CHRONIC OPIOID THERAPY AND THE RECEIPT OF PREVENTIVE SERVICES IN RURAL PRIMARY CARE

by

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A THESIS

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CERTIFICATE OF APPROVAL

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LIST OF ABBREVIATIONS

BRFSS	Behavioral Risk Factor Surveillance System
CI	Confidence Interval
CNMP	Chronic Non-Malignant Pain
COAT	Chronic Opioid Analgesic Therapy
CRC	Colorectal Cancer
Non-COAT	Not (using) Chronic Opioid Analgesic Therapy
ORPRN	Oregon Rural Practice-based Research Network
PBRN	Practice Based Research Network
PCP	Primary Care Physician /Provider
RR	Relative Risk
RRC	Regional Research Coordinator
U.S.	United States
USPSTF	United States Preventive Services Task Force

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ABSTRACT

Background

Chronic non-malignant pain is a common and important public health issue associated with broad and profound effects, including decreased quality of life, disability, and increased use of health services. The use of chronic opioid therapy for non-malignant pain often presents primary care clinicians with a conflict between their desire to care for their patients' pain and fears of addiction, diversion of medication, and/or legal action. The resulting dilemmas can lead to "time-consuming activities" and "failures in patient-physician relationship". Such stresses on the clinical encounter, along with physician ambivalence about working with patients with chronic non-malignant pain, might be expected to adversely affect many aspects of the clinical care of these patients, including the provision of clinical preventive and screening services.

Objective

The study was conducted to evaluate a possible association between chronic opioid therapy for chronic non-malignant pain and the receipt of clinical preventive and screening services.

Methods

The study used a retrospective cohort design to compare the receipt of four preventive services between patients on chronic opioid therapy for non-malignant pain and patients not on chronic opioid therapy. The four preventive services studied were: Pap testing, colorectal cancer screening, lipid screening, and smoking cessation

counseling. The study was conducted in 7 clinics in a rural practice-based research network. We used medical record data of 704 subjects, 35 to 85 years old, seen in participating clinics over a three year period, and frequency matched by gender and smoking status. We used multivariable regression analyses to calculate the relative risk of receipt of each preventive service for patients on chronic opioid therapy compared to patients not on opioid therapy, while adjusting for potential confounding factors.

Results

The adjusted relative risk (RR) of receipt of each service by patients using chronic opioid therapy compared to patients not using opioid therapy was as follows: Pap testing, RR = 0.60 [95% confidence interval (95% CI) = 0.47, 0.76]; colorectal cancer screening, RR = 0.42 [95% CI = 0.22, 0.80]; lipid screening, RR = 0.77 [95% CI = 0.54, 1.10]; and smoking cessation counseling, RR = 0.95 [95% CI = 0.78, 1.15].

Conclusions

We found that patients using chronic opioid therapy were less likely to receive each preventive or screening service. The relative risk estimates were statistically significant for Pap testing and colorectal cancer screening. The specific reasons for these disparities in preventive care cannot be definitively determined from our study, but might include time-consuming activities focused on pain and prescribing opioids and/or failures in the patient-physician relationship. These findings suggest the need for a better understanding of barriers to and improved methods for providing preventive services for patients using opioids for chronic pain.

"Three respectable London druggists, in widely remote quarters of London, from whom I happened lately to be purchasing small quantities of opium, assured me that the number of amateur opium-eaters (as I may term them) was at this time immense; and that the difficulty of distinguishing those persons to whom habit had rendered opium necessary from such as were purchasing it with a view to suicide, occasioned them daily trouble and disputes."

Thomas De Quincey
Confessions of an English Opium-Eater (1822)

INTRODUCTION

The Challenges of Chronic Non-Malignant Pain and Opioids

In 1822, the English author Thomas De Quincey published *Confessions of an English Opium-Eater*,[1] in which he described his experience as an opium addict, and in which he provided a glimpse of the social, moral, and medical views of opium use at that time.[2] By De Quincey's account, opium use presented problems and challenges for doctors and druggists nearly two hundred years ago. In fact, most primary care clinicians practicing today would recognize with sympathy the dilemma around opium use faced by our 18th century counterparts. We, too, may be experience "daily trouble and disputes" when caring for our patients who are on chronic opioid therapy. And, yet, the issues of chronic pain and pain management have never been more pressing for public health and primary care.

Chronic non-cancer related pain is a common and important public health issue associated with broad and profound effects, including decreased quality of life, disability, increased use of health services, high direct costs for treatment, and loss of productivity.[3-7] Population-based data on the prevalence and duration of pain in the United States were reported in a recent annual publication of the National Center for

Health Statistics.[8] These data, from the National Health and Nutrition Examination Survey, indicate that approximately a quarter of the U.S. population 20 years of age and older have pain on a monthly basis and that roughly 40% of those reporting pain the previous month have had that pain for a year or longer.[8] This amounts to more than 75 million Americans with chronic or recurrent pain.[9] Not surprisingly, pain is one of the most common reasons that people seek medical care in the U.S. and elsewhere,[10-17] and the majority of those seeking medical attention receive their care in the primary care setting.[12, 13, 18, 19] A World Health Organization study found the prevalence of chronic pain to be 22% across 15 primary care centers in Asia, Africa, Europe, and the Americas, with a prevalence of 17.3% in the U.S. clinic studied.[16] A study conducted among older U.S. veterans (mean age of 64 years) in a general medicine clinic found the prevalence of non-cancer related pain to be 48%.[12]

Despite its high prevalence and its high cost to individuals and society, chronic pain is often poorly managed and inadequately treated.[4, 5, 10, 17, 20-22] Studies suggest that from 40% to 70% of patients with chronic pain continue to experience pain after treatment.[4, 5, 10] The inadequate management of chronic pain is likely due to a combination of numerous factors, some of which relate to general societal perceptions and attitudes toward pain, some of which relate to aspects of the health care system and regulations, and some of which relate to characteristics of physicians, patients, and their interactions.

The subjective nature of pain makes it difficult to measure and presents challenges for assessing treatment.[9] Many physicians and others in the health care system believe that psychological characteristics and/or psychiatric disorders are the

primary cause of much chronic pain, despite a lack of evidence to support this view, and as a consequence may not adequately understand or manage chronic pain.[4] Many physicians and others believe that disability benefits provide a disincentive for patients with pain to recover and return to work, although evidence to support this view is also lacking, and this may place patients and physicians at odds with one another.[4] One study found that physicians' approach to pain management varied according to the type of pain and patient demographic characteristics.[23] The study found that physicians were more likely to provide optimal pain treatment for men with postoperative or cancer-related pain, and that treatment goals were generally lower for chronic non-cancer pain.[23] Physicians report the need for practice guidelines and best practice standards.[22, 24] Additionally, studies have concluded that relatively few physicians are adequately trained in pain management, many have low confidence in their knowledge and abilities in pain management, and few find it satisfying.[22, 23, 25-28]

A key factor in this situation is the complexity associated with the use of opioid medications for the treatment of chronic non-malignant pain (i.e., chronic pain that is not due to cancer). Opioid medications are generally accepted as appropriate therapy for cancer pain and pain related to other terminal illnesses. However, although the use of opioid therapy to treat chronic non-malignant pain (CNMP) has become increasingly accepted in primary care practice, this is still with some controversy.[6, 29-34] For the practicing primary care physician, multiple factors contribute to this controversy and present dilemmas regarding treatment with opioids for CNMP. These factors include: the lack of definitive data on the risks and benefits of opioids for CNMP; concerns about physical dependence, tolerance and addiction; concern about adequate and appropriate

treatment of patients' pain; concern about possible diversion of opioid medication for other purposes; and concern about possible sanctions by state and federal regulatory agencies.

A recent systematic review and meta-analysis of 17 studies found the evidence base regarding chronic opioid therapy for CNMP to be of generally low quality and limited.[30] The investigators concluded that many patients discontinue long-term opioid therapy due to adverse effects or insufficient pain relief, and that weak evidence does suggest that opioids reduce pain long-term in the small proportion of patients who continue therapy.[30] However, the paucity of data from included studies that describe long-term efficacy and safety means that the implications of these conclusions for clinical practice are unclear. Another recent systematic review and meta-analysis of 34 randomized trials concluded that opioids out-performed placebo for pain and functional outcomes.[35] This review also found that strong, but not weak, opioids provided better pain relief, but that non-opioid drugs produced better functional outcomes than opioids. A third recent systematic review concluded that moderate to high quality evidence suggests that long-term treatment with opioids for CNMP can improve functional outcomes.[36] Another recent, non-systemic, review reports conflicting findings in the literature with regard to the long-term efficacy of opioids for CNMP.[37] This review also notes that evidence is limited regarding functional and quality of life outcomes, which are broadly regarded as the most meaningful outcomes. Aside from the variation in the studies included in these reviews and the possible implications this may have for the results, it is understandable that, based on the reported conclusions, clinicians might be unclear about the efficacy and safety of long-term opioid therapy for CNMP.

Clinical decisions about the long-term use of opioids for CNMP are further complicated by concerns about possible addiction, physical tolerance, dependence and withdrawal.[38-42] Each of the previously cited reviews notes that the potential for addiction should be considered when prescribing opioids.[30, 35-37] Although studies indicate that the risk for development of addiction when opioids are used to treat pain is low,[17, 43] the evidence is not unequivocal.[37, 44] Clearly, some risk does exist, and clinicians have a responsibility to somehow assess this risk for their patients with chronic pain.[45-48] Furthermore, many physicians misunderstand the difference between addiction, pseudo-addiction, physical dependence, and tolerance.[17, 49, 50] A considerable amount of research has been conducted to understand how to better identify those at increased risk and avoid iatrogenic addiction.[43, 45-47, 51] To date, however, issues related to addiction present many complex questions that have still not been clearly answered.[37, 47] This uncertainty complicates clinical decision-making and is a major element in the dilemmas experienced by clinicians when prescribing opioids for CNMP.[52]

Physicians are also concerned that they may be misled by patients who wish to obtain opioid medications for purposes other than treatment of pain, such as diversion for sale and profit, treatment of non-pain symptoms, recreational use, or maintenance of addiction.[17, 32, 37, 40, 41, 49, 52-55] One study found that concern about patient "drug-seeking" behavior was a consideration in 44% of those cases in which primary care physicians experienced dilemmas regarding opioid prescriptions, and that suspected drug abuse was a consideration in 14% of cases.[52] A related issue is the fear that physicians have of incurring regulatory or other legal action for either over-prescribing opioid

medications or under-treating patient pain.[38, 54, 56-59] These concerns, too, contribute to the dilemmas that face physicians when deciding to prescribe opioid therapy, and have been shown to undermine the "therapeutic alliance" and contribute to strains in the patient-physician relationship.[52]

In summary, the clinical management of chronic non-malignant pain, particularly when using opioid medications, is complex and influenced by a myriad of often conflicting factors. Physicians are normally empathetic toward the pain of their patients and want to ease their suffering.[9, 60, 61] This is often complicated, however, by uncertainty related to the subjective nature of pain; misconceptions about the causes of chronic pain; lack of physician confidence or experience in the management of chronic pain; lack of clear and definitive data on the efficacy and safety of long-term opioid therapy; concerns about possible diversion of opioids for non-pain related purposes; and concern about possible legal or regulatory sanctions. Given the potential conflict between physicians' desire to care for their patients' pain and fears of addiction, diversion of medication, and/or legal action, it would not be surprising if primary care clinic encounters involving patients with CNMP and opioids were especially complicated or challenging for physicians, clinic staff, and/or patients.

In fact, researchers have found that the process of deciding whether or not to prescribe medications is complex, and is often characterized by physicians struggling to balance several disparate considerations such as those mentioned above.[62-64] One study of the reasons that primary care physicians experience dilemmas in prescribing opioids also examined the multiple consequences of these dilemmas. The two leading

consequences of dilemmas experienced by physicians in prescribing opioids were found to be "time-consuming actions" (37% of cases) and "failures in patient-physician relationship" (25% of cases).[52] Another study found that patient pain during clinic visits is associated with physicians spending more time on technical tasks, and less time on preventive services and other activities designed to encourage the patient's active participation in their own health care.[10] Many physicians are ambivalent about working with patients who have chronic non-malignant pain and few enjoy it, with one survey reporting only 15% of physicians "enjoy working with patients who have CNMP". [32]

It is reasonable to consider that the complexity and conflicts associated with chronic opioid therapy and CNMP might place stresses on clinical encounters between physicians and patients, such as the time-consuming actions and failures in the patient-physician relationship noted above. It is also reasonable to consider that such stresses, along with physician ambivalence about working with patients with CNMP, might be expected to adversely affect many aspects of the clinical care of these patients, including the provision of clinical preventive and screening services.

Clinical Preventive and Screening Services

Abundant research clearly demonstrates that receiving good quality, evidence-based clinical preventive and screening services is integral to helping people live healthier lives.[65] The U. S. Preventive Services Task Force (USPSTF), sponsored by the Agency for Healthcare Research and Quality, systematically reviews and evaluates the scientific evidence regarding a large number of preventive and screening services for a wide variety of conditions, including cancers, cardiovascular disease, infectious

diseases, injury and violence, mental health conditions, and metabolic conditions. These rigorous reviews evaluate the benefits of primary and secondary preventive services in apparently health individuals, in order to make recommendations as to which services should be incorporated into routine primary care practice.[65] The USPSTF recommendations are widely considered to be the "gold standard" for preventive services.

Providing recommended preventive and screening services is an essential aspect of good quality primary care. Although USPSTF recommended preventive services have been shown to decrease morbidity and mortality, they are not always received as indicated. For example, data from the 2006 Behavioral Risk Factor Surveillance System (BRFSS) survey indicate that only 57.1% of adults aged ≥ 50 years have ever received colorectal cancer screening with sigmoidoscopy or colonoscopy, and only 24.1% report having had a fecal occult blood test within the past two years.[66] This is despite the highest level recommendation (level "A") by the USPSTF for colorectal cancer screening.[65] The USPSTF also makes an "A" level recommendation for routine screening for lipid disorders in men aged 35 years or older and women aged 45 years or older, yet the 2007 BRFSS survey data indicate that only 74.9% of these individuals had been screened in the previous five years and 21.7% had never been screened.[66] Similarly, tobacco cessation counseling ("A" recommendation) is not systematically addressed.[67] Although rates of cholesterol screening and cervical cancer screening (also "A" recommendation) are generally higher, variations in the rates of all preventive and screening services have been noted between different groups and sub-populations, and depending on various patient and clinic characteristics.[66] For instance, multiple studies have found that adults with mobility impairments are less likely than those

without mobility impairments to receive preventive and screening services.[68-71] And, studies have also found rural residents to be less likely than urban residents to receive indicated preventive and screening services.[72-75] Another subgroup that may have lower rates of preventive services is patients with chronic non-malignant pain receiving opioid medication therapy.

As the number of appropriate screening and preventive services grows, the time and resources required for providing these services grows, as well.[76] Physicians are increasingly under time constraints during office visits, and time-consuming activities related to prescribing opioids might detract from time that would otherwise be spent addressing and/or arranging for preventive care or screening services. Similarly, failures of the patient-physician relationship that derive from the challenges of caring for patients with CNMP with opioids might reduce the likelihood that physicians would deliver, or that patients would receive, recommended preventive and screening services.

OBJECTIVES

The study was conducted to test the hypothesis that patients who receive chronic opioid analgesic therapy (COAT) for non-malignant pain in the primary care setting receive preventive and screening services at lower rates than those who do not receive chronic opioid therapy. The specific preventive and screening services evaluated were: 1) screening for cervical cancer; 2) screening for colorectal cancer; 3) screening for hyperlipidemia; and, 4) counseling for smoking cessation. These particular services were chosen for a number of reasons. First, each of these preventive services has been the subject of a rigorous systematic review by the U.S. Preventive Services Task Force and has the highest level recommendation based on evidence of its effectiveness. Secondly, each of these services is recommended for a different subgroup of patients, defined by particular characteristics of age, gender and/or smoking behavior. By addressing this variety of services, the study is applicable to a broader population of patients. Thirdly, the four services differ not only in the particular health condition that each is designed to detect or prevent, but also in the nature of what each service requires of patients, physicians and other elements of the healthcare system. Obtaining some services is more logistically complicated and demanding than others (e.g., colorectal cancer screening received off-site versus lipid screening at the primary care clinic). The services also differ in their technical complexity, the interpersonal skills required, level of inconvenience and/or discomfort for patients, time required, and cost. By including this variety of services, the study accounts for a range of other factors that might influence the performance preventive services.

METHODS

Overview of Study Design

The study used a retrospective cohort design to compare the receipt of the four clinical preventive services between patients on chronic opioid analgesic therapy (COAT) for non-malignant pain to those not on chronic opioid analgesic therapy (Non-COAT). We used the medical records of participating primary care medical practices to identify study subjects comprising a single general cohort. The medical records for all patients aged 35 or older seen in clinic by the participating clinicians during the month of April 2000 were reviewed to determine eligibility. When necessary to obtain adequate sample size, we extended the sampling time frame to include the last two weeks of March 2000 and the first two weeks of May 2000. Eligible potential study subjects were classified into "exposure" categories as either "COAT" (those receiving chronic opioid therapy) or "Non-COAT" (those not receiving chronic opioid therapy), according to opioid use during calendar year 2000. All eligible subjects classified as COAT were enrolled, and those classified as Non-COAT were frequency matched by gender and smoking status to COAT subjects at a 2:1 ratio.

Data for all study variables were then abstracted from the medical records of enrolled subjects for the three-year period of observation defined by calendar years 2001, 2002, and 2003. These data included information on the performance of the four preventive and screening services (the outcome variables), demographic information (e.g., age, gender, ethnicity), and other pertinent co-variables. We conducted analyses to compare a variety of demographic, medical, clinic utilization, and other descriptive characteristics between COAT and Non-COAT subjects. We conducted these analyses

for the entire sample of study subjects, and for each of the four subgroups of subjects corresponding to the four preventive service outcomes of interest. We then conducted regression analyses to determine the relative risk of receipt of each preventive service in the COAT subjects compared with the Non-COAT subjects, while adjusting for plausible confounders.

Study Setting

The study was conducted in the Oregon Rural Practice-based Research Network (ORPRN), a practice-based research network of 45 primary care practiced located throughout rural Oregon. A practice-based research network (PBRN) is a network of clinical practices that collaborate in research to better understand disease, health, and healthcare needs in the primary care setting, where most people receive most of their healthcare. Regional and national PBRNs have been active in the United States since the 1970s.[77, 78] PBRNs have been recognized as "the only organized setting dedicated to research on clinical preventive services, the diagnosis and management of common and important medical problems, and the delivery of primary care health services."[77] Given that CNMP and the dilemmas surrounding chronic opioid therapy are a common and difficult problem in primary care, and since most clinical preventive and screening services occur as an element of primary care, a PBRN is the ideal setting for conducting this study.

The Oregon Rural Practice-based Research Network (ORPRN) is a collaboration of rural primary care clinical practices and academic researchers at Oregon Health and Science University, with the mission of carrying out research that addresses the needs of

rural Oregonians and the rural medical practitioners who serve them. ORPRN includes more than 140 clinicians, in 45 practices, serving approximately 225,000 patients in 35 communities throughout the state of Oregon. (See Appendix A for Map) The rural medical practices within ORPRN are not otherwise formally associated. ORPRN practices do not share data, nor do they use a common medical record or data system. The study was conducted in seven ORPRN practices in six rural Oregon communities.

Data for the study were abstracted from patient medical records by three "Regional Research Coordinators". The Regional Research Coordinators, or "RRCs", are core staff members of ORPRN, each of whom lives and works in a different rural community located in one of three different geographical regions of the state. Each RRC participates in different aspects of research projects carried out in their respective regions. The seven clinics that participated in this study were located throughout the state, with two clinics from each of two regions and three clinics from the third region.

Data Source and Data Collection

Data for the study were abstracted from patient medical records on-site at each of the seven clinics. The clinics use a variety of both paper and electronic medical record systems, with no uniform system among the practices for recording specific study variables. For this reason, we developed a single, uniform data collection instrument for use in all of the participating practices. (See Appendix B) To develop this data collection instrument, a co-investigator (JC) and I visited two ORPRN practices with a research assistant who had chart review experience. We reviewed a sample of medical records in both clinics to: 1) test a prototype data collection tool for its ease of use, and 2) to refine

the operational definitions of the study variables so they conformed more closely to the clinic medical records. For this latter objective, we identified the sections within the medical records where data on each variable were likely to be found and the form that those data were likely to take. For example, information on whether a serum lipid test was performed might be recorded on a laboratory report in the "Lab Results" section, in a computerized list of preventive services, and/or written by hand in the clinic notes. Through this process, two iterations of the data collection instrument were tested in the clinics and modified. The final iteration of the data collection instrument was converted into a scan-able form used in the study by the RRCs (Appendix B). All sections of the medical record that might plausibly contain data on the study variables (as determined by the "preliminary pilot phase") were reviewed, including clinic notes, medication lists, laboratory reports, nursing notes, chronic disease flow-sheets, and preventive services checklists.

