Published in final edited form as:
Ann Epidemiol. 2019 August ; 36: 26–32. doi:10.1016/j.annepidem.2019.06.007.

Association between trends in county-level opioid prescribing and reported rates of gonorrhea cases in the United States

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Abstract

Purpose: We investigated the association between county-level trends in opioid prescribing rates, a proxy for opioid misuse, and rates of reported gonorrhea (GC) among males in the United States.

Methods: We used linear mixed-model regression analyses to evaluate the association between county-level trends in opioid prescribing rates and rates of reported GC among males during 2010–2015.

Results: There was a positive association between trends in county-level opioid prescribing rates and rates of GC among males (β = 0.068, 95% confidence interval [CI] = 0.030, 0.105) during 2010–2015.However, magnitude of this association decreased significantly over time in counties where opioid prescribing rates decreased (β = −0.018, 95% CI = −0.030, −0.006) and remained stable (β = −0.020, 95% CI = −0.038, 0.002) but was unchanged in counties where opioid prescribing rates increased (β = −0.029, 95% CI 0.058, 0.001).

Conclusions: During 2010–2015, we found a positive association between increases in county-level opioid prescribing rates, a proxy for opioid misuse, and rates of reported GC among males especially in counties most affected by the opioid crisis. Integrating sexual health with opioid misuse interventions might be beneficial in addressing the GC burden in the United States.

Keywords

Prescription opioids; Gonorrhea; Opioid crisis; Opioid misuse; Sexual risk behaviors

Introduction

The opioid crisis is a significant public health issue in the United States [1]. During 1999–2017, prescription opioid–related overdose deaths increased more than four-fold [2, 3].

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The views expressed are those of the authors and do not necessarily represent those of the Centers for Disease Control and Prevention.

Although national opioid prescribing rates in the United States declined during 2010–2015, opioid prescribing rates increased in nearly 1 in 5 U.S. counties [4]. High opioid prescribing rates increase the availability of prescription opioids in the community; prior analyses have demonstrated that increases in opioid prescribing parallel increases in opioid overdose deaths and admissions for opioid use disorder [1,5–7]. Thus, high opioid prescribing rates are associated with opioid misuse and its adverse outcomes [6, 7]. In addition to contributing to opioid-related deaths, prescription opioid misuse is associated with risky sexual behaviors, such as condomless sex, casual sex, multiple sex partners, exchanging sex for drugs and money, and group sex [8–14]; all of which may increase the risk of sexually transmitted diseases (STDs), such as gonorrhea (GC).

GC is the second most commonly reported nationally notifiable disease in the United States [15]. After a historically low rate in 2009, overall rates of reported GC cases have since increased. From 2010 to 2017, the rate of reported GC cases increased 70.5% from 100.8 cases per 100,000 population to 171.9 cases per 100,000 population [15]. From 2010 to 2017, the rate of reported GC cases among males increased 115.2% from 94.1 cases per 100,000 males to 202.5 cases per 100,000 males and increased 33.1% from 106.5 cases per 100,000 females to 141.8 cases per 100,000 females [15]. The rate of reported GC cases also vary by county. In 2017, 50% of all reported GC cases occurred in just 70 counties in the United States, most of which were urban [15]. Because prescription opioid misuse is associated with sexual risk behaviors [8–14] and may place individuals at heightened risk for GC, the objective of this ecological analysis was to examine the potential association between trends in county-level opioid prescribing rates, a proxy for opioid misuse, and county-level rates of reported GC cases among males during 2010–2015.

Materials and methods

National and county-level data on the number of opioid prescriptions for males and females were obtained from IQVIA Xponent® [16]. IQVIA Xponent is a health data system that tracks retail drug prescription sales in the United States. The estimated number of opioid prescriptions dispensed in the United States from 2010 to 2015 was based on a sample of approximately 59,000 pharmacies, which represent 88% of all prescriptions in the United States [4]. Annual county-level opioid prescribing rates were calculated by dividing the number of opioid prescriptions in each county by the U.S. census county-level population estimates of each year. Annual county-level opioid prescribing rates are measured per 100 persons. Cold and cough products containing opioids and buprenorphine products indicated for conditions other than pain were excluded [4]. We used opioid prescribing as a proxy for opioid misuse because high opioid prescribing rates increase the availability of prescription opioids in the community, which is in turn associated with opioid misuse [1,5–7].

