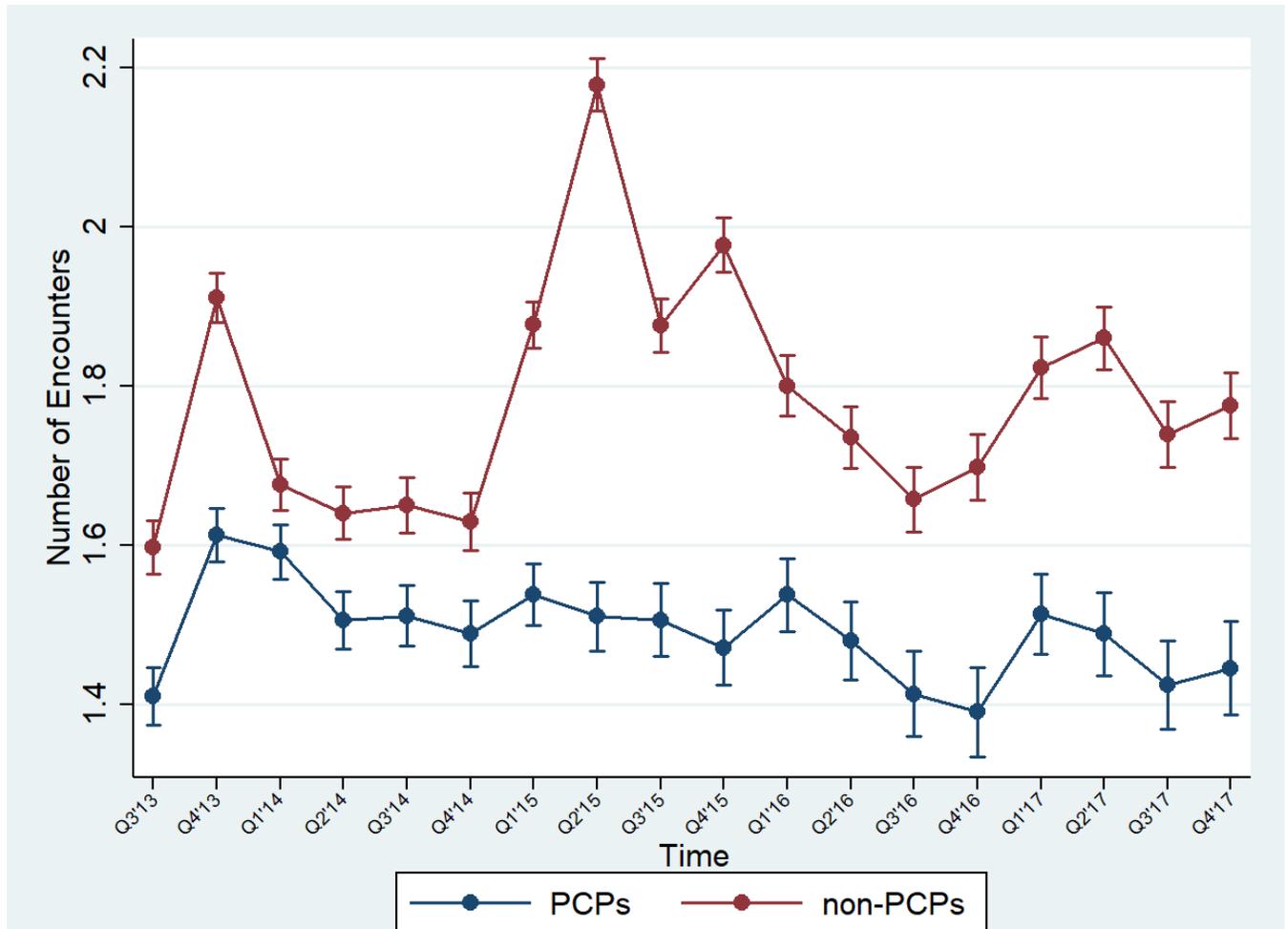
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