Prior to the chart reviews at the study sites, the RRCs attended a one-day training session in Portland, at which they received instruction on working with the study sites, standardized procedures for the study, operational definitions of study variables, and a standardized approach to data abstraction. We developed an "operations manual" (See Appendix D) that outlines the details of the study procedures and contains references for the operational definitions of the variables, codes, forms, etc. We used this manual during the training session, and the RRCs conducted approximately 10 practice chart abstractions during the training session in order to address and resolve any confusion or ambiguities around the procedures and definitions. The RRCs then used the manual as a reference during the field work and data abstraction. [For clarity, the reader should note

that the manual, included as Appendix D of this document, has numerous appendices of its own, and these are numbered "1" to "11". The individual appendices of the manual are herein referred to using the letter "D" and the corresponding number for the appendix in the manual, for example, as "D-1", "D-2", "D-3", etc. See page 77 for details of the manual, its appendices, and its page numbering.]

Selection of Study Subjects

Initially, the RRCs randomly selected one to four clinicians at each study site. These were selected from among all clinicians (including physicians (M.D. or D.O.), nurse practitioners, and physician assistants) who saw patients at one of the seven participating clinics on a full time basis at least four days a week during the entire month of April 2000. The number of clinicians randomly selected at each study site was determined by the total number of practicing clinicians, with fewer selected for smaller sites and more for larger sites (Appendix D-2). Then, the medical records of all patients aged 35 and older who were seen by one of the selected clinicians during April 2000 were reviewed to determine COAT status, sex, and smoking status. When necessary to obtain adequate sample size, we extended the sampling time frame to include the last two weeks of March 2000 and the first two weeks of May 2000. This "First Pass" record review was to gather data on COAT status, sex, and smoking status, only.

Patients were then classified into one of the 2 comparison groups: COAT and Non-COAT. All COAT subjects were enrolled, and Non-COAT subjects were then frequency matched with the COAT subjects at a 2 to 1 ratio, according to sex and smoking status. For example, for each female smoker on COAT, 2 female smokers not on

COAT were also enrolled. Non-COAT subjects were considered for inclusion according to the chronology of their first clinic visit during April 2000. So, for example, if 25 female smokers on COAT were identified at a particular clinic, the 50 Non-COAT female smokers who had the earliest clinic visits during April 2000 were first considered for inclusion. In those cases when a Non-COAT patient was ineligible, we considered the Non-COAT patient with the next earliest clinic visit, instead. In this way, we were assured to have study subjects for each of the four preventive services, which are each recommended according to age, gender, and/or smoking status. And, we avoided the time and cost of performing a complete record review on those Non-COAT patients who were not matched into the study. Additionally, we restricted the study to adults aged 35 and older in order to increase the likelihood that a study subject would be eligible for multiple preventive services, thereby reducing the total number of subjects required. Only after the frequency-matched COAT and Non-COAT cohorts were determined were the full chart reviews performed with abstraction of all study variables.

The inclusion and exclusion criteria are summarized below:

Inclusion Criteria:

1) Patient seen in participating clinic during the sampling time frame in March, 2000 to May, 2000;

2) Patient 35 years or older as of 4/1/00;

3) Either gender;

4) Patient with a medical record beginning no later than 1/1/00.

Exclusion Criteria:

1) Patient younger than 35 years of age as of 4/1/00;

2) Medical record of insufficient time span to establish the patient's classification as "COAT" or "Non-COAT", per protocol;

3) Patient medical record without at least one clinic visit during the study period, 1/1/00 to 12/31/03.

COAT Definition

Chronic Opioid Analgesic Therapy (COAT) status was defined as a dichotomous variable ("Yes/No") indicating whether or not the subject received chronic opioid therapy during calendar year 2000. Chronic opioid therapy was defined in either one of two ways:

1) **Direct**:

- ⇨ Evidence of ≥30 days of prescribed opioid medication per month for at least 6 months during calendar year 2000,

OR,

2) **Indirect** (by Inference):

- ⇨ Evidence of ≥30 days of prescribed opioid medication per month for at least 6 months during calendar year 1999, **AND**
- ⇨ Evidence of ≥30 days of prescribed opioid medication per month for at least 6 months during calendar year 2001, **AND**
- ⇨ At least one chart entry indicating opioid use during calendar year 2000.

The direct definition was preferred and tried first. As with all variables evaluated in the study, the evidence might have come from any of a variety of sources. The most likely sources were: medication lists, physician or nursing clinic notes, or prescription copies.

Preventive Services Subgroups

The study's four outcomes of interest were derived from the recommendations of the U.S. Preventive Services Task Force (USPSTF). As noted below, each service is recommended for a particular age and/or gender. Our analysis for each preventive service outcome was restricted to the subgroup of study subjects who met the criteria by which that preventive service would be recommended in usual clinical practice. Individual subjects were included in all subgroups for which they fit the criteria. For example, a 55-year old woman who smokes would have been included in the analysis of each preventive service outcome, and a 40-year old man who does not smoke would only be included in the analysis of the lipid screening outcome. Although Pap testing is recommended for most women between the ages of 21 and 65 years, this study only included subjects 35 years of age or older, in order to maximize the number of services for which subjects would potentially be eligible.

For the purposes of this study, each outcome variable is defined as dichotomous (yes or no), indicating whether or not the particular screening test or preventive service was performed at least one time during the three year period of observation. There are six outcome variables representing only four preventive or screening services, since three of the variables represent three different possible methods for colorectal cancer screening. Screening for cervical cancer (Pap testing) was assessed in women 35 to 65 years old. Screening for colorectal cancer (CRC) was assessed in men and women aged 50 years and older. CRC screening was measured as having received at least one of three different methods: home fecal occult blood testing, flexible sigmoidoscopy, or colonoscopy. Screening for lipid disorders was assessed in men aged 35 years or older and women

aged 45 years or older. Counseling for smoking cessation was assessed in all smokers. In addition, for each of the CRC screening variables and for the lipid screening variable, data were collected to confirm that the test was for screening purposes. The four preventive/screening services, corresponding outcome variables, and corresponding subgroup of study subjects are summarized in Table 1, below.

Table 1. Preventive and Screening Services Included in the Study, with Corresponding Outcome Variables Measured and Study Subject Subgroups

Preventive Service	Measured Variable	Patient Subgroup
Cervical Cancer Screening	Pap testing	Women ≥35 years old and ≤65 years old
Colorectal Cancer Screening	*At least one* of : fecal occult blood test; sigmoidoscopy; *or* colonoscopy	Men and Women ≥50 years old
Lipid Screening	Serum cholesterol or lipid testing	Men ≥35 years old, and Women ≥45 years old
Smoking Cessation Counseling	Counseling by clinician or other professional	All smokers

Other Variables

Data on a variety of additional variables were also gathered, to make comparisons between the COAT and Non-COAT subjects, and to evaluate for possible confounders in any observed association between COAT status and the receipt of preventive services. These variables included data about a variety of patient characteristics, including demographics, insurance status and type, number and type of medical conditions, history of substance abuse, and several measures of clinic utilization. Detailed descriptions and operational definitions of these variables are included in the operations manual (Appendix D-7). Variable types included continuous and categorical (both dichotomous

and polychotomous). Data were also gathered on more than 30 distinct coexisting medical diagnoses, or "comorbidities" (Appendix D-10). A list of other variables assessed in the study is presented in Table 2, below.

Table 2. Other Variables Assessed in the Study

Age	Date of Last Visit
Sex	Diagnosis for Opioid Use
Ethnicity and Race	Comorbid Diagnoses
Zip Code	Number of Comorbid Diagnoses
Insurance Status	Lipid Disorder History
Clinic	Substance Abuse History
Primary Care Physician (PCP)	Controlled Substance Contract
Number of Visits	Date Subject Discontinued at Clinic
Number of Visits with PCP	Date of Death

Analyses

Distribution of Demographic and Other Characteristics by COAT Status:

I calculated the distributions of demographic and other descriptive characteristics between COAT subjects and Non-COAT subjects as mean values (continuous variables) and percentages (categorical variables). I used the independent samples *t* test and the Pearson chi-squared ($\chi 2$) test to compare the mean values and percentages, respectively, between the subjects in each of the two "exposure" groups (COAT and Non-COAT). These analyses were conducted for the total study sample and for each of the subgroups corresponding to the four preventive service outcomes. In addition, for each preventive service subgroup, I calculated the percentage of COAT subjects and the percentage of Non-COAT subjects that received the particular preventive service.

Assessment of potential confounders

Before conducting regression analyses to calculate the relative risk of receiving each preventive service among COAT versus Non-COAT subjects, I first used a three-part process to evaluate various factors for their potential confounding effects. By definition, a confounder is associated with both the exposure and the outcome of interest. To be a plausible confounder in this study, therefore, a variable would first need to be associated with both COAT status and the particular preventive service outcome. Only those variables that appeared to be plausible possible confounders were considered in the regression modeling that followed. Given the large number of variables relative to the number of study subjects, I used this approach as a logical way of narrowing the set of co-variables considered in the model building, and excluding those variables that were unlikely to have a confounding effect. Although, this approach might not be appropriate for building *predictive* models, it is a reasonable step in assessing variables for possible confounding when regression modeling is used only to adjust for confounding, as in this study.

For each of the four preventive service outcomes, I conducted statistical testing to determine if each co-variable was: 1) significantly associated with COAT status (exposure), and 2) significantly associated with the particular preventive service (outcome). I used the independent samples *t* test for continuous variables and the Pearson chi-squared ($\chi 2$) test for categorical variables. A p-value of ≤ 0.05 was considered significant. For these analyses, I converted the variable "Age" from a continuous to a categorical variable with three categories (35-44 years old; 45-54 years old; 55-65 years old). "Race/Ethnicity" was categorized as: "White/Non-Hispanic"; "Other"; or "Not

Specified". I classified "Insurance" status into one of 5 categories, each of which was tested as a dichotomous variable. Individual subjects with more than one type of insurance were counted for each type of insurance they had. I conducted these statistical tests only for 9 of the 35 medical and psychiatric comorbidities for which we originally gathered data. These 9 conditions were the only comorbidities for which a statistically significant difference ($p \leq 0.20$) in distribution between COAT and Non-COAT subjects was found in at least one of the outcome subgroups or in the total study population.

In addition to testing for associations with both COAT status and each of the respective outcomes, I also included each co-variable in a bivariable log-binomial regression model with COAT status to see if this changed the effect of COAT status *alone* on receipt of the preventive service. I considered that a change in the relative risk of 10% or more was meaningful. These models were analyzed for each of the four preventive service outcomes.

The results of the tests described above were considered together in assessing the variables for plausible confounding effects. If a variable was not close to statistically significantly associated with both COAT status and the particular preventive service, and if it did not change the effect of COAT alone when included in a bivariable model, then the variable was clearly not a plausible confounder. If, on the other hand, a variable was significantly associated with both COAT status and the preventive service, and if including that variable in a bivariable regression model with COAT changed the effect of COAT alone by 10% or more, then that variable was clearly a plausible confounder. Plausible confounders were then considered in the multivariable regression modeling that followed. In those few instances in which this assessment was equivocal or only one of

the two main criteria (association with both exposure and outcome; change in effect in bivariable model) were met, I considered other factors such as small cell size that might underlie the statistical findings. If still in doubt about the potential confounding effects, I included the variable in the multivariable regression modeling process.

Multivariable Regression Modeling

To calculate the relative risk of receiving each preventive service among COAT versus Non-COAT subjects, I fit multivariable log-binomial regression models to estimate the prevalence ratios for receipt of each service. I considered for inclusion in the models those covariates found to be plausible possible confounders. Various models for each preventive service were compared and assessed for effect size and for the significance of covariates in the model. I used the Wald statistic to assess the significance of the covariates. The best model for each preventive service outcome was considered to be the model with the greatest number of significant covariates that also contained no non-significant covariates. However, because of their likely clinical significance, the variables "Age" and "Clinic" were retained in all final models, regardless of their statistical significance in the model.

This retrospective cohort study was designed to classify subjects according to their exposure status (COAT or Non-COAT) and to then determine if they received the outcomes of interest (preventive services) at any time during a subsequent three-year study period. Although we did measure the time from the beginning of the study period until each patient's last clinic visit during the study period, we only considered this as a possible confounding covariate, and did not include it in the measure of effect. As such,

the study is prospective in nature, although the measure of effect that we used is a prevalence ratio. When a risk ratio or prevalence ratio is the parameter of interest for a dichotomous outcome, log-binomial regression is a more appropriate method than logistic regression, which estimates odds ratios.[79, 80] Log-binomial regression is a generalized linear model that uses the log function, *log (p)*, as the link function and yields a direct measure of the relative risk, as compared with logistic regression, in which the link function is the logit, *log (p/1-p)*, which yields an odds ratio.[79]

A possible complication of using the log-binomial model is that it is not as numerically stable as the logistic model, and problems with convergence may arise. A valid method for addressing this short-coming is to use the Poisson regression model with robust variance, which approximates the log-binomial maximum likelihood estimators.[81, 82] Current versions of various statistical software packages now allow for direct calculation of risk or prevalence ratios using the Poisson regression model with robust variance as an approximation of the log-binomial model.[81] I used the log-binomial capacity of SPSS statistical software (Version 15.0) to conduct the regression modeling for this study. In fact, I found that several log-binomial models did not converge, and, therefore, I used the modified Poisson regression approach. For the sake of consistency, I used this approach for all models.

Sample Size

To reduce the number of subjects required for the study, individual subjects were included in all preventive service subgroups for which they fit the criteria. With this strategy, the sample sizes for the different subgroups differed. This is because different

individuals would contribute differentially to the four subgroups. Again, for example, a 55-year old woman who smokes would contribute to the sample size of each preventive service outcome, and a 40-year old man who does not smoke would only contribute to the lipid screening outcome. Furthermore, the statistical power afforded by a given sample size is affected by many factors, including the prevalence of the outcome being studied. Given this variability, we designed the study to have sufficient power to detect an effect size of 20% for the cervical cancer screening outcome (Pap testing), with the understanding that the different resulting sample sizes for the other outcomes would provide power to detect different effect sizes for each outcome. The calculated required sample size was for 192 COAT subjects and 384 Non-COAT subjects, assuming: two-sided testing; α=0.05; β=0.20; and at least 50% of the sample being female.

Data Management

Each study subject was assigned a unique study identification number. All data abstracted from medical records were stripped of any personal identifiers and stored with this identification number. Similarly, each clinic and clinician was assigned a unique identification number and corresponding data were "de-identified". Each RRC generated a key to the identification numbers and these keys were securely stored in computers with restricted password access. Data on the electronic scan forms contained no personal identifying information. Data forms were scanned and a file was created, which was converted into SPSS statistical software (Version 15.0) for analysis, and was securely stored with restricted access only by the principal investigators. The study was approved by the Institutional Review Board (IRB) of Oregon Health & Science University.

RESULTS

Overall Study Subject Characteristics

Table 3 presents the distribution of demographic and other characteristics by COAT status among all study subjects (N = 704). We identified a total of 234 patients without cancer on COAT who were eligible and included in the study. These 234 were frequency matched with 470 eligible patients who were not on COAT. The values in the columns for each of these groups (COAT and Non-COAT) represent percentages, unless otherwise noted for continuous variables, such as "Age" and "Time Active", which are reported as means. For example, the mean age of all COAT subjects was 54.9 years and the percentage of all COAT subjects who were female was 64.1%. The p-values of the statistical testing comparing the mean values or percentages between COAT subjects and Non-COAT are reported in the last column.

Subjects on chronic opioid therapy were slightly younger (54.9 years vs. 57.7 years) and more likely to be White/Non-Hispanic. Fewer COAT subjects had commercial insurance (32.1% vs. 47.2%); more had Medicaid (38.0% vs. 23.6%); and fewer were uninsured (6.4% vs. 11.5%). Because individual subjects with more than one type of insurance were counted for each type of insurance they had, the sum of the percentages of insurance types is greater than 100%. This is reflected in Table 3 and in each of the following similar tables that correspond to each preventive service subgroup. A higher percentage of COAT subjects had a history of substance abuse (15.0% vs. 10.0%); had 2 or more medical comorbidities (85.5% vs. 78.1%); had anxiety (13.7% vs. 8.9%) or depression (48.7% vs. 28.1%); or had gastric reflux or a sleep disorder. The COAT subjects also had a higher mean number of clinic visits during the study period (24.6 vs.

15.4), with a slightly higher percentage of visits to their primary clinician (83.0% vs. 79.2%), and were more likely to have either voluntarily or involuntarily discontinued being a patient at the clinic (7.7% vs. 3.0%). There was no significant difference in sex or smoking status between the COAT and Non-COAT groups, which confirms that the frequency matching was accurate.

Table 3: Distribution of Demographic and Other Characteristics by COAT Status among All Study Subjects (N = 704), reported as percentages unless otherwise noted

Variable	COAT (N = 234)	Non-COAT (N = 470)	p-value
Age*	54.9*	57.7*	0.015
Female	64.1	63.4	0.856
Ethnicity/Race			
White, Non-Hispanic	69.7	60.0	0.012
Other	4.3	7.4	0.105
Not Specified	26.1	32.6	0.078
Insurance**			
Commercial	32.1	47.2	< 0.001
Medicaid	38.0	23.6	< 0.001
Medicare	42.7	40.0	0.487
Uninsured	6.4	11.5	0.033
Other	11.1	6.2	0.021
Substance Abuse History	15.0	10.0	0.056
Smoker	44.4	43.4	0.793
Number of Comorbidities ≥2	85.5	78.1	0.02
Comorbidities with p ≤0.20‡			
Anxiety	13.7	8.9	0.053
CHF	5.1	8.1	0.15
Depression	48.7	28.1	< 0.001
GERD/PUD	28.2	19.8	0.012
Hepatitis	5.6	2.8	0.064
Osteoporosis	4.7	7.0	0.231
Sleep Disorder	5.1	2.3	0.05
Same Zip Code as Clinic	32.1	30.0	0.578
Time Active* (months)	30.5*	29.3*	0.2
Total Number Visits*	24.6*	15.4*	< 0.001
Percentage Visits with PCP*	83.0*	79.2*	0.03
Record of Discharge	7.7	3.0	0.005

* Mean value

** Subjects with more than one type of insurance were counted for each type that they had; therefore the sum of the percentages of insurance types is greater than 100%.

‡ The comorbidities included in the table are those for which a difference between COAT and Non-COAT was seen in the total study sample or in at least one study subgroup.

Cervical Cancer Screening

Subgroup Characteristics

Table 4 presents the distribution of demographic and other characteristics by COAT status among the subgroup of study subjects who were analyzed for the receipt of Pap testing for cervical cancer screening (N = 321). This subgroup was comprised only of women aged 35 to 65 years. Of the total 234 COAT subjects in the study, 110 were women in this age range, and, of the total 470 Non-COAT subjects, 211 were women in this age range. Compared with the group of all 704 study subjects, this subgroup of 321 subjects was younger, with a higher percentage of people on Medicaid, a higher percentage with a history of substance abuse, a higher percentage of smokers, and a higher percentage with depression.

For most variables, the essential differences between COAT and Non-COAT subjects that we found for the total study sample (N = 704) were also observed in the cervical cancer screening subgroup (N = 321). Although, in this smaller subgroup, a few of the statistical relationships between COAT and Non-COAT were no longer significant, even when similar differences were noted. Unlike the total sample, the mean age of COAT and Non-COAT subjects did not differ in this subgroup (48.4 vs. 48.1), nor did the percentage of subjects with anxiety disorders (11.8% vs. 12.8). And, although the p-values for tests of differences between COAT and Non-COAT were no longer significant, we still found differences in the percentage of subjects with a history of substance abuse (21.8% vs. 16.6%) and with a sleep disorder (6.4% vs. 2.8%). Similarly, although not statistically significant in this smaller subgroup, we still found COAT patients to have a higher mean percentage of visits with their primary clinician (77.3% vs.

73.0%). A significantly lower percentage of COAT subjects received Pap testing during the study period, compared with Non-COAT subjects (42.7% vs. 59.2%).

Table 4: Characteristics by COAT Status among Cervical Cancer Screening Subjects (N = 321), reported as percentages unless otherwise noted

Variable	COAT (N = 110)	Non-COAT (N = 211)	p-value
Age*	48.4*	48.1*	0.752
Female	100.0	100.0	n/a
Ethnicity/Race			
White, Non-Hispanic	73.6	60.7	0.021
Other	4.5	11.8	0.033
Not Specified	21.8	27.5	0.269
Insurance**			
Commercial	26.4	38.9	0.025
Medicaid	46.4	33.2	0.021
Medicare	22.7	15.6	0.117
Uninsured	10.0	19.4	0.03
Other	11.8	6.2	0.078
Substance Abuse History	21.8	16.6	0.251
Smoker	50.0	55.5	0.353
Number of Comorbidities ≥2	80.9	71.1	0.056
Comorbidities with p ≤0.20‡			
Anxiety	11.8	12.8	0.801
CHF	0.0	3.3	0.053
Depression	59.1	38.9	0.001
GERD/PUD	35.5	24.6	0.041
Hepatitis	9.1	4.3	0.082
Osteoporosis	2.7	3.8	0.619
Sleep Disorder	6.4	2.8	0.129
Same Zip Code as Clinic	30.9	38.4	0.185
Time Active* (months)	29.4*	29.6*	0.906
Total Number Visits*	25.7*	14.1*	< 0.001
Percentage Visits with PCP*	77.3*	73.0*	0.116
Record of Discharge	11.0	3.3	0.006
Received Pap testing	42.7	59.2	0.005

* Mean value

** Subjects with more than one type of insurance were counted for each type that they had; therefore the sum of the percentages of insurance types is greater than 100%.

