AN ANALYSIS OF THE NORTH CAROLINA NURSING HOME POLYPHARMACY INITIATIVE

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ABSTRACT

TROY TRYGSTAD Pharm. D., M.B.A.: An Analysis of the North Carolina Nursing Home Polypharmacy Initiative
(Under the direction of Dale Christensen, Ph.D.)

This dissertation is an evaluation of the North Carolina Polypharmacy Initiative (Initiative). The Initiative was a demonstration project that remunerated nursing home consultant pharmacists for value-added drug regimen reviews using a claims-generated patient profile that flagged targeted drugs and drug classes for review.

Shewhart's PDSA (Plan-Do-Study-Act) cycle is used as the framework to guide this evaluation. The Initiative brought about three distinct PDSA cycles throughout its history. The first was the pilot project, and the second was a statewide endeavor, while the third continues through other programs and settings in North Carolina. It is the goal of this dissertation to inform the planning stage of future PDSA cycles of pharmacist services in nursing home settings.

Three formal evaluations of the initiative were conducted. The first evaluation, a before-after without comparison group study found a per member per month (PMPM) drug cost savings of $30.33 due to initiative activities. The second, a before-after with comparison group study found a PMPM drug cost savings of $19.04. The third, a before-after with propensity matched comparison group found a PMPM drug cost savings of $21.36. Flags (alerts) were reduced for two types of alert categories across all evaluations and their sub-group evaluations. The first, alerts for drugs on the Prescription Advantage List (PAL)

were substantially reduced with a percentage reduction of 19.2% for all persons having a pharmacist review. The PAL list a voluntary preferred drug list sponsored by North Carolina Medicaid. The second, alerts for drugs on the Clinical Initiatives List were also substantially reduced with a percentage reduction of 9.6% for all residents having a pharmacist review. The Clinical Initiatives List was a list of drugs submitted by consultant pharmacy organizations that were targeted for cost-effectiveness and quality concerns. Overall, Phases 1, 2 and 3 of the Initiative produced consultant pharmacist reviews for 19,144 nursing home residents. These reviews generated 17,545 recommendations that resulted in greater than 10,000 drug changes.

Findings from this dissertation support the conclusion that a targeted program using pharmacists to review patient profiles may be quickly launched and expeditiously conducted across large numbers of patients, at least in long-term-care settings.

ACKNOWLEDGEMENTS

I have been so fortunate in my formative years to have been subjected to a culture of academic inquiry. Certainly, my parents are to blame, but also many teachers, coaches and mentors over the years who prodded me along. I cannot list them all here, for there are so many to which I owe a debt of mentorship. I am truly fortunate.

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ongoing as well as terminal evaluations of the Initiative. Many others employed with and affiliated with AccessCare were quick to assist in all matters related to this work. In over four years, I was never placed second in line for help, not once.

My other committee members should be applauded for their support as well. I have had the privilege to work with an engaged, active and diverse committee membership that are leaders in their respective areas of expertise. Dr. Michael Murray was rather benevolent to accept my request for committee service given his responsibilities as Chair of the Division of Pharmaceutical Outcomes and Policy, all the while engaged in many research projects of his own and other students to mentor as a major advisor. I want to thank Dr. Richard Hansen, who, aside from my major advisor, provided the most critical and valuable of comments in this dissertation. Every dissertation committee should have a member with his fortitude. Dr. Rob Sullivan is, quite possibly, the most sincere and well-intended health care provider of all time. For the benefit of all of us, we can only hope that his commitment to improving the quality of care provided to the elderly and his willingness to collaborate with allied health professionals translates to future generations of physicians.

I leave my final thanks to Dr. Dale Christensen. What is written below is an excerpt from a nomination letter for the newly created, "Faculty Award for Excellence in Doctoral Mentoring". I know not weather he will receive this award as it remains open for nomination, but I feel obligated to include some of the nomination's contents since they most accurately describe my heartfelt gratitude.

"I have found Dr. Christensen's advising philosophy of "it's not mine it's yours" exceptionally valuable in the development of my research skills. Always present to reassure and redirect, he was steadfast in his role as an *advisor* and not a director of human labor. He

excelled at creating a culture of research ownership that required his graduate students pave their own way and troubleshoot their own problems, while ever-presently watching closely over their work. I recall many instances during my stay here in Chapel Hill, where I was certain that my five year dissertation project was going to kill me. In every instance, he knew exactly what to say, when to say it and how to go about fixing the problem.

I am very fortunate to be his very last student in a long line of graduate students that have had the privilege to work under his tutelage. Recent advisees have left this university to excel in their respective research endeavors as well as become leaders within their community. His former students are often at forefront of evolving Pharmaceutical Care practices, holding chair or other leadership positions within their respective academic or commercial units, all the while acting as mentors to countless other students such as myself.

He has effectively passed the torch to his students, and receiving it is humbling indeed. The only true measure of repayment for his kind and genuine mentorship to us is to offer the same to others.

His dedication to this university and its students should be unquestioned. I often tell the story to anyone in doubt, of the near certainty of his vehicle being parked in the very first space at the School of Pharmacy every day for years on end. This was a parking spot that was highly coveted but assigned to nobody, there solely for the first to arrive in the morning. A late worker myself, I frequently found him working late into the night as well.

As I finish my own work here, I am left to ponder how I may best use the skills I have acquired during my stay here in Chapel Hill. Leaving will not be easy, though he would insist I take my own path. Undoubtedly, my own footprints will bear some resemblance to a dear old friend, my best advisor, Dale Christensen."

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LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
AJGP	American Journal of Geriatric Pharmacotherapy
CCNC	Community Care of North Carolina
DRR	Drug Regimen Review
DTP	Drug Therapy Problem
DUR	Drug Utilization Review
Initiative	The North Carolina Polypharmacy Initiative
ITT	Intention-To-Treat
JMCP	Journal of Managed Care Pharmacy
MAI	Medication Appropriateness Index
MMA	Medicare Modernization Act
MTMP	Medication Therapy Management Program
NC	North Carolina
NSAID	Non-Steroidal Anti-Inflammatory Drug
OBRA	Omnibus Budget Reconciliation Act
OT	On-Treatment
PAL	Prescription Advantage List
PDCA	Plan Do Check Act
PDP	Prescription Drug Plan
PDTP	Potential Drug Therapy Problem
PMPM	Per Member Per Month
RCT	Randomized Clinical/Controlled Trial

SQL	Structured Query Language

CHAPTER 1

DISSERTATION SCOPE

This dissertation presents an overall evaluation of the North Carolina Polypharmacy Initiative (Initiative). The Initiative was a demonstration project that remunerated nursing home consultant pharmacists for value-added drug regimen reviews using a claims-generated patient profile that flagged targeted drugs and drug classes for review.

Shewhart's PDSA (Plan-Do-Study-Act) cycle is used as the framework to guide this evaluation. The Initiative brought about three distinct PDSA cycles throughout its history. The first was the pilot project, which was used for planning and justification of the statewide implementation of the Initiative. The second PDSA cycle, Phase 1 of the statewide program was of sufficient success to warrant pilot projects in other settings within the state. The third and final PDSA cycle occurred with Phases 2 and 3 and could be replicated throughout many other programs and settings either nationally our through initiatives not affiliated with the North Carolina Polypharmacy Initiative.

As pharmacist intervention programs such as this Initiative begin to proliferate, guidance from previous experience is prudent. It is the goal of this dissertation to inform the planning stage of the third PDSA cycle. To this end, the main objective of this work is to:

1) Determine if the Initiative was successful in reducing drug expenditures while simultaneously maintaining or improving the quality of care received by nursing home patients

The overall objective will be met by accomplishing the following sub-objectives:

A) Determine if pre-determined potential drug therapy problems decreased following pharmacist action

B) Determine if drug costs decreased following pharmacist action

C) Determine if hospitalization rates either decreased or remained constant following pharmacist action

D) Establish which pharmacist actions and in which sub-groups patients experienced the greatest decrease in alert rates

E) Establish which pharmacist actions and in which sub-groups patients experienced the greatest decrease in drug costs

After these objectives are met, I continue with interpretation and comment on these findings in the context of the PDSA cycle. I end the dissertation by offering lessons learned and provide suggestions for developing future drug review services: both generally for ambulatory settings and specifically for Medicare recipients receiving drug coverage through prescription drug plans (PDPs) beginning in 2006. Finally, I outline six policy implications resulting from the findings of this dissertation.

CHAPTER 2

THE PROBLEM OF POLYPHARMACY IN THE ELDERLY

2.1 Quality

Elderly persons are especially vulnerable to drug-related problems. Drug-related morbidity and mortality have been identified as major problems in the elderly, and the two major causes are therapeutic failure (i.e., inadequate drug therapy) and adverse drug reactions.[1-4]A study of 1492 nursing homes in five states showed that 33% of residents received at least one potentially inappropriate drug.[5] Two studies in particular have documented a link between elderly hospital readmissions and drug related problems in 18%-28% of the cases.[6,7] Compounding the problem is high prescription drug use; elders are at greater risk for experiencing sub-optimal drug therapy (i.e., polypharmacy, inappropriate use, or underutilization), which can lead to therapeutic failure or adverse drug reactions.[8-10] The risk of adverse drug reactions increases with the number of regularly scheduled medications.[11]

Among residents of long-term care facilities, potential drug therapy problems (PDTPs) are magnified because of the typical resident's more frail state of health, and greater use of prescription drugs. Several studies have noted the prevalence of drug related problems in nursing home settings.[12-19] Studies have also shown that pharmacists are effective at reducing the number of drug related problems.[20,21]

2.2 Cost

National attention has been directed to the problem of rapidly rising costs of medications for the greater part of the last two decades. Growing pressure from Medicare recipients, especially those with fixed income, led to a crescendo of pleas for drug coverage over the past decade. Subsequent passage of the Medicare Modernization Act of 2003 (MMA 2003) provided prescription drug coverage beginning in 2006. Medicare will soon become the largest single payor of drug benefits in the United States, with a projected $70 billion in expenditures in 2006.[22]

CHAPTER 3

THE GENESIS OF THE NORTH CAROLINA POLYPHARMACY INITIATIVE

3.1 Escalating Medicaid Drug Expenditures

Prior to MMA 2003, State Medicaid programs were bearing the brunt of rising prescription drug costs for low income nursing home residents. State Medicaid programs and insurers faced a double-digit rise in prescription drug costs per insured person. Within NC, Medicaid costs approximated $ 7.4 billion per year in 2003, [23] with prescription drugs approximating $ 1.2 billion per year.[24] The drug component was rising at rate of 17% annually.[25] Of particular interest to this dissertation, the elderly accounted for only 11% of enrollees[26], but 32% of all prescription drug costs prior to the implementation of MMA 2003.[27] Countercyclical demands of Medicaid's fiscal requirements compounded the problem of escalating per member per month drug expenditures. In periods of economic recession, governmental income tax receipts shrink as a result of declining personal as well as corporate income. Simultaneously, more citizens become eligible for means-tested Medicaid benefits, putting further strain upon state budgets. In North Carolina, two cost-reduction strategies emerged from this period of budgetary strain: 1) reduce provider fees (pay less for services) 2) reduce drug costs (pay less for products).

3.2 AccessCare Network of Physicians (Community Care of North Carolina)

In response to the possibility of a reduction in provider fees, physician groups began to solicit proposals for a program that would help constrain drug expenditures within the

most costly strata of Medicaid recipients, nursing home residents. AccessCare, a component of Community Care of North Carolina (CCNC) physician provider system, was chosen to generate possible strategies to this end. AccessCare is one of the largest provider networks within CCNC, representing approximately 1,500 physicians in 200 group practices, 14 counties and 20 communities throughout the state North Carolina. AccessCare has been responsible for administering many demonstration projects within North Carolina Medicaid since 1991. CCNC operates through collaborative agreements with local community organizations and physician group practices that work together to enhance the quality and control costs of care for Medicaid recipients. CCNC providers are care for nearly 70% of the State's Medicaid enrollees.

3.3 The Long-Term-Care Pharmacy Alliance

The North Carolina Long Term Care Pharmacy Alliance is a group that is broadly representative of pharmacists serving nursing homes throughout the state. Long-term-care pharmacies were concerned that reduction in both dispensing fees (fees charged for the service of dispensing of the drug product) as well as drug product reimbursement (the amount paid for the drug product itself) would be particularly burdensome. Motivated by the possibility of a reduction in operating margins together with the emergence of a group of primary care providers willing to work collaboratively, long-term-care pharmacists began to generate ideas for a polypharmacy reduction program in nursing homes using their network of pharmacists and pharmacy organizations. These pharmacists were familiar with the patients in their respective nursing homes, and had existing relationships with physicians providing care at each site, allowing such a program to gain broader acceptance with fewer hurdles to prevent implementation.

3.4 Program Scope and Objectives

Initially, the polypharmacy reduction program was conceived as a short-term, single intervention activity in response to a cyclical decline in Medicaid fiscal health. However, the AccessCare network, along with other CCNC network provider groups, had a engaged in many types of demonstration projects that ultimately changed processes of care provided by primary care givers in North Carolina. The institutional memory these projects created along with the networks' predisposition for progressive care processes ultimately nurtured the development of the pilot project and ultimately the statewide initiative. Thus, the AccessCare network conceived and launched a polypharmacy program that aimed to demonstrate the long-term viability of a value-added drug regimen review system that would be conducted by consultant pharmacists working in collaboration with the attending physician. This program was titled The North Carolina Medicaid Polypharmacy Initiative (Initiative). Key to this long-term viability was a formal evaluation of the cost-effectiveness of the Initiative and its ultimate effect on drug expenditures. Additionally, stakeholders (i.e., NC Medicaid, CCNC providers) sought to determine that the Initiative would be scalable, expeditiously disseminated to all nursing homes in the state), and continuously modified to respond to both the needs of North Carolina Medicaid as well as the prescription drug marketplace. Most importantly, physicians, pharmacists, and administrators strongly believed that any endeavor to reduce drug costs could be conducted while preserving the quality of care provided to patients.

As a result of these requirements, the PDSA (Plan-Do-Study-Act) framework was chosen to guide the evaluation and continuously improve of the Initiative.

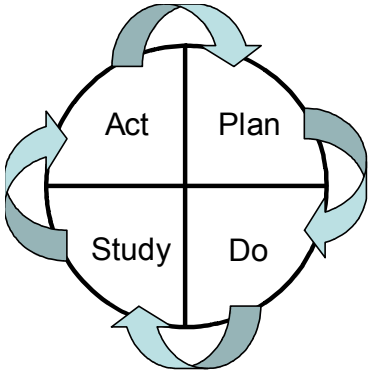
CHAPTER 4

TESTING THE EFFECT OF CHANGE IDEAS ON THE PERFORMANCE OF THE HEALTHCARE SYSTEM: SHEWHART'S PDSA CYCLE

4.1 Walter A. Shewhart's PDSA cycle

Walter Shewhart introduced "statistical control" to Bell Telephone laboratories in the 1920's, and to the world in 1931 through his seminal work, *Economic Control of Quality of Manufactured Product.*[28] He became known as the "Godfather of Total Quality Management" for promoting continuous improvement through recycling through the PDCA (Plan-Do-Check-Act) framework. It was the continual and perpetual use of critical appraisal and subsequent implementation of the cycle which compelled manufacturing industries such as automakers to adopt his strategies to improve their products. Later coined the PDSA (Plan-Do-Study-Act) cycle (Figure 4.1), and expanded upon by his colleague at Bell Laboratories, W. Edwards Deming, the process was applied in "real-time" and most recently in a more general manner, was found to be applicable to all products and services.

Figure 4.1 The Shewhart-Deming PDSA Cycle



The hallmark of the PDSA cycle is its repetitive evaluation of real-world experiences. This feature makes employment of the PDSA cycle compelling for evaluation and improvement of an intervention program such as a polypharmacy reduction program in nursing homes where drug regimens are subjected a quality review at scheduled intervals.[29] Furthermore, the cycle emphasizes effectiveness over efficacy, through process improvement and transformation. Many researchers agree that an operational gap exists between closely monitored and controlled randomized clinical trials (RCTs) environment and resource and behavioral constraints of the health care marketplace. However, the PDSA framework does not stop at emphasizing effectiveness. The findings from a program's **Study** or analysis of what was **Done** are to be **Acted** upon and inform the next cycle's **Planning** phase.

4.2 Theodore Speroff's Healthcare Application

While PDSA techniques began to infiltrate manufacturing industries in the 1930's, only recently have they been applied in service industries, with healthcare among the more newly emerging areas of PDSA principles. Theodore Speroff, an epidemiologist by training was one of the first healthcare researchers to apply PDSA techniques in a healthcare setting. He rendered a set of guidelines for appraisal and publication of quality improvement research.[30] His focus was on application of research findings to real world practice. As Speroff and colleagues put it in their guidelines publication, "The focus on implementation in everyday practice is the single most important factor that distinguishes quality improvement from traditional evaluative research".[30] moreover, they note that traditional observational research stops short of applying findings in the **S**tudy stage, whereas quality improvement research uses those findings to implement and operationalize "change ideas"[30] resulting from past evaluations. The authors of these guiding principles purport the PDSA cycle to be "the

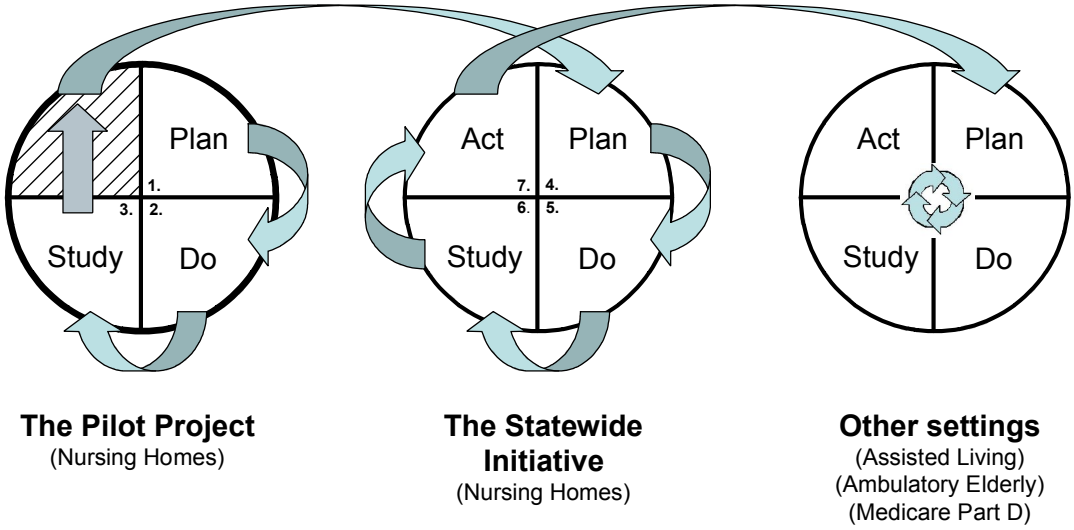
application of the scientific method to implement and test the effects of change ideas on the performance of the health care system". Three core activities as outlined by Speroff to guide both researcher and administrator:

1) To seek an understanding of the sources of systematic as well as unwanted and unnecessary variation
2) To implement cost-effective strategies to reduce unwanted variation
3) To produce organization-wide knowledge on structured approaches to change process and improve outcomes

4.3 Initiative PDSA Cycles

In the planning and launch of a demonstration project in nursing homes in North Carolina, leaders of the Initiative implicitly adopted these core activities. First, they needed to acquire an understanding of the main drivers of prescription drug costs within their patient population. Any unnecessary variations from the standard of care had to be identified to clarify specific operational objectives. Second, it was imperative to understand what perpetuated these deviations and find a cost-effective manner in which to reduce the incidence of sub-optimal prescribing. Activities one and two are of no value unless the third, dissemination of knowledge is successfully performed. If proven successful, the proliferation of the Initiative to other geographic locations, settings, and populations will ultimately decide its success or failure. As such, I strive in this dissertation to employ all three activities from inception of the initiative, its pilot project, Phases 1, 2, and 3 of the statewide initiative to the guidance provided for future Initiatives addressing Polypharmacy via drug review (Figure 4.2).

Figure 4.2 The North Carolina Polypharmacy Initiative's PDSA Cycles



The Pilot Project
(Nursing Homes)

The Statewide Initiative
(Nursing Homes)

Other settings
(Assisted Living)
(Ambulatory Elderly)
(Medicare Part D)

While I make use of all three core activities in this dissertation, the primary focus is to the second core activity (**S**tudy) stage of the PDSA cycle. Its aim, to employ robust statistical techniques to rigorously evaluate the success of the Initiative in reducing drug costs while simultaneously ensuring the standard of care has not been compromised, will be accomplished through quasi-experimentation and statistical matching of study and comparison subjects. The results herein are intended to inform programmatic planning and budgetary outlays for future PDSA cycles.

CHAPTER 5

PLANNING AND DEVELOPMENT OF A CHANGE IDEA: SUPPLEMENTARY REVIEW OF PATIENT DRUG THERAPY REGIMENS

5.1 Engendering Value-Added Reviews to Reduce Drug Costs

To meet program objectives of drug cost reduction and maintained or improved drug-related quality, Initiative administrators determined that using existing infrastructure of pharmacists and prescribers in already employed in long-term-care settings would be most expedient. Program administrators determined that a supplemental review that emphasized a critical appraisal of both sub-optimal therapy *as well as* sub-optimal value could most effectively be carried out by a pharmacist-prescriber team that was already engaged in ongoing reviews.

5.2 History and Context of OBRA 87

Beginning in the 1970s, federal regulations were adopted that required monthly drug regimen reviews (DRR) be conducted in long-term care facilities by consultant pharmacists at least once per month.[29] Subsequent revisions to the Omnibus Reconciliation Act (OBRA 87) required that this review be accomplished in collaboration with the attending physician. These regulations contained explicit requirements for reviewing therapy for targeted drugs and drug classes with a high probability of overuse or inappropriate use in long term care settings. While such reviews have resulted in improved care since first mandated[16], there seems to be room for improvement [1]and a more comprehensive approach based aimed at

optimizing both the type and use of *all* drugs taken by the elderly seems prudent. Program administrators believed that augmenting the existing drug regimen review process with a supplementary review that targeted drugs and drug classes not explicitly addressed by OBRA 87 legislation would lead to reductions in total drug costs while simultaneously improving the quality of therapies prescribed.

5.3 OBRA 90: Drug Utilization Review and Population Level Interventions

The passage of OBRA-90 placed additional drug utilization review (DUR) requirements on state Medicaid programs. The legislation compelled states to establish committees and systems to conduct retrospective and prospective review patterns of drug use believed to be problematic in ambulatory enrollees. Prospective reviews are defined as review activities occurring at the time the prescription is dispensed, while retrospective reviews are focused on periodic reviews of prescribing and drug usage patterns based on claims data.

Prospective DUR is most widely employed through pharmacy-based computer algorithms that alert the dispensing pharmacist to potential drug therapy problems (PDTPs) during online adjudication of claims. While the alert is patient-level, it is not patient-specific. Alerts are usually drug-specific and sometimes drug-condition-specific, but are rarely customized based upon the characteristics and nuances of the individual patient. This deficiency is most pronounced in the high incidence of false positive alerts.[31] Retrospective DUR is operationally less standardized and is managed at the state level. Typically, work is done at the committee level with an emphasis on patterns of drug use with interventions of various types to achieve the desired result. The most common intervention is through

advisory letters to physicians. To date, retrospective DUR activities have emphasized reviews of drug therapy based upon population-level observation.

5.4 Using Administrative Claims to Generate Targeted Alerts

Program administrators set out to design a program that combined the state-level, top-down administration characteristics of retrospective DUR activities with patient-level, pharmacist-driven activities typical of OBRA-97 DRR reviews. During Phase I, records were retrieved and examined for Medicaid recipients' prescription usage in 13 selected nursing homes served by physicians in the AccessCare network. Patient drug profiles for each nursing home were then created. Algorithms were developed to screen patient records for signs of potential inappropriate and/or polypharmacy drug therapy problems such as therapeutic duplication, inappropriate drugs being used (based on the Beers drug list), multiple prescribers, and higher than normal drug usage. The consultant/ pharmacist verified the completeness of the patient database as well as the completeness of the drug profile for each patient during the first visit to the nursing home facility. The consultant/pharmacist reviewed and confirmed the patients' prescription regimen and then made recommendations to prescribers.

Based on the consultant/pharmacist recommendations, the prescriber was to decide on one of three alternatives: (1) no change/recommendation rejected, (2) recommendation accepted, or (3) recommendation accepted with other changes. Consultant/pharmacists were to document their process activities, including: which patients were reviewed, the type of recommendation made, whether or not the recommendations were accepted, and what drug therapy changes were made. Supplemental notes, records, and hard copies of the recommendation orders were maintained by participating pharmacist-physician pairs to

verify the integrity of the databases and maintain consistency of data entry across nursing homes.

5.5 Implementing the Nursing Home Pilot Project

Beginning in March 2002, the pilot program was launched in 13 nursing homes. The intervention consisted of a drug therapy management service provided by a pharmacist-physician team. The team 1) reviewed drug profiles and other medical records of Medicaid patients in nursing homes, 2) determined if a drug therapy problem existed, 3) recommended a change, and 4) followed up to determine if the change was implemented.

A variety of drug regimen review approaches to this review were allowed. Most pharmacists superimposed the profile review onto their monthly DRR reviews. Some pharmacists initiated a separate review cycle incident to the Initiative. In five of the nursing homes in one particular county, medical residents were utilized as part of the pharmacist-physician team. In some of the homes, both targeted as well as non-targeted residents were reviewed. In other homes, recommendations were reviewed with Access II and III Medical Directors. Subsequently, the pharmacist/consultant and medical directors met with attending physicians to discuss specific recommendations.

Pharmacists reviewed patients only after obtaining permission of the Department of Medical Assistance and the nursing homes as well as their Medical Directors and attending physicians. Confidentiality agreements were in place as a condition for Medicaid enrollee and providers participation.

All review documents were returned to AccessCare Inc. for evaluation. To assess cost impact, each specific drug recommendation was tracked and labeled as to whether or not it led to a *therapy change*, *discontinued drug* or *added drug* for each patient. For each drug

change (addition or deletion), its cost impact was calculated by determining the average baseline drug cost per month and projecting these costs to the after period (one year). The data source for determining costs was baseline Medicaid claims data for three months prior to the start of the intervention (i.e., November 1, 2001 to January 31, 2002) in the pilot nursing homes. All projected drug costs were determined by taking the average amount paid by Medicaid for a month's supply of each prescription identified by its unique drug name and dose (if available).

A payor perspective was used, focusing on the amount paid by Medicaid to pharmacies. While North Carolina Medicaid has a 6 prescription per patient per month benefit cap, many elderly patients had exceeded this cap under an exception procedure. Some patients without documented exemptions may have nevertheless received prescriptions but their drug claims (greater than 6 drug fills) were paid directly by the nursing home.

CHAPTER 6

RESULTS FROM THE NURSING HOME PILOT PROJECT

6.1 Pilot Project Results

Of the 13 pilot nursing homes, all but one completed the intervention and provided data available by the end of the requested period. Results for the remaining 12 homes are briefly summarized below.[32] A more detailed report if the findings from the pilot project are found in Appendix C.

Baseline Use: Medicaid nursing home patients used, on average, 6.1 prescriptions per month (median = 6, standard deviation = 3.3, range = 1-18). The average cost of a single prescription for a 30 day supply of a drug $54.81. The average cost per patient per month for prescription drugs was $336.68 (median cost = $269.19)

Frequency of Recommendations: Consultant/pharmacists reviewed 673 Medicaid patients in 12 of the assigned 13 nursing homes (One of the nursing homes did not report back results) The pharmacist-physician team made drug change recommendations for 37.7% (254/673) of all patients reviewed.

Frequency of Changes: Of the 4,134 prescriptions reviewed, 408 (10%) had a recommendation for some type of change. Of the 408 drug change recommendations made by the consultant/pharmacist, 236 (57.8%) were acted upon (accepted or rejected) by the physician. A recommendation to discontinue (D/C) a drug occurred in 124 or

30%, and another 69 (17%) involved a recommendation to change therapy from one drug to another. 20 drugs were added to patients' regimens for new indications.

Drug Cost Savings: The baseline costs for one month of prescription drug usage across 12 nursing home sites was $226,588. The resultant cost after the reviews was $217,143, representing a 4.2% savings of $9,445 for the first month. An annualized gross annual savings of $113,340 would be achieved assuming these changes in drug therapy persisted for the entire year for all patients reviewed.

Cost Minimization Ratio: Subtracting the $8,700 cost to hire pharmacist consultants and reimburse special physician consultant panels for their review services, the first year annual savings to costs ratio is estimated at 13 to 1.

6.2 Informing the Statewide Implementation of the Polypharmacy Initiative

Analyzing the results from the pilot study enabled project administrators to make informed changes before the rollout of the Statewide Initiative. PDSA cycles are recurring, and the study phase was immaterial without actionable results to inform the next cycle. The pilot program was formed loosely, without rigid construction, to identify alternative strategies that reduce drug costs. This strategy enabled a viable and practicable model to emerge that could be replicated many times over for the Statewide Initiative. Several notable points were found in the analysis of the results from pilot project study.

Variation in Intervention Intensity: There was considerable variation in the number of reviews conducted by consultants/pharmacists. In some cases, all of the patients in a home were reviewed. Some homes (five nursing homes in one particular county), only targeted patients (i.e., those flagged with possible drug therapy problems) were reviewed,

whereas all patients who where Medicaid eligible received reviews in other homes. Across nursing homes, the number of patients reviewed ranged from 12 to 195.

There was also variation across nursing homes in the percentage of patients receiving change recommendations by the consultant-pharmacist team. Though the team in aggregate made some type of recommendation for change in drug therapy for 37.7% (254/673) of the patients reviewed, the percentage of patients with problems identified and recommendations made ranged from 5% to 100% across nursing homes.

Variation in Intervention Provider: Interventions were initiated by consultant pharmacists in most homes. However, in five of the nursing homes in one particular county, medical residents were utilized as part of the pharmacist-physician team. In these homes, recommendations were reviewed with Access II and III Medical Directors. Subsequently, the pharmacist/consultant and medical directors met with attending physicians to discuss specific recommendations.

Variation in Recommendation Type: The drugs most frequently involved in drug discontinuation and change decisions were, in descending order of frequency: Prevacid, Prilosec, Celebrex, Zyprexa, and Norvasc. However, quite often consultant pharmacists made differing recommendations for drugs in the same class. While differing therapeutic rationales may have driven this divergence, it was frequently the case that pharmacists and physicians who initiated interventions tended to make the same types of recommendations and drug changes. Despite the variation in recommendation type and alternative drug preference, the average savings from a prescription discontinuation was $57.68 for a month's supply. The average savings for the replacement of one drug with another was $33.23 for a month's supply.

Acceptance of Recommendations: Across nursing homes, 42% of recommendations to change therapy were either ignored or rejected. In four homes, all recommendations were accepted by prescribers. Yet one home garnered 56 recommendations without any acceptance from prescribers. The cause of this success disparity was not determined.

Time to Intervention: Patient profiles were generally returned in a timely fashion (within three months of program initiation). However, given the time-sensitive nature of the interventions and resultant costs savings projections, the pilot project analysis made evident the need for better tracking of the time of the intervention. Both the date of the recommendation as well as the date of the follow-up would be needed to accurately track intervention activities, and follow-up for laggard profile reviews.

North Carolina Medicaid's Six-Prescription Limit: There was considerable variation across nursing home settings in terms of the number and costs of prescriptions consumed by elderly residents. Findings showing that nursing home patients used a high number of drugs at high cost to Medicaid are consistent with what is generally known about elderly nursing home patients' drug use patterns nationally. The finding that patients used a median of 6 prescriptions per month indicates that at least half of them obtained drugs through an exceptional use procedure or had their medications covered directly by the nursing home itself. It became evident through feedback from pharmacists in the field that the vast majority of persons using more than 6 prescriptions per month had filed and received an exemption from this limit. Thus the likelihood of drug use not captured in administrative claims was low. However, program administrators suggested that all drugs, including over-

the-counter medications be reported on patient profiles provided in future Initiative cycles to accurately and comprehensively depict resident drug use.

Variable Overall Success Across Homes: Considerable variation was observed across homes with regard to intervention intensity and success. The reasons for this variation were not entirely clear. It was not determined why the pilot program was more successful in some of the nursing homes than in others, especially recognizing that all have, by regulatory requirement, review and quality assurance systems in place as outlined in OBRA 87 regulations and updates. It may be that consultants typically audited for safety, compliance, quality, and legalities or liabilities/risk exposure but gave less emphasis to cost effectiveness. In this pilot, however, a special emphasis was given to the potential for cost savings. Secondly, perhaps "another pair of eyes" provided by the pharmacist-physician team detected more problems or more opportunities for drug cost savings. Third, it may have been that problems/opportunities were previously detected or noted in records by consulting pharmacists, but simply not acted upon because of the lack of follow-up.