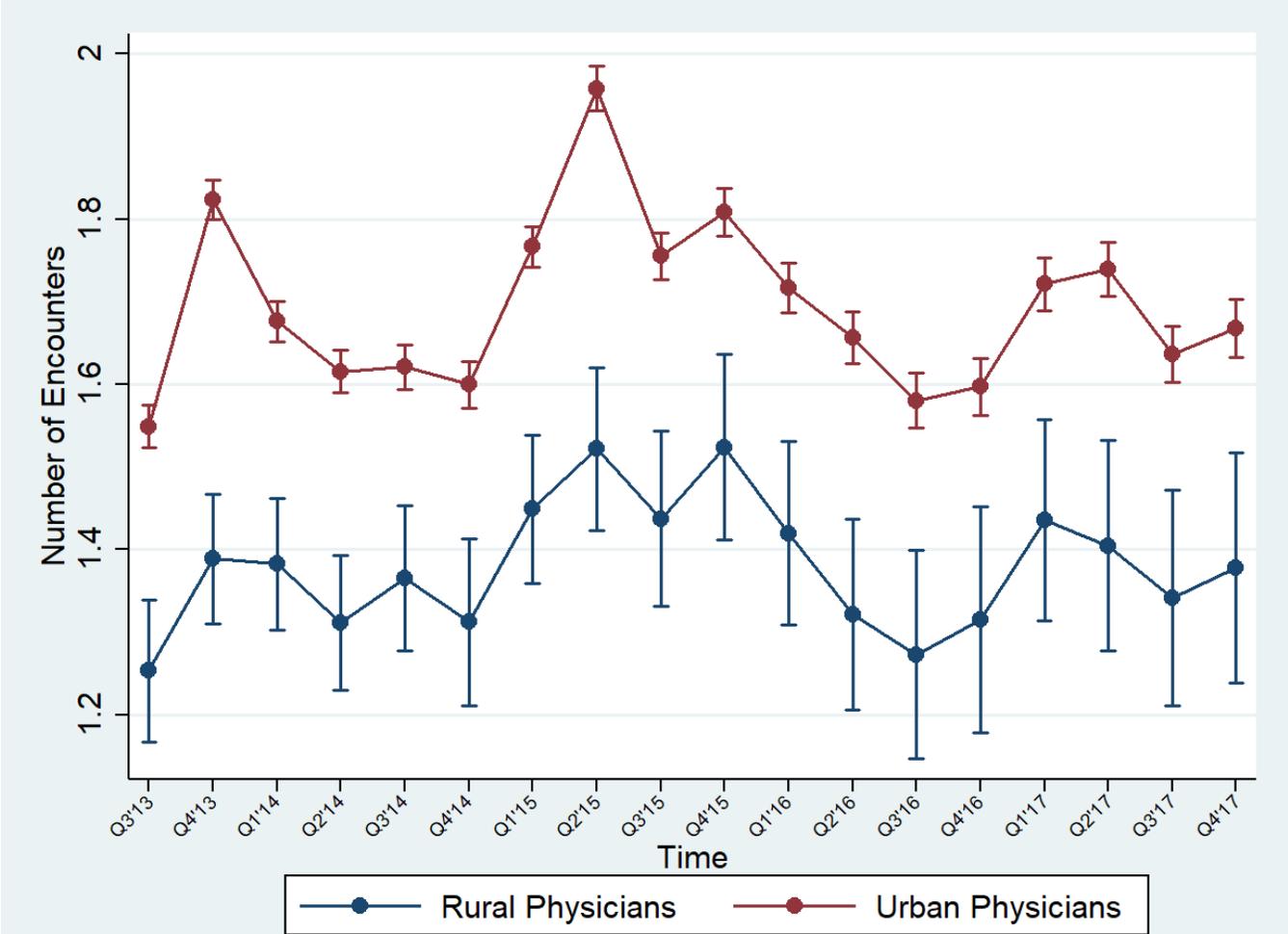
## eAppendix