We obtained national and county-level data on the number of reported GC cases among males from the national STD surveillance records at the Centers for Disease Control and Prevention (CDC). The national STD surveillance records include data on all reported GC cases in the United States. GC is a nationally notifiable disease and all 50 states and the District of Columbia report cases to the CDC. Annual rates of reported GC cases among males are calculated by dividing the number of GC cases in each county by the U.S. census county-level population estimates for males of each year[17]. Annual county-level rates of reported GC cases are measured per 100,000 males.

We selected rates of reported GC cases among males as the outcome rather than overall rates of reported GC cases or rates of reported GC cases among females. Gonorrheal infections are more often symptomatic (especially urethral infections) among men than among women; infections among women are often only detected by screening [18]. Therefore, rates of reported GC cases among men may better approximate the rate of newly acquired, acute gonococcal infections compared to rates in women, which can be heavily influenced by screening practices [19, 20].

We selected area-level covariates that may confound the ecologic relationship between opioid prescribing rates and rates of GC among males from the existing literature. We obtained county-level sociodemographic data among males for 2010–2015 from the American Community Survey (ACS). The ACS is an annual survey conducted by the U.S. Census Bureau that collects data on social, economic, housing, and population data at the national, state, county, census tract, census block group level, and other geographic level subtypes [21]. We obtained five-year estimates of county-level percentage of males by age (categorized as ≤ 19 years, 20–29 years, 30–39 years, 40–49 years, and ≥50 years), race/ethnicity (non-Hispanic black, Hispanic, non-Hispanic white, and other), highest level of education (<high school, high school/GED, some college, and ≥ college), and poverty level (living below federal poverty level and at or above federal poverty level) from ACS. County urbanicity (rural or urban county) was based on the rural-urban continuum codes of the Economic Research Service, the United States Department of Agriculture [22]. The rural-urban continuum codes are assigned to counties based on the population of the county and whether the county is in a metropolitan area.

Statistical analysis

Descriptive statistics were used to calculate percent change in annual opioid prescribing rates and rates of reported GC cases among males during 2010–2015. We used a linear mixed effects model with a random intercept to examine the bivariate and multivariable association between county-level trends in opioid prescribing rates and rates of reported GC cases among males in the United States during 2010–2015. Significant covariates in the bivariate model were included in the multivariable model. The multivariable model included county-level opioid prescribing rate, year, the interaction term between county-level opioid prescribing rate and year, and covariates (county urbanicity and county-level percentage of males by age, race/ethnicity, highest level of education, and poverty level). The interaction term was included in the model to determine if the association between county-level opioid prescribing rates and rates of reported GC cases among males varied by year. We estimated adjusted unstandardized regression coefficients (β) and 95% confidence intervals (CIs).

We evaluated the association between county-level trends in opioid prescribing rates and rates of reported GC cases among males in the United States separately for counties where opioid prescribing rates decreased, increased, or remained stable from 2010 to 2015. This categorization was based on data published by CDC [3]. A county-level change in opioid prescribing rate of ≥ 10% from 2010 to 2015 was considered to be an increase or decrease, whereas changes <10% were considered stable [3]. We conducted stratified analyses for each category (counties where opioid prescribing rates decreased, increased, or remained stable) using linear mixed effects. We estimated adjusted unstandardized regression coefficients and 95% CI. All analyses were conducted in R, version3.5.1, and the lmer function in the lme4 package was used for fitting linear mixed effects model [23]. Statistical significance was set at $P < .05$. This research was reviewed by the Institutional Review Board of the CDC and was considered exempt because it was determined not to be research involving human subjects.