6.3 Major Findings

A. Baseline drug use was significant, especially for enrollees using greater than 18 prescription fills in 90 days

B. Individual variation existed in number of recommendations, recommendation type, reviewer type, and success

C. Substantial numbers of recommendations could be garnered in this setting and with this approach

D. Substantial savings resulted recommendations when accepted

E. The six prescription limit was inconsequential to overall results, but nonetheless needs to be addressed in future phases of the Initiative

F. More emphasis on follow-up would be required for future phases of the Initiative

G. Monitoring of the review process throughout its life-cycle will help maintain Initiative inertia and ensure quality reviews

H. Requirements for follow-up are critical to recommendation attribution and subsequent program measurement and evaluation

6.4 Lessons Learned from the Pilot Project

Given the results of the pilot project, it became apparent that a program of review of Medicaid nursing home patients by pharmacist-physician consultants was cost-beneficial based solely on drug cost savings. Assuming that the drug use experiences of other NC Medicaid nursing home patients is similar to those in these homes, there seemed to be an opportunity to expand the Initiative and attempt to optimize therapy among NC nursing home Medicaid patients. Using a value-added, supplemental review had proven successful through piloting.

Additionally, the findings supported the role of pharmacists working collaboratively with physicians in this activity. A recent Cochrane database review indicated that clinical pharmacists, working collaboratively with physicians, can be effective in addressing drug related problems among patients.[33] These studies imply that interventions of the type conducted in this pilot study have the potential for additional savings from reduced hospitalizations and other health care system costs.

The pilot project results suggest that having pharmacist-physician review teams make periodic visits to targeted nursing homes may improve both the quality and cost of drug therapy reviews. These findings supported the conclusions of other researchers that drug therapy received by the elderly could be improved from a qualitative as well as a cost-effectiveness standpoint. Based upon those conclusions, the statewide initiative was approved by the Division of Medical Assistance (Medicaid) with the approval of the Office of Rural Health and Demonstration Projects.

CHAPTER 7

ACTING ON THE FINDINGS OF THE PILOT PROJECT AND PLANNING FOR THE STATEWIDE INITIATIVE

7.1 Programmatic Changes Resulting from the Findings of the Pilot Project

One of the resulting themes of the pilot project was a lack of standardization in terms of which patients received (e.g. targeted patients, all Medicaid patients, or all patients in the home), who conducted the reviews (e.g., traveling pharmacists, physicians, or both; on-site consultant pharmacists). and what the focus of those reviews (e.g., which drugs and/or drug classes would be emphasized for review). Conducting a statewide initiative with review of greater than 10,000 residents would require a more streamlined approach that utilized a more well-defined intervention that was reproducible and measurable. Some programmatic changes included:

Emphasis of consultant pharmacists as point persons for coordinating profile reviews: To decrease the lag time to review and recommendation, existing consultant pharmacists were chosen as the primary coordinators of review activities. Reasons for this decision included: Existing consultant pharmacists would be were familiar with coordinating reviews at both the dispensing settings as well as on-site, through scheduled OBRA-87 required DRRs. Additionally, the long-term-care pharmacy market in North Carolina was relatively concentrated and top-heavy, with five organizations responsible for DRR reviews

of greater than 70% of the state's nursing home residents, making it easier to coordinate and efficiently implement new review requirements. All nursing home pharmacy consulting organizations were members of the Long-Term-Care Pharmacy Alliance that had endorsed the initiative prior to the pilot project. Unlike the pilot project, thousands of patients in hundreds of homes would require review. A relatively small number of uniformly-trained pharmacists could review drug profiles for the majority of Medicaid enrollees in nursing homes in a short period of time (2-3 months), reducing time to launch and program uptake.

A more well-defined patient profile: To aid in the efficiency and yield of profile reviews, AccessCare collaborated with the NC Long Term Care Pharmacy Alliance to develop an action plan and a Toolkit© for consulting pharmacists. The Toolkit© contained instructions for documenting consultations and explained the screening criteria used to select (flag) drugs for attention (Figure 6.1). The Toolkit was introduced consultant pharmacists to the project during two one-hour group meetings and one hour-long conference call in September and October 2002. Pharmacists were provided with the Toolkit©, and received individual training from the lead consultants in their organizations. Each consultant pharmacist was provided with a Toolkit© as well as printed drug profiles of screened patients which contained computer-generated prompts for selected drugs and classes of drugs.

The Toolkit and patient profile were developed to ensure consistency of interventions. Since many different pharmacists were involved in this project, these two documents provided a guide and standard procedure for documenting interventions. The toolkit criteria were used to prompt the pharmacist to review specific drug(s) or classes of drugs that had the potential to achieve cost-savings as well as increased quality of care in targeted patients. The first criterion was receipt of a drug generally considered to be inappropriate for use in the

elderly (Beers drug list).[3] A second criterion was receipt of a drug on the CCNC Prescription Advantage List ("PAL"), which encourages substitution of less expensive drugs within a therapeutic class. For each of the ten drug classes represented on the list, certain medications offered potential cost-savings to the Medicaid program (PAL-1) while others either offered no clear cost advantage (PAL-2) or would incur significant costs (PAL-3). The third criterion was receipt of a drug on a list of 'Clinical Initiatives.' This list was developed by the consultants participating in this project, and included 16 drugs and/or drug classes that have the potential for quality improvement and cost savings. The list was derived from NC Medicaid's Top 100 drugs by expenditures for fiscal year 2001. Examples include the review of proton pump inhibitors for appropriate length of therapy and possible switch to a H2 receptor blocker, and the evaluation of residents taking chronic sleep aids for a possible drug holiday or discontinuation. By soliciting input from both prescribers as well as pharmacists, each had ownership in the review process, greatly enhancing the acceptance of the PDTP alerts and the Initiative as a whole.

To further diminish review ambiguity and increase the specificity of the subsequent analyses, the recording procedures were altered to be more specific and all-encompassing of the potential universe of recommendation and result-types (Figure 7.1). Consultant pharmacists were asked to record both the *result of the review* (i.e., the recommendation) and the *result of the intervention* (i.e. the outcome) onto a specially prepared documentation form (i.e. The Intervention Tool™). The following types of problems were documented: Unnecessary Drug Therapy, More Cost Effective Drug Available, Wrong Dose/Delivery, Potential for Adverse Drug Reaction, Needs Additional Therapy, and Other Problem. The following intervention results were coded: Dose/Delivery Changed, Drug Added, Drug

Changed (from one to another), Drug Discontinued, No change, and Other. If an intervention resulted in drug therapy change of any type, the original drug, dose, and quantity was noted as well as the changed drug, dose, and quantity. Drug, dose and quantity were also reported for each new drug added for previously untreated indication.

Overall, the patient profile for the statewide initiative was designed to reduce unwanted variation in response. In line with the traditional manufacturing roots of PDSA, the profile utilizes a standardized format, with replicable and structured data sources.

Figure 7.1 Example Resident Profile

Nursing Home PolyPharmacy Project - Patient Profile **Patient Name** Medicaid ID Page 1 of 4 5/7/2003

Nursing Home Practice: Nursing Home Name and Number

Patient ID: XXXXXXX **Last Name:** XXXXXXX **First Name:** XXXXXXX

Gender: F **Age:** 82 **DOB:** xx/xx/xxxx **Avg # of Drugs/month:** 7.67 **Avg monthly drug $:** $625.85

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Fill Date	Drug Class	Medication	Amount Paid	Prescriber	PAL	Potential Theraputic Duplication	Clinical Initiatives/Quality	Consider Length of treatment*	Beers List ≥ 65	Problem Type	Results Type	New Drug and Strength
7/30/02	ANALGESICS, NARCOTIC	ULTRACET TABLET *d*	$164.96	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
8/16/02	ANTINAUSEANTS	METOCLOPRAMIDE 10MG TABLET	$11.81	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
6/5/02	ANTISPASMODIC-ANTICHOLINERGICS	HYOSCYAMINE 0.375MG TAB SA	$16.04	Prescriber Name					X	A B C D E F G	1 2 3 4 5 6	
8/7/02	ANTI-ULCER/OTHER GASTROINTESTINAL PREPS	NEXIUM 40MG CAPSULE	$131.32	Prescriber Name	PAL 3 Prefer Protonix		X			A B C D E F G	1 2 3 4 5 6	
8/9/02	BRONCHIAL DILATORS	ALBUTEROL .83MG/ML SOLUTION	$16.70	Prescriber Name	PAL 1					A B C D E F G	1 2 3 4 5 6	
8/29/02	DIURETICS	FUROSEMIDE 40MG TABLET *a*	$7.52	Prescriber Name						A B C D E F G	1 2 3 4 5 6	

*Please refer to toolkit for further explanation.

Problem Type (Circle all that apply)
A. Unnecessary Drug Therapy
B. More Cost Effective Drug Available
C. Wrong Dose or Strength
D. Drug has High Potential for ADRs
E. Needs Additional Therapy
F. Not a problem at this time
G. Other - Any other problem not listed above

Results Type (Circle all that apply)
1. Dose/Delivery Changed - Dosage or administration was changed
2. Drug Added - New drug was added for previously untreated indication.
3. Drug Change - Drug was changed from one to another.
4. Drug Discontinued - Drug was discontinued or was changed to PRN.
5. No Change - Physician Responded but did not make any changes.
6. Other - Any result not listed above.

Medication Superscripts
***a.* Recommended check for K+ need**
***b.* Recommended use with Ca+ supplement.**
***c.* Recommended check for FE+ need**
***d.* Recommended check for Stool Softener need**
***e.* Recommend check for Folic Acid therapy.**
***f.* Recommend check for supplemental calcium need..**
***g.* TB test needed?**
***h.* Does patient have BPH and HTN? Consider Cardura.**
***i.* Consider dose reduction/excessive dose.**

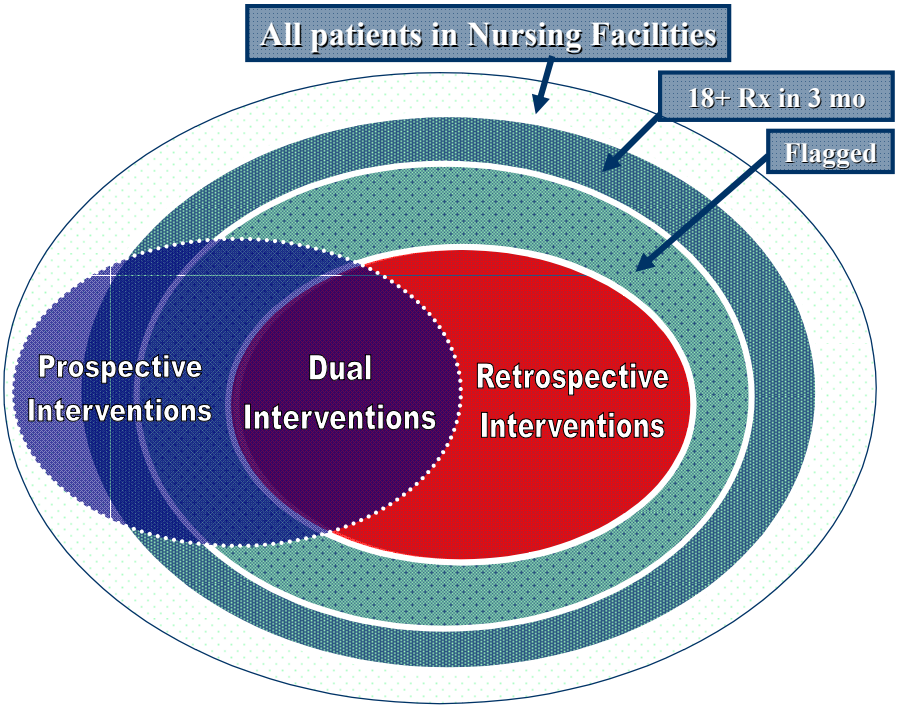
PAL Codes
PAL Code 1 - Preferred Drug
PAL Code 2 - No Preference
PAL Code 3 - Avoid
PA - Prior Authorization Required

Targeting reviews: Rather than generate profiles for all Medicaid enrollees residing in long-term-care facilities, program administrators chose to employ a targeted approach. For phase I, all persons having more than 18 drug fills in 90-days had profiles generated and sent to consultant pharmacists for review activities (Figure 7.2). This decision was based

upon a two-fold motivation: 1) Initiative funds could not bear to compensate pharmacists for the total number of potential reviews for a long-term-care Medicaid population of greater than 25,000 and 2) Targeted reviews were believed to be more cost-beneficial based upon the results of the pilot project. The primary rationale for reviewing targeted patients was to increase the percentage of patients receiving recommendations to maximize return on the payments to pharmacists for review activities. Furthermore, an evolving set of alerting algorithms would be desirable given changes in practice, drug cost and patient setting. This evolution over time is consistent with the PDSA cycle process. Each cycle should have renewed targeting strategies since practice standards and resource use for given products and services change over time.

Prospective Interventions: Consultant pharmacists approached program administrators about performing prospective interventions in addition to targeted retrospective profile reviews. They argued that retrospective profile reviews target and address potential problems well after the problematic drug(s) are dispensed. An earlier review (i.e. targeting the first dispensing of a new prescription order) would delay the detection of a potential drug therapy problem and/or miss an additional drug cost savings opportunity. Their arguments were persuasive, and the Initiative agreed to pay for both types of interventions ensured that high-use patients as well as low-use patients with a high probability for review success (Figure 7.2)

Figure 7.2 Targeting Strategy



Action-driven vs. results-driven incentives: It is advantageous to review the decisions regarding payment rules under the Initiative in the context of health care industry practices. Two general types of payment incentives have developed in the health care industry over time. Action driven incentives such as payment for procedures performed reward caregivers for their services, for example, number and type of visits or interventions performed. In contrast, results driven incentives such as "pay for performance" programs reward providers for achievement of pre-specified metrics. Both types of remuneration for services can align patient-provider incentives to achieve better care. The Initiative employed both of these types of incentives.

Pharmacists were compensated for all profile reviews completed, regardless of the resultant outcome of the review. This action driven incentive encouraged widespread adoption of the Initiative by providing front-end compensation for services performed. If Initiative administrators had required results driven payment for profile reviews, many pharmacist consultant organizations may have seen the up-front costs of establishing a successful review process to be too burdensome to participate in the Initiative, and would have incentivized them to intervene in patients which they had a strong *a priori* belief that their interventions would result in positive results (i.e., drug changes). Pharmacists were compensated at a per retrospective profile review at the rate of $12.50 in phase I of the Initiative. This level of compensation seemed reasonable since targeted reviews would occur at the time of a separately funded regularly scheduled OBRA-87 drug regimen review.

Conversely, payment only for services performed without providing an incentive might have led to stale reviews without diligent effort to vigorously uncover PDTPs. Thus, a results-driven prospective payment system was set up alongside the action-driven profile reviews. Pharmacists were allowed to bill for interventions occurring at the time of dispensing for drugs ordered for patients not targeted in Phase I of the Initiative, or for new drugs ordered for targeted patients. Compensation was allowed if the drug order was changed or not dispensed as a result of dispensing pharmacist review. These "line-item" interventions were compensated at the rate of $6.50 per drug.

Using both action-driven and results-driven incentives provided a balance of motivations among pharmacists and their organizations. Furthermore, the payment system was set up to ameliorate start-up costs associated with the disruption in workflow caused by the implementation of the Initiative in the consultant organizations. One-time overhead

payments were granted to participating pharmacies to encourage participation. All of these elements of payment in combination are believed have aided in the widespread adoption and success of the program from the beginning of the Initiative.

CHAPTER 8

OPERATIONALIZING A STATEWIDE PHARMACIST REVIEW PROGRAM

8.1 Toolkit Orientation

Consultant pharmacists were oriented to the project during a group meeting in October 2002. Pharmacists were provided with the specially prepared Toolkit©, and received individual training by nursing home consulting organization administrative personnel. Individual orientations in person and by teleconferencing were also given for those consultant-pharmacists unable to attend the group orientation.

8.2 Meeting with Prescribers and Administrators

Meetings with prescribers and administrators both within Medicaid as well as Medical Directors at nursing facilities were held in the Fall of 2002 to elicit their support and advocacy for Phase 1 of the Initiative. Attendees learned about the results of the pilot program, the potential qualitative and economic value of the program were it successful, and detailed plans for Phase 1 of the statewide intervention.

8.3 Profile Generation

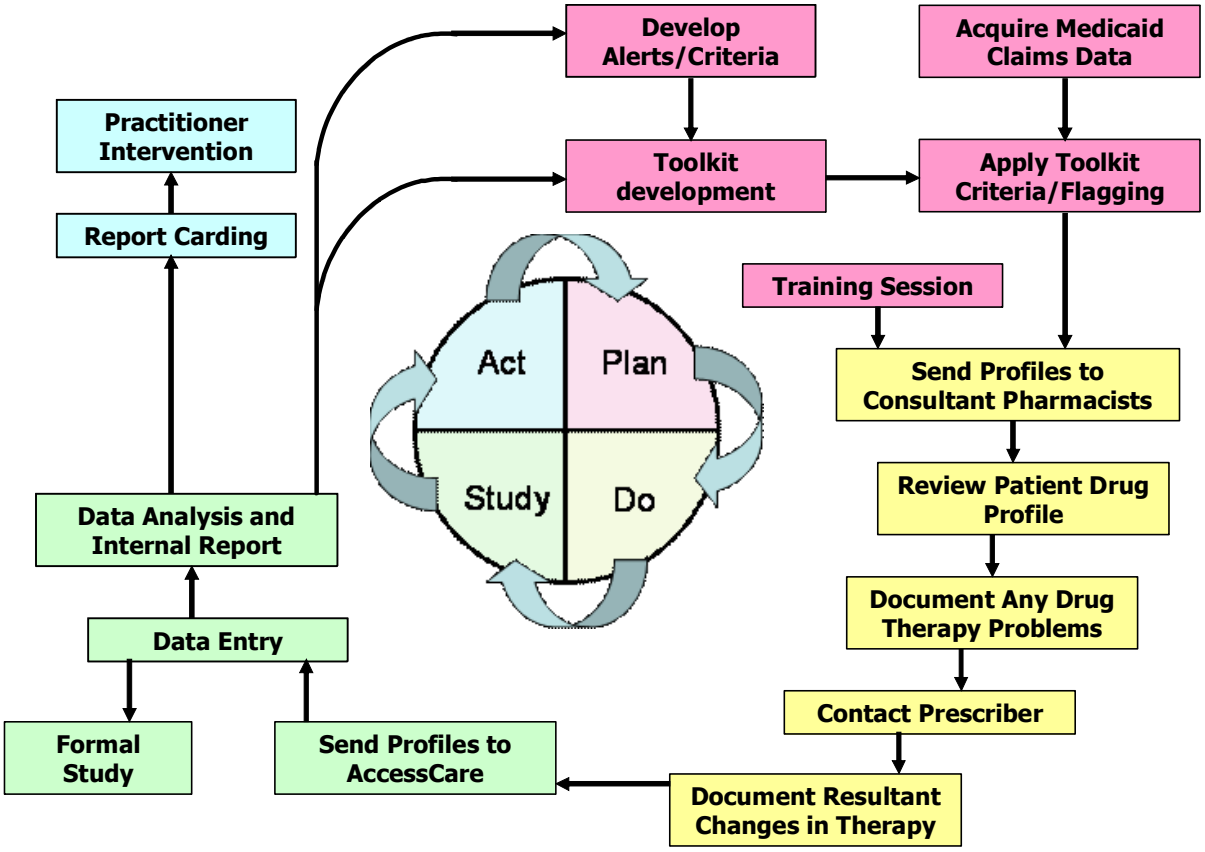
Two weeks prior to the rollout of the Statewide Initiative, Medicaid prescription claims data was retrieved from the archival vendor. As is typical of the administrative data archival process, a two-week lag time was required before data became available for use in the Initiative. Three months of data beginning three and one-half months prior to profile

generation and ending at two weeks prior to rollout were acquired. Prescription claims data were aggregated into an electronic profile using the SQL programming software. This process took approximately one day of computer processing since programming was written prior to the acquisition of claims. Once resident profiles were electronically generated, three days of printing ensued. Ultimately, greater than 10,000 eligible profiles were printed. With multiple pages per profile, and in many instances multiple pages of drug listings, printing and sending profiles to consultant pharmacists became the rate limiting step in the process once data was acquired from the vendor.

8.4 Workflow that Mimics the PDSA cycle

The PDSA cycle provides an ideal framework for assessing the steps followed designing, demonstrating, and evaluating this Initiative. This cycle is illustrated in Figure 8.1. Planning activities such as determination of criteria for profile-based alerts and eligibility for review precede the application of claims data to generate patient profiles. After profiles are sent, utilized and returned for evaluation, an analysis of the effect of a given cycle is studied and acted upon until the next cycles planning phase.

Figure 8.1 Program Workflow



CHAPTER 9

DESCRIPTIVE RESULTS FROM PHASE 1 OF THE NORTH CAROLINA POLYPHARMACY INITIATIVE

9.1 Pharmacist Reported Data

Pharmacists were required, as a condition of payment, to record problem types (including "no problem"), results types (including "no change") and new drugs and strengths when introduced. Documentation was required for both complete profile as well as individual drug reviews regardless of its retrospective or prospective nature. Thus, upwards of 10,000 documents were returned to AccessCare for payment and ultimately, entry into a primary data set for analysis.

A computerized data entry program was created to assist in data processing. Pharmacy students were hired as data-entry personnel. They were selected over non-medically trained personnel because of their familiarity with prescription drugs and nomenclature. Each person was screened for their proficiency in interpreting hand written documentation. When written documentation was insufficient to make an absolutely clear determination of the intended notation, profiles were marked for further review in the computerized data entry program. These determinations were ultimately made by licensed pharmacists. Less than 3% of all drug documentations and/or recommendation types required pharmacist interpretation. Data reported in this chapter are derived from this

primary data source with the exception of Table 9.1, for which administrative claims data was used as a source.

9.2 Phase 1 Scope

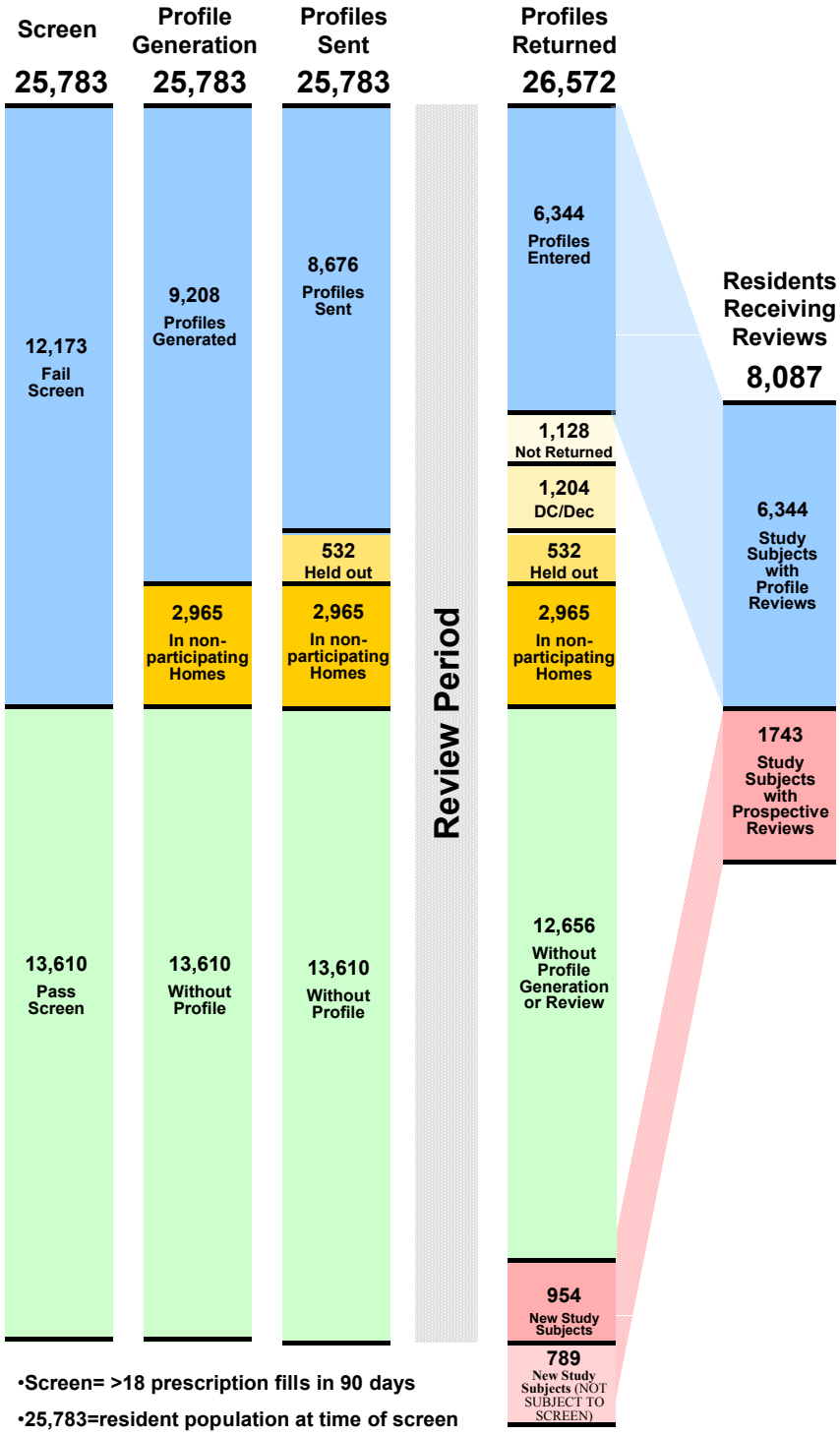
9.2.1 Number of pharmacists, nursing homes, residents and counties

One-hundred and ten consulting pharmacists participated in the first phase of the Initiative with a total of 253 nursing homes served by a participating consultant pharmacy organization participating. Ninety-three of North Carolina's 100 counties had nursing homes participating in Phase I of the Initiative. There were 25,783 residents in nursing homes in the state of North Carolina at the time of screening and profile generation (Figure 9.1). Of the 12,173 residents failing the screen of greater than or equal to 18 prescription fills in 90 days, 9,208 resided with pharmacy consultant organizations that expressed interest in taking part in the Initiative.

9.2.2 Profiles generated, sent and returned

Prescription profiles were generated from Medicaid claims data and sent to consultant pharmacists for 9208 patients, representing 75.6% (9,208/12,173) of all residents in North Carolina failing a screen of greater than 18 prescription drug fills in the 90-day period preceding the rollout of the statewide Initiative (Figure 9.1). Pharmacists returned 82% (7,548/9,208) of all profiles generated. After excluding 1,204 (13%) patients who were discharged or deceased prior to initial reviews, and 532 (5.8%) resident profiles held out from the Initiative due their inclusion in an ongoing, unrelated study, a response rate of 85% (6,344/7,472) was observed, with 1,128 profiles unreturned.

Figure 9.1 Residents Screened, Profile Generation, Distribution and Receipt



9.2.3 Residents selected for reviews by pharmacists

Another 1,743 residents were introduced to the Initiative through prospective interventions. Interventions were considered prospective if they occurred under one of two circumstances: 1) a review was performed in lieu of a profile (the resident passed the screen for profile generation, yet the pharmacist sought to make a recommendation) or 2) a resident had a profile that did not list a drug for which pharmacists desired to make a recommendation (drugs are customarily added and removed residents' regimens over time, and there was a lag period of time from profile generation to profile review, creating the opportunity to intervene on these newly prescribed drugs). 1,743 residents met the former criteria with 1,399 residents meeting the later (Figure 9.2).

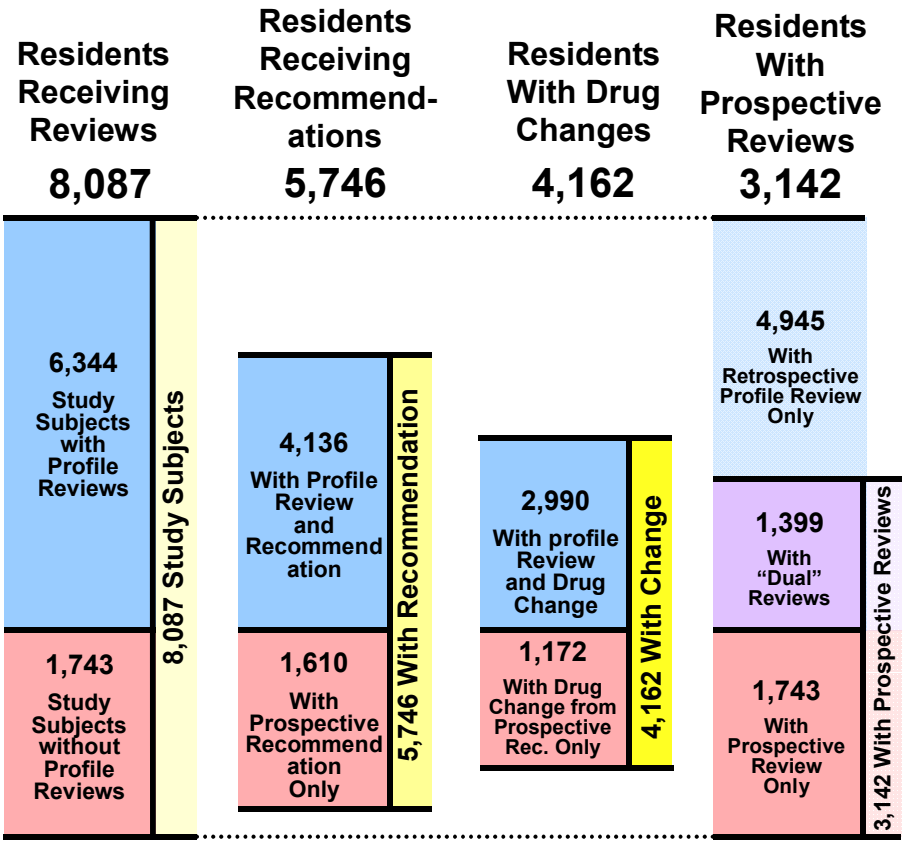
There is a historical and relatively constant rate of discharge or death in North Carolina nursing homes of 36% per year. Thus, approximately 2,300 new residents entered homes during the three month review period and pharmacists chose to make recommendations for many of those new residents. Of the 1,743 residents receiving recommendations without the direction of a computer generated profile, 45.3% (789/1,743) were new residents not subject to screening prior to the review period. The remaining 954 (54.7%, 9,54/1743) were residents that resided in the home during the review period, passing the screen. These residents were selected for review by pharmacists without the aid of a profile. In total, 8,807 nursing home residents in North Carolina were subject to reviews performed by consultant pharmacists in Phase 1 of the Statewide Initiative.

9.2.4 Types of reviews received by residents

Of the 8,087 residents receiving reviews by consultant pharmacists, recommendations were offered for 71% (5,746/8,087) of them, with successful recommendations (drug change

accepted by prescriber) garnered by 51.4% (4,162/8,087) of residents receiving reviews (Figure 9.2). For residents with retrospective profile reviews, 47.1% (2,990/6,344) ultimately had a drug change. Among those residents selected for review by pharmacists prospectively, 67.2% (1,172/1,743) had changes in drug therapy resulting from recommendations as recorded by pharmacists. There were 1,399 residents who had both a retrospective, claims generated profile review in addition to prospective recommendations based upon drugs not used during the baseline period. These residents were considered to have had "dual" type interventions. In total, the three types of interventions possible were: 1) Prospective-Only 2) Retrospective-Only and 3) Dual-Type (prospective and retrospective).

Figure 9.2 Residents Receiving Reviews, Recommendations and Drug Changes by Type of Intervention



9.2.5 Baseline characteristics

Table 9.1 presents the baseline characteristics for residents with reviews, by type. In order to obtain comparable baseline characteristics among intervention types, criteria were imposed to limit the analysis to only those residents who: 1) were Medicaid eligible for the three month period leading up to the review period, 2) resided in a nursing home for the three month period leading up to the review period, and 3) had not been deceased or discharged up to the time of review. All patients having a profile generated and reviewed met these criteria. Similarly, all 954 residents passing the screen, but selected by pharmacists for review met the criteria.

