2011

Case-Mix Adjustment of Adherence Based Pharmacy Quality Indicator Scores

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CASE-MIX ADJUSTMENT OF ADHERENCE BASED PHARMACY QUALITY INDICATOR SCORES

A Thesis
Submitted to the Faculty of
The University of Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Master of Science
in the Department of Pharmacy Administration
The University of Mississippi

by

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B.Pharm., Birla Institute of Technology and Science, 2009

December, 2011

ABSTRACT

Medication adherence has been shown to be influenced by demographics, health status and socio-economic status of the patient. Thus, adherence-based measures of pharmacy quality may be influenced by patient-related risk factors outside of the healthcare provider's control.

This study examines the performance of a classical logistic regression model containing only patient characteristics and a random-effect model including patient characteristics and a pharmacy-specific effect in predicting medication adherence. These models were used to compute three different risk-adjusted scores on adherence-based pharmacy quality indicators: based on the classical logistic regression model (Method 1), the random effects model (Method 2) and the shrinkage estimators of the random-effects model (Method 3). Finally, we compared the classification as low, medium or high quality pharmacies based on unadjusted and adjusted scores.

This retrospective cohort study used the 2007 Mississippi Medicare administrative claims dataset. Patient medication adherence was measured using the proportion of days covered (PDC) measure for seven therapeutic classes of medications. Pharmacy Quality scores on adherence-based measures were computed for all pharmacies serving Medicare beneficiaries in the state.

The logistic regression model and the random-effect model displayed good predictive ability (c-statistic>0.7) for all therapeutic classes. The residual intra class correlation coefficient ranged from 0.008 to 0.012 indicating that although pharmacy level factors may have a

significant impact, they may not be as important as patient level factors in determining adherence. Higher levels of agreement was observed between pharmacy classification based on unadjusted scores and risk-adjusted scores obtained from Methods 1 and 2 ($0.5<\kappa<0.74$) with the percentage change in classification ranging from 16.3%-28.4%. Scores based on Method 3 produced fewer outliers and showed minimal agreement with unadjusted scores ($0.19<\kappa<0.35$). When compared to risk-adjusted scores, unadjusted scores classified 8-12% of the low performing pharmacies as high performing and classified 20-30% of the pharmacies in the top 20% as low performers.

Risk-adjusted scores produced more robust indicators of pharmacy quality than unadjusted scores. Not adequately addressing the effects of patient case-mix while measuring quality could have severe implications if these measures are used for pay for performance programs or generating quality report cards.

LIST OF ABBREVIATIONS AND SYMBOLS

PQA	Pharmacy Quality Alliance
NCQA	National Committee for Quality Assurance
CMS	Centers for Medicare and Medicaid Services
ICD-9-CM	International Classification of Diseases, 9th Revision, Clinical Modification
CDS	Chronic Disease Score
GHC	Group Health Cooperation
CCI	Charlson Comorbidity Index
EI	Elixhauser Index
PDC	Proportion of Days Covered
ACEI/ARB	Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptor Blockers
SAS	Statistical Analysis Software
κ	Cohen's Kappa

ACKNOWLEDGEMENTS

I would like to acknowledge the members of this thesis committee Dr. Donna West-Strum and Dr. John P. Bentley who guided my activities in this undertaking. I would like to extend special thanks to the thesis committee Chair, Dr. Benjamin Banahan III, for his constant support and encouragement without which this would not have been possible.

I would also like to thank Vennela Thumula whose exemplary work as the lead analyst on the Pharmacy Quality Indicators project aided in the timely completion of this thesis.

TABLE OF CONTENTS

		PAGE
	ABSTRACT	ii
	LIST OF ABBREVIATIONS AND SYMBOLS	iv
	ACKNOWLEDGEMENTS	v
	LIST OF TABLES	viii
CHAPTER		
I.	INTRODUCTION	1
II.	LITERATURE REVIEW	3
	Measuring Pharmacy Quality	4
	Quality Indicators and the Importance of Case-Mix Adjustment	5
	Influence of Patient Characteristics on Medication Adherence	6
	Risk-adjustment Models	8
III.	METHODOLOGY	10
	Study Design and Data Sources	10

	Medicare	10
	Study Variables	11
	Pharmacy Quality Indicator Scores	12
	Statistical Analysis	17
IV.	RESULTS	24
	Beta Blockers	24
	Calcium Channel Blockers	30
	Angiotensin Converting Enzyme Inhibitor/ Angiotensin Receptor Blocker	36
	Sulfonylurea	42
	Biguanides	48
	Thiazolidinediones	54
	Statins	58
	Identifying High Quality Outliers – Top 20%	64
V.	DISCUSSION & CONCLUSIONS	66
BIBLIOGRAPHY		72
APPENDIX		76
VITA		84

LIST OF TABLES

TABLE		PAGE
1.	Claims based exclusions Table	15
2.	Odds ratio estimates of baseline patient characteristics in risk adjustment models – Beta Blockers	25
3.	Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Beta Blockers	28
4.	Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – Beta Blockers	29
5.	Odds ratio estimates of baseline patient characteristics in risk adjustment models – Calcium Channel Blockers	31
6.	Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Calcium Channel Blockers	34
7.	Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods –Calcium Channel Blockers	35
8.	Odds ratio estimates of baseline patient characteristics in risk adjustment models –ACEI/ARBs	37
9.	Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores –ACEI/ARBs	40
10.	Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – ACEI/ARBs	41
11.	Odds ratio estimates of baseline patient characteristics in risk adjustment models	

– Sulfonylurea 43

12. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Sulfonylurea 46

13. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – Sulfonylurea 47

14. Odds ratio estimates of baseline patient characteristics in risk adjustment models – Biguanides 49

15. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Biguanides 52

16. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – Biguanides 53

17. Odds ratio estimates of baseline patient characteristics in risk adjustment models – Thiazolidinediones 55

18. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Thiazolidinediones 57

19. Odds ratio estimates of baseline patient characteristics in risk adjustment models – Statins 59

20. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Statins 62

21. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – Statins 63

22. Summary of agreement between unadjusted and risk-adjusted pharmacy quality indicator scores in identifying high quality outliers as those pharmacies in top 20% of the distribution 65

23. Summary of agreement between unadjusted and risk-adjusted pharmacy quality indicator scores in identifying high quality outliers as those pharmacies in top 20% of the distribution 65

CHAPTER I

INTRODUCTION

In their landmark study, Johnson and Bootman[1] estimated that nearly 5 million hospital admissions and more than 100,000 deaths each year could be attributed to medication misuse. A newer study estimated that $45 billion could be saved annually if medications are used appropriately.[2] Pharmacies and pharmacists play an important role in the healthcare system, improving health outcomes through better pharmaceutical care, disease management and medication therapy management, thereby preventing medication misuse.[3] Yet, little information is available to evaluate the impact of these services. In November 2006, the Pharmacy Quality Alliance (PQA) contracted the National Committee for Quality Assurance (NCQA) to come up with pharmacy performance measures in 37 concept areas identified by the PQA.[4] In collaboration with the Advanced Pharmacy Concepts (APC), the NCQA developed detailed specifications for 22 measures in the area of medication adherence and persistence, efficiency, safety, diabetes, cardiovascular and respiratory care. PQA has promoted the use of these standardized measures for the evaluation of pharmacy service quality at various levels within the healthcare system.

However, it must be noted that these measures may be influenced by demographics, health status and socio-economic status of the patient population, which are factors outside of

payers' or healthcare providers' control. For example, the researchers at RAND Health Corporation conducted a systematic review of the barriers to medication adherence and concluded that apart from costs and provider-related factors, patient characteristics such as diagnosis of depression and regimen complexity are among the most important barriers to medication adherence.[5] They also found evidence that the number of prescribed medications may be related to adherence but not always in a specific direction.[6] This study and numerous other studies of the predictors of medication adherence suggest a need to risk-adjust for patient characteristics while computing pharmacy quality scores that will be used to compare different payers or providers on adherence-related indicators.[6-15] Failure to do so may result in comparisons that do not accurately reflect the effect of the individual providers and potential unfair rewards or penalties in pay-for-performance programs or other incentive/disincentive arrangements.

The objectives of the current study were:

- To examine the predictive ability of patient characteristics in medication adherence
- To compute risk-adjusted scores on adherence-related pharmacy performance indicators
- To compare unadjusted and adjusted scores on adherence-related pharmacy performance indicators

This study sought to answer the important questions: Are case-mix adjustments needed when computing Pharmacy Quality Indicator scores for individual pharmacies and if so, what are the best adjustments to use?

CHAPTER II

LITERATURE REVIEW

Measuring Pharmacy Quality

As healthcare in the United States moves to a value-driven model, there is an increased emphasis being placed on the measurement of quality of the service provided. The purpose of quality measurement is to identify problems in a system and track the effect of changes on quality, thereby ensuring continuous quality improvement.[16] Over the past two decades, accreditation standards for providers have been modified to include collection and reporting of performance data.[17] The data on performance have been used extensively by payers in the reimbursement of hospitals and physicians, better known as pay-for-performance.[18] As of 2005, nearly two-thirds of the physicians in large group and staff model health maintenance organizations and greater than 30% of family practice physicians reported that quality had a role in their compensation.[19] Public reporting of performance data has further stimulated quality improvement. Reports comparing the quality of hospitals,[20] nursing homes[21] and other institutional providers have been made available on a public domain by the Centers for Medicare and Medicaid Services (CMS) and the Joint Commission. The National Center for Quality Assurance provides information on the quality of health plans and managed care organizations using its set of measures (Health Effectiveness Data and Information Set-HEDIS).[22] Physician report cards are now available at the clinic level and the demand for these at the individual level

is growing.[23] However, quality measurement of medication use systems has remained relatively unexplored.[17]

In 2006, the Pharmacy Quality Alliance (PQA) was formed with the mission of improving the quality of medication use across healthcare settings through a collaborative process in which key stakeholders agree on a strategy for measuring and reporting performance information related to medications.[24] PQA is a voluntary, membership-based collaborative comprising organizations from the pharmacy, patient, employer, and health insurance plan communities, as well as state and federal government.[24] At its outset PQA sought to identify pharmacist performance indicators or measures relevant to patients enrolled in Medicare Part D drug plans which could be put into place using existing data.[24] On finding little evidence about the extensive use of any quality measures in the ambulatory or community pharmacy setting, PQA convened a Quality Metrics Workgroup which identified a starter set of 37 measure concepts in the areas adherence and persistence, efficiency, safety, and diabetes, cardiovascular and respiratory care.[4]

After a competitive bidding process involving organizations with expertise in measure development the contract was awarded to the National Committee for Quality Assurance (NCQA). NCQA collaborated with Advanced Pharmacy Concepts (APC) to achieve the tasks of evaluating the feasibility of creating measures in each concept area, developing detailed specifications for each measure, and conducting initial measure testing using drug claims data.[25] NCQA created a set of 22 feasible measures which were pilot tested by Pillittere-Dugan et al.[25] using prescription claims data. The authors examined the variation of different performance measures within four different health plans. The authors concluded that performance measures related to medication adherence may be feasible and scientifically sound as there was found to be

sufficient variation in these measures across different pharmacies within a health plan suggesting possible room for improvement for some pharmacies. The study also points out some limitations in the implementation of these measures. Most importantly, only few pharmacies were reliably evaluated as most pharmacies did not meet the eligibility criterion of serving at least 30 members for each measure. Thus, the quality measures may not apply to all the pharmacies in a health plan. Another important limitation is the assumption that the measures used were at the control of the pharmacist and not influenced by any patient characteristics.

Quality Indicators and the Importance of Case-Mix Adjustment

Failure to account for patient case mix may result in unfair and improper assessment of the healthcare provider. Studies examining hospital quality indicators such as mortality rates, rates of readmission, complication rates have shown that risk-adjusting for age, race, gender, disease severity and comorbidity burden yield different hospital ratings from unadjusted performance measures.[26] This is indicative of the fact that hospitals with a patient mix of poor health status to begin with are expected to perform worse on such measures; case mix or risk adjustment provides us with ratings that are potentially corrected for the effect of these risk factors. Recently, a study found that accounting for patient characteristics and treatment opportunity affected hospital rankings based on process measures such as adherence to treatment guidelines, for acute myocardial infarction.[26] At the individual physician-level, numerous studies have shown the need for risk-adjusting for patient demographic characteristics and comorbidity burden while comparing specialist referral rates.[27-29] The Center for Healthcare Strategies (CHCS) showed the importance of risk-adjustment in the evaluation of health-plan performance in the care provided to patients with chronic diseases.[30] This report assessed the performance of six managed care plans participating in the Maryland Medicaid program. The care provided to

enrollees with asthma, diabetes, HIV/AIDS and schizophrenia was analyzed using healthcare utilization rates for emergency room visits and inpatient admissions as the outcome performance measures. It was found that health status of the population was strongly related to these measures and adjusting for the health status improved the accuracy of the performance measures.

