Sex and racial disparities in cardiovascular risk continue to exist, and the risk factors fueling these disparities will require redress. The enormous progress in reducing cardiovascular disease mortality realized since the 1960s represent public health and health care improvement successes, yet more progress in reducing the remaining colossal burden of cardiovascular disease in the United States awaits.

Earl S. Ford, MD, MPH
Julie C. Will, PhD
Carla I. Mercado, PhD
Fleetwood Loustalot, PhD, FNP

Author Affiliations: Division of Population Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia (Ford); Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia (Will, Mercado, Loustalot).

Corresponding Author: Earl S. Ford, MD, MPH, Centers for Disease Control and Prevention, 4770 Buford Hwy, MS F78, Atlanta, GA 30341 (eford@cdc.gov).

Published Online: December 8, 2014. doi:10.1001/jamainternmed.2014.6403.

Author Contributions: Dr Ford had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Ford, Will.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Ford.
Critical revision of the manuscript for important intellectual content: Will, Mercado, Loustalot.
Statistical analysis: Ford, Will.
Administrative, technical, or material support: Loustalot.
Study supervision: Ford.

Conflict of Interest Disclosures: None reported.

Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

1. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. ACC/AHA Guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(25)(suppl 2):S49-S73.

2. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. http://www.cdc.gov/nchs/nhanes.htm. Accessed July 11, 2013.

3. Muntner P, Colantonio LD, Cushman M, et al. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. *JAMA*. 2014;311(14):1406-1415.

Prescription Drug Abuse: A National Survey of Primary Care Physicians

Chronic pain is one of the most common reasons for seeking medical attention in the United States, and such pain is frequently treated with prescription opioids. The clinical use of these products nearly doubled between 2000 and 2010,[1] with simultaneous increases in the incidence of opioid abuse, addiction, injury, and death.[2] Because primary care physicians play a critical role in maximizing the safe use of these products, we examined their beliefs and self-reported practices regarding prescription opioid use.

Related article page 186

Invited Commentary page 194

Table 1. Physician Characteristics

Characteristic	Value (N = 420)
Age, mean (SE), y	50 (0.4)
Male sex, %	55
Specialty, %	
Family practice	52
Internal medicine	46
General practice	2
Ethnicity, %	
White	70
Asian	19
African American or other	11
Practice type, %[a]	
Solo or small group practice	45
Academic medical center-based practice	13
Managed care organization	12
Public or government-based practice	11
Other	23
Works in academic or teaching hospital, %	24
Ownership in practice	
Full	21
Partial	14
None	65
No. of patients seen per month, mean (SE)	285 (8.4)
No. of patients prescribed an opioid per month, mean (SE)	35 (2.9)
Pharmaceutical companies visit primary site of clinical practice, %	56

Abbreviation: SE, standard error.

[a] Column total may exceed 100% because more than 1 response may apply.

Methods | We used the Dillman[3] approach to conduct a nationally representative postal mail survey. We sampled 1000 practicing US internists, family physicians, and general practitioners using the American Medical Association Masterfile. Participants were sent a questionnaire, $2 cash incentive, and self-addressed stamped envelope in February 2014, and nonrespondents were contacted a maximum of 3 times in approximately 6-week intervals. Response patterns between early and late responders were similar, suggesting the absence of nonresponse bias. However, because of modest sociodemographic differences between respondents and nonrespondents, we incorporated poststratification weights in our analyses. The questionnaire and study protocol were exempted from review by the institutional review board of the Johns Hopkins Bloomberg School of Public Health. The study did not require informed consent because it did not qualify as human subjects research.

Results | Our adjusted response rate was 58%, and physician characteristics are reported in **Table 1.** Most physicians (90%) reported prescription drug abuse to be a "big" or "moderate" problem in their communities, and more than four-fifths (85%) reported that opioids are overused in clinical practice (**Table 2**). A majority of physicians (65%-84%) reported being "very" or