For the 7,298 residents with baseline data, 74.9% (5,464/7,298) were female and 68.5% (5001/7,298) where white with an average age of 77.8. An average of $1,444.73 in paid pharmacy claims from an average of 26.97 drugs was utilized during the 90-day pre-review screening period. Notably, one resident had $99,630.33 in baseline drug costs and thus, the mean and standard deviation are highly skewed for the overall group as well as the group with retrospective-only reviews, underscoring the importance of using median results and non-parametric testing when outliers skew the distribution. As expected, residents with prospective-only type reviews utilized fewer than half of the drugs of their targeted counterparts with profiles. The resulting $702.06 average drug cost for the 90-day pre-period is also less than half of the drug costs incurred by residents receiving retrospective-only and dual-type interventions.

Table 9.1 Baseline Characteristics of Residents Receiving Reviews by Type (N=8,087)

Characteristic	All Residents with Reviews (N=7,298)*	Residents with Retrospective Reviews Only (n=4,945)	Residents with Dual Retrospective and Prospective Reviews (n=1,399)	Residents with Prospective Reviews Only (n=954)*
Sex, # (%)				
Male	1834 (25.13)	1269 (25.66)	327 (23.37)	238 (24.95)
Female	5464 (74.87)	3676 (74.34)	1072 (76.63)	716 (75.05)
Race, # (%)				
White	5001 (68.53)	3411 (68.98)	994 (71.05)	596 (62.47)
Other	2297 (31.47)	1534 (31.02)	405 (28.95)	358 (37.53)
Age, years, mean ±SD	77.78 ± 12.46	77.37 ± 12.62	77.53 ± 12.22	80.26 ± 11.62
(median)	(80.0)	(80.0)	(80.0)	(82.0)
# of prescription fills, 3 mo. period, mean ±SD	26.97 ± 11.22	28.76 ± 9.96	30.84 ± 10.56	12.00 ± 4.82
(median)	(25.0)	(26.0)	(28.0)	(12.0)
amount of paid claims, $ in 3 mo., mean ±SD	$1444.73 ± 1489**	$1526.48 ± 1681**	$1662.23± 987.44	$702.06 ± 478.99
(median)	($1247.67)	($1304.19)	($1473.87)	($608.49)

* Of the 1,743 residents receiving only prospective reviews, 954 maintained baseline eligibility throughout the 3 month baseline period prior to screening and reviews and resided in a nursing home during that time
**One resident had $99,630.33 in baseline drug costs and thus the mean and standard deviation for "amount of paid claims" are unduly affected and focus should be given to median values
Note: Administrative claims were used as a data source

9.3 Descriptive Results

9.3.1 Overall response

Overall, 8087 residents with consultant pharmacist reviews generated 9883 recommendations for a drug change (Table 9.2), or an average of 1.22 recommendations per resident. The most frequent reason cited for change was for the substitution of a more cost-effective therapy representing 55.4% (5473/9883) of all recommendations to change therapy.

A total of 6115 changes in drug therapy occurred as a result of recommendations by consultant pharmacists (Table 9.3), or an average of 0.84 drug changes per resident with review.

Approximately two-thirds of all recommendations were accepted, with 61.9% (6115/9883) of suggested therapy changes resulting in changed therapy. The most common result was that of a change from one drug to another, representing 55.9% (3418/6115) of resulting changes in drug therapy.

Table 9.2 Recommendations for Changed Therapy by Type (N=8,087 residents)

Problem Type	Frequency (%)	Average Number per 100 residents*
Unnecessary Drug Therapy	1887 (19.0)	23.3
More Cost Effective Drug Available	5473 (55.4)	67.7
Wrong Dose or Strength	734 (7.4)	9.1
Drug has High Potential for ADRs	936 (9.5)	11.6
Needs Additional Therapy	234 (2.7)	2.9
Other-Any other problem not listed above	619 (6.3)	7.7
Total	**9883 (100)**	**122.2**

ADR= Adverse Drug Reaction

* Denominator is the total number of residents receiving a completed review by consultant pharmacists

Note: Pharmacist report was used as a data source

Table 9.3 Resultant Changes in Therapy by Type (N=8087 residents)

	Frequency (%)	Average Number per 100 Residents*
Dose/Delivery Changed	852 (13.9)	10.5
-Dose or administration was changed		
Drug Added	97 (1.7)	1.2
-Drug added for untreated indication		
Drug Change	3418 (55.9)	42.3
-Drug was changed from one to another		
Drug Discontinued	1748 (28.6)	21.6
-Drug was discontinued or changed to PRN		
Total**	**6115 (100)**	**75.6**

* Denominator is the total number of residents receiving a completed review by consultant pharmacists

** A result type of "Other-Any result not listed above" occurred in 1,111 instances but was not considered to be verified drug changes.

Note: Pharmacist report used as a data source.

9.3.2 Response by Intervention Type

Overall, an average of 1.21 recommendations were made per resident with any review resulting in 0.74 drug changes per resident (Table 8.3). Residents with retrospective-only type reviews received the fewest recommendations per resident (0.99) and drug changes (0.57), whereas residents with dual-type interventions garnered the greatest rate of recommendations (2.05) and resultant drug changes per patient (1.31).

Table 9.4 Response by Intervention Type (N=7,298)

	All Residents with Reviews (N=7,298)*	Residents with Retrospective Reviews Only (n=4,945)	Residents with Dual Retrospective and Prospective Reviews (n=1,399)	Residents with Prospective Reviews Only (n=954)*
Recommendations	8850	4878	2869	1103
-per resident	**(1.21)**	**(0.99)**	**(2.05)**	**(1.16)**
Drug Changes	5425	2822	1828	775
-per resident	**(0.74)**	**(0.57)**	**(1.31)**	**(0.81)**

* Of the 1,743 residents receiving only prospective reviews, 954 maintained baseline eligibility throughout the 3 month baseline period prior to screening and reviews and resided in a nursing home during that time
Note: Administrative claims were used as a data source

CHAPTER 10

METHODOLOGICAL CONSIDERATIONS FOR EMPIRICAL EVALUATIONS OF PHARMACIST SERVICES

10.1 Methodological Considerations

The objective of this dissertation is to determine if the Initiative was effective in reducing drug expenditures while simultaneously maintaining or improving the quality of care received by nursing home patients in North Carolina. At first glace, this proposition may seem relatively straightforward given readily available primary data (patient profiles) as well as secondary data sources (administrative claims data) with large samples sizes brought about by the broad scope and successful launch of the Initiative. Yet observational studies suffer from methodological limitations unique to their design, setting, and treatment. Tantamount is their universal failure to assure that unmeasured and maldistributed risk factors do not induce biased results. This dissertation attempts to minimize, to the greatest extent possible, this threat to internal validity that has plagued many prior studies of pharmacist services in real world settings to date.

10.1.1 Intention-To-Treat versus On-Treatment Analysis

Intention-to-treat (ITT) analysis is a compelling research strategy employed to increase the internal validity of experimental studies. It requires the researcher to steadfastly retain subject subjects by including all initially enrolled subjects and their results in the final

analysis regardless of circumstance or adherence.[34] Gerard Dallal identifies four major lines of justification for intention-to-treat analysis[34]:

1) Intention-to-treat simplifies the task of dealing with suspicious outcomes, that is, it guards against conscious or unconscious attempts to influence the results of the study by excluding odd outcomes.
2) Intention-to-treat guards against bias introduced when dropouts are related to the outcome.
3) Intention-to-treat preserves the baseline comparability between treatment groups achieved by randomization.
4) Intention-to-treat reflects how treatments will perform in the population by ignoring adherence when the data are analyzed.

These are persuasive reasons to employ ITT analysis for empirical evaluation of the Statewide Initiative. It is now widely accepted among researchers conducting randomized clinical trials (RCT) that ITT analysis is superior to *on-treatment* analysis (OT), where only those receiving treatment or otherwise finishing the study are accounted for in the results.

Yet there are practical challenges and methodological risks associated with employing an ITT approach for an evaluation of a program of this type and scope. First, the Initiative was neither conceived as nor conducive to an RCT. The Initiative was formed as voluntary program for consultant pharmacist organizations. Response to solicitations for involvement was a great success with 235 homes with roughly 80% of the states residents responding with reviews. Attempts to randomize homes within participating pharmacy providers would have been difficult, if not impossible to practically employ. Prescribers and

pharmacists would have practiced in "experimental" as well as "control" homes, increasing the likelihood of spillover or contamination effects. Further, as in most real-world settings, the administrative goal was very pragmatic: to initiate a program that produced desired results in the shortest time frame possible, and not to conduct a prolonged and rigorous randomized study.

Dallal's first three justifications deal with a misdistribution of risk factors between subject and comparison homes. In the absence of an RCT protocol with randomization, his first three points are moot. For the Initiative, there was never an attempt (experimental or otherwise) to create baseline comparability. Thus, there was no comparability to maintain by subjecting study inclusion to ITT based upon Dallal's first three principles. Of importance to this analysis, the absence randomization does not preclude the use of non-randomized comparison groups, or the determination of comparison groups that maintain homogenous distributions of risk between subject and comparison homes. Because no active attempt was ever undertaken to achieve a prospective control group, the preservation of this non-existent control group is non-sensical. For the observational researcher, the burden of baseline comparison lies within retrospective statistical adjustment or comparison group matching, not within the preservation of prospective randomization.

Dallal's fourth and final justification for ITT analysis, performance in a population, speaks to a chosen research focus: emphasizing either efficacy or effectiveness. For the purposes of the initiative, we may be interested in both efficacy *as well as* effectiveness. This issue is addressed in the next chapter.

Based upon the requisite need for retrospective statistical adjustment and matching of a comparison group, the first three of Dallal's ITT justifications are moot with respect to the

Initiative. Further, an OT analysis offers diminished potential of committing a Type II error. One of the disadvantages of ITT analysis is its tendency to be biased toward the null with treatments having low adherence and/or response, even in the face of high efficacy in sub-populations.

Unlike RCTs of drug products where the active agent is highly standardized, pharmacist services are often unique to each participating pharmacist in their focus, actions, and results. Add to this diversity of response, a historical 36% dropout rate due to death or discharge in the nursing home setting in North Carolina and an ITT analysis of the Initiative becomes quite likely to bias toward the null. An OT analysis of the Initiative is more likely to prevent type II errors in hypothesis testing due to low adherence and/or specific response. Dallal's own appraisal suggests that program with high efficacy may have low effectiveness if adherence is low.

Depending on the research question at hand, OT analyses may be more adept at proving efficacy whereas an ITT analysis produces results indicating effectiveness. He states that ITT analysis answers research questions at the "public health" level, whereas OT analysis indicates effect where adherence to treatment may be greater.[34] For this evaluation, an OT analysis would be favored since we are interested in the effect of pharmacist intervention at various levels of adherence, or success. In the next chapter, I discuss the various levels of adherence (success) of interventions and why it is important to measure each treatment level in order to make conclusions about the Initiative. Regardless of the chosen method (ITT vs. OT), the researcher must assure baseline comparability to prevent biased results.

10.1.2 Efficacy versus Effectiveness

Consideration of the term *effectiveness* as a synonym of *efficacy* is a regrettably common mistake among lay analysts. These research concepts retain important and distinctive differences for both methodological consideration and interpretation of study results. Most of the products and services used in health care differ in their performance in a "real world" or "naturalistic" environment versus a well controlled, idyllic environment. For health services in particular, a great disparity exists between the ability of a service to produce a desired outcome in a controlled environment (efficacy) and its operation in actual practice (effectiveness). This begs the researcher to conduct experiments in "real world" settings.

Yet seeking effectiveness must follow research establishing efficacy. A service may be ineffective, but efficacious. Thus, establishing efficacy is the primary research goal, with establishment of effectiveness to follow. Foremost is proving efficacy is establishing causality, and doing so requires strong internal validity. Strong internal validity is brought about in an RCT through experimentation. Experimentation is possible through randomization, a process that ensures both study and control subjects have equal risk on the whole at baseline.

Two requirements must be maintained throughout the study period to ensure valid results following randomization:

1) Once randomized, the researcher must ensure that control group is not subject to any treatment effects
2) Once randomized, the researcher must ensure that the treatment is correctly applied to all study patients

Satisfaction of these requirements is exceptionally challenging for the researcher when engaged in intervention or service studies. First, spillover effects often threaten the non-treatment of comparison subjects in "real world" settings. Second, applying a standardized and equi-potent treatment across all study subjects is nearly impossible. Such is the case with pharmacist services studies, where pharmacist action and intensity vary across sites.[35] Even if both requirements are satisfied and internally valid results emerge, randomization still does nothing to ensure external validity.

External validity is the capacity of the study to mimic results found in the population and setting of interest. Thus an RCT might be completely internally valid, while not meaningful at all in practice. Extraneous factors not present or nor controlled for during the study cause treatment effectiveness to be unequal to treatment efficacy. While some extraneous factors enhance efficacy, most detract from it, underscoring the importance of measuring effectiveness in parallel with efficacy.

Dallal proposes that the combination of efficacy and adherence produce effectiveness. Adherence in this sense is meant to represent all extraneous factors not defined in treatment, which presumably has been proved efficacious. An example using corticosteroid inhalers provides an excellent example of his summative statement.

Inhaled corticosteroids are advantageous in preventing asthma exacerbations due to their anti-inflammatory properties. Reductions of inflammation in the lungs are at least partially responsible for increased airflow to patients' bronchial cavities. They have been proven to be efficacious in producing this effect with repeated administrations, often requiring more than one administration per day. Many factors are at play when considering the seemingly simple task of repeated administration. First and foremost is the consideration

of the traditional definition of adherence. If the patient neglects to administer the drug to oneself and fails to follow a pre-defined schedule established through tests of efficacy, effectiveness is reduced. Many human factors bring about self-limiting compliance. Out-of-pocket costs, social stigma, and inability to properly activate the inhaler and administer the medication properly are only a few. Yet for Dallal's statement to hold unequivocally true, the consideration of all environmental factors not explicitly defined as treatment in RCT trials proving efficacy are required to establish effectiveness. Other factors extraneous to the patient that affect efficacy in this example may include dysfunctional or outdated metered dose inhaler, co-morbid conditions that vary over time such as seasonal allergies, or other factors not considered during the efficacy proving trial. However, the most likely cause of decreased effectiveness with inhaled corticosteroids is self-limiting compliance. One might make the case that this applies generally to all drug products.

A similar example using the example of an x-ray as a diagnostic tool for a broken leg illustrates the added importance of considering adherence beyond that of the patients with health services. Once ordered, the patient must comply with a physicians order to arrive at the x-ray machine on time and maintain the proper anatomical position to create the desired x-ray image. Beyond these actions, nothing further is required of the patient to produce the image properly. However, many other factors may influence the quality of the image as well as the interpretation of image and subsequent diagnosis. The quality of the film and the x-ray machine itself affect the service. The x-ray technician, the radiologist, and the ordering physician must all perform as prescribed. Even personnel charged with transporting, keeping, and uploading the images into the medical record is crucial to the performance of the service. It is unlikely that all of these factors were considered in an efficacy trial for x-

rays in diagnosing a broken leg. That is, if an efficacy trial was ever performed in the first place. To do so with the consideration of all adherence factors would have established effectiveness. Pharmacist services are subject to even greater challenges to adherence due to their consulting and augmentive nature. This fact in combination with multiple practitioners, activities and outcomes to consider, create a challenging research environment.

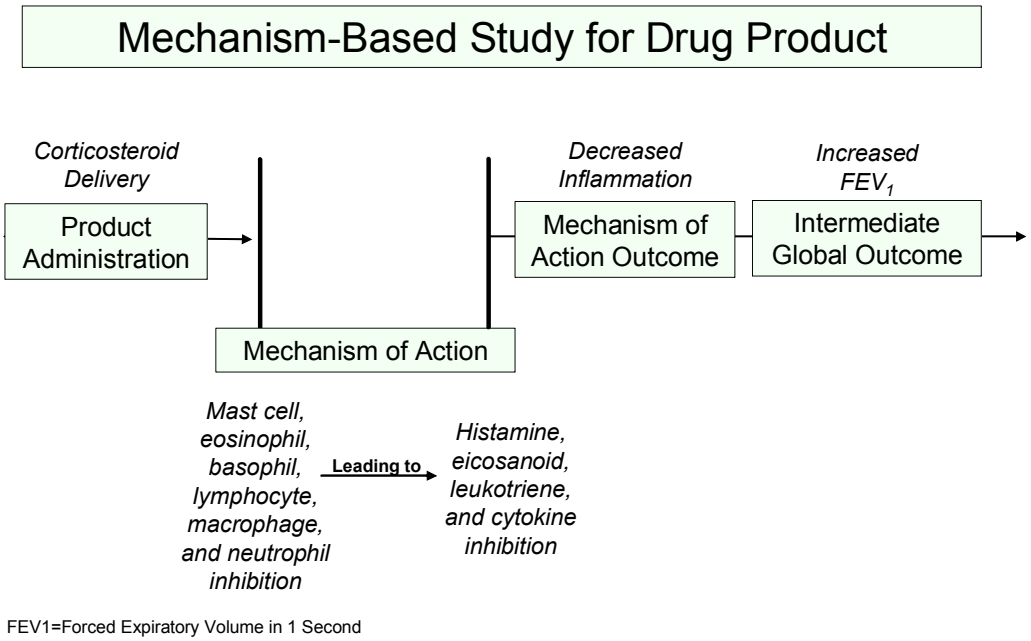
10.1.3 The causal pathway between interventions and outcomes

With ever-evolving technologies and well-informed practitioners, services researchers are inevitably asked to assess the outcomes of a new procedure, intervention, or service. Often, these advances are complex and multifaceted, intermingling many technologies and health care professions. This evolution places greater pressure on researchers to engage in translational or practice-based research. Demonstration projects are notorious for their inability to capture all relevant factors that effect treatment outcomes. The challenge for this proposed study is a familiar one: how to discern and distinguish the impact of a single intervention with multiple stages in the context of many other factors and forces affecting the ultimate outcomes of interest. In this chapter, I briefly describe this challenge by comparing it to the relatively simple case of a randomized clinical trial of a drug. In ensuing chapters, I then describe how I will handle these methodological challenges in this study.

Historically, products have been the subject of a great many more RCTs than services, especially within the pharmaceutical industry. Close proximity to the outcome on the causal pathway permits researchers of drug products to minimize the numbers of study subjects enrolled in efficacy studies because of the high likelihood of adherence in a controlled trail. Small sample sizes require less resource consumption for a study. This proximity also affords the researcher a stronger claim of efficacy. Yet another advantage for

drug products when establishing efficacy is the close proximity of the end point to the mechanism. Figure 10.1 illustrates this point.

Figure 10.1: Hypothetical Causal Pathway for Drug Product Efficacy Trial



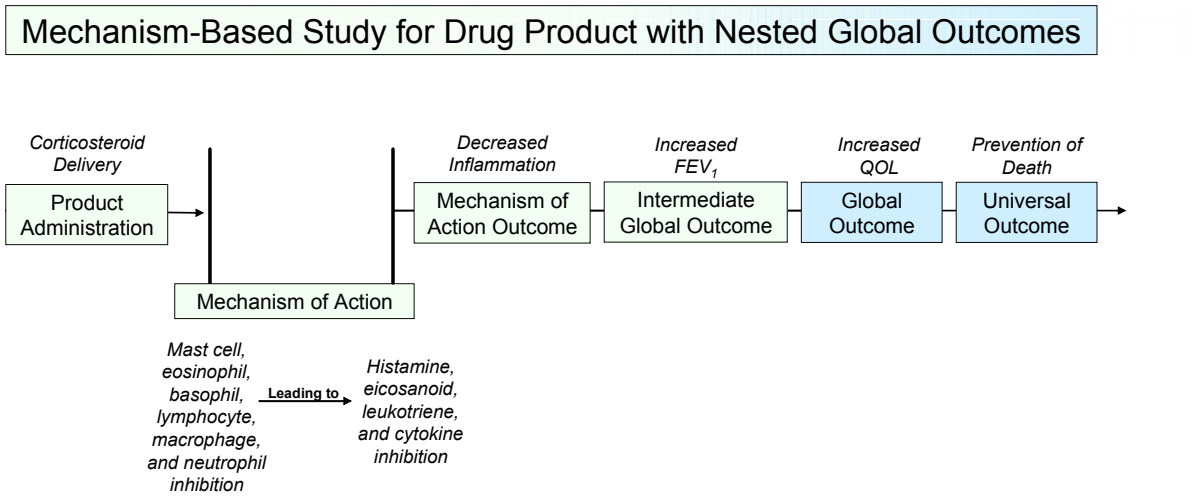
FEV1=Forced Expiratory Volume in 1 Second

Although recently criticized, historical end-points for RCTs of drug products tended to be mechanistic or anatomical and not clinical or global with respect to patient functioning. This approach aided establishment of efficacy claims for drug products. Recent calls for global measures and increased emphasis on effectiveness may at least partially explain increasing sample sizes for RCTs of drug products. Both product and service studies are challenged by the objective of proving effectiveness due to the distal nature of global functioning and patient quality of life. Figure 10.2 illustrates the added complexity and burden of effectiveness with global outcomes trials.

Service trails are at an especially magnified disadvantage. Unlike product trials, service trails are distal in the causal pathway *prior to and following* the mechanism of action (Figure 10.3). This dual disadvantage puts additional burden on the services researcher when

establishing both efficacy as well as effectiveness, with severe bias toward the null. Pharmacist services trials are especially burdensome as they often maintain more complex causal pathways than other health services due to the peripheral nature of ambulatory pharmacy practice.

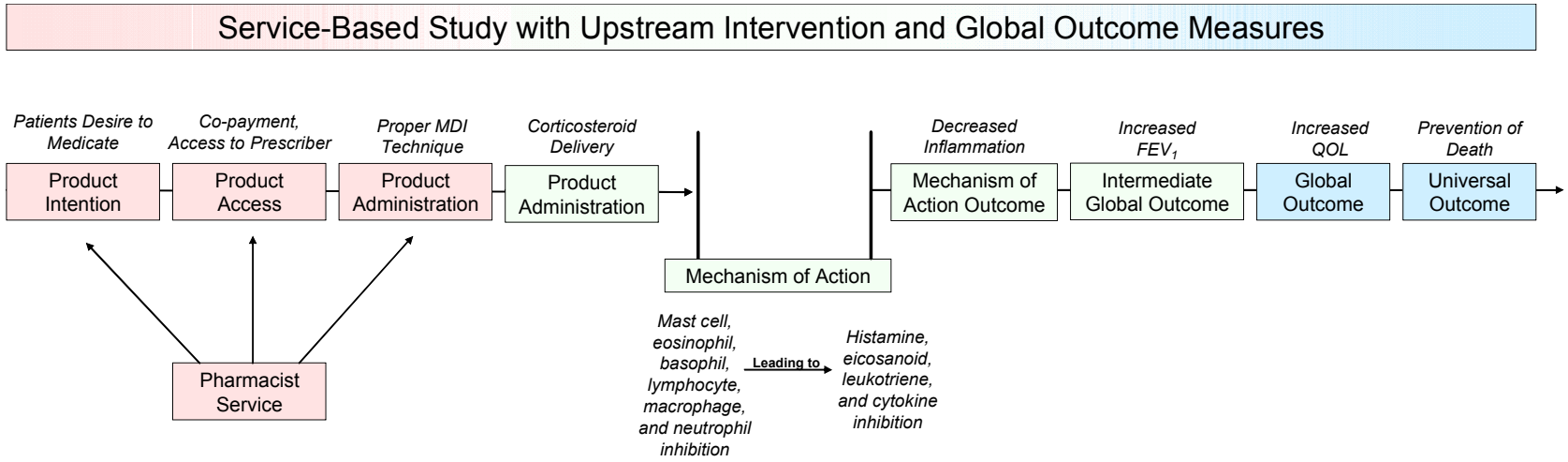
Figure 10.2 Hypothetical Causal Pathway for Drug Product Efficacy Trial with Global Outcomes for Effectiveness



FEV1=Forced Expiratory Volume in 1 Second
QOL=Quality of Life

In the first part of this chapter of the dissertation I reason that Dallal's first three justifications for ITT analyses are moot with respect to non-randomized, quasi experimental approaches required of pharmacist services studies. With respect to effectiveness, Dallal's final justification, I make the point above that the Initiative is subject to a great many extraneous factors both controllable and not controllable effecting the treatment. To use an ITT analyses severely biases the results toward the null. Furthermore, the treatment itself is subjugated to three distinct core activities, as shown later in the chapter, each of which may result in differing efficacies. Thus, showing that Dallal's justifications for ITT are not valid with respect to an analysis of the Initiative, I choose to use an OT method of analysis, using only those patients actually receiving treatment and existing throughout the study period.

Figure 10.3 Hypothetical Causal Pathway for Service Effectiveness Study



MDI=Metered Dose Inhaler

FEV_1=Forced Expiratory Volume in 1 Second

QOL=Quality of Life

10.1.4 Defining the treatment

To establish the causal pathway for the Initiative, I will first define the treatment(s). No single treatment may be identified to fully encompass the interventions of the Initiative. Multiple activities took place with multiple types of practitioners. At a minimum, core events that are perceived to affect chosen outcome measures to the greatest extent should be outlined for empirical testing. Testing of multiple core events strengthens the external validly of the program evaluation while simultaneously informing future PDSA cycles.

Arguably the first actionable event in the causal pathway of the initiative was the download of administrative claims and subsequent screening process. After screening, profiles were generated using pre-determined drug-level algorithms for the presence of alerts. Once generated, profiles were sent to pharmacists for review.

Three main treatments or "core" events remain in the causal pathway and can be reasonably defined and empirically tested for causal links following the receipt of profiles for review. The three treatment classifications defined below are the most logical and testable treatment nodes since the focus of our analysis is on the effects of pharmacist actions. Until this point in the causal pathway, only fixed costs were incurred by program administrators. At the point of pharmacist review, the Initiative began to garner incremental program costs. Pharmacists were paid for reviews, and thus increased reviews resulted in increased costs to the program sponsor.

Pharmacist Profile/Prospective Review: Arguably the most important treatment classification, pharmacists were paid for this action in the causal pathway and this action alone. This treatment classification is imperative to the establishment of effectiveness, program valuation, and ultimately a cost-minimization-ratio.

Pharmacist Recommendation: Another compelling treatment classification, pharmacist recommendations may be required for billable claims in many pharmacist services associated with Medicare Part D. Furthermore, as a treatment definition, it is the first action in the causal pathway that is pharmacist dependent. That is, the intensity of the review and the ability of the reviewer to identify potential drug therapy problems determine the frequency and distribution of recommendations among nursing home residents.

Accepted Recommendation/Drug Change: An accepted recommendation is the most proximal event to the Initiative's mechanism of action (the use of a new drug regimen) that can be analyzed given the available data. As a treatment definition, it is the first action in the causal pathway that requires pharmacist interaction with other health care providers. Whereas the *pharmacist recommendation* treatment classification is pharmacist dependent, the *accepted recommendation* treatment classification is both pharmacist and prescriber dependent, with prescribers weighing the merit of the pharmacist recommendation.

These three core treatment classifications encompass the spectrum of causality in the initiative from the more distal (Profile Review) to the more proximal (Accepted recommendation/Drug Change). While the more distal treatment definitions better establish effectiveness, the more proximal treatment definitions better establish efficacy. Each of these three treatment classifications answers a different research question.

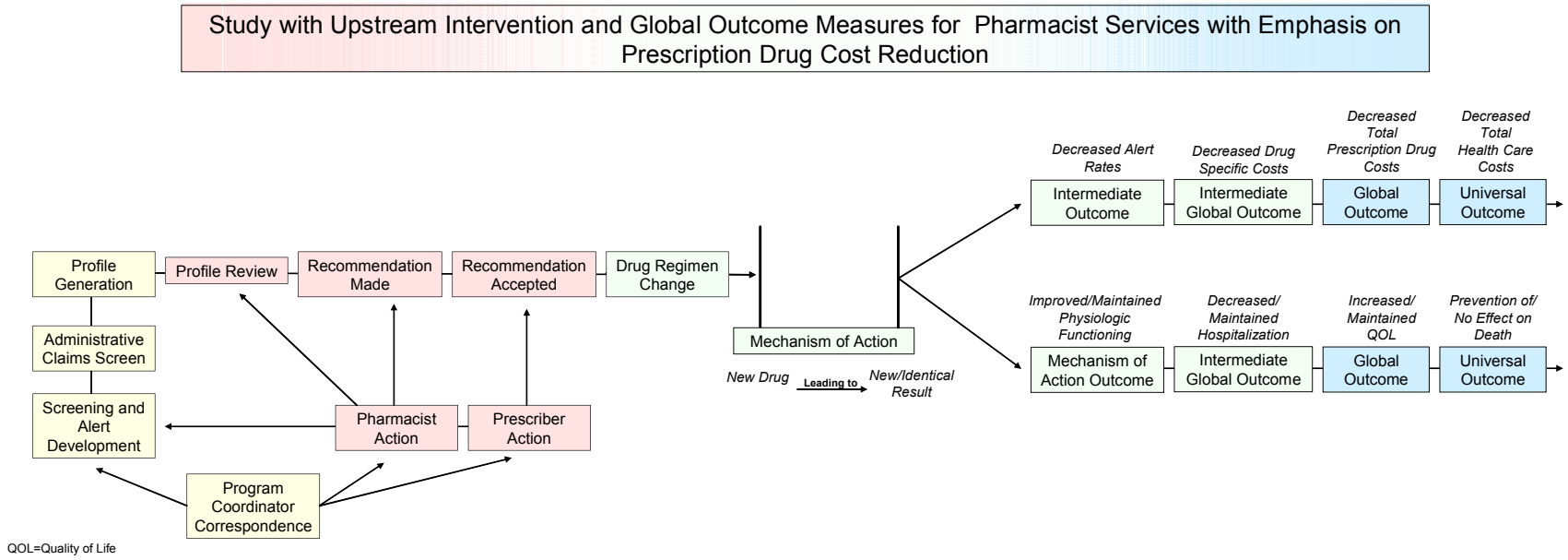
It is most certainly in the spirit of the PDSA method to analyze efficacy at each treatment nodule to aid in the improvement of the entire process. One of the goals of the PDSA process in the context of the Initiative would be to maximize treatment adherence to the greatest extent possible once efficacy has been established. By evaluating treatment efficacy and multiple nodes in the treatment process, the researcher can elucidate

effectiveness limiting processes and make improvements for future initiatives, interventions, and associated activities.

Arguments certainly exist for other events, actions or intentions to be considered as treatment if time, resources, and data allowed. Profile generation may be considered the best category to fit a research objective aimed at public health policy. Certainly, it was the goal of program administrators to have as many profiles reviewed as were generated. However, it is the consultant pharmacist who intended to review profiles to make recommendations. What if a profile was generated, but never arrived to the pharmacist to review? Of what significance is the program feature that affords payment only for completed reviews? Furthermore, intent may hold an important research question if it is further drilled down to "intention to make recommendations", but not the action of communicating with a physician. What about a research objective with consideration of prescribers as the actionable health care provider? Patients may only be treated if a recommendation is accepted, and thus, the prescriber's intention is may dominate the choice of the on treatment-group selection.

There are more potential treatment nodes in the causal pathway than can be addressed in a single dissertation, especially given the limitations of the data with respect to the involved health care practitioners. The above groups seem most relevant to the objective of the dissertation and were the motivation for the genesis of Initiative at the outset. Figure 10.4 attempts maps the causal pathway for Phase 1 of the Initiative.

Figure 10.4 Hypothesized Causal Pathway for Outcomes Arising from the North Carolina Polypharmacy Initiative



The more distal the treatment from the mechanism of action, the more its evaluation represents effectiveness over efficacy. The more proximal the treatment, the more it represents efficacy over effectiveness. Each of the chosen treatments of interest answers a different research question:

Treatment Level #1: Profile Review: How effective are adjunct profile reviews conducted by consultant pharmacists in a nursing home setting at reducing drug costs while maintaining health?

Treatment Level #2: Recommendation Made: How effective are recommendations made by consultant pharmacists in a nursing home setting at reducing drug costs while maintaining health?

Treatment Level #3: Accepted Recommendation: How effective are accepted recommendations resulting from consultant pharmacists in a nursing home setting at reducing drug costs while maintaining health?

10.2 In Search of a Comparable Group

In this part, I present the concept of the counterfactual ideal. Then I proceed to outline selection biases that may exist at each proposed treatment level in the Initiative. Then I explore implications of the resultant baseline differences in risk and the necessary cohort strategy to address it.