‡ The comorbidities included in the table are those for which a difference between COAT and Non-COAT was seen in the total study sample or in at least one study subgroup.

Assessment of Potential Confounders

In the process of assessing variables for their potential as viable confounding factors in a possible association between COAT status and the receipt of Pap testing, I used

a worksheet to summarize the findings of the three tests I performed, and as an aid in considering the three tests together. This worksheet, like those for the other three preventive services we studied, is included in Appendix C, and is labeled on the top as "PAP: COVARIATE ASSESSMENT". Using the independent samples *t* test for continuous variables and the Pearson chi-squared ($\chi 2$) test for categorical variables, I first tested for a significant association of the variable in question with COAT status and then tested for a significant association with the receipt of Pap testing. The p-values of these tests are reported in the worksheet under the columns labeled "COAT Cross" and "Cross PAP". "COAT Cross" is the result of testing for an association of the variable with COAT status, and "Cross PAP" is the result of the testing for an association with Pap testing. The third test was actually a comparison of the results of a bivariable log-binomial regression model that included both COAT status and the variable in question as predictor variables and Pap testing as the outcome, with a univariable model including only COAT status as predictor. In some cases, the log-binomial model did not converge, and I used the modified Poisson model with robust variance, instead. For this comparison, I considered the Wald statistic p-value of the variable in question, as well as changes in the COAT β-coefficient and the COAT relative risk (RR) between the univariable and the bivariable model. Pertinent information regarding these findings are summarized under the column labeled "Bivar Regress", with "No Significance" meaning that none of these values supported consideration of the variable as a plausible confounder in the model building. Comments regarding details, such as small sample size or empty cells that would affect the numerical stability of a regression model, and other considerations in the assessment are included in the last column.

Of the numerous variables assessed, only "**Total Number of Visits**" was unequivocally a plausible confounder. This variable represents the number of clinic visits that patients had during the three year study period from 2001 to 2003. It had a statistically significant association with both COAT status and Pap testing, and including the variable in the bivariable regression produced a 17.48% change in the RR associated with COAT. Although the variable "**Record of Discharge**" was significantly associated with both COAT status and Pap testing, its inclusion in the bivariable model only changed the COAT relative risk by 3.33%, and change in the RR is considered a more meaningful measure of the variable's influence in the bivariable model than the change in the COAT β-coefficient. A more critical factor in my decision not to use this variable in the model building was the small number of subjects with a record of discharge from the clinic (n = 19) and the smaller number of those who received a Pap test (n = 4). Such a small cell size would be insufficient for a numerically stable regression model. The variable "**Percentage of Visits to PCP**" was associated with Pap testing and close to significantly associated with COAT status, but its inclusion in the bivariable model also produced only a small change in the COAT relative risk (2.36%). Although many of the other variables were associated with either COAT status or Pap testing, only one, the medical condition "**CHF**" (Congestive Heart Failure), was associated with both, and this variable had an even smaller cell size of zero. Of the variables assessed, I used three as possible confounders in regression modeling. One of these, "**Total Number of Visits**", satisfied the criteria for a plausible confounder, as described above. The other two, "**Age**", and "**Clinic**", did not meet the statistical criteria for plausible confounders, but were included in the model building because of their clinical plausibility as confounders.

Multivariable Regression Modeling

Results of the multivariable regression model building for the cervical cancer screening outcome are presented in Table 5. The various models that were compared and assessed are presented in the first column, labeled "Model". The principal predictor variable, COAT status, was included in each model, and the additional covariates included in each model are listed in parentheses next to "COAT". For each model, the table reports the β-coefficient for COAT, the relative risk (RR) estimate associated with COAT, and the 95% confidence interval (CI) surrounding the RR estimate. These values are presented in the columns labeled "COAT β_1", "COAT RR", and "(95% CI)", respectively. The last four columns present the p-values of the Wald statistics of the covariates included in the particular model. In each model, the p-value of the Wald statistic for COAT is presented first, in the column labeled "COAT p-val". The following columns present the Wald statistic p-values for the other covariates in the model, and are presented in the order in which the covariates are listed in the column labeled "Model". For example, in the model with COAT and the two additional covariates, "**Total Number of Visits**" and "**Age**", there are two additional Wald p-values reported. These are listed in the two columns labeled "p-val 1" and "p-val 2". For this model, "**Total Number of Visits**" is listed in the table as the first of the two additional covariates, with "**Age**" listed second. Therefore, for this model, the p-value in the column "p-val 1" corresponds to "**Total Number of Visits**" and the p-value in the column "p-val 2" corresponds to "**Age**". Similarly, the Wald statistic p-values are presented in the order in which the covariates are listed for all models reported in this table and in the corresponding tables for the other three preventive services in the study.

Table 5. Multivariable Regression Modeling for the Cervical Cancer Screening Outcome

Model	COAT β_1	COAT RR	(95% CI)	COAT p-val	p-val 1	p-val 2	p-val 3
COAT	-0.327	0.721	(0.565; 0.920)	0.009			
COAT (+Age)	-0.351	0.704	(0.552; 0.899)	0.005	0.113		
COAT (+Clinic)	-0.325	0.722	(0.569; 0.916)	0.007	0.007		
COAT (+Total Visits)	-0.519	0.595	(0.466; 0.759)	< 0.001	< 0.001		
COAT (+Total Visits + Age)	-0.531	0.588	(0.462; 0.749)	< 0.001	< 0.001	0.259	
COAT (+Total Visits +Clinic)	-0.502	0.605	(0.476; 0.769)	< 0.001	< 0.001	0.005	
COAT (+Total Visits + Age + Clinic)	-0.517	0.597	(0.470; 0.757)	< 0.001	< 0.001	0.211	0.007
COAT (+Age + Clinic)	-0.353	0.703	(0.554; 0.891)	0.004	0.082	0.008	

The variable "**COAT**" was significant in the univariable model and in each multivariable model. The Wald statistic for "**Age**" was not statistically significant in any of the models, but was close to significance in the model with "**COAT**" and "**Clinic**". As we learned in the assessment for plausible confounders, "**Clinic**" was significant in the bivariable model with COAT; it was also significant in each model in which it was included. However, neither "**Age**" nor "**Clinic**", when included in a bivariable model with "COAT", substantially changed the RR associated with COAT. Similarly, neither "**Age**" nor "**Clinic**", nor the two together, substantially changed the RR when added to a bivariable model with "**COAT**" and "**Total Number of Visits**". Still, these variables were included in the final model because of their clinical plausibility as confounders, as previously mentioned. The final model included the variables "**COAT**", "**Total Number of Visits**", "**Age**" and "**Clinic**". The RR associated with COAT in this model was 0.597, with a 95% confidence interval of (0.470; 0.757). This indicates that, with statistical significance, women receiving COAT for non-malignant pain were approximately 60% as likely to receive a Pap test compared to women not receiving COAT.

Colorectal Cancer Screening

Subgroup Characteristics

Table 6 presents the distribution of demographic and other characteristics by COAT status among the subgroup of study subjects who were analyzed for the receipt of colorectal cancer (CRC) screening (N = 425). This subgroup was comprised of both men and women aged 50 years and older. Of the total 234 COAT subjects in the study, 128 were in this age range, and, of the total 470 Non-COAT subjects, 297 were in this age range. Compared with the group of all 704 study subjects, this subgroup of 425 subjects was older, with a higher percentage of people on Medicare or commercial insurance and a lower percentage on Medicaid, a lower percentage with a history of substance abuse, a lower percentage of smokers, and a higher percentage with two or more medical comorbidities. A lower percentage of COAT subjects received CRC screening during the study period, compared with Non-COAT subjects (7.8% vs. 13.8%), although the difference was not statistically significant (p = 0.081).

Again, for most variables, the essential differences between COAT and Non-COAT subjects that we found for the total study sample (N = 704) were also observed in the CRC screening subgroup (N = 425). In this subgroup, the percentage of female COAT subjects was higher than female Non-COAT subjects (65.6% vs.59.9%), although not statistically significant. A few findings regarding insurance coverage are noteworthy. Although the percentage of people with commercial insurance was higher for both COAT and Non-COAT in the CRC screening subgroup compared to the total group of 704 subjects, still, statistically fewer COAT patients than Non-COAT patients had commercial insurance (39.8% vs.51.5%). And, although the percentage of the CRC

screening subgroup (both COAT and Non-COAT) on Medicaid was lower compared to the total study group, still, more COAT subjects than Non-COAT were on Medicaid (30.5% vs. 16.8%). A higher percentage of both COAT and Non-COAT subjects in the

Table 6. Characteristics by COAT Status among Colorectal Cancer Screening Subjects (N = 425), reported as percentages unless otherwise noted

Variable	COAT (N = 128)	Non-COAT (N = 297)	p-value
Age*	64.7*	67.0*	0.047
Female	65.6	59.9	0.268
Ethnicity/Race			
White, Non-Hispanic	71.1	62.0	0.07
Other	3.1	4.0	0.649
Not Specified	25.8	34.0	0.094
Insurance**			
Commercial	39.8	51.5	0.027
Medicaid	30.5	16.8	0.002
Medicare	56.3	60.3	0.439
Uninsured	5.5	6.4	0.714
Other	10.9	5.1	0.027
Substance Abuse History	8.6	5.8	0.282
Smoker	32.0	35.7	0.467
Number of Comorbidities ≥2	94.5	86.5	0.016
Comorbidities with p ≤0.20‡			
Anxiety	13.3	6.7	0.028
CHF	7.8	12.1	0.19
Depression	43.0	23.2	< 0.001
GERD/PUD	27.3	16.2	0.008
Hepatitis	2.3	1.0	0.285
Osteoporosis	6.3	10.1	0.202
Sleep Disorder	2.3	1.3	0.459
Same Zip Code as Clinic	35.9	28.3	0.116
Time Active* (months)	31.0*	30.2*	0.51
Total Number Visits*	24.6*	17.4*	< 0.001
Percentage Visits with PCP*	84.7*	82.7*	0.34
Record of Discharge	6.3	2.7	0.081
Received CRC Screening	7.8	13.8	0.081

* Mean value

** Subjects with more than one type of insurance were counted for each type that they had; therefore the sum of the percentages of insurance types is greater than 100%.

‡ The comorbidities included in the table are those for which a difference between COAT and Non-COAT was seen in the total study sample or in at least one study subgroup.

CRC subgroup were on Medicare, as would be expected with the higher mean age. The ratio of COAT to Non-COAT on Medicare, however, is the reverse of that for the total

study group, with fewer Non-COAT subjects on Medicare (56.3% vs. 60.3%). We also found that the ratio of COAT to Non-COAT subjects in the CRC subgroup who were smokers was the reverse of that for the total study group, with more Non-COAT smokers, but this was not statistically significant. Although we frequency matched COAT and Non-COAT on sex and smoking status, we matched for the total study group of 704 individuals, and not at the level of the four preventive service subgroups. Therefore, it was possible that the proportions of these factors between COAT and Non-COAT might differ between the subgroups, as was the case.

Assessment of Potential Confounders

As described above for cervical cancer screening, in the process of assessing variables for their potential as viable confounding factors in an association between COAT status and colorectal cancer screening, I used a worksheet to summarize the findings of the three tests I performed, and as an aid in considering the three tests together. This worksheet is included in Appendix C, and is labeled on the top as "CRC: COVARIATE ASSESSMENT". The details of this process, and a guide to the interpretation of the worksheet (Appendix C), were presented in the results section for cervical cancer screening. That explanation also applies to the worksheet for each of the four preventive services, including CRC screening, and will not be repeated here. The reader is referred to the section beginning at the bottom of page 29 as a guide to Appendix C.

As with cervical cancer screening, the variable "**Total Number of Visits**" was unequivocally a plausible confounder. In addition, the variables "**Medicaid**" and "**GERD**" appeared to be plausible confounders. "**Medicaid**" is a dichotomous variable indicating

whether or not the patient had Medicaid coverage, and "**GERD**" indicates whether or not the patient had gastroesophageal reflux disease. Each of these variables was significantly associated with both COAT status and the receipt of colorectal cancer screening. Including "**Medicaid**" in a bivariable model with "**COAT**" changed the COAT-associated RR by 9.35%, and including "**GERD**" in a bivariable model with "**COAT**" changed the COAT-associated RR by 8.48%. Although each of these changes in the RR was less than 10%, they were close enough to warrant inclusion in the model building process. Another variable, "**Number of Comorbidities ≥2**", was associated with both COAT status and CRC screening, and resulted in a change of 7.07% in the RR in the bivariable model with "**COAT**". This variable, however, was rejected for the model building because only one study subject fit the category of having fewer than 2 comorbidities and receiving CRC screening, which would result in numerically unstable models.

Of the variables assessed, I used five as possible confounders in regression modeling of an association between COAT and CRC screening. Three of these, "**Total Number of Visits**", "**Medicaid**", and "**GERD**" either satisfied the criteria for a plausible confounder, outright, or were close enough to warrant inclusion in the model building process. As with all of the preventive services we studied, "**Age**" and "**Clinic**" were included in the model building because of their clinical plausibility as confounders, regardless of their statistical plausibility.

Multivariable Regression Modeling

Results of the multivariable regression model building for the colorectal cancer screening outcome are presented in Table 7. For guidance in interpreting this table, the

Table 7. Multivariable Regression Modeling for the Colorectal Cancer Screening Outcome

Model	COAT β_1	COAT RR	(95% CI)	COAT p-val	p-val 1	p-val 2	p-val 3	p-val 4	p-val 5
COAT	-0.569	0.566	(0.293; 1.094)	0.091					
COAT (+Age)	-0.519	0.595	(0.308; 1.149)	0.122	0.259				
COAT (+Clinic)	-0.391	0.677	(0.293; 1.094)	0.244	< 0.001				
COAT (+Total Visits)	-0.840	0.432	(0.229; 0.813)	0.009	< 0.001				
COAT (+Medicaid)	-0.622	0.537	(0.278; 1.038)	0.064	0.031				
COAT (+GERD)	-0.636	0.530	(0.268; 1.046)	0.067	0.006				
COAT (+Tot Vts +Clinic)	-0.782	0.457	(0.241; 0.869)	0.017	< 0.001	< 0.001			
COAT (+Tot Vts +Age)	-0.873	0.418	(0.217; 0.804)	0.009	< 0.001	0.181			
COAT (+Tot Vts +Medicaid)	-0.924	0.397	(0.208; 0.756)	0.005	< 0.001	0.103			
COAT (+Tot Vts +GERD)	-0.934	0.393	(0.204; 0.756)	0.005	< 0.001	0.021			
COAT (+Tot Vts +Clinic +Age)	-0.736	0.479	(0.251; 0.914)	0.026	< 0.001	< 0.001	0.033		
COAT (+Tot Vts +Age+Clinic +GERD)	-0.873	0.418	(0.218; 0.800)	0.008	< 0.001	0.001	< 0.001	0.003	
COAT (+Tot Vts +Clinic +Age +Medcd)	-0.770	0.463	(0.244; 0.878)	0.018	< 0.001	< 0.001	0.035	0.329	
COAT (+Tot Vts +Clinic +Age +Medcd + GERD)	-0.852	0.427	(0.223; 0.815)	0.010	< 0.001	< 0.001	0.001	0.403	0.002
COAT (+Medicaid +GERD)	-1.012	0.363	(0.187; 0.707)	0.003	< 0.001	0.139	0.027		
COAT (+CoM #)	-0.644	0.525	(0.272; 1.013)	0.055	0.054				
COAT (+Tot Vts +CoM #)	-0.892	0.410	(0.220; 0.764)	0.005	< 0.001	0.152			
COAT (+Tot Vts +Age+Clinic +CoM #)	-0.796	0.451	(0.240; 0.849)	0.014	< 0.001	0.026	< 0.001	0.190	
COAT (+Tot Vts +Age+Clinic +GERD +CoM #)	-0.870	0.419	(0.221; 0.795)	0.008	< 0.001	0.001	< 0.001	0.005	0.267

reader is referred to the description of the regression modeling summary table for cervical cancer screening on page 32. The variable "COAT" was significant in the univariable model and in each multivariable model, except the bivariable models with "**Age**" and "**Clinic**". Adding either "**Medicaid**" or "**GERD**", individually, to the bivariable model with "**COAT**" and "**Total Number of Visits**" reduced the RR associated with COAT status. Adding "**Medicaid**" reduced the RR (95% CI) from 0.432 (0.229; 0.813) to 0.397 (0.208; 0.756), and adding "**GERD**" reduced it to 0.393 (0.204; 0.756), although only "**GERD**" was significant in the model. The variable "**Medicaid**" was included in three additional models, but was not significant in any of these, and did not substantially change the RR associated with COAT status. The variable "**GERD**", on the other hand, was significant in every model in which it was included.

Including "**Age**" and "**Clinic**" in a model with "**COAT**" and "**Total Number of Visits**" changed the RR (95% CI) associated with COAT from 0.432 (0.229; 0.813) to 0.479 (0.251; 0.914), compared with the bivariable model that included "**Total Number of Visits**". Both "**Age**" and "**Clinic**" were significant in this model. In fact, the variable "**Age**" was only significant in those models that also included "**Clinic**", suggesting a possible interaction effect. I compared the basic model that included "**COAT**", "**Total Number of Visits**", "**Age**", and "**Clinic**" with models that added "**Medicaid**" and/or "**GERD**" to these basic four variables. As noted above, "**Medicaid**" was not significant. Adding "**GERD**" to the model, however, changed the RR (95% CI) from 0.479 (0.251; 0.914) to 0.418 (0.218; 0.800), with all covariates significant. Finally, despite the issue of small cell size, I included the variable "**Number of Comorbidities ≥2**" in several models

to check its possible effect. The variable was not significant except in the bivariable model with "**COAT**".

The final model included the variables "**COAT**", "**Total Number of Visits**", "**Age**", "**Clinic**", and "**GERD**". The RR associated with COAT in this model was 0.418, with a 95% confidence interval of (0.218; 0.800). This indicates that, with statistical significance, men and women receiving COAT for non-malignant pain were approximately 42% as likely to receive colorectal cancer screening compared to those not receiving COAT.

Lipid Screening

Subgroup Characteristics

Table 8 presents the distribution of demographic and other characteristics by COAT status among the subgroup of study subjects who were analyzed for the receipt of blood screening for abnormal lipid levels, or dyslipidemia (N = 303).

Table 8. Characteristics by COAT Status among Lipid Screening Subjects (N = 303), reported as percentages unless otherwise noted

Variable	COAT (N = 109)	Non-COAT (N = 194)	p-value
Age*	57.3*	60.4*	0.076
Female	61.5	58.2	0.584
Ethnicity/Race			
White, Non-Hispanic	78.0	68.6	0.08
Other	4.6	5.7	0.686
Not Specified	17.4	25.8	0.097
Insurance**			
Commercial	31.2	42.8	0.047
Medicaid	34.9	24.7	0.061
Medicare	44.0	43.8	0.97
Uninsured	7.3	6.2	0.698
Other	11.0	7.2	0.258
Substance Abuse History	18.3	7.2	0.003
Smoker	49.5	44.8	0.432
Number of Comorbidities ≥2	82.6	73.2	0.065
Comorbidities with p ≤0.20‡			
Anxiety	15.6	7.2	0.021
CHF	8.3	11.9	0.328
Depression	46.8	28.9	0.002
GERD/PUD	24.8	18.6	0.201
Hepatitis	9.2	2.6	0.011
Osteoporosis	7.3	6.7	0.834
Sleep Disorder	5.5	1.0	0.02
Same Zip Code as Clinic	38.5	33.5	0.38
Time Active* (months)	28.2*	27.2*	0.531
Total Number Visits*	22.5*	14.0*	< 0.001
Percentage Visits with PCP*	82.5*	82.0*	0.858
Record of Discharge	10.1	3.1	0.011
Received Lipid Screening	28.4	29.9	0.789

* Mean value

** Subjects with more than one type of insurance were counted for each type that they had; therefore the sum of the percentages of insurance types is greater than 100%.

‡ The comorbidities included in the table are those for which a difference between COAT and Non-COAT was seen in the total study sample or in at least one study subgroup.

This subgroup was comprised of men aged 35 years and older and women aged 45 years and older. Of the total 234 COAT subjects in the study, 109 were in this subgroup, and, of the total 470 Non-COAT subjects, 194 were in this subgroup. A slightly lower percentage of COAT subjects received lipid screening during the study period, compared with Non-COAT subjects (28.4% vs. 29.9%), although the difference was not statistically significant.

