THE IMPACT OF THE PRACTITIONER MANAGED PRESCRIPTION DRUG PLAN ON HEALTH SERVICE UTILIZATION FOR OREGON HEALTH PLAN FEE- FOR-SERVICE LONG-ACTING OPIOID USERS WITH NON-CANCER PAIN

by

Natalie R. Jacuzzi

A THESIS

Presented to the Department of Public Health and Preventive Medicine

and the Oregon Health and Science University

School of Medicine

in partial fulfillment of

the requirements for the degree of

Master of Public Health

June 2007

School of Medicine
Oregon Health & Science University

CERTIFICATE OF APPROVAL

This is to certify that the Master's thesis of

Natalie Jacuzzi

has been approved

[redacted]
Mentor/Advisor

[redacted]
Member

[redacted]
Member

TABLE OF CONTENTS Page #

Acknowledgements

The process of completing this project has been challenging and very rewarding. I am very thankful for the considerable support I received from my advisor and mentor Dr. K. John McConnell. I feel privileged to have worked with such a successful and intelligent researcher this early in my career. I will confidently attack my next challenge because of his enthusiasm for my project and confidence in my abilities. I would also like to extend my gratitude to Dr. Roger Chou for his clinical perspective and Dr. Rochelle Fu for her statistical expertise. Thank you for steering me through a very complex project. I would also like to thank Dr. Daniel Hartung for allowing me to elaborate on his recently published work and for acting as my Medicaid guide. Finally, I would like to thank George Wu, my friend and partner, for his continual support through this very busy year.

Abstract

The purpose of this study was to evaluate the impact of changes in prescription practices related to Oregon's Practitioner Managed Prescription Drug Plan (PMPDP) on emergency department (ED) visits and hospitalizations for persons receiving long-acting opioid analgesics for non-cancer pain. Pharmacy and medical reimbursements claims from Oregon's Medicaid fee-for-service were used to investigate the impacts of this policy change. We established an open-cohort of continuous long-acting opioid users treated for non-cancer pain during the year prior to implementation of the PMPDP prescription practices guidelines. The cohort was separated into two groups: switchers and non-switchers. Switchers were defined as those persons who received an opioid not listed on the preferred drug list prior to policy implementation and who switched to an opioid listed on the formulary after policy implementation. Subgroups were defined by time period of switch. Non-switchers were defined as persons who received opioid prescriptions prior to policy implementation and were not switched to an opioid listed on the formulary after policy implementation. For the year period preceding PMPDP policy implementation and the year following its prohibition, ED visits and hospitalizations were quantified and changes in service use were compared. A difference-in-differences analysis was performed between defined time periods to assess changes associated with the policy. Sensitivity analyses were conducted for the subgroups and aggregate analyses were conducted for all opioid users combined. Results indicate that ED visits and hospitalizations were not different in individuals subject to prescription changes due to the PMPDP policy compared to persons not affected by the formulary.

Introduction

Research Question

How did changes in prescription practices related to Oregon's Practitioner Managed Prescription Managed Drug Plan (PMPDP) differentially impact service utilization for patients receiving long-acting opioids analgesics for non-cancer pain who were subject to prescription changes compared to individuals not affected by the policy?

Specific Aims

The medical and pharmacy reimbursement claims dataset from the Oregon fee-for-service Medicaid program were utilized to investigate the impacts of this policy change. The following specific aims were addressed:

1. We established an open-cohort of long-acting opioid users treated for non-cancer pain for the year prior to implementation of the PMPDP. This cohort was followed until 1-year after active enforcement of policy was prohibited. Cohort was divided into two groups: switchers and non-switchers.

2. For the year period preceding PMPDP policy implementation and the year following its prohibition, we quantified and compared differences in health service utilization (ED visits, hospitalizations) and opioid toxicity.

3. We performed a difference-in-differences analysis between defined time periods to quantify changes associated with the policy change. Separate analyses were conducted for the subgroups and aggregate analyses were conducted for all opioid users combined.

Hypotheses:

2-1 Overall rates of ED utilization and hospitalizations would increase following policy implementation relative to the proceeding 1-year period.

3-1 Changes for ED utilization and hospitalizations would be greater in individuals subject to prescription changes due to restrictive drug formulary after policy implementation than persons not affected by the policy change.

Background and Significance

Medicaid provides prescription drugs for persons whose income and resources are insufficient to pay for their care. However, spending increases for state Medicaid programs appear to be unsustainable. Prescription drug costs have increased by approximately 18 percent per year since 1997 and national expenditures exceeded $20 billion dollars in 2000.[1] Rising health care costs and federal budgetary restraints have necessitated the implementation of cost-containment policies that specifically target this drug benefit. Enforcement of preferred drug lists (PDLs) have been utilized to control costs in multiple states. PDLs influence the prescription of less expensive drugs in the face of costly, equally beneficial alternatives. Presently, there is not consensus on the magnitude of risk associated with these interventions.

Oregon's approach to a PDL was an evidence-based Practitioner Managed Prescription Drug Plan (PMPDP).[2] The PMPDP used a systematic, transparent, and evidence-based approach to make the preferred drug selections which were briefly enforced with prior authorization restrictions in the OHP fee-for-service (FFS) population. Market share trends indicated that the policy effectively increased the use of

preferred agents and decreased total opioids dispensed, translating into reduced costs to the state.[3] Enforcement of the PMPDP was ultimately revoked by the Oregon state legislature due to pharmaceutical lobbying pressure and public reaction to increasing restrictions in a Medicaid population.

