Evaluating a Program to Lower Prescription Opioid Doses for Patients With Chronic Pain

Michael Von Korff¹; Sascha Dublin, MD, PhD¹; Ryan Hansen, PhD, PharmD²; Evette Ludman, PhD¹; Michael Parchman, MD, MPH¹; Katie Saunders, JD¹; Karen Sherman, PhD¹; Susan Shortreed, PhD¹; Manu Thakral, PhD, NP¹; Rod Walker, MS¹; Megan Addis, BA¹; Patient Advisory Committee: Catherine Cartwright, Penney Cowan, David Duhrkoop, Mariann Farrell, Ada Giudice Tompson, Kathryn Guthrie, Catherine Lippincott, Max Sokolnicki, Betts Tully

AFFILIATIONS:

¹Kaiser Permanente Washington Health Research Institute, Washington, DC
²University of Washington, Seattle

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# TABLE OF CONTENTS

## ABSTRACT

- Care of Chronic Pain—A National Challenge ......................................................... 8
- Lack of Controlled Research and Gaps in Knowledge ................................................. 9
- The Need for Evidence Relevant to CDC Opioid Guideline Implementation ............. 12

## BACKGROUND

- Care of Chronic Pain—A National Challenge ......................................................... 8
- Lack of Controlled Research and Gaps in Knowledge ................................................. 9
- The Need for Evidence Relevant to CDC Opioid Guideline Implementation ............. 12

## PARTICIPATION OF PATIENTS AND OTHER STAKEHOLDERS IN THE DESIGN AND CONDUCT OF RESEARCH AND DISSEMINATION ................................................................. 14

- Patient Advisory Committee .................................................................................. 14
- Patient-defined Values Guiding the Evaluation ........................................................ 14
  - Figure 1. Care study values defined by the patient advisory committee .................. 15
- Patient Advisory Committee Guidance ................................................................... 15

## METHODS

- Study Setting .............................................................................................................. 16
  - Figure 2. Evaluation design and timeline: Interrupted time series for opioid-related adverse event outcomes ................................................................. 17
  - Figure 3. Evaluation design and timeline: Telephone survey of long-term COT patients (after-only) Patient-reported Outcomes: Pain & Rx Opioid Use Disorder ........................................ 19
- Analytic Methods for Survey Data .......................................................................... 29
- Implementation of the COT Risk Reduction Initiatives .......................................... 30
  - Figure 4. GH-IGP risk reduction initiatives ............................................................. 32
  - Figure 5. Trends in number of COT patients in the intervention (GH-IGP) and control (GH-CC) ......................................................................................................................... 34
  - Figure 6A. Trends in average daily MED among COT patients ................................. 36
  - Figure 6B. Estimated average change per year (with 95% CI) in the mean daily milligrams of MED among COT patients by setting and period .............................................. 36
  - Figure 7. Trends in percentage of COT patients with average daily dose ≥ 120 mg MED ................................................................................................................................. 37
  - Figure 8. Trends in percentage of high COT dose among GH-IGP COT patients by risk factors ......................................................................................................................... 38
  - Figure 9A. Trends in percentage of COT patients with chronic sedative use (45+ days’ supply) ................................................................................................................................. 39
  - Figure 9B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients with concurrent chronic sedative use by setting and period ................. 40
RESULTS ................................................................................................................................ 43

Characteristics of COT Patients in Intervention and Control Settings ..................................... 43

Table 1. COT Patient Characteristics for Individuals Included in the Interrupted Time Series Analyses (as of each patient’s first COT eligibility quarter during the study period) .................................................................................. 45

Table 2. Characteristics of COT Patient Survey Respondents Measured at the Time of the Survey Interview in the Intervention (GH-IGP) and Control (GH-CC) Clinics .................................................................................................................. 47

Adverse Event Rates by Study Period .......................................................................................... 49

Figure 13A. Overdose rate per 100 person-years (with 95% CI) among COT patients .......................................................... 50

Figure 13B. Motor vehicle crash rate per 100 person-years (with 95% CI) among COT patients .................................................................................................................. 51

Figure 13C. Medically attended injury rate per 100 person-years (with 95% CI) among COT patients .................................................................................................................. 51

How This Research Differs From Previous Evaluations ............................................................... 52

Interrupted Time Series Analyses for Adverse Events From 2006 Through 2014 ................. 52

Figure 14A. Percentage of COT patients with an opioid overdose (fatal or nonfatal) by quarter (2006-2014) .................................................................................................................. 53

Figure 14B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients experiencing an overdose by setting and period .................................................................................................................. 54

Figure 15. Percentage of all enrollees with an opioid overdose (fatal or nonfatal) by quarter (2006-2014) .................................................................................................................. 55

Figure 16. Relative risk of opioid overdose by average daily MED (compared to former COT patients no longer using opioids) .................................................................................................................. 56

Figure 17A. Percentage of COT patients with motor vehicle crash by quarter (2006-2014) .................................................................................................................. 57

Figure 17B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients experiencing a motor vehicle crash by setting and period .................................................................................................................. 58

Figure 18. Relative risk of motor vehicle crash by average daily MED (compared to former COT patients no longer using opioids) .................................................................................................................. 59
Figure 19A. Percentage of COT patients with medically attended injuries (2006-2014) ............................................................................................................................... 60

Figure 19B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients experiencing a medically attended injury by setting and period ........................................................................................................... 61

Figure 20. Relative risk of medically attended injury by average daily MED (compared with former COD patients no longer using opioids) ................................................................. 61

Survey Results for Patient-reported Outcomes ............................................................................................................................... 62

Figure 21. COT patient survey dispositions ............................................................................................................................... 62

Figure 22. Survey response rates by variables measured with EHR data ................................................................. 64

Figure 23. PEG pain severity and interference ratings (0-10) ............................................................................................................................... 65

Figure 24. PEG pain severity ratings (0-10) after implementation of dose reduction and RSM initiatives ............................................................................................................................... 65

Figure 25. PEG pain interference rating (0-10) after implementation of dose reduction and RSM initiatives ............................................................................................................................... 66

Figure 26. Perceived helpfulness of opioids after implementation of dose reduction and RSM initiatives ............................................................................................................................... 67

Figure 27. Perceived bothersomeness of opioids after implementation of dose reduction and RSM initiatives ............................................................................................................................... 68

Figure 28. Percentage of COT patients with DSM-5 prescription opioid use disorder after full implementation of dose reduction and RSM initiatives for 4+ years ............................................................................................................................... 68

Figure 29. Most common prescription opioid use disorder symptoms by prescription opioid use disorder status ............................................................................................................................... 69

Figure 30. Patient rating: “I trust my doctor’s judgment in managing my opiate pain medicine.” ........................................................................................................................................... 70

Figure 31. Patient rating: “I feel my doctor trusts me in how I manage my opiate pain medicine.” ........................................................................................................................................... 71

Figure 32. Patient rating: “I sometimes worry that my doctor will stop prescribing my opiate pain medicine.” ........................................................................................................................................... 71

Figure 33. Patient rating: “My doctor, pharmacist, or other providers made sure I was well informed about potential problems with opiate pain medicines.” ........................................................................................................................................... 72

Expanded Dialogue With Patient and Family Stakeholders ............................................................................................................................... 72

Figure 34. Characteristics of patient/family stakeholder participants ........................................................................................................................................... 73

Figure 35. Online responses from patient/family stakeholders: Preference for clinics with differing approaches to COT management before and after learning about evaluation results ........................................................................................................................................... 74
DISCUSSION ................................................................. 76
Context ........................................................................... 76
Study Results in Context ..................................................... 76
Implementation of Study Results .......................................... 79

Figure 38. Key Observations from the Workshop on Chronic Pain Management and Opioids, April 21, 2017 ......................................................... 81

Generalizability .................................................................. 81
Subpopulation Considerations .............................................. 82
Limitations ........................................................................ 82
Future Research ................................................................ 85

CONCLUSIONS ................................................................ 87
REFERENCES .................................................................... 90
ACKNOWLEDGMENTS .................................................... 100
APPENDIX ...................................................................... 101
ABSTRACT

Background: In 2007, Washington State released a guideline for chronic opioid therapy (COT) that recommended a ceiling dose. In 2010, the guideline was enhanced with recommendations for risk stratification and monitoring (RSM) and enacted as state law. In response to the guideline, Group Health’s Integrated Group Practice (GH-IGP; intervention setting) reduced opioid doses for COT patients beginning in 2007. In October 2010, the practice implemented a multifaceted RSM initiative. Group Health Contracted Care practices (GH-CC; control setting) did not implement either organized dose reduction or RSM initiatives. The marked differences in COT management between intervention and control settings permitted a natural experiment in which relevant outcomes among COT patients in the 2 care settings were compared, providing the first controlled evaluation of COT dose reduction and RSM initiatives.

Objectives: This research evaluated the effects of the GH-IGP dose reduction and RSM initiatives on patient outcomes by comparing intervention setting patients with those from the GH-CC control setting.

Methods: We used quarterly time series data from 2006 through mid-2014 to compare trends in opioid-relevant adverse outcomes (opioid overdose, medically attended injuries, motor vehicle crashes) among COT patients in intervention (N = 22,673) and control (N = 8,469) settings. We compared trends among COT patients in the 2 settings over 3 periods:

2. Dose reduction phase (2008-September 2010)
3. RSM phase (October 2010-June 2014)

In 2014-2015, we interviewed 935 intervention and 653 control COT patients (persons aged 18 years or older with chronic opioid use in each of the previous 4 quarters) who had been exposed to differences in COT management for at least 1 year in order to compare patient-reported outcomes (eg, pain ratings, perceived effectiveness of opioids, prescription opioid use disorder) between intervention and control settings.

Implementation: Starting in 2008, intervention COT patients showed substantially greater reductions in opioid dose than control COT patients. These differences were sustained through 2014. Starting in October 2010, the use of urine drug tests and COT care plans increased substantially among intervention COT patients but not among control patients.

Results: During the dose reduction phase (2008-2010), changes in overdose rates did not differ significantly between intervention and control COT patients. But among intervention COT patients, opioid overdose rates declined significantly during the dose reduction phase, a change of –17% per year (95% CI: –1% to –30%). Concurrently, among control COT patients the rates of opioid overdose did not decline significantly, a change of –2% per year (95% CI: –30% to +39%). After RSM initiatives were implemented, no further decline in overdose rates in intervention or control settings was observed. Overdose rates in the entire population, regardless of opioid use, did not change over the study period in either the intervention or control setting. Neither
GH-IGP dose reduction nor RSM initiatives were associated with changes in rates of motor vehicle crashes or rates of medically attended injuries among COT patients in the intervention setting.

Interviews with COT patients in 2014-2015, after sustained implementation of dose reduction and RSM initiatives for more than 4 years, showed no differences between intervention and control patients in pain severity, pain-related interference with activities, or ratings of opioid helpfulness, and no difference in the prevalence of prescription opioid use disorder. More than 20% of COT patients met diagnostic criteria for prescription opioid use disorder. While COT patients in both settings typically gave positive ratings to physician collaboration and trust regarding opioid management, these ratings were somewhat less favorable among intervention patients than among controls.

Conclusions: Whether the dose reduction initiative reduced rates of opioid overdose is uncertain. The difference between intervention and control settings in the change in overdose rate was nonsignificant, but the reduction in overdose rate in the intervention setting was significant. The reasons for this inconsistency are unclear. In any case, the practice-level population overdose rate did not show a measurable change during the dose reduction period in either setting. Other adverse events (motor vehicle crashes and medically attended injuries) were not affected by COT dose reduction. Greater reductions in opioid dose and opioid therapy prescribing may have been necessary to yield reductions in adverse event rates. The RSM initiatives did not influence the rates for opioid overdose, motor vehicle crashes, or medically attended injuries. Patient ratings of pain and opioid effectiveness were not adversely affected by reductions in opioid dose, suggesting that COT dose reduction did not have large deleterious effects on COT patients’ pain outcomes. The RSM initiatives did not enhance patient safety or reduce prescription opioid addiction, although health care teams perceived fewer difficulties in COT management.

Limitations: The control population was much smaller than the intervention population, which limited our ability to compare opioid overdose trends. It was possible to compare patient-reported outcomes only after sustained (4 or more years) implementation of the initiatives in the intervention setting. While large and sustained differences were seen between the intervention and control settings in opioid dose, use of COT care plans, and use of urine drug tests among COT patients, the state guideline may have influenced COT management in the control setting. This evaluation assessed the incremental effects of the health plan initiatives relative to care settings influenced only by the state guideline.
BACKGROUND

Care of Chronic Pain—A National Challenge

An estimated 60 million American adults (25%) have moderate to severe chronic pain, and annual US health care costs attributable to chronic pain are $560 billion to $635 billion.\(^1\) Twenty-five million Americans (10% of adults) have substantial social role disability because of chronic pain,\(^2\) and 7 in 10 say that pain management should be one of the medical community’s top priorities (16%) or at least a high priority (55%).\(^3\)

One option for chronic pain care—the use of opioids—is mired in controversy, reflecting deficiencies in scientific evidence regarding their effectiveness and safety.\(^4\)\(^-\)\(^8\) Currently, 5 to 8 million American adults receive chronic opioid therapy (COT) for chronic pain.\(^9\)\(^,\)\(^10\) Our research addressed the needs and concerns of the millions of Americans who consider opioids for long-term management of chronic pain, as well as those who currently receive COT. These individuals expect reliable information in order to weigh the potential risks of opioids against the perceived benefits, and they expect clinicians who prescribe opioids to minimize the risks of serious adverse consequences, including addiction, overdose, and other potentially serious adverse effects.\(^11\) A recent pragmatic randomized trial with 1-year follow-up found that chronic pain patients who received opioids had somewhat less favorable long-term pain outcomes than those who received nonopioid alternatives.\(^11\)\(^4\) This finding supports a growing national consensus that COT has been overprescribed for long-term chronic pain management. Short-term trials of opioids for chronic pain report a one-third reduction in pain intensity and less robust benefits for functioning.\(^8\) As a recent review concluded, “Existing evidence suggests that analgesic efficacy, although initially good, is not always sustained during continuous and long-term opioid therapy (months to years).”\(^22\) Short-term COT benefits appear modest on average, with new randomized trial evidence that any short-term benefits are not typically sustained over the long term, while risks include death and addiction. Severe chronic pain leads some patients and their clinicians to conclude that partial pain relief outweighs the seemingly remote risks of addiction and overdose. Unfortunately, universal precautions, such as risk stratification and monitoring (RSM), intended to reduce opioid risks\(^23\)\(^,\)\(^24\) are inconsistently implemented, and
the effectiveness of RSM for reducing COT risks has never been evaluated by controlled research. In the words of the former director of the Centers for Disease Control and Prevention (CDC), “Prescription opioid abuse . . . is a major public health problem and it is getting worse and getting worse rapidly.”68 Health care organizations nationwide are seeking guidance on how to minimize opioid-related risks and harms.