Influence of Patient Characteristics on Medication Adherence

Numerous studies have shown that patient characteristics influence medication adherence, indicating a need for case-mix adjustment of adherence-related pharmacy quality measures. A commonly employed conceptual framework in explaining adherence consists of patient-related factors, provider-related factors and health-system factors as the predictors of medication adherence. Patient-related factors can further be categorized as demographics, coexisting illness, medication characteristics and cognitive functioning, all of which may influence health beliefs thereby affecting medication compliance behavior.[5] Factors such as depression, beliefs about medication and medication characteristics such as number of prescriptions and regimen complexity, have been extensively studied.[5]

In a recently published systematic review of studies examining the barriers to medication adherence for the RAND Corporation, Gellad et al.[5] reported that evidence about the effect of number of chronic conditions and number of medications on medication adherence is unclear. Some studies suggest a positive relationship while others suggest a negative or a lack of relationship. For example, Billups et al.,[6] using computerized prescription records, found that increased age, higher number of chronic conditions, and higher number of concurrent drugs were positively correlated with drug therapy compliance. Similarly Siegel et al.[7] reported a positive association between antihypertensive medication adherence and older age, number of

cardiovascular medications and total number of medications using veterans' pharmacy claims database. Similar results were obtained by Shalansky and Levy[8] who report lower adherence to chronic cardiovascular regimens in patients taking fewer medications and Eagle et al.[9] who found that patients with myocardial infarction and hypertension were more likely to be adherent to beta-blocker therapy than patients with just one of those conditions. Other studies using patient surveys, computerized prescription records from national pharmacy chains and pharmacy claims data have also shown an increase in adherence rates with an increase in the number of comorbidities especially in those treated with cardiovascular drugs.[5]

However, Chapman et al.[10] using managed care prescription claims and medical service data, report that patients with higher disease burden (52.1%) and patients with any complex chronic condition (48.1%) were more likely to be non-adherent. These findings are similar to the findings of other studies like that by Sung et al.,[11] who found that patients with comorbidities, patients with multiple doses of antihyperlipidemic medications are less likely to be compliant. The complexity of dosing regimen has been recognized as an important predictor of medication adherence. Systematic reviews by Saini and colleagues[12] as well as Ingersoll and Cohen[13] concluded that dosing frequency and regimen complexity (defined as multiple medications, multiple doses, and specific time requirements) are associated with poorer adherence rates. Apart from clinical characteristics, adherence rates have also been found to vary with age, gender and race-ethnic grouping.[5, 14-15] Thus, in order to obtain an accurate assessment of pharmacy quality, the effects of patient characteristics must be adjusted for while computing pharmacy quality scores.

Risk-Adjustment Models

Risk assessment models such as the Ambulatory Clinical Groups (ACG) system, Hierarchical Coexisting Conditions (HCCs) system and the Chronic and Disability Payment System (CDPS) have been widely used in risk-adjustment of capitated health plan payments and provider performance ratings.[31] These diagnosis-based instruments provide a risk assessment based on the population health status and demographic profile. Diagnosis information based on International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM), codes available on automated information systems or from claims data is used.[31] However, a few drawbacks of these diagnosis-based measures are worth mentioning. They are susceptible to coding-related issues, and may not reflect medication characteristics. Further, diagnosis information may not be available to pharmacies or other agencies tasked with the measurement of pharmacy performance using pharmacy data.

Thus, a prescription-based risk-assessment model like the Rx-Risk system which aims to produce a risk assessment which reflects the comorbidity burden, medication characteristics such as the number of medications and the complexity of the medication regimen, would be ideal for the purpose of this study. The Rx-Risk system is a revised and expanded version of the Chronic Disease Score (CDS), a risk assessment instrument based on automated pharmacy data developed at Group Health Cooperation (GHC) of Puget Sound.[31] The risk assessment produced is based on an individual's age, sex and chronic condition profile measured by pharmacy dispenses linked to chronic conditions rather than diagnosis codes. Each drug dispensed is associated with a particular Rx-Risk category representing a chronic condition. A single dispensing of a drug is enough to be classified into an associated category. This helps to assure that adherent patients are not classified into more disease categories than non-adherent patients,

which would happen if multiple doses of a drug were required for classification into an associated chronic condition category. The Rx-Risk was designed to overcome some of the barriers of the earlier CDS in forecasting costs. Some categories in the CDS had to be modified to be used as a financial model for capitation adjustment. Further, the CDS was also developed and estimated within the GHC system, which meant that risk weights may reflect practice pattern and drug-use bias present in GHC and thereby limit its applicability. The Rx-Risk model was estimated and validated using data from approximately 1.5 million people sample of three large HMOs: GHC, HealthPartners of Minnesota and the Northeast Ohio and Rocky Mountain regions of Kaiser Permanente. The Rx-Risk system has been shown to perform at par with ACG and better than the Charlson comorbidity index (CCI) and the Elixhauser Index (EI) in the forecasting future healthcare costs[31]. More recently, the Rx-Risk instrument was found to have a better predictive ability compared to the CCI, the EI and the Health-related Quality of Life comorbidity index (HRQL-CI) in the prediction of adherence to treatment by physicians.[32] More importantly, this study also found that the risk assessment based on the Rx-Risk system was found to be a predictor of medication adherence in diabetic patients, whereas diagnosis-based comorbidity indices, like the CCI and the EI, performed poorly in the prediction of adherence.[32]

In this study, risk-adjusted scores on pharmacy performance measures were computed using patient demographic information and a chronic condition profile as measured by the Rx-Risk instrument to adjust for patient characteristics. Pharmacy rankings based on unadjusted and risk-adjusted scores on adherence-related pharmacy performance measures were compared.

CHAPTER III

METHODOLOGY

Study Design and Data Sources

A retrospective study was conducted using the 2007 Mississippi Medicare administrative claims datasets to compute and compare adjusted and unadjusted Pharmacy Quality scores on adherence-based Proportion of Days Covered (PDC) measures for pharmacies serving Medicare beneficiaries in the state.

Medicare

Medicare is a federally-funded, public health insurance program for patients 65 years of age or older, or those who meet special criteria, in the United States of America. The components of Medicare include hospital insurance (Part A), supplemental medical insurance (Part B), Medicare Advantage Plans (Part C) and prescription drug coverage (Part D). Medicare data are made available in the form of Research Identifiable Files which contain person-specific data on providers, beneficiaries and recipients including individual identifiers such as age, date of birth, race, sex, residence information. The de-identified form of these files, with an encrypted ID to link all records for patients on different files, was used. Use of these data files was covered by a Data Use Agreement with CMS. The following files were used in this study:

- Beneficiary Summary File: This file contains demographic and enrollment information for each Medicare beneficiary

- The Outpatient (submitted by institutional outpatient providers) and the Carrier (submitted by non-institutional outpatient providers) Standard Analytical Files or claim files which contain the final action claims data submitted by providers for reimbursement to CMS.
- The MedPAR File which contains inpatient hospital and skilled nursing facility (SNF) final action stay records. Each record on this file represents a hospital or a skilled nursing facility stay.
- Part D Drug Event (PDE) File: This file contains a summary record of each filled prescription by a beneficiary under Medicare Part D.

This study used the Beneficiary Summary file to retrieve demographic and eligibility information on patients. The claims files and MedPAR files helped identify patients who met inclusion criteria for the computation of the adherence based performance measures. Further, the RX and PDE files were used to compute these measures at a patient and pharmacy-level. The RX and PDE files were also used to measure a patient's RxRisk score based on the prescribed medications during the study period. Approval from the Institutional Review Board of the University of Mississippi was obtained under the exempt category.

Study Variables

Demographic Variables

Information on patient demographics was obtained from the Beneficiary Summary (beneficiary_summary) file of the Medicare data. Specifically the variables listed in table BENE_AGE_AT_END_REF_YR, BENE_SEX_IDENT_CD, BENE_RACE_CD were used to obtain information on patient age, sex and race respectively.

Additionally, information on the Low-income subsidy status of Medicare individuals was obtained from the Beneficiary_summary file of the Medicare data. In the Medicare Part D program, enrollees are eligible for cost-sharing assistance programs based on income levels and other criteria. Based on income levels, enrollees may receive drug benefits without any premium or co-pay, or may be required to pay a premium but no co-pay, or may be required to pay both a premium and a co-pay. The variable COST_GRP from the beneficiary_summary file was used to determine low-income subsidy status.

Rx-Risk System

The Rx-Risk system or a chronic disease score uses patients' prescription claims data to quantify their co-morbidity burden. The Rx-Risk model developed by Fishman et al. identifies 29 chronic disease categories (see Appendix A) and specifies all the classes of medications that belong to each category. Patients were assigned to a chronic disease category if they filled a prescription for any medication in that chronic disease category during the measurement period. Patients could have been assigned to multiple categories based on their prescription fills in the measurement period.

For each prescription record, the medication class was identified using the associated National Drug code. The Product Service ID (PROD_SRVC_ID) field of the Medicare prescription drug event file was used to obtain the National Drug Code of the prescribed medication.

Pharmacy Quality Indicator Score

NCQA developed a set of performance measures based on the conceptual foundations provided by Pharmacy Quality Alliance that could be widely implemented in the reporting and

assessment of pharmacy quality. This study evaluated pharmacy performance on a subset of these measures in the area of medication adherence. Specifically, pharmacies were evaluated on the proportion of days covered (PDC) measure. The quantification of pharmacy performance was based on the technical specifications and implementation guidelines provided by NCQA.

Proportion of Days Covered (PDC) Measure

As defined by the NCQA, PDC measures assess the proportion of patients "covered" by a drug or another drug in the same therapeutic class during the measurement period. At the patient-level PDC is calculated as the proportion of days in the measurement period covered by prescription claims for a given medication or any other medication in that therapeutic category. A PDC threshold of 0.8 (80%), was used to classify patients as "covered". Pharmacy performance on the PDC measure was assessed following the steps below:

- Step 1: Each patient's measurement period was identified as the period beginning on the date of the index prescription (first prescription in the calendar year) and ending on the date of disenrollment, death, the last day of the year or the last day covered by the final prescription fill in the year if it was before the last date of the year
- Step 2: In the measurement period the number of days for which the patient is covered by prescription claim for a drug or another medication in the same class was counted. If the dates covered by different prescription claims for the same drug overlapped, then an adjustment was made to start counting the days covered by the subsequent prescription claim after the last date covered by the previous prescription.
- Step 3: The number obtained in step 2 was divided by that in step 1 to get the PDC for each patient.

- Step 4: Patients were attributed to a particular pharmacy if they received at least 75% of their prescription fills at that pharmacy
- Step 5: Within each pharmacy, the number of patients who met the PDC threshold of 0.8 (measure numerator) was divided by the number of patients eligible for the PDC measure (measure denominator) to arrive at the final measure of Pharmacy performance.

A separate proportion was calculated for each of the following six classes of medications:

- Beta-blocker (BB)
- Angiotensin-converting enzyme (ACE) inhibitor or Angiotensin-receptor blocker (ARB)
- Calcium Channel Blocker (CCB)
- Biguanide
- Sulfonylurea
- Thiazolidinedione
- Statin

To have been eligible for measure computation, a patient must have filled at least two prescriptions for a medication or a combination medication in that therapeutic class (see Appendix B for list of medications) on two unique dates of service in the measurement year. The lists of medications in each class as specified in the NCQA guidelines is given below.

Additionally, the NCQA lists the following eligibility criteria for including a patient in the denominator of the pharmacy performance measure:

- Age – Patient must be 18 years or older as of the last day of the measurement year.

- Enrollment – The patient must be enrolled to receive Medicaid/Medicare benefits for the measurement year and must have no more than one gap of up to 45 days during the enrollment year. For Medicaid beneficiaries the member should not have a gap of more than one month in the year when enrollment status is measured on a monthly basis.
- Pharmacy benefits - The patient must be enrolled to receive pharmacy benefits during the measurement year.