10.2.1 The counterfactual ideal

For each treatment level, the counterfactual ideal is desired for comparison of post-treatment outcome measures. The counterfactual is the theoretical dual existence where study subjects can exist in treatment and comparison groups simultaneously, thus ensuring

comparability. Of course, this theoretical dual-existence is quite difficult to arrange, let alone measure. In the absence of divine assistance in the matter, the RCT, through randomization approximates the counterfactual by creating a comparable group of study subjects that act as a proxy for the experience of the treatment group given no treatment. Two central concerns arise in the absence of randomization and both are manifest in the initiative: 1) Pharmacist imposed selection bias (introduced by selection of patients for prospective interventions as well as recommendation-based treatment selection) and 2) the presence of baseline differences in important risk factors related to the outcomes of interest among some treatment groups and their sub-groups unbeknownst to the pharmacist. To aid in reading comprehension, I heretofore refer to pharmacist imposed bias as "active bias" and baseline differences as "passive bias", with passive bias defined as the introduction of bias without the knowledge of pharmacists, prescribers, or program administrators, but present nonetheless. Both types result in selection bias, despite the action implied term--selection.

10.2.2 Treatment specific selection bias

Unlike randomized clinical trials (RCTs), where experimental and control groups are determined prior to experimentation, the Initiative operated under an open enrollment policy where new patients could enter respective phases of the project based upon evolving screening criteria and/or a consultant pharmacist's judgment of need.

Treatment Level #1: Active selection bias is unlikely at this level for residents receiving profile reviews since profile generation was guided by the 18 prescription fills in 90-day criteria and not by pharmacists. If a nursing home was a participant in the Initiative, all residents failing the screening criteria were reviewed. This prevented active patient selection on the part of the pharmacist. To find a comparable group for these residents at this

level of treatment, identical criterion could be applied in non-participating homes to determine which residents would have received reviews if residing in participating homes. Any bias that does exist at this treatment level does so because of self-selection of participating homes. However, while patients within homes may be different with respect to each other, patients between homes are not likely to differ in aggregate with respect to participating and non-participating homes. This point becomes important later as I acknowledge a propensity matched group cannot exist for this treatment level among patients failing the 18 drug criteria without using replacement matching methods. This limitation is the result of an insufficient number of comparison subjects to match 1:1.

For the 1,743 patients who were introduced to the initiative through prospective review and without the generation of a profile, a great deal of selection bias is likely to have occurred at this treatment level. For residents with less than 18 prescription drug fills in 90-days, pharmacists were able to select out those residents for whom they determined a drug therapy problem (DTP) existed. No pre-determined screening or selection criterion existed to apply to the same population of low-utilizers in non-participating homes.

Treatment Level #2: For residents with recommendations resulting from consultant reviews, an inherent active selection bias exists that is propagated by the pharmacist conducting the reviews. All residents receiving recommendations were selected out by pharmacists for changes to their respective drug regimens. Any differences in risk for an outcome of interest between residents receiving recommendations and residents who did not receive recommendations bring about biased results emanating from this selection. This selection prevents comparisons of residents with recommendations in study homes to patients in non-participating homes in the absence of a method of adjusting for bias. Unlike the

profile review level, where the screening criteria can be applied to non-participating homes. No explicit criterion exists for residents receiving recommendations that can be applied to residents in non-participating homes to determine which residents *would have received a recommendation* had their respective homes been participants in the Initiative. This problem holds true for all residents with prospective-only, dual type and retrospective-only recipients of recommendations.

Treatment Level #3: For residents with accepted recommendations, an inherent selection exists above and beyond that of selection at the recommendation treatment level. At the profile review and recommendation received treatment levels, pharmacists play the central role in selecting out residents based upon characteristics that put them at risk for adverse outcomes. At the accepted recommendation level, prescribers play the central role in selecting out patients for change. They are the gatekeeper to the mechanism of action (drug regimen changes). The same reasons for non-comparability to non-participating homes exist in this treatment level as with the recommendation received level, only with greater and compounded selection effect since two or more health care providers have now screened patients for drug changes and must be in agreement for a change to occur. This congruence is most proximal to the mechanism of action for the service with empirical testing at this level best establishing efficacy.

10.2.3 Baseline differences in risk

Ultimately, selection bias results quite often in maldistributed risk, leading to misattribution of effect, and subsequently invalid results. There are two possible causes of maldistributed risk factors resulting from the causal pathway in the Initiative: 1) selection (above) and 2) concentric relationships among treatment levels. The former is inherent to all

observational studies and can result from active selection (e.g. pharmacist action) or passive selection (e.g. participation of home) with the latter being more unique to this dissertation.

Each treatment level is a function of the prior treatment level along the causal pathway. Figure 10.5 illustrates this relationship. If comparisons are made between residents having a recommendation accepted and those that did not, only those that did not *and had a recommendation made* can qualify for comparison. In other words, comparisons would stray further from the counterfactual if we allowed those with accepted recommendations to be compared with study subjects having a profile review and no recommendation. This unfortunate reality limits the number of eligible comparison subjects for each treatment level. Also it prevents the use of research methodologies that could attribute effect for each treatment level simultaneously due to lack of independent choice among treatment alternatives.

Figure 10.5 Concentric Relationships among On-Treatment Groups

This limitation has a unique advantage, though. The conditional nature of the concentric circles illustrated above harkens back to the discussion of efficacy versus effectiveness. If the Accepted Recommendation group best establishes efficacy, then

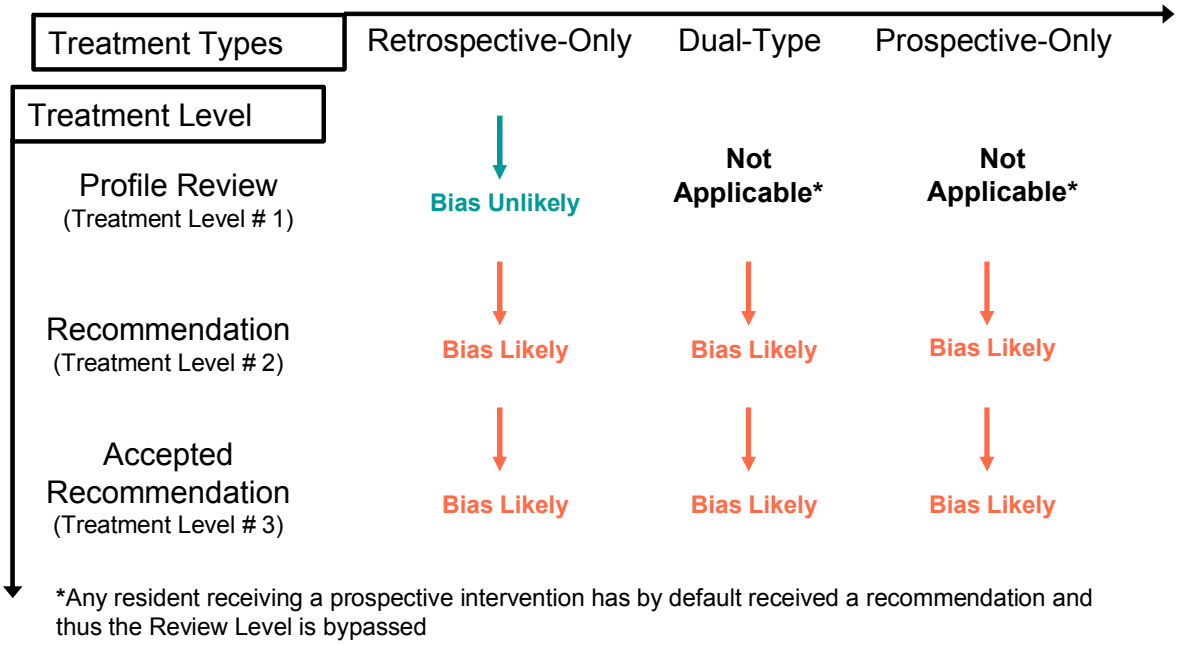
differences that exist in successive distal rings may be attributed to adherence. An accepted recommendation is contingent upon a recommendation received. A recommendation is contingent upon a review. I am not suggesting that, given perfect adherence, every person receiving a review should experience a drug regimen change. However, given perfect adherence, all persons that *should* have drug changes, *do* have drug changes. Fortunately, predictive models as well as propensity models are now available to model which residents should have received drug changes and did not. These non-adherent residents and the factors that led to non-adherence have important ramifications for future PDSA cycles.

Earlier in this chapter, I made the case for an on-treatment (OT) analysis of three treatment levels (profile review, recommendation, and accepted recommendation) spanning the efficacy-effectiveness spectrum with the goal of parsing out event-specific treatment effect. When combined with the three types of treatment (retrospective-only, prospective-only, and dual-type) determined earlier, nine possible sub-groupings (3x3) emerge for analyses and comparison (Figure 10.6). Since residents with dual-type and prospective-only interventions had at least one recommendations by default (prospective interventions were single drug interventions submitted only when a PDTP was identified), no cohorts exist at the review level for these treatment types.

As shown previously, the results of this analysis are only valid if a comparable group of study subjects not receiving treatment can be formed to test for differences in effect. In the next chapter I discuss statistical adjustment and matching techniques that increase comparability. Note that residents having Retrospective-Only type interventions are not likely to be subject to bias at the review level since all residents were reviewed regardless of the presence of a PDTP and all failed the screening criteria. The only bias that may exist for

this cohort may have resulting from selection at the nursing facility level through solicitation for Initiative participation.

Figure 10.6 Study Cohort Schematic and Likelihood of Bias



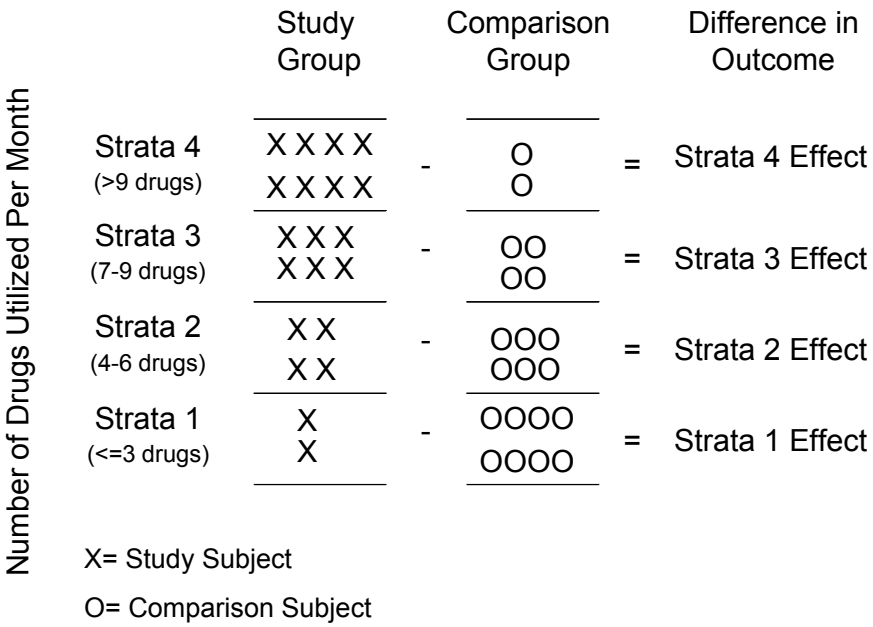
CHAPTER 11

RESEARCH METHODS THAT ACCOUNT FOR SELECTION BIAS AND BASELINE RISK

11.1 Stratification

The most straightforward approach to risk adjustment is simple stratification. It is most appropriately employed when a single important risk factor for the outcome is maldistributed between study and comparison groups. In the Initiative, it is likely that residents using more drugs were more likely to receive reviews, with subsequent recommendations leading to drug changes than residents with fewer drugs. Baseline differences in drug utilization between study and comparison groups and selection bias imposed by providers likely led to a maldistribution of risk with respect to number of drugs per month. If taking more drugs is related to an outcome of interest, than this factor is considered confounding and must be accounted for in the analysis. This factor is not a problem in and of itself if the distribution of drug counts per resident is balanced between study and comparison groups. This may not be the case, though, especially as the treatment level becomes more proximal to a drug change. Stratifying both study and comparison groups by number of drugs attempts to balance the distributions of this risk factor so that study subjects with high utilization are evaluated against comparison subjects with high utilization and vice versa (Figure 11.1).

Figure 11.1 Stratification Example for Number of Drugs Utilized in One Month



Kelsey et al. outline hypothesis testing to determine stratum specific effect as well as aggregate effect and a method to determine if effect is differential based upon strata.[36] The foundation of the latter hypothesis test becomes important when discussing propensity scoring.

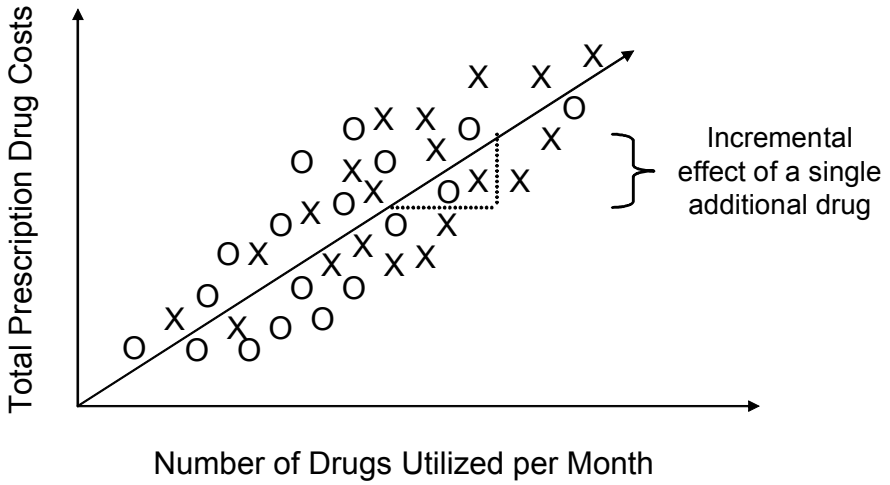
11.2 Simple Linear Regression

Not mentioned above is the number of strata needed to balance subgroups. The greater the effect of the independent variable (number of drugs) on the dependent variable with respect to the maldistribution, the more strata required to balance risk appropriately. Regression techniques attempt to eliminate the need to stratify altogether. They utilize a hypothesized linear relationship between independent variables (e.g. the number of drugs taken) and the outcome of interest. The linear adjustment for differences in resident-specific drug utilization affords a more precise theoretical balance because of the extrapolation of

effect. This is both an advantage of linear regression with its predictive capabilities well as an oft-cited disadvantage as shown later when misspecification distorts effect.

Using drug utilization as a single independent variable, one could regress the number of drugs taken on total prescription drug expenditures. This would allow us to calculate the incremental effect of a single additional drug on total prescription drug expenditures (Figure 11.2).

Figure 11.2 Regression Example for Number of Drugs Utilized in One Month



X= Study Subject

O= Comparison Subject

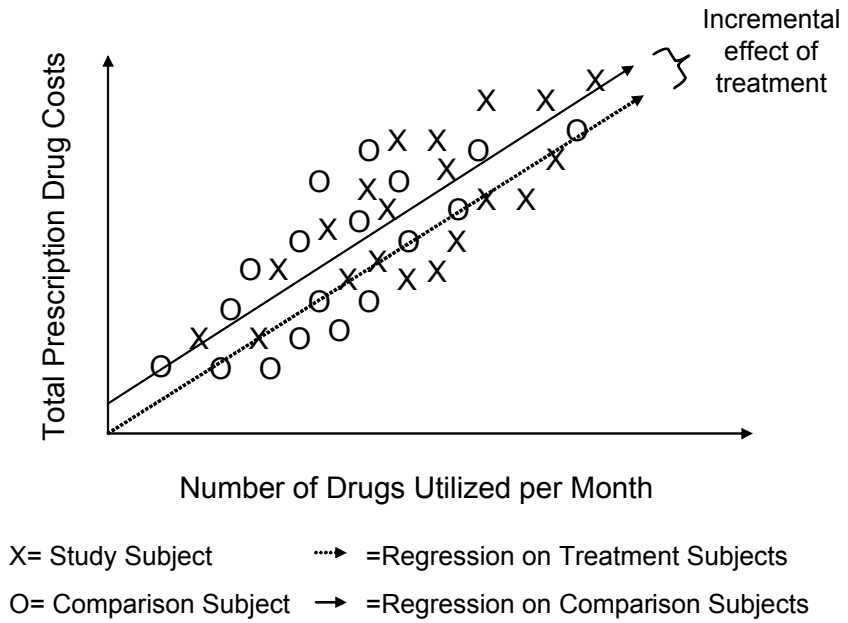
To estimate the effect of a treatment requires another independent variable, and subsequently, multivariate regression.

11.3 Multivariate Regression

Adding a treatment dummy variable allows the model to differentiate study subjects from comparison subjects and provides the effect of the treatment on drug costs. This of course assumes that the number of drugs per month used is the only variable affecting drug

costs outside of treatment. Figure 11.3 illustrates the addition of a treatment variable to a regression model predicting drug costs with number of drugs used per month.

Figure 11.3 Multivariate Regression Example for Number of Drugs Utilized in One Month



Often, many independent variables have effects on the dependent variable of interest. Stark and Mantel present a classic study of confounding introduced by the mixing of effects by two independent variables.[37] Their study illustrated potential misguided conclusions that may be formed by simple associations in the absence of consideration of all relevant risk factors. As presented by Rothman,[38] Stark and Mantel considered the mixing of effects of birth order and age. Since birth order and age are highly correlated, the researcher might overestimate the effect of birth order on the prevalence of Down Syndrome in the absence of age from the model. If age has a greater effect than birth order, but only birth order is factored into the analysis, biased results ensue. If birth order has no effect at all, then an entirely unfounded result is elucidated. A multivariate regression that includes age would not

create the illusion of the dominant effect of birth order since the effects birth order and age are partialled out.[39] Stark and Mantel ultimately find that birth order has no effect on the prevalence of Down Syndrome. However, if both age and birth order did have and effect, we are presented with an entirely different problem: interactive effects.

Quite frequently co-dependent interactions occur with simultaneous effects on the dependent variable of interest. If birth order and age effects are additive, no bias exists with the interpretation of the marginal (incremental) effect estimates resulting from the regression, though multicollinearity may exist. However, if a synergistic effect exists, these estimates will be biased, requiring further specification of the model with an interaction term. Other specification problems may result from multivariate regression as well. Out of sample, or outlier observations may unduly affect the estimates of effect due to the presumptive linear associations in the absence of specification modifications. Furthermore, the regression example above in Figure 11.3 relies heavily on two study subject observations with low utilization and two comparison subjects with high utilization for extrapolations of effect at the extremes. If, in fact, there is relationship between the treatment and the magnitude of effect at the extremes, results will be biased with respect to the overall marginal effect estimate on treatment. This suggests a combination of stratification strategies to parse out treatment effect in the face of heterogeneous risk factors and regression to maintain precision may be most appropriate when the specification of either the dependent or independent variables is uncertain.

11.4 Co-morbidity Scoring

One challenge associated with studies having global outcome measures is the sheer number of risk factors or and/or co-morbidities that must be accounted for when attributing effect to global treatments. For the initiative, the pharmacist service was not limited to a single class of drugs, nor a pre-defined disease state. Any drug treating any condition was subject to review at the pharmacist's discretion. Furthermore, global outcomes such as total prescription drug costs are influenced by a great variety of risk factors, many of which may have little to do with pharmacist activities.

Adjusting for risk factors associated with global outcomes in a regression requires many co-morbidity variables, often with required interactions. Joffe and Rosenbaum give the example of a study with 74 covariates that requires 148 tests to verify covariate balance.[40] Assuming a 95% confidence level, at least 7 of these covariates are likely to be significant based on chance alone. Schneeweiss and Maclure identify two overall problems with this approach: 1) decreased statistical efficiency (as outline above by Joffe and Rosenbaum) and 2) increased complexity of variable selection and subsequent decreased comparability to other studies.[41]

Co-morbidity scoring attempts to increase regression efficiency and standardize the effect of co-morbidity across studies by condensing all co-morbid conditions into a single proxy score. However, achieving the ideal proxy variable (score) for co-morbid conditions has proven to be quite a challenge. Co-morbidity scoring has shown some usefulness in exploratory data analysis, but is plagued by residual confounding and imprecise measurement in administrative databases, with age remaining a more desirable proxy.[41] Another type of

score, propensity to receive treatment or be exposed, has been shown robust in a number of health care studies.

11.5 Propensity Scoring

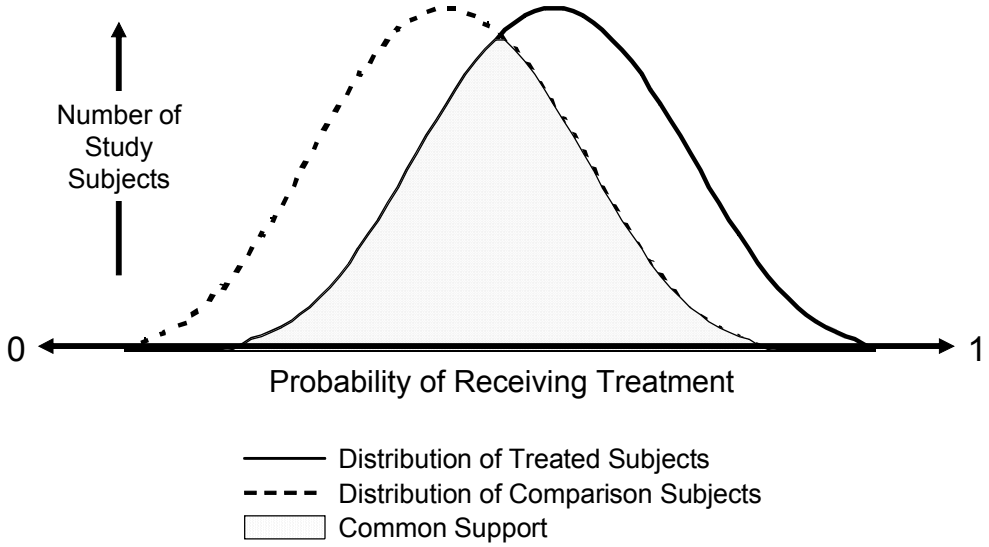
With all the advantages of increased statistical efficiency, interpretability, and reliability in combination with the reduced risk of mis-specification, propensity scoring has steadily gained popularity among researchers reporting on health care interventions in the 22 years since Rosenbaum and Rubin first introduced the concept in 1983.[42,43] The approach is to essentially condense all baseline risk factors into a single probability metric ranging from zero to one. This is done using standard regression techniques that are modeled to predict treatment group selection. The logarithmic function is utilized to constrain the probability (score) between zero and one.

Once an estimated probability of treatment is assigned, study subjects may be stratified by probability and subsequently matched with comparison subjects with similar likelihoods of receiving treatment. Those with similar likelihood have "common support" (Figure 11.4). This commonality with respect to the propensity for treatment selection allows for non-randomized comparisons.

Once matched, regression is no longer required since risk is presumably equalized, though regression after matching is sometimes preferred when attribution of effect is desired for risk factors outside of treatment. This feature affords the researcher greater flexibility with respect to the type of statistical test employed upon comparison. This quality of propensity scoring is particularly important for analyses of the Initiative. For instance, total prescription drug costs can be highly variable at or near the end of life, irrespective of interventions on the part of health care providers. More importantly, this effect may be

limited to a few residents at a time causing skewness, as seen in the baseline characteristics of one initiative subject with nearly $100,000 in drug costs in 90 days. This single resident caused the standard deviation of drug costs to be greater than the average drug cost for all study subjects. Quite frequent in nursing homes, the presence of these outliers, the incidental fluctuation in their continuous outcomes, and the ultimate inevitability of the effect beg the researcher to use non-parametric testing. This testing is very convenient once subjects are stratified by propensity score. For this dissertation, the distribution of difference-in-differences will ultimately determine the chosen test (parametric or otherwise).

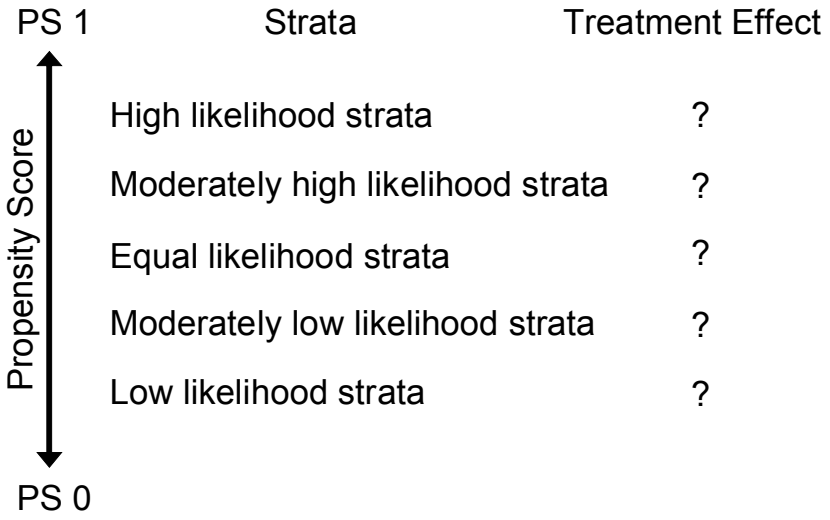
Figure 11.4 Common Support Following Logistic Regression on Treatment



Also advantageous are the strata-specific comparisons that can be made to measure the effect of interventions at various probabilities of receiving an intervention (Figure 11.5). It is likely, given more drug use that more treatment effect of a single intervention may result. For instance, persons having more drugs might be more likely to receive more than one recommendation or drug change. The potential exists for a threshold that may be established as a breakeven point with respect to cost-effectiveness focused interventions such

as the Initiative. Furthermore, because comparison subjects are scored from within a group having the access to the intervention, those residents not receiving reviews, recommendations, and drug changes at each respective treatment level may be quite informative to future PDSA cycles. Identifying residents that should have received an intervention but did not should aid in future targeting algorithms and provider report carding.

Figure 11.5 Strata Specific Treatment Effects



Unfortunately, one major limitation exists with propensity scoring methods despite its widespread appeal. Unmeasured risk factors may still bias results. Propensity scoring does nothing in its score assignment to address any factor not taken into consideration in modeling the probability of receiving treatment.

11.6 Instrument Variables

Unlike previously described methods, regression methods using instrument variables have the capacity to account for unmeasured baseline risk. It does so by using a identifying a factor that is associated with treatment but has no bearing on the outcome of interest. Patient assignment in an RCT is often considered the perfect Instrument variable as it is

perfectly correlated with treatment and has absolutely no association with the outcome of interest. While at face value the approach is clearly theoretically superior compared against other approaches that do not account for unobserved or unmeasured risk factors, finding a reliable and precise instrument is difficult. Also, the resulting effect estimates are only a reflection of variation introduced by the instrument, biasing the approach toward the null.[44]

11.7 Heckman Two-Step Selection Method

Two-step selection models offer the advantage of including all study subjects, regardless of outlying or unmatched subjects. The first step models treatment, much like propensity scoring. The second incorporates an Inverse Mills Ratio resulting from the first step into the second regression. Choosing between Heckman two-step methods versus propensity scoring methods becomes a tradeoff between inclusion of all study subjects (two-step), but with out-of-sample extrapolations, or the potential exclusion of non-matched study subjects (propensity scoring). Two-step regressions have the added disadvantage of estimating potential outcomes, rather than actual outcomes, adding to an already cumbersome interpretation of results from the method.

11.8 Difference in Difference Models

Difference in difference models utilize the passage of time to reduce the effects of maldistributed risk on treatment differences between study and comparison groups. Since the measure of interest is the before-after difference in the outcome of interest, characteristics such as gender that remain fixed over time cannot confound the pre-period outcome of interest. If the effect of treatment differs for any fixed effect characteristic that is maldistributed between groups, confounding by that characteristic remains. This begs the researcher to employ a regression in combination with the difference-in-difference approach

to account for maldistributed risk. The method still suffers from omitted variable bias, though any bias is limited to the effect of treatment on fixed effects and not the outcome of interest itself. When used in combination with propensity scoring, the difference-in-difference approach may be employed without regression since fixed effect characteristics have been balanced prior to analyzing differences in before-after differences between study and comparison groups.

CHAPTER 12

PROPOSED METHOD OF EVALUATION FOR PHASE 1 OF THE NORTH CAROLINA POLYPHARMACY INITIATIVE

12.1 Proposed Method

Given the constraints of Initiative in its design, data sources, and scope, I propose an on-treatment analysis of two different types of interventions, alone and in combination (Retrospective, Prospective, Dual-Type) with three core activities (Review, Recommendation, Drug Change) performed by consultant pharmacists and attending physicians. This analysis would utilize propensity scoring with difference in difference modeling.

12.2 Cohort Assignment and Model Selection

To evaluate overall Initiative success, three primary cohorts will be evaluated against propensity matched residents in non-participating nursing facilities. These cohorts (#1,#2,#3 below in Figure 12.1) include all intervention types (retrospective-only, dual-type, and prospective-only) and will be evaluated at the three levels of treatment (review, recommendation, and drug change). As discussed previously, nine possible sub-groupings could be considered separately to determine sub-group effects and also prevent any mixing of treatment effects in the event of incomplete balancing from propensity score matching in the aggregated groups (#1, #2, and #3). Evaluation of the sub-groupings separately ensures appropriate comparison group matching with homogenous baseline risk by parsing out the

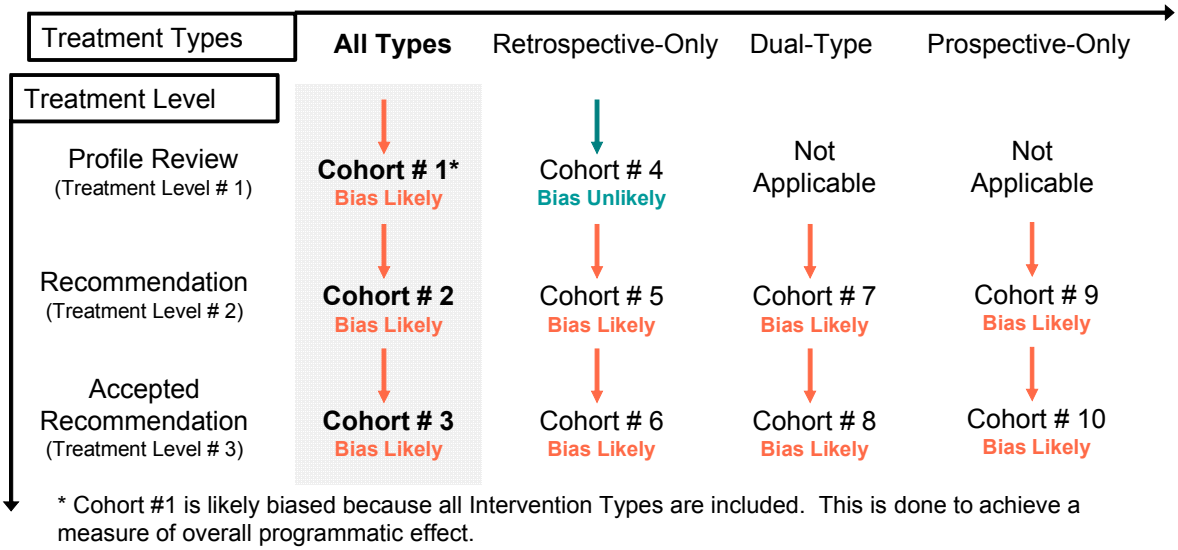
type of biased imposed by practitioners involved with the intervention. Two of these sub-groupings are not-applicable for this particular initiative since prospective reviews required a recommendation as a requirement of submission.

In Chapter 10.2.4, I discussed the types of bias that are likely for each of the potential cohorts. Of the seven relevant sub-groupings, Cohort #4 (below, retrospective-only profile reviews) is the only cohort that is not likely to have active selection bias. It is also the largest Cohort, subsequently outnumbering its potential comparison group approximately 5 to 3, preventing 1:1 propensity matching. It is possible that no baseline differences will be found between Cohort #2 and its counterpart comparison group (those with at least 18 drug fills in 90 days in non-participating homes). One of the previous analyses published in the Journal of Managed Care Pharmacy (Appendix E) using this cohort found that the Initiative was successful in reducing drug costs as well as alert rates for PAL List drugs as well as Clinical Initiatives List drugs. Only race was found to maintain a statistically significant mal-distribution between study and comparison group. Findings using a propensity scoring approach could validate the internal validity of that study in two ways: 1) demonstration of similar results and 2) demonstration of co-variate balance prior to matching. The remaining eight cohorts have been shown to have active selection bias and thus require propensity score matching prior to difference-in-difference analysis (Figure 12.1). To be consistent, all cohorts in this analysis will be propensity matched regardless of the extent of bias found after modeling treatment selection.