**eAppendix Figure 1.** Total Quarterly Testosterone Marketing Encounter per Physician by Physician Specialty, Adjusted Predictive Margins with 95% CIs



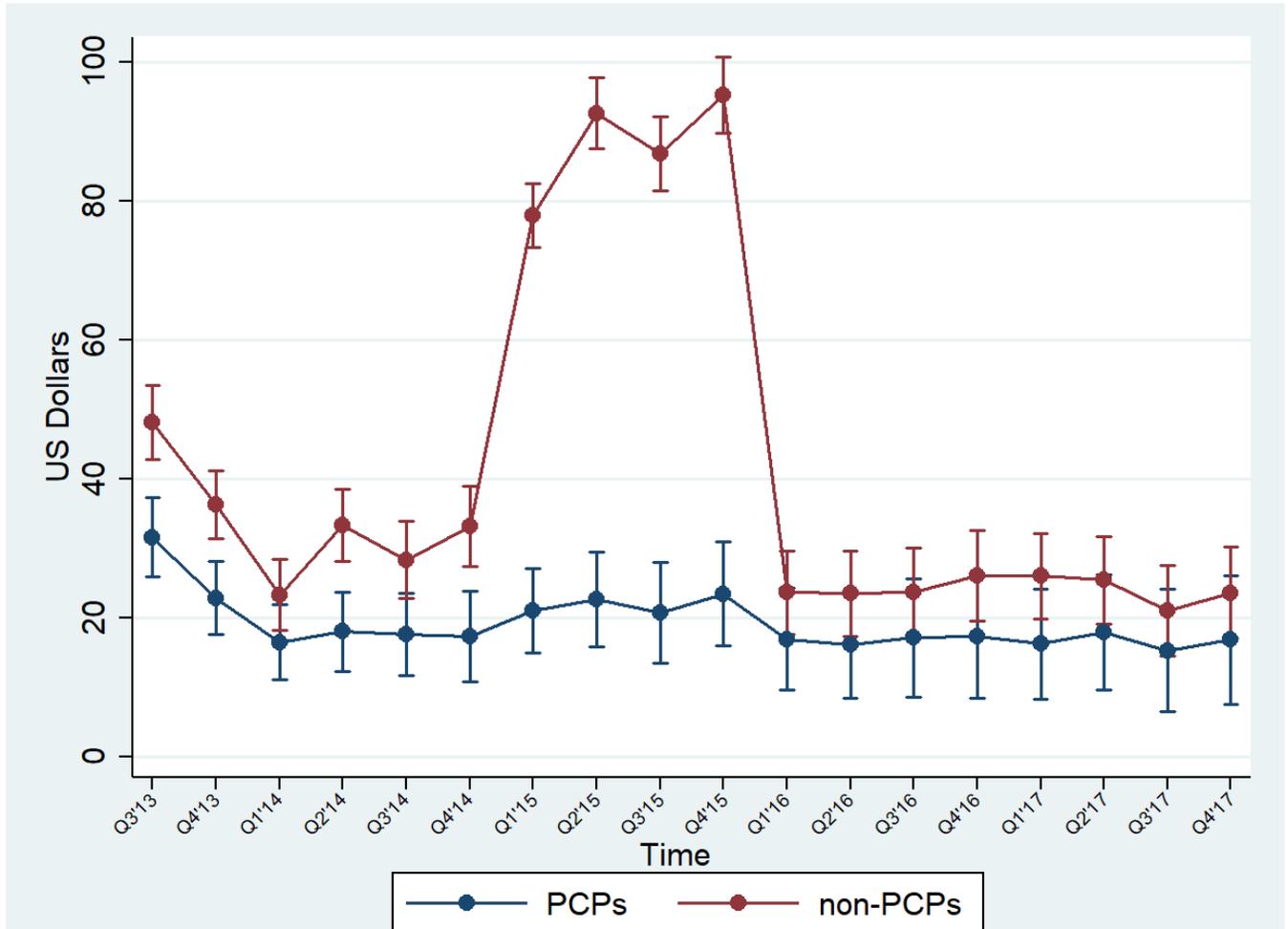
Note: Trends adjusted for physician type (PCP vs non-PCP), physician census region, and physician location in urban or rural primary care service areas (PCSAs). Quarters are interacted with physician type and 95% CI bars for the adjusted trends are shown extending from each data point.

**eAppendix Figure 2.** Quarterly Testosterone Marketing Encounter per Physician by Geography, Adjusted Predictive Margins with 95% CIs