Table 2. Attitudes and Beliefs Regarding the Use of Opioids in Clinical Practice

Attitude or Belief	Respondents, % (N = 420)			
	No Problem at All	A Small Problem	A Moderate Problem	A Big Problem
Belief Regarding Prescription Drug Abuse				
Magnitude of prescription drug abuse in the community	0	10	37	53
	Strongly Disagree	**Somewhat Disagree**	**Somewhat Agree**	**Strongly Agree**
Belief Regarding Opioid Use in Clinical Practice				
In general, opioids are overused to treat pain today	2	13	39	46
Patients commonly embellish or fabricate their pain symptoms to obtain opioids	3	15	46	36
	Not at All	**Slightly**	**Moderately**	**Very**
Attitude Toward Opioid Prescribing				
Confidence in clinical skills related to opioid prescribing	2	10	56	32
Comfort in prescribing opioids for chronic noncancer pain	13	38	36	13
Concern About Potential Patient Outcomes				
Addiction	1	15	29	55
Deaths related to opioids	6	24	22	48
Motor vehicle accidents related to opioids	1	22	33	44
Nonadherence	11	24	32	33
Tolerance	3	22	44	31
Impaired cognition	1	25	44	30
Sedation	2	27	44	27
Concern About Potential Prescriber Outcomes				
Malpractice claim	17	37	20	26
Prosecution	25	30	20	25
Censure by state medical board	26	30	19	25
	Never	**Rarely**	**Sometimes**	**Often**
Belief Regarding Frequency of Potential Adverse Events When Opioids Are Used as Directed				
Tolerance	0	5	33	62
Physical dependence	1	6	37	56
Ceiling effects	1	9	54	36
Addiction	1	22	50	27
Hypersensitivity to pain (hyperalgesia)	3	27	43	27

"moderately" concerned about each potential adverse patient outcome that was assessed, including opioid-related addiction (55% reporting "very concerned"), deaths (48%), and motor vehicle accidents (44%). Furthermore, most physicians reported high frequencies of adverse events—such as tolerance (62% reported occurring "often"), physical dependence (56%), and ceiling effects (36%)—even when prescription opioids are used as directed to treat chronic pain. Physicians expressed somewhat lower degrees of concern for potential adverse prescriber outcomes associated with opioid prescribing, such as malpractice claims and censure by state medical boards. Approximately one-half of physicians (45%) reported being less likely to prescribe opioids compared to 1 year ago. Despite this, nearly all physicians (88%) expressed confidence in their clinical skills related to opioid prescribing, and nearly one-half (49%) were "very" or "moderately" comfortable using these drugs for chronic noncancer pain.

Discussion | Primary care physicians appear to recognize many elements of the prescription drug abuse epidemic, such as the high prevalence of adverse outcomes associated with opioid use.[4,5] Although our study did not allow for longitudinal assessment of these physicians' attitudes or knowledge over time, substantial publicity and raising of awareness on the part of many stakeholders may have contributed to these findings. Physicians' high levels of confidence in their own prescribing are also of note and may reflect a combination of their experiences, as well as cognitive biases that have been demonstrated in other settings.[6,7]

Our study has limitations. First, our results are based on self-report and prone to socially desirable response bias. We minimized this potential by ensuring participant confidentiality and avoiding leading questions. Second, nonresponse bias may have influenced our findings. To reduce this impact, we maximized survey participation rates using the Dillman method and implemented poststratification weights in our analyses.

Given the increasing use of opioids in clinical practice and its attendant morbidity and mortality, understanding primary care physicians' prescribing patterns, as well as their perception of adverse events associated with the use of these products, is crucial. Our investigation suggests that most primary

care physicians are aware of many risks of opioids, and many have decreased their prescribing of these products during the past 12 months.

Catherine S. Hwang, MSPH
Lydia W. Turner, MHS
Stefan P. Kruszewski, MD
Andrew Kolodny, MD
G. Caleb Alexander, MD, MS

Author Affiliations: Center for Drug Safety and Effectiveness, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland (Hwang, Turner, Kruszewski, Alexander); Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland (Hwang, Turner, Alexander); Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland (Kruszewski); Stefan P. Kruszewski, MD, and Associates, Harrisburg, Pennsylvania (Kruszewski); Phoenix House Foundation, New York, New York (Kolodny); Division of General Internal Medicine, Department of Medicine, Johns Hopkins Medicine, Baltimore, Maryland (Alexander).

Corresponding Author: G. Caleb Alexander, MD, MS, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe St, W6035, Baltimore, MD 21205 (galexand@jhsph.edu).

Published Online: December 8, 2014. doi:10.1001/jamainternmed.2014.6520.

Author Contributions: Ms Hwang and Dr Alexander had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: Hwang, Turner, Kolodny, Alexander.
Drafting of the manuscript: Hwang, Turner, Kolodny, Alexander.
Critical revision of the manuscript for important intellectual content: Hwang, Kruszewski, Kolodny, Alexander.
Statistical analysis: Hwang, Kolodny.
Obtained funding: Turner, Alexander.
Administrative, technical, or material support: Turner, Kruszewski, Alexander.
Study supervision: Turner, Alexander.