Compared with the group of all 704 study subjects, the lipid screening subgroup of 303 subjects was slightly older. The subgroup was, otherwise, similar to the total study sample for most variables, with few differences in the essential distributions between COAT and Non-COAT status. A smaller percentage of Non-COAT subjects in the lipid screening subgroup had commercial insurance, but, as with the total group, significantly fewer COAT subjects were covered by commercial insurance. Unlike in the total study group, we found no difference in the percentage uninsured between COAT and Non-COAT in the lipid screening subgroup. Compared with the total group of 704, a slightly higher percentage of COAT subjects had a record of discharge from the clinic.

Assessment of Potential Confounders

The worksheet labeled "LIPID: COVARIATE ASSESSMENT" in Appendix C presents a summary of the process I followed to determine which variables might be plausible confounders of an association between COAT status and receipt of lipid screening. An explanation of the process and a guide the interpretation of the appendix was presented above. The reader is referred to the section beginning at the bottom of page 29 as a guide to Appendix C.

As before, the variable "**Total Number of Visits**" was unequivocally a plausible confounder, although with a smaller change (7.47%) in the RR associated with COAT in the bivariable model. Although the variable "**Record of Discharge**" was associated with COAT status and was close to significantly associated with lipid screening ($p = 0.099$), it was not used in the modeling building because of its small effect on the RR of COAT (a change of only 3.79%), in combination with the issue of small numbers. The variable "**Commercial Insurance**" was also associated with COAT, was close to significantly associated with lipid screening ($p = 0.144$), and had a small effect on the RR of COAT (change of 3.47%).

Of the variables assessed, I used four as possible confounders in regression modeling of an association between COAT and lipid screening. Only "**Total Number of Visits**" was unequivocally a plausible confounder. The variables "**Age**" and "**Clinic**" were included in the model building because of their clinical plausibility as confounders, as before. I also included the variable "**Commercial Insurance**" because of its borderline significance with both COAT and lipid screening.

Multivariable Regression Modeling

Results of the multivariable regression model building for the lipid screening outcome are presented in Table 9. For guidance in interpreting this table, the reader is referred to the description of the regression modeling summary table for cervical cancer screening on page 32. The variable "**COAT**" was not significant in the univariable model, or in any of the multivariable models. The variable "**Commercial Insurance**" did not substantially change the RR of COAT and was not significant in any model. The final

model included the variables "**COAT**", "**Total Number of Visits**", "**Age**" and "**Clinic**". The RR associated with COAT in this model was 0.769, with a 95% confidence interval of (0.536; 1.104). This indicates that men and women receiving COAT for non-malignant pain were approximately 77% as likely to receive lipid screening compared to those not receiving COAT, although the difference was not statistically significant at $\alpha \leq 0.05$.

Table 9. Multivariable Regression Modeling for the Lipid Screening Outcome

Model	COAT β_1	COAT RR	(95% CI)	COAT p-val	p-val 1	p-val 2	p-val 3	p-val 4
COAT	-0.050	0.951	(0.659; 1.374)	0.790				
COAT (+Age)	-0.066	0.936	(0.651; 1.344)	0.719	0.306			
COAT (+Clinic)	-0.076	0.927	(0.654; 1.315)	0.670	<0.001			
COAT (+Total Visits)	-0.208	0.812	(0.559; 1.180)	0.275	<0.001			
COAT (+Commercial)	-0.019	0.981	(0.678; 1.419)	0.919	0.149			
COAT (+Tot Vts +Age)	-0.238	0.788	(0.541; 1.148)	0.214	<0.001	0.329		
COAT (+Tot Vts +Clinic)	-0.240	0.786	(0.547; 1.129)	0.193	0.001	<0.001		
COAT (+Tot Vts +Commercial)	-0.176	0.838	(0.575; 1.222)	0.359	<0.001	0.190		
COAT (+Tot Vts +Age +Clinic)	-0.263	0.769	(0.536; 1.104)	0.154	0.001	0.371	<0.001	
COAT (+Tot Vts +Age +Clinic +Commercial)	-0.253	0.776	(0.541; 1.115)	0.171	0.001	0.367	<0.001	0.418

Smoking Cessation Counseling

Subgroup Characteristics

Table 10 presents the distribution of demographic and other characteristics by COAT status among the subgroup of study subjects who were analyzed for the receipt of smoking cessation counseling (N = 298). This subgroup was comprised of all men and

Table 10. Characteristics by COAT Status among Smoking Cessation Counseling Subjects (N = 298), reported as percentages unless otherwise noted

Variable	COAT (N = 101)	Non-COAT (N = 197)	p-value
Age*	50.4*	51.8*	0.347
Female	64.4	65.5	0.847
Ethnicity/Race			
White, Non-Hispanic	72.3	68.5	0.505
Other	5.9	5.6	0.9
Not Specified	21.8	25.9	0.435
Insurance**			
Commercial	16.8	37.1	< 0.001
Medicaid	51.5	32.0	0.001
Medicare	38.6	26.9	0.038
Uninsured	8.9	16.2	0.082
Other	8.9	7.1	0.581
Substance Abuse History	27.7	17.9	0.049
Smoker	100.0	100.0	n/a
Number of Comorbidities ≥2	78.2	78.2	0.993
Comorbidities with p ≤0.20‡			
Anxiety	15.8	11.2	0.252
CHF	5.0	4.6	0.883
Depression	49.5	36.5	0.031
GERD/PUD	24.8	23.4	0.788
Hepatitis	5.9	3.6	0.34
Osteoporosis	3.0	4.6	0.506
Sleep Disorder	5.9	4.1	0.468
Same Zip Code as Clinic	32.7	34.0	0.817
Time Active* (months)	29.1*	29.1*	0.994
Total Number Visits*	23.8*	14.3*	< 0.001
Percentage Visits with PCP*	81.1*	75.9*	0.064
Record of Discharge	10.0	2.0	0.002
Received Smoking Counseling	61.4	56.9	0.452

* Mean value

** Subjects with more than one type of insurance were counted for each type that they had; therefore the sum of the percentages of insurance types is greater than 100%.

‡ The comorbidities included in the table are those for which a difference between COAT and Non-COAT was seen in the total study sample or in at least one study subgroup.

women of all ages who where smokers. Of the total 234 COAT subjects in the study, 101 were smokers, and, of the total 470 Non-COAT subjects, 197 were smokers. A higher percentage of COAT subjects received smoking cessation counseling during the study period, compared with Non-COAT subjects (61.4% vs. 56.9%), although the difference was not statistically significant.

Compared with the group of all 704 study subjects, the smoking cessation counseling subgroup of 298 subjects was slightly younger, with no significant difference in age between COAT and Non-COAT. The smokers differed somewhat from the total study group in terms of the percentages of various characteristics, but the general relationships between COAT and Non-COAT were mostly the same. Compared with the total study group, a smaller percentage of the smokers had commercial insurance, though the difference between COAT and Non-COAT was still seen. Similarly, a larger percentage of this subgroup had Medicaid coverage, with the difference in COAT and Non-COAT still seen. Fewer subjects in this subgroup were on Medicare, with a significantly higher percentage of the COAT group covered by Medicare, a difference between COAT and Non-COAT not seen in the total group. And, a larger percentage of smokers were uninsured.

Compared with the total study group, a larger percentage of smokers had a history of substance abuse, though, still, more COAT than Non-COAT smokers had that history. Unlike in the total group, there was no difference in the percentage of COAT and Non-COAT smokers with two or more medical comorbidities, nor was there a difference in the percentage of COAT and Non-COAT smokers with GERD. A slightly higher percentage of smokers had anxiety disorders, and, compared with the total Non-COAT

group, a higher percentage of Non-COAT smokers had depression. Compared with the total group of 704, a slightly higher percentage of COAT smokers had a record of discharge from the clinic. The subgroup was, otherwise, similar to the total study sample for most variables, with few differences in the essential distributions between COAT and Non-COAT status.

Assessment of Potential Confounders

The worksheet labeled "SMOKING: COVARIATE ASSESSMENT" included in Appendix C presents a summary of the process I followed to determine which variables might be plausible confounders of an association between COAT status and receipt of smoking cessation screening. An explanation of the process and a guide the interpretation of the appendix was presented above. The reader is referred to the section beginning at the bottom of page 29 as a guide to Appendix C.

Of the variables assessed, I used six as possible confounders in regression modeling. As with each of the other preventive services, the variable "**Total Number of Visits**" was unequivocally a plausible confounder. In addition, three other variables appeared to be plausible confounders. These were "**Medicaid**", "**Percentage of Visits with PCP**", and "**Depression**". When included in a bivariable model with COAT, none of these latter three variables had a large effect on the relative risk associated with COAT. Each of the three, however, was significantly or nearly significantly associated with both COAT status and smoking counseling. On this basis I included the three variables in the model building process. As before, the variables "**Age**" and "**Clinic**" were included in the model building because of their clinical plausibility as confounders.

Multivariable Regression Modeling

Results of the regression model building for the smoking cessation counseling outcome are presented in Table 11. For guidance in interpreting this table, refer to the description of the modeling summary table for cervical cancer screening on page 32.

The variable "**COAT**" was not significant in the univariable model, or in any of the multivariable models. The variable "**Total Number of Visits**" was significant in every model in which it was included. As with the CRC screening outcome, I compared the basic model that included "**COAT**", "**Total Number of Visits**", "**Age**", and "**Clinic**" with models that added "**Medicaid**", "**Percentage of Visits with PCP**", and/or "**Depression**" to these basic four variables. Neither "**Medicaid**" nor "**Depression**" substantially changed the RR associated with COAT in any model in which they were included, nor was either of these variables significant in any model. The variable "**Percentage of Visits with PCP**", as the name suggests, is the percentage of their total clinic visits at which a patient was seen by their primary clinician. This variable was significant in every model in which it was included. In every instance, adding "**Percentage of Visits with PCP**" to a model had the effect of increasing the relative risk of receiving smoking cessation counseling in COAT patients compared with Non-COAT patients.

The final model included the variables "**COAT**", "**Total Number of Visits**", "**Age**", "**Clinic**", and "**Percentage of Visits with PCP**". The RR associated with COAT in this model was 0.949, with a 95% confidence interval of (0.783; 1.150). This indicates that smokers receiving COAT for non-malignant pain were only slightly less likely to receive counseling for smoking cessation than were those not on COAT, and that the difference was not statistically significant at $\alpha \leq 0.05$.

Table 11. Multivariable Regression Modeling for the Smoking Cessation Counseling Outcome

Model	COAT β_1	COAT RR	(95% CI)	COAT p-val	p-val 1	p-val 2	p-val 3	p-val 4	p-val 5
COAT	0.077	1.080	(0.887; 1.315)	0.445					
COAT (+Age)	0.075	1.078	(0.885; 1.312)	0.457	0.180				
COAT (+Clinic)	0.076	1.079	(0.901; 1.292)	0.408	<0.001				
COAT (+Total Visits)	-0.103	0.902	(0.743; 1.096)	0.300	<0.001				
COAT (+Medicaid)	0.046	1.047	(0.858; 1.279)	0.650	0.114				
COAT (+PCP%)	0.119	1.126	(0.926; 1.369)	0.235	<0.001				
COAT (+Tot Vts +Age)	-0.106	0.900	(0.738; 1.097)	0.296	<0.001	0.256			
COAT (+Tot Vts +Clinic)	-0.079	0.924	(0.769; 1.111)	0.401	<0.001	<0.001			
COAT (+Tot Vts +Medicaid)	-0.111	0.895	(0.737; 1.086)	0.262	<0.001	0.466			
COAT (+Tot Vts +PCP%)	-0.065	0.937	(0.770; 1.140)	0.516	<0.001	0.002			
COAT (+Tot Vts +Age +Clinic)	-0.078	0.925	(0.766; 1.117)	0.417	<0.001	0.322	<0.001		
COAT (+Tot Vts +Age +Clinic +Medcd)	-0.082	0.921	(0.763; 1.111)	0.390	<0.001	0.329	<0.001	0.710	
COAT (+Tot Vts +Age +Clinic +PCP%)	-0.053	0.949	(0.783; 1.150)	0.591	<0.001	0.395	<0.001	0.062	
COAT (+Tot Vts +Age +Clinic +Medcd +PCP%)	-0.058	0.944	(0.779; 1.144)	0.557	<0.001	0.408	<0.001	0.691	0.062
COAT (+Tot Vts +Depress)	-0.112	0.894	(0.735; 1.086)	0.258	<0.001	0.114			
COAT (+Tot Vts +Age +Depress)	-0.116	0.891	(0.731; 1.086)	0.252	<0.001	0.260	0.149		
COAT (+Tot Vts +Clinic +Depress)	-0.083	0.921	(0.764; 1.109)	0.384	<0.001	<0.001	0.683		
COAT (+Tot Vts +Age +Clinic +Depress)	-0.083	0.920	(0.760; 1.114)	0.392	<0.001	0.299	<0.001	0.593	

Summary of Results

Table 12 summarizes the findings of the regression analyses for all four preventive and screening services. The table presents the relative risk of receipt of each preventive service by patients with CNMP on COAT compared to patients not on COAT. It shows both the unadjusted relative risks and the relative risks from the multivariable regression models, with 95% confidence intervals. For each of the four preventive services, the final regression model adjusted for patient age, the clinic at which they received their care, and the total number of clinic visits they had during the three-year study period. In other words, each of the final models adjusted for three variables in common: "**Age**", "**Clinic**", and "**Total Number of Visits**". For cervical cancer screening and lipid screening, these three variables were the *only factors* for which the model adjusted. In the models for CRC screening and smoking cessation counseling, however, additional factors were found to be significant. For CRC screening, the final model adjusted for the diagnosis of gastroesophageal reflux disease, or "**GERD**", *in addition to* the common set of three variables, "**Age**", "**Clinic**", and "**Total Number of Visits**". And, for smoking cessation counseling, the final model adjusted for the percentage of visits a patient had with their primary clinician, or "**Percentage of Visits with PCP**", *in addition to* the common set of three variables, "**Age**", "**Clinic**", and "**Total Number of Visits**".

The first column of Table 12, labeled "Unadjusted" presents the unadjusted RR (95% CI) of COAT compared to Non-COAT for each of the four services. The second column, labeled "Adjustment for 3 common factors", presents the RR (95% CI) after adjustment for the same set of three variables, "**Age**", "**Clinic**", and "**Total Number of Visits**". This provides a common basis for comparing the relative effect of COAT on the

receipt of the different preventive services, albeit with some limitations related to differences in the specific subgroups, including sample sizes. The last column, labeled "'Final model' adjustment", presents the RR (95% CI) after adjustment for all variables in the final and best model for each service.

Table 12. Summary of Unadjusted and Multivariable Adjusted Relative Risks of Receipt of Preventive Services by Patients Using COAT Compared to Those Not Using COAT

	Unadjusted	Adjustment for 3 common factors*	"Final model" adjustment**
Service	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**
Pap testing	**0.72** (0.57; 0.92)	**0.60** (0.47; 0.76)	**0.60** (0.47; 0.76)
CRC screening	**0.57** (0.29; 1.09)	**0.48** (0.25; 0.91)	**0.42**† (0.22; 0.80)
Lipid screening	**0.95** (0.66; 1.37)	**0.77** (0.54; 1.10)	**0.77** (0.54; 1.10)
Smoking counseling	**1.08** (0.89; 1.32)	**0.93** (0.77; 1.12)	**0.95**‡ (0.78; 1.15)

* Each model adjusted for the same set of 3 covariates: Age; Clinic; and Total Number of Clinic Visits.
** Each model adjusted for the basic set of 3 covariates: Age; Clinic; and Total Number of Clinic Visits, with additional variables included in the CRC model and the Smoking model, as noted.
† Adjusted for Age; Clinic; Total Number of Clinic Visits; *and* GERD.
‡ Adjusted for Age; Clinic; Total Number of Clinic Visits; *and* Percentage of Visits with PCP.

In univariable analyses, COAT subjects were found to have a lower relative risk of Pap testing and CRC screening, compared with Non-COAT subjects. The unadjusted RR for Pap testing was statistically significant, and the unadjusted RR for CRC screening was close to statistically significant. In multivariable analyses adjusting for age, clinic, and number of clinic visits, we found the likelihood of receiving each of these preventive services to be lower for patients on COAT compared to patients not on COAT. This effect was statistically significant for both Pap Testing (RR = 0.60; 95% CI: 0.47, 0.76) and CRC Screening (RR=0.48; 95% CI: 0.25, 0.91). Although the RRs for lipid screening (RR=0.77; 95% CI: 0.54, 1.10) and smoking counseling (RR=0.93; 95% CI: 0.77, 1.12)

did not reach statistical significance in the multivariable analyses, in each case the RR decreased compared to the univariable analysis, and the findings came closer to statistical significance. When GERD was added to the model for CRC screening, the relative risk further decreased (RR=0.42; 95% CI: 0.22, 0.80), indicating that a diagnosis of GERD decreased the likelihood of COAT patients receiving CRC screening. When the percentage of visits a patient had with their primary clinician was added to the model for smoking cessation counseling, the RR increased slightly (RR=0.95; 95% CI: 0.78, 1.15), indicating that a higher percentage of visits with one's PCP slightly increased the likelihood of COAT patients receiving counseling, although the overall relative risk was still slightly decreased and not significant.

DISCUSSION

In this study we found that patients who receive chronic opioid therapy for non-malignant pain in the primary care setting are less likely to receive certain preventive and screening services than patients who do not receive chronic opioid therapy. These findings were significant and most pronounced for cervical cancer screening and colorectal cancer screening. Women receiving COAT were only 60% as likely to receive a Pap test compared with women not receiving COAT. Men and women receiving COAT were only 42% as likely to receive any form of CRC screening compared with those not receiving COAT. In addition, patients receiving COAT were only 77% as likely to be screened for lipid disorders, compared with those not receiving COAT, although this finding was not statistically significant. We did not find a significant difference in the likelihood of receiving counseling for smoking cessation between patients on COAT and those not on COAT.

The specific reasons for these disparities in preventive care cannot be definitively determined from our study, but a number of factors might explain the findings. Although I am not aware of any published study that has specifically examined the relationship between chronic opioid therapy for CNMP and the receipt of preventive and screening services, our findings are consistent with the hypothesis that the challenges and demands of caring for these patients may compromise the quality of preventive care they receive. Specifically, time-consuming activities focused on pain and prescribing opioids might detract from time that would otherwise be spent addressing and/or arranging for preventive care or screening services. Similarly, failures of the patient-physician relationship that derive from the challenges of caring for patients with CNMP on opioids

might reduce the likelihood that physicians would deliver, or that patients would receive, recommended preventive and screening services.

Another possible explanation might be that patients with CNMP receiving COAT are simply more medically complex than average, and that this added complexity itself, aside from any of the challenges related to CNMP and COAT, explains the poorer quality of preventive care. In fact, we found a significantly higher percentage of COAT patients with 2 or more medical comorbidities compared to Non-COAT patients, for each the three services that COAT patients were less likely to receive, but not for smoking cessation counseling. Despite these differences, however, the number of comorbidities was only related to receipt of a preventive service in the case of CRC screening. And, although the variable had a small cell size, the number of comorbidities was not significant in any of the CRC regression models. In addition to the number of comorbidities, we evaluated 35 specific medical conditions, of which only GERD appeared to have a significant influence on receipt of a service. Although one might logically predict that having a higher number of medical conditions would negatively affect the quality of care received, a recent study of 7680 patients in a variety of healthcare settings across the U.S. found that the reverse was true.[83] In this study, quality of care, including preventive care, was higher among patients with a higher number of chronic medical conditions.

We were interested in evaluating the possible effect of COAT on a variety of preventive and screening services, in order to account for a range of factors that might differentially influence the performance preventive services. We found that the effect of COAT on preventive services varied between the four services we studied. Although our

study did not address the specific reasons that services were not received, we can speculate that the higher technical complexity, logistical complexity, inconvenience, and time requirements associated with Pap test or CRC screening, relative to lipid screening or smoking counseling, may contribute to this variation between the different services. Furthermore, compared to lipid screening or smoking counseling, discussing or performing a Pap test or CRC screening may require a higher degree of trust and comfort, which may be compromised if the patient-physician relationship were strained.

The apparent influence of a number of other variables on the receipt of preventive services also warrants discussion. A recent study found that having chronic pain was associated with higher levels of health care use.[11] Our finding that patients with CNMP receiving COAT had a higher number of clinic visits is consistent with this study. In addition, we found that the total number of clinic visits patients had was also associated with the receipt of each preventive service. In fact, the number of clinic visits was the only variable that clearly was a likely confounder for all of the services. It is interesting to note that for COAT patients in our study, having a higher number of visits actually lowered the likelihood of receiving preventive care. This finding may seem counterintuitive, and, in fact, one reason we gathered data on clinic utilization was to control for the possibility that more frequent clinic visits might provide more opportunities for providing needed preventive services. One explanation for this finding might be that until recently U.S. Drug Enforcement Administration policy limited opioid prescriptions to 30 days without refills,[84] which made more frequent clinic visits necessary, and added a time-consuming and inconvenient element to the management of chronic pain with opioids, for both patients and physicians. It is possible that such clinic

visits might center around refilling the opioid prescription, and, to that extent, become somewhat "ritualistic", to the exclusion of other elements of primary care. For our study, we only counted visits in which the patient was seen by a clinician, and not those visits that were exclusively for medication refills. Another explanation, which is consistent with the previously cited study,[11] might be that patients whose CNMP is most poorly controlled have the highest frequency of clinic visits. If this were the case, it is also possible that relatively more of the clinic visit would be spent on issues related to poorly controlled pain, thereby reducing the likelihood that preventive care would be addressed.