Finally, the NCQA guidelines specify that patients who meet the above eligibility criteria but had a non-acute stay in the measurement year be excluded from the denominator of the measure. To identify patients receiving non-acute care the claims based exclusions table (Table 1) below was used.

Table 1 - Claims based exclusions table

Description	HCPCS	UB Revenue	UB Type of Bill	DRG	POS
Hospice		0115, 0125, 0135, 0145, 0155, 0650, 0656, 0658, 0659	81x, 82x		34
SNF		019x	21x, 22x, 28x		31, 32
Hospital transitional care, swing bed or rehabilitation			18x		
Rehabilitation		0118, 0128, 0138, 0148, 0158		462	
Respite		0655			
Intermediate care facility					54
Residential substance abuse treatment facility		1002			55
Psychiatric residential treatment center	T2048, H0017-H0019	1001			56
Comprehensive inpatient rehabilitation facility					61
Other nonacute care facilities that do not use the UB Revenue or Type of Bill codes for billing (e.g., ICF, SNF)					

If event codes are not available patients were excluded if they met one of the following conditions:

- Long-term care indicator field was populated on claims
- The NCPD or NABP code on the claim identified a long-term care specific pharmacy
- PBM pharmacy indicator type indicated a long-term care specific pharmacy
- Medicare claims with a zero co-pay were present

Scores on pharmacy performance measures were only calculated for pharmacies with at least 30 patients in the measure denominator.

Pharmacy Attribution

It is imperative that patients are accurately attributed to pharmacies. Inaccuracy may lead to some pharmacies being unfairly penalized for the quality of services received by the patient when the pharmacy has not had enough opportunities to impact it. Alternatively, pharmacies may unfairly benefit from the higher quality of prior services received by the patient elsewhere. Taking this into consideration, the NCQA developed specific rules for pharmacy attribution which were followed in this study:

- If patients qualifying for the denominator of a measure receive all of their prescriptions from one pharmacy they were attributed to that pharmacy.
- If patients qualifying for the denominator of a measure receive their prescriptions for a medication within the identified drug class or drug classes, from multiple pharmacies, they were attributed to the pharmacy which filled at least 75% of their prescriptions for

the medications in the identified drug class or drug classes when data from multiple pharmacies are available.

Statistical Analysis

Unadjusted pharmacy quality indicator score

As outlined above, the unadjusted measure of pharmacy performance or unadjusted pharmacy quality indicator score was calculated as the proportion of eligible patients within each of the pharmacies who met the PDC threshold of 0.8. A 95 % confidence interval for this measure was calculated using a normal approximation as:

$$O_j \pm 1.96 * \sqrt{O_j(1 - O_j)/n_j} \quad (1)$$

Where O_j is the unadjusted quality indicator score for pharmacy j, and n_j is the number of patients in pharmacy j.

Objective 1: To examine the predictive ability of patient characteristics in medication adherence

Method 1

Medication adherence for patient i in pharmacy j was defined as a binary variable Y_{ij} which equaled '1' for patients classified as being adherent (PDC>=0.8) and '0' for patients classified as being non-adherent (PDC<0.8). A classical logistic regression model was estimated to predict the log odds of adherence (equation 1) for each patient in the sample. This included all patients meeting the enrollment criteria and found to be eligible for the denominator of the corresponding pharmacy performance measure. The predictor variables in this model included categorical variables for race, sex and low income subsidy status, continuous variables for age

and the average number of prescriptions per 30 days, and dichotomous variables indicating the presence of each RxRisk category.

The logistic regression model was estimated as:

$$ln\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_0 + \beta_1 x_{1ij} + \beta_2 x_{2ij} \dots \dots + \beta_n x_{nij} \quad (2)$$

where p_{ij} is the probability of being adherent for patient *i* in pharmacy *j*, β_k are model parameters, x_{hij} are values of individual predictor variables.

The predictive ability of the model was examined using the c-statistic which is equal to the area under the receiver operating characteristic curve. The c-statistic provides a measure of the model's ability to discriminate between adherent and non-adherent patients. The c-statistic ranges from 0.5 (no discrimination, might as well flip a coin) to 1.0 (perfect discrimination).

Method 2

Alternatively, a hierarchical logistic regression model with a random intercept was estimated on the same data as:

$$ln\left(\frac{p_{ij}}{1-p_{ij}}\right) = \alpha_j + \beta_1 x_{1ij} + \beta_2 x_{2ij} \dots \dots + \beta_n x_{nij} \quad (3)$$

where p_{ij} is the probability of being adherent for patient *i* in pharmacy *j*, β_k are model parameters, x_{hij} are values of individual predictor variables, α_j is the random intercept for pharmacy *j*. This model consists of the same predictor variables used in the classical logistic regression model but accounts for the nesting of patients within a pharmacy by including an intercept term that is different for each pharmacy. This intercept term is taken to be random and

is expressed as a linear combination of the average intercept α and a group dependent deviation given by the random variable u_j. The random variable u_j was assumed to follow a normal distribution with mean of zero and variance of σ_u^2 and independent of the patient-level residuals:

$$\alpha_j = \alpha + u_j \quad (4)$$

$$u_j \sim N(0, \sigma_u^2) \quad (5)$$

The pharmacy-specific intercepts provide a measure of the effect of the pharmacy on adherence controlling for all the patient-level variables in the model. The predictive ability of this model was also examined using the c-statistic.

Additionally, the residual intraclass correlation coefficient was computed to provide a measure of variation between pharmacies. The residual intraclass correlation coefficient is a measure of the correlation between two individuals chosen at random from any random pharmacy. It translates to the proportion of the unexplained variation after controlling for the effect for the explanatory variables that can be attributed to variation at the pharmacy-level (or group membership). The patient-level residuals follow a logistic distribution which implies a fixed variance of $\pi^2/3$. The intraclass correlation coefficient for the random-intercept model was estimated as suggested by Snijders and Bosker[33] as:

$$\rho = \frac{\sigma_u^2}{\sigma_u^2 + \pi^2/3} \quad (6)$$

Where ρ is the intraclass coefficient, σ_u^2 is the variance of the random part of the pharmacy specific intercepts, $\pi^2/3$ is the variance of patient-level residuals.

Objective 2: To compute risk-adjusted scores of pharmacy performance on medication adherence-related measures

Method 1

The classical logistic regression model outlined above was used to estimate the predicted probability of adherence $\hat{p}_{ij1}$ for patient i in pharmacy j. For a given pharmacy the expected quality indicator score was calculated as the average of the individual predicted probabilities of patients within that pharmacy.

$$E_{j1} = \frac{1}{n_j} * \sum_{i=1}^{n_j} \hat{p}_{ij1} \quad (7)$$

Where E_{j1} is the expected quality indicator score for pharmacy j, $\hat{p}_{ij1}$ is the predicted probability of adherence for patient i, and n_j is the number of patients at pharmacy j.

The risk-adjusted performance measure for each pharmacy was calculated as the ratio of observed (or unadjusted) quality indicator score to the expected quality indicator score: O_j/E_{j1}.

The 95 % confidence intervals of O_j/E_{j1} was calculated as suggested by Hosmer and Lemeshow,[34] as:

$$\frac{O_j \pm 1.96 * \frac{\sqrt{\sum_{i=1}^{n_j} \hat{p}_{ij1}\left(1-\hat{p}_{ij1}\right)}}{n_j}}{E_{j1}} \quad (8)$$

Method 2

Alternatively, the hierarchical logistic regression model with a random intercept outlined above was used to estimate the predicted probability (assuming null effect of u_j) of adherence $\hat{p}_{ij2}$ for patient *i* in pharmacy *j*. For a given pharmacy the expected quality indicator score was calculated as the average of the individual predicted probabilities of patients within that pharmacy.

$$E_{j2} = \frac{1}{n_j} * \sum_{i=1}^{n_j} \hat{p}_{ij2} \quad (9)$$

Where E_{j2} is the expected quality indicator score for pharmacy *j* and $\hat{p}_{ij2}$ is the predicted probability of adherence for patient *i* based on Method 2 and n_j is the number of patients at pharmacy *j*.

Once again, the risk-adjusted performance measure for each pharmacy was calculated as the ratio of observed (or unadjusted) quality indicator score to the expected quality indicator score: O_j/E_{j2}.

The upper and lower bounds of the confidence interval of the risk-adjusted measure O_j/E_{j2} was calculated using the same formula described in equation 8.

Method 3

As mentioned earlier, the pharmacy specific intercepts provide a measure of the effect of the pharmacy after accounting for the patient-level explanatory variables. Specifically, the exponentiation of the random variable, $exp(u_j)$ is equal to the ratio of the odds of adherence at pharmacy j to the odds of adherence at the average pharmacy controlling for patient

characteristics. This final method uses the exponentiation of the random variable u_j (or shrinkage estimator u_j) as a risk-adjusted measure of pharmacy performance. The 95 % confidence interval of this risk-adjusted measure was calculated using the 95 % CI of u_j.

Objective 3: To compare unadjusted and adjusted scores on adherence-related pharmacy performance measures.

Based on their quality indicator scores pharmacies were classified as low-quality outliers, medium-quality pharmacies and high-quality outliers.

The average unadjusted pharmacy quality indicator score on each PDC measure was calculated as the sum of quality indicator scores of all pharmacies divided by the total number of pharmacies. Pharmacies were classified as low-quality outliers if their unadjusted score was less than the average unadjusted score and their 95 % CI of their unadjusted score did not contain the average unadjusted score. Pharmacies were classified as high-quality outliers if their unadjusted score was higher than the average unadjusted score and their 95 % CI of their unadjusted score did not contain the average unadjusted score. Pharmacies were classified as medium-quality if the 95 % CI of their unadjusted score contained the average unadjusted score.[35]

Similarly, for all three risk adjustment methods which yield a ratio as the final measure of performance, pharmacies were classified as follows: Pharmacies were classified as low-quality outliers if their risk-adjusted score was less than 1 and their 95 % CI of their unadjusted score did not contain 1. Pharmacies were classified as high-quality outliers if their risk-adjusted score was higher than 1 and their 95 % CI of their risk-adjusted score did not contain 1. Pharmacies were classified as medium-quality if the 95 % CI of their risk-adjusted score contained 1.[35]

The agreement in pharmacy classification based on unadjusted and adjusted scores obtained from the three different methods detailed above was evaluated using Cohen's Kappa (κ) coefficient.

Further, agreement in the identification of high quality pharmacies, defined as the top 20% of the distribution, using unadjusted and adjusted scores was also evaluated.

All analyses were conducted using SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina).

CHAPTER IV

RESULTS

Beta Blockers

At the patient-level, PDC measures for this class of medications were computed for 53,975 Medicare patients who met eligibility criteria. These patients were attributed to a total of 620 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 2 shows the odds ratio estimates of patient characteristics used to predict adherence to beta blockers using a classical logistic regression model and a random-intercept model. The odds ratio estimates of all patient characteristics were similar in both models. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to beta blockers. Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent to beta blockers. The c-statistic was 0.721 for the classical logistic regression model and 0.729 for the random intercept model which shows good discriminative ability for both models.