Legislative reversal of the policy was rooted in insecurities over the effect a decrease in prescriptions for non-cancer pain could have in this vulnerable population. Evaluation of health utilization changes associated with implementation of the PMPDP had not been assessed at the time of policy removal. It was thought that a decrease in opioids dispensed could have resulted in an overall reduction in appropriate pain management and associated decrease in health status for this population. Evaluation of health utilization changes associated with the implementation of this cost-containment policy is required to assess the necessity of its prohibition.

PMPDP List Development Process

In 1994, Oregon enacted the Oregon Health Plan (OHP) to cover persons eligible for Medicaid and other uninsured residents. Enrollment and utilization exceeded initial budgetary projections. Prescription drug spending accounted for 62% of the increase in OHP costs and 26.5 % of the total OHP budget.[4] Medicaid fee-for-service (FFS) spending threatened the viability of the program and the prescription drug benefit was the focus of Oregon's Medicaid cost containment efforts.[5]

In August 2001, Oregon enacted Senate Bill (SB) 819 which mandated the development of the PMPDP FFS Medicaid Program.[6] Legislation called for the PMPDP to be created by "considering first the effectiveness of a drug and second its relative

cost."[7] The Oregon Department of Human Services (DHS) adopted the administrative rule OAR 410-121-0030(2) (2003) to establish which prescription drugs to include on the PDL. The rule gave the Health Resources Commission (HRC) the authority to determine the most effective drug within a given class.

The Evidence Based Practice Center (EPC) was contracted by HRC to conduct the review. The EPC found insufficient evidence to determine that any long-acting opioid was safer or more effective.[8] Therefore, the selections for the long-acting opioid PDL were determined by price based on a systematic process outlined in 410-121-0030(2).[9] Drugs selected for the formulary by the HRC were the following: morphine sulfate long-acting (generic, Kadian, Oramorph SR), methadone(generic), and levorphanol (generic).[10] Some have considered more restrictive than other comparable state Medicaid PDLs.[11]

Implementation

The PMPDP was initially implemented with a voluntary policy. Prescribers could request non-preferred drugs by indicating "dispense as written" (DAW) on the prescription blank. Long-acting opioids and proton pump inhibitors were rolled out in August and statins and NSAIDS in September of 2002. Although practitioners were made aware of the PMPDP, they were not required to comply. Fiscal targets were not met with this voluntary program. In order to change prescribing towards the use of less-expensive drugs on the PMPDP, the state authorized a more rigid enforcement mechanism in May of 2003 requiring prescribers to contact the state's pharmacy benefit manager to receive an educational message about the evidence-based drug review prior to approval. Because

this policy did not require clinicians to submit clinical justification for prescribing the drug in common practice in other commercial and public health plans, it has been termed a "soft" prior authorization. After enforcement of the PMPDP, pharmacy costs decreased 9.1 and 17.7 percent after implementation of the DAW and soft PA policies for all drug classes subjected to the PMPDP, translating into an estimated $1,727, 392 and $2,223,300 actual savings to the state during these periods.[12]

Although this decision complied with the PMPDP, the policy disregarded the 1990 Omnibus Budget Reconciliation Act when the PDL became authorized to enforce prior authorization restrictions. According to this act, Medicaid programs must guarantee that drugs approved by the FDA will be made available unless they are specifically put on prior authorization status for justifiable therapeutic reasons. Drug excluded from the formulary must be shown to "not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcome of such treatment for such population over other drugs included in the formulary and there is written explanation for the basis of exclusion." [13]

Policy Prohibition

In 2003, legislation was passed that prohibited active enforcement of the PA.[14] HB 3624 forced the state to remove the PA requirement in November 2003. Immediate increases in costs were observed after the soft PA was repealed. Legislation was passed in reaction to claims from multiple stakeholders that the PA process restricted beneficiary access to necessary drugs and did not comply with initial PMPDP language. Specifically, Purdue Pharma and Purdue Frederick filed a lawsuit in Oregon state court to contend the

decision to not include two opioids manufactured by Purdue, Pharma-Oxycontin and MsContin, on the formulary.[15] These companies sustained substantial market losses as a result of the new drug formulary and their lawsuit was interpreted as a move to protect their business interests.

Purdue sought judicial review of the DHS administrative rule that lists drugs that are approved for reimbursement by the state for OHP beneficiaries. Petitioners "contended that the amended rule was adopted without compliance with applicable rulemaking procedures and exceeded the statuary authority of DHS."[16] Petitioners claimed that creating a PDL without sufficient evidence of comparative evidence was unlawful. Their claim was based largely on the statement from the EPC that "there is insufficient evidence to draw any conclusions about the comparative effectiveness of long-acting opioids."[17] The court of appeals concluded from this statement that "all [opioids] were of equal effectiveness" and determined the commission's decision in compliance with the administrative rules. The Court of Appeals, Landua, P.J. rejected the petitioner's challenge to the amended rule and declared that OAR 410-121-0030 was valid April 20, 2005. Petition for review was denied August 9, 2005.

Medicaid OHP FFS Population

The OHP FFS population is a pool of high-risk low-income beneficiaries not eligible for managed care coverage including the disabled, elderly, person residing in state institutions and those with certain complex medical conditions.[18] FFS beneficiaries are sicker than other Medicaid beneficiaries. As a result they were covered separately because the state was unable to contract them out to managed care plans. The elderly and

disabled represent 27 percent of Medicaid beneficiaries nationally.[19] Prior to January 1, 2006, the Medicaid prescription drug benefit was the only prescription drug coverage for Medicare enrollees. In the absence of a Medicare drug benefit, qualified elderly persons received their drug coverage through Medicaid.[20] These dual eligible beneficiaries made up a large proportion of the FFS pool.