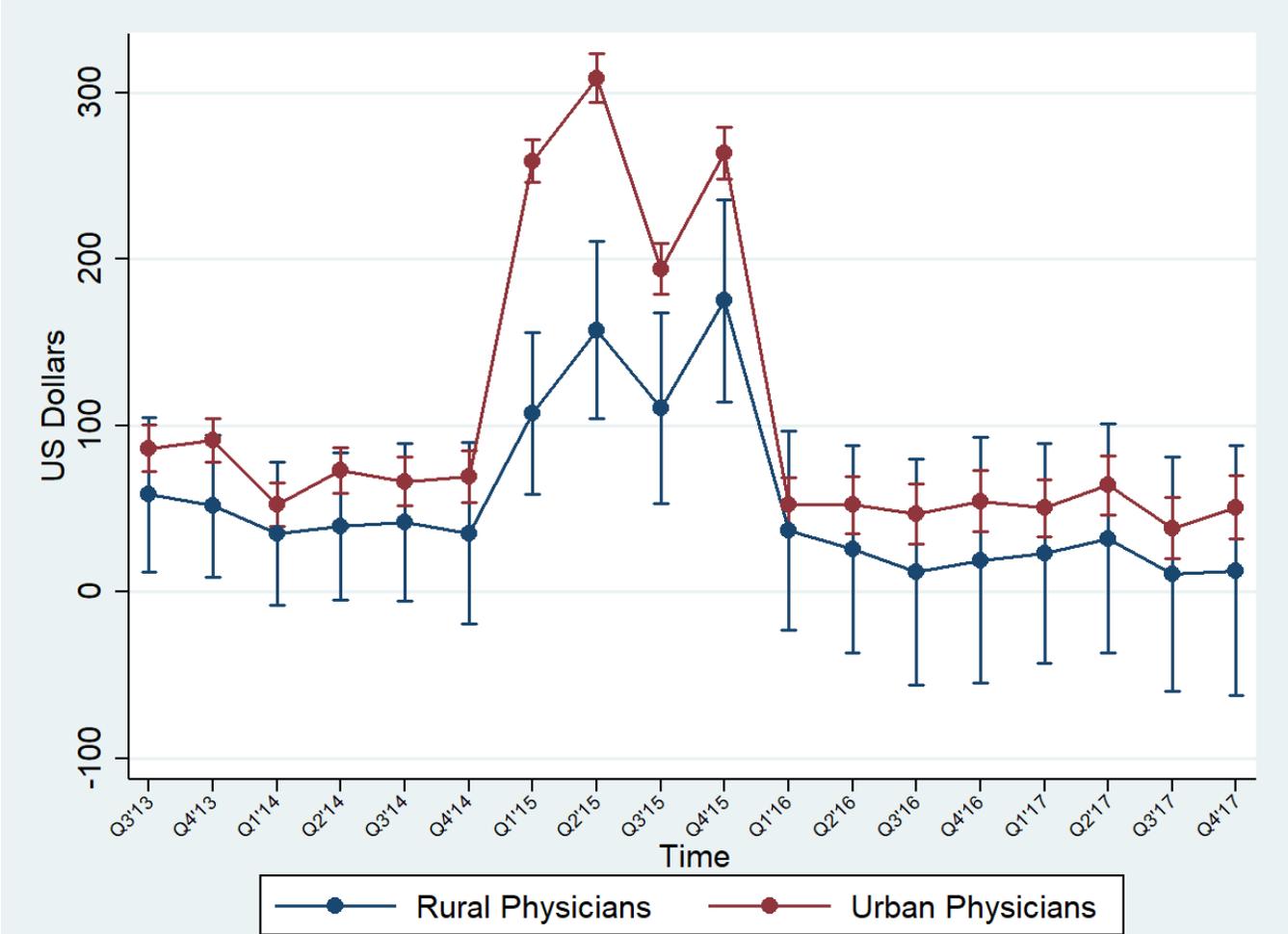
Note: Trends adjusted for physician type (PCP vs non-PCP), physician census region, and physician location in urban or rural primary care service areas (PCSAs). Quarters are interacted with physician rural/urban location and 95% CI bars for the adjusted trends are shown extending from each data point.

**eAppendix Figure 3.** Quarterly Testosterone Marketing Spending per Encounter to Physicians by Physician Specialty, Adjusted Predictive Margins with 95% CIs