Table 2. Odds ratio estimates of baseline patient characteristics in risk adjustment models – Beta Blockers

Baseline Characteristics	Prevalence(%) or Mean ± SD	Classical Logistic Regression Model		Random Intercept Model	
		Point Estimate	P-Value	Point Estimate	P-Value
RxRisk Category					
• **Anxiety and tension**	12.47	0.678	<.0001	0.676	<.0001
• **Asthma**	20.58	0.645	<.0001	0.647	<.0001
• **Bipolar disorder**	0.25	1.043	0.8344	1.031	0.8792
• **Cardiac disease**	12.19	0.534	<.0001	0.533	<.0001
• **Vascular disease**	13.05	0.761	<.0001	0.757	<.0001
• **Cystic fibrosis**	0.06	0.316	0.0029	0.322	0.0038
• **Depression**	28.53	0.630	<.0001	0.629	<.0001
• **Diabetes**	29.97	0.641	<.0001	0.638	<.0001
• **Epilepsy**	14.87	0.644	<.0001	0.644	<.0001
• **ESRD**	0.19	0.672	0.0886	0.665	0.0808
• **Gastric acid disorder**	34.55	0.681	<.0001	0.680	<.0001
• **Gout**	7.62	0.764	<.0001	0.763	<.0001
• **AIDS**	2.56	0.850	0.0090	0.846	0.0076
• **Hyperlipidemia**	51.88	0.800	<.0001	0.797	<.0001
• **Inflammatory bowel disorder**	10.39	0.788	<.0001	0.789	<.0001
• **Liver disease**	1.55	0.639	<.0001	0.635	<.0001
• **Malignancies**	9.97	0.773	<.0001	0.774	<.0001
• **Parkinson's**	3.84	0.739	<.0001	0.731	<.0001
• **Psychotic illness**	5.77	0.726	<.0001	0.725	<.0001
• **Renal disease**	0.34	0.920	0.6289	0.916	0.6122
• **Rheumatoid arthritis**	14.55	1.074	0.1097	1.071	0.1265
• **Thyroid disorder**	14.59	0.744	<.0001	0.741	<.0001
• **Transplant**	0.28	0.907	0.6138	0.906	0.6124
• **Tuberculosis**	0.31	0.705	0.0505	0.702	0.0479
• **Pain**	44.47	0.661	<.0001	0.664	<.0001

• **Pain and inflammation**	23.15	0.867	<.0001	0.868	<.0001
• **Glaucoma**	7.74	0.818	<.0001	0.817	<.0001
Race					
• **North American Native**	0.11	Reference	Reference	Reference	Reference
• **Unknown race**	0.03	0.613	0.0450	0.574	0.3917
• **White**	65.74	2.887	<.0001	2.769	0.0008
• **Black**	33.71	1.636	0.9285	1.578	0.1341
• **Other**	0.18	2.593	0.0502	2.514	0.0165
• **Asian**	0.18	2.253	0.1692	2.145	0.0466
• **Hispanic**	0.06	1.997	0.5840	1.921	0.1843
Sex					
• **Female**	64.47	Reference	Reference	Reference	Reference
• **Male**	35.53	0.893	<.0001	0.894	<.0001
Age	71.07±11.54	1.010	<.0001	1.010	<.0001
Cost share group[a]					
• **No Premium Subsidy**	47.47	Reference	Reference	Reference	Reference
• **Subsidy group 1**	3.13	1.234	0.0026	1.253	0.0129
• **Subsidy group 2**	47.28	0.901	<.0001	0.908	<.0001
• **Subsidy group 3**	2.11	0.972	0.4017	0.976	0.7351
Prescriptions per month	5.58±3.11	1.454	<.0001	1.459	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Using the random-intercept model, the pharmacy-level variance component was estimated to be 0.03382 with a standard error of 0.005714. Testing the null hypothesis of no random effects and complete independence of all the observations using a likelihood ratio test based on residual pseudo likelihoods yielded a chi-square of 73.36 ($p<0.0001$), indicating non-zero covariance parameters (or presence of random effect). The residual intraclass correlation coefficient (ρ) for the random intercept model was estimated to be 0.01017 which indicates that

1.02% of the unexplained variation after controlling for patient-level variables could be attributed to variation between pharmacies.

Table 3 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Agreement between pharmacy classification based on unadjusted and risk-adjusted scores was similar when risk adjustment was done using a classical logistic regression model (κ=0.61) and when adjustment was based on a random intercept model (κ=0.59) and the least when risk adjustment was based on the shrinkage estimators of the random intercept model (κ=0.34).

Table 3. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Beta Blockers

Outlier status based on unadjusted performance rating	**Outlier Status Based on Risk Adjustment**								
	Method 1[a]			Method 2[b]			Method 3[c]		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Low	90	49	1	92	47	1	40	99	1
Medium	27	283	28	33	277	28	2	332	4
High	1	33	108	1	36	105	1	98	43
Percentage change in classification (%)[d]	23.7	22.5	21.2	26.7	23.1	21.6	6.97	37.2	10.4
Overall κ[e]	0.61			0.60			0.34		

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Percentage change was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Table 4 shows a comparison of the three different risk adjustment methods used. Pharmacy classification based on risk-adjusted scores obtained using Method 1 and 2 showed nearly perfect agreement (κ=0.97). Classification based on Method 3 showed only moderate agreement with classification based on Method 1 (κ=0.43) and Method 2 (κ=0.42). Method 3 also identified fewer high and low quality outliers compared to the other risk adjustment methods.

Table 4. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – Beta Blockers

Outlier status Based on Risk Adjustment Method	**Outlier Status Based on Risk Adjustment Method**					
	Method 1[a]			Method 2[b]		
Method 2[b]						
	Low	Medium	High			
Low	118	8	0			
Medium	0	357	3			
High	0	0	134			
Overall κ[d]		0.97				
Method 3[c]						
	Low	Medium	High	Low	Medium	High
Low	43	0	0	43	0	0
Medium	75	365	89	83	360	86
High	0	0	48	0	0	48
Overall κ[d]		0.43			0.42	

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Calcium Channel Blockers

At the patient-level, PDC measures for this class of medications were computed for 50,577 Medicare patients who met eligibility criteria. These patients were attributed to a total of 606 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 5 shows the odds ratio estimates of patient characteristics used to predict adherence to calcium channel blockers using a classical logistic regression model and a random-intercept model. The odds ratio estimates of all patient characteristics were similar in both models. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to calcium channel blockers. Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent to calcium channel blockers. The c-statistic was 0.728 for the classical logistic regression model and 0.734 for the random intercept model which shows good discriminative ability for both models.

Table 5. Odds ratio estimates of baseline patient characteristics in risk adjustment models – Calcium Channel Blockers

Baseline Characteristics	Prevalence(%) or Mean ± SD	Classical Logistic Regression Model		Random Intercept Model	
		Point Estimate	P-Value	Point Estimate	P-Value
RxRisk Category					
• **Anxiety and tension**	11.45	0.647	<.0001	0.646	<.0001
• **Asthma**	20.62	0.687	<.0001	0.688	<.0001
• **Bipolar disorder**	0.18	0.850	0.5077	0.844	0.4927
• **Cardiac disease**	7.87	0.535	<.0001	0.535	<.0001
• **Vascular disease**	9.89	0.766	<.0001	0.762	<.0001
• **Cystic fibrosis**	0.09	0.789	0.5201	0.775	0.4908
• **Depression**	25.22	0.661	<.0001	0.659	<.0001
• **Diabetes**	30.87	0.653	<.0001	0.652	<.0001
• **Epilepsy**	13.53	0.654	<.0001	0.653	<.0001
• **ESRD**	0.26	0.611	0.0173	0.610	0.0172
• **Gastric acid disorder**	32.82	0.667	<.0001	0.664	<.0001
• **Gout**	6.60	0.704	<.0001	0.702	<.0001
• **AIDS**	2.24	0.984	0.8264	0.987	0.8641
• **Hyperlipidemia**	44.15	0.752	<.0001	0.750	<.0001
• **Inflammatory bowel disorder**	10.60	0.747	<.0001	0.749	<.0001
• **Liver disease**	1.74	0.734	0.0003	0.736	0.0003
• **Malignancies**	9.88	0.742	<.0001	0.740	<.0001
• **Parkinson's**	3.23	0.667	<.0001	0.667	<.0001
• **Psychotic illness**	5.73	0.685	<.0001	0.680	<.0001
• **Renal disease**	0.31	0.587	0.0042	0.593	0.0052
• **Rheumatoid arthritis**	14.42	1.006	0.9024	1.003	0.9567
• **Thyroid disorder**	13.18	0.775	<.0001	0.775	<.0001

• **Transplant**	0.29	0.669	0.0425	0.670	0.0441
• **Tuberculosis**	0.28	0.742	0.1279	0.738	0.1222
• **Pain**	43.45	0.653	<.0001	0.655	<.0001
• **Pain and inflammation**	25.92	0.891	<.0001	0.890	<.0001
• **Glaucoma**	10.28	0.899	0.0040	0.898	0.0036
Race					
• **North American Native**	0.19	Reference	Reference	Reference	Reference
• **Unknown race**	0.05	2.796	0.5424	2.557	0.0929
• **White**	52.63	3.405	<.0001	3.218	<.0001
• **Black**	46.76	2.145	0.9664	2.031	0.0075
• **Other**	0.16	2.143	0.9808	2.051	0.0480
• **Asian**	0.15	2.807	0.2994	2.601	0.0118
• **Hispanic**	0.06	1.759	0.5697	1.691	0.2771
Sex					
• **Female**	67.96	Reference	Reference	Reference	Reference
• **Male**	32.04	1.034	0.1736	1.034	0.1774
Age	71.76±11.6	1.015	<.0001	1.015	<.0001
Cost share group[a]					
• **No Premium Subsidy**	41.02	Reference	Reference	Reference	Reference
• **Subsidy group 1**	3.23	0.933	0.8906	0.965	0.6974
• **Subsidy group 2**	53.71	0.857	0.0133	0.862	<.0001
• **Subsidy group 3**	2.04	0.914	0.8571	0.915	0.2630
Prescriptions per month	5.27±3.01	1.474	<.0001	1.477	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Using the random-intercept model, the pharmacy-level variance component was estimated to be 0.02887 with a standard error of 0.005844. Testing the null hypothesis of no random effects and complete independence of all the observations using a likelihood ratio test based on residual pseudo likelihoods yielded a chi-square of 45.48 ($p<0.0001$), indicating non-

zero covariance parameters (or presence of random effect). The residual intraclass correlation coefficient (ρ) for the random intercept model was estimated to be 0.0087 which indicates that 0.87% of the unexplained variation after controlling for patient-level variables could be attributed to variation between pharmacies.

Table 6 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Agreement between pharmacy classification based on unadjusted and risk-adjusted scores was similar when risk adjustment was done using a classical logistic regression model (κ=0.51) and a random intercept model (κ=0.52) and the least when risk adjustment was based on the shrinkage estimators of the random intercept model (κ=0.23).

Table 6. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – Calcium Channel Blockers

Outlier status based on unadjusted performance rating	Outlier Status Based on Risk Adjustment								
	Method 1[a]			Method 2[b]			Method 3[c]		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Low	79	50	0	80	49	0	25	104	0
Medium	39	267	31	39	268	30	1	329	7
High	2	49	89	2	49	89	1	111	28
Percentage change in classification (%)[d]	34.2	27.0	25.8	33.9	26.7	25.2	7.4	39.5	20
Overall κ[e]	0.51			0.52			0.23		

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Percentage change was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Table 16 shows a comparison of the three different risk adjustment methods used. Pharmacy classification based on risk-adjusted scores obtained using Method 1 and 2 showed nearly perfect agreement (κ=0.97). Classification based on Method 3 showed less than moderate agreement with classification based on Method 1 (κ=0.33) and Method 2 (κ=0.33). Method 3 also identified fewer high and low quality outliers compared to the other risk adjustment methods.

Table 7. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – Calcium Channel Blockers

Outlier status Based on Risk Adjustment Method	**Outlier Status Based on Risk Adjustment Method**					
	Method 1[a]			Method 2[b]		
Method 2[b]						
	Low	Medium	High			
Low	120	1	0			
Medium	0	365	1			
High	0	0	119			
Overall κ[d]		0.99				
Method 3[c]						
	Low	Medium	High	Low	Medium	High
Low	27	0	0	27	0	0
Medium	93	366	85	94	366	84
High	0	0	35	0	0	35
Overall κ[d]		0.33			0.33	

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Angiotensin-Converting Enzyme Inhibitor/Angiotensin-Receptor Blocker (ACEI/ARB)

At the patient-level, PDC measures for this class of medications were computed for 87,220 Medicare patients who met eligibility criteria. These patients were attributed to a total of 682 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 8 shows the odds ratio estimates of patient characteristics used to predict adherence to ACEI/ARBs using a classical logistic regression model and a random-intercept model. The odds ratio estimates of all patient characteristics were similar in both models. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to ACEI/ARBs. Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent to ACEI/ARBs. However, patients with Rheumatoid Arthritis had higher odds of being adherent compared to those without the condition. The c-statistic was 0.715 for the classical logistic regression model and 0.723 for the random intercept model which shows good discriminative ability for both models.