12.3 Eligibility and Loss to Follow-Up

Residents in participating homes are considered eligible for analysis if they were continuously eligible throughout the 90-day pre-intervention period as well as the 90-day post-intervention period. Residents in non-participating homes are considered eligible for propensity matching if they satisfied the same 90-day pre and post-intervention eligibility criteria. The 90-day post-period is selected to mimic the 90-day pre-period to allow for a difference in difference study design. The 90-day period was also chosen as a tradeoff between a need to minimize drop-out and ensuring a long enough time-period was available to assess the effects of the intervention in terms of changes in prescribing and dispensing.

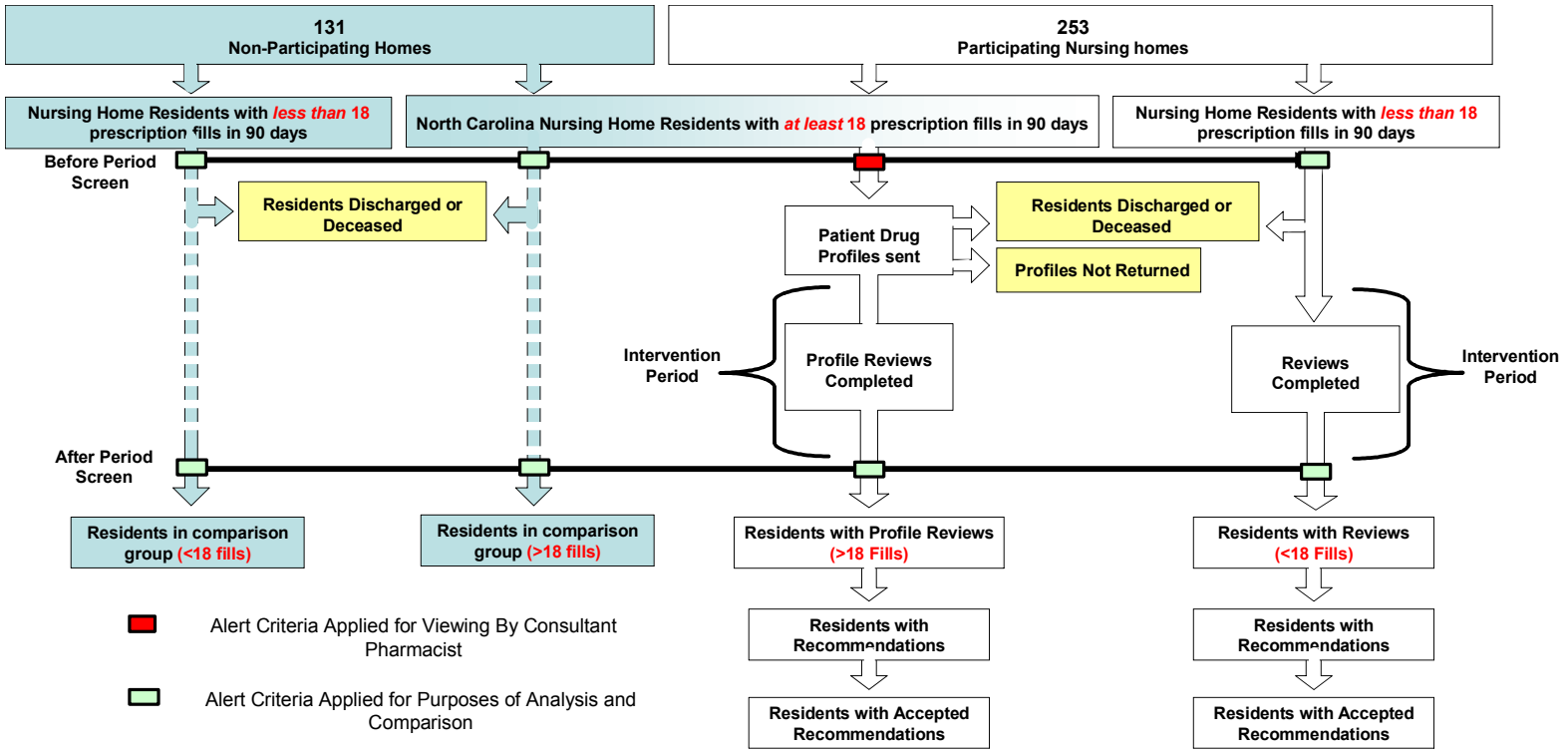
Figure 12.1 Cohort Schematic and Model Assignment



* Cohort #1 is likely biased because all Intervention Types are included. This is done to achieve a measure of overall programmatic effect.

Roughly 18% of residents were lost to follow-up during the six-month study period. This is consistent with a historic rate of discharge and death of 36% annually for the North Carolina Medicaid population. Figure 12.2 illustrates the evolution of study and comparison groups throughout the study period. Loss to follow-up occurred in the six months between screens designated with red and green boxes.

Figure 12.2 Study Design and Cohort Development



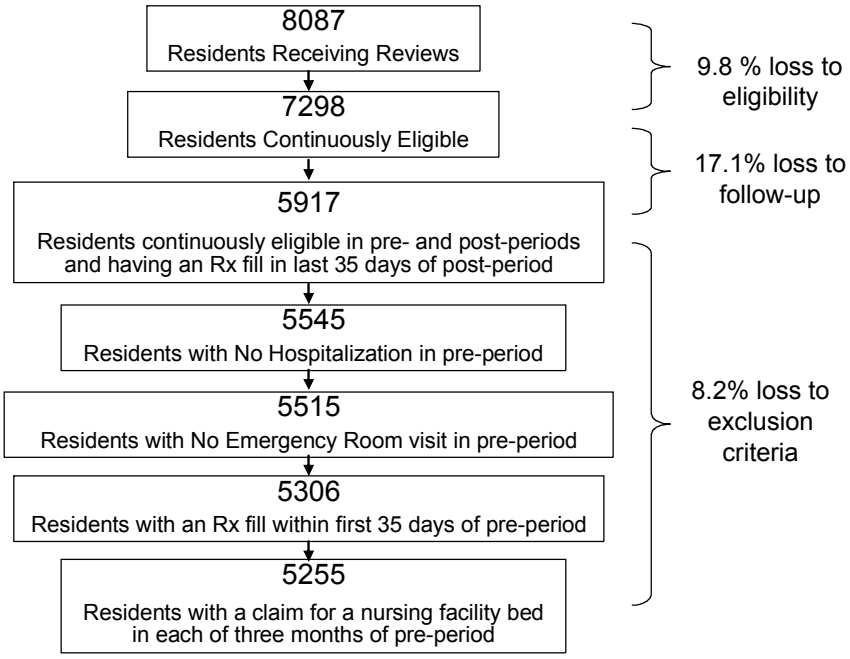
Residents are also required to have at least one prescription fill within the last 35 days of the post-period. This is done to minimize, to the greatest extent possible, including any residents in the analysis that may have died during the study or post-periods, subsequently preventing a downward utilization bias. Medicaid had a 34-day supply limit on prescription drugs at the time of the study. Dates of death are not recorded in the Medicaid database, and can only be inferred if a long period of non-use of services exists up to the month of disenrollment. Since prescriptions are the units of service used most often in a nursing home population, prescription use during the last month (35 days) of the study period was thus felt to be a reasonable proxy for persistence when used in conjunction with eligibility files stating continued eligibility throughout the study period.

I reported descriptive results earlier that included individuals eventually lost to follow-up for the empirical analysis. These descriptive analyses are included in this dissertation to depict the total intervention effort, irrespective of drop-out. A description of the overall intervention effort was required to evaluate general intervention activities, intensity of interventions, and overall pharmacist intention. The descriptive analysis in chapter 9 presents results based upon the cross-section in time immediately following the intervention period. For the empirical analysis, more strict eligibility criteria are applied and a follow-up period is required to screen post-period drug use for utilization and PDTP alert prevalence.

In addition to the previously described eligibility criteria and post-period analysis, pre-period exclusion criteria were added to further limit maldistribution of risk emanating from differences in disease severity among study and comparison groups that could not

otherwise be measured. Any residents having a hospitalization or an emergency room visit in the pre-period were excluded. Additionally, any resident not having a prescription fill in the first 35 days of the pre-period was excluded to restrict the inclusion of any study subjects using any third-party payor other than North Carolina Medicaid. Finally, the presence of a "hotelling" charge (claim for the use of a nursing facility bed) was required in all three months of the pre-period to ensure subject residency in respective facilities. Resultant sample sizes are shown in Figure 12.3. Considerable but comparable sample size reductions were observed in all groups, both study and comparison.

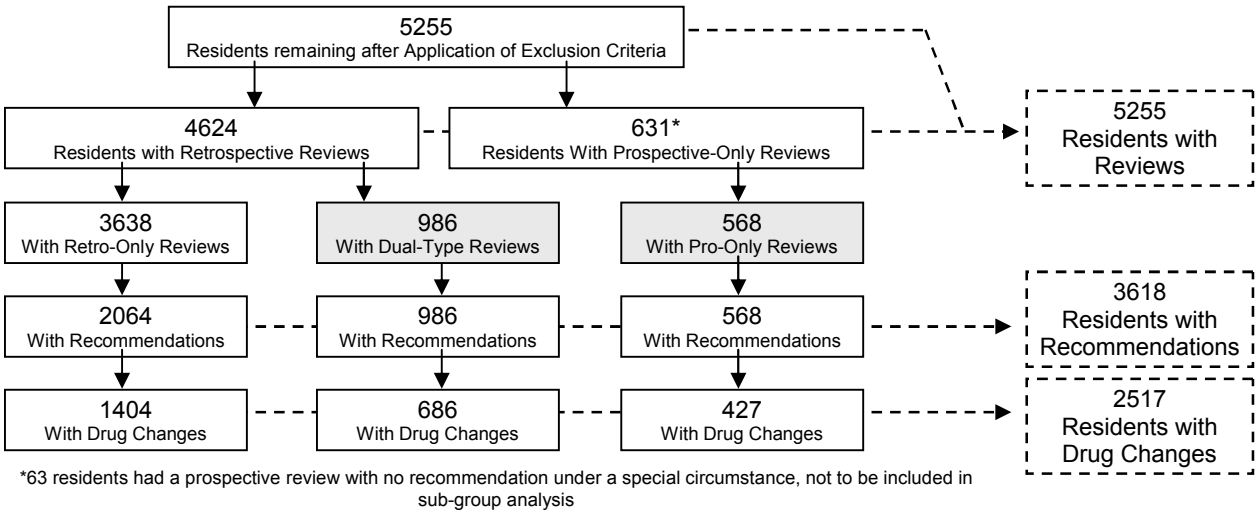
Figure 12.3 Study Subjects Remaining After Application of Exclusion Criteria



Sample size reductions were most evident for Prospective-Only Cohorts, where only 954 residents were eligible during the entire pre-period. When followed throughout the post period and with application of the exclusion criteria, 5,255 remain for analysis in Treatment Level #1 (Review), 3,618 for Treatment Level # 2 (Recommendation) and 2,517 for Treatment Level # 3 (Drug Change) as illustrated in Figure 12.4. Fortunately, all 6,344

residents receiving reviews were eligible throughout the entire pre-period. For Retrospective-Only Type interventions, 3,638 remained at the review level, 2,064 at the recommendation level, and 1,404 at the drug change level. For Dual-Type interventions, 986 remained that had a review and recommendation while 686 remained that also had a drug change. For Prospective-Only Type interventions, 568 remained that had a review and recommendation while 427 remained that had also had a drug change. 63 residents had a prospective review with no recommendation under a special circumstance, not to be included in sub-group analysis.

Figure 12.4 Sub-Group Sample Sizes Following Application of Exclusion Criteria



12.4 Previous Evaluations

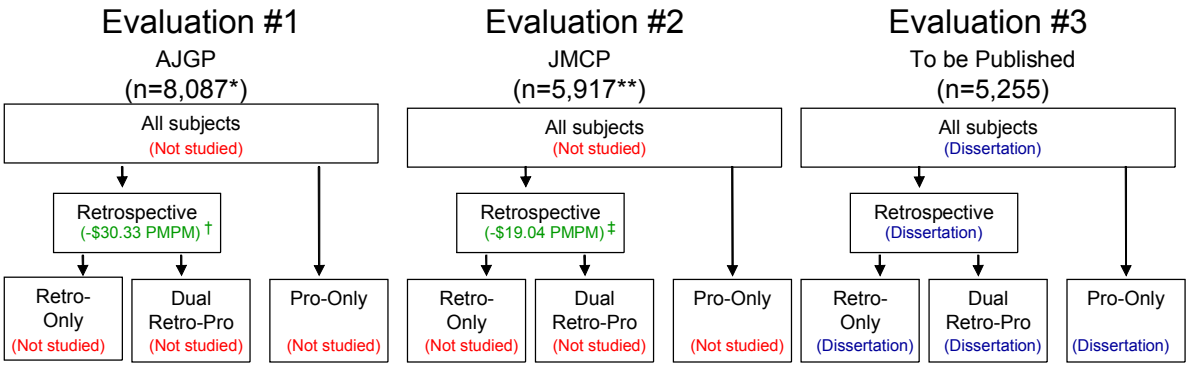
Two evaluations of the Initiative have been conducted prior to this dissertation. The first, published in The American Journal of Geriatric Pharmacotherapy (Appendix D) included a portion of the descriptive results found in Chapter 9 of this dissertation. A cost minimization ratio was reported (12:1) as well as a per member per month (PMPM) drug cost savings of $30.33. This study was based solely on pharmacist report and a projection of savings based upon the derived result type (Drug Added, Drug Discontinuation, Drug

Regimen Change, and Drug Change) and the cost differential between the before reported drug and the after reported result. This study was followed by another published in The Journal of Managed Care Pharmacy (Appendix E) analyzing PDTP alert rate reductions and drug cost reductions using administrative claims. PMPM drug savings were found to be $19.04. Study residents were compared against a comparison group in non-participating homes to establish before-after difference-in-difference results. No matching was performed.

To date, results have not yet been reported for an all intervention types. All three primary comparison groups (All Intervention Types at the Review, Recommendation, and Change Levels) are subject to many types of inherent bias resulting from selection as discussed in Section 10.2.3. One of the likely drivers of selection bias was the prospective intervention, where only residents perceived to have PDTPs where selected for intervention by a pharmacist. The other main driver of bias likely resulted from prescriber selection during recommendation acceptance. As such, at least 9 of the 10 possible cohort-comparison groupings were subject to maldistribution of risk resulting from substantial selection pressures. Since the propensity matching method balances this risk, all 10 cohort-comparison grouping may be evaluated for treatment effects. Findings from this dissertation will be the first to assess the overall effects (All Intervention Types) of the Initiative (Figure 12.5).

This third planned analysis will allow me to more accurately assess the overall (program level) effects, as well as the effects among each sub-group. Since only one of the seven relevant sub-groups is likely to be without significant selection bias, propensity scoring is needed to match groups based on pre-period risk factors.

Figure 12.5 Cohort Inclusions of the Three Initiative Evaluations



† Mean drug cost savings resulting from interventions

‡ Median drug cost savings resulting from interventions

* 8,087 represents the number of study subjects receiving any intervention without exclusion criteria. Since only retrospective reviews were studied in Evaluation #1, n=6334.

* 5917 represents the number of study subjects receiving any intervention with exclusion criteria the first inclusion criteria (continuously eligible in pre- and post- period and having an Rx fill in the last 35 days of the post period). Since only retrospective reviews were studied in Evaluation #2, n=5,160.

AJGP = American Journal of Geriatric Pharmacotherapy
JMCP = Journal of Managed Care Pharmacy

The first evaluation utilized a projected before-after study design. The second applied a before-after design using administrative claims and added a comparison group. The third and final evaluation is designed to have the greater amount of internal validity based upon study design as a before-after with matched comparison group. Thus, the final analysis as outlined in this dissertation is not only the first to analyze all types of interventions, but also to apply strict exclusion criteria and matching based on patient pre-period characteristics having influence on the outcomes of interest.

Figure 12.6 illustrates the tradeoff between no and strict exclusion criteria that strengthen internal validity versus generalizability and Figure 12.7 illustrates the sample size reductions resulting from a longer time horizon. Evaluation #1 is preferable when calculating a cost-minimization ratio since fixed costs are correctly spread over all subjects and interventions. Additionally, Evaluation #1 is preferred when stronger external validity

(generalizability) is paramount. Evaluation #3, (more strict criteria with strong study design) is preferred when more emphasis is placed upon internal validity.

Figure 12.6 Study Design, Data Sources, and Exclusion Criteria of Initiative Evaluations

	Evaluation #1 (n=6,334)	Evaluation #2 (n=5,160)	Evaluation #3 (n=4,624*)
Data Sources	-Pharmacist Report	-Pharmacist Report -Pharmacy Claims	-Pharmacist Report -Pharmacy Claims -Non-Pharmacy Claims
Methods	-Before-After	-Before-After -With comparison	-Before-After -With comparison -And propensity matching
Exclusion Criteria	-None	-Absence of Rx Claim in post last 35 days of post-period**	-Absence of Rx Claim in post last 35 days of post-period** -ER Visit in Pre-Period -Hospitalization in Pre-Period -Absence of claim for LTC bed in all three months of pre-period

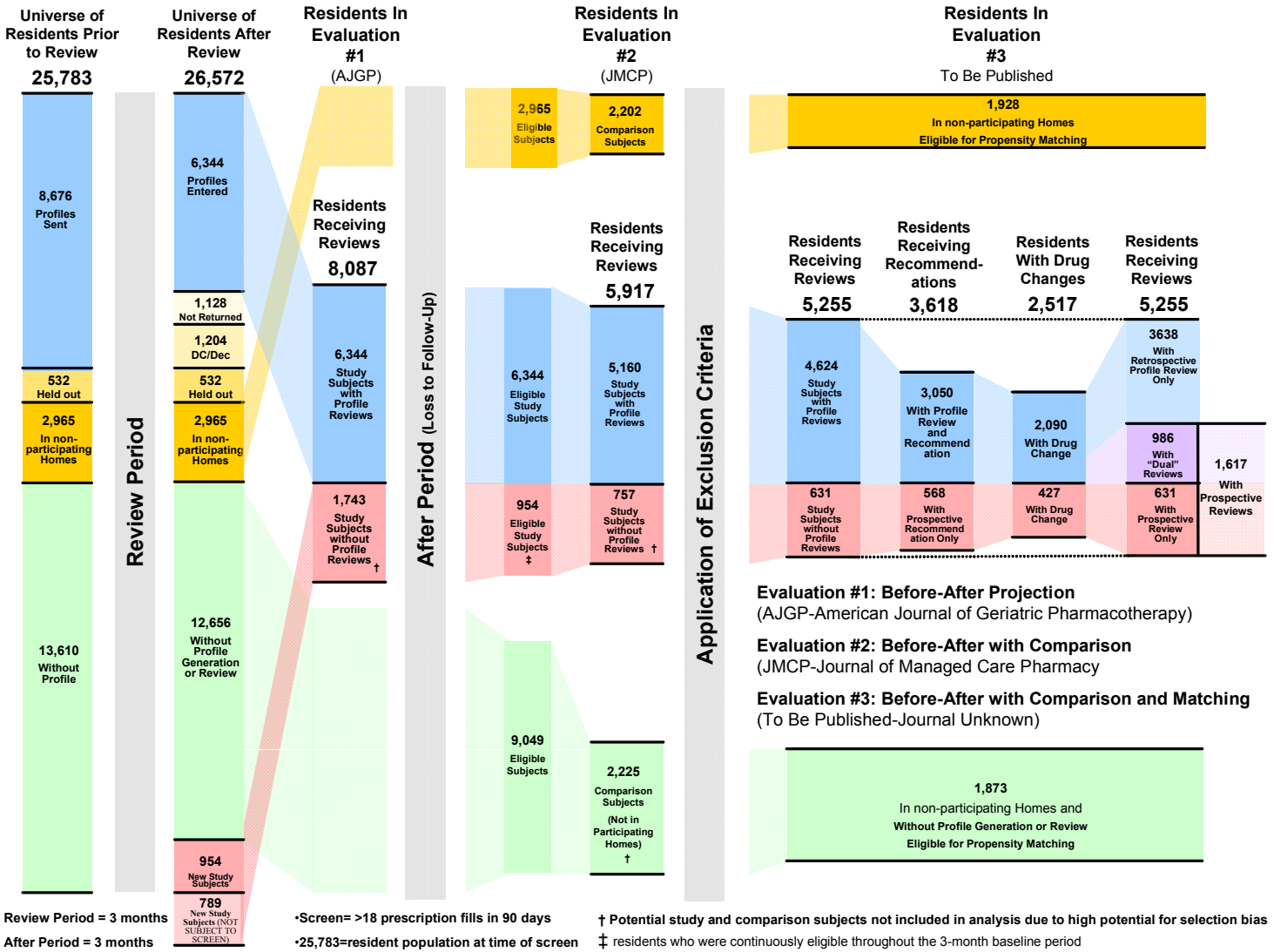
* 4,624 represents the number of study subjects receiving any retrospective intervention for Evaluation #3. It was the first to include subjects with prospective interventions and has a total n=5255.

** Continuous eligibility was required in both pre- and post- periods with this criteria. For Evaluation #3 an Rx fill was required in the first 35 days of the pre-period as well.

12.5 Comparison Group Assignment

At the outset, Phase # 1 of the Initiative sought to target nursing home residents for review that had at least 18 prescription drug fills in 90 days. During program development, the pool of review-eligible residents evolved to include all residents existing in participating homes. Though only residents with 18 or more prescription fills had claims-generated profiles sent to pharmacists, reviews could be sought for all residents in participating homes.

Figure 12.7 Cohort Developments for the Three Initiative Evaluations



As stated earlier, treatment selection was brought about by: 1) pharmacist and prescriber-specific characteristic(s), where a resident might not have received a review with one pharmacist but would have with another (or a drug change from one prescriber and not another) as well as 2) resident-specific characteristic(s). These characteristics, both pharmacist and resident, may have caused selection into and out of the group of residents receiving reviews and recommendations. The 20 co-variates outlined are an attempt to model treatment selection as accurately and precisely as possible given the available data. Endogeneity most certainly remains since there are no available co-variates that describe pharmacist or prescriber characteristics, nor do the co-variates completely describe resident-specific response to drug therapy. As such, the safer approach is to model treatment selection versus residents in non-participating homes, rather than against persons not receiving treatment in participating homes. This approach is illustrated in Figure 12.8.

Figure 12.8 Propensity Matching Strategy for Study and Comparison Subjects

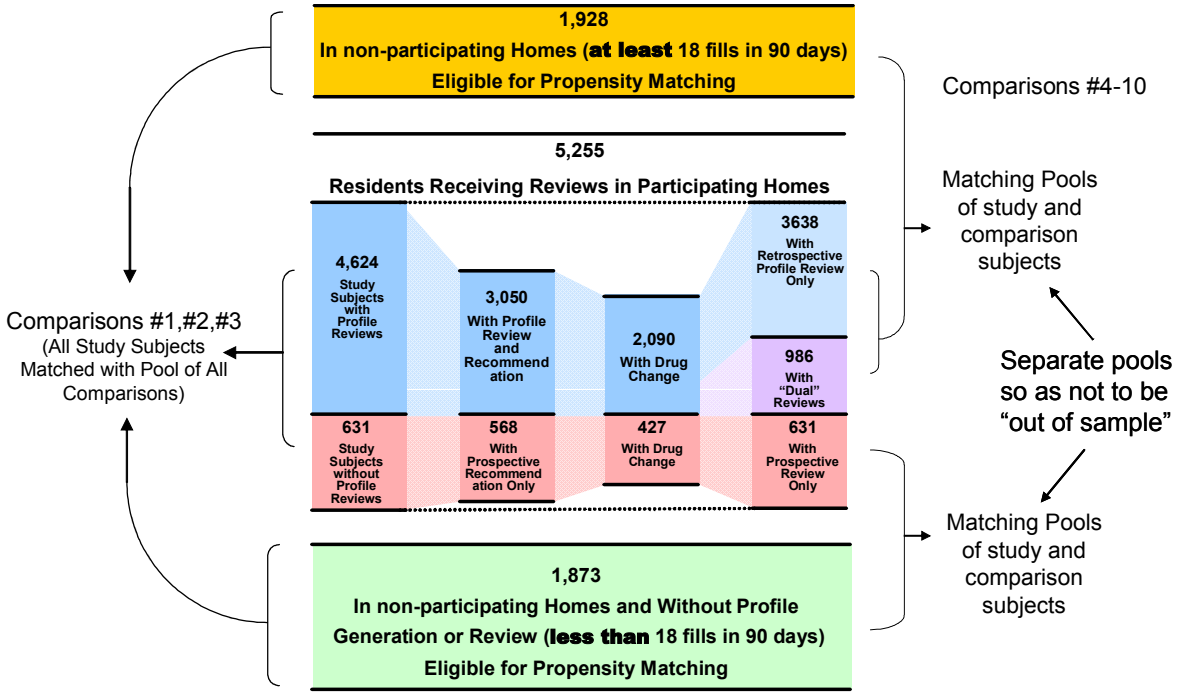
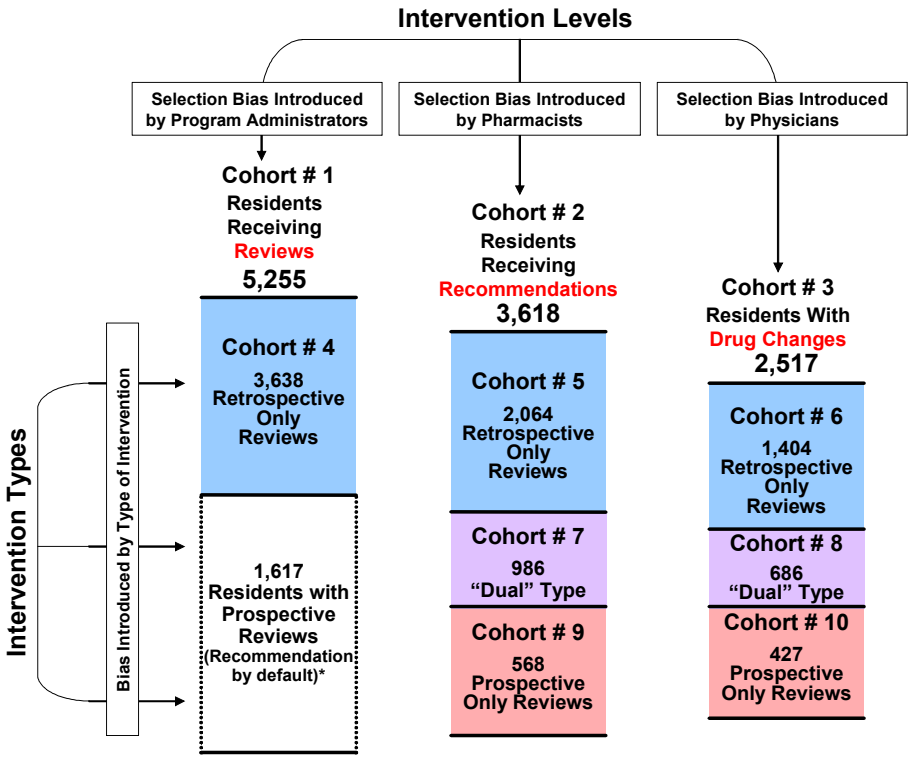


Figure 12.9 further illustrates the importance of separate analysis and treatment selection modeling for each of the nine proposed cohorts. Notice that the three cohorts with drug changes are a function of the three cohorts of recommendations, which are a function of the three cohorts with reviews. As discussed previously, each of these nine cohorts is subject to different selection pressures, both in type of intervention and in health practitioner involvement. At the review level, selection bias may be imposed by program administrators through nursing home solicitation for participation. At the recommendation level, selection bias may be introduced by pharmacists as they select out those residents for whom they believe to have a PDTP that warrants change. At the drug change level, prescribers introduce selection bias since they ultimately determine which changes are made. The same holds for each of the type of interventions taking place in the initiative. Each type of intervention (Retrospective-Only, Dual-Type, and Prospective Only) are subject to different selection pressures based upon the methods and characteristics of each. For instance, Retrospective-Only type reviews have profiles for the pharmacist to view with alerts that require the reviewer to actively disregard in order to receive payment whereas Prospective-Only reviews do not. This feature alone would has the potential to create large amount of selection bias to occur since drugs and their respective types of PDTP alerts on a given residents profile might cue a pharmacist towards a recommendation that he/she may not have otherwise been aware of without a profile.

Since the three main cohorts as well as their seven sub-groupings may be subject to different selection pressures, all must be subjected to a treatment selection model separately when propensity scoring since different co-variates will have differing significance and

resultant effects in differing cohorts. The following illustration depicts the nine proposed cohorts.

Figure 12.9 Study Subject Cohorts



*63 residents had a prospective review with no recommendation under a special circumstance, not to be included in sub-group analysis

12.6 Propensity Scoring

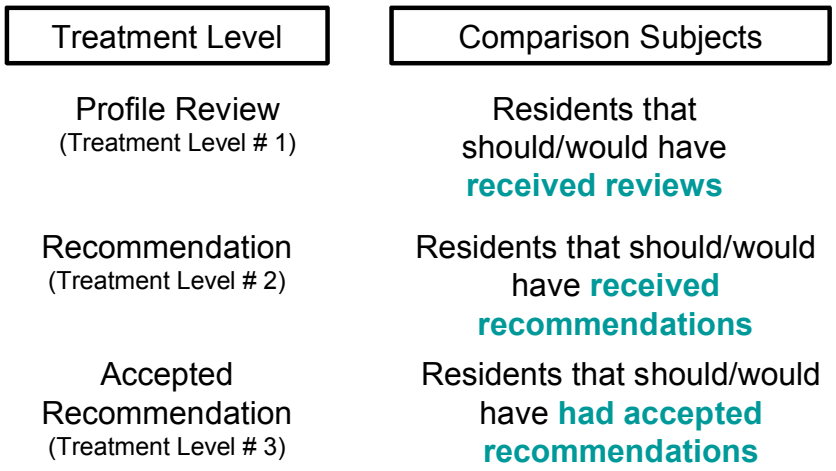
Perkens et al.[45] outline five steps for conducting an evaluation of observational data using propensity scoring:

1) Estimate the propensity score by modeling treatment selection
2) Stratify Observations
3) Check the balance achieved by step 1 modeling
4) If balance not achieved, revisit step one with additional variables or interactions
5) Calculate subclass-specific estimates

12.6.1 Step 1: Modeling Pharmacist Response

Estimating the propensity of receiving treatment requires a model that predicts how pharmacists respond in terms of resident-specific reviews and subsequent action. Any resident characteristics that influence a pharmacist's inclination to make reviews, recommendations, and changes should ideally be included in a logistic regression of treatment selection. If all relevant characteristics are included, a counterfactual match can be assigned to every study subject that receives treatment at each respective treatment level (Figure 12.10). For each treatment level (review, recommendation, and change) the counterfactual represents those residents that would or should have received treatment had they been eligible for treatment. For treatment level #1 (profile review), the counterfactual is represented by residents who should or would have received a review had they been eligible for treatment. For treatment level #2 (recommendation), the counterfactual is represented by residents who would have received a recommendation. For treatment level #3 (drug change), the counterfactual is represented by residents who would have received a drug change had they been eligible for treatment.

Figure 12.10 Comparison Subject Modeling



Potential matches are not mutually exclusive among treatment levels. A comparison subject may be a potential match for any or all treatment levels. Because the model is performed at respective treatment levels (review, recommendation, and drug change) and treatment types (prospective-only, retrospective-only and dual-type), different sets of patient, pharmacist or physician characteristics may be in play as potential sources of bias and every potential comparison subject is likely to have a slightly different propensity score for each of the seven sub-cohorts.