The potential impact of restricting access to necessary medications on health and cost in this already vulnerable population has not been addressed. Previous studies suggest that limitations on Medicaid prescriptions for chronic pain in vulnerable populations can result in a 35% reduction in the use of clinically essential drugs and an increase in the use of health services related to a reduction in pain management that exceeded the costs of discontinued drugs.[21] Overall, there is insufficient research to assess the impact of restrictive drug policies in Medicaid populations.

Long-acting Opioids for Chronic Non-Cancer Pain

Chronic pain conditions are highly prevalent. Approximately twenty percent of the adult population is currently diagnosed with a chronic pain condition.[22] These conditions include: osteoarthritis, peripheral neuropathies, fibromyalgia, and low back pain. Opioids are commonly prescribed to manage non-cancer pain in the general population.[23] Opioids are a class of medications that act on common receptors and are natural derivatives of morphine.[24] They are the most potent medications available for the treatment of non-cancer pain. Specifically, opioids are classified as long or short based on their metabolic half-lives. Long-acting opioids have increased half-lives with longer

duration of analgesic effects, and are considered more appropriate for sufferers of chronic pain. [25]

Prescription changes of long-acting opioids pose significant risks for chronic non-cancer pain management. Opioid therapy can fail to be effective and well tolerated if the choice of opioid is inappropriate due to prescribing restrictions. Opioids as a drug class elicit heterogeneous patient responses and side effects. Studies have demonstrated that targeting this drug class with cost-containment restrictions is associated with lower quality care.[26] Opioid prescription choices based on compliance with a drug formulary without regard to individual patient factors could adversely affect health status and cause shifts to more costly types of care.[27]

The FFS population was hypothesized to be more sensitive to drug use limitation than the general population. Prescription changes were hypothesized to elicit adverse effects for three primary reasons: (1) physiologic variation in organ system function increases with disease severity; (2) poly-pharmacy is more common in this population due to high co-morbidity of complex medical conditions; and (3) prescription restrictions are expected to disproportionately impact this population due to decreased access. The use of multiple medications is associated with an increased risk for adverse event with opioid prescription changes. Formulary restrictions add one more barrier to receiving medications in a population that already suffers from decreased ability to advocate for their health.[28]

Limiting access to medications through stricter drug formularies has been associated with increased incidence of adverse health events and higher utilization of costly health services. Health outcomes associated with drug formulary restrictions

include: mortality, opioid toxicity, constipation, nausea, and decreased pain management. Health service utilization increases associated with drug formulary restrictions include: office visits, emergency department encounters, hospitalizations, and increased usage of other classes of drugs.[29]

Indication for Study

Market share trends indicated that soft PA policy effectively increased the use of preferred agents and decreased total opioids dispensed.[30] Health outcomes related to the observed decrease in utilization of long-opioid analgesics have not been previously assessed. As a result of PMPDP policy implementation, it was expected that higher incidences of adverse health outcomes and associated increased utilization of health services would be seen in FFS beneficiaries using opioids for non-cancer pain. Specifically, it was hypothesized that persons who switched opioids as a result of the policy would have higher utilization rates in comparison to individuals not affected by the policy. Moreover, it was expected that the effects would be modified by age, indication for drug therapy, disability status, disease severity and number of concurrent medications. The purpose of this study was to assess the unintended consequences associated with a restrictive drug formulary for patients with chronic non-cancer pain.

Methods

Study Design and Data Sources

This study employed a retrospective cohort design utilizing administrative claims from the State of Oregon Medicaid Program. Data was abstracted from pharmacy and

medical encounter claims from the Oregon FFS Medicaid database. Pharmacy claims are compiled electronically at the point of prescription fill. Medicaid claims are submitted both electronically and in paper forms.

Cohort assignments and outcome measures were based on algorithms generated from eligibility criteria and International Classification of Diseases, 9th edition (ICD-9) codes abstracted from Medicaid pharmacy claims and Medicaid medical claims respectively.

Time Periods

Time periods for the analyses were specified as follows: 1 year prior to policy implementation (August 2001-August 2002), during voluntary practitioner enforced PMPDP (DAW) (September 2002-May 2003), "soft" prior authorization (PA) (June 2003-October 2003), and 1 year post- policy prohibition (November 2003-November 2004). The DAW and PA periods were used to determine time of switch for cohort assignments.

Study Population

We included beneficiaries of the OHP FFS program to investigate the impacts of the PMPDP policy changes. Beneficiaries in the OHP program are qualified based on low income and significant financial need.

Selection of individuals for analyses required multiple steps. Initially, we selected adult long-acting opioid users during the year prior to implementation of the PMPDP prescription practice guidelines and who were continuously enrolled for the

entire study period (August 2001- November 2004). Because the purpose of this study was to understand the effects of prescribing changes on persons using opioids for chronic pain, persons with a diagnosis of cancer pain were excluded from the analyses. The indication for opioid usage in cancer patients is acute pain associated with the progression of their illness.

Second, we excluded persons diagnosed with an opioid abuse condition (opioid dependence or opioid abuse) from analyses. Substance abuse by itself is an indicator for increased health utilization. Persons diagnosed with a substance abuse condition were excluded to minimize the potential confounding effects of these conditions.

A third exclusion was based on a 2003 policy change that divided OHP members into two groups: Standard and Plus. OHP Plus was offered to all federally mandated Medicaid eligibility groups and maintained the same level of benefits. OHP standard covered the state's Medicaid expansion population for the working poor and offered reduced benefits, higher co-payments, and higher premiums. FFS beneficiaries who were part of this "Standard" benefit package and thus subject to coverage changes were excluded due to potential confounding from this policy change.