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Table 8. Odds ratio estimates of baseline patient characteristics in risk adjustment models – ACEI/ARB

Baseline Characteristics	Prevalence(%) or Mean ± SD	Classical Logistic Regression Model		Random Intercept Model	
		Point Estimate	P-Value	Point Estimate	P-Value
RxRisk Category					
• **Anxiety and tension**	11.45	0.699	<.0001	0.697	<.0001
• **Asthma**	20.43	0.629	<.0001	0.631	<.0001
• **Bipolar disorder**	0.21	1.019	0.9152	1.002	0.9919
• **Cardiac disease**	8.66	0.534	<.0001	0.532	<.0001
• **Vascular disease**	9.69	0.715	<.0001	0.712	<.0001
• **Cystic fibrosis**	0.06	0.273	<.0001	0.274	<.0001
• **Depression**	26.28	0.620	<.0001	0.617	<.0001
• **Diabetes**	35.48	0.718	<.0001	0.714	<.0001
• **Epilepsy**	14.21	0.667	<.0001	0.667	<.0001
• **ESRD**	0.17	0.564	0.0029	0.557	0.0025
• **Gastric acid disorder**	32.05	0.683	<.0001	0.679	<.0001
• **Gout**	6.48	0.706	<.0001	0.702	<.0001
• **AIDS**	2.35	0.944	0.2728	0.941	0.2462
• **Hyperlipidemia**	49.31	0.800	<.0001	0.797	<.0001
• **Inflammatory bowel disorder**	10.21	0.758	<.0001	0.761	<.0001
• **Liver disease**	1.32	0.648	<.0001	0.648	<.0001
• **Malignancies**	9.35	0.770	<.0001	0.772	<.0001
• **Parkinson's**	3.48	0.698	<.0001	0.692	<.0001
• **Psychotic illness**	5.57	0.741	<.0001	0.736	<.0001
• **Renal disease**	0.29	0.392	<.0001	0.394	<.0001
• **Rheumatoid arthritis**	13.98	1.083	0.0219	1.077	0.0329
• **Thyroid disorder**	13.25	0.731	<.0001	0.728	<.0001
• **Transplant**	0.25	0.897	0.5107	0.891	0.4858
• **Tuberculosis**	0.27	0.678	0.0084	0.672	0.0073
• **Pain**	42.89	0.665	<.0001	0.667	<.0001
• **Pain and inflammation**	25.49	0.903	<.0001	0.901	<.0001

• **Glaucoma**	9.17	0.881	<.0001	0.881	<.0001
Race					
• **North American Native**	0.17	Reference	Reference	Reference	Reference
• **Unknown race**	0.04	1.964	0.8912	1.606	0.2728
• **White**	60.10	3.541	<.0001	2.916	<.0001
• **Black**	39.26	2.291	0.1868	1.907	0.0032
• **Other**	0.20	2.623	0.1338	2.179	0.0048
• **Asian**	0.17	1.675	0.2357	1.353	0.2883
• **Hispanic**	0.05	2.197	0.8098	1.887	0.1010
Sex					
• **Female**	65.29	Reference	Reference	Reference	Reference
• **Male**	34.71	0.996	0.8180	0.992	0.6472
Age	70.81±11.49	1.011	<.0001	1.011	<.0001
Cost share group[a]					
• **No Premium Subsidy**	44.35	Reference	Reference	Reference	Reference
• **Subsidy group 1**	2.94	1.121	0.1876	1.130	0.0959
• **Subsidy group 2**	50.70	1.028	0.4040	1.035	0.0753
• **Subsidy group 3**	2.01	1.049	0.9916	1.057	0.3507
Prescriptions per month	5.14±3.01	1.452	<.0001	1.458	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Using the random-intercept model, the pharmacy-level variance component was estimated to be 0.03459 with a standard error of 0.004477. Testing the null hypothesis of no random effects and complete independence of all the observations using a likelihood ratio test based on residual pseudo likelihoods yielded a chi-square of 151.99 ($p<0.0001$), indicating non-zero covariance parameters (or presence of random effect). The residual intraclass correlation coefficient (ρ) for the random intercept model was estimated to be 0.0104 which indicates that 1.04% of the unexplained variation after controlling for patient-level variables could be attributed to variation between pharmacies.

Table 9 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Agreement between pharmacy classification based on unadjusted and risk-adjusted scores was least when risk adjustment was based on the shrinkage estimators of the random intercept model (κ=0.38). Similar levels of agreement was seen when risk adjustment was done using a random intercept model (κ=0.59) and a classical logistic regression model (κ=0.57).

Table 9. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores – ACEI/ARB

Outlier status based on unadjusted performance rating	**Outlier Status Based on Risk Adjustment**								
	Method 1[a]			Method 2[b]			Method 3[c]		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Low	98	61	1	106	53	1	44	115	1
Medium	30	298	26	32	299	23	6	342	6
High	2	54	112	2	54	112	1	97	70
Percentage change in classification (%)[d]	26.7	27.8	19.4	24.3	26.3	17.6	13.7	38.3	9.09
Overall κ[e]	0.57			0.59			0.38		

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Percentage change was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Table 10 shows a comparison of the three different risk adjustment methods used. Pharmacy classification based on risk-adjusted scores obtained using Method 1 and 2 showed nearly perfect agreement (κ=0.97). Classification based on Method 3 showed less than moderate agreement with classification based on Method 1 (κ=0.56) and Method 2 (κ=0.55). Method 3 also identified fewer high and low quality outliers compared to the other risk adjustment methods.

Table 10. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods – ACEI/ARB

Outlier status Based on Risk Adjustment Method	**Outlier Status Based on Risk Adjustment Method**					
	Method 1[a]			Method 2[b]		
Method 2[b]						
	Low	Medium	High			
Low	130	10	0			
Medium	0	403	3			
High	0	0	136			
Overall κ[d]		0.97				
Method 3[c]						
	Low	Medium	High	Low	Medium	High
Low	51	0	0	51	0	0
Medium	79	413	62	89	406	59
High	0	0	77	0	0	77
Overall κ[d]		0.56			0.55	

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Sulphonylurea

At the patient-level, PDC measures for this class of medications were computed for 13,280 Medicare patients who met eligibility criteria. These patients were attributed to a total of 275 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 11 shows the odds ratio estimates of patient characteristics used to predict adherence to sulphonylurea medications using a classical logistic regression model and a random-intercept model. The odds ratio estimates of all patient characteristics were similar in both models. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to sulphonylurea medications. Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent to medications. The c-statistic was 0.702 for the classical logistic regression model and 0.7124 for the random intercept model which shows good discriminative ability for both models.

Table 11. Odds ratio estimates of baseline patient characteristics in risk adjustment models - Sulfonylurea

Baseline Characteristics	Prevalence(%) or Mean ± SD	Classical Logistic Regression Model		Random Intercept Model	
		Point Estimate	P-Value	Point Estimate	P-Value
RxRisk Category					
• **Anxiety and tension**	11.18	0.689	<.0001	0.686	<.0001
• **Asthma**	17.42	0.736	<.0001	0.736	<.0001
• **Bipolar disorder**	0.27	1.438	0.3690	1.408	0.3974
• **Cardiac disease**	9.12	0.685	<.0001	0.687	<.0001
• **Vascular disease**	9.50	0.866	0.0500	0.861	0.0420
• **Cystic fibrosis**	0.09	1.268	0.7195	1.326	0.6699
• **Depression**	26.05	0.670	<.0001	0.666	<.0001
• **Hypertension**	92.87	0.702	<.0001	0.700	<.0001
• **Epilepsy**	16.58	0.711	<.0001	0.711	<.0001
• **ESRD**	0.23	0.804	0.5974	0.816	0.6229
• **Gastric acid disorder**	31.40	0.651	<.0001	0.652	<.0001
• **Gout**	8.17	0.855	0.0349	0.854	0.0347
• **AIDS**	2.09	0.810	0.1163	0.801	0.0985
• **Hyperlipidemia**	54.89	0.787	<.0001	0.789	<.0001
• **Inflammatory bowel disorder**	11.31	0.794	0.0002	0.796	0.0003
• **Liver disease**	1.39	0.971	0.8689	0.966	0.8443
• **Malignancies**	9.19	0.880	0.0671	0.883	0.0762
• **Parkinson's**	3.95	0.895	0.3036	0.891	0.2857
• **Psychotic illness**	6.62	0.761	0.0017	0.759	0.0016
• **Renal disease**	0.29	0.679	0.2743	0.676	0.2715
• **Rheumatoid arthritis**	11.08	1.028	0.7572	1.028	0.7589
• **Thyroid disorder**	12.27	0.878	0.0424	0.876	0.0413

• **Transplant**	0.20	0.572	0.1911	0.587	0.2123
• **Tuberculosis**	0.34	0.656	0.2106	0.658	0.2164
• **Pain**	43.33	0.690	<.0001	0.690	<.0001
• **Pain and inflammation**	26.47	0.895	0.0152	0.893	0.0138
• **Glaucoma**	10.93	0.843	0.0077	0.840	0.0066
Race					
• **North American Native**	0.66	Reference	Reference	Reference	Reference
• **Unknown race**	0.05	0.534	0.2158	0.511	0.4182
• **White**	49.79	2.315	0.0018	2.191	0.0069
• **Black**	49.18	1.734	0.0968	1.643	0.0848
• **Other**	0.19	1.862	0.3389	1.822	0.2515
• **Asian**	0.07	1.191	0.9372	1.127	0.8734
• **Hispanic**	0.06	1.003	0.7357	1.001	0.9987
Sex					
• **Female**	63.01	Reference	Reference	Reference	Reference
• **Male**	36.99	1.009	0.8391	1.015	0.7325
Age	70.16±11.06	1.014	<.0001	1.014	<.0001
Cost share group[a]					
• **No Premium Subsidy**	37.04	Reference	Reference	Reference	Reference
• **Subsidy group 1**	3.81	0.870	0.4594	0.872	0.3730
• **Subsidy group 2**	56.75	0.825	0.0119	0.829	<.0001
• **Subsidy group 3**	2.39	1.094	0.1561	1.103	0.4771
Prescriptions per month	5.99±3.10	1.371	<.0001	1.374	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Using the random-intercept model, the pharmacy-level variance component was estimated to be 0.03888 with a standard error of 0.01235. Testing the null hypothesis of no random effects and complete independence of all the observations using a likelihood ratio test

based on residual pseudo likelihoods yielded a chi-square of 15.83 ($p<0.0001$), indicating non-zero covariance parameters (or presence of random effect). The residual intraclass correlation coefficient (ρ) for the random intercept model was estimated to be 0.01168 which indicates that 1.17% of the unexplained variation after controlling for patient-level variables could be attributed to variation between pharmacies.

Table 12 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Agreement between pharmacy classification based on unadjusted and risk-adjusted scores was the same ($\kappa=0.61$) when risk adjustment was done using a classical logistic regression model and a random intercept model and much lesser when risk adjustment was done using the shrinkage estimators of the random intercept model ($\kappa=0.29$).

Table 12. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores - Sulfonylurea

Outlier status based on unadjusted performance rating	Outlier Status Based on Risk Adjustment Method								
	Method 1[a]			Method 2[b]			Method 3[c]		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Low	40	16	0	40	16	0	12	44	0
Medium	8	134	14	8	134	14	0	156	0
High	2	21	40	2	21	40	0	47	16
Percentage change in classification (%)[d]	20	21.6	25.9	20	21.6	25.9	0	36.8	0
Overall κ[e]	0.61			0.61			0.29		

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Percentage change was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Table 13 shows a comparison of the three different risk adjustment methods used. Pharmacy classification based on risk-adjusted scores obtained using Method 1 and 2 showed perfect agreement ($\kappa=1$). Classification based on Method 3 showed less than moderate agreement with classification based on Method 1 and Method 2 ($\kappa=0.35$). Method 3 also identified fewer high and low quality outliers compared to the other risk adjustment methods.

Table 13. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods - Sulfonylurea

Outlier status Based on Risk Adjustment Method	Outlier Status Based on Risk Adjustment Method					
	Method 1[a]			Method 2[b]		
Method 2[b]						
	Low	Medium	High			
Low	50	0	0			
Medium	0	171	0			
High	0	0	54			
Overall κ[d]		1				
Method 3[c]						
	Low	Medium	High	Low	Medium	High
Low	12	0	0	12	0	0
Medium	38	171	38	38	171	38
High	0	0	16	0	0	16
Overall κ[d]		0.35			0.35	

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Biguanides

At the patient-level, PDC measures for this class of medications were computed for 15,468 Medicare patients who met eligibility criteria. These patients were attributed to a total of 311 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 14 shows the odds ratio estimates of patient characteristics used to predict adherence to biguanides using a classical logistic regression model and a random-intercept model. The odds ratio estimates of all patient characteristics were similar in both models. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to biguanide medications. Beneficiaries in subsidy group 2 i.e., beneficiaries with 100% premium-subsidy and low copayment/high copayment and those with a low income subsidy, a 100% premium-subsidy and high copayment were less likely to be adherent when compared to beneficiaries with no premium subsidy or cost sharing with an estimated odds ratio of 0.856 (using classical logistic regression model) and 0.857 (using the random intercept model). Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent to medications. The c-statistic was 0.723 for the classical logistic regression model and 0.73 for the random intercept model which shows good discriminative ability for both models.