Results

Nationally, from 2010 to 2015, there was a 13.1% decrease in annual opioid prescribing rates (81.2 prescriptions per 100 persons to 70.6 prescriptions per 100 persons) and a 49.7% increase in the annual rate of reported GC cases among males (from 94.1 cases per 100,000 males to 140.9 cases per 100,000 males). However, during this period, the opioid prescribing rate increased in 19.6% of counties [3] and the rate of reported GC cases among males increased in 59.7% of U.S. counties. All covariates were significant in the bivariate model and thus were included in the multivariable model. The multivariable model included county-level opioid prescribing rate, year, the interaction term between county-level opioid prescribing rate and year, and covariates (county urbanicity and county-level percentage of males by age, race/ethnicity, highest level of education, and poverty level).

County-level opioid prescribing rates were positively associated with county-level rates of reported GC cases among males (β = 0.068, 95% CI = 0.031, 0.105) (Table 1). For every one unit increase in county-level opioid prescribing rates, the county-level rate of reported GC cases among males increased by 0.068 per 100,000. However, the interaction term, county-level prescribing rate and year, was negatively associated with county-level rates of reported GC cases among males (β = −0.014, 95% CI = −0.023, −0.006). Therefore, although the association between county-level opioid prescribing rate and county-level rate of reported GC cases was positive, the magnitude of this association decreased significantly over time from 2010 to 2015 (Fig. 1). The association between county-level rates of GC cases among males and all covariates were positive.

We further evaluated the association between opioid prescribing rates and rates of reported GC among males separately in counties where opioid prescribing rates decreased, remained stable, or increased from 2010 to 2015. In counties where opioid prescribing rates decreased from 2010 to 2015, the opioid prescribing rate was positively associated with rates of reported GC cases among males (β = 0.104, 95% CI = 0.173) but the magnitude of this association decreased significantly over time (β = −0.018, 95% CI = −0.030, −0.006) (Table 2). Similarly, in counties where opioid prescribing rates remained stable, opioid prescribing rate was positively associated with rates of reported GC cases among males (β = 0.206, 95% CI = 0.118, 0.344), but the magnitude of this association decreased, significantly over time (β = −0.020, 95% CI = −0.038, −0.002). However, in counties where opioid prescribing rates increased, opioid prescribing rate was positively associated with rates of reported GC cases among males (β = 0.181, 95% CI = 0.045, 0.324) and the magnitude of this association remained stable over time (β = −0.029, 95% CI = −0.058, 0.001). Figure 2 shows the change in the, slope categorized by counties where opioid prescribing rates decreased, remained stable, or increased from 2010 to 2015.

Discussion

Although national opioid prescribing rates declined and rates of reported GC cases among males increased during the study period, more granular analyses at the county level revealed that opioid prescribing rates were positively associated with county-level rates of reported GC cases among males in the United States. However, the magnitude of this association decreased over time and varied across counties. In counties where the opioid prescribing rate increased from 2010 to 2015, the magnitude of this association remained the same over time, in contrast to counties where opioid prescribing rate decreased or remained stable (where the magnitude of this association decreased over time).

Sexual risk behaviors are important correlates of GC [24]. Increased risk behaviors may account for the positive association between trends in opioid prescribing rates and the rates of reported GC cases among males, especially in counties where opioid prescribing rates increased. High levels of prescription opioid use, even as prescribed, and particularly for long duration can lead to misuse and addiction [1,5–7]. Prescription opioid misuse, in turn, is associated with sexual risk behaviors such as condomless sex, casual sex, multiple sexual partners and decision-making, and exchange sex for drugs or money, which may increase the risk of infection with GC.[8–13] These risk behaviors may increase the risk of acquisition or transmission of *Neisseria gonorrhoeae* [8, 11, 12]. Although opioids in general are traditionally associated with dampening of sexual desire, recent studies have reported that prescription opioids may heighten sexual impulsivity and risk, especially if used with other illicit drugs.[12, 13] Clustering of other risk behaviors with opioid misuse can also account for the positive association in trends between opioid prescribing (proxy for opioid misuse) and rates of reported GC observed in this study. Clustering of sexual risk behaviors and illicit drug use behaviors such as opioids has been reported [25]. Persons who engage in one of these behaviors are likely to engage in the other, and this may account for the association between opioid prescribing rates and GC rates in this study [25]. Furthermore, drug-using networks sometimes overlap with sexual networks; thus, persons who misuse opioids might be at elevated risk for STDs such as GC [9]. The decline in the magnitude of the association between trends in opioid prescribing and GC rates during 2010–2015 in counties where opioid prescribing rate decreased or remained stable that was observed in this study may be attributable to the increasing public health response efforts to address in the opioid crisis in the United States in the past decade.