Fourth, included beneficiaries must have continuously filled prescriptions for the 1-year period preceding the policy change (August 1 2001 to August 31 2002). Continuous fill was defined as one prescription fill per quarter for any long-acting opioid during the pre-policy period. Individuals that discontinued use during the entire active policy period, DAW stage (September 1 2002 to May 31 2003) and the Soft PA stage (June 1 2003 to October 31 2003) were excluded. Although discontinuation is an

accepted adverse outcome of a prohibitory policy change, sample size proved to be inadequate for analysis of this group.

Finally, two groups were defined to create a comparison between persons affected by the policy change and persons not affected by the policy change. *Switchers* were defined as those persons who continuously filled prescriptions for any long-acting opioid not on the PMPDP formulary during the year preceding the voluntary practitioner enforced formulary and were switched to a long-acting opioid on the PMPDP formulary (long-acting morphine (generic), Oramorph SR, Kadian, methadone (generic), or levorphanol (generic)) during one of the two policy periods. Time of switch, DAW or Soft-PA period, was specified for sensitivity analyses. *Non-switchers* were defined as those persons who continuously filled prescriptions for any long-acting opioid during the year preceding the voluntary practitioner enforced formulary and who either continued to have these medications dispensed or switched to an opioid not on the PMPDP preferred list.

Outcome Variables

We had two primary outcome variables: emergency department (ED) utilization and hospitalizations. ED services that did not lead to an admission were identified by procedure codes and revenue center codes. An ED visit that billed any Current Procedural Terminology (CPT) code of 99281-99285 or a visit that resulted in advanced life support (CPT code 99288) was considered an ED encounter. ED visits that generated a revenue center code of 45x or 981 were also included. Hospitalizations were identified using the diagnosis-related group (DRG) coding system. Claims submitted with a DRG payment

were considered a hospitalization. The number of ED encounters and hospitalizations for each study period was quantified for analyses.

The occurrence of opioid toxicity was described in preliminary analyses. Medical encounters with a diagnosis code of 9650X were considered opioid toxicity. While opioid toxicity is thought to be a serious adverse event associated with opioid prescription changes, final analyses were not done on this variable due to a low event rate.

Predictor Variables

In addition to cohort assignment, the following baseline demographic variables were quantified for analysis: age, race, and sex, as defined by the first recorded medical encounter form. The presence of the following origin of pain indicators was included: osteoarthritis, low back pain, peripheral nervous system disorders, and fibromylagia, defined by ICD codes abstracted from medical records pain diagnoses. These diagnoses are the most common chronic pain diagnoses for this population and were expected to identify a majority of appropriate persons suffering from non-cancer chronic pain.

We included a disease severity indicator, the Charlson Co-morbidity Index. The index score serves as a proxy measure for mortality prediction based on prevalence of co-morbidity conditions and is an accepted indicator for health status in observational studies.[31 32] It has been successfully applied to administrative claims databases.[33 34] Diagnosis codes and weights presented in table 1 were used to calculate each beneficiaries Charlson index during the study period.

Table1: Adapted Charslon Co-morbidity Index

Field	Condition	ICD-9-CM Code	Weight
MI	MI	410,411,412	1
CHF	CHF	428	1
PVD	Peripheral Vascular	4439, 4402	1
DEM	Dementia	290	1
CVD	Cerebrovascular	430-438	1
COPD	Chronic lung disease	490-496, 500-505, 506.4	1
DM	Dm	2500, 250.7	1
RHEUM	Rheumatologic dz	714.0-714.2, 7100, 710.1, 710.4, 714.81, 725	1
PUD	Peptic ulcer dz	531-534	1
MLD_LVR_DZ	Mild liver disease	571.2, 571.3, 571.4, 571.5, 571.6	1
SVR_LVR_DZ	Severe liver disease	572.2-572.4, 572.8	2
H_P_PLEGIA	Hemiplegia/paraplegia	344.1, 342	2
CRF	Renal Disease	582, 583, 585, 586, 588	2
DM_COMP	Dm with complications	250.4-250.6	2
CA	Cancer	140-165, 166-169, 174-195.8, 200-208.9	2
CA_MTS	Cancer with mets	196-198	6
HIV	Human Immunodeficiency Virus	042	6

A poly-pharmacy variable was constructed to estimate the number of unique medications a beneficiary was exposed to that could potentially contribute to adverse health events. The following drug classes known to have pharmacodynamic interactions with long-acting opioids were specified and include: benzodiazepines (e.g. lorazepam), skeletal muscle relaxants (e.g. carisprodol), barbiturates (e.g. Phenobarbital), sedative hypnotics (e.g. zolpidem), and short-acting narcotics (e.g. hydrocodone/ acetaminophen). Relevant drugs were indicated by their National Drug Code. Poly-pharmacy was quantified as number of unique drugs used per person during the pre-policy period.

Statistical Analysis

A "difference-in-differences" approach was utilized to assess the changes in ED visits and hospitalizations before and after the OHP PMPDP policy change. In this approach, the first "difference" refers to health service event changes in those affected (switchers) 1 year prior to policy implementation (August 2001-August 2002) and 1 year post- policy prohibition (November 2003-November 2004). The second "difference" was achieved through a comparison group (non-switchers) that is observed during the same period but was not subject to prescription changes as a result of the policy change. This group provided baseline data on any secular changes that could be driving changes in our outcome that are not related to the policy change. Remaining significant differences are considered effects of the policy change.

Association between cohort group (switcher vs, non-switcher) and change in emergency room utilization and hospitalizations before the OHP PMPDP policy change and after its prohibition were assessed by using a matching estimators analysis and fitting generalized estimating equations (GEE) population-averaged negative binomial regression models. Treatment effect refers to the causal effect of the binary variable (switcher, non-switcher) on health service utilization (ED utilization and hospitalizations). The following baseline variables were included for both preliminary estimations: age, race. disability status, long-term care, osteoarthritis, low back pain, peripheral neuropathies, fibromyalgia, poly-pharmacy, and co-morbidity index. Variables were selected based on a prior knowledge of clinically significant predictors of health service utilization.