All variables related to both treatment and response will be included in the propensity scoring model estimating treatment selection.[45] Post-treatment variables were not be included, as bias would result from over matching.[46] As discussed earlier, both active and passive selection occurred during the deployment of the Initiative. Using both primary (data entry from hard-copy profiles) and secondary (administrative claims data) sources, the following variables were chosen to estimate treatment selection:

Passive Treatment Selection: Age, Race, Gender

Active Treatment Selection: Number of Potential Drug Therapy Alerts (PDTPs),
Number of Drugs Filled in 90-days,
Total Cost of Drugs in 90-days

In addition to the total number of PDTP alerts, a separate explanatory variable is used for each type of PDTP since each PDTP has different origins and meanings as an alert. Pharmacist interpretation of these alerts is likely to vary considerably among PTDPs, and thus each PDTP must be modeled separately:

Potential Drug Therapy Alerts: Number of: Therapeutic Duplications

Beers List Drugs

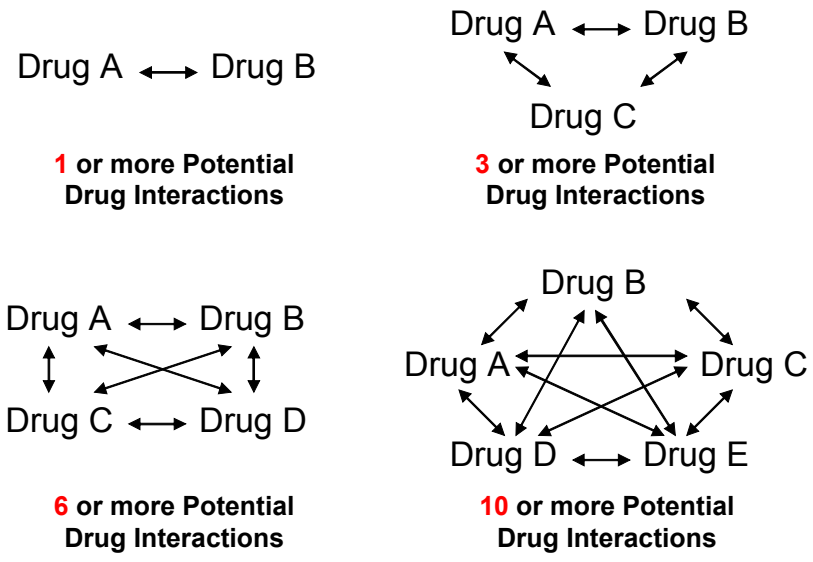
Consider Length of Therapy

PAL List Drugs

Clinical Initiatives Drugs

Further specification using interaction terms, squared terms, and potentially cubed terms should be employed when treatment selection is not fully understood.[47] Thus, I added a squared term for age to model the potential effects of exponential treatment selection with respect to age. Additionally, since I chose to model number of alerts linearly rather than categorically, I included squared terms for each of the PDTP alert categories. It is possible that an exponential relationship exists between pharmacist response and the number and type of alerts presented to them. This effect is illustrated below in Figure 12.11.

Figure 12.11 Relationships between Number of Alerts and Number of Drug Interactions



1...3…6...10….exponential gain with each additional drug

Interactive effects may exist between PDTPS, Number of Drugs, and Total drug cost as well. If interactive effects do occur among these variables, construction of a co-variate of interacting terms assures appropriate treatment selection modeling. If no interactive effect is observed, little is lost, since one of the advantages of propensity scoring is the diminished concern for overspecification, given large sample sizes.[48]

Squared terms: Age^2, (No. of Therapeutic Duplications)^2, No. of Beers list)^2, (No. of Consider Length)^2, (No. of PAL List)^2, (No. of Clinical Initiatives)^2

Interacted terms: No. of Drugs x No. of PDTP Alerts, No. of Drugs x Total Cost of Drugs, No. of PDTP alerts x Total Cost of Drugs

In summation, the fully specified, fully interacted model is as follows:

Treatment selection = Age + Age2 +Race + Sex + Number of Drugs + Cost of Drugs+ Number of Alerts + No. of Duplications + No. of Beers + No. of Consider Length + No. of PAL + No. of Clinical Initiatives + (No. of Duplications)^2 + (No. of Beers)^2 +(No. of Length)^2 + (No. of PAL)^2 + (No. of Clinical Initiatives)^2 + (No. of Drugs x No. of Alerts) + (No. of Drugs x Cost of Drugs) + (No. of alerts x Cost of Drugs) + error term

Rubin et al.[49] found that it is more important to include unimportant co-variates than to exclude important co-variates. Wang et al. notes that the goal of treatment selection modeling is to try to over-fit the model by including as many potential confounding co-variates as possible.[50] Additionally, Drake found no additional bias imposition from misspecification of co-variates.[48] Indeed, propensity scores are most useful when the

relationship between baseline risk factors and treatment selection are not fully understood.[51] To date, there are no established or recommended criteria for propensity score model development available,[52] though consensus dictates that I include all potentially relevant co-variates with higher order terms as well as interacted terms.

12.6.2 Step 2: Stratify (Match) Observations

Once scored, both study and potential comparison subjects must be matched to achieve balance among baseline characteristics. A multitude of matching techniques are available to the researcher employing a propensity scoring approach. Generally, six types of matching are available to researchers (Stratification, Nearest Neighbor, Caliper, Mahalanobis, Kernel, and Radius).[53]

Stratification methods assign study and comparison observations to strata based proximity of propensity score. Once stratified, treatment effect is determined by weighting the outcome measure by sample sizes of the strata.

Nearest neighbor matching simply matches study and comparison subject scores that are most closely aligned in value. Different matching types can take place (1:1, 2:1, with or without replacement), but all matching is at the subject level. Nearest match without replacement works as well as replacement methods when a sufficient number of "relevant comparison units" are available.[47]

Caliper matching utilizes the propensity score variance to limit the distance between the propensity scores for potential study and comparison matches. A pre-defined fraction of the variance is set, whereby a match must fall within this distance to be eligible for comparison. Doing this ensures that propensity scores are not matched that are "out of sample".

Radius matching employs a predefined distance requirement rather than a variance fraction. It also ensures matches are not "out of sample", but has the additional limitation of a fixed distance restraint. Thus, unlike caliper matching, the potential for making an "out of sample" match is further reduced if variation in propensity scores is high.

Kernel matching uses weighting to adjust for the distance between matches. Thus, matches that have fewer distance between them are more influential in the resultant analysis, whereas matches with greater distance between them have less influence on the results.

Mahalanobis metric matching uses matrices to find the smallest difference between a study subjects and all eligible comparison subjects based upon the distribution of all co-variates for each comparison subject. It is essentially a more sophisticated manner in which to match with the true nearest neighbor based on the treatment selection model. It may be combined with Radius or Kernal techniques to ensure study subjects are not matched to any comparison subject that is "out of sample". It may be performed with or without replacement.

Mahalanobis matching provides for the most comprehensive and precise matching based upon the chosen co-variates in the selection model. Another convenient feature is its ability to use with or without replacement matching once a Mahalanobis metric has been established to which comparison subjects are matched. The method is robust at determining the closest matches since it determines simultaneously considers all co-variates when determining distance to nearest neighbor. Additionally, as shown previously, cohorts #4, and #5 have study sample sizes that are greater than the number eligible comparison subjects, necessitating a matching technique that allows for with replacement matching. Radius and

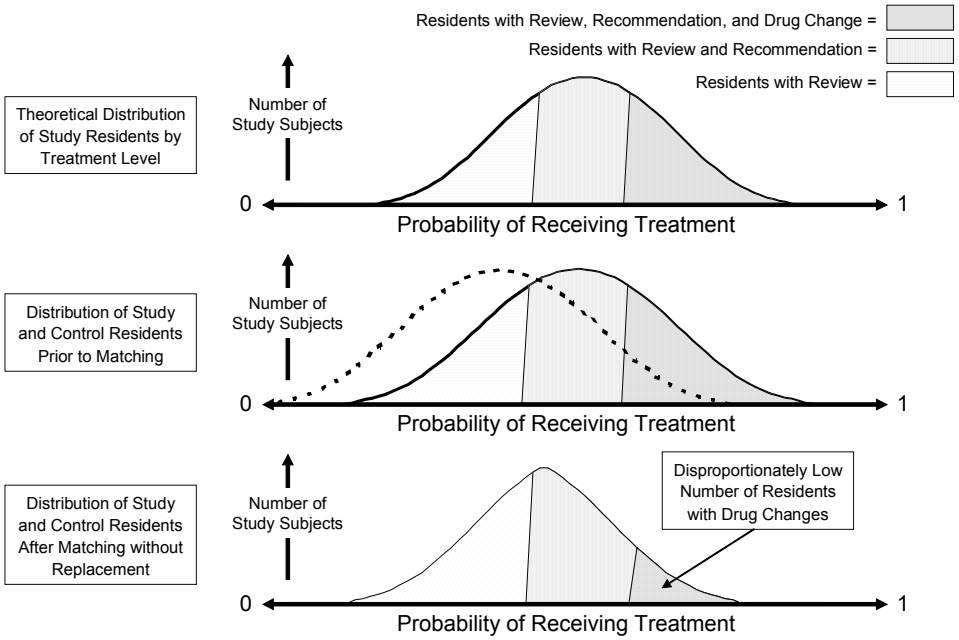
caliper restrictions are not placed upon the matching method since analysis of all study subjects is desired.

One of the caveats when utilizing any propensity matching procedure with replacement is the replication of comparison observations when evaluating outcomes. The method simply matches study subjects with its nearest neighbor regardless of the frequency with which it has been replaced. The number of times a particular observation may be replaced is referred to as its weight. To date, no consensus or thorough review of matching techniques exist, though most researchers imply that choice of method depends on a variety of factors specific to each particular study.[54,55]

Regardless of the particular advantages or disadvantages of replacement methods, they have been shown to be robust in practice,[47,53] especially when evaluating interventions,[56,57] and when the degree of overlap between treatment and comparison groups in large.[47] Unlike drug products, which are standardized so that each patient receives nearly identical treatment upon administration, services such as those that pharmacists provide differ depending on the pharmacist providing the service and as well as the patient-specific needs of the person receiving the service. Thus, when possible, all subjects in intervention studies should be included in the analysis when possible unless these inherent differences are accounted for in the analysis, a difficult proposition at best given the nuance in the delivery of a service. In this investigation, matching with replacement is preferred, since treatment selection may predict subsequent treatment levels. For example, in the case of matching at the review level, it is quite possible that more of persons not having a recommendation will have nearest neighbor matches, as opposed to persons with recommendations by pharmacists. This maldistribution of propensity to receive a recommendation may bias the estimate for

effect at the review level. The same holds at the recommendation level, were a disproportionate number of persons not having drug changes will have a nearest neighbor match, since the overall propensity of receiving treatment is likely higher in the study group than in the comparison group. Figure 12.12 illustrates this phenomenon.

Figure 12.12 Potential Bias Imposed by Matching without Replacement



12.6.3 Step 3: Check the Balance Achieved by Step 1 Modeling

Once matched, I will check to assure successful balancing by statistically testing for differences in baseline risk. For categorical variables, I will use chi-square testing and Student T-testing for continuous variables. Despite multiple comparisons, I do not plan to use a Bonferroni-type adjustment. Joffe and Rosenbaum support this decision, arguing that randomization (the gold standard) tends to elicit at least one significant difference for every 20 co-variates[40], so that we should expect some random associations to prove statistically significant at a 95% confidence level given enough comparisons. Using a Bonferroni type

adjustment makes the balancing test *less* conservative, not *more* conservative (As the adjustment intends) since the null hypothesis is no balance in co-variate distributions.

12.6.4 Step 4: If Balance Not Achieved, Revisit Step 1 and Remodel

If balance is not achieved ($p<=0.05$) for each of the covariates, I will revisit the treatment selection model and adjust variables or include additional variables such as co-morbid conditions. If multiple iterations of the treatment selection model do not achieve balance among all co-variates, I will relax the requirement of a fully balanced set of baseline characteristics so as not to limit the inclusion of all study subjects in the analyses.

12.6.5 Step 5: Calculate Subclass-Specific Estimates

Since I am using the Mahalanobis method of matching, I will not use pre-determined strata following propensity scoring. Instead, I will form quintiles for sub-class analysis following successful matching as described in Chapter 11. (Figure 11.5 Strata Specific Treatment Effects).

12.7 Outcome Measures

I have selected outcome measures for their relevance to the previously stated dissertation objective:

Determine if the Initiative was effective in reducing drug expenditures while simultaneously maintaining or improving the quality of care received by nursing home patients.

The required measures are conveniently found in the treatment selection model. The before-after with comparison study design allows for both: 1) a difference in difference calculation as well as 2) a measurement of effect using the same co-variates that described baseline risk. In addition to the selected co-variates, a

categorical measurement (hospitalization) is added as an event (Medicare crossover payments precluded the used of this variable in the selection model).

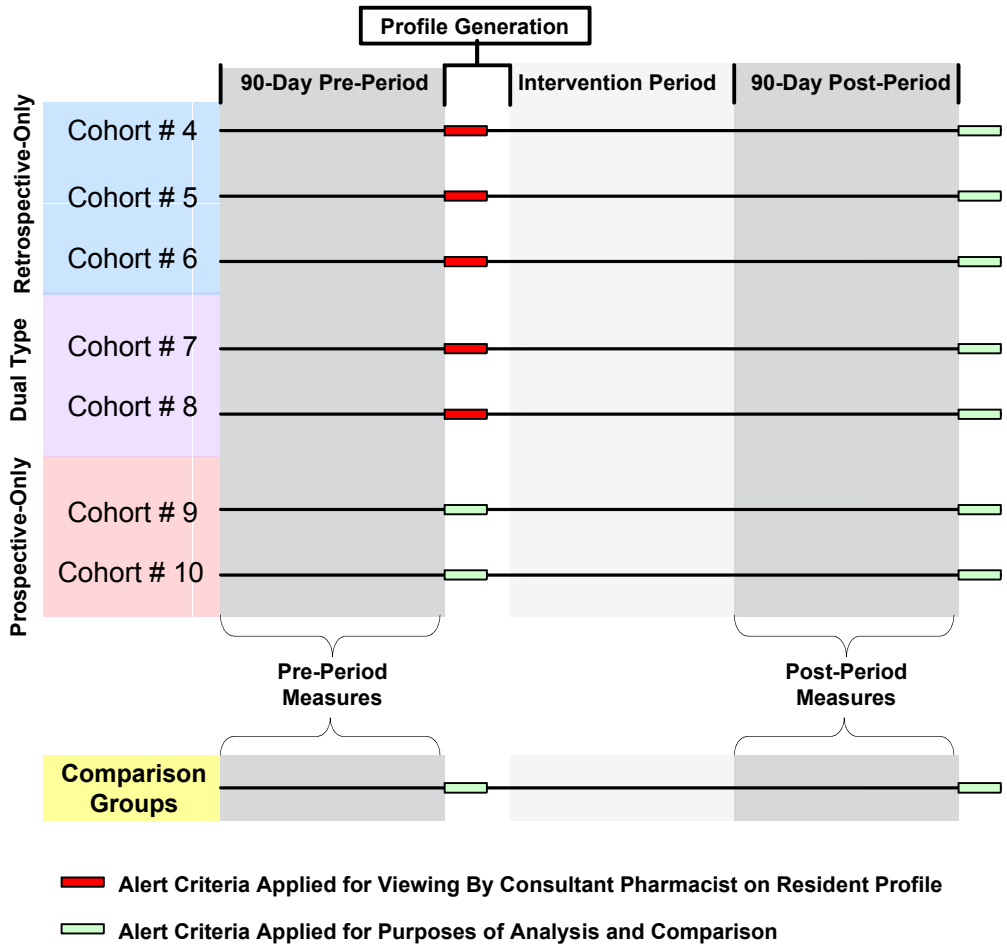
Proposed Outcome Measures

Intermediate Quality:	Prevalence of Beers List Drug Alerts Prevalence of Consider Length of Therapy Alerts Prevalence of Therapeutic Duplication Drug Alerts
Intermediate Cost:	Prevalence of PAL List Drug Alerts
Intermediate Cost /Quality:	Prevalence of Clinical Initiatives List Drug Alerts
Global Utilization:	Number of Prescription Drug Fills
Global Cost:	Total Prescription Drug Cost
Global Quality:	Prevalence of Hospitalizations in Post Period

With a balanced sample, post treatment differences in co-variates may be attributed to treatment alone, assuming no relevant variables were omitted when modeling treatment selection. This assumption is never satisfied fully in practice, but a well-developed treatment selection model limits any bias that may occur. Figure 12.13 illustrates pre and post period screenings that occurred. These screenings served two functions: 1) to populate alert categories on patient profiles for those failing the 18 drug in 90 day criteria and 2) to measure drug utilization with total drug use, cost, and prevalence of PDTP alerts. Notice that six of the nine proposed cohorts used pre-period screens to populate resident profiles, while three categories received screens for the purposes of the analysis, but were never used to inform consultant pharmacists of PDTP alerts. All nine cohorts were subjected to post-period screens to compare to pre-period screens to determine the before after difference in drug utilization. Similarly, comparison groups from non-participating homes are subjected

to the same alert criteria and screen, though profiles never became available to their consultant pharmacists or their prescribers (Figure 12.13).

Figure 12.13 Before-After Screening by Cohort



Noticeably absent from the proposed outcomes are qualitative measures. One such measure is the Medication Appropriateness Index (MAI). Like other qualitative or subjective measures, this index is not particularly useful for an evaluation of this Initiative. The consultant pharmacists were charged with deciding the appropriateness of the drug regimens. The MAI, like pharmacist action, requires a subjective evaluation of medications and uses 10 criteria quite similar to the criteria employed in this study as part of the possible problems identified on the drug profile (e.g. dose problems, therapeutic duplications, duration), thus

rendering the MAI is impractical for use in this study. Furthermore, recent evidence has shown only moderate inter-group agreement is found using the MAI when multiple raters are used.[58] While the MAI has been validated in circumstances where no prior review had taken place,[59] no meaningful validation has been performed in a circumstance such as the Initiative, were consultant pharmacists would be rating other consultant pharmacists; as it would be a redundant exercise.

12.8 Statistical Testing

If difference-in-difference results are generally not skewed by outliers, t-testing will be used to determine statistical significance. If evidence of skewed distributions exist, I will use non-parametric testing. Specifically the Wilcoxin two-sample test for changes in alert rates, number of drug fills, and total cost of drugs between study and comparison groups. Relative risk estimates will be determined for hospitalization events and between groups testing performed using the Chi Square Distribution. Though McNemar's Chi Square is a popular test to apply for before-after studies, it is infeasible for the evaluation of hospitalization risk since persons having hospitalizations in the pre-period were excluded from the analysis. STATA (StataCorp. 2005. *Stata Statistical Software: Release 9*. College Station, TX: StataCorp LP) statistical software version 9.0 was utilized for all statistical testing. Mahalanobis matching was performed using the PSMATCH2 file available at http://ideas.repec.org/c/boc/bocode/s432001.html.[60]

This evaluation and its predecessors received Institutional Review Board approval from The University of North Carolina at Chapel Hill.

CHAPTER 13

PHASE 1 RESULTS, INTERPRETATION, AND STUDY LIMITATIONS

13.1 Co-variate Balance

Ultimately, the goal of propensity scoring with subsequent matching is to match study subjects with comparison subjects based upon relevant co-variates as closely as possible given a choice of matching methods. For this analysis, participant behavior was modeled using 20 variables presumed to influence treatment selection at all three levels (Review, Recommendation, and Change) as well as all three types (Retrospective-Only, Dual-Type and Prospective-Only) of intervention.

The Mahalanobis method of matching produced substantial reductions in bias for most cohort-comparison groups. Table 13.1 displays the percentage of absolute bias that was present in both unmatched as well as matched cohort-comparison groups for Comparison #1 (Review Level, All Intervention Types).

Absolute bias was introduced to propensity scoring methods by Rosenbaum and Rubin[61] in 1985 using the following calculation in Figure 13.1:

Figure 13.1 Formula to Calculate Absolute Bias Percentage

$$\%\text{Absolute Bias} = 100\left(\frac{|\ \mu_t - \mu_c\ |}{\sqrt{\frac{Var_t - Var_c}{2}}}\right)$$

Where: μ_t = Mean of the Treatment Group

μ_c = Mean of the Comparison Group

Var_t = Variance of the Treatment Group

Var_c = Variance of the Comparison Group

This calculation standardizes the magnitude of difference in means across treatment and comparison groups to enable bias comparisons between co-variates as well as comparisons among and between treatment selection models. While offering no easily interpretable result, the effect of standardization of distance between groups provides a convenient manner in which to identify quickly and readily variables that remain problematic. Table 13.1 lists the percentage of absolute bias by co-variate both before and after matching as well as the percentage reduction in bias achieved by propensity scored matching using the Mahalanobis with replacement method.

The magnitude of the difference in means between study and comparison groups is directly related to the bias measurement, while the variance is inversely related. This point is important when considering a co-variant such as Total Amount Paid since its standard deviation is greater than its magnitude, correctly suppressing the reported bias. Conversely, if the variance around a measurement is small, such as the case with age where less than a 2% absolute difference exists between groups but the variance in age is small, pre-matching bias is much higher (14.1%).

Table 13.1 also reports the average percentage bias for both matched and unmatched comparisons as well as the Pseudo R^2, a measure of goodness of fit. This measure is similar to R^2, in that it approximates the amount of variance explained by the model. The unmatched cohort-comparison group shown above has bias that explains 10.5% of treatment selection, whereas the matched group has only 0.8%.

Table 13.1 Bias Measurements, Reductions and Significance for Comparison #1

Comparison #1 (All Residents with any Type of Review)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.6	79.4	-14.1		-6.62	0.000
	Matched	77.6	78.5	-7.1	50%	-3.83	0.000
(Age)^2	Unmatched	6,175	6,455	-15.7		-7.38	0.000
	Matched	6,175	6,286	-6.2	61%	-3.35	0.001
Race	Unmatched	32.2%	24.9%	16		7.48	0.000
(Non-White)	Matched	32.2%	30.5%	3.6	78%	1.79	0.074
Sex	Unmatched	75.1%	78.8%	-8.7		-4.05	0.000
(Female)	Matched	75.1%	76.2%	-2.6	70%	-1.3	0.195
Total Number of Drugs	Unmatched	26.9	20.4	57.5		27.22	0.000
	Matched	26.9	25.6	11	81%	6.11	0.000
Total Amount Paid	Unmatched	$1,442	$1,088	27.1		12.19	0.000
	Matched	$1,442	$1,340	7.8	71%	4.04	0.000
Total Number of Alerts	Unmatched	9.37	6.73	48.1		22.57	0.000
	Matched	9.37	8.86	9.4	81%	4.98	0.000
Number of Duplication Alerts	Unmatched	4.47	3.04	41.9		19.55	0.000
	Matched	4.47	4.14	9.8	77%	5.1	0.000
Number of Beers List Alerts	Unmatched	0.686	0.522	18.4		8.55	0.000
	Matched	0.686	0.645	4.6	75%	2.29	0.022
Number of PAL List Alerts	Unmatched	1.47	1.14	27.9		13.03	0.000
	Matched	1.47	1.42	3.5	87%	1.82	0.069
Number of Clinical Initiatives Alerts	Unmatched	2.60	1.89	42.1		19.72	0.000
	Matched	2.60	2.51	5.5	87%	2.87	0.004
Number of Consider Length Alerts	Unmatched	0.150	0.135	3.3		1.55	0.121
	Matched	0.150	0.143	1.6	51%	0.8	0.423
(Number of Duplication Alerts)^2	Unmatched	32.4	20.1	25.4		11.82	0.000
	Matched	32.4	27.3	10.6	58%	5.57	0.000
(Number of Beers List Alerts)^2	Unmatched	1.35	0.98	12.5		5.78	0.000
	Matched	1.35	1.20	5.1	59%	2.53	0.012
(Number of PAL List Alerts)^2	Unmatched	3.63	2.60	20.6		9.53	0.000
	Matched	3.63	3.31	6.4	69%	3.19	0.001
(Number of Clinical Initiatives Alerts)^2	Unmatched	9.62	6.33	29.7		13.75	0.000
	Matched	9.62	8.76	7.8	74%	3.87	0.000
(Number of Consider Length Alerts)^2	Unmatched	0.230	0.187	4.7		2.17	0.030
	Matched	0.230	0.218	1.4	71%	0.66	0.511
Total Number of Alerts x Total Number of Drugs	Unmatched	293.7	187.8	37.7		17.54	0.000
	Matched	293.7	264.3	10.5	72%	5.45	0.000
Total Amount Paid x Total Number of Drugs	Unmatched	44,936	29,281	22.5		10.05	0.000
	Matched	44,936	39,467	7.9	65%	4.04	0.000
Total Amount Paid x Total Number of Alerts	Unmatched	16,183	10,170	23.9		10.69	0.000
	Matched	16,183	14,049	8.5	65%	4.33	0.000
Average Bias	Unmatched			**24.89**			
	Matched			**6.53**	**74%**		
Pseudo R2	Unmatched	0.105					
	Matched	0.008					

Sample Sizes: Study Group n=5,255
Unmatched Comparison Group n=3

Also reported in Table 13.1, is the statistical significance of the difference in means between treatment and comparison groups using between groups t-testing, as well as the reduction in percentage absolute bias. Results of the T test determine whether or not the reductions in bias between the matched and unmatched samples were sufficient to balance co-variates. Significant differences ($p<0.05$) indicate that the co-variate remains unbalanced. Despite Mahalanobis matching, 15 of the 20 co-variates remain unbalanced using the between groups t-testing at a p-value < 0.05. While the number of covariates with statistically significant differences remained high, the magnitude of the unbalance/difference is not great. The percentage bias remaining post-match ranged from 1.4% for the co-variate (Number of Consider Length Alerts) to 11.0% for the (Number of Drugs) co-variate. On the whole, balancing was improved with a 6.53% post-match bias, compared with 24.89% pre-matching bias. This represented a 74% reduction in overall bias.

This remaining imbalance must be viewed in context. It is not uncommon for many co-variates to remain unbalanced following matching. Further, with such large sample sizes employed (N>10,000), even small differences become statistical significant and may not result in much bias in effect estimates. Of note, the matched cohort-comparison for Comparison #12 (Prospective-Only, Drug Change) has no statistically significant differences between study and comparison subjects for any of the 20 co-variates, yet its average percentage bias was 6.67%, greater than matched subjects for Comparison #1 (6.53%). This effect may be due in large part from the smaller sample size (n<3000). Replications of Table 12.1 for all comparison groups maybe found in Appendix A.

Table 13.2 displays the mean percentage bias existing in the unmatched comparison groups for all 10 comparisons. As expected, bias exists to the greatest extent when

considering all types of Interventions. The greatest existence of bias is found in the group receiving drug changes for all types of interventions with a percentage bias of 30.18%. Also as expected, the group with the least amount of percentage bias was for Comparison #4 (Review Level, Retrospective-Only). Since reviews were performed on all residents in participating homes failing the screening criteria, program administrators were the only likely source of selection bias.

Table 13.2 Mean Percentage Bias among Comparison Groups (Pre-Match)

Pre-Matching Bias (Mean %)	**Intervention Type**			
	All Types	Retrospective	Dual-Type	Prospective
Review	**24.89**	4.92	N/A	N/A
Review and Reccommendation	**28.90**	6.55	12.75	17.66
Review, Recommendation, and Drug Change	**30.18**	8.61	16.36	18.93

It is apparent from Table 13.2 that prospective interventions imposed the greatest selection pressures. This finding is consistent with the nature of prospective interventions as conducted in the Initiative, where pharmacists initiated treatment only when a problem was discovered.

Table 13.3 shows the extent of percentage bias among all comparison groups following matching. Following successful Mahalanobis matching, the extent of remaining bias is remarkably similar across comparison groups.

Table 13.3 Mean Percentage Bias among Comparison Groups (Post-Match)

Post-Matching Bias (Mean%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**6.53**	5.06	N/A	N/A
Review and Reccommendation	**7.83**	6.97	7.48	5.78
Review, Recommendation, and Drug Change	**7.97**	6.80	7.64	6.67

Percentage bias ranges from 5.06% in Comparison #4 (Review Level, Retrospective-Only) to 7.97% in Comparison #3 (Drug Change Level, All Intervention Types). Just as with the unmatched comparison groupings, bias increased slightly across Intervention Types as the Intervention Level became more proximal to the mechanism of action (changed drug utilization). This finding is consistent with the notion that additional selection bias occurs as one nears the drug change event on the causal pathway. The exception to this rule was found at the Recommendation Level in the Retrospective-Only intervention group, which maintained a higher level of bias than its Drug Change Level counterpart.

Table 13.4 shows reductions in mean percentage bias among all comparison groups following matching.

Table 13.4 Reduction in Mean Percentage Bias among Comparison Groups

Pre-Post Bias Difference (Mean % Reduction)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**73.76**	**-2.95**	N/A	N/A
Review and Reccommendation	**72.90**	**-6.37**	**41.33**	**67.29**
Review, Recommendation, and Drug Change	**73.59**	**21.06**	**53.32**	**64.76**

Large bias reductions were observed in all comparison groups. Though none approached the desired 100% reduction, 6 of 10 comparison groups experience reductions of greater than 50%. Interestingly, the Review and Recommendation Levels for the Retrospective-Only Intervention Type experienced greater levels of bias after matching. This is possible, as Rosenbaum and Rubin have stated,[61] if the pre-matching bias is substantially less than 20%.

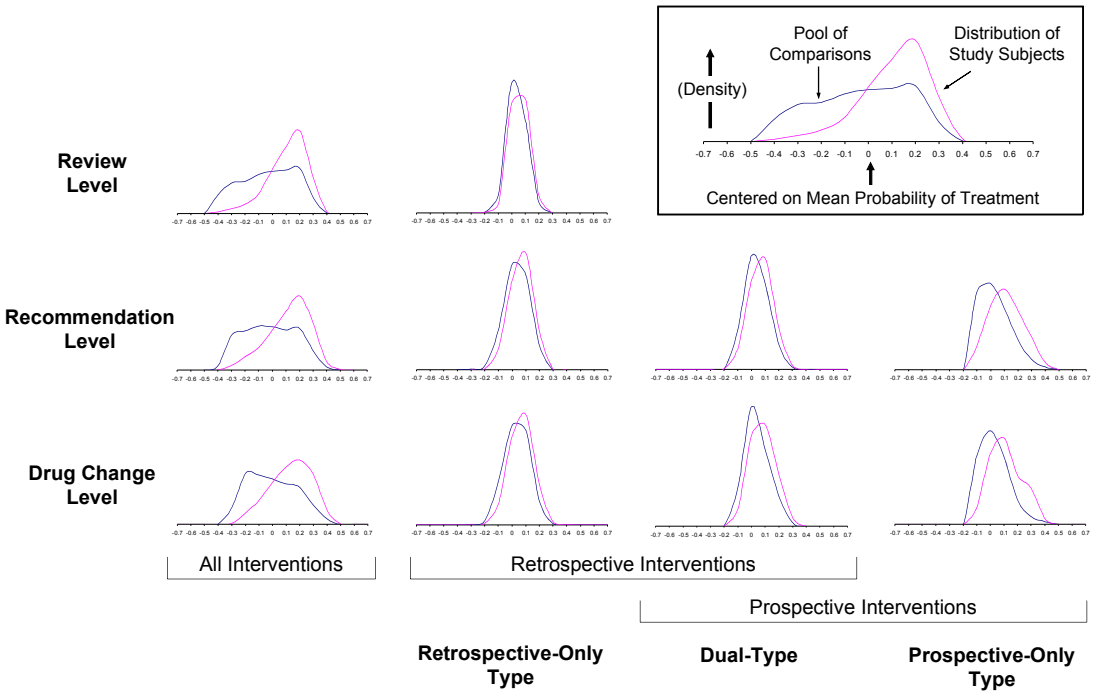
13.2 Distribution of Propensity Scores

Mahalanobis matching is preferred when treatment selection may be non-linearly related to many co-variates.[62] It is also the method of choice for multiple treatments[63] and multi-level treatments. Its advantage is drawn from its inclusion of all co-variates as well as the propensity score when calculating distances between study and comparison subjects. While this strategy ensures substantial bias reduction on all co-variates, it may do so at the cost of increased distance between propensity scores for study and comparison subjects compared to other methods of matching that only consider the propensity score itself.[61] In practice, it is possible to employ a method of nearest propensity scored neighbor as a first method of matching to ensure equal propensity to receive treatment, followed the Mahalanobis method.[61]

When Mahalanobis matching is applied alone, a check on the distributions of propensity scores between study and comparison groups is prudent to ensure that the distance between study and comparison subjects is minimal for both: 1) co-variates as well as the 2) the propensity to receive treatment. Propensity score distributions both pre and post matching for both study and comparison groups in all 10 comparisons are shown below.

Figure 13.2 contains graphical representations of the distributions of propensity to receive treatment *prior to* Mahalanobis matching.