Increasing rates of reported GC cases overall can have significant economic and health consequences in counties already affected by the opioid crisis. Over 500,000 GC cases were reported nationally in 2017, most of which were reported among males [13], and CDC estimates that over 800,000 infections may actually occur each year[26]. The estimated annual direct cost of GC in the United States in 2008 was approximately $162 million ($81.1e$243.2 million) [27]. Increasing rates of reported GC cases may further exacerbate health care costs associated with prescription opioid misuse in affected communities [28], most of which are already low income [4]. GC is a risk factor for the sexual transmission of

HIV [29], so increasing rates of GC in communities hardest hit by the opioid crisis might further contribute to HIV transmission, particularly if these communities have limited access to HIV testing and high-quality clinical care. Increasing rates of reported GC cases are of particular concern in an era of emerging antimicrobial resistance. N. gonorrhoeae has progressively developed resistance to most antimicrobials used to treat it [30, 31]. Currently, there is only one recommended regimen for the treatment of GC, a single dose of 250 mg of ceftriaxone administered intramuscularly and 1g of azithromycin administered orally [32], and susceptibility to this treatment may be declining [33, 34].

This analysis used opioid prescribing rate as a proxy for opioid misuse. The positive association between county-level opioid prescribing rates and GC cases underscores the importance of prevention interventions that focus on opioid misuse and sexual risk behaviors and suggests the potential value of partnerships between opioid use treatment programs and STD prevention programs. Programs that serve persons at risk for opioid misuse (including those taking prescribed opioids for long duration) or who have opioid use disorder can consider conducting sexual risk assessments, including assessments of sexual risk behaviors, STD history, sexual partners, condom use, and other sexual risk-reduction behaviors as part of their services [32]. This approach may identify persons who are also at risk for GC and who may benefit from sexual health services and screening. Making condoms freely available at these locations may further promote condom use in this population. STD programs can also consider including brief opioid- and substance-use assessments as part of their sexual health care services and offer behavioral counseling and education and/or referrals to at-risk clients. The screening, brief intervention, and referral to treatment service model implemented in New York City STD clinics provide opportunities to identify clients with substance-use disorders and refer them to substance-abuse counseling and support services [35]. This integrated STD and substance-use disorder service model was associated with a reduction in substance use and risky sexual behaviors among clients [35].

There are limitations to this ecologic analysis. This analysis cannot prove causation because it was an ecologic analysis examining the association between trends in county-level opioid prescribing and rates of reported GC cases among males during 2010–2015. We used opioid prescribing rate as a proxy for opioid misuse because opioid misuse data were unavailable. However, its use as a proxy for opioid misuse might have biased its association with GC in this analysis. Residual confounding is another limitation of this analysis. We did not adjust for all potential residual confounders of the association between opioid misuse and GC such as county-level rates of arrest or incarceration, exchange sex, injection drug use, and alcohol and other substance use because these data were unavailable. County-level opioid prescribing data used in this analysis are aggregated by the county where the pharmacy from which a prescribed opioid is dispensed and exclude prescriptions obtained by persons outside the county, prescriptions dispensed directly by prescribers, pharmacies that did not supply prescription information to IQVIA, or prescription opioids obtained through other means. Therefore, this analysis might have underestimated opioid prescribing rates in some counties. The rates of reported GC cases among males used in this analysis are based on cases reported to the CDC from state health departments; underreporting of GC cases from any jurisdiction could underestimate the county-level rate of reported GC cases used in this analysis. GC rates have increased sharply among men, likely reflecting increasing rates among MSM. The steep increases among MSM might have confounded the association between county-level rates of reported GC cases among males and opioid prescribing rates observed in this study.