The ***match*** command in Stata version 9.2 (Stata Corp., College Station, TX) was utilized to match estimators for average treatment effects.[35] The average treatment effect for the treated (ATT) was estimated with and without a bias correction. The bias-corrected matching estimator specified the same set of covariates as the matching. Three different treatment groups were analyzed: switchers (overall), switcher (DAW), and switchers (soft-PA). A sensitivity analysis was conducted; estimations were calculated using one-to-one matching as well as one-to-five matching as part of a sensitivity analysis. The Mahalanobis metric was chosen to measure the difference between two vectors of covariates. The variance was estimated allowing for heteroskedasticity, assuming that the variance was not constant for both treatment groups and all covariates. The number of matches used for the variance estimation was consistent with the number of matches used to estimate the treatment.

The ***xtnbreg*** command in STATA version 9.2 (Stata Corp., College Station, TX) was utilized to fit a GEE negative binomial model with an exchangeable correlation matrix. The GEE negative binomial model was used to account for over dispersion in the data and adjust for within subject correlation.[36] As part of our sensitivity analysis, we also examined a negative binomial random effects model. The results of the GEE and random effects models were qualitatively consistent. We present the GEE results here.

Based on a prior knowledge of clinically significant predictors of ED utilization and hospitalizations, all predictor variables aforementioned were included in preliminary multiple regression models. Significance of predictor variables was based on the likelihood ratio test. Level of significance was set at $p < .05$. Osteoarthritis, peripheral neuropathies, and fibromyalgia were not significant in preliminary models for ED

utilization and were excluded from the final model. Osteoarthritis and peripheral neuropathies variables were excluded from the regression estimate of hospitalizations. The model goodness of fit was assessed using the deviance statistics.

Results of GEE negative binomial models were used to interpret the significance of baseline variables. The policy effect, the interaction term, is commonly interpreted incorrectly in non-linear models.[37] Matching estimators provides an easily interpretable estimate of the policy effect and was used for interpretation.

Sensitivity analyses for poly-pharmacy and co-morbidity were conducted to investigate the impact of extreme outliers, excluding persons with greater than 50 concurrent medications or persons with an index score of greater than 5. Results were not qualitatively different from full sample models. Therefore, outliers were not excluded in interpreted models.

Sensitivity analyses of DAW and Soft-PA switchers did not indicate significant differences in outcomes based on assignment. Therefore, all analyses reported hereafter reflect a comparison between switchers and non-switchers.

Results

Tables 2 and 3 compare the descriptive statistics of individual characteristics for persons affected by the policy change and persons not affected by the policy change, switchers and non-switchers respectively. Descriptive statistics indicate similar characteristics between groups. The only statistically significant difference between groups was for low back pain, as indicated by the Pearson chi-square test. A greater proportion of switchers were diagnosed with low back pain than non-switchers (p=.001)

Table 2: Continuous Predictor Variables Descriptive Statistics by Group

	Switchers, n=140			Non-switchers, n=907			Difference of the Means	
Variable	Mean	Std	Range	Mean	Std	Range	Score	Pr >|t|
Age	57.35	15.99	24-92	57.83	16.54	19-99	0.4629	.6437
Poly-pharmacy	18.96	16.06	0-94	20.77	17.04	0-150	1.814	0.067
Co-morbidity	1.32	1.59	0-10	1.39	1.76	0-13	-.234	.8149

Note: Differences of the means for age is a two-sample t-test with unequal variances,Welch.
Difference of the means for poly-pharmacy and co-morbidity is a Wilcoxon rank-sum Mann-Whitney

Table 3: Categorical Predictor Variable Descriptive Statistics by Group

	Switchers, n= 140		Non-switchers, n= 807		Difference of the Mean	
Variable	Frequency	Percent	Frequency	Percent	Pearson Chi- square	P-value
Sex						
Male	35	25.00	233	28.87	0.8817	0.348
Female	105	75.00	574	71.13		
Race						
Non-white	9	6.43	59	7.31	.0.1394	0.709
white	131	93.57	748	92.69		
Disability Status						
Yes	69	49.29	336	41.64	2.8525	0.091
No	71	50.71	471	58.36		
Language Spoken						
Non-English	1	0.71	4	50	NA	NA
English	139	99.29	803	99.5		
Long term care						
Yes	34	24.29	250	30.98	2.5456	0.111
No	106	75.71	557	69.02		
Osteoarthritis						
Yes	44	31.43	232	28.75	0.4150	0.519
No	96	68.57	575	71.25		
Low Back Pain						
Yes	96	68.57	435	53.90	10.4210	0.001
No	44	31.43	372	46.01		
Peripheral Neuropathies						
Yes	36	25.71	173	21.44	1.2688	0.260
No	104	74.29	634	78.56		
Fibroroyalgia						
Yes	28	20.00	132	16.36	1.1277	0.288
No	112	80.00	675	83.64		

Table 4 displays simple statistics for outcomes by treatment group. Switchers and non-switchers had similar mean values for pre and post ED utilization [(1.22(SD 2.69) vs. 1.54 (SD 3.56) and (0.99 (SD 1.46) vs. 1.23 (SD 3.53)]. Switchers and non-switchers also had similar mean values for pre and post hospitalizations [(0.42 (SD 1.22), 0.44 (SD 0.97)) and (0.34 (SD 0.84) vs. 0.35 (SD 0.82)]. The pre and post differences were significant for both outcomes between groups. Mean ED visits for switchers significantly decreased in comparison to non-switchers (t=3.08, p=.001). Mean hospitalizations for switchers significantly decreased in comparison to non-switchers (t=2.58, p=.005).