Since 1990, life expectancy among white Americans with low education has dropped by 4 years,12 an unprecedented decline attributable in large measure to increased rates of fatal prescription drug overdose.13 Adverse effects of opioids affect not only individuals using prescription drugs nonmedically but also the millions of COT patients who receive opioids from physicians. In 2011, the White House Office of National Drug Control Policy declared an epidemic of prescription drug overdose and abuse, stating, “Prescription drug misuse and abuse is a major public health and public safety crisis. As a nation, we must take urgent action to ensure the appropriate balance between the benefits of these medications and the risks they pose.”14

COT use for chronic pain has quadrupled since the 1980s.15 As opioid prescribing increased, fatal overdoses involving opioid analgesics increased 4-fold from 1999 to 2010, to more than 16 500.16,17 Hospitalizations for prescription opioid overdose doubled between 1999 and 2006.18 Estimates vary,19,20 but the most rigorous study found that more than 90% of opioid overdose decedents had obtained opioids from a physician by prescription in the year before overdose death.21

Lack of Controlled Research and Gaps in Knowledge

The opioid dose received by a COT patient affects the risk of adverse events.11 Direct risks of opioids for COT patients increase with dose, including risks of drug overdose,25-27 serious fractures,28,29 depression,31 motor vehicle accidents,30-33 and other adverse health effects.11 Community risks also rise with opioid dose. Prescription opioids used nonmedically are most often obtained from family or friends or from the family medicine cabinet.34 The amount of opioid medication available for diversion in the community is affected by the
prevalence of high-dose COT: More than 60% of all legally prescribed morphine equivalents are dispensed to COT patients on higher-dose regimens.4

For these reasons, reducing opioid dose could have benefits for COT patients and for community health. Clinical guidelines have always urged care in prescribing opioids, but guidance regarding COT dosage has been contentious.35,36 Some experts have recommended a low-to-moderate dose ceiling, while others have advocated increasing a patient’s opioid dose until pain is controlled, with no dose ceiling.7,36 We do not know if these 2 distinctly different COT dosing strategies result in long-term differences in pain outcomes for patients, and we have no evidence from long-term controlled trials regarding differences in COT effectiveness and safety by dose.8

This study assessed whether reducing opioid dose among COT patients reduced the risk for serious adverse events (overdose, fractures, motor vehicle crashes) as well as the risk of prescription opioid use disorder. Before this evaluation, no controlled studies had been conducted to assess the effect of initiatives to lower opioid doses among COT patients on the risks of opioid overdose, other dose-related adverse events, or rates of prescription opioid use disorder. Before-and-after studies in states that have lowered opioid doses or reduced opioid prescribing have shown reduced numbers of fatal opioid overdoses,108-110 but there are no studies with a control group and none that have assessed adverse effects other than fatal opioid overdose.

Population-based surveys of people with chronic pain have found, after adjusting for potential confounders, that COT patients on higher-dose regimens have poorer functional status and lower quality of life than patients on low-dose regimens.37-41 Cohort studies of patients receiving workers’ compensation found, after adjusting for confounders, that patients who used opioids were delayed in returning to work compared with patients who did not use opioids, and that patients who received higher-dose COT were delayed returning to work compared with patients receiving lower doses.42-46 COT patients receiving rehabilitative services who were withdrawn from opioids have improved pain and function.47-54 These results could be explained by adverse selection, as COT patients with unfavorable prognostic indicators are
more likely to use opioids long term and more likely to escalate dose. One recent randomized pilot test (N = 35) found that COT patients whose opioid dose was tapered had more favorable pain outcomes at long-term follow-up than control patients who were not tapered. However, no controlled studies have evaluated the effects of health plan COT dose reduction initiatives on pain outcomes among COT patients.

Guidelines for COT management recommend close monitoring and periodic use of urine drug screening, but COT monitoring in community practice is typically lax. Krebs et al found that of 7 guideline-recommended COT monitoring practices, the mean number documented in a 6-month period was 1.7, with pain reassessment being the most common. Only 11% of COT patients had an opioid treatment agreement documented in their medical record. Starrels et al found that only 8% of COT patients had urine drug screening and only half had regular monitoring visits. Morasco et al also found low rates of urine drug screening. No controlled research has determined whether enhanced COT monitoring reduces the risk of opioid abuse, overdose, or other potential adverse outcomes. Controlled research is needed to determine whether closer monitoring of COT patients can lower the risk of adverse health effects.

A significant gap in knowledge is that the long-term safety of COT has not been established. As of 2011, randomized trials evaluating COT add up to only 1500 person-years of observation, compared with hundreds of thousands of person-years for trials of antihypertensive agents, statins, and nonsteroidal inflammatory drugs. The person-years of observation in COT randomized trials is too small by a wide margin to assess the risk of important adverse effects such as overdose and addiction. Controlled observational studies using electronic health record (EHR) data for large populations of COT patients (such as this evaluation) provide a means of addressing this knowledge gap.

An action plan from the White House Office of National Drug Control Policy to reduce prescription drug abuse proposed risk mitigation strategies that included education, monitoring, proper medication disposal, and enforcement. Unfortunately, evidence regarding these strategies is limited. The US Food and Drug Administration (FDA) proposed a Risk Evaluation and Mitigation Strategy for long-acting opioids, but opinions vary on whether the
strategy is likely to reduce opioid-related morbidity and mortality. Our research addressed these gaps by determining whether implementation of an RSM initiative for COT patients lowered the risks of opioid abuse, overdose, and other potential adverse effects.

The Need for Evidence Relevant to CDC Opioid Guideline Implementation

In March 2016, the CDC disseminated a national guideline that recommended, among other things, a COT dose ceiling and stepped-up monitoring of opioid therapy guided by assessment of patient risk factors. Health care organizations nationwide are considering how to implement the CDC guideline. They need information on which of the multifaceted CDC recommendations should be emphasized and how they should be implemented to reduce opioid-related risks and harms. Unfortunately, as established by the evidence review that accompanied the release of the CDC guideline, no controlled studies of COT guideline implementation are available to direct their efforts. The structured review that informed the CDC guideline concluded, “No study evaluated the effectiveness of risk mitigation strategies for improving outcomes related to overdose, addiction, abuse, or misuse.”

In 2007, almost a decade before the CDC guideline was released, Washington State was the first to disseminate a COT guideline with a recommended dose ceiling. In 2010, a revised version of the Washington State guideline (http://www.agencymed directors.wa.gov/guidelines.asp), including recommendations for RSM, was enacted into state law. Group Health (now Kaiser Permanente Washington) implemented opioid dose reduction efforts in its group practice clinics (intervention setting) starting in 2007, almost a decade before the CDC opioid guideline recommended a dose ceiling. In October 2010, 6 years before the release of the CDC guideline, Group Health (GH) implemented a multifaceted RSM initiative in its integrated group practice clinics (IGP; the intervention setting). These initiatives were not implemented for enrollees who received opioid therapy in Group Health’s contracted care clinics (GH-CC; the control setting). Many recommendations embodied in the Washington State guideline foreshadowed the recommendations in the 2016 CDC opioid prescribing guideline. Because the GH-IGP practices achieved sustained implementation of key elements of the Washington State guideline while GH-CC practices with
similar COT patients did not implement the guideline, it is possible to compare the 2 sets of COT patients in a natural experiment: a controlled evaluation of the effects of guideline implementation. The results of this natural experiment are relevant to current efforts by health care organizations nationwide to implement the CDC guideline.

The Group Health COT risk reduction initiative received national attention with an overview in *Health Affairs* and was selected for dissemination through the Agency for Healthcare Research and Quality (AHRQ)’s Innovation Exchange program. In November 2012, the Alliance for Community Health Plans cited this initiative as a response to prescription opioid misuse, and elements of it were incorporated into an implementation guide and toolkit developed for disseminating best practices (the Six Building Blocks model for improved opioid management).

This evaluation provides evidence regarding the long-term effects of the COT dose reduction and RSM initiatives. Because the initiatives were sustained over the long term in the intervention setting, differences in opioid dose and COT monitoring between the intervention and control settings were used to evaluate the effects on key patient outcomes of dose reduction and stepped-up COT monitoring.
PARTICIPATION OF PATIENTS AND OTHER STAKEHOLDERS

Patient Advisory Committee

This study was guided by a patient advisory committee that included 5 persons from the American Chronic Pain Association (ACPA), 2 persons from organizations seeking to reduce the overprescribing of opioids, and 2 volunteer COT patients from GH-IGP who had been study subjects in previous research on chronic pain and opioids. The committee members were selected on the basis of their ability to articulate their point of view, work effectively in a group, and listen respectfully to those who might hold different opinions about the topics being discussed. One member of the patient advisory committee, Penny Cowan, was the director of the ACPA and was affected by chronic pain herself. The committee held regular 90-minute telephone conferences (usually monthly) over the course of the evaluation. Each member received a $1000 honorarium for each year of participation, and the committee chair received $3000. All committee members remained active throughout the study.

An in-person meeting was held in Seattle, Washington, at the beginning of the study, and a workshop was held in Seattle at the conclusion of the evaluation, with clinicians and experts in chronic pain care and opioids. The patient advisory committee members were active and vocal participants in the workshop. The appendix of this report includes the opening statements made by 2 committee members at the workshop; they exemplify the diversity of opinions and experiences represented by members of the committee.

Patient-defined Values Guiding the Evaluation

The patient advisory committee defined a set of values for patient-centered care for chronic pain that informed the conduct and reporting of this research; these values included safety, respect, autonomy, compassion, knowledge, and teamwork (Figure 1). Over the course of the study, the patient advisory committee made critically important contributions to the research, including the following:
Figure 1. Care study values defined by the patient advisory committee

Patient Advisory Committee Guidance

The patient advisory committee reviewed the study interview before it was finalized, reviewed analysis plans before data analyses were implemented, reviewed and discussed each of the papers reporting study results, and discussed key issues that arose over the course of the study. Members of the research team participated in the committee meetings when appropriate. The patient advisory committee was chaired by David Duhrkoop. Michael Von Korff (principal investigator) and Megan Addis (project manager) participated in all committee meetings, and Evette Ludman (who studied the process of involving patients in the evaluation) participated in most meetings. Attendance at patient advisory committee meetings over the course of the study consistently exceeded 90%.
METHODS

Study Setting

This research was conducted at Group Health (GH), an insurer and integrated health care delivery system in Washington State, which became part of Kaiser Permanente in 2017 (after the period covered by the study). The study assessed the implementation of dose reduction and RSM initiatives in GH integrated group practice settings. It did not evaluate the Washington State COT guideline per se, as the guideline applied to both the intervention setting (which took steps to implement it) and the control setting (which did not).

Intervention and Control Settings

GH provided care in both integrated group practice (IGP) and contracted care (CC) settings. Approximately two-thirds of GH’s enrollees received care delivered by providers in the IGP at GH’s own facilities, while the remaining enrollees received care from community clinicians in diverse clinical settings not operated by GH. Research study procedures for analyses using electronic health care data were approved by the GH Human Subjects Review Committee with a waiver of individual informed consent.

Time Series Evaluation Design Overview

We used quarterly time series data from 2006 through mid-2014 to compare trends in opioid-relevant adverse outcomes (opioid overdose, medically attended injuries, motor vehicle crashes) among COT patients in intervention (N = 22,673) and control (N = 8,469) settings (Figure 2). We compared trends among COT patients in intervention and control settings over 3 periods:

2. Dose reduction period (2008-September 2010)
3. RSM period (October 2010-June 2014)
Figure 2. Evaluation design and timeline: Interrupted time series for opioid-related adverse event outcomes

The interrupted time series design compared trends in opioid-relevant adverse event rates among persons who were receiving COT at the time of the adverse event. Because some patients initiated, discontinued, and reinitiated COT, we did not follow a fixed cohort over time. That is, we compared adverse event rates among persons who currently met the GH-IGP operational definition of COT—the patients targeted by the dose reduction and RSM initiatives as implemented by the IGP. The interrupted time series evaluation compared adverse event rates before, during, and after the dose reduction and RSM initiatives were implemented in dynamic (changing over time) sets of COT patients. We compared changes in adverse event rates in the intervention and control settings during baseline, dose reduction, and RSM periods, and between the intervention and control settings during each of these periods. Comparison of rates of change in adverse event rates between the intervention and control settings during the dose reduction and the RSM periods were defined as primary for assessing effects of the initiatives.
Cross-sectional (after-only) Survey Design Overview

In 2014-2015, we interviewed 935 intervention and 653 control patients who had been exposed to intervention versus control setting differences in COT management for at least a year in order to compare patient-reported outcomes (eg, pain ratings, perceived effectiveness of opioids, prescription opioid use disorder) between the settings (Figure 3). The survey analyses were after-only, reflecting the accumulated effects of the initiatives on patients who had been receiving COT for at least a year before being sampled for the survey. Since this evaluation was not funded by PCORI until 2014, it was not possible to conduct surveys before implementation of the initiatives, nor was it possible to conduct a longitudinal panel survey of COT patients while the initiatives were being implemented.

Opioid Dose and Risk Reduction Initiatives

In April 2007, the State of Washington published a COT guideline; in 2010 the guideline was enacted into law.36 Shortly after initial dissemination of the guideline in 2007, GH implemented its own initiative to change COT prescribing in primary care, with emphasis on discouraging dose escalation and reducing high-dose prescribing for COT patients.76 In September 2010, a COT risk stratification and monitoring initiative was implemented in the GH-IGP.73 The implementation of these initiatives is described in detail under Implementation of the COT Risk Reduction Initiatives.

While the state guideline and legislation could potentially influence management of COT patients in all health care settings in Washington, GH’s initial opioid dose reduction initiative and its later, more extensive RSM initiative were implemented only in the IGP, not in the CC settings. This study took advantage of this natural experiment to investigate differences in relevant outcomes between patients who received care in the IGP and those who received care in the CC. Under “Summary of Implementation of Dose Reduction and RSM Initiatives,” we show that large, clinically significant differences in opioid dose trends between intervention and control settings emerged in 2008 and were sustained through 2014. We also establish that large, clinically significant differences in COT monitoring emerged starting in October 2010; these differences were also sustained. Before we analyzed trends in the study outcomes, we set
the start of the dose reduction and RSM periods to coincide with clinically important diverging trends in opioid dose and RSM process measures between the intervention and control settings. During the baseline period, trends in opioid dose and COT monitoring did not differ significantly between the 2 settings, even though the Washington State guideline was released in the last year of the baseline period (2007), and GH-IGP took initial steps to implement its dose reduction initiative.

Figure 3. Evaluation design and timeline: Telephone survey of long-term COT patients (after-only) Patient-reported Outcomes: Pain & Rx Opioid Use Disorder

Implementation Process Measures

Process measures for guideline implementation included temporal changes in the average daily morphine equivalent dose (MED) received by each patient and the proportion of patients receiving average daily doses of ≥ 50 mg MED and ≥ 120 mg MED (potentially important dose thresholds). We based these measures on GH automated pharmacy data and calculated them in each 3-month period (quarter) of the study. To calculate average daily dose, we added the morphine equivalents for all prescriptions dispensed during the roughly 90 days of a given quarter and divided by 90, using methods and conversion factors described in
previous work\textsuperscript{77-79} and accounting for prescription run-out dates that extend beyond the given quarter or extend into the given quarter from a fill in a previous quarter. We also compared the percentage of intervention and control patients who were chronic users of both opioids and sedatives in the same quarter, although this topic was not targeted by either the Washington State guideline or the GH-IGP initiatives.

In the patient survey conducted in 2014-2015, we asked COT patients if they had received all their opioid prescriptions in the previous year through their GH insurance benefits. In both the intervention and control settings, 96\% of patients reported receiving all their opioid prescriptions through their GH insurance benefits. This suggests that data capture of opioid prescriptions filled was likely to be very high in the patient population eligible for this research.

In preliminary analyses, we determined that divergent trends in COT dose between intervention and control settings were largely due to lower rates of dose escalation and higher rates of partial tapers among GH-IGP patients compared with GH-CC patients. No sustained differences in rates of COT discontinuation existed between the intervention and control settings.

We used the percentage of patients who received at least 1 urine drug test in a year to compare COT monitoring in the intervention and control settings. We also report the percentage of patients with a COT care plan documented in their EHR in the intervention setting. No flag for a COT care plan existed in the control setting, so it was not possible to compare differences in this indicator. However, it is unlikely that many COT care plans were developed for patients in the control setting in the absence of an initiative to ensure that all COT patients had such a plan.\textsuperscript{64,65}

**Adverse Event Outcome Measures**

Adverse event outcome measures included (1) rates of motor vehicle crashes, an outcome associated with opioid use in other studies\textsuperscript{80-82}; (2) rates of medically attended injuries (fractures, concussions, and other head injuries) previously found to be associated with opioid use\textsuperscript{83-85}; and (3) rates of opioid overdose (fatal and nonfatal), a risk that increases markedly
with opioid dose.\textsuperscript{86-89} We estimated rates of these adverse events per person receiving COT in the quarter prior to the study quarter in which the adverse event occurred. We determined COT status for the quarter prior to rather than concurrent with the adverse event, because such adverse events (overdose, motor vehicle crash, medically attended injuries) could potentially increase or decrease opioid use during the study quarter in which they took place (ie, after the event).