In conclusion, a positive ecological association was found between increases in county-level opioid prescribing rates and increases in rates of reported GC cases among males during 2010–2015 especially in counties most affected by the opioid crisis. These data highlight the potential value of forging creative linkages between opioid use treatment programs and STD prevention and control programs.

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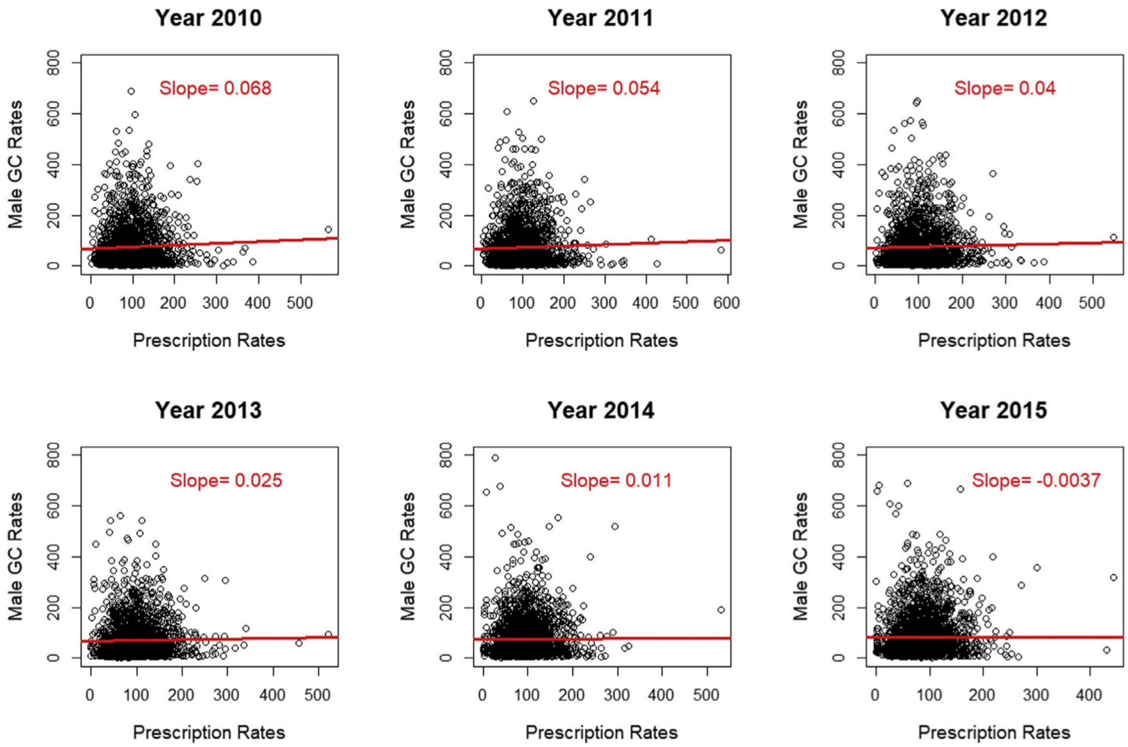
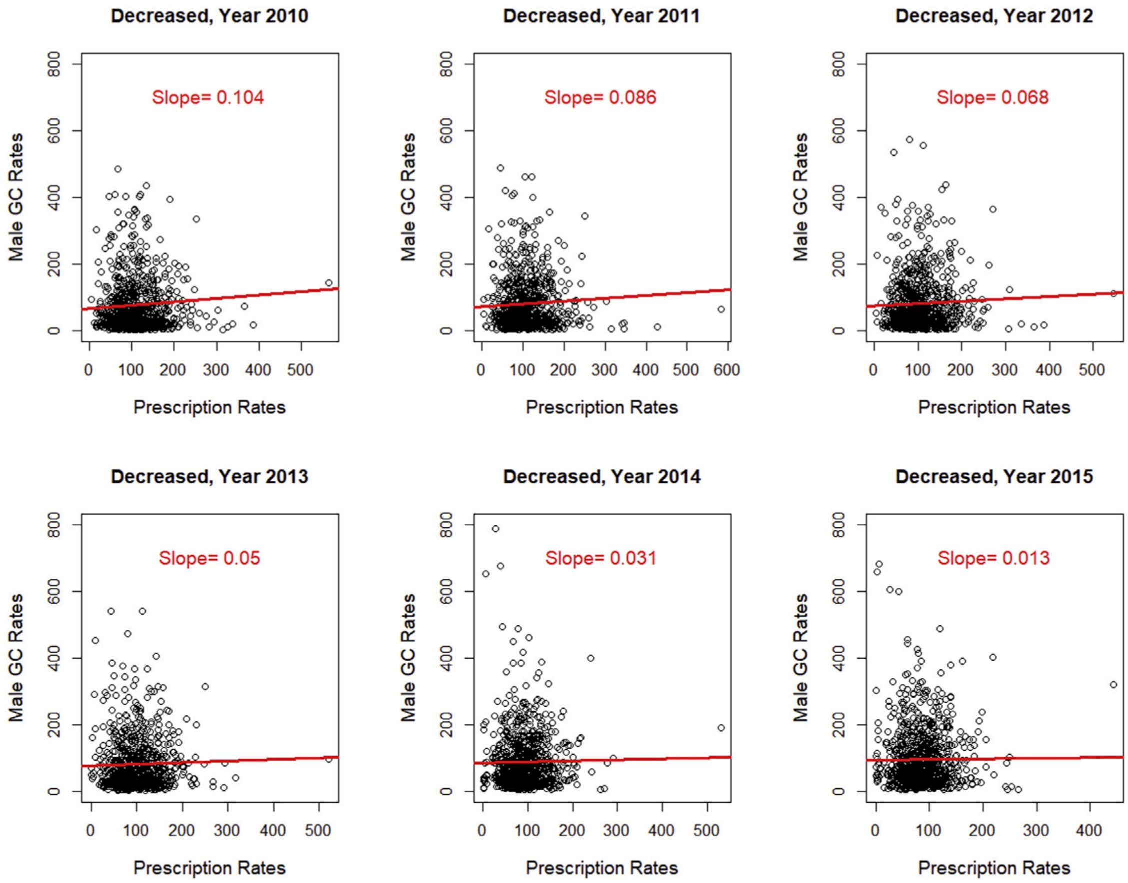
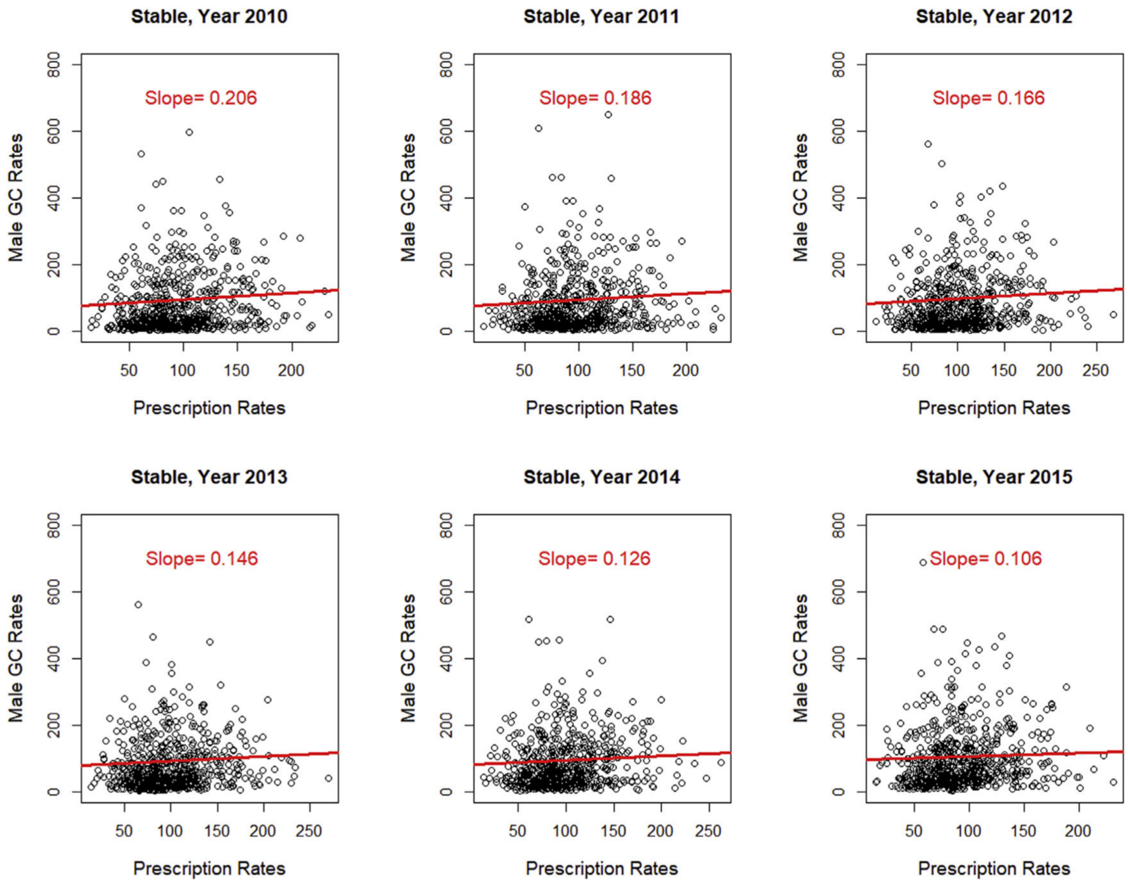