Table 4: Simple Statistics for Outcomes by Treatment Group

	Switchers		Non-Switchers		Mean Difference (pre-post)	
Policy Period	**Mean**	**Std**	**Mean**	**Std**	**t-score**	**P-value**
ED_Pre_policy	1.22	2.69	1.54	3.56	3.08	0.001
ED_Post_policy	0.99	1.46	1.23	3.53		
Hosp_Pre_policy	0.42	1.22	0.44	0.97	2.58	0.005
Hosp Post Policy	0.34	0.84	0.35	0.82		

Matching Estimators

Estimates of average difference for ED utilization between switchers and non-switchers from matched analysis, reported in Table 7, suggest that the policy change did not have a differential effect on switchers. The bias corrected estimate (0.0678) indicates that the effect of the policy change on ED visits is not significantly different from zero (p= .836).

Table 5 reports the matching estimators for average treatment effects for hospitalizations. Estimates confirm that the policy change did not have a differential

effect on switchers. The bias corrected estimate (0.05338) indicates that the effect of the policy change on hospitalizations in not significantly different from zero (p=.624).

Table 5: Matching Estimators for Average Treatment Effects, Matching 1:1

SATT	Coef.	SE	Z	P>|z|	95% C.I.	
ED Utilization	-.1	.3273268	-0.31	.760	-.7415	.5415
Bias Corrected	.0678	.3273268	0.21	0.836	-.5737	.7094
Hospitalizations	-.0143	.10997	-0.13	0.897	-.2298	.2012
Bias Corrected	.05388	.10997	0.49	0.624	-.1616	.2694

The sensitivity analyses results displayed in Table 6 indicate that differential matching techniques were qualitatively consistent, indicating that the 1:1 matching estimations were efficient.

Table 6: Sensitivity Analysis, Matching 1:5

SATT	Coef.	SE	Z	P>|z|	95% C.I.	
ED Utilization	-.1057143	.1592623	-0.66	.507	-.4178627	.2064341
Bias Corrected	.0247305	.1592623	0.16	0.877	-.2874179	.3368789
Hospitalizations	-.1028571	.0729061	-1.41	0.158	-.2457506	.0400363
Bias Corrected	-.0149917	.0729061	-0.21	0.837	-.1578852	.1279017

Generalized Estimating Equation Negative Binomial Regression Models

Table 7 reports the GEE negative binomial regression model risk ratios with associated statistics for ED utilization. All of the following estimates of risk are stated as a part of the model, controlling for the other predictors. The following variables were determined to be significant predictors of ED utilization: sex ($p<.001$), low back pain ($p<.0001$), number of concurrent medications ($p<.0001$), and co-morbidity score ($p<.0001$). ED utilization rate by male is .66 times (RR=.66 (95% C.I., .55, .78)) the ED utilization rate by female. Diagnosis with low back pain is associates with a 62% increase in ED utilization rate (RR=1.62 (95% C.I., 1.38, 1.90)). Each additional concurrent medication increases the rate of ED utilization by a factor of 1.01 (RR= 1.01 (95% C.I., 1.009, 1.017)). Each additional co-morbidity index unit increases the rate or ED utilization by a factor of 1.24 (RR= 1.24 (95% C.I., 1.20, 1.29)).

Table 7: GEE Negative Binomial Regression Model for ED Utilization

Analysis of Parameter Estimates						
Parameter	RR	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Sex	.65617	.05786	.55202	.77997	-4.78	<0.0001
Race	1.0913	.15511	.82597	1.4418	0.61	0.539
Age	.98836	.00305	.98240	.99437	-3.79	<0.001
Disability Status	1.0806	.09091	.91636	1.2743	0.92	0.357
Long Term Care	.84148	0.0849	.69058	1.0254	-1.71	0.087
Low Back Pain	1.6220	.13217	1.3826	1.9029	5.94	<0.0001
Polypharmacy	1.0127	.00215	1.0085	1.0169	5.95	<0.0001
Comorbidity Score	1.2431	.0244	1.1962	1.2918	11.09	<0.0001
Policyperiod	.79091	.04340	.71027	.88071	-4.27	<0.0001
Switchers	.75814	.09827	.58805	.97743	-2.14	0.033
Switchers_Policyperiod	1.0450	.15426	.78243	1.3956	0.30	0.766

Table 8 reports the GEE negative binomial regression model risk ratios with associated statistics for hospitalizations. After controlling for all other variables in the model, the following variables were determined to be significant predictors of ED utilization: sex (p=.002), low back pain (p<.0001), fibromyalgia (p=.05) number of concurrent medications (p=.001), and co-morbidity score (p<.0001). Hospitalization rate for males is .69 times (RR= .69 (95% C.I., .55, .86)) the hospitalization rate for females. Disability status is associated with a 30% increase in hospitalizations (RR= 1.30 (95% C.I., 1.04, 1.63)). Diagnosis of low back pain is associated with a 47% increase in hospitalizations (RR=1.47 (95% C.I., 1.19, 1.82)). Each additional concurrent medication increases the rate of hospitalizations by a factor of 1.008 (RR=1.008(95% C.I., 1.003, 1.014)). Each additional index unit increases the rate of hospitalizations by a factor of 1.29 (RR= 1.29 (95% C.I., 1.23, 1.35)).