Police-reported motor vehicle crash information was provided by the Washington Department of Transportation and linked to study subjects through the use of GH membership files and a publicly available algorithm for converting names and dates of birth to drivers’ license numbers.\textsuperscript{90,91} We identified medically attended injuries from GH’s electronic data systems using combinations of \textit{ICD-9 (International Classification of Diseases, Ninth Revision)} diagnosis codes from inpatient, ambulatory, and emergency department encounters and the presence of X-rays (if any), with algorithms developed and tested through a limited medical record review that established positive predictive value of greater than 80\% for each of the conditions used in the analyses. We based the types of injuries and encounter settings included on input from the patient advisory committee, which played a key part in recommending that injuries other than fractures and injuries treated in outpatient settings be included, owing to the impact such injuries can have on a person’s quality of life. We identified opioid overdoses based on validated methods\textsuperscript{92} using diagnosis codes from GH electronic health records for inpatient care, emergency department, urgent care, and observation unit encounters, and from Washington State death records. We ascertained opioid overdoses and medically attended injuries for patients from the control setting through claims submitted for reimbursement of health care services. While it is possible that ascertainment of these adverse events was more complete in the intervention setting than in the control setting, we found that the rates of opioid overdose and medically attended injury were similar among COT patients in both settings during the baseline period. The rates of motor vehicle crashes were also similar among intervention and control patients during the baseline period. The similarity in the rates of all 3 adverse events before the risk reduction initiatives were implemented suggests baseline comparability of the 2 populations despite some differences in population characteristics and
methods of data capture. The time series design controls for differences in population characteristics and data capture by measuring rates of adverse events before, during, and after the dose reduction and RSM initiatives were implemented.

Interrupted Time Series Analyses

To assess differences in these outcomes in the 2 settings, we performed a nonconcurrent (retrospective) cohort study of COT patients analyzed using an interrupted time series design from 2006 through 2014. First we divided the study period into 3 intervention phases: (1) a baseline period from 2006 through 2007 that predated sustained differences in COT management between the intervention and control settings; (2) a dose reduction period from 2008 through September 2010, during which the intervention setting achieved much larger reductions than the control setting in opioid dose among COT patients; and (3) an RSM period from October 2010 through June 2014, during which the intervention setting achieved much larger increases than the control setting in monitoring (eg, use of urine drug tests) among COT patients.

The rationale for starting the dose reduction period on January 1, 2008, was that preliminary analyses reported in the grant proposal indicated that divergent trends in opioid dose emerged and were sustained between the intervention and control settings beginning in 2008. Our evaluation sought to assess whether trends in adverse outcome rates differed between COT patients in practices that lowered opioid dose compared with patients in practices that did not reduce opioid dose to the same extent. By placing the start of the dose reduction period at 2008 (rather than mid-2007, when the state guideline was initially disseminated), we assumed that one-time transient effects of guideline release in both intervention and control settings would have dissipated before the beginning of the GH-IGP dose reduction period. The 2008 start date also provided lag time for implementation of the GH-IGP dose reduction initiatives to gain momentum. We did not expect differences in trends in opioid dose to be sustained between intervention and control settings immediately upon guideline release and initial implementation of the dose reduction initiative. Upon preliminary inspection of dose trends data, we found that the baseline period was characterized by modest
but statistically significant reductions in opioid dose among patients in both intervention and control settings. After January 1, 2008, we observed large reductions in opioid dose among patients in the intervention setting but not in the control setting. We saw small, statistically significant reductions in COT dose in both intervention and control settings in the RSM period, but the large differences in dose between the 2 settings that developed during the dose reduction period were sustained until the end of the study.

Analyses of the RSM initiative showed that large changes in rates of urine drug testing and documentation of COT care plans started in October 2010 and were sustained through the end of the study.

We made decisions about boundaries for dose reduction and RSM periods after preliminary analyses of process measures data but before analyses of adverse outcome data. Our intent was to maximize trend differences in dose reduction and RSM process measures to maximize opportunities to observe outcome differences if changes in COT dose and management influenced patient outcomes.

Within each 3-month window (quarter) of the study period, we identified all GH members in the IGP and CC who (1) were aged ≥ 18 years, (2) had been enrolled in the health plan for at least a year, and (3) were recipients of ≥ 70 days’ supply of opioids in the given quarter (a threshold for defining a COT patient consistent with GH’s operational definition used to target the GH-IGP initiatives). Because GH initiatives focused on COT for noncancer pain, we excluded person-quarters from patients with multiple cancer diagnoses and those who were receiving hospice care. Among eligible COT patients in each quarter, we computed the opioid prescribing process measures in the quarter itself and the 3 adverse event outcomes in the subsequent quarter.

We used a quarter (3-month) interval to measure opioid use and rates of adverse events because that was the period used to define COT (a 70-day supply in 90 days) and because it struck a balance between yielding sufficient numbers of adverse events for stable rate estimation and characterizing the time trends in adverse event rates.
The rationale for measuring the adverse event in the quarter following the quarter used to determine COT status and opioid dose is that the adverse event could alter COT status and dose if it were measured in the same quarter. For the medically attended injury outcome only, we also required a wash-out period of 18 months after each type of injury before an eligible COT patient could experience another injury event of that type, to guard against misclassifying follow-up care for the initial injury as a new injury.

We then estimated and compared temporal changes in the outcomes of interest between COT patients who received care in the IGP and those who received care in CCs across the 3 periods. We used regression models: logistic or modified Poisson regression for binary outcomes.95 We used linear regression for comparing continuous measures of opioid dose. We included main effects in these models for health plan setting (IGP versus CC) and for calendar time measured quarterly. We used linear splines96 with knots at the first quarter of 2008 and the fourth quarter of 2010 (ie, the times separating the 3 periods), and interactions between calendar time and health plan setting. These interactions allowed for estimation of different temporal trends in the adverse outcomes within the 2 populations across the 3 periods. Models also included covariate adjustment terms for demographic and health characteristics collected from GH electronic enrollment and health data.

The following covariates were controlled in multivariate analyses. Characteristics assessed for each COT patient in each quarter of the analyses included age, gender, geographic region of residence in the state, season, smoking status, comorbid illnesses and other health diagnoses, and medication fills. For most comorbid conditions, diagnoses, and medications in which the underlying health condition was of primary interest, we assessed comorbidities by considering the presence or absence of diagnostic codes and medication prescriptions filled in the past 3 years. For medications for which current use was of primary interest, we determined use strictly on the basis of fills within a given study quarter. Exact choice of construct and inclusion set of adjustment variables in regression models differed somewhat across analyses, depending on the adverse event outcome under investigation and scientific evaluation regarding potential confounders. Previous before-and-after evaluations of how prescribing
policy changes have affected opioid overdose rates have not controlled for patient characteristics, and they have not had a contemporaneous control group.

To estimate regression model parameters, we used generalized estimating equations (GEEs) assuming an independence working correlation matrix and then computed robust standard errors via the sandwich estimator to account for the potentially mis-specified variance and within-person correlation across time. In this evaluation, it was possible to model clustering within patient over time but not clustering owing to prescribing clinician. We think it is unlikely that inability to model the latter was an important limitation, because there was a large number of clusters and few adverse events occurred within each clinician cluster.

On the basis of the estimated models, we then presented adjusted odds ratios, relative risks, or differences of means with 95% CI representing the change per year in outcomes among COT users in the IGP and CC in each period. We computed Wald-based *P* values to test whether rates of change were different.

To accompany these estimates, we plotted both unadjusted quarterly outcome rates and curves showing standardized rates based on adjusted estimates from the regression model. The latter showed the estimated time trends in the outcomes when the results for both the intervention and control COT population were standardized to a common distribution of patient characteristics.

As noted, these regression models accounted for within-patient clustering over time. In planning the analyses, we decided not to account for within-prescriber clustering for several reasons. The patients in the control setting were dispersed over 977 different prescribers; of these, 17% had only 1 COT patient and 38% had 3 or fewer. In the control setting, 94% of the prescribers had no opioid overdose events among their COT patients and less than 1% reported 2 or more overdoses. The COT patients in the intervention setting were dispersed over 536 different prescribers; of these, 3.5% had only 1 COT patient and 7.7% had 3 or fewer. In the IGP, 73% of clinicians had no opioid overdoses among their COT patients, 17% had 1 overdose, and 10% reported 2 or more. In addition, COT patients sometimes changed prescribers over time.
Given these considerations, accounting for clustering both within patient over time and within prescriber would have introduced significant difficulties in GEE model estimation, including possible failure to converge for analyses with smaller numbers of adverse events. Modeling the effects of within-patient clustering over time controls for part of the variance owing to higher-order clustering (eg, by prescriber, by practice, by geographic area). Since the time series analyses were conducted and reported sequentially, starting with more common adverse outcomes (motor vehicle crashes, medically attended injuries) and ending with the least common adverse event (opioid overdose), we wanted to avoid having to change analytic methods.

We performed various subgroup analyses, including (1) comparing trends in motor vehicle crash rates between COT patients in intervention and control settings with and without concurrent exposure to sedative-hypnotic medications; (2) comparing trends in opioid dose process measures among COT patient groups in the intervention setting stratified on the basis of factors (age, gender, sedative-hypnotic use, substance use disorders, and mental health conditions) associated with higher risk for opioid-related problems; and (3) comparing trends in medically attended injury rates between COT patients stratified on the basis of age and concomitant sedative-hypnotic use, groups that may be at particularly high risk for injury.

Because data were largely from GH electronic health records, with variables defined as present or absent in the EHR over the specified ascertainment period, it was possible to specify values based on electronic health care data for almost all study subjects for most covariates. A notable exception was race/ethnicity, which was not captured in GH’s electronic data for a relatively large proportion of the sample. However, as it was not considered to be an important potential confounder, we did not include it in interrupted time series analyses. In the patient survey, we asked respondents whether they had obtained all their opioid prescriptions in the previous year through their GH insurance benefits. In both intervention and control settings, 96% of respondents said “yes,” which suggests that GH insurance claims records were a reasonably complete source of data for opioid prescriptions for the study population.
To identify motor vehicle crashes, we used a fuzzy matching algorithm to link our study cohort to state records; the algorithm accounted for possible mismatches owing to missing information on middle initials and used GH membership files to account for name changes that occurred during the study period, even though 93% of crashes matched with an exact name and initial. Rates of motor vehicle crashes were lower in rural areas than in urban areas, and older persons had higher rates of crashes than younger persons. Intervention setting patients were more likely to reside in urban areas and tended to be older than control setting patients. These covariates (and others) were controlled in our analyses.

**Dose-Response Analyses**

We conducted additional analyses to examine the dose-response relationship between opioid dose and risk of the adverse outcomes to understand how dose changes might affect the incidence of each adverse outcome. For these analyses, we included COT patients from the primary analyses plus all calendar quarters of follow-up, including those in which the patients were no longer receiving opioid therapy. This allowed us to identify an appropriate reference group of individuals who had previously received COT, rather than those who had never received it. We modeled the association between daily opioid dose (in mg MED) and the risk of adverse outcomes using modified Poisson regression with natural cubic splines for dose, linear splines for time trends, indicators for current COT use and care setting (IGP versus CC), adjustment for other patient covariates, and estimation of confidence intervals, as in the primary analysis models.

**Survey of Patient-Reported Outcomes**

We conducted a separate study to investigate patient-reported outcomes among COT patients who received care in the GH-IGP or CC settings, outcomes that could be collected only via patient survey. Primary patient-reported outcomes of interest included PEG (Pain, Enjoyment, General Activities) scale items such as average ratings of pain severity (scale of 0-10, with higher scores representing worse pain); pain-related interference in daily activities (scale of 0-10); and pain-related interference in enjoyment of life (scale of 0-10). The
prevalence of prescription opioid use disorder was also a primary patient-reported outcome. Prevalence was analyzed overall (mild, moderate, and severe) and then limited to moderate or severe cases. The disorder was ascertained according to the Psychiatric Research Interview for Substance and Mental Disorders for DSM-5 (PRISM5). The PRISM5 is a validated diagnostic assessment102,103 that determines whether patients have experienced any of 9 symptoms of prescription opioid use disorder, as well as opioid tolerance or withdrawal. On the basis of COT patient responses to the PRISM survey questions, the disorder was classified as mild (2-3 symptoms), moderate (4-5 symptoms), or severe (≥ 6 symptoms). Our primary opioid use disorder outcome did not consider opioid withdrawal and tolerance; however, a secondary outcome did consider these 2 indicators.

Other secondary patient-reported outcomes analyzed from the survey included (1) depressive symptoms as measured by PHQ (Patient Health Questionnaire)-8 score (scale of 0-24, with higher scores indicating worse depression),104 a tool that has been validated for telephone administration105; (2) perceived helpfulness of opioids (Likert-type scale categorized as not at all/little, moderately, or very/extremely helpful); (3) perceived bothersomeness of opioids (Likert-type scale categorized as not at all/little, moderately, or very/extremely bothersome); and (4) trust in patient–doctor relationship related to prescribing and managing opioid therapy (4 questions with Likert-type scale categorized as totally agree/agree, neutral, or disagree/totally disagree).

Research study procedures for survey-based analyses were approved by the GH Institutional Review Board, with verbal consent for the telephone interviews. We conducted interviews from September 2014 through January 2016 among COT patients who were receiving care in either the IGP or CC settings and who agreed to the use of their electronic health care data for research purposes. The interview was administered by telephone and required 30 to 40 minutes to complete. Eligible COT patients received a $2 preincentive with the study invitation letter and a $10 postincentive upon completing the telephone interview. GH enrollees were eligible for the survey if they were aged ≥ 18; had been a GH member for at least 1 year before sample selection; and (according to electronic pharmacy data) had received
a ≥ 70 days’ supply of opioids in the 90 days before sample selection, a ≥ 70 days’ supply of opioids in at least 1 other quarter in the previous year, and a ≥ 45 days’ supply of opioids in all 4 quarters in the previous year. These criteria were required to identify patients who had been using opioids regularly for at least a year. We excluded those who had been admitted to hospice in the previous year and those who had had 2 or more cancer diagnoses (excluding nonmelanoma skin cancer). These criteria limited the study population to patients with noncancer chronic pain.

Measures of the patient-reported outcomes of interest (ie, those pertaining to prescription opioid use disorder, pain, and perceptions of the impact of opioids and doctor–patient relationships) were collected from the survey responses. The telephone interview also collected patient-reported information regarding marital status, educational attainment, and race/ethnicity.

GH enrollment and electronic health care data provided additional COT patient information on age; gender; residence in eastern or western Washington; chronic disease comorbidities; previous diagnoses of mental disorders or of tobacco, alcohol, or opioid or nonopioid drug use disorders; and hepatitis C or cirrhosis. Diagnoses were obtained for up to 3 years prior to the date of the telephone interview, while information on chronic disease comorbidity was summarized using the Romano version of the Charlson comorbidity score for the year prior to the telephone interview. We used electronic pharmacy data available on each sampled patient to compute the average daily opioid dose received over the 90 days before he or she was sampled for the survey, as well as to determine whether the patient had received more than 20% excess opioid days supplied in any of the 4 quarters in the previous year.