Fig. 1.

Change in the magnitude of the association between county-level opioid prescribing rate and county-level rates of reported gonorrhea cases among males by year, 2010–2015.


Decreased, Year 2010
Slope= 0.104
Decreased, Year 2011
Slope= 0.086
Decreased, Year 2012
Slope= 0.068
Decreased, Year 2013
Slope= 0.05
Decreased, Year 2014
Slope= 0.031
Decreased, Year 2015
Slope= 0.013
Male GC Rates
Prescription Rates


Stable, Year 2010
Slope= 0.206
Male GC Rates
Prescription Rates
Stable, Year 2011
Slope= 0.186
Stable, Year 2012
Slope= 0.166
Stable, Year 2013
Slope= 0.146
Stable, Year 2014
Slope= 0.126
Stable, Year 2015
Slope= 0.106

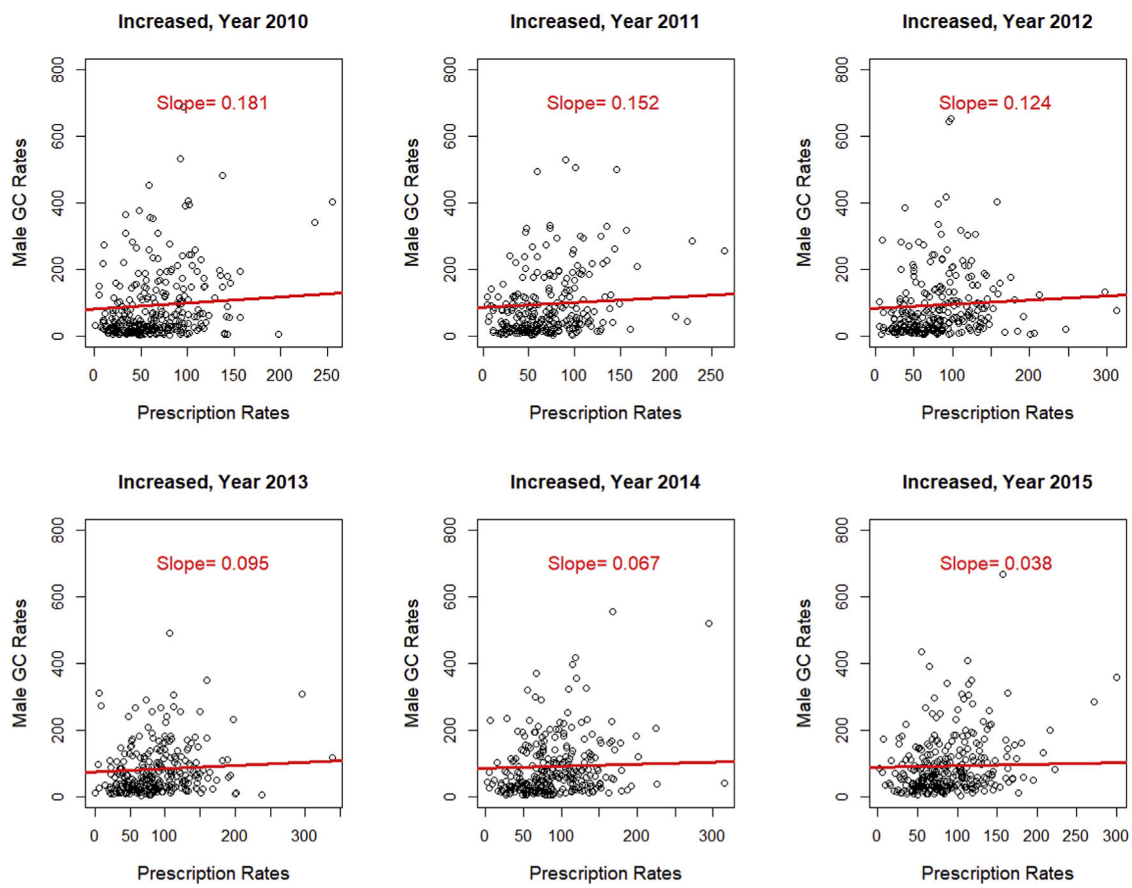


Fig. 2.

Changes in the magnitude of the association between county-level opioid prescribing rate and county-level rates of reported gonorrhea cases among males over time, 2010–2015; counties where opioid prescribing rates decreased, 2010–2015; counties where opioid prescribing rates remained stable, 2010–2015; counties where opioid prescribing rates increased, 2010–2015.

Table 1

Multivariable linear mixed effects model analysis of the association between county-level opioid prescribing rates and county-level rates of reported gonorrhea cases among males, 2010–2015

Variable	β *	95% confidence interval
Intercept	−98.36	−163.551, −33.157
Prescribing rate	0.068	0.031, 0.105
Year	4.52	3.601, 5.446
Prescribing rate *year †	−0.014	−0.023, −0.006