Figure 13.2 Distributions of Propensity Scores between Study and Comparison Subjects (Pre-Match)



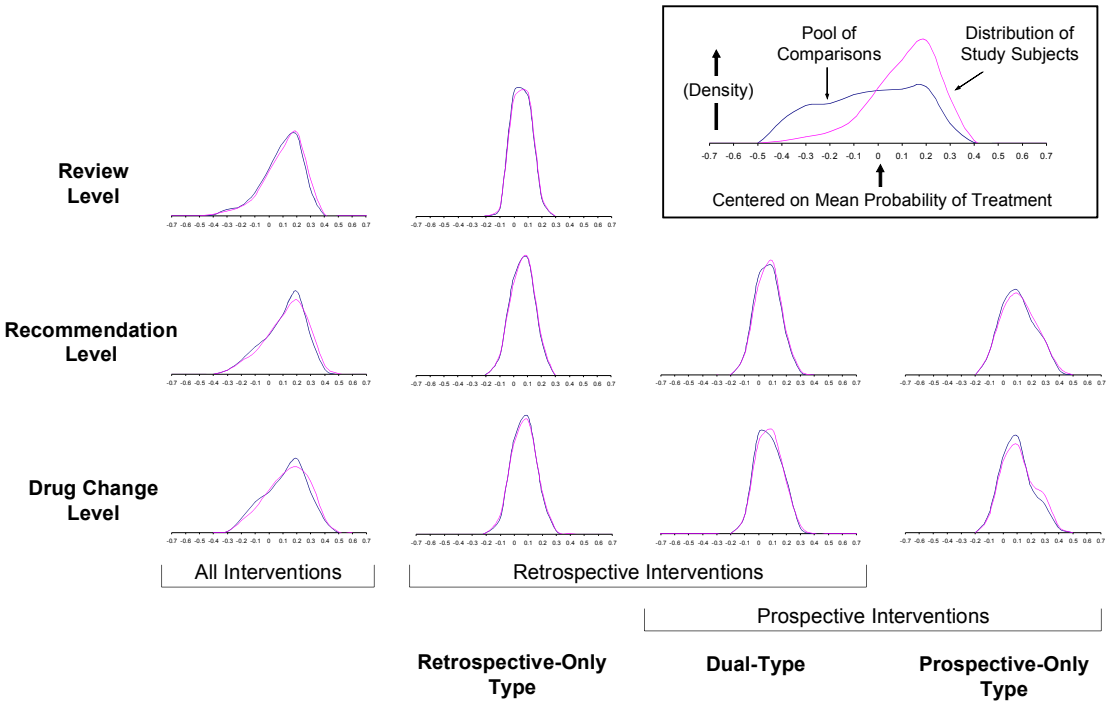
Upon visual inspection, the greatest differences in the distribution of propensity to receive treatment between study and comparison groups are found in the three primary comparisons (All Levels, All intervention Types). This is not surprising since these cohort-comparison groups contained all study participants, regardless of the result if the 18 drug fill in 90 day criteria. Similarly, the pool of comparisons for these cohort-comparison groupings contained all residents in non-participating homes meeting the inclusion criteria, regardless of the number of drugs filled in the 90 day pre-period.

Substantial distributional differences also exist for the Prospective-Only treatment sub-groups and are likely the result of increased selection pressures for that type of intervention. Interestingly, the Dual-Type interventions do seem to have some distributional

differences on propensity score, though this is likely a result of selection from prospective selection rather than retrospective selection since the Retrospective-Only sub-groupings have little distributional differences, especially at the review and recommendation levels.

Figure 13.3 contains graphical representations of the distributions of propensity to receive treatment *following* Mahalanobis matching.

Figure 13.3 Distributions of Propensity Scores between Study and Comparison Subjects (Post-Match)

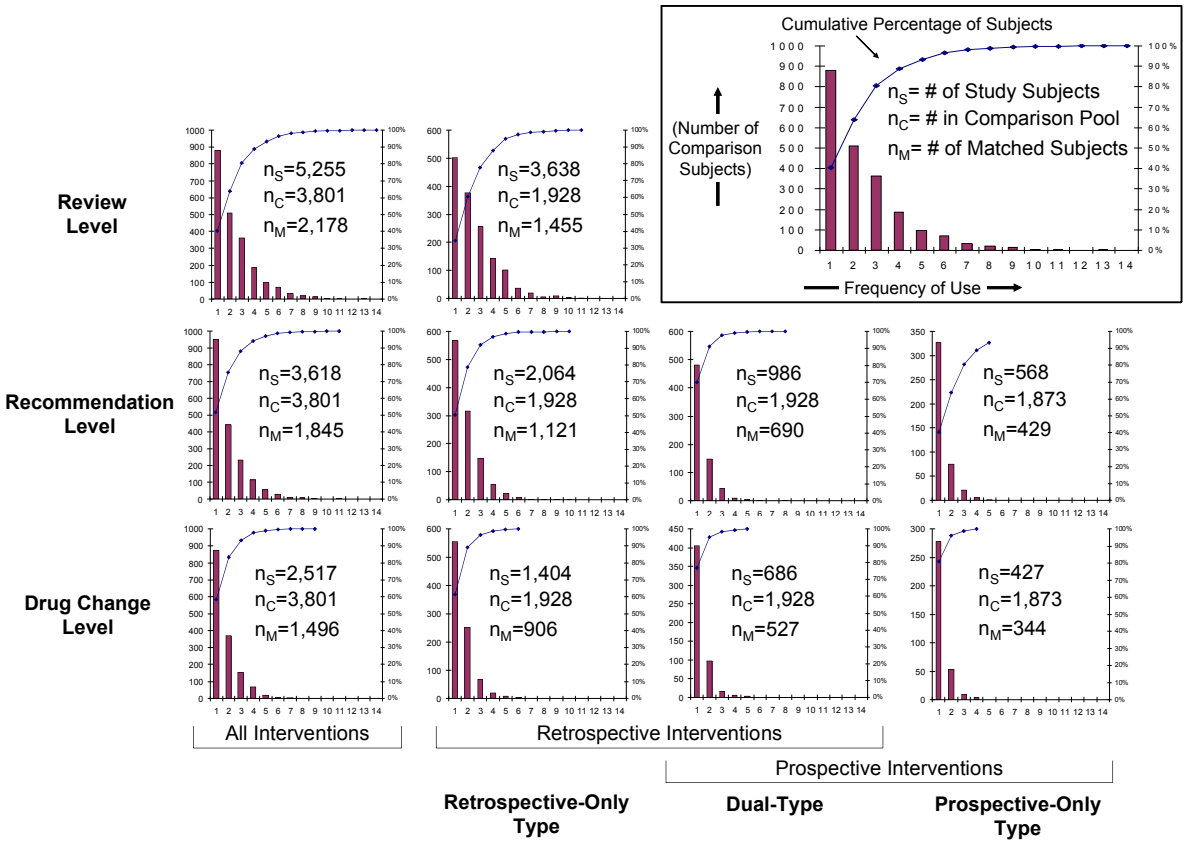


From visual inspection of Figure 13.3, it is apparent that the Mahalanobis provided a close match on propensity scores in addition to the 20 co-variates of interest.

13.3 Frequency of Re-Sampling

With replacement methods are not bounded by the number of instances in which a potential match may be used to make comparisons against a study group. Figure 13.4 shows the frequency of re-sampling of comparison subjects across all 10 comparison groups.

Figure 13.4 Frequency of Re-Sampling from Pool of Comparison Subjects (Post-Match)



The x-axis represents the frequency of re-sampling on a given comparison subject. The y-axis represents the number of comparison subjects having the re-sampling frequency. The smoothed line represents the cumulative frequency with 100% representing cumulative number of matched comparison subjects, or n_M. This sample size (n_M) represents the number of unique comparison observations without the inclusion of re-sampling observations. The denotation n_S represents the number of study subjects for each cohort-comparison grouping.

The denotation n_C represents total number of comparison subjects eligible for matching that meets all of the inclusion criteria.

The maximum number of instances in which a comparison subject was re-sampled was 14 in Comparison #1 (Review Level, All Intervention Types). Comparison #1 (Review Level, All Intervention Types) had the greatest frequency of re-sampling as well as the lowest cumulative frequency throughout. This is largely due to the ratio between study subjects and possible comparison subjects at 5,255:3,801. Where the ratio of study subjects to comparison subjects is greater, a greater required frequency of replacement occurs. The sparse number of eligible comparison subjects from non-participating nursing homes further supports the use of replacement method matching since we are interested in comparing possible study subjects due to heterogeneous intervention effects. While the study subject to comparison pool ratio largely determined the frequency of re-sampling, it was also necessitated to some extent by the amount of common support available from which to draw comparison subjects. The farther the inter-subject distances resulting from the 20 co-variates of interest and the propensity score, the greater the required frequency of replacement to maximize balance.

13.4 Results from Comparison #1 (Review Level, All Intervention Types)

Comparison #1 (Review Level, All Intervention Types) is an important cohort-comparison grouping for evaluation of overall intervention effect. Since all study subjects meeting the inclusion criteria are evaluated regardless of intervention type, this comparison may be viewed as a "main effect". The remaining primary comparisons (Comparison #2 and #3, Recommendation and Drug Change levels for all Intervention Types) test overall effect as well, yet not at the level of initiation of treatment. The thrust of the Initiative was to have

pharmacists review computer generated profiles, with payment for services at the Review Level of Treatment. Thus, programmatically this comparison is best used for any cost-minimization analyses subsequent to this dissertation (For prospective interventions, the review and recommendation levels were co-incidental with this particular program since payment for services was conducted at the recommendation level).

A statistically significant difference-in-difference three month prescription cost reduction of $64.09 was found, equal to a 4.4% reduction in overall expenditures for pharmaceuticals. This translates to a per member per month (PMPM) drug cost savings of $21.36. Difference-in-difference reductions were also found for three of five alert types. PAL list alerts experienced at 19.2% reduction, while Clinical Initiative Alerts were reduced by 9.6%. A small, but statistically significant reduction in Duplication Alerts was observed (3.8%) as well.

Table 13.5 underscores the importance of using a difference-in-difference approach for intervention studies. Note that the within-group drug cost reduction was only 0.7% for the study group, while it *increased* in the comparison group (4.7%). This seems intuitively feasible since we would expect the number of drugs and their aggregate costs to increase given the progression of time, especially at a late stage in life. This result also highlights the imperative need for a comparison group.

Table 13.5 Comparison #1 Treatment Effects (Review Level, All Intervention Types)

Comparison #1 (All Residents with any Type of Review)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,442	-9.60	-0.7%			
	Comparison	$1,341	54.49	4.1%	**-64.09**	**-4.4%**	**0.000**
Total number of drugs	Review	26.9	-0.33	-1.2%			
	Comparison	25.6	-0.38	-1.5%	**0.05**	**0.2%**	**0.781**
Number of PAL list alerts	Review	1.47	-0.42	-28.7%			
	Comparison	1.42	-0.14	-9.8%	**-0.28**	**-19.2%**	**0.000**
Number of Clinical Initiatives alerts	Review	2.60	-0.25	-9.6%			
	Comparison	2.51	0.001	0.1%	**-0.25**	**-9.6%**	**0.000**
Number of Beers List alerts	Review	0.69	-0.05	-8.0%			
	Comparison	0.64	-0.04	-6.7%	**-0.01**	**-1.7%**	**0.488**
Number of duplication alerts	Review	4.47	-0.30	-6.6%			
	Comparison	4.14	-0.13	-3.1%	**-0.17**	**-3.8%**	**0.013**
Number of Consider Length alerts	Review	0.15	-0.01	-5.5%			
	Comparison	0.14	0.001	0.9%	**-0.01**	**-6.3%**	**0.363**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=5,255
Unmatched Comparison Group n=3

Note also that PAL list alerts declined by 9.8% in the comparison group. This decline is likely a result of a concerted statewide effort to encourage all physicians serving Medicaid recipients to prescribe preferred drugs on the PAL list. Comparison group prescribers and pharmacists were not isolated from these effects. Had a difference-in-difference approach not been employed, an overestimation of PAL List Alert reductions may have been erroneously reported.

One concern addressed in this dissertation is whether or not interventions that resulted in drug changes had the undesired effect of adversely affecting health consequences. As explained earlier, I chose the occurrence of one or more hospitalization events per person over the 3 month post period was the most tangible (and easily obtained) measure. The resulting in a 2x2 contingency table and Chi-Square testing are shown in table 13.6.

Table 13.6 Hospitalization Events, Comparison #1
(Review Level, All Intervention Types)

Comparison #1 (All Residents with any Type of Review)

	Treatment Group	Comparison Group	
Hospitalization Event	311	358	669
No Event	4,944	4,897	9,841
Total	5,255	5,255	10,510
Relative Risk	0.87		
chi2(1)	3.53		
p-value	0.06		
95% Confidence Interval	(0.75 - 1.01)		
Fisher's Exact (p-value)	0.066		

Notes: Events are person level. Repeat hospitalizations are not reflected in the 2x2 contingency table. Person time is equal 3-month post-period intervals.

The estimate of relative risk of having a hospitalization, given the treatment (Pharmacist Review) was 0.87 with a 95 % confidence interval of (0.75-1.01) and a p-value of 0.060. Fisher's exact test produced a p-value of 0.066. This result indicates that there may be an association between intervention activities and a reduction in the risk of a hospitalization event, though not statistically significant with 95% confidence.

13.5 Evaluation of Treatment Effects Using Multiple Testing Methods

Matching with replacement, while justified as a techique to achieve balance between comparison and study groups, does create a statistical inference dilemma. The assumption of independence with standard statistical testing techniques is violated. For instance, in Comparison #1 (Review Level, All Intervention Types), the study subject sample size was 5,255, with a resultant unweighted comparison sample of 2,178 after matching. For between groups t-testing, the STATA function PSTEST (a command designed to test balance and outcome measures) uses standard, equal variance testing with 10,508 reported degrees of freedom (the study sample size plus the weighted sample size minus two [5,255 + 5,255 -2]). Intuitively, it would seem the number of unique observations (7,433) should determine the degrees of freedom since there are, in fact, 7,431 observations free to vary [5,255 + 2,178 -2].

Similarly, weighting or over-sampling in survey analysis causes similar inferential challenges, and often a primary sampling unit (PSU) adjustment is made to the variance of estimates. The situation arising with replacement matching methods may be distinctly different in one important feature; the repeated observation when matching is meant to represent more than one occurrence of the risk factor, outcome, or event. In other words, surveys that leave sub-populations under or over represented are sampled from an existing population with unknown parameters. In the case of the initiative, the population parameters

are known and the repeated observations are in essence drawn from a non-existent population, thus violating the assumption of independence.

Indeed, this issue is yet to be resolved, especially with difference in difference models,[64] though some have suggested bootstrapping effect estimates.[47,65] Mention of this particular problem is remarkably sparse in the literature to date, possibly due to lack of statistical programming that specifically deals with difference-in-difference estimates of effect.[64] As disease management programs evolve from a predominately pilot project existence to widespread, more all-inclusive programs, a limited number of potential comparison subjects will necessitate the use of with replacement methods of evaluation.[66]

I chose to address this issue by re-testing the results for Comparison #1 (Review Level, All Intervention Types) using additional statistical evaluations to validate the statistical significance of reported treatment effects for the remaining nine comparisons using the standard t-testing method. I used a threefold approach in addition to the standard approach: 1) I report p-values using the degrees of freedom from unique observations, 2) I report p-values based upon an unequal variance assumption that determines the degrees of freedom based upon distributional variance and 3) I show that bootstrapped standard errors are not dissimilar to standard errors reported from t-testing, rendering bootstrapping redundant. Table 13.7 displays the results from this threefold approach.

Table 13.7 Comparison of Statistical Testing (Review Level, All Intervention Types)

Comparison #1 (All Residents with any Type of Review)

Variable	DID Estimate	p-value (df=10,508)	p-value (df=7,431)	p-value (unequal variance)*	t-test Lower Bound (2.5%)**	Bootstrap Lower Bound (2.5%)***	t-test Upper Bound (2.5%)**	Bootstrap Upper Bound (2.5%)***
Total amount paid	**-$64.09**	0.000	0.001	0.001	-$92.27	-$98.62	-$35.91	-$28.47
Total number of drugs	**0.045**	0.781	0.830	0.833	-0.28	-0.33	0.37	0.55
Number of PAL list alerts	**-0.28**	0.000	0.000	0.000	-0.33	-0.33	-0.24	-0.20
Number of Clinical Initiatives alerts	**-0.25**	0.000	0.000	0.000	-0.30	-0.29	-0.20	-0.15
Number of Beers List alerts	**-0.012**	0.488	0.594	0.597	-0.044	-0.042	0.021	0.028
Number of Duplication alerts	**-0.17**	0.013	0.055	0.059	-0.30	-0.36	-0.036	0.014
Number of Consider Length alerts	**-0.010**	0.363	0.482	0.490	-0.030	-0.033	0.011	0.016
Risk of Hospitalization	**-0.0089**	0.06****	n/a	n/a	-0.0183	-0.0217	0.0004	0.0044

* p-value reported for t-test with unequal variance imposes a separate number of degrees of freedom for each outcome measure
** t-test applie

determination of degrees of freedom

For outcome metrics Total Amount Paid, Number of PAL List Alerts, and Number of Clinical Initiatives Alerts, none of the three additional statistical tests provided a different conclusion from hypotheses tests, and had very minimal effects on the p-value. Bootstrapped confidence intervals were remarkably similar to those resulting from two-tailed t-testing with unequal variance assumptions in all cases, though the 95% confidence interval was slightly larger in all cases. For Total Amount Paid, the confidence interval using t-testing was (-$92.27 to -$35.91) while bootstrapping replicates produced a confidence interval of (-$98.62 to -$28.74).

Testing using the three additional methods did produce a different hypothetical result using a standard of 95% confidence for reductions in Consider Length Alerts. Using the standard method, the resultant p-value was p=0.013. Using the reduced degrees of freedom representing unique observations, the resultant p-value was p=0.055, scarcely outside the popular range for rejecting the null hypothesis. Using the unequal variance assumption, the resultant p-value was p=0.059, also just outside the 95% confidence interval. Interestingly, bootstrapping produced a similar finding to the previous two supplementary methods of statistical testing with an upper bound estimate of 0.014, also remarkably close to rejecting the null hypothesis of no effect.

13.6 Sub-Group Results

Difference-in-difference drug cost reductions were found in all ten comparisons of interest (Table 13.8). As expected, drug cost reductions increased in magnitude at subsequent levels of treatment. Comparison #2 (Recommendation Level, All Intervention Types) produced a drug cost reduction of -$91.94, or 30.64 PMPM. Residents having a

review, recommendation and ultimately a drug change (Comparison #3, Drug Change Level, All Intervention Types) had three-month difference-in-difference reduction of -$114.15, or -$38.05 PMPM. Results were similar for Retrospective-Only Type Interventions at all treatment levels (Comparisons #4, #5, and #6) with PMPM reductions of -$20.80, -$30.52, and -$41.96 respectively. Prospective-Only Type Interventions also produced similar results with PMPM reductions of -$36.94 for Recommendation Level (Comparison #9) and -$40.05 for Drug Change Level (Comparison #10). Interestingly, Dual-Type Interventions produced the least drug cost savings. Using a two-tailed t-test, Comparison #7 (Recommendation Level, Dual-Type Intervention) produced a difference-in-difference estimate of -$37.18, or $12.39 PMPM at a p-value of 0.28, though the Drug Change Level comparison resulted in an estimate of -$83.34, or $27.95 PMPM. This intervention type (Dual-Type) produced, somewhat paradoxically, the greatest number of recommendations per reviewed person while producing the least amount of drug cost savings. Detailed results tables for each sub-group may be found in Appendix B.

Table 13.8 Drug Cost Reductions Resulting from Initiative Activities

Drug Cost DID Mean $, (%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**-64.09* (-4.4%)**	-62.39* (-4.1%)	N/A	N/A
Review and Recommendation	**-91.94* (-6.3%)**	-91.58* (-5.9%)	-37.18 (-2.3%)	-110.83* (-15.0%)
Review, Recommendation, and Drug Change	**-114.15* (-7.8%)**	-125.89* (-8.0%)	-83.84* (-5.0%)	-120.15* (-16.4%)

Notes: DID=Difference in Difference
Drug Costs measurements were obtained from a 90-day post-period
* statistically significant at p<0.05 using a two tailed t-test with equal variance assumption

On average, a retrospective review produced a drug cost savings of 4.4%. Among all comparisons, the greatest percentage reduction in drug costs was found for residents having a drug change in the Prospective-Only intervention group, with a reduction of 16.4%. This makes intuitive sense since these residents, on average, had baseline drug costs substantially smaller than there Retrospective Intervention counterparts (~$250 PMPM vs ~$500 PMPM) due to the 18 drug fill screening criteria.

With the exception of Dual-Type Interventions at the Review Level (Comparison #7), no difference-in-differences were found in the number of drugs used in the 90-day post period (Table 13.9). A 2.62% difference or an increase of 0.81 drug fills in 90-days was found in Comparison #7. This result is similarly paradoxical to drug cost savings for Dual-Type Interventions in that the expected result was the reverse. It may indicate incomplete matching for Dual-Type study subjects, or more likely, the presence of some unmeasured endogenous factor not included as a co-variate in the treatment selection model.

Table 13.9 Number of Drug Fill Reductions Resulting from Initiative Activities

Number of Drugs DID Mean, (%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**0.045 (0.17%)**	-0.035 (-0.12%)	N/A	N/A
Review and Recommendation	**0.19 (0.70%)**	0.047 (0.16%)	0.81* (2.6%)	0.16 (1.3%)
Review, Recommendation, and Drug Change	**-0.092 (-0.34%)**	-0.46 (-1.6%)	0.41 (1.3%)	0.15 (1.2%)

Notes: DID=Difference in Difference
Number of Drug fill measurements were obtained from a 90-day post-period
* statistically significant at p<0.05 using a two tailed t-test with equal variance assumption

Substantial and significant percentage reductions in the incidence of PAL List alerts were found in all 10 comparison groups (Table 13.10). Percentage reductions ranged from 18.1% in the Review Level, All Intervention Types (Comparison#1) grouping 37.7% reduction at the Drug Change Level of the Prospective-Only Intervention Group (Comparison #10). Absolute reductions in PAL List Alerts were similar at respective intervention levels with the Recommendation Level producing reductions of -0.36, -0.36 and -0.30 for Retrospective-Only, Dual-Type, and Prospective-Only interventions respectively. The Drug Change Level produced reductions of 0.49, 0.47 and 0.38 respectively. These results indicate that, on average approximately one PAL List drug was dropped from a resident's drug regimen for every two residents having a successful review, recommendation and drug change. At the review level, approximately one of every three residents with a review had a PAL List drug removed, on average. As observed with drug cost reductions, the percentage reductions in PAL list alerts becomes more pronounced moving closer to the mechanism of action (changed drug consumption).

Table 13.10 PAL List Alert Reductions Resulting from Initiative Activities

PAL List Alert DID Mean, (%)	**Intervention Type**			
	All Types	Retrospective	Dual-Type	Prospective
Review	**-0.28* (-19.2%)**	-0.27* (-18.1%)	N/A	N/A
Review and Recommendation	**-0.35* (-21.7%)**	-0.36* (-21.3%)	-0.36* (-20.3%)	-0.30* (-30.6%)
Review, Recommendation, and Drug Change	**-0.44* (-26.6%)**	-0.49* (-27.9%)	-0.47* (-25.6%)	-0.38* (-37.7%)

Notes: DID=Difference in Difference
Number of PAL List Alert measurements were obtained from a 90-day post-period
* statistically significant at $p<0.05$ using a two tailed t-test with equal variance assumption

Patterns for percentage of Clinical Initiatives Alert reductions also mimicked drug cost reductions findings and findings of PAL List reductions. Cohort-comparison groupings experienced proportionally similar reductions (Table 13.11). The smallest percentage reduction was found at the Review Level for All Intervention Types (9.6%) and the largest at the Drug Change Level for Prospective-Only Type (13.9%). In absolute terms, the number of reductions in Clinical Initiative Alerts was 0.25, 0.25, and 0.31 for the Review, Recommendation, and Drug Change Levels for all intervention types. Approximately one-third of all residents having a successful review, recommendation and drug change, had a Clinical Initiatives List drug removed from their regimen, on average.

Table 13.11 Clinical Initiative Alert Reductions Resulting from Initiative Activities

Clinical Initiatives Alert DID Mean, (%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**-0.25* (-9.6%)**	-0.30* (-11.6%)	N/A	N/A
Review and Recommendation	**-0.25* (-8.9%)**	-0.30* (-10.4%)	-0.22* (-7.0%)	-0.17* (-10.3%)
Review, Recommendation, and Drug Change	**-0.31* (-10.9%)**	-0.37* (-12.3%)	-0.31* (-9.6%)	-0.24* (-13.9%)

Notes: DID=Difference in Difference
Number of Clinical Initiatives Alert measurements were obtained from a 90-day post-period
* statistically significant at $p<0.05$ using a two tailed t-test with equal variance assumption

No statistically significant reductions were found for Beers List Alerts (Table 13.12) for any of the ten comparisons of interest, nor for Consider Length Alerts (Table 13.13).

Table 13.12 Beers List Alert Reductions Resulting from Initiative Activities

Beers List Alert DID Mean, (%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**-0.012 (-1.7%)**	-0.030 (-4.2%)	N/A	N/A
Review and Recommendation	**-0.018 (-2.6%)**	-0.021 (-2.8%)	-0.028 (-3.3%)	-0.042 (-16.4%)
Review, Recommendation, and Drug Change	**-0.030 (-4.2%)**	-0.033 (-4.5%)	-0.41 (-4.4%)	-0.037 (-14.3%)

Notes: DID=Difference in Difference
Number of Beers List Alert measurements were obtained from a 90-day post-period
* statistically significant at p<0.05 using a two tailed t-test with equal variance assumption

Table 13.13 Consider Length Alert Reductions Resulting from Initiative Activities

Consider Length Alert DID Mean, (%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**-0.010 (-6.4%)**	-0.008 (5.2%)	N/A	N/A
Review and Recommendation	**-0.007 (5.2%)**	0.00 (0.0%)	-0.016 (-10.5%)	-0.030 (-36.2%)
Review, Recommendation, and Drug Change	**-0.010 (7.9%)**	-0.009 (-6.6%)	-0.022 (-15.5%)	-0.023 (-27.8%)

Notes: DID=Difference in Difference
Number of Consider Length Alert measurements were obtained from a 90-day post-period
* statistically significant at p<0.05 using a two tailed t-test with equal variance assumption

Statistically significant reductions in Duplication alerts were found at the Review Level for All Intervention Types and Retrospective-Only Type interventions produced statistically significant reductions of 3.8% and 6.9% respectively (Table 13.14). However, this finding should be taken with some caution since these reductions are inconsistent with subsequent intervention levels. Each subsequent level of treatment should produce

progressively greater effects. The lack of this hypothesized effect suggests serendipity may be at play, owing possibly to multiple comparisons or incomplete matching.

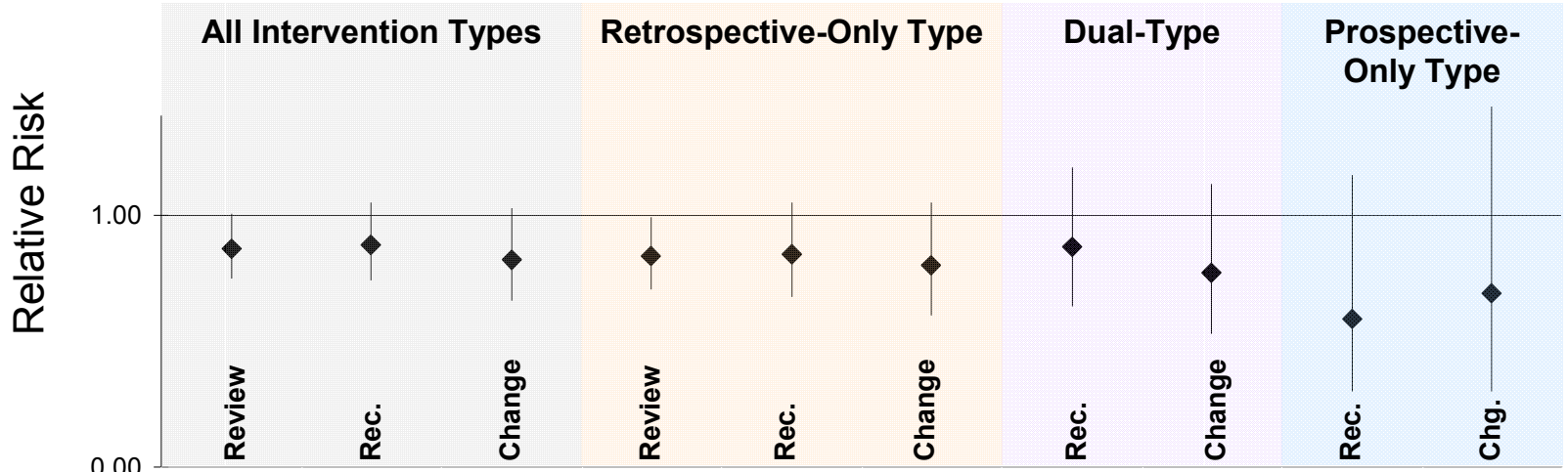
Table 13.14 Duplication Alert Reductions Resulting from Initiative Activities

Duplication Alert DID Mean, (%)	Intervention Type			
	All Types	Retrospective	Dual-Type	Prospective
Review	**-0.17* (-3.8%)**	-0.333* (-6.9%)	N/A	N/A
Review and Recommendation	**-0.067 (-1.5%)**	-0.167 (-3.5%)	0.116 (2.3%)	-0.035 (-2.3%)
Review, Recommendation, and Drug Change	**-0.104 (-2.4%)**	-0.193 (-3.9%)	0.016 (0.3%)	-0.087 (-5.6%)

Notes: DID=Difference in Difference
Number of Duplication Alert measurements were obtained from a 90-day post-period
* statistically significant at $p<0.05$ using a two tailed t-test with equal variance assumption

As a qualitative measure of downstream impact of interventions, hospitalization events were obtained for the 90-day post intervention period. All point estimates of relative risk were less than one, though only one cohort-comparison grouping elicited a significant reduction in risk using Fisher's Exact Test (Comparison #4, Review Level, Retrospective-Only). More comparisons may have elicited statistically significant results with sufficient sample size. Figure 12.5 shows point estimates of relative risk of a hospitalization event in the post period with upper and lower boundaries for a 95% confidence interval.

Figure 13.5 Relative Risk of Having a Hospitalization Resulting from Intervention



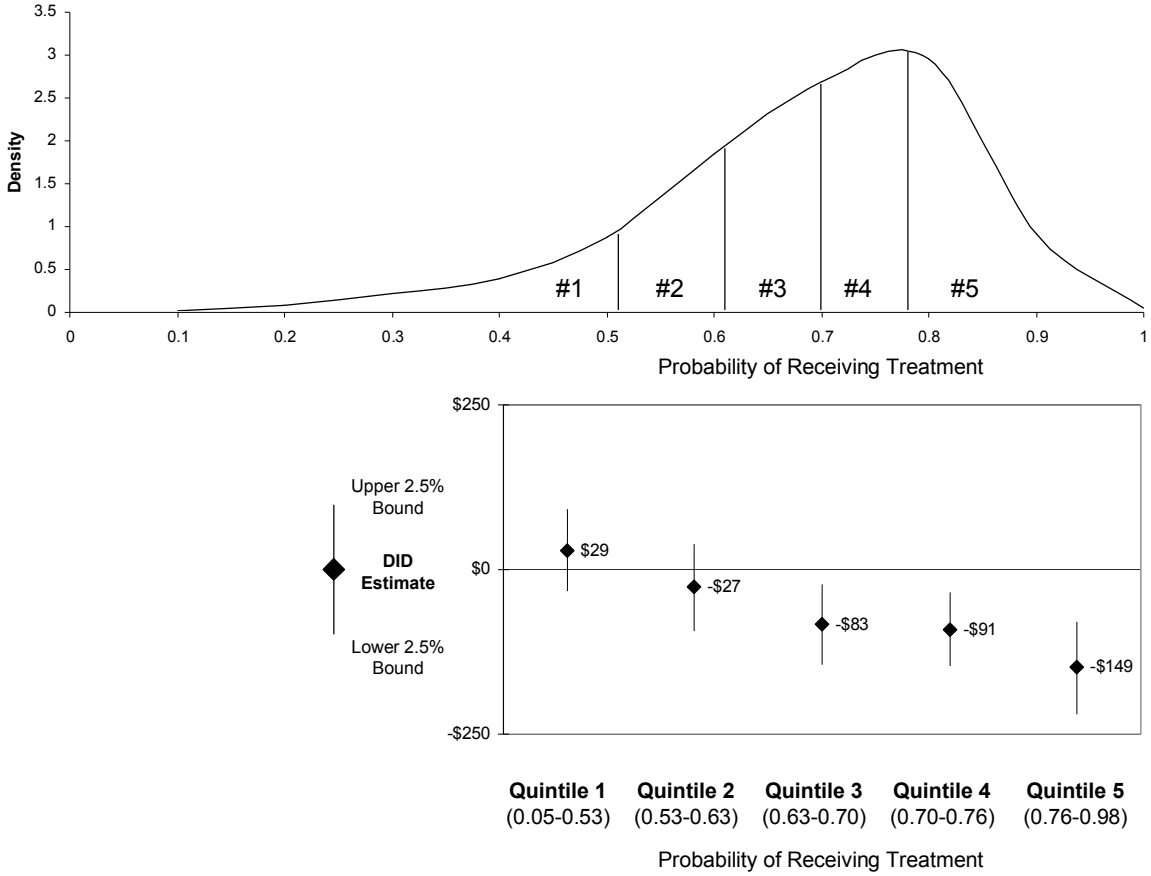
	Comparison #1	Comparison #2	Comparison #3	Comparison #4	Comparison #5	Comparison #6	Comparison #7	Comparison #8	Comparison #9	Comparison #10
Upper 2.5% Bound	1.01	1.05	1.03	1.00	1.05	1.06	1.19	1.13	1.16	1.60
Lower 2.5% Bound	0.75	0.74	0.66	0.71	0.68	0.61	0.64	0.53	0.30	0.30
◆ Relative Risk	0.87	0.88	0.83	0.84*	0.85	0.80	0.87	0.78	0.59	0.69

*Statistically significant using Fisher's Exact Test

13.7 Sub-Strata Results from Comparison #1

One of the many advantages of propensity scoring is the ability to parse out effect by level of treatment selection. Figure 13.6 shows the drug cost difference-in-difference by propensity score quintile for Comparison #1 (Review Level, All Treatment Types). Statistically significant reductions in 90-day drug costs were found for Quintiles #3, #4, and #5. Mean difference-in-difference reductions increased proportionally with treatment selection. This finding is logical since program administrators, pharmacists and prescribers are likely to select out those residents most in need of a drug therapy change.