Analytic Methods for Survey Data

The data collected from electronic enrollment, diagnoses, and pharmacy sources were available on all patients who were eligible and selected for the survey (ie, nonrespondents as well as respondents). We compared survey response rates by these patient demographic and health characteristics (measured relative to the sample selection data) and used logistic
We used regression models to estimate parameters (with 95% CIs)—such as odds ratios, relative risks, and differences of means—that quantify differences in the patient-reported outcomes between COT patients in the IGP and the CC. Depending on whether the outcome was continuous, binary, or ordinal, we used inverse probability of response weighted linear, modified Poisson,95 or ordinal logistic (proportional odds) regression models, respectively. In these models, we included main effects for the health plan setting (IGP versus CC) and some combination of adjustment terms (depending on the outcome under investigation) for patient age; gender; region of residence; employment; education; marital status; race/ethnicity; comorbidity; mental disorders; pain; and tobacco, alcohol, and nonopioid drug use disorders. We estimated model parameters using GEEs assuming an independence working correlation matrix, with 95% CIs computed based on robust standard errors estimated via the sandwich estimator.97

We performed additional subgroup analyses for the pain and opioid use disorder outcomes, investigating results in groups defined by age, gender, race/ethnicity, mental health disorders, comorbidity scores, and alcohol and nonopioid substance use disorders. We had very low rates of missing data for covariate and outcome measures ascertained from the telephone survey. Because missing information for variables used in any particular analysis was relatively minor, we performed and reported results from complete-case analyses.

Implementation of the COT Risk Reduction Initiatives

The following section describes the intervention and control settings and the implementation of the COT dose reduction and RSM initiatives in the intervention setting.
Intervention and Control Settings

The intervention setting consisted of clinics within Group Health’s Integrated Group Practice in which the clinical staff and medical staff leadership were GH employees and the clinics and clinical information systems were owned and operated by GH. The control setting consisted of contracted care practices that provided medical care to GH enrollees. The clinicians were not GH employees, and the practices and clinical information systems were not owned and operated by GH. In the contracted care practices, GH enrollees were generally a small minority of the patients receiving care (typically < 15%). For these reasons, it was not possible for Group Health to implement the opioid dose or RSM reduction initiatives among its contracted care patients receiving opioid therapy. The GH-IGP clinics were medium-to-large primary care clinics serving 10 000 to 25 000 GH enrollees. The GH-CC practices were diverse primary care settings reflecting community practice in Washington State. The control practices were more likely to be located in the eastern part of the state, while the intervention practices were more likely to be in the greater Puget Sound area in the western part of the state. The interrupted time series design permitted comparison of adverse event rates in the intervention and control patient populations before the opioid risk reduction initiatives were implemented. As noted earlier, the rates of opioid overdose, motor vehicle crashes, and medically attended injuries were similar in the 2 patient populations during the baseline period, suggesting their comparability.

The rates of COT patients who moved from the intervention to the control setting were negligible over the course of the study (< 1%): Less than 4% of COT patients moved from the control setting to the intervention setting, so the potential for contamination was low.

Opioid Dose Reduction Initiative. Washington State first disseminated its COT guideline in April 2007. Consistent with the state guideline, GH medical staff leadership and consulting rehabilitation medicine specialists encouraged greater caution in prescribing opioids for chronic pain and discouraged dose escalation and the use of higher doses for COT patients in the IGP clinics. These steps were not taken in the CC practices. Over several years, the medical director of rehabilitation medicine delivered periodic voluntary educational
presentations about managing chronic pain and opioid prescribing. Typically, about one-fourth of group practice primary care physicians (PCPs) attended any given presentation. Group Health established a clinical policy that made PCPs responsible for overall opioid management of their COT patients. PCPs and clinic medical directors received lists that flagged those of their COT patients who were receiving high daily opioid doses (≥ 120 mg MED). PCPs with unusually large numbers of COT patients taking high opioid doses received feedback and supervisory guidance from clinic medical directors. Elements of the GH-IGP dose reduction initiative are summarized in the left-hand column of Figure 4.

Figure 4. GH-IGP risk reduction initiatives

**Dose reduction (2007+)**
- State guideline (4/2007)
- Doses ≥120 mg discouraged
- Opioid management in Primary Care
- Lists of high-dose COT patients
- Specialty consult advised caution
- Voluntary CME
- Supervisory guidance for PCPs with long lists of high-dose COT patients

**Risk stratification & monitoring (2010+)**
- Guideline enacted into state law (3/2010)
- Components for implementation
- On-line CME (87% participation)
- Standardized materials on-line
- Single prescriber per patient
- EHR-documented care plans
- Risk-stratified monitoring with minimum annual urine drug tests
- Advance notice for opioid refills

*Risk Stratification and Monitoring Initiative.* In 2010, Washington State enacted legislation mandating the use of its COT guideline for long-term opioid prescribing for chronic noncancer pain. Prescribers were required to check medical records to assess the appropriateness of chronic opioid therapy and to screen for risk of drug abuse and diversion. The guideline recommended assessment of addiction risk factors, developing a treatment plan,
periodic monitoring visits and urine drug testing (frequency guided by patient risk factors), and use of a written agreement outlining patient responsibilities. In October 2010, GH-IGP implemented a multifaceted opioid risk reduction initiative in the intervention clinics. This initiative included a guideline establishing minimum standards for risk-stratified COT monitoring (including urine drug testing); documentation of standard care plans in the medical record, including the treatment regimen and the PCP responsible for COT management; periodic monitoring visits; and modifications to the prescription refill process to prevent urgent refill requests.73 The initiative sought to increase the conformity of opioid prescribing and management for chronic noncancer pain with the recently enacted state legislation, but neither the state guideline nor the GH initiatives explicitly sought to reduce the percentage of patients receiving COT. Clinical decisions about whether and how long to prescribe COT for chronic pain were left to physician discretion.

To support implementation in the IGP settings, the RSM initiatives employed practice tools such as patient education materials, a COT care plan template, and an online calculator for estimating MED; performance measures tracking the development of COT care plans in the EHR; medical staff leader advocacy; expert consultation for physicians in each primary care clinic; and financial incentives for completing COT care plans. Medical staff leadership mandated a 90-minute online continuing medical education course about chronic pain management and opioids, which 87% of group practice PCPs completed.76 After taking the course, staff clinicians in each intervention clinic met for a 1-hour discussion. Elements of the RSM initiatives implemented in the intervention clinics are summarized in the right-hand column of Figure 4.

The GH-IGP dose reduction and RSM initiatives were not implemented in the control setting. The GH-CC prescribers were exposed to the statewide guideline and legislation but not to the augmented implementation of the guidelines that took place in the intervention clinics. COT patients in the CC clinics served as controls for evaluating the incremental effects of the more extensive changes in opioid prescribing and management implemented in the group practice settings, as described under “Intervention and Control Settings.”
Prevalence of Chronic Opioid Therapy. In both intervention and control settings, the percentage of adults receiving COT increased over the study period. In the intervention setting, the prevalence of COT among adults increased from 1.9% in 2006 to 2.7% in June 2014. In the control setting, the percentage of adults currently receiving COT increased from 1.4% in 2006 to 2.8% in June 2014. (See Figure 5 for trends in the number of COT patients in each quarter in the intervention and control settings from January 2006 through June 2014.)

Figure 5. Trends in number of COT patients in the intervention (GH-IGP) and control (GH-CC)

From 2006 to 2014, the percent of adults (age-sex standardized) receiving COT increased from 1.9% to 2.7% in the GH-IGP and from 1.4% to 2.8% in GH-CC.

COT Dose. The intervention setting achieved and sustained substantially larger reductions in opioid dose among COT patients than those observed among patients in the control setting. In the baseline period (2006-2007), patients in intervention clinics received an average daily dose of around 75 mg MED, while patients in control settings received an average daily dose of around 85 mg MED.

By October 2010 (when the RSM interventions were implemented), the average daily dose for intervention COT patients was around 50 mg MED, compared with 70 mg MED for
control patients. By the end of the study period (June 2014), intervention COT patients were receiving an average daily opioid dose of 40 mg MED (a 47% reduction from baseline), compared with around 65 mg MED for control patients (a 24% reduction from baseline) (Figure 6A).

When we applied interrupted time series methods to average daily opioid dose, we found statistically significant reductions in average daily dose in the baseline period, with an annual decrement of −7.7 mg MED (95% CI, −13.9 to −1.6) in the control setting and an annual decrement of −4.6 mg MED (95% CI, −6.5 to −2.7) in the intervention setting (Figure 6B). The difference in change in average daily dose between intervention and control settings in the baseline period was not statistically significant (p = 0.343). It is not possible to determine whether these changes in average daily dose were due to the dissemination of the Washington State opioid guideline or if they reflected general changes in opioid prescribing practice norms. In any case, the reductions proved to be transient in the control setting. During the dose reduction period, annual reduction in average daily opioid dose was a nonsignificant −0.6 mg MED (−3.0, 1.7) in the control setting, compared with a significant annual reduction in average daily dose in the intervention setting: −7.0 mg MED (−8.0, −6.0) (Figure 6B). The difference in annual change in average daily opioid dose between intervention and control settings during the dose reduction period was highly significant (p < 0.001). During the RSM period, modest reductions in average daily opioid dose occurred that exceeded chance expectation, with an annual decline of −1.9 mg MED (−3.6, −0.3) in the control setting and −1.8 mg MED (−2.4, −1.1) in the intervention setting (Figure 6B). The difference in dose reduction between intervention and control settings during the RSM period was nonsignificant (p = 0.839). The large difference in average daily opioid dose that emerged during the dose reduction period was sustained over the RSM period as the rates of dose reduction did not differ; however, the dosage levels in the intervention setting started from a much lower level at the beginning of the RSM period. It is noteworthy that the multifaceted RSM initiative did not sustain the high levels of dose reduction achieved in the intervention setting during the dose reduction period.
Figure 6A. Trends in average daily MED among COT patients

Note: The solid and dashed lines are trends adjusted for covariates. The triangles and squares show trends unadjusted for covariates.

Figure 6B. Estimated average change per year (with 95% CI) in the mean daily milligrams of MED among COT patients by setting and period

<table>
<thead>
<tr>
<th>Care Setting</th>
<th>Time period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>Control</td>
<td>-7.7 (-13.9, -1.6)**</td>
</tr>
<tr>
<td>Intervention</td>
<td>-4.6 (-6.5, -2.7)**</td>
</tr>
</tbody>
</table>

*p-values for tests of difference in annual opioid dose reduction within time period between Intervention and Control settings:

Does the rate of change differ between Intervention and Control within a given period?

<table>
<thead>
<tr>
<th></th>
<th>Not Significant</th>
<th>&lt;0.001</th>
<th>Not Significant</th>
</tr>
</thead>
</table>


In 2007, the Washington State guideline recommended a ceiling COT dose of 120 mg MED. The percentage of COT patients receiving more than 120 mg declined from about 17% at the beginning of 2006 to about 6% in June 2014 among intervention patients (a 65% reduction from baseline), compared with a decline from about 20% in 2006 to about 13% in June 2014 among control patients (a 35% reduction from baseline) (Figure 7).

**Figure 7. Trends in percentage of COT patients with average daily dose ≥ 120 mg MED**

![Graph showing trends in percentage of COT patients with average daily dose ≥ 120 mg MED]

Note: The solid and dashed lines are trends adjusted for covariates. The triangles and squares show trends unadjusted for covariates.

Among intervention patients, we observed reductions in opioid dose among men and women and among individuals with and without a substance use disorder diagnosis, with and without a mental disorder diagnosis, and with and without sedative use. The reductions in the percentage receiving doses of 120 mg MED were somewhat larger among higher-risk patients (men, those with sedative use, and those with mental or substance use disorders) because the percentage of patients receiving high doses was larger at baseline. However, differences in dose reduction between individuals with and without these risk factors were nonsignificant among the intervention patients (Figure 8).
Figure 8. Trends in percentage of high COT dose among GH-IGP COT patients by risk factors

Percent receiving ≥ 120 mg. MED

Note: The triangles and squares show trends unadjusted for covariates.
Concurrent Sedative Use. Trends in frequent concurrent use of opioids and sedatives were generally stable from 2006 through 2014 among both intervention and control patients, although there was a slight upward trend among control patients in concurrent opioid and sedative use in the dose reduction period and a slight downward trend among intervention patients in the RSM period. The trends in concurrent opioid and sedative use among control patients differed from the trends among intervention patients by greater than chance expectation in the dose reduction and RSM periods (Figures 9A and 9B). Over the study period, about 35% of current COT patients received 45 or more days’ supply of sedatives in the same quarter.

Figure 9A. Trends in percentage of COT patients with chronic sedative use (45+ days’ supply)

Note: The solid and dashed lines are trends adjusted for covariates. The triangles and squares show trends unadjusted for covariates.
Figure 9B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients with concurrent chronic sedative use by setting and period

<table>
<thead>
<tr>
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<th>Time period</th>
<th></th>
<th>Risk Stratification Monitoring</th>
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<td>Baseline</td>
<td>Dose Reduction</td>
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<tr>
<td>Control</td>
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<td>1.04 (1.01, 1.06) **</td>
<td>1.00 (0.98, 1.02)</td>
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<tr>
<td>Intervention</td>
<td>0.99 (0.97, 1.02)</td>
<td>1.01 (0.99, 1.02)</td>
<td>0.97 (0.96, 0.98) **</td>
</tr>
</tbody>
</table>

*p-values for tests of difference in annual opioid dose reduction within time period between Intervention and Control settings:*

- Relative risk of 1.04 indicates a 4% increase in the rate of concurrent chronic sedative use per year
- Relative risk of 0.97 indicates a 3% decrease in the rate of concurrent chronic sedative use per year

Does the rate of change in overdose rate differ between Intervention and Control within a given period?

| Does the rate of change in overdose rate differ between Intervention and Control within a given period? | Not Significant | 0.037 | 0.015 |

**Percentage of Patients With COT Care Plans.** Among intervention patients, the percentage with a COT care plan in the EHR increased from less than 10% in the first half of 2010 to more than 70% in the last quarter of 2010. From 2012 through June 2014, more than 80% of intervention patients had COT care plans documented in their EHRs (Figure 10). No flag for COT care plans existed in electronic health care data for the control patients.
**Figure 10. Trends in percentage with COT care plans: Intervention COT patients**

Percentage of Patients With Annual Urine Drug Tests. Periodic urine drug tests were recommended by the Washington State guideline (and other COT guidelines) to assess whether COT patients were taking prescribed opioids, to identify the use of nonprescribed opioids, and to detect the use of illicit drugs, including cocaine, methamphetamine, heroin, and marijuana. The percentage of intervention patients with an annual urine drug test increased from less than 15% before October 2010 to 40% to 50% from 2011 through June 2014 (Figure 11). Among control patients, the percentage with an annual urine drug test was less than 15% before 2011 and remained below 20% through June 2014. In exploratory analyses, we found that the sharp increase in the ordering of urine drug tests coincided with the implementation of RSM initiatives in October 2010.
Summary of Implementation of Dose Reduction and RSM Initiatives. Our analyses of process data found that clinically meaningful differences in opioid dose emerged between intervention and control settings among COT patients starting in 2008 and that these differences were sustained through the end of the evaluation period in 2014. Similarly, large changes in indicators of enhanced risk stratification and monitoring (documentation of care plans, use of urine drug tests) emerged with the implementation of the RSM initiatives in the fall of 2010, and these changes were sustained through the end of the evaluation period in 2014.
RESULTS

Characteristics of COT Patients in Intervention and Control Settings

Figure 12 shows the characteristics of 22,673 patients in the intervention setting (GH-IGP) and 8,469 patients in the control setting (GH-CC). The control patients were evenly split between eastern and western Washington, while the intervention patients were predominantly from western Washington. Other characteristics were similar between the 2 patient populations. All variables shown in Figure 12 were controlled in comparative analyses. We assessed whether the composition of the intervention and control patients based on these characteristics was sustained over the study period, at the beginning of the dose reduction period, at the beginning of the RSM period, and at the end of the study. The similarities and differences in intervention and control patients were sustained over the study period (data not shown). Detailed data on patient characteristics from the interrupted time series analyses is shown in Table 1. Detailed data on patient characteristics from the survey analyses is provided in Table 2.