Table 14. Odds ratio estimates of baseline patient characteristics in risk adjustment models - Biguanides

Baseline Characteristics	Prevalence(%) or Mean ± SD	Classical Logistic Regression Model		Random Intercept Model	
		Point Estimate	P-Value	Point Estimate	P-Value
RxRisk Category					
• **Anxiety and tension**	11.26	0.670	<.0001	0.671	<.0001
• **Asthma**	17.35	0.747	<.0001	0.749	<.0001
• **Bipolar disorder**	0.41	1.171	0.5989	1.159	0.6251
• **Cardiac disease**	7.27	0.570	<.0001	0.572	<.0001
• **Vascular disease**	8.02	0.780	0.0004	0.779	0.0004
• **Cystic fibrosis**	0.08	0.189	0.0158	0.193	0.0176
• **Depression**	28.63	0.662	<.0001	0.662	<.0001
• **Hypertension**	91.80	0.683	<.0001	0.683	<.0001
• **Epilepsy**	17.71	0.697	<.0001	0.701	<.0001
• **ESRD**	0.08	2.161	0.2575	2.282	0.2272
• **Gastric acid disorder**	32.00	0.705	<.0001	0.703	<.0001
• **Gout**	6.24	0.680	<.0001	0.679	<.0001
• **AIDS**	2.04	0.923	0.5300	0.928	0.5544
• **Hyperlipidemia**	59.57	0.818	<.0001	0.817	<.0001
• **Inflammatory bowel disorder**	10.86	0.767	<.0001	0.769	<.0001
• **Liver disease**	1.08	0.744	0.0944	0.743	0.0946
• **Malignancies**	8.74	0.767	<.0001	0.770	<.0001
• **Parkinson's**	4.34	0.860	0.1081	0.857	0.1006
• **Psychotic illness**	7.29	0.890	0.1349	0.887	0.1265
• **Renal disease**	0.25	0.472	0.0332	0.476	0.0357
• **Rheumatoid arthritis**	10.69	0.910	0.2567	0.906	0.2369

• **Thyroid disorder**	12.28	0.783	<.0001	0.781	<.0001
• **Transplant**	0.18	0.604	0.2195	0.618	0.2413
• **Tuberculosis**	0.25	0.995	0.9895	1.021	0.9552
• **Pain**	43.53	0.614	<.0001	0.614	<.0001
• **Pain and inflammation**	27.99	0.833	<.0001	0.831	<.0001
• **Glaucoma**	9.84	0.927	0.2155	0.923	0.1953
Race					
• **North American Native**	0.41	Reference	Reference	Reference	Reference
• **Unknown race**	0.03	1.593	0.8995	1.448	0.7043
• **White**	53.01	2.572	0.0408	2.373	0.0061
• **Black**	46.11	1.566	0.5194	1.446	0.2386
• **Other**	0.22	2.273	0.4933	2.114	0.1297
• **Asian**	0.12	3.079	0.2419	2.853	0.0853
• **Hispanic**	0.10	1.179	0.4108	1.096	0.8839
Sex					
• **Female**	63.91	Reference	Reference	Reference	Reference
• **Male**	36.09	1.047	0.2498	1.049	0.2279
Age	67.94±10.98	1.012	<.0001	1.012	<.0001
Cost share group[a]					
• **No Premium Subsidy**	38.65	Reference	Reference	Reference	Reference
• **Subsidy group 1**	2.82	1.207	0.1434	1.220	0.2211
• **Subsidy group 2**	56.32	0.856	0.0011	0.857	0.0003
• **Subsidy group 3**	2.21	1.031	0.8820	1.032	0.7997
Prescriptions per month	5.86±3.08	1.404	<.0001	1.405	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Using the random-intercept model, the pharmacy-level variance component was estimated to be 0.02726 with a standard error of 0.01020. Testing the null hypothesis of no random effects and complete independence of all the observations using a likelihood ratio test

based on residual pseudo likelihoods yielded a chi-square of 10.34 (p=0.0013), indicating non-zero covariance parameters (or presence of random effect). The residual intraclass correlation coefficient (ρ) for the random intercept model was estimated to be 0.00821 which indicates that 0.82% of the unexplained variation after controlling for patient-level variables could be attributed to variation between pharmacies. Table 15 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Agreement between pharmacy classification based on unadjusted and risk-adjusted scores was similar when risk adjustment was done using a random intercept model (κ=0.54) and a classical logistic regression model (κ=0.53) and the least when risk adjustment was done using the shrinkage estimators of the random intercept model (κ=0.19).

Table 15. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores - Biguanides

Outlier status based on unadjusted performance rating	Outlier Status Based on Risk Adjustment								
	Method 1[a]			Method 2[b]			Method 3[c]		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Low	36	26	0	36	26	0	8	54	0
Medium	17	156	17	17	156	17	0	189	1
High	1	17	41	1	16	42	0	49	10
Percentage change in classification (%)[d]	33.3	21.6	29.3	33.3	21.2	28.8	0	35.3	0.09
Overall κ[e]	0.53			0.54			0.19		

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Percentage change was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Table 16 shows a comparison of the three different risk adjustment methods used. Pharmacy classification based on risk-adjusted scores obtained using Method 1 and 2 showed nearly perfect agreement (κ=0.99). Classification based on Method 3 showed less than moderate agreement with classification based on Method 1 (κ=0.23) and Method 2 (κ=0.23). Method 3 also identified fewer high and low quality outliers compared to the other risk adjustment methods.

Table 16. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods - Biguanides

Outlier status Based on Risk Adjustment Method	**Outlier Status Based on Risk Adjustment Method**					
	Method 1[a]			Method 2[b]		
Method 2[b]						
	Low	Medium	High			
Low	54	0	0			
Medium	0	198	0			
High	0	1	58			
Overall κ[d]		0.99				
Method 3[c]						
	Low	Medium	High	Low	Medium	High
Low	8	0	0	8	0	0
Medium	46	199	47	46	198	48
High	0	0	11	0	0	11
Overall κ[d]		0.23			0.23	

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Thiazolidinediones

At the patient-level, PDC measures for this class of medications were computed for 3,955 Medicare patients who met eligibility criteria. These patients were attributed to a total of 92 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 17 shows the odds ratio estimates of patient characteristics used to predict adherence to thiazolidinediones (TZDs) using a classical logistic regression model. A random intercept model could not be specified due to sample size restrictions. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to TZDs. Beneficiaries in subsidy group 1, i.e., beneficiaries with 100% premium-subsidy and no copayment and those in subsidy group 2, i.e., beneficiaries with 100% premium-subsidy and low copayment/high copayment and those with a low income subsidy, a 100% premium-subsidy and high copayment were significantly more likely to be adherent when compared to beneficiaries with no premium subsidy or cost sharing with an estimated odds ratio of 2.575 and 2.055 for subsidy groups 1 and 2 respectively. Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent to medications. The c-statistic was 0.727 which shows good discriminative ability for the classical logistic regression model.

Table 17. Odds ratio estimates of baseline patient characteristics in risk adjustment models - Thiazolidinediones

Baseline Characteristics	Prevalence (%) or Mean ± SD	Classical Logistic Regression Model	
		Point Estimate	P-Value
RxRisk Category			
• **Anxiety and tension**	11.88	0.606	<.0001
• **Asthma**	17.72	0.788	0.0706
• **Bipolar disorder**	0.2	1.254	0.7666
• **Cardiac disease**	7.36	0.535	<.0001
• **Vascular disease**	8.42	0.647	0.0012
• **Cystic fibrosis**	0.03	<0.001	0.9677
• **Depression**	28.39	0.685	<.0001
• **Hypertension**	92.47	0.520	<.0001
• **Epilepsy**	18.1	0.797	0.0212
• **ESRD**	0.63	0.584	0.2632
• **Gastric acid disorder**	34.97	0.694	<.0001
• **Gout**	7.0	0.743	0.0342
• **AIDS**	1.87	0.661	0.1143
• **Hyperlipidemia**	59.62	0.792	0.0016
• **Inflammatory bowel disorder**	12.19	0.751	0.0096
• **Liver disease**	1.95	1.074	0.7839
• **Malignancies**	8.80	0.820	0.1279
• **Parkinson's**	4.12	0.745	0.1301
• **Psychotic illness**	7.79	0.755	0.0598
• **Renal disease**	0.46	0.773	0.6191
• **Rheumatoid arthritis**	10.49	1.131	0.4471
• **Thyroid disorder**	10.87	0.843	0.1458
• **Transplant**	0.10	0.739	0.7642
• **Tuberculosis**	0.53	0.910	0.8471
• **Pain**	47.05	0.630	<.0001
• **Pain and inflammation**	27.84	0.741	0.0002
• **Glaucoma**	13.0	0.715	0.0015

Race			
• **Unknown race**	1.49	Reference	Reference
• **White**	39.9	2.480	0.0448
• **Black**	58.3	1.769	0.6331
• **Other**	0.18	1.475	0.8973
Sex			
• **Female**	65.66	Reference	Reference
• **Male**	34.34	1.218	0.0114
Age	68.76±11.48	1.013	0.0001
• **No Premium Subsidy**	25.99	Reference	Reference
• **Subsidy group 1**	7.16	2.575	0.0018
• **Subsidy group 2**	65.56	2.055	0.0095
• **Subsidy group 3**	1.29	1.239	0.2611
Prescriptions per month	6.18±3.35	1.331	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Table 18 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Table 18. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores

Outlier status based on unadjusted performance rating	**Outlier Status Based on Risk Adjustment** Using Classical Logistic Regression		
	Low	Medium	High
Low	19	3	0
Medium	1	40	5
High	1	5	18
Percentage change in classification (%)[d]	9.5	16.7	21.7
Overall κ[e]		0.74	

[d]Percentage change in classification was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Statins

At the patient-level, PDC measures for this class of medications were computed for 60,913 Medicare patients who met eligibility criteria. These patients were attributed to a total of 644 pharmacies in the state for which quality indicator scores were computed according to NCQA specifications.

Table 19 shows the odds ratio estimates of patient characteristics used to predict adherence to statins using a classical logistic regression model and a random-intercept model. The odds ratio estimates of all patient characteristics were similar in both models. Adherence was strongly associated with the average number of prescriptions per month. Patients with a greater number of average prescriptions per month had higher odds of being adherent to statins. Presence of most medical conditions, as measured by the RxRisk measure, was associated with significantly lesser odds of being adherent statins. Beneficiaries with no copayment and 100% premium subsidy were more likely to be adherent when compared to beneficiaries with no premium subsidy or cost sharing with an estimated odds ratio of 1.99 (using classical logistic regression model) and 2.08 (using the random intercept model). The c-statistic was 0.723 for the classical logistic regression model and 0.7316 for the random intercept model which shows good discriminative ability for both models.