The clinic at which patients received their primary care was not associated with COAT status in any of the four preventive service subgroups. However, clinic site was associated with the receipt of each of the services, which is consistent with previous research.[85] This association, and the fact that clinic site was usually significant in our modeling, underscores the importance of adjusting for this factor. The variability in preventive care between different primary care clinics also has important implications for programs or interventions designed to improve preventive services. Such interventions require an understanding of the unique workings and characteristics of individual clinics.[86-90]

Gastroesophageal reflux is known to be associated with opioid medications, as a result of the slowing of peristalsis and delayed stomach emptying, but the association we also found of GERD with CRC screening is harder to explain. One could speculate that more gastrointestinal symptoms might lead to more gastrointestinal evaluations, including fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy. However, we found that COAT patients with GERD were *less* likely to receive these procedures.

Furthermore, in our study, we confirmed that these procedures were received for screening purposes, not for diagnostic purposes, as would be the case if they were performed due to GERD symptoms. This finding may be an anomaly of our data, and/or may warrant further investigation.

Our finding that patients with CNMP receiving COAT are more likely to have an anxiety disorder or depression is consistent with previous research.[16] And, I recognize that information bias might have played a role in our finding that COAT patients are more likely to have a history of substance abuse. This finding might be an artifact of differential screening by clinicians, with patients on COAT more likely to be asked about a history of substance abuse.

Our results should be viewed with a number of considerations in mind. First, the study relied on data abstracted from medical records, which may be inaccurate. Studies have shown that recording bias in medical records tends toward underreporting of delivery of services compared to review of recorded visits or reports by standardized patients.[90-92] The overall sensitivity of medical record abstraction for evidence of appropriate care has been reported to be 70%, with specificity of 81%. One study found that the specificity of the medical record was high for most services, and that the sensitivity was low for measuring health habit counseling and moderate for laboratory testing, physical examination and immunization.[90] For the four outcomes in our study, the reported sensitivities ranged from 41% (smoking cessation counseling) to 90% (Pap testing), with cholesterol screening, home FOBT, and sigmoidoscopy between 64% and 67%. All specificities were 99%, except cholesterol screening at 96%. This potential bias

would not be expected to change the essential effect observed in our analyses, however, unless inaccuracies in recording were systematically associated with COAT status, which seems unlikely.

Although the data abstractors in our study were not blinded to COAT status, we took a number of measures to assure high quality, reliable record review and data abstraction. The RRCs received training in a standardized study protocol, explicit data abstraction criteria, explicit variable definitions, and a standardized data abstraction form. In addition, we evaluated the concordance in data abstraction between all three RRCs. The RRCs each used the standardized form to conduct data abstractions of the same set of ten medical records, which were not otherwise used in the study. Comparison of the abstracted data from these 10 medical records showed a generally high level of concordance among all three of the RRCs. The concordance was 100% for COAT status, 97% for CRC screening and 90% for Pap testing. It was lower for smoking cessation counseling, at 70%, and lipid screening at 50%.

The preventive service outcomes in our study were defined as "at least one occurrence" during the three year study period, and not as "up-to-date" status. For certain services, a large baseline difference in up-to-date status between COAT and Non-COAT subjects might explain some or all of the difference in receipt of the service over the following three years. For example, if a larger portion of COAT patients were up-to-date for a particular service at a given time, then fewer COAT patients would be "due" for that service and fewer would be expected to receive it at that time. In our study, this would not affect Pap testing, because, based on its recommended frequency of at least every three years, all eligible women would be expected to receive a Pap test at some time

during the three year study period. And, it would not be expected to affect smoking cessation counseling, which, although not recommended for a specific frequency, is generally brief (less than 3 minutes) and provided at every opportunity. The optimal frequency for lipid screening is not certain,[65] but based on other guidelines and expert opinion it is reasonable to screen approximately every five years. This interval is longer than our three year study period, so a baseline difference between COAT and Non-COAT might explain some of our finding. However, approximately 27% of COAT patients would have to have been up-to-date with lipid screening at baseline to explain the difference we observed, and this seems unlikely. And, although the shortness of our three year study period relative to the longer (up to ten year) screening period for CRC screening is likely to be a factor in the generally low percentages of receipt of CRC screening among all of our study subjects, more than twice as many COAT patients as Non-COAT patients would have to have been up-to-date at baseline to explain the difference we observed, and this also seems unlikely.

Finally, we did not adjust for the possible effect of patient pain, distinct from COAT status. Chronic non-malignant pain and chronic opioid therapy may each influence the clinical encounter and preventive care in both similar and different ways. Adjustment for the level of patient pain, both general pain level and pain level at the time of clinic visits, might provide a means for distinguishing the unique effects of pain and chronic opioid therapy.

CONCLUSIONS

We found that patients who receive chronic opioid therapy for non-malignant pain in the primary care setting are less likely to receive certain preventive and screening services than patients who do not receive chronic opioid therapy. The reasons for this association cannot be clearly and definitively determined from this study, although a number of possible explanations have been posited. Further investigation is warranted to more clearly characterize the nature of the relationship. Follow-up studies could employ qualitative methods to explore and more clearly define the characteristics of patients, physicians, clinics, and clinic systems that affect the quality of preventive care received by these patients. Such studies could lead to interventions that guide clinic practice changes toward improving the quality of care for patients with a chronic problem that is common to most primary care practices.

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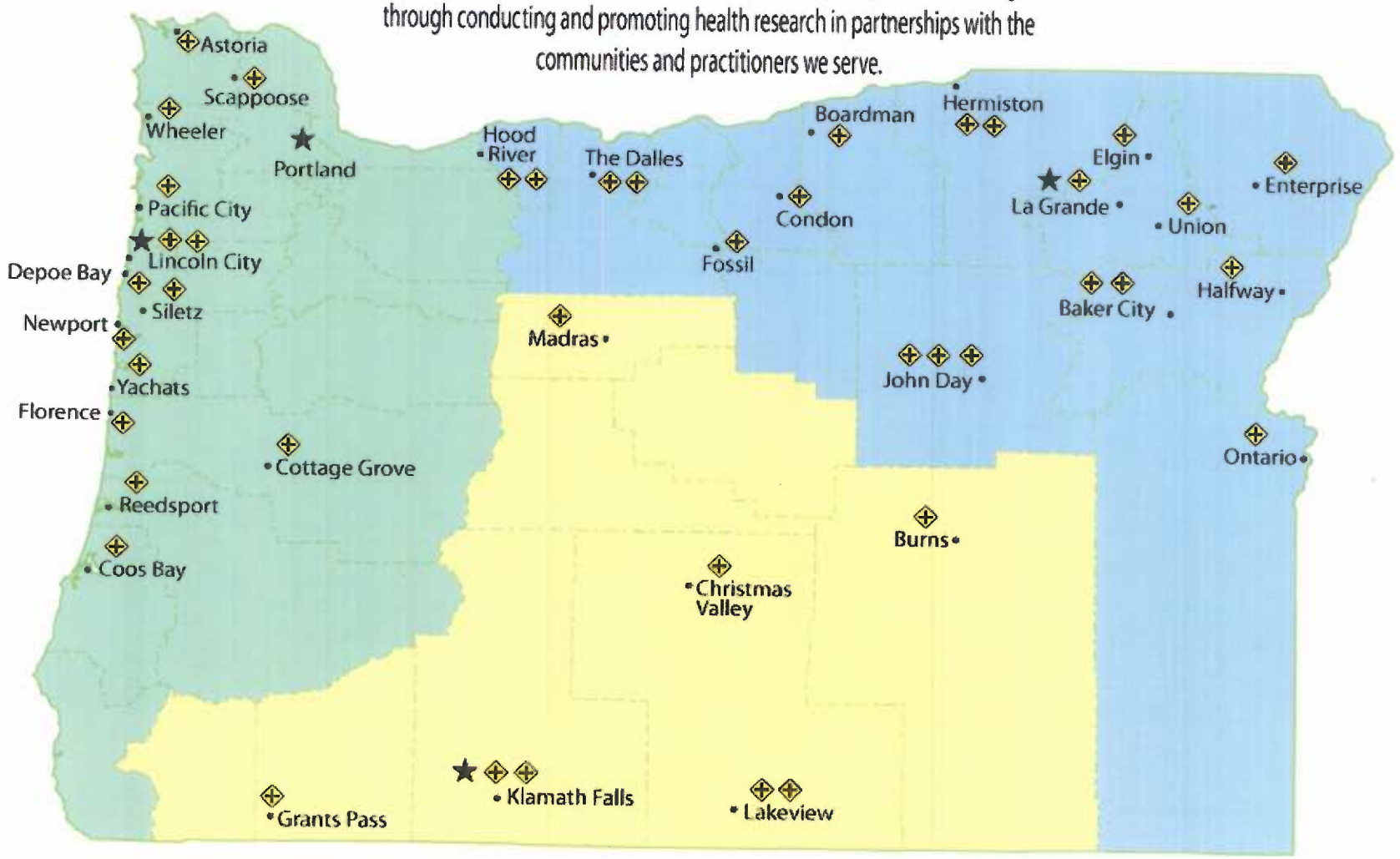
APPENDIX A: Map of ORPRN

A map of the Oregon Rural Practice-based Research Network (ORPRN) is on the following page (page 68).

Oregon Rural Practice-Based Research Network

The mission of ORPRN is to improve the health of rural populations in Oregon through conducting and promoting health research in partnerships with the communities and practitioners we serve.



APPENDIX B: Data Abstraction Form

The two-page scan-able data abstraction form used in the medical chart review is on the following two pages (pages 70-71, unnumbered).

5613134687

ORPRN

04/01/05 (Version 1)

ORPRN Opioid Study Data Collection Instrument

Instructions: Using a black pen please mark the appropriate box.

1. ID Number ☐☐☐☐☐

2. Clinic ☐☐

3. First Pass Clinician ☐☐☐

4. PCP ☐☐☐

5. Year of Birth ☐☐☐☐

6. Gender
   - ☐ Male
   - ☐ Female

7. Zip Code ☐☐☐☐☐

8. Insurance Status **(check all that apply)**
   - ☐ Commercial
   - ☐ Medicaid
   - ☐ Medicare
   - ☐ Uninsured
   - ☐ Other

9a. Ethnicity
   - ☐ Hispanic or Latino
   - ☐ Not Hispanic or Latino
   - ☐ Not specified

9b. Race **(check all that apply)**
   - ☐ White
   - ☐ Black/African American
   - ☐ Asian
   - ☐ Native Hawaiian/Other Pacific Islander
   - ☐ American Indian/Alaska Native
   - ☐ Not specified

10. Smoking Status (as of 1/1/2001)
   - ☐ Yes
   - ☐ No
   - ☐ Not recorded **(If NO or Not recorded, go to 11)**

10a. If yes, Smoking Counseling?
   - ☐ Yes
   - ☐ No

10b. If yes, Counseling Date
☐☐ / ☐☐ / ☐☐
month / day / year

11. COAT Status
   - ☐ Yes
   - ☐ No **(If NO, go to 12)**

11a. If yes, Contract?
   - ☐ Yes
   - ☐ No

11b. If yes, Contract Date
☐☐ / ☐☐ / ☐☐
month / day / year

11c. Diagnosis (reason for Opioid use)
a) ☐☐☐.☐
b) ☐☐☐.☐
c) ☐☐☐.☐
d) ☐☐☐.☐
e) ☐☐☐.☐

11d. Anatomic Site of Pain
a) ☐☐
b) ☐☐
c) ☐☐
d) ☐☐
e) ☐☐

12. Comorbidities
a) ☐☐☐.☐
b) ☐☐☐.☐
c) ☐☐☐.☐
d) ☐☐☐.☐
e) ☐☐☐.☐

12a. Comorbidities Dates

	month	day	year
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐

7934134685

13. Total # of Visits
(between 1/1/01 to 12/31/03)

14. # of visits with PCP
(between 1/1/01 to 12/31/03)

15. Date of Last Visit
(prior to 12/31/03)
month / day / year

16. Lipid Disorder
(Prior to 1/1/01)
☐ Yes
☐ No
☐ Not Recorded

17. Lipid Screening
(1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 18)**

17a. If yes, Lipid Screening Date
(earliest between 1/1/01 to 12/31/03)
month / day / year

18. Pap
(1/1/01 to 12/31/03)
☐ Yes
☐ No
☐ Male **(If NO or Male, go to 19)**

18a. If yes, Pap Date
(earliest between 1/1/01 to 12/31/03)
month / day / year

19. Fecal Occult Blood Testing (FOBT)
(1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 20)**

19a. If yes, FOBT Dates
(1/1/01 to 12/31/03)
month day year
a) / /
b) / /
c) / /

19b. FOBT for screening?
☐ Yes ☐ No
☐ Yes ☐ No
☐ Yes ☐ No

20. Flex Sig
(1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 21)**

20a. If yes, Flex Sig Dates
(1/1/01 to 12/31/03)
month day year
a) / /
b) / /
c) / /

20b. Flex Sig for sceening?
☐ Yes ☐ No
☐ Yes ☐ No
☐ Yes ☐ No

21. Colonoscopy
(1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 22)**

21a. If yes, Colonoscopy Dates
(1/1/01 to 12/31/03)
month day year
a) / /
b) / /
c) / /

21b. Colonoscopy for screening?
☐ Yes ☐ No
☐ Yes ☐ No
☐ Yes ☐ No

22. Substance Abuse
(past or present)
☐ Yes
☐ No **(If NO, go to 23)**

22a. If yes, Substance Abuse Date
month / day / year

23. Record of Discharge from clinic
☐ Yes
☐ No **(If NO, go to 24)**

23a. If Yes, Date
month / day / year

24. Record of Subject's Death
☐ Yes
☐ No

24a. If Yes, Date
month / day / year

Notes: _____

APPENDIX C: Worksheets for Assessment of Confounders

Worksheets used for assessing variables for their potential as confounding factors are on the following four pages (73-76, unnumbered). A separate worksheet was used for each of the four preventive services to summarize the findings of the three tests performed in the process of assessing co-variables and as an aid in considering the three tests together. Each worksheet is labeled at the top with the particular preventive service to which the worksheet applies. A description and guide to these worksheets begins at the bottom of page 29.

PAP: COVARIATE ASSESSMENT

Variable		PAP (N = 321) COAT Cross	Cross PAP	Bivar Regress	Comments
COAT		n/a	0.005	n/a	
Age	X	0.059	0.227	%Δβ 13.15	Wald p-value of model effect=0.127. %Δ RR = 4.33. Use Age because of clinical plausibility and these stats, but don't necessarily keep it in model.
Sex	^	n/a	n/a	n/a	All subjects female.
Ethnicity/Race	^	0.032	0.194	No Significance	Examine the significant differences in DICHOTOMOUS categories (3) between COAT and Non-COAT. Note small number of "Other".
Clinic	X	0.536	0.009	Wald p-value = 0.007 (Poisson)	COAT 2:1 freq. matched at clinic level, did not carry through for each subgroup. COAT Cross not valid. Log-binomial did not converge. Poisson %Δβ = 0.61 and %Δ RR = 0.14
Same Zip	^	0.185	0.430	No Significance	
Insurance (5 categories)	^	0.004	0.543	No Significance	Examine the significant differences in DICHOTOMOUS categories (5) between COAT and Non-COAT.
Commercial	^	0.025	0.911	No Significance	
Medicaid	^	0.021	0.672	No Significance	
Medicare	^	0.117	0.546	No Significance	
Uninsured	^	0.030	0.119	No Significance	Validity of model uncertain. Cells sufficient. Poisson almost identical. Log-Bi shown.
Other	^	0.078	0.661	No Significance	
Insurance (7 categories)	^	0.441	0.004	Wald p-value <0.001	Wald p-value of model effect=0.003. But, %Δβ = 1.53 and %Δ RR = 0.55. Validity of model uncertain. Will not use this variable for NAPCRG. ? Final model?
Time Active, Months	^	0.906	< 0.001	Wald p-value <0.001	Wald p-value of model effect < 0.001. But, %Δβ = 1.53 and %Δ RR = 0.55.
Total Number Visits	X	< 0.001	< 0.001	p-value <0.001 %Δ RR = 17.48	Log-binomial model did not converge. Poisson Robust %Δβ = 58.72 and %Δ RR = 17.48.
Percent Visits PCP	^	0.116	0.007	Wald p-value = 0.015 (Poisson)	Log-binomial model did not converge. Poisson Robust %Δβ = 7.03 and %Δ RR = 2.36.
Visit Density	^	< 0.001	0.206	No Significance	Validity of model uncertain. Poisson Robust also with no significance.
PCP Visit Density	^	0.003	0.118	No Significance	
Record of Discharge	^	0.006	0.003	p-value=0.050; %Δβ = 10.09	Despite significance of Wald p-value of model effect and %Δβ, %Δ RR = 3.33. Only 19 "Yes". Small cell (n = 4).
Substance Abuse Hx	^	0.251	0.015	Wald p-value = 0.008	%Δβ = 4.28; %Δ RR = 1.39.
Number of Comorbidities ≥2 [yes/no]	^	0.056	0.312	No Significance	No model indicators significant, but Validity Warning. Poisson Robust also with no significance.
Comorbidities with p ≤ 0.20					
Anxiety	^	0.801	0.848	No Significance	
Arthritis	^	0.001	0.471	No Significance	Will not use this variable for any subgroup, due to prob. low report for COAT as CM
CHF	^	0.053	0.035	%Δβ = 13.25	Empty cell. Validity of bivariate model uncertain.
Chronic Pain NOS	^	0.19	0.129	No Significance	Will not use this variable for any subgroup, due to prob. low report for COAT as CM
Depression	^	0.001	0.398	No Significance	
GERD/PUD	^	0.041	0.121	%Δβ = 19.27	Wald p-value=0.011. %Δ RR = 6.10. Validity uncertain. Poisson less significant.
Hepatitis	^	0.082	0.576	No Significance	
Osteoporosis	^	0.619	0.948	No Significance	Small cells (3) and (8)
Sleep Disorder	^	0.129	0.557	No Significance	

CRC: COVARIATE ASSESSMENT

Variable		CRC (N = 425) COAT Cross	Cross CRC	Bivar Regress	Comments
COAT		n/a	0.081	n/a	
Age	X	0.313	0.175	%Δβ = 10.54	Wald p-value of model effect = 0.276. %Δ RR = 6.18. Include as a clinically plausible confounder. Not necessarily in final model.
Sex	^	0.268	0.454	No Significance	
Ethnicity/Race	^	0.195	0.697	No Significance	Examine the significant differences in DICHOTOMOUS categories (3) between COAT and Non-COAT. Note small number of "Other".
Clinic	X	0.523	< 0.001	%Δ RR = 13.78	COAT 2:1 freq. matched at clinic level. COAT Cross not valid. Wald p-value of model effect = 0.001. %Δβ = 22.50; %Δ RR = 13.78. Small cells (four cells with "1").
Same Zip	^	0.116	0.897	No Significance	
Insurance (5 categories)	^	0.003	0.032	%Δβ = 10.90	Although %Δβ = 10.90, Wald p-value of model effect = 0.281, and %Δ RR = 6.01. Validity of model fit uncertain. Small (empty) cells.
Commercial	^	0.027	0.293	No Significance	
Medicaid	X	0.002	0.051	%Δ RR = 9.36	Wald p-value of model effect = 0.270. %Δβ = 17.22; %Δ RR = 9.36.
Medicare	^	0.439	0.239	No Significance	
Uninsured	^	0.714	0.052	validity doubtful	Non-convergence log-binomial and Poisson due to empty cell.
Other	^	0.027	0.142	No Significance	
Insurance (7 categories)	^	0.614	0.398	%Δβ = 11.60	Although %Δβ = 11.60, Wald p-value of model effect = 0.509, and %Δ RR = 6.89. Small cells.
Time Active, Months	^	0.510	< 0.001	Wald p-value = 0.003	Although Wald p-value= 0.003, %Δβ = 7.38 and %Δ RR = 4.06. Because we are looking for confounding, will not use, given no diff. In COAT/Non-COAT and small %Δ RR.
Total Number Visits	X	< 0.001	< 0.001	%Δ RR = 10.42	Wald p-value of model effect < 0.001. %Δβ = 19.51; %Δ RR = 10.42.
Percent Visits PCP	^	0.340	0.097	p-value=0.079; %Δβ = 9.31	Although Wald p-value of model effect = 0.079 and %Δβ = 9.31, %Δ RR = 5.48. Will not use as potential confounder, given no diff. In COAT/Non-COAT and small %Δ RR.
Visit Density	^	< 0.001	0.283	No Significance	
PCP Visit Density	^	< 0.001	0.661	No Significance	Validity of model fit uncertain. Poisson robust regression converged without warning of validity, but results essentially the same.
Record of Discharge		0.081	0.490	%Δβ = 9.67	Although %Δβ = 9.67, Wald p-value of model effect = 0.578, and %Δ RR = 5.65. Small cell (n=1).
Substance Abuse Hx	^	0.282	0.428	No Significance	Small cell (n = 2).
Number of Comorbidities ≥2 [yes/no]		0.016	0.027	p-value=0.055; %Δβ = 13.01	Although Wald p-value of model effect = 0.055 and %Δβ = 13.01, %Δ RR = 7.07. Small cell (n = 1)
Comorbidities with p ≤ 0.20					
Anxiety	^	0.028	0.409	No Significance	
Arthritis	^	< 0.001	0.675	No Significance	Will not use this variable for any subgroup, due to prob. low report for COAT as CM
CHF	^	0.190	0.233	%Δβ = 11.25	Validity of model fit uncertain. Wald p-value of model effect = 0.232; %Δ RR = 6.71.
Chronic Pain NOS	^	0.117	0.001		Will not use this variable for any subgroup, due to prob. low report for COAT as CM
Depression	^	< 0.001	0.537	No Significance	Validity of model fit uncertain.
GERD/PUD	X	0.008	0.023	%Δβ = 15.47	Wald p-value of model effect = 0.005 and %Δ RR = 8.48. GI CM clinically plausible.
Hepatitis	^	0.285	0.362	No Significance	Small cell sizes (3) and (3). Validity of model fit uncertain. Empty cell cross with CRC.
Osteoporosis	^	0.202	0.818	No Significance	
Sleep Disorder	^	0.459	0.851	No Significance	Small cell sizes (3) and (4). Validity of model fit uncertain.