The rates of COT patients who moved from the intervention to the control setting were negligible over the course of the study (< 1%), and less than 4% of patients moved from the control setting to the intervention setting. The potential for contamination was low.
Figure 12. Comparison of COT patients from intervention and control clinics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (GH+GP) (N=22,673)</th>
<th>Control (GH-CC) (N=8,469)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Washington</td>
<td>Percent</td>
<td>Percent</td>
</tr>
<tr>
<td>Female</td>
<td>63.7</td>
<td>61.6</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-34</td>
<td>8.5</td>
<td>6.9</td>
</tr>
<tr>
<td>35-44</td>
<td>13.9</td>
<td>15.7</td>
</tr>
<tr>
<td>45-54</td>
<td>24.7</td>
<td>29.5</td>
</tr>
<tr>
<td>55-64</td>
<td>24.0</td>
<td>26.8</td>
</tr>
<tr>
<td>65-74</td>
<td>12.9</td>
<td>11.1</td>
</tr>
<tr>
<td>75+</td>
<td>16.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Opioid abuse or dependence</td>
<td>3.5</td>
<td>3.0</td>
</tr>
<tr>
<td>Non-opioid drug abuse or dependence</td>
<td>5.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td>5.5</td>
<td>4.2</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>15.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>9.2</td>
<td>5.9</td>
</tr>
<tr>
<td>Mental disorders (including use of antipsychotics)</td>
<td>56.2</td>
<td>51.2</td>
</tr>
<tr>
<td>Use of tricyclic antidepressant</td>
<td>15.4</td>
<td>10.3</td>
</tr>
<tr>
<td>Use of sedatives/muscle relaxants</td>
<td>46.6</td>
<td>52.3</td>
</tr>
<tr>
<td>Romano-Charlson Comorbidity score 3+</td>
<td>19.0</td>
<td>14.9</td>
</tr>
</tbody>
</table>
Table 1. COT Patient Characteristics for Individuals Included in the Interrupted Time Series Analyses (as of each patient’s first COT eligibility quarter during the study period)

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Intervention (GH-IGP)</th>
<th>Control (GH-CC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Total</td>
<td>31 142</td>
<td></td>
<td>22 673</td>
</tr>
<tr>
<td>Western Washington</td>
<td>24 081</td>
<td>77.3</td>
<td>19 926</td>
</tr>
<tr>
<td>Female</td>
<td>19 664</td>
<td>63.1</td>
<td>14 444</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-34</td>
<td>2519</td>
<td>8.1</td>
<td>1935</td>
</tr>
<tr>
<td>35-44</td>
<td>4483</td>
<td>14.4</td>
<td>3153</td>
</tr>
<tr>
<td>45-54</td>
<td>8090</td>
<td>26.0</td>
<td>5595</td>
</tr>
<tr>
<td>55-64</td>
<td>7714</td>
<td>24.8</td>
<td>5441</td>
</tr>
<tr>
<td>65-74</td>
<td>3867</td>
<td>12.4</td>
<td>2926</td>
</tr>
<tr>
<td>75+</td>
<td>4469</td>
<td>14.4</td>
<td>3623</td>
</tr>
<tr>
<td>Opioid abuse or dependence</td>
<td>1038</td>
<td>3.3</td>
<td>783</td>
</tr>
<tr>
<td>Nonopioid drug abuse or dependence</td>
<td>1583</td>
<td>5.1</td>
<td>1273</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td>1597</td>
<td>5.1</td>
<td>1244</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>4595</td>
<td>14.8</td>
<td>3468</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2595</td>
<td>8.3</td>
<td>2094</td>
</tr>
<tr>
<td>Mental health disorders (including use of antipsychotics)</td>
<td>17 067</td>
<td>54.8</td>
<td>12 731</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>Intervention (GH-IGP)</td>
<td>Control (GH-CC)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------------</td>
<td>-----------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Use of tricyclic antidepressant*</td>
<td>4376 14.1</td>
<td>3501 15.4</td>
<td>875 10.3</td>
</tr>
<tr>
<td>Use of sedatives/muscle relaxants*</td>
<td>14996 48.2</td>
<td>10570 46.6</td>
<td>4426 52.3</td>
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<tr>
<td>Romano-Charlson comorbidity score**</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>0</td>
<td>18184 58.4</td>
<td>13095 57.8</td>
<td>5089 60.1</td>
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<tr>
<td>1</td>
<td>2903 9.3</td>
<td>1950 8.6</td>
<td>953 11.3</td>
</tr>
<tr>
<td>2</td>
<td>4481 14.4</td>
<td>3320 14.6</td>
<td>1161 13.7</td>
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<tr>
<td>3+</td>
<td>5574 17.9</td>
<td>4308 19.0</td>
<td>1266 14.9</td>
</tr>
</tbody>
</table>

Note: Most covariates were defined using information from the previous 3 years. Exceptions (*) are based on the current quarter only except for the Romano-Charlson comorbidity score (**), which was calculated based on the previous year.
Table 2. Characteristics of COT Patient Survey Respondents Measured at the Time of the Survey Interview in the Intervention (GH-IGP) and Control (GH-CC) Clinics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (GH-IGP)</th>
<th>Control (GH-CC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%a</td>
</tr>
<tr>
<td>Total</td>
<td>935</td>
<td>100.0</td>
</tr>
<tr>
<td>Age (at time of interview)</td>
<td></td>
<td></td>
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<tr>
<td>20-44</td>
<td>73</td>
<td>7.8</td>
</tr>
<tr>
<td>45-54</td>
<td>130</td>
<td>13.9</td>
</tr>
<tr>
<td>55-64</td>
<td>304</td>
<td>32.5</td>
</tr>
<tr>
<td>65-74</td>
<td>291</td>
<td>31.1</td>
</tr>
<tr>
<td>75+</td>
<td>137</td>
<td>14.7</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>589</td>
<td>63.0</td>
</tr>
<tr>
<td>Male</td>
<td>346</td>
<td>37.0</td>
</tr>
<tr>
<td>Race</td>
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<td></td>
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<td>87.0</td>
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<tr>
<td>African American</td>
<td>19</td>
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<td>Asian/Pacific Islander</td>
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<td>1.2</td>
</tr>
<tr>
<td>Native American</td>
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<td>0.8</td>
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<td>Multiple or other</td>
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<td>9.0</td>
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<td>Missing</td>
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<td>1.2</td>
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<td>Hispanic ethnicity</td>
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<td>904</td>
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<td>27</td>
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<td>Education</td>
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<td>High school or less</td>
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<tr>
<td>Some college</td>
<td>436</td>
<td>46.7</td>
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<td>4-year college or graduate</td>
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<td>Missing</td>
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<td>0.1</td>
</tr>
<tr>
<td>Condition</td>
<td>Intervention (GH-IGP)</td>
<td>Control (GH-CC)</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-----------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%²</td>
</tr>
<tr>
<td><strong>Mental disorder diagnosed</strong> (past 36 months, includes depression or anxiety)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>312</td>
<td>33.4</td>
</tr>
<tr>
<td>Yes</td>
<td>623</td>
<td>66.6</td>
</tr>
<tr>
<td><strong>Alcohol use disorder diagnosed</strong> (past 36 months, does not include if in remission)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>885</td>
<td>94.7</td>
</tr>
<tr>
<td>Yes</td>
<td>50</td>
<td>5.3</td>
</tr>
<tr>
<td><strong>Nonopioid drug use disorder diagnosed</strong> (past 36 months)</td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>846</td>
<td>90.5</td>
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<tr>
<td>Yes</td>
<td>89</td>
<td>9.5</td>
</tr>
<tr>
<td><strong>Opioid drug use disorder diagnosed</strong> (past 36 months)</td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>834</td>
<td>89.2</td>
</tr>
<tr>
<td>Yes</td>
<td>101</td>
<td>10.8</td>
</tr>
<tr>
<td><strong>Tobacco use disorder diagnosed</strong> (past 36 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>711</td>
<td>76.0</td>
</tr>
<tr>
<td>Yes</td>
<td>224</td>
<td>24.0</td>
</tr>
<tr>
<td><strong>Location in Washington State</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>East</td>
<td>242</td>
<td>25.9</td>
</tr>
<tr>
<td>West</td>
<td>693</td>
<td>74.1</td>
</tr>
<tr>
<td><strong>Married or living as married</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>318</td>
<td>34.1</td>
</tr>
<tr>
<td>Yes</td>
<td>615</td>
<td>65.9</td>
</tr>
<tr>
<td>Missing</td>
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<td>0.2</td>
</tr>
<tr>
<td><strong>Romano-Charlson comorbidity score</strong> (based on past 12 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>426</td>
<td>45.6</td>
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<td>1</td>
<td>75</td>
<td>8.0</td>
</tr>
<tr>
<td>2</td>
<td>144</td>
<td>15.4</td>
</tr>
<tr>
<td>3-5</td>
<td>195</td>
<td>20.9</td>
</tr>
<tr>
<td>6+</td>
<td>95</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td>Intervention (GH-IGP)</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hepatitis C or cirrhosis diagnosed (past 36 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>851</td>
<td>91.0</td>
</tr>
<tr>
<td>Yes</td>
<td>84</td>
<td>9.0</td>
</tr>
<tr>
<td>20%+ opioid excess days supplied in any of past 4 quarters (108 or more days of opioids supplied in a 90-day period)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>734</td>
<td>78.5</td>
</tr>
<tr>
<td>Yes</td>
<td>201</td>
<td>21.5</td>
</tr>
<tr>
<td>Average COT dose (in prior quarter)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No use</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>&lt; 15 mg</td>
<td>232</td>
<td>24.8</td>
</tr>
<tr>
<td>15 - &lt; 50 mg</td>
<td>432</td>
<td>46.2</td>
</tr>
<tr>
<td>50 - &lt; 120 mg</td>
<td>199</td>
<td>21.3</td>
</tr>
<tr>
<td>120+ mg</td>
<td>72</td>
<td>7.7</td>
</tr>
<tr>
<td>Continuously enrolled (past 24 months)</td>
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<td></td>
</tr>
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<td>No</td>
<td>48</td>
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</tr>
<tr>
<td>Yes</td>
<td>887</td>
<td>94.9</td>
</tr>
</tbody>
</table>

<sup>a</sup> % is among nonmissing. Missing information included race (n = 24), Hispanic ethnicity (n = 8), education (n = 3), and marital status (n = 3).

**Adverse Event Rates by Study Period**

We estimated numbers and overall rates per 100 person-years for each of the adverse events (opioid overdose, motor vehicle crashes, medically attended injuries) in each study period (baseline, dose reduction, RSM) for the intervention and control settings. Figure 13A shows the estimates for opioid overdoses, Figure 13B for motor vehicle crashes, and Figure 13C for medically attended injuries. We observed motor vehicle accidents and medically attended injuries for 2% to 4% of current COT patients per person-year of receiving chronic opioid therapy, whereas opioid overdoses (fatal or nonfatal) were less common, occurring for about 0.5% of current COT patients per person-year of receiving COT. The unadjusted motor vehicle crash rates were lower among the control patients than among the intervention patients over
the study period. This difference is likely explained, in part, by the fact that control patients were more likely to live in rural areas (where crash rates are lower) and were generally younger (crash rates are lower for younger people). The evaluation results we report are adjusted for differences in patient characteristics.

**Figure 13A. Overdose rate per 100 person-years (with 95% CI) among COT patients**

<table>
<thead>
<tr>
<th>Care Setting</th>
<th>Time period</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Dose Reduction</td>
<td>Risk Stratification Monitoring</td>
<td>OVERALL</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.56 (0.33, 0.96)</td>
<td>0.41 (0.26, 0.66)</td>
<td>0.48 (0.34, 0.67)</td>
<td>0.47 (0.37, 0.60)</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>0.68 (0.53, 0.88)</td>
<td>0.53 (0.42, 0.66)</td>
<td>0.40 (0.32, 0.49)</td>
<td>0.49 (0.43, 0.56)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Control (person-years)</th>
<th>2318.5</th>
<th>4135.25</th>
<th>8198.25</th>
<th>14652</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (events)</td>
<td></td>
<td>13</td>
<td>17</td>
<td>39</td>
<td>69</td>
</tr>
<tr>
<td>Intervention (person-years)</td>
<td></td>
<td>9214.5</td>
<td>14907.25</td>
<td>25250</td>
<td>49371.75</td>
</tr>
<tr>
<td>Intervention (events)</td>
<td></td>
<td>63</td>
<td>79</td>
<td>100</td>
<td>242</td>
</tr>
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</table>
### Figure 13B. Motor vehicle crash rate per 100 person-years (with 95% CI) among COT patients

<table>
<thead>
<tr>
<th>Care Setting</th>
<th>Time period</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Dose Reduction</td>
<td>Risk Stratification</td>
<td>Monitoring</td>
<td>OVERALL</td>
</tr>
<tr>
<td>Control</td>
<td>2.09 (1.59, 2.73)</td>
<td>2.30 (1.88, 2.81)</td>
<td>2.39 (2.07, 2.77)</td>
<td>2.32 (2.07, 2.59)</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>3.45 (3.08, 3.86)</td>
<td>3.24 (2.96, 3.55)</td>
<td>2.96 (2.75, 3.18)</td>
<td>3.13 (2.97, 3.31)</td>
<td></td>
</tr>
</tbody>
</table>

| Control (person-years) | 2445.5 | 4306 | 8609 | 15360.5 |
| Control (events)       | 51     | 99   | 206  | 356     |
| Intervention (person-years) | 9541.75 | 15344.75 | 26159.5 | 51046 |
| Intervention (events)  | 329    | 497  | 774  | 1600    |

### Figure 13C. Medically attended injury rate per 100 person-years (with 95% CI) among COT patients

<table>
<thead>
<tr>
<th>Care Setting</th>
<th>Time period</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Dose Reduction</td>
<td>Risk Stratification</td>
<td>Monitoring</td>
<td>OVERALL</td>
</tr>
<tr>
<td>Control</td>
<td>3.48 (2.79, 4.33)</td>
<td>3.50 (2.95, 4.15)</td>
<td>4.11 (3.67, 4.60)</td>
<td>3.84 (3.51, 4.19)</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>4.17 (3.75, 4.64)</td>
<td>4.23 (3.90, 4.58)</td>
<td>4.55 (4.27, 4.84)</td>
<td>4.38 (4.18, 4.59)</td>
<td></td>
</tr>
</tbody>
</table>

| Control (person-years) | 2272.25 | 4085.25 | 8105.5 | 14463 |
| Control (events)       | 79      | 143     | 333    | 555   |
| Intervention (person-years) | 8916.25 | 14617.25 | 24939.75 | 48473.25 |
| Intervention (events)  | 372     | 618     | 1134   | 2124  |
How This Research Differs From Previous Evaluations

Previous evaluations of the effect of reducing access to opioids or lowering opioid dose have reported before-and-after comparisons of the number of fatal opioid overdoses. Because overdoses were not linked to prescription medicine data in these evaluations, they reported numbers of overdoses, not rates of opioid overdose per person-year at risk. The evaluations also lacked a contemporaneous control group, and because the overdose data were not linked to COT patient population data, the studies did not compare adverse event rates adjusted for differences in patient characteristics. In contrast, our evaluation estimates fatal and nonfatal overdose rates per current COT patient, employs a contemporaneous control group, examines trends over an extended period, and adjusts for differences in patient characteristics. No previous studies have evaluated the effects of COT risk reduction initiatives on rates of motor vehicle accidents or medically attended injuries among opioid therapy patients; this is the first evaluation of the effects of dose reduction and RSM on these outcomes.