Table 8: GEE Negative Binomial Regression Model for Hospitalizations

Analysis Of Parameter Estimates						
Parameter	RR	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Sex	.68672	.08207	.54332	.86797	-3.14	0.002
Race	.91152	.17594	.62441	1.3307	-0.48	0.631
Age	.99987	.00410	.99187	1.0079	-0.03	0.974
Disability Status	1.3034	.14748	1.0442	1.6271	2.34	0.019
Long Term Care	1.0824	.13695	.84467	1.3870	0.63	0.531
Low Back Pain	1.4738	.15907	1.1928	1.8210	3.59	<0.001
Fibromyalgia	.76048	.10707	.57710	1.0021	-1.94	0.052
Polypharmacy	1.0087	.00274	1.0033	1.0141	3.20	0.001
Comorbidity Score	1.2862	.02976	1..2292	1.3459	10.88	<0.001
Switchers	.85226	.15209	.60072	1.2091	-0.90	0.370
Policyperiod	.79205	.06908	.66759	.93971	-2.67	0.008
Switchers_Policyperiod	1.0163	.23827	.64197	1.6092	0.07	0.945

Discussion

Market share trends indicated that the PMPDP effectively increased the use of preferred agents and decreased total opioids dispensed.[38] Our study results show that ED visits and hospitalizations were not different in individuals subject to prescription changes due to PMPDP policy implementation compared to persons not affected by the formulary. Findings suggest that policy restrictions did not increase health service utilization as a result of a reduction in pain management for patients with chronic, non-cancer pain. Moreover, our study implies that legislation prohibiting enforcement of the drug list in reaction to the pharmaceutical company's lawsuit was not evidence-based.

Strengths and Limitations

The validity of this finding is strengthened by the significance of multiple clinically relevant parameter estimates. For example, the number of concurrent medications and the disease status of a beneficiary significantly predicted ED utilization and hospitalizations. Since these variables are clinically known risk factors, our finding of significance demonstrates the sensitivity of our study design to detect differences in utilization based on operationally defined characteristics.

Generalizations of these findings to other Medicaid populations are supported by similarities between our cohort and the general OHP long-acting opioid user population. In a sample of approximately 14, 000 OHP beneficiaries, the mean age (55.7), percent female (63.7%), percent white (91.4%), and percent in long-term care (15.9%) were comparable to our study cohort with the exception of percent disabled (31.7%). These comparisons indicate that we formed a representative sample. However, our results

represent a restrictive sample of beneficiaries and generalizations should be cautioned by inherent limitations of retrospective cohort studies.

This policy change analysis is an observational study design and is complicated by factors not measured or accounted for in an administrative database. Comparison group specification and analysis methods were carefully chosen to minimize this bias. Specifically, a control was chosen within the Medicaid FFS population to reduce the amount of between subject variance. An alternative design could have designated a comparison group outside of the FFS population during the same time period. In addition, the difference-in-differences analysis was chosen because it is considered a valid quasi-experimental design to estimate intervention effects in non-randomized settings. Difference-in-differences analysis controls for secular trends in the outcome measure and quantifies change in response to an intervention in non-randomized settings.

A principal concern in the estimation of treatment effects is selection bias, switchers systematically differ from non-switchers for reasons other than group status.[39] The observational retrospective study design did not allow for control of all relevant factors and bias may exist from unobserved and uncontrolled differences between the treatment groups. For example, mental health status was not quantified and controlled for in the analysis. If degree of mental illness was related to cohort specification, this differential distribution of a relevant factor could have biased the results.

The Medicaid database may not be appropriate for answering the research question. The purpose of the study was to determine whether a reduction in pain management due to a restrictive drug formulary translated into increased health utilization. The Medicaid database is an administrative claims database and is potentially

biased for three reasons. First, outcomes are only included in the database if a utilized service was reimbursed by the states and do not necessarily account for all services rendered by a beneficiary and, therefore, represent a minimum level of utilization. Second, diagnosis misclassification bias is common in administrative claims databases. Medical diagnosis coding could be influenced by reimbursement incentives and may not reflect the true medical condition. Third, medical encounter and claims forms only allow for the development of proxy measures for changes in pain management. These outcomes lack specificity and interpretations of direct causality are not appropriate with this type of analysis. Moreover, the outcome measures available in an administrative database are markers for serious outcomes. ED utilization and hospitalizations are indirect and insensitive measures of decreased pain management.

To ensure validity, the study cohort was created with very restrictive inclusion and exclusion criteria. Although approximately 8, 000 FFS beneficiaries used long-acting opioids for non-cancer pain, our study cohort only included approximately 947 persons. This small sample size could have provided limited statistical power to detect a difference between insensitive outcomes such as hospitalizations and ED visits. However, point estimates were clinically irrelevant and increased sample size would have arguably not led to a different conclusion.

Future Research

Follow-up studies that included the incorporation of clinical outcomes would strengthen the interpretation of our results. Selecting a small sample of beneficiaries to create a detailed clinical picture would be a more appropriate design for addressing

fluctuations in pain management. Outcome measures such as number of provider visits per month, adherence to prescribed opioid regimen, and self-reported adverse effects and pain management would be necessary to more directly address the impact of formulary restrictions on patient-centered outcomes.

In our study, health utilization was predicted by factors such as disability status and specific pain diagnoses. The increased risk for ED visits and hospitalizations due to disability status warrants attention. Although, it is expected that this would be significant it pronounces an unmet need in this population. Future studies should address the additional access barriers disabled persons have that result in higher utilization rates of the ED and hospital.