* Adjusted for county-level age, race/ethnicity, highest level of education, poverty level, and county urbanicity.

† Interaction between county-level opioid prescribing rate and year.

Table 2

Multivariable linear mixed effects model analysis of the association between county-level opioid prescribing rate and county-level rates of reported gonorrhea cases among males by trends in opioid prescribing rates, 2010–2015

Variable	Counties where opioid prescribing rates decreased during 2010–2015* (*n* = 946)		Counties where opioid prescribing rates remained stable during 2010–2015* (*n* = 675)		Counties where opioid prescribing rates increased during 2010–2015* (*n* = 308)	
	β†	95% Confidence interval	β†	95% Confidence interval	β†	95% Confidence interval
Intercept	−149.02	−257.233, −40.753	−189.73	−331.378,−48.041	−75.833	−308.385,−157.197
Prescribing rate	0.104	0.042, 0.173	0.206	0.118, 0.344	0.181	0.045, 0.324
Year	6.449	5.111, 7.823	5.172	3.253, 7.186	2.592	−0.223, 5.494
Prescribing rate *year‡	−0.018	−0.030, −0.006	−0.020	−0.038, −0.002	−0.029	−0.058, 0.001

*Based on data from Guy JG, Zhang K, Bohm MK et al. Vital Signs: Changes in Opioid Prescribing in the United States, 2006–2015. MMWR Morbidity and Mortality Weekly Report. 2017; 66:697–704.

†Adjusted for county-level age, race/ethnicity, highest level of education, poverty level, and county urbanicity.

‡Interaction between county-level opioid prescribing rate and year.