Interrupted Time Series Analyses for Adverse Events From 2006 Through 2014

Opioid Overdose

The primary comparison of annual rates of change in opioid overdose rates between the intervention and control settings during the dose reduction period (2008 through September 2010) was nonsignificant. Overdose rates were about 0.10% to 0.15% per quarter among current COT patients; however, a preplanned secondary analysis showed a different result. The annual decline in opioid overdose rate was −17% per year in the intervention setting (95% CI = −1% to −30%, as shown in Figures 14A and 14B), a statistically significant decline (p = 0.038). Among control patients in the same period, the annual decline in overdose rate was 2% per year (95% CI = −30% to +39%), a nonsignificant change.

In summary, the evaluation results for opioid overdose in the dose reduction period were inconsistent. The primary analysis found that the difference in the change in opioid overdose rates between the intervention and control settings was nonsignificant, but a preplanned secondary analysis of annual change in overdose rates in the 2 settings found a
significant decline in these rates in the intervention setting but not in the control setting (Figure 14B).

No further decline in overdose rates occurred in the intervention setting after the implementation of RSM interventions. During the RSM period, the annual year-to-year change in overdose rates among intervention patients was –2% (95% CI = –20% to +21%). The annual rate of change in overdose rates among control patients was the same: –2% (95% CI = –11% to +21%). This evaluation found no support for the effectiveness of the RSM initiatives in reducing opioid overdose rates (Figures 14A and 14B).

Figure 14A. Percentage of COT patients with an opioid overdose (fatal or nonfatal) by quarter (2006-2014)

Note: The solid and dashed lines are trends adjusted for covariates. The triangles and squares show trends unadjusted for covariates.
Figure 14B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients experiencing an overdose by setting and period

<table>
<thead>
<tr>
<th>Care Setting</th>
<th>Baseline</th>
<th>Dose Reduction</th>
<th>Risk Stratification Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.79 (0.41, 1.54)</td>
<td>0.98 (0.70, 1.39)</td>
<td>0.98 (0.80, 1.21)</td>
</tr>
<tr>
<td>Intervention</td>
<td>0.92 (0.68, 1.24)</td>
<td>0.83 (0.70, 0.99) **</td>
<td>0.98 (0.85, 1.13)</td>
</tr>
</tbody>
</table>

\*p-values for tests of difference in annual opioid dose reduction within time period between Intervention and Control settings:

- Relative risk of 0.83 indicates a 17% reduction in opioid overdose rate per year

Does the rate of change in overdose rate differ between Intervention and Control within a given period?

- Not Significant
- Not Significant
- Not Significant

When we examined overdose rates among the entire enrolled populations of the intervention and control settings, regardless of whether they received prescribed opioids, there was no indication of a decline in overdose rates and no significant difference in the rate of decline in overdose rates between intervention and control patients in any of the study periods (Figure 15).

Using the statistical models estimated for the analyses reported here, it was possible to estimate whether changes in overdose rates from baseline to the dose reduction period and from the dose reduction period to the RSM period differed between the intervention and control settings (ie, difference in difference [DID] analyses). The results of these post hoc analyses were consistent with the planned primary analyses for overdose rates; that is, they failed to reject the null hypothesis of no change in overdose rates between the intervention and control settings.
Analyses of overdose rates by average daily opioid dose indicated that the dose reduction achieved in the intervention clinics occurred between 40 mg MED and 80 mg MED rather than on the steepest part of the overdose dose-response curve (0 mg MED to 30 mg MED). Among COT patients who received an average daily dose of around 15 mg MED, the relative risk of overdose was about 3.0 for persons receiving opioid doses of > 80 mg MED (Figure 16). This might explain why larger differences in opioid overdose trends were not observed between the intervention and control settings. The divergence of trends in opioid dose between the intervention and control settings was not large enough to expect large differential effects on opioid overdose rates.
Figure 16. Relative risk of opioid overdose by average daily MED (compared to former COT patients no longer using opioids)

Note: See “Dose-response Analyses” section for explanation of methods used to estimate dose-response curve.

**Motor Vehicle Crashes**

No evidence existed that either the dose reduction initiative or the RSM initiative influenced the rates of motor vehicle crashes among COT patients (Figures 17A and 17B). While the vehicle crash rates in the intervention setting decreased in the dose reduction period, this was counterbalanced by a significant increase in crash rates in the intervention setting in the RSM period (Figure 17B), suggesting differences unrelated to changes in opioid prescribing and management. Post hoc analyses of the DID in rates of motor vehicle crashes from baseline to the dose reduction period and from the dose reduction period to the RSM period gave similar results; that is, they failed to reject the null hypothesis of no change in motor vehicle crash rates between the intervention and control settings.
Figure 17A. Percentage of COT patients with motor vehicle crash by quarter (2006-2014)

Note: The solid and dashed lines are trends adjusted for covariates. The triangles and squares show trends unadjusted for covariates.
Compared with former COT patients currently not using opioids at all, the relative risk of a motor vehicle crash was less than 1.2 among COT patients currently receiving a dose of 80 mg MED (Figure 18). Thus, the dose-response curve for vehicle crashes was much weaker than that observed for opioid overdose. The relatively weak dose-response curve for crashes suggests that very large differences in opioid dose trends between the intervention and control settings would have been needed to produce differences in crash trends.
Figure 18. Relative risk of motor vehicle crash by average daily MED (compared to former COT patients no longer using opioids)

Note: See “Dose-response Analyses” section for explanation of methods used to estimate dose-response curve.

Medically Attended Injuries

Medically attended injuries included fractures, intracranial lacerations, concussions, and other head injuries. No evidence existed that either the dose reduction initiative or the RSM initiative influenced the rates of medically attended injuries among COT patients (Figures 19A and 19B). Compared with COT patients receiving about 10 mg MED, the relative risk of a medically attended injury was about 1.2 among COT patients currently receiving a dose of 80 mg MED (Figure 20). Post hoc analyses of the DID in rates of medically attended injuries from baseline to the dose reduction period and from the dose reduction period to the RSM period
gave similar results; that is, they failed to reject the null hypothesis of no change in medically attended injury rates between the intervention and control settings.

The dose-response curve for medically attended injuries was much weaker than that observed for opioid overdose. As with motor vehicle crashes, the relatively weak dose-response curve for medically attended injuries suggests that very large differences in opioid dose trends between intervention and control settings would have been needed to yield differences in medically attended injury trends.

**Figure 19A. Percentage of COT patients with medically attended injuries (2006-2014)**

Note: The solid and dashed lines are trends adjusted for covariates. The triangles and squares show trends unadjusted for covariates.
Figure 19B. Estimated relative risk and 95% CI for the relative change per year in the proportion of COT patients experiencing a medically attended injury by setting and period

<table>
<thead>
<tr>
<th>Care Setting</th>
<th>Time period</th>
<th>Risk Stratification / Close Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Baseline</td>
<td>0.86 (0.68, 1.10)</td>
</tr>
<tr>
<td></td>
<td>Dose Reduction</td>
<td>1.13 (1.00, 1.28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.95 (0.88, 1.03)</td>
</tr>
<tr>
<td>Intervention</td>
<td>Baseline</td>
<td>0.98 (0.87, 1.11)</td>
</tr>
<tr>
<td></td>
<td>Dose Reduction</td>
<td>1.01 (0.95, 1.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.99 (0.95, 1.04)</td>
</tr>
</tbody>
</table>

*p-values for tests of difference in annual medically attended injury rate within time period between Intervention and Control settings:*

<table>
<thead>
<tr>
<th>Does the rate of change differ between Intervention and Control within a given period?</th>
<th>Not Significant</th>
<th>Not Significant</th>
<th>Not Significant</th>
</tr>
</thead>
</table>

Figure 20. Relative risk of medically attended injury by average daily MED (compared with former COD patients no longer using opioids)

Note: See “Dose-response Analyses” section for explanation of methods used to estimate dose-response curve.
Survey Results for Patient-reported Outcomes

Survey Response Rates and Nonresponse Predictors

The response rates for the postinitiative survey were low: 39.7% among COT patients in the intervention (GH-IGP) setting and 27.8% among patients in the control (GH-CC) setting. Figure 21 provides a flow diagram for recruitment for the telephone survey, including reasons for ineligibility and reasons for nonresponse. A major factor contributing to the lower survey response rates in the control setting was the much higher percentage of patients who were eligible but not reached owing to problems with telephone contact information.

The survey employed techniques that typically achieve much higher response rates: advance letter with $2 preincentive, $10 postincentive, contact materials written in “plain English” with a low reading grade level, and multiple contact attempts.

Figure 21. COT patient survey dispositions

<table>
<thead>
<tr>
<th></th>
<th>Intervention setting COT patients eligible for survey</th>
<th>Control setting COT patients eligible for survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampled for survey</td>
<td>2353</td>
<td>2351</td>
</tr>
<tr>
<td>Completed interview</td>
<td>39.7% (N=935)</td>
<td>27.8% (N=653)</td>
</tr>
<tr>
<td>Active refusal</td>
<td>31.4%</td>
<td>29.0 %</td>
</tr>
<tr>
<td>Passive refusal or not reached after many attempts</td>
<td>24.9%</td>
<td>25.8 %</td>
</tr>
<tr>
<td>Not reached due to problems with telephone contact information</td>
<td>3.8%</td>
<td>17.4 %</td>
</tr>
</tbody>
</table>

The low response rates may be attributed to a patient population that can be difficult to reach and engage in survey research, the requirement that participants agree to the use of their electronic health care data, a general decline in survey response rates in the United States, the sensitive nature of some of the survey content concerning misuse of prescription

62
opioid medications, and the length of the survey interview (30 to 40 minutes). The lower response rate in the control (GH-CC) setting may be attributable, in part, to the poorer quality of telephone contact information for those GH enrollees and the lower level of identification of CC enrollees with the Group Health organization.

**Predictors of Survey Response**

We performed unique analyses of variables predicting survey response using deidentified electronic health care data available for all persons eligible for the survey. After removing identifying information, records of the grouped characteristics for respondents and nonrespondents sampled for the survey were retained for nonresponse analyses. The variables found to predict survey nonresponse were the same characteristics generally found in other surveys to predict nonresponse: younger age, male gender, and tobacco use.¹⁰⁷

Individuals with mental disorder diagnoses were more likely to participate than those without. As found in a previous study,¹⁰⁷ strong risk indicators for prescription drug abuse (eg, substance use disorder diagnoses, opioid dose, and receiving more than 20% excess days of opioid supply) were not associated with differences in response rates in this survey. Figure 22 summarizes the variables that were and were not found to be associated with survey response rates. We used all the variables listed in Figure 22 to estimate analysis weights that adjusted for differences in survey response rates by patient characteristics.
Figure 22. Survey response rates by variables measured with EHR data

<table>
<thead>
<tr>
<th></th>
<th>Intervention (GH-IGP)</th>
<th>p-value</th>
<th>Control (GH-CC)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survey response rate</td>
<td>39.7 %</td>
<td>.0001</td>
<td>27.8 %</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-44</td>
<td>29.5 %</td>
<td>&lt;.0001</td>
<td>17.2 %</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>45-54</td>
<td>28.9 %</td>
<td></td>
<td>21.4 %</td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>37.6 %</td>
<td></td>
<td>28.6 %</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>51.8 %</td>
<td></td>
<td>37.5 %</td>
<td></td>
</tr>
<tr>
<td>75 +</td>
<td>48.9 %</td>
<td></td>
<td>39.0 %</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>41.7 %</td>
<td>0.018</td>
<td>28.8 %</td>
<td>0.139</td>
</tr>
<tr>
<td>Male</td>
<td>36.8 %</td>
<td></td>
<td>26.0 %</td>
<td></td>
</tr>
<tr>
<td>Mental disorder dx</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>36.5 %</td>
<td>0.016</td>
<td>24.1 %</td>
<td>0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>41.6 %</td>
<td></td>
<td>30.4 %</td>
<td></td>
</tr>
<tr>
<td>Tobacco use disorder dx</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>42.4 %</td>
<td>&lt;.0001</td>
<td>29.3 %</td>
<td>0.003</td>
</tr>
<tr>
<td>Yes</td>
<td>32.6 %</td>
<td></td>
<td>22.9 %</td>
<td></td>
</tr>
<tr>
<td>Eastern/Western Washington</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>East WA</td>
<td>39.3 %</td>
<td>0.790</td>
<td>24.0 %</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>West WA</td>
<td>39.9 %</td>
<td></td>
<td>32.0 %</td>
<td></td>
</tr>
</tbody>
</table>

Note: Variables unrelated to response rate: Alcohol use disorder Dx; Non-opioid drug use disorder Dx; Opioid use disorder Dx; Hepatitis C or cirrhosis Dx; Average daily opioid dose; Receiving excess days supply of opioids.

Pain Severity and Pain-Related Interference With Activities

Among COT patients interviewed in 2014-2015, after full implementation of intervention setting opioid dose and RSM initiatives for many years, ratings of pain severity and pain-related interference with activities did not differ between intervention and control patients. The pain ratings employed are shown in Figure 23. In both settings, more than 30% had pain ratings in the severe range (7 or higher on a 10-point scale) and more than 40% had pain-related interference ratings in the severe range (7 or higher; Figures 24 and 25). Most of the rest had pain severity and pain-related interference ratings in the moderate range (4-6). The covariate mean adjusted differences in these pain ratings between intervention and control patients were nonsignificant (Figures 24 and 25): COT patients in both settings reported similar levels of pain severity and interference even though intervention COT patients were, on average, receiving much lower opioid doses.
Figure 23. PEG pain severity and interference ratings (0-10)

In the past 7 days, how would you rate your pain on average?

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Worst Imaginable Pain</td>
</tr>
</tbody>
</table>

In the past 7 days, how much did pain interfere with your day-to-day activities?

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not Interfere at all</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Completely interferes</td>
</tr>
</tbody>
</table>

Figure 24. PEG pain severity ratings (0-10) after implementation of dose reduction and RSM initiatives

Covariate adjusted mean difference (Intervention minus Control) = 0.17 (95% CI = -0.02, 0.35)
Depressive Symptoms

Differences in PHQ-8 scores were statistically significant, with less depression among intervention patients, but the adjusted mean difference was modest (−0.64; 95% CI, −1.19 to −0.08). The mean PHQ-8 score among intervention patients was 7.5 (SD = 5.4); among control patients, it was 8.1 (SD = 5.8). The percentage with PHQ-8 scores of 10 or higher (indicative of clinically significant depressive symptoms) was 31.2% among intervention patients and 37.3% among control patients.

Ratings of Opioid Helpfulness and Bothersomeness

No differences in ratings of opioid helpfulness or bothersomeness appeared between the intervention and control patients (Figures 26 and 27). In both settings, more than 60% of patients who had been using opioids regularly for at least a year rated them as very or extremely helpful, and less than 5% rated them as very or extremely bothersome. The favorable ratings of opioid helpfulness stand in contrast to the ratings of pain severity and pain-related interference among the same patients, which suggests that most COT patients continued to have considerable pain dysfunction.
Prevalence of Prescription Opioid Use Disorder

After full implementation of dose reduction and RSM initiatives in the intervention setting for many years, no difference occurred in the prevalence of DSM-5 prescription opioid use disorder between intervention and control COT patients (Figure 28). In both settings, more than 20% of the patients met DSM-5 criteria for mild, moderate, or severe prescription opioid use disorder. The percentage with moderate or severe use disorder was 5.2% among intervention patients and 4.2% among control patients. Common symptoms of this disorder reported by COT patients were being unable to stop or cut down, having a strong urge or desire to take opioids, being preoccupied with their use, using opioids more or longer than intended, and giving up or cutting down important activities because of opioid use (Figure 29).