Public Health Importance

Determining the implications of cost-containment policies in vulnerable Medicaid populations is pertinent for the current Oregon Medicaid debate and for future state and federal policy development. Due to increased costs in health care and a growing number of uninsured, cost containment policies will continue to be employed in the future. Understanding the magnitude of risks associated with these interventions is essential for prioritizing policies and improving population health. Public health professionals have a responsibility to create policies based on best evidence practices and to design policies that place the least harm on beneficiaries. Findings of these studies will be disseminated to state and federal officials, policy makers, and the academic community at large. We hope that our findings will be utilized to advise future policy

decisions and determine necessary areas of health outcome research that deserve attention.

References

[1] Kaiser Commission on Medicaid and the Uninsured. Medicaid: purchasing prescription drugs. Policy Brief (4025). 2002 [cited 16 October 2003]. Available from: http://www.kff.org/content/2002/20020213/4025a.pdf. (accessed 16 October 2007).
[2] Bernasek C, Mendelson D, Padrez C, Harrington C; The Health Strategies Consulting LLC. Oregon's Medicaid PDL: will an evidence based formulary with voluntary compliance set a precedent for Medicaid. In: Kaiser Commission of Medicaid for the Uninsured; 2004.
[3] Hartung D, Ketchum K, and Haxby D. An evaluation of Oregon's evidence-based Practitioner Managed Prescription Drug Plan. Health Affairs. 2006; 25(5): 1423-1432.
[4] Oregon Department of Human Services, Finance and Policy Analysis, Office of Rate Setting.
[5] Associated Press. State draws up first prescription drug list. Associated Press Newswire. 2002 June 15.
[6] Oregon House Bill 3624, ch 897, ξ 1-3. (2001).
[7] Oregon Senate Bill 819. ORS 414.330. (2001).
[8] Chou R, Clark E, Helfand M. Comparative efficacy and safety of long-acting opioids for chronic non-cancer pain: a systematic review. J Pain Symptom Manage. 2003 Nov; 26(5): 1026-48.
[9] Bernasek C. 2004.
[10] Oregon Senate Bill 819. OAR 410-121-0030(2). (2001).
[11] Bernasek C. Appendix G. 2004.
[12] Hartung D. 2006.
[13] Social Security Act ξ 1927 (d)(4)(E). (1991).
[14] Oregon House Bill 3624. (2003).
[15] Appleby J. Oregon's list of preferred drugs skips some big names. USA Today. 2002 October 10.
[16] Purdue Pharma L.P. and Purdue Frederick Company v, Oregon Department of Human Services. Court of Appeals of the State of Oregon. 199 Or App 199. (2005).
[17] 199 Or App 199 (2005).
[18] Bernasek C. 2004.
[19] Bruen B. Medicaid and prescription drugs: an overview. Kaiser Commission of Medicaid and the Uninsured; 2000 [cited 16 Oct 2006]. Available from: http://www.kff.org/content/2000/2202/mcaidandrx.pdf.
[20] Crowley J, Ashner D. Medicaid outpatient prescription drug benefits: findings from a national survey, 2003. Kaiser Commission on Medicaid and the Uninsured; 2003.
[21] Soumerai S. Benefits and risks of increasing restrictions on access to costly drugs in Medicaid. Health Affairs. 2004; 23(1):135-146.
[22] Joranson DE, Ryan KM, Gilson AM, Dahl JL. Trends in the medical use and abuse of opioid analgesics. JAMA. 2000; 283(13):1710-1714.
[23] Strumph M, Dertwinkel R, Wiebalck A, Bading B, Zenz M. Role of opioid analgesics in the treatment of non-cancer pain. CNS Drugs. 2000;14(2):147-155.
[24] Schug SA, Merry AF, Acland RH. Treatment principles for the use of opioids in pain of non-malignant origin. Drugs. 1991; 42(2):228-239.

[25] Julien, RM. A Primer of Drug Action. 9th ed. New York: Worth Publishers; 2001.
[26] Horn SD, Sharkey PD, Gassaway J. Managed care outcomes project: study design, baseline patient characteristics, and outcome measures. American Journal of Managed Care. 1996;2(3):237-247.
[27] Soumerai S. 2004.
[28] Horn SD, Sharkey PD, Tracy DM, Horn CE, James B, Goodwin F. Intended and unintended consequences of cost containment strategies: results from the managed care outcomes project. American Journal of Managed Care. 1996; 2(3): 253-264.
[29] Horn SD, Sharkey PD, Tracy DM, Horn CE, James B, Goodwin F. 1996
[30] Hartung D. 2006.
[31] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of Chronic Diseases. 1987;40:373-383.
[32] Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. Journal of Clinical Epidemiology. 1994; 47:1245-1251.
[33] Schneeweiss S, Seeger JD, Maclure M, Wang PS, Avron J, Glynn RJ. Performance of comorbidity scores to control for confounding in epidemiologic studies using claims data. American Journal of Clinical Epidemiology. 2001; 154: 854-864.
[34] Romano PS, Roos LL, Jollis JG. Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. Journal of Clinical Epidemiology. 1993;46: 1075-1079.
[35] Abadie A, Drukker D, Herr JL, Imbens GW. Implementing matching estimators for average treatment effects in Stata. The Stata Journal. 2001;1(1):1-18.
[36] Diggle PJ, Heagerty P, Liang K, Zeger SL. Analysis of longitudinal data, 2nd edition. New York: Oxford (2002).
[37] Chunrong A., Norton EC. Interaction Terms in Nonlinear Models. Triangle Health Economics Working Paper No. 2. 2001 July [cited 2007 June 18]. Available from: http://ssrn.com/abstract=303862
[38] Hartung D. 2006.
[39] Abadie A, Imbens G. Simple and bias corrected matching estimators. Tech rep., Department of Economics, UC Berkely. 2002 [cited 2007 May 17]. Available from: http://enlab.berkeley.edu/users/imbens/. Retrieved May 17, 2007.