Table 19. Odds ratio estimates of baseline patient characteristics in risk adjustment models - Statins

Baseline Characteristics	Prevalence(%) or Mean±SD	Classical Logistic Regression Model		Random Intercept Model	
		Point Estimate	P-Value	Point Estimate	P-Value
RxRisk Category					
• **Anxiety and tension**	11.72	0.674	<.0001	0.672	<.0001
• **Asthma**	20.15	0.644	<.0001	0.645	<.0001
• **Bipolar disorder**	0.29	0.804	0.2129	0.803	0.2115
• **Cardiac disease**	8.05	0.618	<.0001	0.616	<.0001
• **Vascular disease**	9.84	0.841	<.0001	0.833	<.0001
• **Cystic fibrosis**	0.06	0.467	0.0358	0.445	0.0248
• **Depression**	28.84	0.658	<.0001	0.657	<.0001
• **Diabetes**	36.24	0.635	<.0001	0.629	<.0001
• **Hypertension**	89.72	0.642	<.0001	0.639	<.0001
• **Epilepsy**	15.17	0.696	<.0001	0.691	<.0001
• **ESRD**	0.18	1.299	0.2549	1.289	0.2702
• **Gastric acid disorder**	34.04	0.654	<.0001	0.651	<.0001
• **Gout**	6.04	0.693	<.0001	0.691	<.0001
• **AIDS**	2.44	0.973	0.6443	0.969	0.5917
• **Inflammatory bowel disorder**	9.98	0.748	<.0001	0.750	<.0001
• **Liver disease**	1.28	0.673	<.0001	0.679	<.0001
• **Malignancies**	8.91	0.732	<.0001	0.734	<.0001
• **Parkinson's**	3.75	0.711	<.0001	0.709	<.0001
• **Psychotic illness**	5.73	0.920	0.0610	0.914	0.0443
• **Renal disease**	0.27	0.820	0.2588	0.827	0.2832
• **Rheumatoid arthritis**	13.60	1.069	0.1003	1.069	0.1015
• **Thyroid disorder**	14.87	0.794	<.0001	0.792	<.0001
• **Transplant**	0.20	0.673	0.0516	0.664	0.0449
• **Tuberculosis**	0.28	0.771	0.1327	0.767	0.1268

• **Pain**	42.18	0.649	<.0001	0.653	<.0001
• **Pain and inflammation**	25.08	0.813	<.0001	0.811	<.0001
• **Glaucoma**	8.86	0.851	<.0001	0.846	<.0001
Race					
• **North American Native**	0.12	Reference	Reference	Reference	Reference
• **Unknown race**	0.05	1.527	0.8305	1.465	0.4451
• **White**	65.32	2.562	<.0001	2.450	0.0021
• **Black**	34.06	1.602	0.7737	1.540	0.1373
• **Other**	0.21	2.294	0.0849	2.206	0.0243
• **Asian**	0.19	1.600	0.8811	1.519	0.2423
• **Hispanic**	0.05	1.431	0.6758	1.303	0.5809
Sex					
• **Female**	63.49	Reference	Reference	Reference	Reference
• **Male**	36.51	1.151	<.0001	1.151	<.0001
Age	70.33±10.59	1.014	<.0001	1.014	<.0001
Cost share group[a]					
• **No Premium Subsidy**	46.15	Reference	Reference	Reference	Reference
• **Subsidy group 1**	2.41	1.990	<.0001	2.080	<.0001
• **Subsidy group 2**	49.41	1.248	0.3423	1.263	<.0001
• **Subsidy group 3**	2.03	1.093	0.0025	1.108	0.1194
Prescriptions per month	5.49±3.10	1.464	<.0001	1.474	<.0001

[a]Subsidy Group 1 consisted of beneficiaries with 100% premium-subsidy and no copayment. Subsidy Group 2 consisted of beneficiaries with 100% premium-subsidy and low copayment/high copayment and beneficiaries with a low income subsidy, a 100% premium-subsidy and high copayment. Subsidy Group 3 consisted of beneficiaries with low income subsidy, 15% copayment and 25%-100% premium-subsidy.

Using the random-intercept model, the pharmacy-level variance component was estimated to be 0.03972 with a standard error of 0.005499. Testing the null hypothesis of no random effects and complete independence of all the observations using a likelihood ratio test based on residual pseudo likelihoods yielded a chi-square of 123.85 ($p<0.0001$), indicating non-zero covariance parameters (or presence of random effect). The residual intraclass correlation coefficient (ρ) for the random intercept model was estimated to be 0.01193 which indicates that

1.19% of the unexplained variation after controlling for patient-level variables could be attributed to variation between pharmacies. Table 20 shows the agreement between the unadjusted quality indicator scores and the risk-adjusted quality indicator scores. Low quality outliers are those pharmacies whose scores on the pharmacy quality indicator are significantly lower than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. High quality outliers are those pharmacies whose pharmacy quality indicator scores are significantly higher than the average quality score in this sample of pharmacies according to the 95% confidence interval of the measures. Pharmacies of medium quality are those whose quality scores are not significantly different from the average quality score in the sample.

Agreement between pharmacy classification based on unadjusted and risk-adjusted scores was similar when risk adjustment was done using a random intercept model (κ=0.50) and a classical logistic regression model (κ=0.49) and the least when risk adjustment was done using the shrinkage estimators of the random intercept model (κ=0.35).

Table 20. Agreement in identifying Pharmacy Quality Outliers: Comparison of unadjusted and risk-adjusted pharmacy quality indicator scores - Statins

Outlier status based on unadjusted performance rating	Outlier Status Based on Risk Adjustment								
	Method 1[a]			Method 2[b]			Method 3[c]		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Low	81	56	1	81	56	1	37	101	0
Medium	51	295	30	51	297	28	5	360	11
High	2	43	85	3	43	84	1	81	48
Percentage change in classification (%)[d]	39.5	25.1	26.7	40	25	25.7	13.9	33.6	18.6
Overall κ[e]	0.49			0.50			0.35		

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Percentage change in classification was calculated for each risk adjustment method using the classification based on the risk adjustment method as the initial classification.
[e]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Table 21 shows a comparison of the three different risk adjustment methods used. Pharmacy classification based on risk-adjusted scores obtained using Method 1 and 2 showed nearly perfect agreement (κ=0.98). Classification based on Method 3 showed less than moderate agreement with classification based on Method 1 (κ=0.49) and Method 2 (κ=0.50). Method 3 also identified fewer high and low quality outliers compared to the other risk adjustment methods.

Table 21. Agreement in identifying Pharmacy Quality Outliers: Comparison of risk adjustment methods - Statins

Outlier status Based on Risk Adjustment Method	Outlier Status Based on Risk Adjustment Method					
	Method 1[a]			Method 2[b]		
Method 2[b]						
	Low	Medium	High			
Low	133	2	0			
Medium	1	392	3			
High	0	0	113			
Overall κ[d]	0.98					
Method 3[c]						
	Low	Medium	High	Low	Medium	High
Low	43	0	0	43	0	0
Medium	91	394	57	92	396	54
High	0	0	59	0	0	59
Overall κ[d]	0.49				0.50	

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement

Identifying High Quality Outliers - Top 20%

Agreement of unadjusted and risk-adjusted pharmacy quality indicator scores in identifying the best pharmacies as defined by the top 20% of all pharmacies was examined for each measure. The results are presented in Table 22. Cohen's Kappa between pharmacy classification based on unadjusted and risk-adjusted quality indicator scores ranged from 0.47-0.63. Kappa values were similar for the three types of risk adjustment methods used indicating that there was not much difference in the level of agreement between pharmacy classification based on risk-adjusted and unadjusted scores when different risk adjustments were used. False positive error rates, calculated as the proportion of pharmacies identified as being in the top 20% by the unadjusted scores and not by the risk-adjusted scores ranged from 7.46%-11%. False negative error rates, calculated as the proportion of pharmacies identified as being in the top 20% by the risk-adjusted scores and not by the unadjusted scores was much higher and ranged from 29%-42%.

We also examined agreement between the different risk adjustment methods used in the identification of the top 20% of the distribution. The results are given in the Table 23. Almost perfect agreement was observed between pharmacy classification based on Method 1 (using classical logistic regression) and Method 2 (using a random intercept model) with Kappa values ranging from 0.97-1.00. Pharmacy rankings based on Method 3 (using shrinkage estimators of random-intercept model) were in strong agreement with rankings based on Method 1 and Method 2 ($0.79<\kappa<0.86$).

Table 22. Summary of agreement between unadjusted and risk-adjusted pharmacy quality indicator scores in identifying high quality outliers as those pharmacies in top 20% of the distribution

Performance measure	Risk Adjustment Method								
	Method 1[a]			Method 2[b]			Method 3[c]		
	κ[d]	False positive (%)[e]	False negative (%)[e]	κ[d]	False positive (%)[e]	False negative (%)[e]	κ[d]	False positive(%)e[e]	False negative (%)[e]
Beta blockers	0.61	7.86	30.6	0.61	7.86	30.6	0.63	7.46	29.03
CCBs	0.52	9.71	38.5	0.52	9.71	38.5	0.53	9.5	37.7
ACE I/ARBs	0.56	8.8	34.8	0.57	8.64	34.1	0.56	8.8	34.8
Sulfonylurea	0.60	8.18	30.9	0.60	8.18	30.9	0.58	8.64	32.7
Biguanides	0.60	8.06	31.75	0.60	8.06	31.8	0.62	7.66	30.2
TZDs	0.47	11	42.1	-	-	-	-	-	-
Statins	0.57	8.54	34.1	0.57	8.54	34.1	0.58	8.35	33.3

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement
[e]False positive and false negative error rates were calculated for each risk adjustment method assuming the classification based on the risk adjustment method to be the correct classification

Table 23. Summary of agreement between unadjusted and risk-adjusted pharmacy quality indicator scores in identifying high quality outliers as those pharmacies in top 20% of the distribution

Performance measure	Risk Adjustment Method		
	Method 1[a] - Method 2[b]	Method 1[a] – Method 3[c]	Method 2[b] - Method 3[c]
	Cohen's Kappa κ[d]	Cohen's Kappa κ[d]	Cohen's Kappa κ[d]
Beta blockers	0.97	0.82	0.81
CCBs	1	0.79	0.79
ACE I/ARBs	0.99	0.81	0.81
Sulfonylureas	1	0.86	0.86
Biguanides	1	0.84	0.84
Statins	0.98	0.85	0.85

[a]Based on classical logistic regression model
[b]Based on random-intercept model
[c]Based on shrinkage estimators of random-intercept model
[d]Overall Kappa coefficient is a measure of agreement between unadjusted performance ratings and ratings based on the risk adjustment method with higher values indicating greater agreement
[e]False positive and false negative error rates were calculated for each risk adjustment method assuming the classification based on the risk adjustment method to be the correct classification

CHAPTER V

DISCUSSION & CONCLUSIONS

With the United States healthcare system moving towards a value-driven model, the demand for evidence of value and quality has reached medication use systems. The Center for Medicare and Medicaid Services (CMS) has already started reporting quality at the drug-plan level thereby intensifying the need for pharmacy-level quality measures. PQA demonstration projects have successfully tested some quality measures, including the adherence-based measures used in this study that are bound to be implemented soon. As measurement of pharmacy performance becomes a reality, we are a step closer to having publicly available report cards and pay-for-performance initiatives for pharmacies. As such, it is imperative that pharmacy quality measures be adjusted for patient case mix so that they accurately reflect pharmacy performance and can be used to make fair comparisons with other pharmacies with a different case mix. This study presents and compares three approaches to address the issue of risk adjustment - the use of a classical logistic regression model, a random intercept model and the shrinkage estimators of the random intercept model.

In order to be a valid risk adjustment method it is necessary that the patient characteristics adjusted for have an influence on the patient outcome used as a measure of facility quality of care. The classical and hierarchical logistic regression models used included the same measures of patient co-morbidity, socio-economic status and demographics as predictors of adherence. The logistic regression model and the random intercept model

displayed good predictive ability (c-statistics>0.7) for all adherence measures thereby justifying the choice of patient characteristics to be adjusted for when measuring pharmacy quality. Also, it is worth mentioning here that accounting for a random effect of a pharmacy only slightly improved the discriminative ability of the model. The highest improvement in c-statistic was only 0.0104, seen in the regression models used to predict adherence to Sulpohnylurea medications. Further, the low intra-class correlation coefficients show that pharmacy-level variation does not explain much of the variation in adherence unexplained by patient characteristics. The residual intraclass correlation coefficient for the random intercept models ranged from 0.008 to 0.012 for the six adherence measures. These findings suggest that although pharmacy-level factors may have a significant impact, they may not be as important as patient-level factors in determining adherence. This also served to reinforce our belief that the use of adherence-based measures which are not adjusted for patient-level factors will lead to unfair assessments of pharmacy quality.

After risk adjusting pharmacy quality indicator scores by three different methods, we compared the pharmacy classification as low, medium or high quality outliers based on the 95% confidence intervals of unadjusted and risk-adjusted scores. It was seen that the classification of pharmacies as low or high quality outliers changed after quality scores were risk-adjusted. Higher levels of agreement was observed between pharmacy classification based on unadjusted scores and risk-adjusted scores obtained from the classical logistic regression model with Cohen's Kappa values ranging from 0.5-0.74 and the percentage change in classification ranging from 16.3%-28.4%. Minimal agreement was seen between pharmacy rankings based on unadjusted scores and risk-adjusted scores obtained from the shrinkage estimators of the hierarchical model with Cohen's Kappa values ranging from 0.19-0.35 and the percentage

change in classification ranging from 30.9%-37%. The lack of agreement between unadjusted and risk-adjusted rankings have been demonstrated for other quality measures. Li et al.[35] studied the impact of different statistical methodologies in risk adjusting quality measures (QMs) of the Nursing Home quality report cards published by CMS. They reported an overall kappa of 0.59-0.76 for the agreement between unadjusted and risk-adjusted measures in identifying quality outliers using the 95% confidence intervals of QMs.