Figure 26. Perceived helpfulness of opioids after implementation of dose reduction and RSM initiatives

Covariate adjusted odds ratio for less perceived helpfulness of opioid for pain relief (Intervention compared to Control) = 1.11 (95% CI= 0.89, 1.40)
Figure 27. Perceived bothersomeness of opioids after implementation of dose reduction and RSM initiatives

\[ \text{Covariate adjusted odds ratio for less perceived helpfulness of opioid for pain relief} \]
\[ \text{(Intervention compared to Control) } = 1.19 \ (95\% \ CI= 0.87, 1.64) \]

Figure 28. Percentage of COT patients with DSM-5 prescription opioid use disorder after full implementation of dose reduction and RSM initiatives for 4+ years

\[ \text{Adjusted difference non-significant} \]
Doctor–Patient Collaboration and Trust Related to Opioid Management

Patients in both settings typically gave highly favorable ratings to physician collaboration and trust regarding opioid management, but the ratings of control patients were somewhat more favorable than those of intervention patients. For example, 86.5% of control patients agreed that “I trust my doctor’s judgment in managing my opiate pain medicine,” compared with 78.0% of intervention patients \( p < 0.001; \) see Figure 30. Similarly, 91% of control patients agreed that “I feel my doctor trusts me in how I manage my opiate pain medicine,” compared with 86.2% of intervention patients \( p = 0.019; \) see Figure 31. Patients in the intervention setting were more likely to say they were worried that their doctors might stop prescribing opioid pain medications (Figure 32). An equal percentage of intervention and control patients agreed that they had been well informed about potential problems with opioid medications (Figure 33).
Subgroup Differences

We performed analyses to identify any differences in patient-reported outcomes between intervention and control patients for the following characteristics: gender, age, race/ethnicity, alcohol use disorder status, medical comorbidity, nonopioid drug use disorder, and opioid use disorder. We assessed interaction effects for the following patient-reported outcomes: pain intensity and pain-related interference ratings, PHQ-8 depressive symptoms, opioid helpfulness and bothersomeness ratings, and prescription opioid use disorder status. Despite the large number of interaction effects screened, none were significant at the 0.05 level.

Figure 30. Patient rating: “I trust my doctor’s judgment in managing my opiate pain medicine.”

Chi-square test  $p<0.001$
Figure 31. Patient rating: “I feel my doctor trusts me in how I manage my opiate pain medicine.”

Chi-square test  $p=0.019$

Figure 32. Patient rating: “I sometimes worry that my doctor will stop prescribing my opiate pain medicine.”

Chi-square test  $p=0.002$
Expanded Dialogue With Patient and Family Stakeholders

Perceptions of Patient and Family Stakeholders Regarding Evaluation Results

After we completed our evaluation, we contacted large groups of patients and family members to solicit their perceptions of the implications of our results. We sent an email to people on the electronic distribution lists of the ACPA and the Steve Rummler Hope Foundation, inviting them to comment on our research results pertaining to the use of opioid medications for chronic pain. The ACPA’s mission is to facilitate peer support and education for individuals with chronic pain and their families so that these people can live more fully in spite of chronic pain. The mission of the Steve Rummler Hope Foundation is to heighten awareness of the dilemma of chronic pain and the disease of addiction, and to improve associated care processes. The characteristics of the participants from the 2 organizations are summarized in Figure 34. About half of the ACPA participants reported current long-term use of opioids for chronic pain, whereas only 5% of the Steve Rummler Hope Foundation participants reported long-term opioid use. More than 70% of ACPA participants had ever used opioids for the long term for chronic pain, compared with about 20% of participants from the Steve Rummler Hope

Chi-square test NS
Foundation. More than 90% of ACPA participants reported ever having had chronic pain, compared with about half of the Steve Rummler Hope Foundation participants.

**Figure 34. Characteristics of patient/family stakeholder participants**

We call this part of the evaluation *expanded dialogue*, because the intent was to understand diverse perspectives of patient and family stakeholders, not to conduct a survey of representative samples of stakeholders. The dialogue was not an interactive exchange in real time.

Before we informed them about the results of our evaluation, most participants from both the ACPA and the Steve Rummler Hope Foundation preferred a clinic that prescribed opioids at lower doses with closer monitoring. These preferences did not change substantially after participants learned about our results (Figure 35). Large majorities of participants from both organizations said that it was important for doctors to offer alternatives to opioid pain medicines (Figure 36).
Figure 35. Online responses from patient/family stakeholders: Preference for clinics with differing approaches to COT management before and after learning about evaluation results

ACPA: American Chronic Pain Association (N=226)
Rummler: Steve Rummler Hope Foundation (N=59)

Figure 36. Online responses from patient/family stakeholders: Importance of doctors offering alternatives to opioids for patients with chronic pain

ACPA: American Chronic Pain Association (N=226)
Rummler: Steve Rummler Hope Foundation (N=59)
Among participants from the Steve Rummler Hope Foundation, most believed that opioids should be prescribed for chronic pain either less often (41%) or rarely (38%). Three percent said opioids should be prescribed more often, and 11% said they should be prescribed about as often as they are now (Figure 37). Among ACPA participants, 20% said opioids should be prescribed more often, 37% said they should be prescribed about as often as they are now, 19% said they should be prescribed less often, and 14% said they should rarely be prescribed for chronic pain (Figure 37). These results highlight the diversity of views about opioids even among stakeholders from the same organization.

Figure 37. Online responses from patient/family stakeholders: How often should opioids be prescribed long-term for chronic pain?

How often should opioids be prescribed long-term for chronic pain?

ACPA: American Chronic Pain Association (N=226)
Rummler: Steve Rummler Hope Foundation (N=59)
DISCUSSION

Context

The use of opioids for long-term management of common chronic pain conditions is mired in controversy, reflecting deficiencies in scientific evidence regarding the effectiveness and safety of the drugs.4-8 Currently, 5 to 8 million American adults receive chronic opioid therapy for chronic pain.9,10 Our research addressed the needs and concerns of the millions of Americans who may consider opioids for long-term management of chronic pain as well as those who currently receive COT. These people expect their prescribing clinicians to use reliable information to weigh the potential risks of opioids against the perceived benefits and to minimize the risks of serious adverse consequences, including addiction and overdose.11

The long-term safety of opioid therapy has not been established.8 No large, long-term experimental studies have assessed major COT risks. Deficiencies in scientific evidence are particularly critical for patients who receive high-dose opioid therapy, for whom the risks of adverse events are greatest. We assessed whether dose reduction in intervention and control settings lowered the rates of relevant adverse events among COT patients. Evidence is limited regarding oft-recommended RSM interventions.4,8 Our research addressed these knowledge gaps by assessing the implementation of initiatives in primary care to lower opioid doses and to increase the use of universal precautions such as stepped-up monitoring, COT care plans, and urine drug screening. We evaluated whether opioid dose reduction and increased use of universal precautions lowered the risks of opioid abuse, overdose, and other potential adverse events while sustaining or enhancing patient-reported outcomes, including pain severity, psychological well-being, and the perceived helpfulness of opioid medications.

Study Results in Context

We found that, beginning in 2008 and continuing through 2010, COT patients in intervention clinics showed larger reductions in opioid dose than those in control clinics. After 2010, the use of COT care plans and urine drug tests increased substantially among patients in the intervention settings, as clinicians took steps to implement Washington State’s opioid
guideline. Organized implementation of the guideline was not evident in the control settings. The resulting large differences in COT management provided an opportunity to evaluate the effects on patient outcomes of opioid therapy dose reduction and RSM initiatives. This is the first controlled evaluation of dose reduction and RSM initiatives, other than before-and-after assessments of changes in state prescribing policies.

Evaluation results assessing whether the dose reduction achieved in the intervention setting was sufficient to reduce opioid overdose rates were inconsistent. During the dose reduction period, the difference in change in overdose rates between intervention and control settings was nonsignificant; however, among intervention patients during this period, the annual change in opioid overdose rate showed a statistically significant 17% decrement per year. In the same period, the annual reduction in overdose rate among control COT patients was 2% per year. We offer 3 explanations for the inconsistent results for opioid overdose:

1. The control group was about one-third the size of the intervention group, reducing statistical power to detect changes in the occurrence of a rarer adverse event such as opioid overdose between intervention and control settings. This lower statistical power was relative to analyses of change in overdose rates within the intervention setting over time with a larger effective sample size.

2. The reductions in opioid dose in the intervention setting typically occurred at moderate dosage levels not characterized by a steep dose-response curve, limiting the magnitude of the change in overdose rates with dose reduction.

3. For whatever reasons, the magnitude of the differences in opioid overdose rates between intervention and control settings after implementation of dose reduction was modest.

The evaluation showed no benefits of the RSM initiatives for reductions in opioid overdose rates. No further decline in overdose rates occurred in the intervention setting after implementation of the RSM interventions.

Overdose rates among the entire enrolled population (ie, among all enrollees regardless of opioid use) did not change over the study period in either the intervention or control settings. This analysis is, of course, less sensitive to changes in opioid therapy prescribing
because most individuals included in these secondary analyses were not exposed to opioids at all and were therefore not at risk of opioid overdose. However, it should be noted that population surveillance of the number of opioid overdose deaths per year reported by the CDC provided the first definitive evidence of increased risk of opioid overdose with increased prescribing of opioids for chronic pain.

Neither the dose reduction initiative nor the RSM initiative influenced rates of motor vehicle crashes or rates of medically attended injuries among COT patients, but these outcomes were not as strongly associated with dose as were opioid overdose rates. This evaluation is the first to report adverse event dose-response curves for opioid overdoses, motor vehicle crashes, and medically attended injuries in the same study population.

Among COT patients interviewed in 2014-2015 after the implementation of dose and risk reduction initiatives, differences in pain severity, pain-related interference with activities, and ratings of opioid helpfulness did not differ between intervention and control patients. Patients in the intervention setting had somewhat lower levels of depressive symptoms, but while this difference was statistically significant, it was modest and of uncertain clinical significance. No difference occurred in the prevalence of prescription opioid use disorder among intervention and control patients. In both settings, more than 20% of patients met DSM-5 criteria for mild, moderate, or severe use disorder.

While patients in both settings typically gave positive ratings to physician collaboration and trust pertaining to COT management, the ratings of patients in the intervention setting were slightly less favorable than those of patients in the control setting.

Recent before-and-after evaluations of overdose rates in settings that have reduced high-dose prescribing have found reductions in the number of opioid overdoses, which suggests that lowering opioid dose may reduce the risk of overdose. In our study, overdose rates were not reduced in the intervention setting among all individuals (including opioid users and nonusers, regardless of COT status), and rates of other adverse events (motor vehicle crashes, medically attended injuries, prescription opioid use disorder) did not differ between
intervention and control patients. Larger reductions in opioid dose or the length of use might have been required to reduce opioid-related risks in the population overall. Previous before-and-after evaluations of opioid overdose mortality have reported reductions in the number of opioid overdose deaths when controls have been placed on opioid prescribing.\textsuperscript{108-110} These evaluations have included fatal opioid overdoses occurring only in large population groups and have not included a control group other than before-and-after comparisons.

The evaluation results did not indicate any additional reductions in opioid-related risks from the RSM initiatives. These negative results do not suggest that universal precautions should be abandoned, but they do suggest that such precautions might not provide a reliable means for lowering risk. Clinicians in the GH-IGP reported anecdotally that the RSM initiatives reduced problems related to COT management in primary care clinics.

After the implementation of the dose reduction and RSM interventions, we found no differences between intervention and control patients in pain severity or pain-related interference ratings or in ratings of opioid helpfulness. This is consistent with recent randomized trials that have reported either no differences in severity and interference ratings with reduced opioid use or more favorable pain and function outcomes.\textsuperscript{114, 115} This finding suggests that on a population basis opioid doses can be lowered among COT patients without notable changes in overall pain status. However, the somewhat lower ratings of doctor–patient trust in the intervention setting than the control setting suggests that lowering the dose and implementing universal precautions may place some stresses on the doctor–patient relationship. The uncertain benefits of opioid therapy should be weighed against the potential strains that opioid management can place on the working relationship of chronic pain patients and prescribers.

**Implementation of Study Results**

The methods used by Group Health to reduce doses and to implement the RSM initiatives were summarized for dissemination to other care settings through the Six Building Blocks model for primary care clinic redesign for prescription opioid management.\textsuperscript{111} The building blocks model is also being applied to opioid risk reduction initiatives in a project
funded by the AHRQ in federally qualified community health centers in rural Washington and Idaho (Michael Parchman, principal investigator). The model was also used by CDC and Abt Associates to develop an implementation package for the 2016 CDC guideline for opioid prescribing for chronic pain. The CDC dissemination package is currently being pilot tested by Abt Associates in MedStar primary care clinics in Maryland. The Oregon Pain Guidance initiative (https://portlandprofessional.oregonpainguidance.org/) has adopted and refined the Six Building Blocks model for use in a statewide initiative to reduce opioid-related risks.

On April 21, 2017, the study team and the patient advisory committee convened a Workshop on Chronic Pain Management and Opioids in Seattle. It was attended by 45 individuals, including Kaiser Permanente Washington leaders responsible for new initiatives to reduce opioid-related risks, national experts on chronic pain management and opioids, and members of the study team and the patient advisory committee. The results of the evaluation were presented, followed by a discussion of the implications for improving chronic pain care and lowering opioid-related risks. As noted earlier, members of the patient advisory committee played an active and important role. (See the remarks by Ada Giudice Tompson and Max Sokolnicki in the appendix of this report.) The key ideas that emerged from the workshop are summarized in Figure 38.
Generalizability

This evaluation assessed a single health care organization’s implementation of a state COT guideline in an integrated group practice setting (not the statewide dissemination of the guideline). The control setting consisted of practices in the same state that did not implement the guideline in an organized fashion.

The opioid dose reduction and RSM initiatives evaluated in this research are likely easier to implement in an integrated group practice setting; however, the Six Building Blocks model has been adapted and implemented in diverse primary care settings. The findings regarding the association of dose reduction with rates of overdose, medically attended injuries, and motor vehicle crashes may depend on the dosage levels before and after prescribing changes, as suggested by the dose-response curves presented in this report. Additional research in the
large health care organizations that have recently achieved notable reductions in opioid dose could help clarify whether dose reductions result in reduced rates of opioid overdose.

The 2010 Washington State guideline is similar in many respects to the 2016 opioid management guideline disseminated by the CDC. The context of this evaluation is analogous to the current national situation, in which the federal government (ie, CDC) has disseminated a guideline for opioid prescribing, and some health care organizations are taking steps to implement the guideline, while others are not implementing it in an organized fashion. Our evaluation results are potentially relevant to health care organizations that are seeking to reduce opioid doses among their COT patients or to increase the use of RSM interventions.

The evaluation methods employed in this research could be used in other settings with electronic health care data to monitor changes in opioid prescribing and assess the effects of changes in opioid prescribing and COT management on key patient outcomes such as overdose. Because randomized trial data are currently insufficient to guide clinical policies regarding long-term opioid prescribing for chronic pain, surveillance and monitoring of initiatives to reduce opioid-related risks will be essential to determine whether hoped-for reductions in these risks are achieved and whether unintended deleterious effects of changes in opioid prescribing are being avoided.

Subpopulation Considerations

We performed extensive secondary analyses to assess whether interactions differed between key patient variables and intervention/control status for key patient-reported outcomes. No indications of differences in study results existed across patient subpopulations.

Limitations

We were not able to develop and follow a fixed cohort of COT patients from the intervention and control clinics. While a prospective design might be preferable for assessing causal effects of dose and risk reduction initiatives among new COT patients, it would take many years to develop an inception cohort of sufficient size, and additional years of follow-up to assess differences in onset rates of prescription opioid use disorder or incidence rates of
opioid overdose. New COT patients discontinue opioid use at high rates, complicating the evaluation of prescribing policies among the subset of patients who sustain long-term use. The dynamic cohort approach used in this evaluation has advantages for studying the effects of risk reduction initiatives targeting a patient population that changes over time depending on whether they are currently receiving chronic opioid therapy. But the dynamic cohort methodology cannot evaluate how risks change for individual patients over time according to how their opioid dose changes. It is possible that the effects of risk reduction initiatives may differ for patients who have recently started COT compared with long-term users, for high-dose patients versus lower-dose patients, or for low-risk versus high-risk patients. Replicating this evaluation in much larger populations to permit adequately powered subgroup analyses and following closed cohorts of COT patients over time could shed light on these substantive and methodological questions.