Conflict of Interest Disclosures: Ms Hwang is a current ORISE Fellow at the Food and Drug Administration. Dr Kruszewski has served as a general and case-specific expert for multiple plaintiff litigations involving OxyContin, Neurontin, and Zyprexa and has had false claims settled as coplaintiff with the United States against Southwood Psychiatric Hospital, Pfizer (Geodon), and AstraZeneca (Seroquel). Dr Kolodny is employed by the Phoenix House and is President of Physicians for Responsible Opioid Prescribing. Dr Alexander is Chair of the Food and Drug Administration's Peripheral and Central Nervous System Drugs Advisory Committee, serves as a paid consultant to IMS Health, and serves on an IMS Health scientific advisory board. This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies. No other disclosures are reported.

Funding/Support: This work was supported by the Robert Wood Johnson Foundation Public Health Law Research Program and the Lipitz Public Health Policy Fund Award from the Johns Hopkins Bloomberg School of Public Health.

Role of the Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: Kenneth Rasinski, PhD, Joint Commission, provided helpful input on survey development, fielding, and analysis. He was not compensated for his contribution.

1. Daubresse M, Chang HY, Yu Y, et al. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000-2010. *Med Care*. 2013;51(10):870-878.

2. Centers for Disease Control and Prevention. Prescription Drug Overdose in the United States: Fact Sheet. Updated October 17, 2014. http://www.cdc.gov/homeandrecreationalsafety/overdose/facts.html. Accessed October 22, 2014.

3. Dillman DA. *Mail and Telephone Surveys: the Total Design Method*. New York, NY: John Wiley and Sons; 1978.

4. Juurlink DN, Dhalla IA. Dependence and addiction during chronic opioid therapy. *J Med Toxicol*. 2012;8(4):393-399.

5. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician*. 2008;11(2)(suppl):S105-S120.

6. Dawson NV, Arkes HR. Systematic errors in medical decision making: judgment limitations. *J Gen Intern Med*. 1987;2(3):183-187.

7. Poses RM, McClish DK, Bekes C, Scott WE, Morley JN. Ego bias, reverse ego bias, and physicians' prognostic. *Crit Care Med*. 1991;19(12):1533-1539.

Association of Cardiovascular Trial Registration With Positive Study Findings: Epidemiological Study of Randomized Trials (ESORT)

Trial registration has been proposed to reduce selective publication and outcome reporting, thereby increasing accountability in the conduct of research.[1] Since 2005, policy makers, journal editors, and research funders have increasingly endorsed and mandated trial registration.[2] However, evidence to support the proposed benefits of trial registration is lacking. Analysis of a select group of randomized trials (RTs) in oncology found that registered and unregistered trials were equally likely to reach conclusions favoring new oncology drugs.[3] We conducted a cross-sectional analysis of published cardiovascular RTs to compare RTs reported as registered with those not reported as registered.

Editor's Note page 307

Methods | An RT was eligible for analysis if it was published on PubMed in December 2012 and focused on a cardiovascular disease, as defined by the *International Classification of Diseases*. Our research group[4] has previously reported a detailed description of the process. Briefly, 2 reviewers independently screened all abstracts and full texts. No language restrictions were applied. Study characteristics and methodological characteristics (**Table 1**) were extracted in duplicate. The International Committee of Medical Journal Editors definition of trial registration was used.[1] The primary outcome was the reported study findings for each trial, categorized as significant positive, nonsignificant, or significant negative. Trials not reported as registered were searched for registry information using the World Health Organization Trials Registry Platform. The χ^2 test, Fisher exact test, and Wilcoxon rank-sum test were applied as appropriate for analysis.

Results | We identified 4190 abstracts of possible reports of RTs, among which 191 cardiovascular RTs were identified. Of these, 86 (45.0%) were reported as registered. Registry information was found for 6 (5.7%) of the 105 trials not reported as registered. Trials reported as registered (median sample size, 111; interquartile range [IQR], 49-360) were larger than those not reported as registered (median sample size, 59; IQR, 24-106) ($P < .001$). Trials reported as registered were also more likely to report a power calculation, explicitly define the primary outcome, and report attrition among study participants. Specific data are reported for all characteristics in **Table 2**; $P < .05$ for all comparison.