LIPID: COVARIATE ASSESSMENT

Variable		LIPID (N = 303) COAT Cross	Cross LIPID	Bivar Regress	Comments
COAT		n/a	0.789	n/a	
Age	X	0.359	0.275	No Significance	Not a likely confounder. Consider including in model for clinical plausibility and consistency with other subgroups/outcomes.
Sex	^	0.584	0.019	p-value=0.024; **%Δβ** = 20.00	Despite significance of Wald p-value of model effect and **%Δβ, %Δ RR** = 0.95. Confounding unlikely, given no difference COAT/Non-COAT.
Ethnicity/Race	^	0.207	0.984	No Significance	
Clinic	X	0.723	< 0.001	p-value<0.001; **%Δβ** = 90.00	COAT freq matched at clinic level. COAT cross not valid. **%Δ RR** = 4.42, a modest change. Include for clinical plausibility and consistency with other subgroups/outcomes.
Same Zip	^	0.380	0.050	p-value=0.058; **%Δβ** = 14.00	Despite significance of Wald p-value of model effect and **%Δβ, %Δ RR** = 0.74. Confounding unlikely, given no difference COAT/Non-COAT.
Insurance (5 categories)	^				
Commercial		0.047	0.144	**%Δβ**=68.00	Wald p-value of model effect=0.148. **%Δ RR** = 3.47. Small %Δ RR, but poss. confound.
Medicaid	^	0.061	0.627	**%Δβ**=10.00	Wald p-value of model effect=0.613. **%Δ RR** = 0.42. Unlikely confounder.
Medicare	^	0.97	0.786	No Significance	
Uninsured	^	0.698	0.949	No Significance	
Other	^	0.258	0.037	**%Δβ**=58.00	Small cell (n = 3). Wald p-value = 0.073, **%Δ RR** = 3.05. Unlikely confounder.
Insurance (7 categories)	^				
Time Active, Months	^	0.531	< 0.001	p-value<0.001; **%Δβ** = 122.00	**%Δ RR** = 5.89, a modest change. Confounding unlikely, given no difference COAT/Non-COAT.
Total Number Visits	X	< 0.001	0.002	p-value<0.001; **%Δβ** = 154.00	**%Δ RR** = 7.47, a modest change. Include for convincing stats, clinical plausibility, and consistency with other subgroups/outcomes.
Percent Visits PCP	^	0.858	0.306	**%Δβ**=28.00	Wald p-value of model effect=0.320. **%Δ RR** = 1.37. Unlikely confounder.
Visit Density	^	< 0.001	0.263	**%Δβ**=96.00	Wald p-value of model effect=0.321. **%Δ RR** = 1.37. Unlikely confounder.
PCP Visit Density	^	< 0.001	0.189	**%Δβ**=98.00	Wald p-value of model effect=0.241. **%Δ RR** = 5.05, a modest change. Unlikely confounder.
Record of Discharge		0.011	0.099	**%Δβ**=74.00	Wald p-value=0.154. **%Δ RR** = 3.79. Small cell (n=2), and small n for discharge "yes" (n=17).
Substance Abuse Hx	^	0.003	0.693	**%Δβ**=20.00	Wald p-value of model effect=0.696. **%Δ RR** = 1.05. Unlikely confounder.
Number of Comorbidities ≥2 [yes/no]	^	0.065	0.251	**%Δβ**=44.00	Wald p-value of model effect=0.253. **%Δ RR** = 2.10. Unlikely confounder.
Comorbidities with p ≤ 0.20					
Anxiety	^	0.021	0.710	**%Δβ**=20.00	Wald p-value=0.615. **%Δ RR** = 0.95. Unlikely confounder.
Arthritis	^	0.002	0.181	**%Δβ**=102.00	Will not use this variable for any subgroup, due to prob. low report for COAT as CM
CHF	^	0.328	0.071	**%Δβ**=62.00	Wald p-value=0.109. **%Δ RR** = 3.05. Unlikely confounder.
Chronic Pain NOS	^	0.680	0.962	**%Δβ**=34.00	Will not use this variable for any subgroup, due to prob. low report for COAT as CM
Depression	^	0.002	0.910	No Significance	
GERD/PUD	^	0.201	0.878	No Significance	
Hepatitis	^	0.011	0.730	**%Δβ**=16.00	Wald p-value=0.717. **%Δ RR** = 0.84. Unlikely confounder.
Osteoporosis	^	0.834	0.160	**%Δβ**=16.00	Wald p-value=0.133. **%Δ RR** = 0.74. Unlikely confounder.
Sleep Disorder	^	0.020	0.609	No Significance	

SMOKING: COVARIATE ASSESSMENT

Variable		SMOKING (N = 298) COAT Cross	Cross SMOKE	Bivar Regress	Comments
COAT		n/a	0.452	n/a	
Age	X	0.085	0.099	**%Δβ=19.48**	Wald p-value of model effect=0.180. **%Δ RR** = 1.48. Use Age because of clinical plausibility and these stats, but don't necessarily keep it in model.
Sex	^	0.847	0.671	No Significance	
Ethnicity/Race	^	0.738	0.149	No Significance	
Clinic	X	0.997	< 0.001	Wald p-value <0.001	COAT 2:1 freq. matched at clinic level. COAT Cross not valid. Log-binomial did converge. **%Δβ** = 2.60 and **%Δ RR** = 0.28. Use in model building due to clinical plausibility.
Same Zip	^	0.817	0.019	p-value=0.025; **%Δβ** = 25.97	Despite significance of Wald p-value of model effect and **%Δβ, %Δ RR** = 2.04. Confounding unlikely, given no difference COAT/Non-COAT.
Insurance (5 categories)	^				
Commercial		< 0.001	0.155	**%Δβ=36.36**	Wald p-value of model effect=0.213. **%Δ RR** = 2.69. Small %Δ RR, but poss. confound.
Medicaid	X	0.001	0.098	**%Δβ=57.14**	Wald p-value=0.125. **%Δ RR** = 4.35. Potential confounder, though small %Δ RR.
Medicare	^	0.038	0.562	No Significance	
Uninsured	^	0.082	0.508	No Significance	
Other	^	0.581	0.529	No Significance	
Insurance (7 categories)	^				
Time Active, Months	^	0.994	< 0.001	p-value<0.001; **%Δβ** = 37.66	Despite significance of Wald p-value of model effect and **%Δβ, %Δ RR** = 2.87. Confounding unlikely, given no difference COAT/Non-COAT.
Total Number Visits	X	< 0.001	< 0.001	**%Δ RR** = 16.48	Wald p-value< 0.001; **%Δβ** = 233.77 and **%Δ RR** = 16.48. Log-Bi did not converge. These values from Poisson Robust.
Percent Visits PCP	X	0.064	< 0.001	p-value<0.001; **%Δβ** = 59.74	Despite significance of Wald p-value of model effect and **%Δβ, %Δ RR** = 4.72 (Poisson) Confounding possible, given borderline differences COAT/Non-COAT and stats above.
Visit Density	^	< 0.001	0.961	**%Δβ=33.77**	Wald p-value=0.747. **%Δ RR** = 2.69. Lacks difference in cross with smoking counselling. Small %Δ RR. Unlikely confounder.
PCP Visit Density		< 0.001	0.373	**%Δβ=71.43**	Wald p-value=0.311. **%Δ RR** = 5.65. Lacks difference in cross with smoking counselling. Unlikely confounder. Of interest, since variable contains TotalVisits and % PCP.
Record of Discharge	^	0.002	0.225	**%Δβ=42.86**	Wald p-value=0.252. **%Δ RR** = 3.43. Lacks difference in cross with smoking counselling. Small %Δ RR. Unlikely confounder.
Substance Abuse Hx	^	0.049	0.708	No Significance	Log-binomial validity uncertain. Poisson robust had no warning on validity, but results were comparable to Log-binomial.
Number of Comorbidities ≥2 [yes/no]	^	0.993	0.005	p-value=0.014; **%Δβ** = 12.99	Despite significance of Wald p-value of model effect and **%Δβ, %Δ RR** = 1.02. Confounding unlikely, given no difference COAT/Non-COAT.
Comorbidities with p ≤ 0.20					
Anxiety	^	0.252	0.016	p-value=0.004	**%Δβ** = 2.60 and **%Δ RR** = 0.28.
Arthritis	^	0.001	0.665		Will not use this variable for any subgroup, due to prob. low report for COAT as CM
CHF	^	0.883	0.311	No Significance	
Chronic Pain NOS	^	0.143	0.861		Will not use this variable for any subgroup, due to prob. low report for COAT as CM
Depression		0.031	0.010	p-value=0.012	**%Δβ** = 22.08 and **%Δ RR** = 1.67. despite small %Δ RR in bivariate, possible confounder.
GERD/PUD	^	0.788	0.008	p-value=0.004	**%Δβ** = 5.19 and **%Δ RR** = 0.46.
Hepatitis	^	0.340	0.417	%Δβ = 19.48	Wald p-value=0.339. **%Δ RR** = 1.57.
Osteoporosis	^	0.506	0.553	%Δβ = 19.48	Wald p-value=0.496. **%Δ RR** = 1.48.
Sleep Disorder	^	0.468	0.001	p-value<0.001	Log-bi non-converge. Poisson converge. Empty cell. **%Δβ** = 12.99 and **%Δ RR** = 1.02

APPENDIX D: Operations Manual

The following pages are a copy of the operations manual used in the study. This manual outlines details of the study procedures, and contains copies of forms used in the study, codes used for data abstraction, and operational definitions of the variables. The manual is reproduced here with its own page numbers, as we used it in the study. Therefore, the following page numbers are discontinuous with those preceding. The manual has its own table of contents, which uses the manual's page numbers. The manual has 11 appendices, 10 of which are reproduced here. *In the text of the thesis*, the manual appendices are referred to using the letter "D" along with the appropriate number for the specific appendix from the manual. For example, Appendix 7 of the manual, which contains the operational definitions of the study variables, is referred to in the thesis text as "Appendix D-7". The table of contents *of the manual* (which follows) indicates that this appendix begins on page 20 *of the manual*.

ORPRN

OPIOIDS AND PREVENTIVE SERVICES STUDY

PERC OPERATIONS MANUAL

2005

"Appearances to the mind are of four kinds.
Things either are what they appear to be;
or they neither are, nor appear to be;
or they are, and do not appear to be;
or they are not, and yet appear to be.
Rightly to aim in all these cases is the wise man's task."

-Epictetus
Discourses, Chapter xxvii

CONTENTS

A. Prepare the Practice Sites

1. Identify the "contact clinician" and "staff contact person" at each site.

2. Contact the "contact clinician" to remind them that the data gathering phase of the study will begin soon, and, if in doubt, to identify the "staff contact person".

3. Send each of these contacts the study "instruction letter" (Appendix 1), which briefly describes what is required of the practice. Add your name and contact information to the letter (and, don't forget to remove the heading, "Appendix, etc.!!).

4. Contact each "staff contact person":

    a. Review the practice requirements of the study with the contact person.
        - Do not assume that they have read and/or understood the "instruction letter", or even that they know that the study will be taking place.
        - Use Appendix 1 and this manual as a guide/checklist.

    b. Clarify and answer any questions. The PERCs will be the study contacts for their respective sites.

    c. Arrange a mutually agreeable schedule for PERC dates and times at the site for both the "First Pass" chart review and the subsequent full data abstraction.
        - Appendix 2 lists the *estimated* time required at each site.
        - These are our best estimates based on multiple assumptions about a variety of factors including patient volume, proportions of patients with particular characteristics, and average abstraction time per record. Actual time required, therefore, may differ from these estimates.
        - The estimates include some extra time for orientation to the sites and unforeseen events, but *do not include travel time.*

    d. Discuss and agree upon the method by which medical records will be pulled as described in Appendix 1.
        - If a clinic is content with having their staff pull the paper records, this will save time for the PERC.
        - On the other hand, the added work of pulling records for the study may be a significant burden for some clinics. So, the PERC should offer to be trained to pull the records. Each PERC should use their judgment in negotiating an arrangement with which the practice is satisfied.

- If an EHR is in place, discuss and agree upon its use by the PERC as in Appendix 1.

5. Review with the "staff contact person" the multi-step process for generating the required list of "First Pass" patient records. Confirm that the responsible person in the practice understands specifically what is being requested in each step. These steps are outlined here and are detailed in the next section on "First Pass" Chart Review (page 3).

    a. Step One: The clinic will identify all clinicians (MD, DO, NP, PA) who saw patients on a full time basis at least four days a week during the entire month of April 2000.
    b. Step Two: The clinic will give this list of clinicians to the PERC, who will randomly select those to be used as "First Pass Clinicians".
    c. Step Three: The PERC will present the list of "First Pass Clinicians" to the clinic. The number of "First Pass Clinicians" will differ for each practice site.
    d. Step Four: For each "First Pass Clinician", the clinic will generate a list of all patients age 35 or older who were seen by that clinician during the month of April 2000 (4/1/2000 through 4/30/2000, inclusive). See the next section on "First Pass" Chart Review for details.

A NOTE ABOUT PAPER VS. ELECTRONIC RECORDS:

The procedures for identifying and getting access to patient lists and medical records will differ in various ways between practice sites. The descriptions of procedures in the next section generally assume a paper record, because identifying and obtaining paper records is usually more logistically complicated than identifying and getting access to electronic records. Often, when an electronic record is in use it will not have been in use for the entire study period, and, therefore, both paper and electronic records will be needed. The basic order and criteria of the steps, however, are the same for both types of records. The PERCs should adapt these guidelines for the specific circumstances of each practice site.

B. "First Pass" Chart Review

1. Goal.

   The goal of the "First Pass" chart review is to classify a cross-sectional sample of patients seen by the "First Pass" clinicians according to *COAT status* (COAT or Non-COAT), *smoking status*, and *gender*. These are the three variables that will be used to frequency match study subjects and produce the list of those who will be enrolled in the study and whose medical records receive full data abstraction.

2. Identify the "First Pass Clinicians".

   a. Each clinic will identify all clinicians (MD, DO, NP, PA) who saw patients on a full time basis at least four days a week during the entire month of April 2000.
   b. For a residency practice (Cascades East), only faculty clinicians are eligible to be "First Pass" Clinicians. (Note: all clinicians, including residents, are eligible to be "PCPs").
   c. Each clinic will give this list of clinicians to the PERC.
   d. The PERC will write the name of each of these clinicians on a separate identical slip of paper, one name per slip. The papers will be folded identically so that the names are not visible and placed together in a hat or other similar container. The PERC will draw the required number of slips from the hat, according to the column "1st Pass Clinician #" in Appendix 2. The clinicians selected in this fashion will be the "First Pass Clinicians" for the given practice site.

3. Assign an ID number to each "First Pass Clinician".

   Using the Clinician Enrollment Log (Appendix 3), the PERC will assign a unique ID number to each "First Pass Clinician". Each clinician's name and clinic ID number will be entered in the Log in the appropriate spaces next to their unique ID number and the box indicating that they are a "First Pass Clinician" will be marked.

4. Generate the list of "First Pass" patients.

   a. The PERC will present the list of "First Pass Clinicians" to the clinic.
   b. For each "First Pass Clinician", the clinic will generate a list of all patients 35 years or older who were seen by that clinician during the month of April 2000 (4/1/2000 through 4/30/2000, inclusive).
   c. Ideally, this list will be in chronologic order of the date and time of visit, with columns containing the patients' names and/or medical record numbers.
   d. The PERC will assign a unique patient study ID number to each patient **at the time that the individual patient's record is reviewed for the "First Pass".** See the details in the following section on gathering the "First Pass" variables.

5. Gather the "First Pass" variables.

   a. The PERC will obtain the medical records of all "First Pass" patients in a systematic fashion according to the agreement with the practice.
      - For paper charts especially, consider the number of records needed for a given day (estimate 12 per hour for the "First Pass") before requesting the records.
      - Consider that records for the year 2000 may be "warehoused" in some practices and, therefore, require more lead-time to pull.
   b. The PERC will review the medical record (paper, electronic, or both) for each "First Pass" patient and enter the appropriate variables into the First Pass Database (Appendix 4) on their laptop. Variable definitions are listed in Appendix 7.
   c. The First Pass Database variables are: Patient ID (automatic); Practice ID (pull down menu); First Pass Clinician ID (enter the number assigned by PERC); gender; smoking status (as defined in Appendix 7); and COAT status (as defined in Appendix 7).
   d. The First Pass Database form is customized for each PERC so that:
      - the PERC name does not need to be entered,
      - the possible entries for clinic code are limited to the appropriate practice sites,
      - the patient ID numbers are automatically generated in sequence and within the range assigned to each PERC.
   e. Because the First Pass Database form automatically enters the next unique ID number in sequence, and because availability of individual charts will likely preclude reviewing records in the order of the "First Pass" patient list, **individual patient ID numbers should be assigned at the time of each "First Pass" chart review, and not before.** The PERC will enter the appropriate patient name and/or medical record number of each "First Pass" patient into the Patient Enrollment Log (Appendix 5) next to the corresponding ID number and with the appropriate Clinic Code number.

A NOTE ABOUT ENROLLMENT LOGS:

The Enrollment Logs for both the clinicians and the patients are the "keys" that link the unique study ID numbers to personal identifying information, including personal health information. For this reason, these enrollment logs must be kept secure, away from all other study data, and must not be entered into a computer. Each PERC is responsible for maintaining and protecting these "keys". These logs will be used by the PERCs to retrieve study subjects' medical records after the "First Pass" chart review. Should it be necessary to refer back to particular medical records after the data collection is complete, the PERCs would use these "keys" to identify the required records. The principal investigators and other analysts should not normally need to refer to these logs.

C. Data Abstraction

1. General Comments.

- The study data set will be comprised of the values of the study variables that are abstracted from subjects' medical records and entered on the "Data Collection Instrument" (hereafter called the "Scan Form"). Although the process of abstracting data from medical records can sometimes be tedious, it is the most important part of the entire study. The data set is the foundation upon which all subsequent analyses and conclusions and fame and fortune depend. In short, the quality of the study depends on the quality of the data abstraction.
- So, the first good news is that this critical process is in the eminently able hands of ORPRN's PERCs.
- The other good news is that we have done everything we can think of to assure the quality and ease of the data abstraction process. The process is described below and will be elaborated during the PERC Opioid Study training.

2. General Principles, Concepts, and Other Information.

- Each of the study variables that are to be abstracted and entered on the Scan Form is defined in Appendix 7. Details of the protocol for recording the abstracted data onto the Scan Form are provided below.
- For some variables, the medical record data will clearly and unequivocally satisfy the definition and will usually be easily, logically, and reliably located (e.g., "Gender" or "Year of Birth"). For other variables, the definition may be satisfied by a variety of types of medical record data found in a variety of chart locations (e.g., evidence of "Lipid Disorder" or "Pap" might be found in clinician progress notes, nursing notes, a problem list, a preventive services flow sheet, a consultant's letter, or laboratory results). The potential range of data type and location in the record can be challenging and is really where the skill of data abstraction comes into play.
- In general, the time required to abstract data decreases with increasing familiarity with the variables and a particular practice's medical records.
- There will be issues that we have not anticipated or prepared for. When you have any question or doubt about how to interpret information in the medical records, how to record data on the Scan Form, what to do in a novel situation, or just for general moral support, put the particular record aside and contact David Buckley, Jim Calvert and/or Jim Wallace.