A second limitation was the evaluation of naturalistic policy changes in opioid dose and risk reduction practices implemented in the intervention clinics in a single health care organization but not in the control setting serving comparable chronic pain patients. The naturalistic design is subject to unmeasured confounding and outcome misclassification due to use of electronic health care data and to differences in ascertainment of adverse events using electronic health care data from different medical record systems (the IGP system and the various systems employed in the CC settings).

Although we found meaningful differences in opioid dose reduction and use of risk reduction practices between the intervention and control clinics, considerable overlap occurred in how the 2 patient populations were managed. For example, many patients in the intervention setting received high opioid doses, and many patients in the control setting received low doses. Because we were comparing patient populations exposed to different health care organization policies for COT guideline implementation, it is not surprising that we found considerable overlap between the intervention and control COT groups in opioid doses received and frequency of urine drug testing. If individual patients had been randomly assigned to different opioid dose schedules or to different COT monitoring regimens, the overlap in
these process measures would likely have been less. However, it would be difficult to randomize sufficient numbers of COT patients to different opioid prescribing policies to evaluate effects on less common events, such as opioid overdose. Recent changes in opioid prescribing in large health plans with electronic health care data could be used to compare the effects of dose reduction on overdose rates with the rates in health plans that have not achieved large reductions in opioid dose among COT patients.

A third limitation was the low survey response rate. Response rates in our survey were comparable to those in previous telephone surveys of COT patients assessing diagnostic criteria for prescription opioid use disorder.113 We sought to control potential nonresponse bias by incorporating weights that adjusted for predictors of survey response, including variables that are direct indicators of substance use disorder and problem opioid use. These weighting variables were available for all individuals sampled for the survey, including nonrespondents. Measures found to predict response were the same variables that predict nonresponse in many health surveys (eg, age, gender, tobacco use, health status) rather than variables that specifically indicate problem opioid use (eg, substance use disorder, excessive opioid use). When we compared analyses weighted to adjust for nonresponse to unweighted analyses, the differences in estimates were trivial. While this suggests that nonresponse bias might not have been important, it is not possible to exclude such bias as a source of measurement error for patient-reported outcomes assessed by survey interview.

We were not able to conduct interviews before, during, and after implementation of the initiatives because implementation began in 2007 and 2010, and our research did not begin until 2014. A prospective evaluation of the changes in COT management was not possible. Still, through the use of electronic pharmacy data to identify large numbers of COT patients, we were able to collect a comprehensive set of pain measures by interviewing almost 1600 COT patients with chronic noncancer pain from across Washington State who had been exposed to differences in COT dose and management in the intervention and control care settings for at least a year.
It is possible that rates of data capture for adverse events differed between the intervention and control settings. While we have no reason to believe that data capture rates for the 3 adverse events were not comparably high in the intervention and control settings, the time series design provides some control for differences in data capture by measuring rates of adverse events before, during, and after the dose reduction and RSM initiatives were implemented. It was reassuring that rates of adverse events assessed were similar in the 2 settings in the baseline period. We also asked COT patients in both settings whether they had received all their prescriptions for opioid medications in the previous year through their health plan insurance coverage; 96% of the patients in both settings said “yes,” indicating that electronic data capture for prescription opioids was likely to have been comparably high in the intervention and control settings.

We did not assess the use of illicit opioids (eg, heroin, illicitly synthesized fentanyl) in this evaluation. In previous research, we found that very few COT patients in the GH-IGP population had urine drug tests indicating heroin use.\textsuperscript{117} Because this evaluation focused on individuals currently receiving opioid therapy rather than those who had been tapered off opioids completely, the study patient population is less relevant to the question of heroin use risks among former COT patients.

Despite its limitations, this study was the first large-scale controlled evaluation of risk reduction initiatives targeting COT patients. Because large health care organizations are implementing similar initiatives to reduce opioid-related risks of overdose and addiction, evaluation of the effects of these initiatives in other settings is possible using methods developed through this research.

Future Research

In light of evidence that widespread prescribing of chronic opioid therapy may be reducing life expectancy on a population basis, that it has contributed to an iatrogenic epidemic of prescription drug addiction and prescription opioid overdose, and that it may not be an effective treatment, future research needs to assess how to de-implement inappropriate prescribing of COT for chronic pain. Recent reductions in opioid prescribing in some large VHA
and Kaiser regions may provide opportunities to evaluate whether larger dose reductions than those achieved in the Group Health setting have resulted in reductions in rates of opioid overdose and other relevant adverse events.
CONCLUSIONS

Whether the dose reduction initiative reduced rates of opioid overdose is uncertain because the difference in the change in overdose rate between intervention and control settings was nonsignificant, although the reduction in overdose rate in the intervention setting was significant during the dose reduction period. The reasons for this inconsistency are uncertain. In any case, the practice-level population overdose rate did not show a measurable change during the dose reduction period in either setting.

Our results did not suggest that the dose reduction initiative influenced rates of motor vehicle crashes or medically attended injuries among COT patients. Dose reduction was not associated with differences in rates of prescription opioid use disorder. Overall, our evaluation results suggest that efforts to lower rates of opioid overdose, addiction, and other adverse events may require lower rates of chronic opioid therapy or lower doses than those observed in the intervention setting. It might be possible to evaluate the effects of COT dose reduction on opioid overdose rates, as the VHA and Kaiser health plans have recently achieved dose reductions in very large populations that are greater than the reductions observed in the Group Health population a decade ago.

After opioid prescribing initiatives were implemented that substantially lowered opioid doses, we found no evidence that COT patients in intervention clinics that lowered doses experienced worse pain or greater pain-related interference with activities or quality of life than patients in control clinics that did not reduce opioid doses to the same extent. No difference in pain intensity, pain-related interference with activities, or enjoyment of life existed between patients in the intervention and control settings. These results are consistent with recent randomized trials that have reported no differences in pain and interference ratings with reduced opioid use or more favorable pain and function outcomes. The intervention patients had slightly lower depression scores, although a difference in PHQ-8 scores of less than 1 point is not clinically meaningful. Intervention patients did not perceive opioid treatment as providing less pain relief, suggesting that limits placed on high-dose opioid prescribing did not
have an identifiable impact on pain intensity ratings among patients who had been using opioids for at least a year on a population basis.

While our results do not argue against close monitoring of COT patients, they do not support RSM as a way to lower overdose rates or other adverse outcomes. This is an important result, because RSM recommendations have been based entirely on expert opinion. While close monitoring of COT patients is prudent (including regular urine drug tests and asking patients about opioid-related problems in more frequent follow-up visits), no evidence from controlled research indicates that such monitoring as typically implemented in community practice settings will reduce opioid-related risks. Along with growing evidence that long-term opioid use is often not effective for improving outcomes among persons with chronic pain, these results suggest that long-term opioid prescribing should be considered only when the benefits clearly outweigh the risks for an individual patient, and when more effective and less risky alternatives are not options.

*DSM-5* prescription opioid use disorder was common among COT patients in both the intervention and control settings who had used opioids regularly for at least a year. In both settings, more than 20% of COT patients met *DSM-5* criteria for the disorder, while 4% to 5% met criteria for moderate or severe opioid use disorder. These results indicate that neither dose reduction nor increased use of guideline-recommended precautions reduced the risks of prescription opioid use disorder to low levels among COT patients who had been using opioids regularly for a year or more.

Patient ratings of doctor–patient trust pertaining to COT were generally high, although they were somewhat lower in the intervention clinics than in the control settings. This finding indicates possible strains that COT can place on the doctor–patient relationship, which may become evident when efforts are initiated to lower doses or to monitor treatment more closely.

This is the first study to evaluate the effects of clinical policy initiatives that implemented opioid dose reduction and RSM on pain outcomes of COT patients. We conclude
that adverse effects of opioids—including addiction, medically attended injuries, and motor vehicle crashes—were not influenced by the RSM initiatives or by the level of opioid dose reduction achieved in the Intervention setting. The results of this evaluation were inconclusive regarding whether overdose rates among COT patients were lowered by dose reduction. In any case, opioid dose reduction did not reduce overdose rates in the entire adult population of the health plan. There is a pressing need for evaluation research that assesses the effects of recent initiatives implemented in large health plans to reduce long-term opioid use and opioid dosage levels among COT patients.
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APPENDIX

Introductory statement by Ada Giudice Tompson, Patient Advisory Committee member
Workshop on Chronic Pain Management and Opioids, April 21, 2017, Seattle, Washington

I expect today’s meeting will bring greater appreciation for the safety of all patients, greater respect for the inherent risks of opioids, and improved understanding of the complexity of chronic pain.

I have been advocating for a resolution to the opioid crisis since 2004, after suffering a personal loss. My son Michael was prescribed Percocet for acute pain caused by repeated bouts of kidney stones. In less than 2 years from the date of his first prescription, Michael was dead of an overdose. You may question, were the opioids prescribed or were they obtained illicitly? Were they taken as directed or misused? Would we say Michael was dependent or addicted? Do the answers to these questions really matter? The tragic outcome is the same. My son is gone. People are dying from overdoses every day, and how we assign blame for these deaths has important implications for policy responses. Why are we focused and blindsided by behaviors to obtain opioids? Why do we judge? Why are we blaming people who are ill, suffering, and vulnerable? Such attitudes serve to demean and disparage individuals. We have a responsibility to respect and understand the crisis, and we must face some unpleasant truths and ask difficult questions in order to make things better for all patients.

A false dichotomy is created engendering stigma when we distinguish between patients who use opioids medically for pain from those who misuse them. This view creates an indefensible moral distinction between “deserving” and “undeserving” patients rather than one community of patients.

The medical community failed to consider the real dangers of opioids and has adopted “safe use” practices such as if taken for pain, slow-release formulations, abuse-deterrent formulations, safe and effective as prescribed, and risk evaluation and mitigation strategies. These safe use approaches align physicians with their patients’ suffering from pain but not with these same patients when they develop an addiction or die of an opioid poisoning. To move
forward, we must acknowledge that these practices were based on poor science and that prescribing opioids liberally was a bad idea. It is a myth that opioid prescribing can be done safely if only the right safeguards are in place. Safe use practices do not make opioids or pharmaceutical grade heroin safe.

Determining analgesic efficacy of opioids is not easy. Relying solely on anecdotal patient reports to support claims of efficacy can be misleading. The effects of opioids on the brain and body cause a neurochemical response and wreak havoc with dopamine. Opioids produce physiological responses that are outside the control of the individual. These physiological responses reinforce continued use to avoid the symptoms of withdrawal. Tolerance, dependence, opioid use disorder, withdrawal symptoms, and opioid-induced hyperalgesia are interrelated, challenging, and act as a surrogate for pain. Patients and their doctors have great difficulty distinguishing one from the other and may lump all of these under the category of pain. Patients may attribute the problems they experience to their pain and not their pain meds. It is not surprising that risk stratification and monitoring initiatives did not reduce opioid overdoses. These approaches are external to the patient and cannot compete with the natural internal physiological opioid responses. Is it any wonder why anyone taking opioids for an extended period of time would resist coming off opioids? And yet we expect them to come off of opioids just as easily as they were put on them. Should patients be put on a drug that is self-perpetuating and difficult to stop?

Patients on COT who had their opioid doses reduced reported the same outcomes as those in the control group. So why continue with high doses? Why are we assuming opioids work and then trying to mitigate the risks associated with taking them, which often turns into a long and difficult battle? Use of alternative therapies and more cautious and judicious prescribing are required to prevent “new starts,” so patients do not transition to COT:

My personal tragedy is a very common scenario for many patients suffering with pain who rely on the legitimacy and integrity of the medical and regulatory systems. Opioids may be necessary in a relatively small number of intractable pain cases. However, it is indisputable at this point that they carry great risks and should be used in very select medical situations. We
need to stop equating opioids with safe pain care. Needing opioids does not equal benefiting from them, and cautious prescribing does not jeopardize quality care, it demands it. No one disputes the need to relieve pain, but the current medical approach is dangerous, and I don’t want my tragedy to become your tragedy. Patients should never be abandoned or arbitrarily taken off opioids or tapered to a lower dose without support and careful management. Prescribers everywhere should be held to the highest ethical standard to not further harm people as they solve this problem.

By the way, my beautiful son Michael was prescribed a new opioid—hydromorphone. He took it as prescribed, went to bed, and never woke up.

Introductory statement by Max Sokolnicki, Patient Advisory Committee member Workshop on Chronic Pain Management and Opioids, April 21, 2017, Seattle, Washington

My own experience with chronic pain and opioids is analogous to this study in that I have been a patient in both types of medical groups as were targets in the study.

In 2002, when my chronic pain began, I was under the care of a practice that did not specialize in pain care. During that time I was not educated in any of the positive or negatives of opioids—I just received them. There was no guideline adherence or information imparted that made me a more knowledgeable patient. As my dosage changed, I found myself in more pain and physical anxiety. I was looking for alternatives, but none was afforded me.

As I became more engaged in my medical condition, I found references for pain specialists from various medical sources. I turned to a well-respected pain practice. What I found there was an eagerness to educate the patient and follow established guidelines for opioids and alternative treatments, as well as risk evaluation and mitigation strategies.

I agreed to a trial with a spinal cord stimulator because I wanted to be more engaged in my life and reduce the amount of opioids that I was taking. The significant point was not that I reduced my opioid use but, more importantly, that I was educated about pain, offered alternatives, and was made to feel like I was an integral part of my own care. There was a
multitiered approach to pain care that I appreciated. Reducing opioid-related risk is apparent at each point in the patient–caregiver relationship.

With so much attention currently focused on the negatives of opioid use, it is important to remember that for some people with chronic pain, opioids are the primary alternative to afford any semblance of an active life at all. For these people, opioid use does not lead to adherent behavior or drug-seeking activity. They understand the risks and live within them. Unfortunately there is a very active minority that exemplifies the opposite.

As guidelines regarding dosage are enacted, it is important not to paint patients with too broad of a brush. Quality of life improvement needs to be the guiding force behind this effort. For some, dose reduction is a sound step. For others, a stable dose or a reduced dose with a reasonable alternative should be the road taken. Only with careful monitoring and consistent risk reduction strategies can this be achieved.

There must be a targeted effort to minimize dosage amounts to an acceptable level that is determined between the patient and the physician. Another goal is to reduce the initial dosage that pain patients are started on. That as well as exploring alternatives before or as opioids are introduced.

A problem lies with alternative therapies in that they are less likely to be accepted by medical insurance. This problem forces the medical community into choosing opioids foremost when treating chronic pain and begins the circuitous issues we are faced with.

I do believe that all medical providers who treat pain, both acute and chronic, should employ risk mitigation strategies and treatment guidelines, and that these strategies and guidelines should be common across all practices.

Early on in the study we were shown 3 examples of individual guidelines from 3 separate providers. Although one was fairly detailed, this exercise highlighted the need for commonality and availability from a consensus-driven set of documents. In short, guidelines that instill these 5 values: safety, respect, autonomy, compassion, and teamwork.
Finally, the patient must accept and be afforded a crucial role in their own health care. Responsibility for a patient’s care does not begin and end with the provider. An active patient or patient advocate enhances the patient–provider relationship to an extraordinary level that benefits both parties. The provider can trust the patient to follow well-designed medical plans, and the informed patient can trust that they are being heard and afforded all the information needed to make sound decisions about their own care.

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