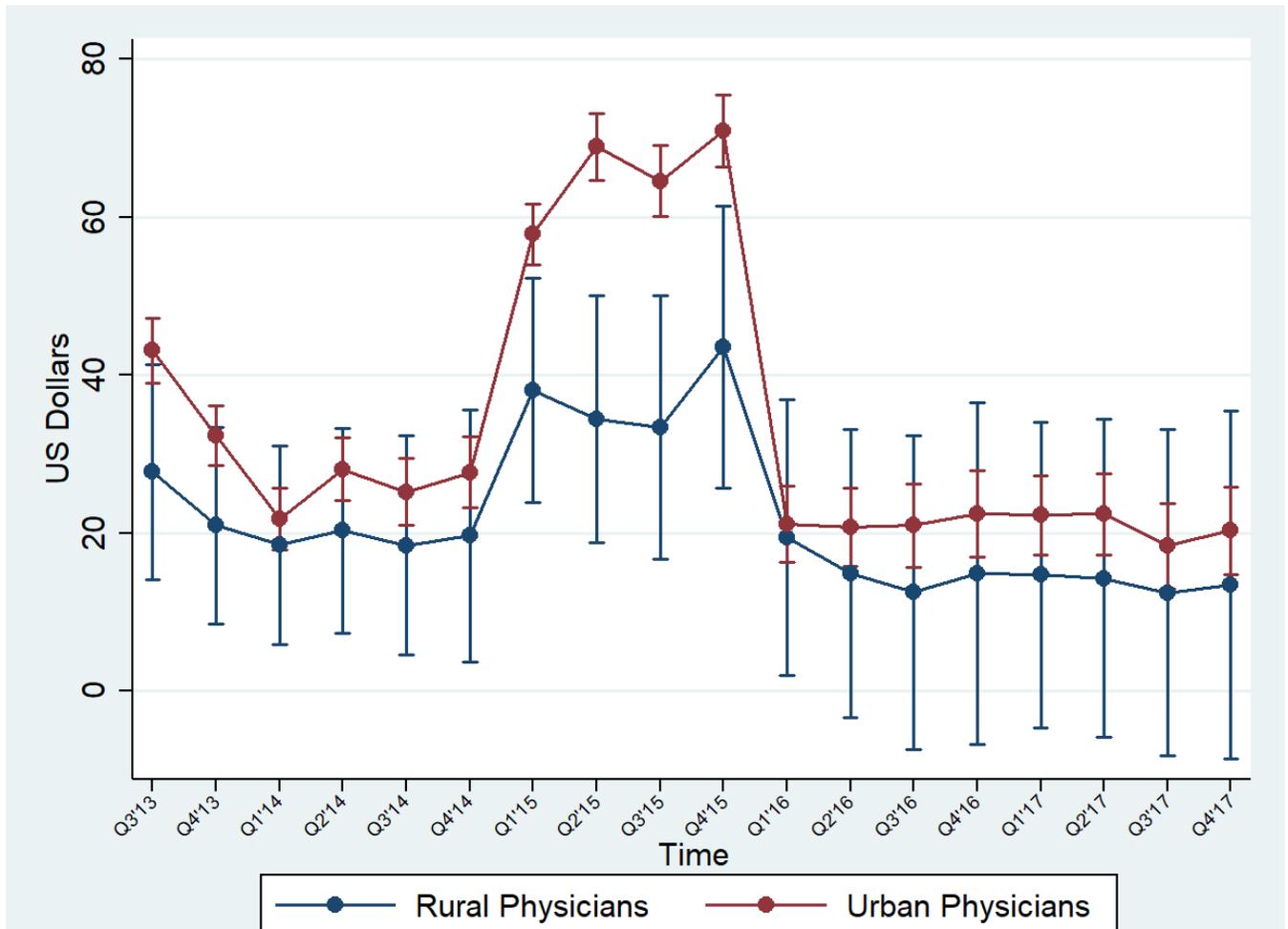
Note: Trends adjusted for physician type (PCP vs non-PCP), physician census region, and physician location in urban or rural primary care service areas (PCSAs). Quarters are interacted with physician type and 95% CI bars for the adjusted trends are shown extending from each data point.

**eAppendix Figure 4.** Testosterone Marketing Spending per Physician by Geography, Adjusted Predictive Margins with 95% CIs



Note: Trends adjusted for physician type (PCP vs non-PCP), physician census region, and physician location in urban or rural primary care service areas (PCSAs). Quarters are interacted with physician rural/urban location and 95% CI bars for the adjusted trends are shown extending from each data point.

**eAppendix Figure 5.** Quarterly Testosterone Marketing Spending per Encounter to Physicians by Geography, Adjusted Predictive Margins with 95% CIs



Note: Trends adjusted for physician type (PCP vs non-PCP), physician census region, and physician location in urban or rural primary care service areas (PCSAs). Quarters are interacted with physician rural/urban location and 95% CI bars for the adjusted trends are shown extending from each data point.