3. Identification of Study Subjects.

- The data gathered in the "First Pass" Chart Review will be sent as file attachments to the principal investigators and used to calculate the number of "First Pass" patients in each category of COAT status, smoking status, and gender. Patients will then be frequency matched on these variables, and a list of enrolled study subjects will be generated. Each PERC will then be given a list of the enrolled

study subjects for their participating practices. *These are the study subjects whose medical records will have a full data abstraction.*

- The PERC will use the Patient Enrollment Log to identify study subjects' medical records (paper, electronic, or both) from their study ID numbers.

4. Using the Data Collection Instrument ("Scan Form").

- General.
  - The Scan Form (Appendix 6) was designed for ease of use after pilot testing, trial and error, and lots of thought. Still, it may be easier to use in some settings than in others, and each PERC will likely find the easiest way for their own situations.
  - Data are entered in two ways:
    1) As numbers in numeric field boxes.
    2) By checking the appropriate box for "Yes/No" or "Multiple choice".
  - As usual with such forms, make clear and dark marks in accordance with the instructions and template presented during the PERC training session. Use a black pen.
  - Before the full data abstraction for each study subject, the six "First Pass" variables, which were already abstracted, should be entered from the First Pass Database onto the Scan Form. <u>These are items #1, #2, #3, #6, #10 and #11</u>.
  - <u>Consult Appendix 7 for operational definitions of the variables.</u>

VARIABLES:
(Consult Appendix 7 for operational definitions of the variables)

- Item 1: (ID Number).
  - Enter the five-digit number exactly as in "Patient ID" from the First Pass Database.
- Item 2: (Clinic).
  - Enter the LAST TWO DIGITS of the "Practice ID" from the First Pass Database.
- Item 3: (First Pass Clinician).
  - Enter the three-digit number from "Clinician ID 1st Pass" from the First Pass Database.
- Item 4: (PCP).
  - After determining the subject's "PCP" (primary care physician, nurse practitioner or physician's assistant) as defined in Appendix 7, enter the clinician's three-digit ID number from the Clinician Enrollment Log.
  - **As each clinician is first identified as a "PCP" in the course of data abstraction, the PERC will assign the clinician a unique ID number.**
  - Using the Clinician Enrollment Log (Appendix 3), the PERC will assign the ID number, and each clinician's name and clinic ID number will be entered in the Log in the appropriate spaces.
  - If a clinician has already been assigned an ID number as a "First Pass Clinician" or a "PCP", they will not be assigned a new number.
  - "First Pass Clinicians" can also be "PCPs", but every clinician will have only one ID number.
- Item 5: (Year of Birth).
  - Enter the subject's four-digit year of birth.
- Item 6: (Gender).
  - Enter the subject's gender from the First Pass Database.
- Item 7: (Zip Code).
  - Enter the subject's most recent five-digit residential zip code.
- Item 8: (Insurance Status).
  - Enter the subject's most recent insurance status.
  - Check all boxes that apply.
- Item 9a: (Ethnicity).
  - Enter the subject's ethnicity (distinct from "Race").
  - Check only one box.
- Item 9b: (Race).
  - Enter the subject's race.
  - Check all boxes that apply.
- Item 10: (Smoking Status).
  - Enter the subject's smoking status from the First Pass Database.
  - Check only one box.
- Item 10a: (Smoking Counseling).

- Only to be filled if response to Item 10 is "Yes".
- Check only one box.

- Item 10b: (Counseling Date).
  - Only to be filled if response to Item 10a is "Yes".
  - Fill each box. Use leading zeroes if needed.
- Item 11: (COAT Status).
  - Enter the subject's COAT status from the First Pass Database.
  - Check only one box.
- Item 11a: (Contract).
  - Only to be filled if response to Item 11 is "Yes".
  - Check only one box.
- Item 11b: (Contract Date).
  - Only to be filled if response to Item 11a is "Yes".
  - Fill each box. Use leading zeroes if needed.
- Item 11c: (Diagnosis).
  - Enter the ICD-9 diagnosis code numbers for up to five principal *diagnoses* as reasons that the patient is treated with opioid medication.
  - <u>These are medical diagnoses that are distinct from the anatomic site of the pain. Anatomic site of pain is entered in Item 11d. A given subject may have an entry in 11c, 11d, neither, or both.</u>
  - Appendix 8 is a list of the most common diagnostic reasons and associated ICD-9 code numbers.
  - If no *diagnostic* reasons are recorded in the medical record, enter "999.9" in the boxes labeled "a".
  - If fewer than five diagnostic reasons are recorded enter the ICD-9 code numbers in the boxes, sequentially beginning with "a", and leave any unused boxes empty (i.e., only use the "999.9" code when *no* diagnostic reasons are recorded).
  - If a diagnostic reason is given in the record that does not appear in Appendix 8, enter the code for "Other" and write the reason in the "Notes" section of the data abstraction form with a notation for "Item 11c".
  - If more than five diagnostic reasons are noted in the medical record, and it is unclear which to include on the data form, contact Jim Calvert or David Buckley.
- Item 11d: (Anatomic Site).
  - Enter the two-digit code number for the anatomical site of the pain for which the patient is treated with opioid medication.
  - Appendix 9 is a list of anatomical sites and code numbers.
  - If no anatomical site is recorded in the medical record, enter "99" in the boxes labeled "a".
  - If fewer than five sites are recorded enter the code numbers in the boxes, sequentially beginning with "a", and leave any unused boxes empty (i.e., only use the "99" code when *no* site is recorded).

- If an anatomical site that does not appear in Appendix 8 is recorded in the record, enter the code for "Other" and write the site in the "Notes" section of the data abstraction form with a notation for "Item 11d".
- If more than five sites are noted, and it is unclear which to include on the data form, contact Jim Calvert or David Buckley.

- Item 12: (Comorbidities).
  - Enter the ICD-9 diagnosis code numbers for up to five chronic illnesses for which the patient is not taking opioid medication.
  - Appendix 10 is a list of common pertinent chronic illnesses and code numbers. See Appendix 10 for more definition-related coding details.
  - If no chronic illnesses are recorded in the medical record, enter "999.9" in the boxes labeled "a".
  - If fewer than five chronic illnesses are recorded enter the ICD-9 code numbers in the boxes, sequentially beginning with "a", and leave any unused boxes empty (i.e., only use the "999.9" code when *no* chronic illnesses are recorded).
  - If an illness is given in the record that does not appear in Appendix 10 write the reason in the "Notes" section of the data abstraction form with a notation for "Item 12". If in doubt about which illnesses to include contact Jim Calvert or David Buckley.
  - If more than five reasons are noted, and it is unclear which to include on the data form, contact Jim Calvert or David Buckley.
- Item 12a: (Comorbidities Dates).
  - Enter one date for each entry in Item 12.
  - Leave blank for code "999.9".
  - Fill each box. Use leading zeroes if needed.
- Item 13: (Total # of Visits).
  - Fill each box. Use leading zeroes if needed.
- Item 14: (# of Visits with PCP).
  - Fill each box. Use leading zeroes if needed.
- Item 15: (Date of Last Visit).
  - Fill each box. Use leading zeroes if needed.
- Item 16: (Lipid Disorder).
  - Check only one box.
- Item 17: (Lipid Screening).
  - Check only one box.
- Item 17a: (Lipid Screening Date).
  - Only to be filled if response to Item 17 is "Yes".
  - Fill each box. Use leading zeroes if needed.
- Item 18: (Pap).
  - Check only one box.
- Item 18a: (Pap Date).
  - Only to be filled if response to Item 18 is "Yes".
  - Fill each box. Use leading zeroes if needed.
- Item 19: (Fecal Occult Blood Testing).
  - Check only one box.

- Item 19a: (FOBT Dates).
  - Only to be filled if response to Item 19 is "Yes".
  - Enter the date of the final result of each instance of a "three card" FOBT.
  - Enter a single date for each set of three (or more) cards. Do not enter a separate date for each card in the set.
  - Fill each box. Use leading zeroes if needed.
- Item 19b: (FOBT for screening?).
  - For each entry in 19a, indicate whether or not the FOBT was for screening.
  - Check only one box.
- Item 20: (Flex Sig).
  - Check only one box.
- Item 20a: (Flex Sig Dates).
  - Only to be filled if response to Item 20 is "Yes".
  - Enter one date for each instance of flexible sigmoidoscopy.
  - Fill each box. Use leading zeroes if needed.
- Item 20b: (Flex Sig for Screening?).
  - For each entry in 20a, indicate whether or not the Flex Sig was for screening.
  - Check only one box.
- Item 21: (Colonoscopy).
  - Check only one box.
- Item 21a: (Colonoscopy Dates).
  - Only to be filled if response to Item 21 is "Yes".
  - Enter one date for each instance of colonoscopy.
  - Fill each box. Use leading zeroes if needed.
- Item 21b: (Colonoscopy for Screening?).
  - For each entry in 21a, indicate whether or not the colonoscopy was for screening.
  - Check only one box.
- Item 22: (Substance Abuse).
  - Check only one box.
- Item 22a: (Substance Abuse Date).
  - Only to be filled if response to Item 22 is "Yes".
  - Fill each box. Use leading zeroes if needed.
- Item 23: (Record of Discharge).
  - Check only one box.
- Item 23a: (Date of Discharge).
  - Only to be filled if response to Item 23 is "Yes".
  - Fill each box. Use leading zeroes if needed.
- Item 24: (Record of Death).
  - Check only one box.
- Item 24a: (Date of Death).
  - Only to be filled if response to Item 24 is "Yes".
  - Fill each box. Use leading zeroes if needed.

APPENDIX 1: PRACTICE SITE "INSTRUCTION LETTER"

Dear ,

The ORPRN Chronic Opioid Therapy and Preventive Services Study will soon begin gathering data. We appreciate your support and participation in this project. This letter is meant as a reminder of some of the key aspects of the study as previously communicated, and to present the following list of "ground work" that is requested of your practice in order to successfully carry it out.

You will be contacted by the ORPRN staff member, called a Practice Enhancement Research Coordinator (PERC), who will serve as the research associate for the study. Your PERC will be able to clarify and answer questions you may have about the "ground work" and/or the study procedures, help you figure out the best and least intrusive way for your practice to do this "ground work", and set up a convenient schedule for visiting the clinic to conduct the chart review.

What does the study consist of?

- A research associate (PERC) will review medical records. A brief initial screening of approximately 600 records will be followed by a full review of approximately 100 records. The actual number of records reviewed will be different for each participating practice.
- Data will be gathered on demographics, pain diagnoses, comorbidities, use of opioid medications, and several preventive and screening services.
- All study data will be gathered from medical records. There will be no direct interaction of the research associate with any patients.

What about confidentiality?

- All provisions have been made in the design of the study to assure anonymity of all patients, clinicians, and practices. No patient identifying, clinician identifying, or practice identifying information will be reported. All data will be aggregated.
- The study has been reviewed and approved by the OHSU Institutional Review Board (IRB) to assure compliance with HIPAA regulations, and the protection of patients' health information.

What is required of the practice?

- Most of the work of data gathering will be performed by your PERC. After being oriented to your practice's medical record system, we expect the PERC will be able to function independently, without disrupting of the normal flow of the clinic.

- Staff time to identify eligible medical records for review according to a clear study protocol that will be presented by your PERC.

- Please identify a contact person in the practice who can:

  1) Arrange for a temporary work space for the visiting PERC. If your clinic uses an electronic health record (EHR), the work space should include a computer with access to the EHR.
  2) Arrange to provide the PERC a brief introduction to the medical record(s) (paper and/or EHR) that were in use from 1/1/2000 until now. If an electronic health record is used, this introduction should include the basic training required for the PERC to be able to independently review all sections of the record.
  3) Arrange brief meetings with any clinicians or others in the practice who may have an interest in meeting with the visiting PERC.
  4) Help to coordinate and arrange for staff to carry out the identification of eligible medical records for review according to a clear study protocol that will be presented by your PERC.
  5) Serve as a resource to address questions or problems that may arise.

Please contact your PERC or any of us if you have any questions: **buckleyd@ohsu.edu**; **fagnanl@ohsu.edu**; **jimcalvert@earthlink.net**

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APPENDIX 2: ESTIMATED TIME REQUIRED BY PRACTICE SITE*

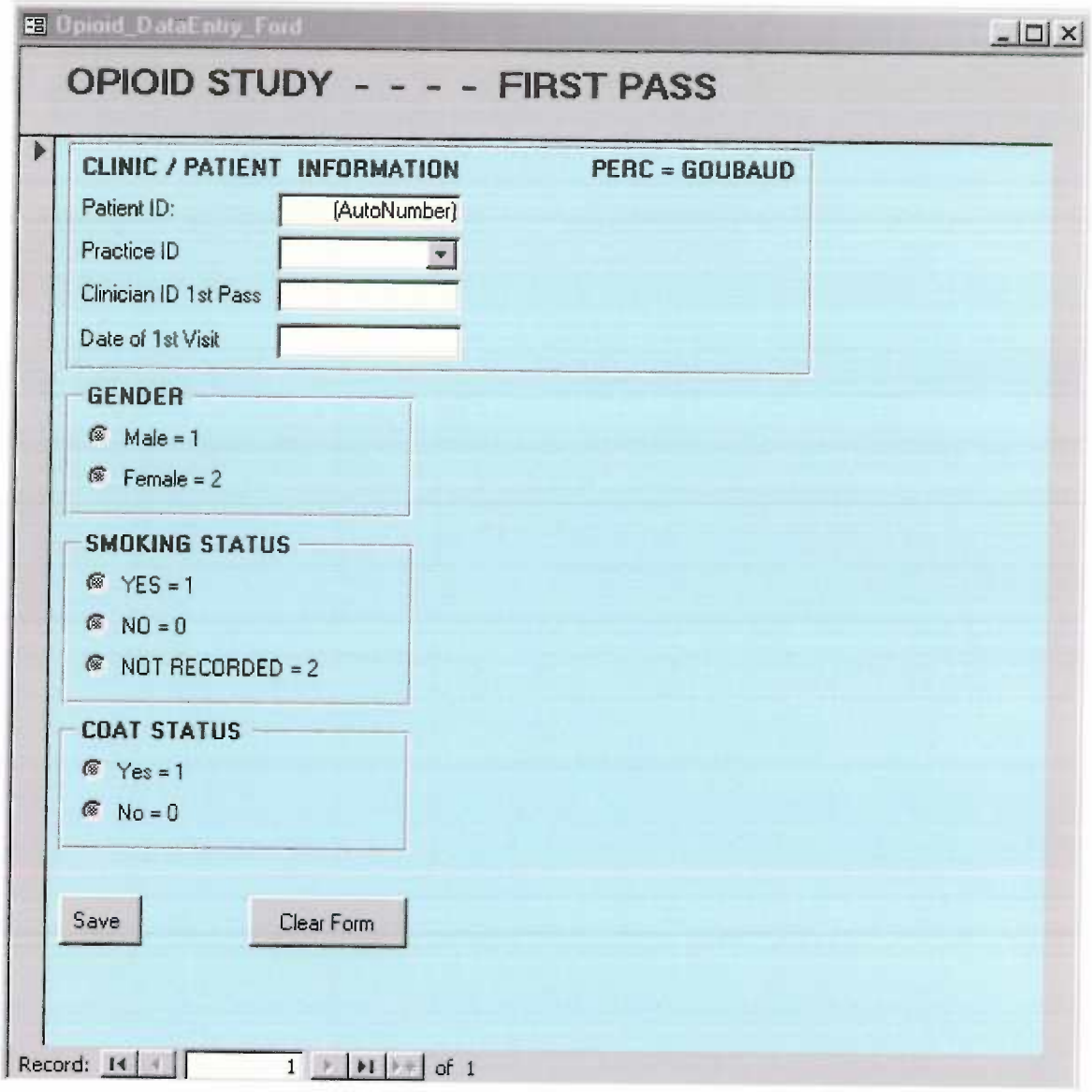
PERC	PRACTICE	1st Pass	FIRST PASS		FULL ABSTRACT		TOTAL DAYS
		Clinician #	Charts	Days	Charts	Days	
Ford	Klamath Open Door	3	675	7.5	99	4.5	13
	Cascades East	3	675	7.5	99	4.5	13
	Strawberry Wilderness	2	450	5	66	3	9
Goubaud	Lincoln City	4	900	10	132	7.5	19
	Wheeler	1	225	2.5	33	1.5	5
Reynolds	Columbia Hills	3	675	7.5	99	4.5	13
	Union	1	225	2.5	33	1.5	5
	Elgin	1	225	2.5	33	1.5	5

* Estimates assume: 1) 225 charts per 1st Pass Clinician; 2) five minutes per 1st pass chart review; 3) 11 COAT subjects per 1st Pass Clinician; 4) 20 minutes per full abstraction; 5) more than one full day added to each clinic; 6) no calculation for travel time.

APPENDIX 3: CLINICIAN ENROLLMENT FORM

Practice ID:	SAMPLE				
PERC:					
	Last name	First name	Degree	Clinic #	X if first pass clinician
X00					
X01					
X02					
X03					
X04					
X05					
X06					
X07					
X08					
X09					
X10					
X11					
X12					
X13					
X14					
X15					
X16					
X17					
X18					
X19					
X20					
X21					
X22					
X23					
X24					
X25					

APPENDIX 4: FIRST PASS DATABASE



APPENDIX 5: PATIENT ENROLLMENT FORM

Practice ID:			
PERC:			
PtID number	Practice Medical Record number	Last name	First name
X0000			
X0001			
X0002			
X0003			
X0004			
X0005			
X0006			
X0007			
X0008			
X0009			
X0010			
X0011			
X0012			
X0013			
X0014			
X0015			
X0016			
X0017			
X0018			
X0019			
X0020			
X0021			
X0022			
X0023			
X0024			
X0025			

APPENDIX 6:

ORPRN Opioid Study Data Collection Instrument

Instructions: Using a black pen please mark the appropriate box.

1. ID Number ☐☐☐☐☐

2. Clinic ☐☐

3. First Pass Clinician ☐☐☐

4. PCP ☐☐☐

5. Year of Birth ☐☐☐☐

6. Gender ☐ Male ☐ Female

7. Zip Code ☐☐☐☐☐

8. Insurance Status **(check all that apply)**

☐ Commercial
☐ Medicaid
☐ Medicare
☐ Uninsured
☐ Other

9a. Ethnicity

☐ Hispanic or Latino
☐ Not Hispanic or Latino
☐ Not specified

9b. Race **(check all that apply)**

☐ White
☐ Black/African American
☐ Asian
☐ Native Hawaiian/Other Pacific Islander
☐ American Indian/Alaska Native
☐ Not specified

10. Smoking Status (as of 1/1/2001)

☐ Yes
☐ No
☐ Not recorded **(If NO or Not recorded, go to 11)**

10a. If yes, Smoking Counseling?

☐ Yes
☐ No

10b. If yes, Counseling Date

☐☐ / ☐☐ / ☐☐
month / day / year

11. COAT Status

☐ Yes
☐ No **(If NO, go to 12)**

11a. If yes, Contract?