In our study, the pharmacy rankings based on the different risk adjustment methods showed moderate to high agreement with each other. These results suggest that the risk-adjusted measures, despite the statistical methodology used, provide a more robust and more useful assessment of pharmacies than the corresponding unadjusted measure. Rankings based on logistic regression models and random intercept models showed nearly perfect agreement in identifying statistical outliers. A similar finding was reported in another study comparing these two methods for the quality assessment of American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) hospitals with regard to colorectal operation morbidity and mortality.[36] This is not surprising given that the estimated coefficients for the covariates used in both models were similar. Although we did not find the outlier classification to vary much in our case, it would be advisable to use the more sophisticated and statistically rigorous approach of hierarchical modeling which accounts for the lack of independence in the data when measuring pharmacy quality for the purposes of pay-for-performance programs or generating quality report cards.

There was only moderate agreement between rankings based on the first two risk adjustment methods which used O/E ratios and the third method which used exponentiation of the random intercept parameters of the hierarchical model as a measure of pharmacy

performance. It was observed that the third method classified fewer pharmacies as outliers. The random intercept parameters are equivalent to shrinkage estimators produced in an empirical Bayes estimation procedure. The shrinkage estimator works on the principle that the precision of the estimate of facility quality produced using the sample of patients served at that facility (unshrunk estimate) will depend upon the sample size and variance. As such, the shrinkage estimator is so designed that the performance of facilities with smaller sample sizes and higher variance within them would be shrunk to an estimate away from their unshrunk estimate and closer to the average performance in the entire population and vice-versa for facilities with a larger sample size. Thus, the shrinkage estimator is biased in nature and this method of risk adjustment often tends to produce fewer outliers. For this reason and its difficulty in interpretation, Mukammel et al. caution against the use of this method for producing risk-adjusted measures to rank providers for quality report cards.[37]

CMS currently rewards the top 20% of hospitals as a part of their Premier Hospital Quality Incentive Demonstration program.[38] The top 10% receive an incentive of 2% and the next 10% receive an incentive of 1% bonus payment per Medicare patient along with their regular Medicare prospective payment.[38] This structure is also used by CMS for a pay-for-performance demonstration program for nursing homes.[35] We examined the effect of case-mix adjustment of pharmacy quality measures on identification of pharmacies eligible for a reward if such a program were to be implemented for pharmacies serving the Medicare beneficiaries. There was moderate to substantial agreement between unadjusted and risk-adjusted pharmacy classification. However, when compared to risk-adjusted scores, unadjusted scores classified 8-12% of the low performing pharmacies as high performing and classified 20-30% of the pharmacies in the top 20% as low performers. When we compared the three risk adjustment

methods in a pairwise manner, we observed almost perfect agreement between them in identifying high performing pharmacies. This suggests that the risk-adjusted measures would provide more robust quality information than the unadjusted measure.

As shown here, not adequately addressing the effects of patient case mix while measuring quality could lead to misclassification of pharmacies. This could have severe implications for pharmacies if these measures are used for pay-for-performance programs or even generating quality report cards. For example, Mehta et al.[26] found that adjusting for patient characteristics (including age, body mass index, race and type of insurance) and treatment opportunities affected hospital rankings and their classification in the CMS pay-for-performance categories based on a process measure for the treatment of acute myocardial infarction. Similar results were reported in studies examining the effect of risk adjustment on New York State and Massachusetts Cardiac Surgery Report cards[39,40] and Nursing Home Compare report cards.[36,41] All these studies demonstrate that unadjusted quality measures will reward facilities with the healthiest patient case mix rather than the best performers. Also, this would unjustly penalize facilities serving sicker patients, minority groups and the lower socio-economic strata. This would ultimately lead to healthcare facilities selecting healthier patients and refusing care for sicker patients in order to obtain a better performance rating. In fact, results from a study of the New York State Cardiac Surgery Report suggest that cardiologists may be "cream skimming" or avoiding the sickest patients because of their concern about their rankings.[42] Preliminary results from another study about the Nursing Home Compare report cards also point towards the occurrence of cream skimming with at least some nursing homes reporting a change in the type of patients they admit following the publication of the report cards.[43]

An important limitation of this study and most studies on methods of case-mix adjustment of quality measures is that there are no true or real quality rankings that can be used to compare the performance of the risk adjustment methods. However, the results of this study show that regardless of the method used, risk-adjusted scores produce more robust indicators of pharmacy quality than unadjusted scores. It was also observed that the use of shrinkage estimators for computing quality score as a risk adjustment method tends to be biased and produce fewer outliers than the conventional methods of using the observed to expected (O/E) ratios. Thus, it may not be desirable to use this method for risk adjustment especially when the intended use of quality scores is to produce quality report cards tailored to the general public. In this study, the quality of pharmacies was evaluated individually for each of the seven medication adherence based measures. Future research should address the question of developing a composite measure of pharmacy performance for each patient that can then be risk-adjusted to arrive at one unique measure of quality for each pharmacy. The pharmacies rankings based on this measure can then be easily used to produce report cards or for pay-for-performance programs.

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APPENDIX

APPENDIX A

RxRisk Chronic Disease Categories and associated Medication Class(es)

Chronic Disease	AHFS (American Hospital Formulary System) medication category	AHFS Category Number
Anxiety and tension	Benzodiazepines, Miscellaneous anxiolytics, Sedative, and Hypnotics	28:24:08, 28:24:92
Asthma	Sympathomimetic agents, Adrenals	12:12, 68:04, 86:16
Bipolar disorder	Antimanic agents	28:28
Cardiac disease	Cardiac drugs	24:04
Coronary/peripheral vascular disease	Anticoagulants, Hemorrheologic agents	20:24, 20:12:04
Cystic fibrosis	Mucolytic agents, Digestants	48:24, 56:16
Depression	Antidepressants	28:16:04
Diabetes	Antidiabetics	68:20
Epilepsy	Anticonvulsants	28:12
End Stage Renal Disease	Hematopoietic agents	20:16
Gastric acid disorder	Miscellaneous GI drugs	56:92, 56:28
Glaucoma		52:40, 52:92
Gout	Unclassified therapeutic agents	92:16
HIV	Antivirals, Miscellaneous antiinfectives	08:18, 08:92
Hyperlipidemia	Antilipemic agent	24:06
Hypertension	Hypotensive agent	24:08, 24:20, 24:24, 24:28, 24:32, 40:28
Inflammatory bowel disorder	Sulfonamide	56:92, 08:12:20
Liver disease	Ammonia detoxicants	40:10
Malignancies	Antineoplastic agents, Hematopoietic antiemetics	10:00, 56:22, 20:16
Pain	Nonsteroidal anti-inflammatory agents	28:08:08
Pain and inflammation	Opiates	28:08:04
Parkinsons disease	Antiparkinsonian agents	28:36
Psychotic illness	Tranquilizers	28:16:08
Renal disease	Potassium removing resins	40:18:18
Rheumatoid arthritis	Adrenals, Gold compounds, Antimalarial agents	68:04, 60:00, 08:30:08

Thyroid disorder	Thyroid agents, Antithyroid agents	68:36
Transplant	Unclassified therapeutic agents	92:44
Tuberculosis	Antituberculosis agents	08:16:04

APPENDIX B

LIST OF MEDICATIONS

Beta-Blocker Medications

- acebutolol HCL
- atenolol
- betaxolol HCL
- bisoprolol fumarate
- carteolol HCL
- carvedilol
- labetalol HCL
- metoprolol succinate
- metoprolol tartrate
- nadolol
- nebivolol HCL
- penbutolol sulfate
- pindolol
- propranolol HCL
- timolol maleate

BB Combination Products

- atenolol & chlorthalidone
- bisoprolol & HCTZ
- nadolol & bendroflumethiazide
- metoprolol & HCTZ
- propranolol & HCTZ
- timolol & HCTZ

Note: Active ingredients are limited to oral formulations only. Excludes the BB sotalol because it is indicated for the treatment of ventricular arrhythmias (and not for hypertension).

Angiotensin-converting enzyme (ACE) inhibitor or Angiotensin-receptor blocker (ARB)

ARB Medications

- candesartan
- eprosartan
- irbesartan
- losartan
- olmesartan
- telmisartan
- valsartan

ACE Inhibitor Medications

- benazepril
- captopril
- enalapril
- fosinopril
- lisinopril
- moexipril
- perindopril
- quinapril
- ramipril
- trandolopril

ACE Inhibitor Combination Products

- amlodipine & benazepril
- benazepril & HCTZ
- captopril & HCTZ
- enalapril & HCTZ
- enalapril & felodipine
- fosinopril & HCTZ
- lisinopril & HCTZ
- moexipril & HCTZ
- lisinopril & nutritional supplement
- quinapril & HCTZ
- trandolopril-verapamil HCL

ARB Combination Products

- candesartan & HCTZ
- eprosartan & HCTZ
- telmisartan & amlodipine
- irbesartan & HCTZ
- losartan & HCTZ
- amlodipine & olmesartan
- olmesartan & HCTZ
- telmisartan & HCTZ
- aliskiren & valsartan
- valsartan & HCTZ
- amlodipine & valsartan
- amlodipine & valsartan & HCTZ

Note: Active ingredients are limited to oral formulations only.

Calcium Channel Blockers

CCB Medications			
• amlodipine besylate	• felodipine	• nicardipine HCL	• verapamil HCL
• diltiazem HCL	• isradipine	• nifedipine (long acting only)	• nisoldipine

CCB Combination Products		
• amlodipine besylate & benazepril HCL	• enalapril maleate & felodipine	• trandolopril & verapamil HCL
• amlodipine & valsartan	• telmisartan & amlodipine	• amlodipine & atorvastatin
• amlodipine & valsartan & HCTZ	• amlodipine & olmesartan	

Note: Active ingredients are limited to oral formulations only. Excludes CCB nimodipine since it has a limited indicatio for use following a subarachnoid hemorrhage.

Biguanide Medications

Biguanides	
• metformin	

Biguanide & Sulfonylurea Combination Products	
• glipizide & metformin	• glyburide & metformin

Biguanide & Thiazolinedione Combination Products	
• rosiglitazone & metformin	• pioglitazone & metformin

Biguanide & Meglitinide Combinations
• repaglinide & metformin

Biguanide & DPP-IV Inhibitor Combinations
• sitagliptin & metformin

Note: Active ingredients are limited to oral formulations only (includes all dosage forms).

Sulfonylureas

Sulfonylureas	
• acetohexamide	• glyburide
• chlorpropamide	• tolazamide
• glimepiride	• tolbutamide
• glipizide	

Sulfonylurea & Biguanide Combination Products	
• glipizide & metformin	• glyburide & metformin

Sulfonylurea & Thiazolidinedione Combination Products	
• rosiglitazone & glimepiride	• pioglitazone & glimepiride

Note: Active ingredients are limited to oral formulations only (includes all salts and dosage forms).

Thiazolidinediones	
Thiazolidinediones	
• pioglitazone	rosiglitazone
Thiazolinedione & Biguanide Combination Products	
• rosiglitazone & metformin	• pioglitazone & metformin
Thiazolidinedione & Sulfonylurea Combination Products	
• rosiglitazone & glimepiride	• pioglitazone & glimepiride
Note: Active ingredients are limited to oral formulations only (includes all dosage forms).	

Statin Medications			
Statins			
• lovastatin • rosuvastatin	• fluvastatin • atorvastatin	• pravastatin	• simvastatin
Statin Combination Products			
• niacin & lovastatin • atorvastatin & amlodipine	• niacin & simvastatin	• pravastatin & aspirin	• ezetimibe & simvastatin
Note: The active ingredients are limited to oral formulations only (includes all dosage forms).			

VITA

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He obtained his Bachelor of Pharmacy degree from the Birla Institute of Technology and Science, Pilani, India in 2009. In August, 2009 he enrolled in the Master's degree program in Pharmacy Administration at The University of Mississippi. He is a recipient of the William E. Farlow Fellowship 2011-2012.