☐ Yes
☐ No

11b. If yes, Contract Date

☐☐ / ☐☐ / ☐☐
month / day / year

11c. Diagnosis (reason for Opioid use)

a) ☐☐☐.☐
b) ☐☐☐.☐
c) ☐☐☐.☐
d) ☐☐☐.☐
e) ☐☐☐.☐

11d. Anatomic Site of Pain

a) ☐☐
b) ☐☐
c) ☐☐
d) ☐☐
e) ☐☐

12. Comorbidities

a) ☐☐☐.☐
b) ☐☐☐.☐
c) ☐☐☐.☐
d) ☐☐☐.☐
e) ☐☐☐.☐

12a. Comorbidities Dates

	month	day	year
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐
Date	☐☐	☐☐	☐☐

13. Total # of Visits (between 1/1/01 to 12/31/03) ☐☐☐

14. # of visits with PCP (between 1/1/01 to 12/31/03) ☐☐☐

15. Date of Last Visit (prior to 12/31/03) ☐☐ / ☐☐ / ☐☐ (month / day / year)

16. Lipid Disorder (Prior to 1/1/01)
☐ Yes
☐ No
☐ Not Recorded

17. Lipid Screening (1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 18)**

17a. If yes, Lipid Screening Date (earliest between 1/1/01 to 12/31/03) ☐☐ / ☐☐ / ☐☐ (month / day / year)

18. Pap (1/1/01 to 12/31/03)
☐ Yes
☐ No
☐ Male **(If NO or Male, go to 19)**

18a. If yes, Pap Date (earliest between 1/1/01 to 12/31/03) ☐☐ / ☐☐ / ☐☐ (month / day / year)

19. Fecal Occult Blood Testing (FOBT) (1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 20)**

19a. If yes, FOBT Dates (1/1/01 to 12/31/03)

	month	day	year	19b. FOBT for screening?
a)	☐☐	☐☐	☐☐	☐ Yes ☐ No
b)	☐☐	☐☐	☐☐	☐ Yes ☐ No
c)	☐☐	☐☐	☐☐	☐ Yes ☐ No

20. Flex Sig (1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 21)**

20a. If yes, Flex Sig Dates (1/1/01 to 12/31/03)

	month	day	year	20b. Flex Sig for sceening?
a)	☐☐	☐☐	☐☐	☐ Yes ☐ No
b)	☐☐	☐☐	☐☐	☐ Yes ☐ No
c)	☐☐	☐☐	☐☐	☐ Yes ☐ No

21 . Colonoscopy (1/1/01 to 12/31/03)
☐ Yes
☐ No **(If NO, go to 22)**

21a. If yes, Colonoscopy Dates (1/1/01 to 12/31/03)

	month	day	year	21b. Colonoscopy for screening?
a)	☐☐	☐☐	☐☐	☐ Yes ☐ No
b)	☐☐	☐☐	☐☐	☐ Yes ☐ No
c)	☐☐	☐☐	☐☐	☐ Yes ☐ No

22. Substance Abuse (past or present)
☐ Yes
☐ No **(If NO, go to 23)**

22a. If yes, Substance Abuse Date ☐☐ / ☐☐ / ☐☐ (month / day / year)

23. Record of Discharge from clinic
☐ Yes
☐ No **(If NO, go to 24)**

23a. If Yes, Date ☐☐ / ☐☐ / ☐☐ (month / day / year)

24. Record of Subject's Death
☐ Yes
☐ No

24a. If Yes, Date ☐☐ / ☐☐ / ☐☐ (month / day / year)

Notes: _____

Appendix 7: Variable Operational Definitions

A NOTE ON MEDICAL RECORD DATA TYPE AND SOURCE:

The nature and location of medical record data that will satisfy each of the following definitions will be diverse. For some variables, the medical record data will clearly and unequivocally satisfy the definition and will usually be easily, logically, and reliably located (e.g., "Gender" or "Year of Birth"). For other variables, the definition may be satisfied by a variety of types of medical record data found in a variety of chart locations (e.g., evidence of "Lipid Disorder" or "Pap" might be found in clinician progress notes, nursing notes, a problem list, a preventive services flow sheet, a consultant's letter, or laboratory results). The evidence for a variable is not, therefore, limited to the types and sources mentioned in the following list. Nor, is it necessary to use the same source or type of evidence for each study subject. (For one subject, evidence of smoking may be in a problem list, and for another the evidence may be in a clinic note). In every case, however, the evidence should clearly indicate the status of the variable. If in doubt about any definitions or novel situations, contact David Buckley or Jim Calvert.

1) ID Number: The unique ID number automatically assigned by the First Pass Database at the time of the subject's "First Pass" chart review.

2) Clinic: Clinical practice where subject received care, and from which study data were gathered. The First Pass Database assigns a unique clinic identification number to each practice site. The same number is used for the Scan Form.

3) First Pass Clinician: Clinician who saw patients in the participating practice during April 2000 and who is used to identify potential study subjects as described in Operations Manual, sections B.2 and B.3.
   - The "First Pass" Clinician **may or may not** be the study subject's PCP.
   - The "First Pass" classification is strictly operational for sampling potential study subjects.
   - For a residency practice (Cascades East), only faculty clinicians are eligible to be "First Pass" Clinicians.
   - The "First Pass" Clinician ID number is assigned as described in section B.3.

4) PCP: The subject's primary care physician, nurse practitioner, or physician's assistant during the study period of 1/1/2001 to 12/31/2003.
   - The PCP may be listed (e.g., on a chart's face sheet) or explicitly mentioned as the designated PCP in another part of the record (e.g., clinician's encounter notes, a consultant's report, nursing note, etc.). Be certain that any such listing pertains to the study period, 1/1/2001 to 12/31/2003.

- If it is clear that the subject had multiple PCPs during the study period, the PCP who saw the subject for the most clinic visits should be used as "PCP".
- In cases where no clinician is explicitly mentioned as the PCP, the number of clinic visits during the study period of 1/1/2001 to 12/31/2003 should be counted and the clinician who saw the subject for the greatest number of visits used as "PCP" (A scratch pad was often used for this purpose in the pilot phase).
- Occasionally a subject will have a designated PCP, but will have had more visits with a different clinician. In such cases, review the content of the clinic notes to see if there was an "official" change in PCP that was not reflected in other sections of the chart. If it appears that the clinician with the most visits is, in fact, addressing the majority of the patient's healthcare issues with continuity, use this *de facto* PCP as the "PCP".

5) Year of Birth: Subject's year of birth. Usually found on a "face sheet".

6) Gender: Subject's gender. Usually found on a "face sheet".

7) Zip Code: Subject's most recent residential zip code. Usually on a "face sheet".

8) Insurance Status: Subject's most recent insurance status. Usually found on a separate sheet with insurance information.

9) Ethnicity: Latino/Hispanic or Not Latino/Hispanic as recorded in the medical record. Either status of this category may apply in conjunction with the various classifications of "Race".

9a) Race: Subject's race, as recorded in the medical record. Categories are: White, Black/African-American, Asian, Native Hawaiian/Other Pacific Islander, American Indian/Alaska Native.

10) Smoking Status: Dichotomous variable (meaning it is a "Yes/No" question) indicating whether or not the subject was a smoker as of 1/01/2001.
- The quantity of smoking should not be considered for this variable.
- Evidence may be in a Problem List or "buried" in clinic notes.
- Occasionally, evidence of smoking on or before 1/01/2001 will be found in clinic notes from a date AFTER 1/01/2001. For example: "Clinic Note, 4/20/2002: 'Mr. Smith smokes a pack a day, and has done so for the past 15 years'". For this reason, if a review of clinic notes is necessary, be certain to review notes for the entire study period of 1/01/2001 to 12/31/2003.

10a) Smoking Cessation Counseling: Dichotomous variable ("Yes/No") indicating whether or not the subject received counseling for smoking cessation on at least one (1) occasion during the study period from 1/01/2001 to 12/31/2003.

- Smoking cessation counseling is any evidence that the issue of the patient's smoking was explicitly addressed with the patient.
- This could include (but is not limited to) giving the patient printed patient education materials, a brief mention the think about quitting, or a referral to a formal smoking cessation program.
- In each case, the action must be recorded somewhere in the record.
- This variable will be entered only for subjects who were recorded as smokers as of 1/01/2001.

10b) Smoking Counseling Date: Earliest date, on or after 1/01/2001, that a subject received smoking cessation counseling as recorded in the medical record. This variable will be entered only if applicable, for subjects who were recorded as smokers as of 1/01/2001 and who had evidence of smoking cessation counseling in the record.

11) COAT Status: Dichotomous variable ("Yes/No") indicating whether or not the subject received **"continuous" opioid therapy during calendar year 2000**.

- "COAT" is the acronym for "Chronic Opioid Analgesic Therapy".
- Opioid medications are also known as "Narcotics" or "Narcotic medications".
- There are a variety of medications that are either purely opioid in composition, or are a combination of opioid medication and other non-opioid medications. Both types of medications are considered opioid for the study.
- The most common opioid medications are listed by generic name and multiple brand names in the "Pocket Pharmacopeia™" provided for each PERC.

"Continuous" therapy may be defined in one of two ways:
(Take careful note of the date ranges in the following)

a) Direct:
   - ✓ Evidence of 30 or more pills prescribed per month for at least 6 months between 1/01/2000 and 12/31/2000,

   OR,

b) By Inference:
   - ✓ Evidence of 30 or more pills prescribed per month for at least 6 months between 1/01/1999 and 12/31/1999,
   - ✓ **AND** Evidence of 30 or more pills prescribed per month for at least 6 months between 1/01/2001 and 12/31/2001,
   - ✓ **AND** at least one entry in the record between 1/01/2000 and 12/31/2000 indicating that the patient was receiving opioid medication during the period between 1/01/2000 to 12/31/2000.

- The Direct definition (a) is preferred and simpler and should be tried first.
- As with all variables the evidence may come from any number of different sources. The most likely sources for this variable are: medication lists, physician or nursing clinic notes, or prescription copies.
- Determination of total time on the medication may require calculation, using the details of prescriptions, number of refills, and the period of time that a given prescription would cover based on number of pills and instructions for dose frequency.
- If in doubt about the nature of a particular medication, the meaning of a particular prescription, or how to interpret the details that are recorded in the medical chart, contact David Buckley or Jim Calvert.

11a) Contract: Dichotomous variable ("Yes/No") indicating whether or not the subject's medical record contains a contract agreement for the use of opioid/narcotic medications.

- A contract for the use of opioids is usually a separate document signed by the patient and at least one witness, and indicates the patient's agreement to specific and limited use of opioids.
- The contract spells out the conditions of use, limits the frequency and size of prescriptions, and stipulates the consequences of violation of the contract.
- It is usually located in the front of the paper medical record, and may be updated periodically.

11b) Contract Date: Earliest date of contract for the use of narcotic medications, if applicable.

11c) Diagnosis: Diagnosis or diagnoses for which an opioid medication was prescribed during the period 1/01/2000 to 12/31/2000.

- Refer to Appendix 8 for a list of common pain-associated diagnoses.
- These are medical diagnoses, and are distinct from the anatomic site of the pain. The anatomic site is entered as Item 11d.
- A subject may have evidence in the chart of either a medical diagnosis (Item 11c), an anatomic site of pain (Item 11d), neither, or both. If evidence of both "diagnosis" and anatomical site is available, then entries should be made for both items.

11d) Anatomic Site: The anatomic site or sites of the pain for which the subject was being treated.

- Refer to Appendix 9 for a list of anatomic sites.
- See Item 11c, above.

12) Comorbidities: These are chronic illnesses aside from those for which the subject was treated with opioids.

- Refer to Appendix 10 for a list of common chronic illnesses as "comorbidities".
- Chronic illnesses are likely to be listed in the "Problem List" (usually in the front of the paper medical chart) or the clinic notes. Hospital discharge summary notes are also a very common location of lists of chronic illnesses.
- Appendix 10 lists multiple names for some conditions, and in these cases the code number for each name is the same. This is to make the identification and abstraction of certain medical conditions easier. In these cases, if the PERC notices that more than one name is recorded in the medical chart for the same essential condition, AND if both names have the same code number in Appendix 10, then it is only necessary to enter the code number once.
- Appendix 10 includes diagnoses that are pain-associated. These are marked with an asterisk. <u>These should ONLY be entered as "Comorbidities" if it is clear that the patient did not receive opioid medication for the condition</u>.

12a) <u>Comorbidities Dates</u>: Date that each comorbid diagnosis was <u>first recorded</u> in the medical record, if applicable.

13) <u>Total # of Visits</u>: Number of the subject's outpatient encounters at the participating clinical practice during the study period <u>from 1/01/2001 to 12/31/2003</u>.
- This ONLY includes visits in which the subject was seen by a "clinician", as defined above (i.e., physician, nurse practitioner, or physician's assistant).
- It does NOT include visits for other services such as laboratory work, blood pressure checks, etc.
- May be recorded on a flow sheet, but will likely require reviewing and counting all clinic notes for the two year study period, 1/1/2001 to 12/31/2003.

14) <u># of Visits with PCP</u>: Number of the subject's outpatient encounters with his or her PCP (as defined in Item 4, above) during the study period from 1/01/2001 to 12/31/2003.

15) <u>Date of Last Visit</u>: Date of subject's latest encounter at the participating clinical practice prior to 12/31/2003. "Visit" is defined as in Item 13, above.

16) <u>Lipid Disorder</u>: Dichotomous variable ("Yes/No") indicating whether or not the subject had a history of any lipid disorder prior to 1/01/2001.
- A lipid disorder results in an abnormal level of cholesterol or triglycerides, fatty substances that circulate in the blood stream.
- The names for this may include: "Hypercholesterolemia", "Hyperlipidemia", Hypertriglyceridemia", or elevation of any of these

substances (cholesterol, lipids, triglycerides) indicated by the words "elevated" or "high" or a "↑" in association with the word.

- The definition for this item can be based upon the diagnosis having been made and recorded somewhere in the chart (generally, in the problem list or clinic notes).
- It is not sufficient for an elevated level to be recorded as the result of laboratory testing, unless there is also a note that the level is abnormally high.
- A subject is also considered to have a lipid disorder, if the subject was taking a medication for elevated lipids on or prior to 1/01/2001, regardless of whether the diagnosis was recorded. Usually, the diagnosis will be recorded if the patient is taking the medication.
- The most common lipid-lowering medications are listed by generic name and multiple brand names in the "Pocket Pharmacopeia™" provided for each PERC.

17) Lipid Screening: Dichotomous variable ("Yes/No") indicating whether or not the subject received at least one (1) screening blood test for hyperlipidemia (as defined in Item 16) during the study period from 1/01/2001 to 12/31/2003. Most often, but not exclusively, found in the laboratory results section or the clinic notes.

17a) Lipid Screening Date: Earliest date, between 1/01/2001 and 12/31/2003, that a subject received a screening blood test for hyperlipidemia, as recorded in the medical record. Only recorded if applicable.

18) Pap: Dichotomous variable ("Yes/No") indicating whether or not the subject had at least one (1) screening Pap test during the study period from 1/01/2001 to 12/31/2003.

- Most often, but not exclusively, in the laboratory results section.
- May be recorded as "Pap", "Pap smear", "Papanicoloau test", or "Cervical Cytology".
- Only recorded for females.

18a) Pap Date: Earliest date, between 1/01/2001 and 12/31/2003, that the subject had a Pap test, as recorded in the medical record. Only recorded if applicable.

19) Fecal Occult Blood Testing (FOBT): Dichotomous variable ("Yes/No") indicating whether or not the subject had a "three card" FOBT at least one (1) time during the study period from 1/01/2001 to 12/31/2003.

- This screening test for colorectal cancer uses a card with a reagent that reacts with unseen ("occult") blood contained within a small sample of stool.
- The cards are known as "hemoccult" or "guiaic" cards, and the testing is sometimes referred to as "hemoccult" or "guiaic" testing.

- For this study, "FOBT" is ONLY considered to be those cases in which the patient was sent home from the clinic with a set of AT LEAST three (3) of these cards to use at home on three different occasions. The patient brings the cards back to the clinic for processing.
- It is common for clinicians to use only one (1) of these cards to check for occult blood in the course of a routine physical exam. These cases DO NOT count as "FOBT" for this study.

19a) Fecal Occult Blood Testing (FOBT) Date: Date or dates, during the study period from 1/01/2001 to 12/31/2003, that a subject had an FOBT. Enter the date that the final card in a set is recorded. Only recorded if applicable. If subject had multiple episodes of FOBT (as defined in Item 19) during the study period from 1/01/2001 to 12/31/2003, the date (as described above) of each episode will be recorded separately.

19b) FOBT Screening: Dichotomous variable ("Yes/No") indicating, for each episode of FOBT, whether or not the episode was for the purpose of routine screening.
- Generally, FOBT will used to screen in asymptomatic patients without signs or symptoms. In such a case, the response to this item is "Yes"
- Occasionally, FOBT might be used for "diagnostic testing" for the evaluation of a patient with signs and/or symptoms such as rectal bleeding. In such a case, the response to this item is "No".

20) Flexible Sigmoidoscopy: Dichotomous variable ("Yes/No") indicating whether or not the subject received flexible sigmoidoscopy at least one (1) time during the study period from 1/01/2001 to 12/31/2003. Commonly (but not exclusively) recorded in the clinic notes, or in consultant's reports.

20a) Flexible Sigmoidoscopy Date: Date or dates, during the study period from 1/01/2001 to 12/31/20034, that a subject received flexible sigmoidoscopy. Only recorded if applicable.

20b) Flexible Sigmoidoscopy Screening: Dichotomous variable ("Yes/No") indicating, for each episode of flexible sigmoidoscopy, whether or not the episode was for the purpose of routine screening.
- Flexible Sigmoidoscopy is often used to screen asymptomatic patients without signs or symptoms. In such a case, the response to this item is "Yes".
- Flexible Sigmoidoscopy might also be used for "diagnostic testing" for the evaluation of a patient with signs and/or symptoms such as rectal bleeding. In such a case, the response to this item is "No".

21) Colonoscopy: Dichotomous variable ("Yes/No") indicating whether or not the subject received colonoscopy at least one (1) time during the study period from 1/01/2001 to 12/31/2003. The procedure is performed by primary care physicians (including some in this study), but is more commonly performed by specialists.

For this reason, it is commonly (but not exclusively) recorded in consultant's reports.

21a) Colonoscopy Date: Date or dates, during the study period from 1/01/2001 to 12/31/2003, that a subject received colonoscopy, as recorded in the medical record. Only recorded if applicable.

21b) Colonoscopy Screening: Dichotomous variable ("Yes/No") indicating, for each episode of colonoscopy, whether or not the episode was for the purpose of routine screening.

- Colonoscopy is often used to screen asymptomatic patients without signs or symptoms. In such a case, the response to this item is "Yes".
- Colonoscopy might also be used for "diagnostic testing" for the evaluation of a patient with signs and/or symptoms such as rectal bleeding. In such a case, the response to this item is "No".

22) Substance Abuse: Dichotomous variable ("Yes/No") indicating whether or not the subject has a past or current history of substance abuse, as recorded in the medical record. The definition includes the use of alcohol, illegal drugs or prescription drugs.

22a) Substance Abuse Date: Date that "Substance Abuse" was first recorded in the medical record, if applicable.

23) Discharge or Discontinuation from clinic: Dichotomous variable ("Yes/No") indicating whether or not the subject formally discontinued care at the clinic on or before 12/31/2003.

- Only recorded if applicable, and if formally noted in the medical record.
- It is not assumed that any specific period of time without a clinic visit constitutes discontinuation of care.

23a) Discontinued Date: If applicable, the date that the subject formally discontinued receiving care at the study clinic, as recorded in the medical record.

24) Record of Subject's Death: Dichotomous variable ("Yes/No") indicating whether or not the subject died on or before 12/31/2003. Only recorded if applicable, and if formally noted in the medical record.

24a) Date of Death: Date that the subject died, if applicable.

APPENDIX 8: LIST OF PAIN DIAGNOSES AND CODES

CONDITION	CODE
Arthritis	716.9
Central Pain Syndromes (after stroke)	806.0
Chronic Pain NOS (Not Otherwise Specified)	307.8
Degenerative Joint Disease (DJD)	716.9
Fibromyalgia Syndrome	307.8
Head Injury (i.e., chronic pain after head injury)	959.0
Headaches (Chronic)	784.0
Migraine	346.0
Myofascial Pain Syndrome	307.8
Neuropathy	356.0
Peripheral Neuropathy	356.0
Postherpetic Neuralgia	053.1
Radiculopathy (cervical, lumbar, or thoracic)	722.6
Sickle Cell Anemia	282.6
Spinal Cord Injury	952.0
Spinal Disorder (e.g., disc disease, facet arthropathy)	722.6
Stroke	436.0
OTHER	999.9

APPENDIX 9: ANATOMIC SITES AND CODES

SITE	CODE
Abdomen	12
Back	23
Chest (chronic)	34
Face	45
Groin	56
Head	67
Hip	78
Joint(s)	89
Limbs (arm, legs, hands, feet)	14
Neck and/or shoulders	26
Pelvis	37
OTHER	99

APPENDIX 10: LIST OF CHRONIC COMORBIDITIES AND CODES

CONDITION	CODE
Alzheimer's Disease	331.0
Angina	413.9
Anxiety Disorder	300.0
Arthritis	716.9
Arrythmia	427.9
Asthma	493.9
Atrial Fibrillation (AF)	427.9
Bipolar Disorder	296.7
Bleeding Disorder	289.9
Blood Pressure (Elevated)	401.0
Cancer (Ca)	199.1
Cirrhosis of Liver	571.0
Congestive Heart Disease/Congestive Heart Failure (CHF)	428.0
Coronary Artery Disease/Coronary Heart Disease (CAD/CHD)	414.0
Cholesterol (Elevated)	272.0
Chronic Liver Disease	571.0
Chronic Renal Failure (CRF)	593.9
Chronic Obstructive Pulmonary Disease (COPD)	493.2
Degenerative Joint Disease (DJD)	716.9
Dementia	331.0
Depression	311.0
Diabetes (DM) (Type 1 or Type 2)	648.0
Dysrythmia	427.9
Eczema	692.0
Emphysema	493.2
Epilepsy	345.0
Gastritis	535.5
Gastric Ulcer	535.5
Gastroesophageal Reflux Disease (GERD)	535.5
Hepatitis	070.0
HIV/AIDS	042.0
Hypercholesterolemia	272.0
Hyperlipidemia	272.0
Hypertension (HTN)	401.0
Hyperthyroidism	240.0
Hypothyroidism	240.0
Ischemic Heart Disease	414.0
Lipid Disorder	272.0
Manic Depression	296.7
Migraine Headaches	346.0
Multiple Sclerosis (MS)	340.0
Myocardial Infarction (MI)	414.0
Osteoporosis	733.0

APPENDIX 10: LIST OF CHRONIC COMORBIDITIES AND CODE

CONDITION	CODE
Parkinson's Disease	332.0
Peptic Ulcer Disase (PUD)	535.5
Seizure Disorder	345.0
Schizophrenia	295.9
Sleep Apnea	780.0
Sleep Disorder	780.0
Stroke (History of)	436.0
Thyroid Disease	240.0
Tuberculosis	010.0
OTHER	999.9