Figure 13.6 Drug Cost Savings by Propensity Score Quintile



13.8 Limitations

This dissertation went to great lengths to address major threats to validity in the assessment of this intervention. Nevertheless, there were several limitations that must be recognized.

Regression to the Mean: As with any non-randomized, observational study, regression toward the mean must be considered. The comparison groups for Evaluations #2 and #3 were selected in the same manner as study group patients, hence both should have equally incurred this regression effect and it is, in essence, neutralized for purposes of differential analysis.

Especially challenging in the evaluation of this particular pharmacist service is the presence of a mandated existing monthly review. The aim of this dissertation was to assess the marginal effect of this review above and beyond pre-existing OBRA-87-mandated monthly reviews (baseline effects). It was not possible to assess, nor infer, the impact of this intervention in the absence of OBRA-87 mandated monthly reviews.

Using a payor perspective, I assessed the impact of *all* drug claims for recipients, not just those just those drugs flagged in patient profiles from pre-intervention screening. It is likely that our broader focus diluted our findings toward the null. Yet we found important drug cost differences on a PMPM basis in all three evaluations.

Use of Administrative Claims Data: Using administrative claims data to measure differences in drug costs is not without limitations. Drugs may have been filled without submission of a claim or nursing homes may have paid for products such as over-the-counter medications out of a separate budget, though there is no evidence that this may have occurred differentially between study and comparison subjects. Further, this study takes a payor

perspective and paid claims are the most meaningful measurement from this perspective. Administrative claims are poor stand-alone proxies for measuring changes in quality, particularly in such areas as adverse effects or health status. On the other hand, claims databases were the only data source with which to measure impact on heath care or economic impact from a payer perspective. The large sample sizes involved in our study suggest that our findings are real and replicable.

Loss to Follow-Up: Resident attrition in North Carolina Nursing Homes remained steady at 36% over the four year study period, making an evaluation of the persistence of intervention effects quite difficult. At a minimum, at least three one-month follow-up periods were required to assure that drug therapy changes were reflected in claims data and persisted for Evaluations #2 and #3. On the other hand, a longer follow-up period of 6-12 months would have incurred problems of patient attrition within the nursing homes, subjecting the study to additional bias resulting from unknown factors associated with attrition. During this study period, attrition rates closely approximated statewide averages, and there was some comfort in the finding that attrition rates were not significantly different between study and comparison groups.

Unknown Intervention Persistence: Despite a robust study design, the downstream effects of repeated interventions, the effects of continually evolving PDTP alerts criteria, and intervention persistence beyond the three month post-period are unknown. The long term impact of these interventions in both cost and quality dimensions remains unknown. Extrapolation of findings beyond the 3 month follow-up window must be done with caution, though patients in long-term care facilities are known to have relatively stable drug therapy regimens over time in the absence of interventions of the type employed in this study.

Internal Validity versus External Validity Tradeoff: This investigation went to great lengths to equalize study and comparison groups for purposes of analyzing the impact of different forms of interventions. In doing so, there is always a tradeoff between internal and external validity. The selection criteria I employed limited my ability to generalize to Medicaid nursing home residents who did not share the same characteristics.

Endogeneity and Omitted Variable Bias: As with nearly all other practice based interventions studies, it was not possible to draw a true random sample of patients across nursing homes or pharmacist consultants due to the intermingling of providers and the need of program administrators to elicit as many participants as possible in the shortest amount of time possible. A randomized controlled trial of a "real world" program such as this is simply not feasible nor practical. Any randomization that would have been employed would have had to account for all clustering effects and interactions between providers common to the long-term-care arena. It would have been difficult, if not impossible, to construct a truly randomized patient-level sample within a nursing home since physicians often provide care to patients in more than one nursing home. Additionally, groups of pharmacists are often clustered through consulting organizations serving multiple nursing homes and multiple nursing homes often operate under a common ownership structure.

Thus, our comparison group was not, by design, a randomized sample of patients. However, propensity scoring approaches are powerful in their ability to reduce bias, and have been shown to perform better than randomization in some circumstances.[42] This quasi-experimentation is only valid, however, if the researcher ensures that all relevant aspects of treatment selection and baseline risk are contained in the propensity scoring model, regardless of balance of observed co-variates. It is always possible that an important

treatment selection variable may have been omitted in this claims data analysis, causing potentially biased results to emerge. Yet I believe the 20 co-variate treatment selection model used in Evaluation #3 to be robust and complete.

Inexact Treatment Selection Modeling: Aside from the problem of unobserved, or omitted variable bias, inexact matching remains a challenge in this and other propensity matching studies. Matching on observed variables rarely produces complete balance using inferential significance testing, especially with large numbers of covariates in the treatment selection model and strong statistical power emanating from sample sizes in the thousands. To the extent that the possibility of bias remains after matching, that bias would be reflected in the results. Generally, this problem is exacerbated when a few comparison observations are available to minimize distance between study and comparison subjects. The propensity matching method in this study has been shown to be robust when large sample sizes exist,[42] and while the method used herein is often employed with far fewer subjects, it is fortunate in this study that sample sizes were relatively large in this evaluation.

Generalizability: The findings of this study must be viewed in the context of the setting, time, and environment in which it was conducted. In NC, Medicaid programs were under considerable pressure to reduce overall costs. There were few options to do so under federal statutes (e.g., prior authorizations and preferred drug lists). One option was certainly to reduce fees to providers, including fees to pharmacist consultants. The threat of reduced fees to providers may have been a motivator for the success of the Initiative. The incentive to participate in earnest may not be present in other environments, decreasing the external validity of the findings herein. However, cost containment pressures and medication safety issues have been paramount in most state Medicaid programs and other federal programs in

most states for quite some time with no sign of abatement. Yet any service study, regardless of research method, control or design is subject to substantial threats to external validity. Pharmaceutical care services in particular, tend to be rather unique to specific geographic regions, settings and patient populations. Foremost among unique qualities are the predispositions of the pharmacists themselves and their disparate abilities to impact patient care in given situations.

Lack of Consideration of Nursing Home, Pharmacist and Prescriber Characteristics: This study did not explicitly examine the decision-making processes of participant pharmacists or physicians regarding drug therapy changes. This was because claims data and pharmacist problem encounter documents were the only data source available for analyses. This lack of consideration has a twofold limitation. First, evaluation of these characteristics could prove valuable to future Initiative phases as well as other fledgling pharmaceutical care programs across the country. Identification of the traits among homes, pharmacists and prescribers that are associated with positive outcomes could lead to better program development. Second, these characteristics may act as confounders of the evaluations herein if they are predictive of intervention success and a maldistribution exists among study and comparison groups with respect to home, pharmacist, and prescriber characteristics and practice patterns. In essence, these characteristics may have served as omitted variables that ultimately imposed bias upon the results. While this possibility exists, there is no apparent rationale that suggests a maldistribution of characteristics exists. To the extent that groups of homes, pharmacists and prescribers behaved similarly by association, some unobserved clustering effects may also have been present.

Unknown or Unrealized Incentives: The amount of compensation to providers may or may not have affected the results. It may have had a positive effect since it was the first explicit recognition, through direct compensation, of drug therapy review services in a Medicaid program. However, since payments were relatively low as compared to rates for service delivery among other health care providers, compensation may have also negatively impacted Initiative response.

Service variability: In all three evaluations undertaken as part of this Initiative, there was an implicit assumption that all pharmacist activities were equipotent. As I stated in Chapter 10 (Methodological Considerations), service studies are subject to much greater variability in practitioner and study subject activities. Unlike drug products which are very standardized, pharmacist services are more heterogeneous in their effects (as are most other professional service interventions). I did not examine differences in individual pharmacist behavior, nor did I address effect differences across pharmacy provider organizations, though some researchers have successfully done so.[67,68] Future work warrants this type of consideration.

Effect Attribution: None of the three Initiative evaluations were designed to distinguish the relative contribution of intervention components (e.g., profile, toolkit, financial reward, pharmacist motivations). Therefore, results must be observed in aggregate.

The Problem of Multiple Comparisons: Evaluation #3 makes multiple comparisons (eight outcome metrics) across ten cohort-comparison groupings. Standard statically inference approaches suggest that one of every twenty comparisons should have a statistically significant and serendipitous relationship with the independent variable of interest using a 95% confidence interval. It is unclear weather a Bonferroni-type adjustment

is warranted or should be applied in this circumstance since all ten comparisons were modeled separately. The safer option seems to be to take the p-values at face value and avoid hypothesis testing conclusions. In this dissertation, I have presented p values of tests unadjusted for multiple comparisons. The reader may wish to apply Bonferroni corrections to observed p values in rendering their own interpretation of these findings. By simply using critical value of $p<0.01$ when hypothesis testing, one effectively reduces the occurrence of an erroneous conclusion resulting from the multiple comparisons problem to 1 in 100. If a critical p value of <0.01 were used, drug cost savings in Comparison # 11 (Recommendation Level, Prospective-Only Type Intervention) would not be statistically significant. Reductions in PAL list alerts and Clinical Initiatives Alerts would remain statistically significant in all comparisons. While I reiterate my belief that the drug cost savings and alert reductions were demonstrated in this project are real, statistically significant, and meaningful. I leave to the reader their own interpretation of statistical significance of reported p values.

CHAPTER 14

PHASE 2 AND 3 DESCRIPTIVE RESULTS

14.1 Phase 2 Descriptive Results

Phase 2 of the North Carolina Nursing Home Polypharmacy Initiative was conducted over a three month period from March-June of 2003. Preliminary results from Phase 1 of the initiative created a desire among administrators to expand the program even further to touch as many Medicaid enrollees residing in North Carolina Nursing Homes as possible. Additional nursing homes and their pharmacist consultant organizations were invited to participate in Phase 2. An additional 12 homes ultimately agreed to participate. Screening criteria were also expanded to allow any resident having any type of drug therapy problem alert to receive comprehensive reviews. Thus, nearly all residents residing in participating nursing homes became eligible for profile reviews in Phase 2.

Results were similar to those found in Phase 1 of the Initiative. An additional 4,123 residents received reviews with 2,639 recommendations, or 0.62 recommendations per resident reviewed. Interestingly, this rate was roughly half that of the 1.21 recommendations per resident reviewed in Phase 1. This reduction was likely the result of a fewer number of drugs to be reviewed since the 18 fill in 90-day screening criteria was lifted for Phase 2. On average, residents receiving reviews in Phase 2 had 4.6 drug fills per month in contrast to the 9.0 per month in Phase 1.

In Phase 2, changes to a more cost-effective drug were again the dominant result type, responsible for 62.5% of all drug regimen changes resulting from intervention activities (Table 14.1). The distribution of result types were remarkably similar to that found in Phase 1. However the number of drug changes per 100 reviewed residents dropped from 75.6 in Phase 1 to 44.7 per 100 in Phase 2, likely owning to less sick residents with fewer drugs being reviewed.

Table 14.1 Resultant Changes in Therapy by Type (N=4,123 residents)

	Frequency (%)	Average Number per 100 Residents*
Dose/Delivery Changed	243 (13.2)	5.9
-Dose or administration was changed		
Drug Added	38 (2.1)	0.9
-Drug added for untreated indication		
Drug Change	1,154 (62.5)	28.0
-Drug was changed from one to another		
Drug Discontinued	410 (22.2)	9.9
-Drug was discontinued or changed to PRN		
Total**	**1,845 (100)**	**44.7**

* Denominator is the total number of residents receiving a completed review by consultant pharmacists

** A result type of "Other-Any result not listed above" occurred in 325 instances but was not considered to be verified drug changes.

Note: Pharmacist report used as a data source.

14.2 Phase 3 Descriptive Results

Phase 3 of the North Carolina Nursing Home Polypharmacy Initiative was conducted from March of 2004 through December of 2005. Unlike the previous two phases, patient profiles were not generated, nor were screening criteria applied. Any resident in any participating Nursing Facility was eligible for any type of intervention at any time.

Phase 3 of the Initiative produced an additional 5,813 residents not previously reviewed by consultant pharmacists as part of the Initiative. Phase 3 reviews produced 5,023

additional recommendations by pharmacist, many times for residents reviewed in previous phases.

CHAPTER 15

CONCLUSIONS AND LESSONS LEARNED FROM THE NORTH CAROLINA POLYPHARMACY INITIATIVE (PHASES 1, 2 AND 3)

This initiative, spanning from the pilot study through Phase III, has contributed to my summary conclusions and lessons learned, outlined below:

1. Plan-Do-Study-Act (PDSA) strategies are valuable for both evaluations as well as for use with programmatic improvements: Real world Initiatives are ever evolving and necessarily responsive to changes in practice, environment and resource demands. Using a PDSA approach enables the program administrator and researcher to find common ground on which to proceed and improve Initiative features.

2. Collaboration is essential among principals involved in any large intervention, and requires administrative support: Having a figure-head, spokesperson, or sponsoring entity is crucial to engendering health care practitioners. In this Initiative, AccessCare provided this role by fostering support from across the state, both geographically as well as across disciplines. AccessCare believed that organizational buy-in was the most effective element in Initiative success.

3. A targeted program using pharmacists to review patient profiles may be quickly launched and expeditiously performed across large numbers of patients, at least in long-term-care settings: The ability of the initiative to be expeditiously executed from

conception to evaluation was essential in this "real world" setting. Each of Phases 1, 2 and the pilot project required less than six months from conception to implementation to evaluation for the next phase. What's more, this program touched 98 of North Carolina's 100 counties and involved roughly two-thirds of all Medicaid enrollees residing in nursing homes during the study period. Most interventions occurred within one month of each respective phase.

4. An expansion of the role of the geriatric consultant pharmacist specialist may help contain drug related health care expenditures in the elderly without adversely affecting total health care costs or quality: The current role for nursing home consulting pharmacists is based on OBRA- 87 and other federal regulations requiring drug regimen reviews to be conducted at least monthly by consultant pharmacists. The Initiative sought to provide an enhanced version of Drug Regimen Reviews (DRRs). This model incorporated a pharmaceutical care plan. Within a pharmaceutical care plan, the pharmacist works with other members of the health care team to implement and monitor patient drug therapy. The results from all three evaluations of the initiative suggest that the addition of PDTP alerts to usual-care DRR reviews was associated with more changes in drug therapy and a reduction in computer-generated drug therapy alerts during the follow-up period.

5. A computerized alerting system can be successful in reducing potential drug therapy problems if an emphasis is placed on specific alerts with pharmacist and prescriber acceptance and collaboration (i.e., "buy-in") to address problem alerts and prudently dismiss false positive alerts: Evaluations #2 and #3 measured PDTP alert reductions among study participants. Two of five alert categories were found to have substantial and statistically significant reductions following interventions using profiles

outlining these alerts (Clinical Initiatives and PAL List Drugs). These two categories were constructed by physician and pharmacist leaders, suggesting that practitioner involvement with a centralized DUR process aids in program response. Beers list and therapeutic duplication alerts decreased in all study groups and in the comparison group in both Evaluations #2 and #3, yet these reductions were not statistically different between study and comparison groups. This finding is consistent with the role of DRRs as outlined in OBRA 87. These types of drugs and drug problems are explicitly mentioned as part of the guidelines for conducting customary mandated DRR reviews. Although residents in comparison homes were not subject to claims-generated drug profile reviews with potential drug therapy problem (PDTP) alerts as part of the Initiative, residents in both study and comparison homes were subject to OBRA-87-based requirements and screening guidelines for the overuse of particular prescription drugs. This may explain the reduction in both groups.

6. Propensity scoring is both an effective evaluation tool as well as prognostic indicator of which patients should receive supplemental services: The advantage of propensity scoring as it relates to these findings lie with its ability to determine a cost-minimization threshold. Given a $12.50 payment for review services, any resident in comparison homes having a propensity score greater than 0.63 should receive a targeted intervention, according to sub-strata results. The treatment selection model suggests that the reviews would be cost-beneficial within the first three months following the intervention alone, with the potential for accruing greater benefits over time. Using a propensity score as a targeting strategy could have major implications for the expansion of pilot projects currently underway in Medicare Part D. Once a pilot project has been conducted, the resulting propensity score match could identify *both* those in need *as well as* those likely to

benefit from supplemental services. This strategy harkens back to the Plan-Do-Study-Act philosophy.

CHAPTER 16

POLICY IMPLICATIONS FOR PHARMACIST SERVICES

The North Carolina Nursing Home Polypharmacy Initiative was a success. Overall, Phases 1, 2 and 3 of the initiative produced 17,545 recommendations for 19,144 nursing home residents in the state of North Carolina. These recommendations generated greater than 10,000 changes in drug therapy over a three year span of time, with an estimated $9-12 million dollars in accrued drug cost savings through December 2005.[69] Results from the pilot project together with Phase 1 results published in a peer reviewed journal suggest annualized cost-minimization ratios of 13:1 and 12:1 respectively.[70,71,72]

This initiative serves as a viable example of a Medication Therapy Management Program (MTMP) called for under Part D of the Medicare Modernization Act of 2003. The Initiative combined a population level, computer-based retrospective drug use review (DUR) profiling system with a comprehensive and patient-specific drug regimen review (DRR) system. Alerts were generated by the payor, in this case NC Medicaid, and were provided to consultant pharmacists for review and recommendation. While the strategy of targeting drugs and drug classes at the population level is far from novel given over 25 years of experience with DUR in dispensing systems, doing so in concert with a comprehensive review of the entire drug regimen at the point of care (the nursing home) has not been done on this scale. In line with usual-care in long term care settings, pharmacists were free to review and recommend therapy changes for any drug in a patient's

profile for any problem they discovered, regardless of any alerts provided on claims-generated resident profiles. Administrative claims alone may only be 65% sensitive and 88% specific when tested against manual review,[73] suggesting a need for combined computerized and manual review of drug use. The Initiative successfully demonstrated that this combined DUR-DRR intervention is feasible and valuable.

Beginning in 2006, PDP and MA-PD sponsors took on this DUR role as required under the Medicare Modernization Act of 2003. Standard DUR approaches have offered little evidence to date of effectively improving patient outcomes for state Medicaid enrollees despite the large budget outlays to these programs,[74-77] yet population specific (targeted) interventions such as the Initiative have shown some success.[78-80]Use of continuous quality improvement strategies such as the PDSA approach in DUR programs may improve both their success and appeal.[81] Designing studies to determine both what *works* and what *does not work* promotes programmatic and operational improvements. To date, evidence of DUR non-success has been offered at highly aggregated levels, without emphasis on specific actions and non-action, subjecting studies to washout effects.[81] DUR activities, as well as their evaluations, lack sufficient sophistication and integration of data, providers and methods, despite available enabling technologies.[82] Focused reviews that utilize claims-generated profiles, in combination with collaborative activities that individualize care,[83] such as DRR reviews, may be a better strategy for PDPs to adopt through the MTMP service requirement.

Robust, multi-center studies are warranted that evaluate downstream health outcomes effects of pharmacist interventions in long-term-care settings. Of the three formal evaluations of the initiative, only Evaluation #3 considered both processes of care *as*

well as global health outcomes resulting from pharmacist activities. Rates of hospitalization were likely an insensitive measure of quality in this study, especially when considering only three months of post-intervention follow-up.

Despite this shortcoming, findings of this study are of great value when viewed in the context of other studies conducted to date. There are a limited number of well-designed studies that focus on pharmacist-physician interventions to improve/change medication therapies in the long-term-care arena. I was able to find only two review articles that studied pharmacist activities that aimed to improve medication use in long-term-care settings.

Hanlon et al.[84] found 14 randomized controlled studies using a MEDLINE search through March of 2003 that evaluated pharmacist interventions in the elderly, yet only two were conducted in long term care settings (five in home settings, three at hospital discharge, three in medical clinics, and one in a community pharmacy setting). They concluded that while evidence of reductions in drug-related problems (DRPs) exists, larger studies involving large numbers of patients, in multiple locations should be conducted.[84]

In an effort to argue for similar legislation in the United Kingdom, Hughes[85] writes one of the few journal articles in existence that specifically outlines the requirements of OBRA 87 legislation and reviews evidence of its impact in the U.S. Findings of change in processes of care were evident in the two studies reviewed, though evidence of translation to improved outcomes remained elusive.[85] Specific evidence of process of care improvements in long-term-care settings include: reductions in antipsychotic prescribing,[86] reductions in psychotropic (antipsychotic, antidepressant, anti-anxiety) medications,[87] targeting of NSAID therapy for cost-effective alternatives,[88] a reduction in preventable adverse drug reactions (ADRs),[89] cost-effective drug substitution,[90] a decrease in polypharmacy and drug costs,[91]

and a strong need for transitional assistance from other institutionalized settings.[92] However, none of these studies demonstrated improved health outcomes.

Robust evaluations of downstream intervention effects have been inhibited by the inability to produce robust study designs in lieu of randomization, the difficulty of capturing essential data and lack of a suitable measure of quality of life.[93] These "real world" constraints have proven challenging to researchers. Few, if any, studies exist that demonstrate with little doubt that pharmacist interventions improve global health outcomes in long-term-care settings, though it is well known that pharmaceutically related problems exist,[11,18,94-98] and that residents of long-term care facilities desire to have these services available to them.[99]

One ongoing examination attempts to fill this void. The American Society of Consultant Pharmacists Foundation is underwriting a multi-phase, multi-year study of drug therapeutic concerns and safety issues labeled, the "Fleetwood Project".[100] For consultant pharmacists in nursing homes involved in the project, a new model of care was employed that emphasized prospective interventions, face-to-face contact and evaluation of high risk patients. The project and its evaluations were conceived in three phases.

Phase 1 was a macro-level pharmacoeconomic evaluation of drug-related morbidity and mortality that would serve as an evaluation model for future Fleetwood evaluations. Results for this preliminary work were based upon survey results from an expert panel that determined the conditional probability of sub-optimal health outcomes. Phase 1 of the Fleetwood project proposed that as much as 3.6 billion is currently saved annually from existing consultant pharmacist activities.[16]

Phase 2 of the project was to serve as a pilot project for conception of Phase 3 that determined which operational activities generate the greatest impact on resident health and cost-related outcomes. This phase served the Fleetwood project in much the same manner as the Pilot Project did for the Initiative using the PDSA strategy of informing future project phases. Phase 2 was to determine the feasibility of a new model of care that placed more emphasis on prospective interventions, face-to-face contact and evaluation of high risk patients. Phase 2 results revealed that the new model increased clinical involvement of the pharmacist, reduced time spent on DRR, greater recognition of pharmacist value within interdisciplinary teams, better communication among team members, and increased workplace efficiency.[101]

The results of Phase 2 were used in the planning of Phase 3, a large-scale demonstration project conducted in NC simultaneously with this project. Phase 3 was a randomized trial involving 26 nursing facilities that evaluated the six specific aims of the Fleetwood Project model: 1) reducing the prevalence of potentially inappropriate medication use, 2) reducing under-treatment of disease, 3) reducing adverse drug events, 4) reducing Resident Assessment Protocols, 5) improved efficiency, workflow, workload and satisfaction among pharmacy staff, and 6) differentiation of nursing homes implementing the new model.[102] All 26 homes involved in the Fleetwood project were exempted from Initiative activities during the course of the trial. Phase 3 results are expected to be published in 2006.

Since the Fleetwood Phase 3 closely approximated some of the goals of this project, and occurred within NC at about the same time, it is important to denote the similarities and differences between programs. Both studies involved interventions to identify potential drug therapy problems in nursing home settings, but in different ways. Compared to Initiative

activities and subsequent evaluation, phase 3 of the Fleetwood project employed much more comprehensive and explicitly framed intervention to make specific recommendations for drug therapy with multi-year follow-up.[103,104] For Fleetwood, the new model of care and subsequent care algorithms were developed over the course of many years[100] instead of weeks, as was the case with the Initiative.

This project and study herein differs from the Fleetwood project in that it was conceived and implemented relatively quickly, with the goal of reducing drug costs as quickly as possible without compromising health. The Initiative sought to acquire additional drug savings, above and beyond what was already being attained as the result of consultant pharmacist activities. The Fleetwood project, at its core, was designed to test a new model of consultant pharmacy. In this study, I show that a supplementary review of existing DRR activities using administrative claims data can be successfully launched relatively quickly on a large scale.

Both pharmacist-initiated prospective interventions and program-initiated retrospective interventions were successful in reducing drug costs and PDTP alerts. Little variation was found among the relative success of prospective-type and retrospective-type interventions as employed by the Initiative. However, care must be taken in interpretation of this finding as it relates to future programmatic planning. During the Initiative, persons that were at high risk (having at least 18 drug fills in the 90-day pre-intervention period) were targeted for retrospective reviews through claims-based profile generation on the part of program administrators. Persons deemed not to be at high risk (having less than 18 drug fills in 90 days) were selected out by pharmacists at the home for recommended drug therapy changes. Results from the evaluation herein *do not* indicate that

non-targeted prospective interventions are equally effective in producing drug cost savings as targeted retrospective interventions wholesale. That is, the finding of equipotentcy should only be considered in light of the screening criteria employed a given program. Variations in screening criteria may have produced different results, namely the superior effectiveness of one type of intervention over another, depending on the accuracy and precision of the screen.

Consultant pharmacists should be explicitly compensated for specific, targeted DRR activities by third-party payors, regardless of the level of care provided, or the relative success of reviews, recommendations, and resultant drug changes. This study found that a program of pharmacist review and intervention achieved reductions in drug costs that were far in excess of the amount paid to pharmacists for the service (i.e., $12.50 for each retrospective review), with additional benefits accruing from enhancing the quality of prescribed drug therapy. Evaluations #1, #2, and #3 found an average reduction in drug costs of $30.33, $19.04, and $21.36 PMPM respectively for the review level of care. That is, on average, these savings were generated regardless of the finding of a PDTP, and were cost-beneficial within the first month of drug cost savings accrual. For the primary comparison group at the Recommendation Level of treatment, average drug cost savings were found to be $30.64 PMPM, while the Drug Change Level generated an average drug cost savings of $38.05 PMPM.

The corollary scenario would be pay-for-performance policies currently being debated at the federal level for Medicare payments to physicians. One alternative method for MTMP programs is to "pay for results," that is, pay pharmacists only for interventions that produce changes in drug therapy (with prescriber consent). This was how pharmacists were paid in the prospective review portion of this study.

An advantage of applying an across the board "pay for results" formula (i.e., for both prospective and retrospective reviews) is that compensation would be efficiently used to generate cost savings. A disadvantage is that this form of compensation would provide economic incentives to focus only on drug cost savings, irrespective of other goals (e.g., improving drug safety or quality). Further, pharmacists may be reluctant to participate in such a plan at a high level because it is not always possible determine which patients would be candidates for drug cost reductions prior to reviews, resulting in uncompensated activities. Thus, payment based on changes in drug therapy may find few willing pharmacists to participate in such a payment plan. In this study, pharmacists completed and submitted patient reviews on an exceptionally high proportion of targeted patient drug profiles that were sent to them for review (85%, 6344/7472). Under a different payment scheme, the percent of reviews conducted relative to the number of residents targeted would likely be less, though the resultant effect on overall return on investment remains unknown and untested.

Activities performed by consultant pharmacists for the North Carolina Polypharmacy Initiative may be reproducible in non-nursing home settings, but with more difficulty. There is evidence that PDTPs are common among ambulatory elderly, as well as in elderly-oriented board and care or assisted living settings. [105-111] Established relationships between pharmacists and prescribers, a trait found to be well-nourished in the Initiative, may not be as prevalent in community pharmacy settings where only early stages of collaboration may have developed.[112] Yet pharmaceutical care programs for ambulatory patients in clinic settings with high levels of collaboration have shown success,[113,114] suggesting a point-of-care approach nurtures collaboration. Additionally, some success has

been found using home health care referrals as a mechanism of targeting,[115] though collaboration among health care providers is more common in that setting as well.

APPENDIX A: BIAS REDUCTION TABLES: COMPARISONS 2-10

Table A.1: Bias Reduction (Comparison #2)

Comparison #2 (Recommendation Level, All Intervention Types)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.7	79.4	-13.4		-5.77	0.000
	Matched	77.7	78.7	-8.1	39%	-3.69	0.000
(Age)^2	Unmatched	6,186	6,455	-15.2		-6.52	0.000
	Matched	6,186	6,315	-7.3	52%	-3.29	0.001
Race	Unmatched	32.6%	24.9%	17		7.33	0.000
(Non-White)	Matched	32.6%	30.9%	3.8	78%	1.57	0.117
Sex	Unmatched	75.7%	78.8%	-7.4		-3.21	0.001
(Female)	Matched	75.7%	76.8%	-2.7	64%	-1.13	0.257
Total Number of Drugs	Unmatched	27.0	20.4	57.2		24.62	0.000
	Matched	27.0	25.6	12.3	79%	5.55	0.000
Total Amount Paid	Unmatched	$1,451	$1,088	40.8		17.6	0.000
	Matched	$1,451	$1,347	11.7	71%	5.19	0.000
Total Number of Alerts	Unmatched	9.61	6.73	52		22.41	0.000
	Matched	9.61	9.02	10.7	80%	4.66	0.000
Number of Duplication Alerts	Unmatched	4.38	3.04	39.2		16.91	0.000
	Matched	4.38	4.02	10.5	73%	4.55	0.000
Number of Beers List Alerts	Unmatched	0.706	0.522	20.4		8.8	0.000
	Matched	0.706	0.670	4	80%	1.64	0.101
Number of PAL List Alerts	Unmatched	1.60	1.14	39.1		16.87	0.000
	Matched	1.60	1.54	5.4	86%	2.27	0.023
Number of Clinical Initiatives Alerts	Unmatched	2.78	1.89	52.6		22.64	0.000
	Matched	2.78	2.65	7.4	86%	3.22	0.001
Number of Consider Length Alerts	Unmatched	0.139	0.135	0.9		0.39	0.700
	Matched	0.139	0.133	1.6	-74%	0.65	0.518
(Number of Duplication Alerts)^2	Unmatched	31.7	20.1	24		10.33	0.000
	Matched	31.7	26.3	11.2	53%	4.91	0.000
(Number of Beers List Alerts)^2	Unmatched	1.42	0.98	14.7		6.34	0.000
	Matched	1.42	1.29	4.6	69%	1.85	0.065
(Number of PAL List Alerts)^2	Unmatched	4.10	2.60	28.9		12.47	0.000
	Matched	4.10	3.70	7.7	73%	3.1	0.002
(Number of Clinical Initiatives Alerts)^2	Unmatched	10.58	6.33	37.3		16.12	0.000
	Matched	10.58	9.55	9.1	76%	3.7	0.000
(Number of Consider Length Alerts)^2	Unmatched	0.214	0.187	3.1		1.32	0.188
	Matched	0.214	0.203	1.3	58%	0.52	0.606
Total Number of Alerts x Total Number of Drugs	Unmatched	305.7	187.8	40.9		17.64	0.000
	Matched	305.7	271.0	12	71%	5.13	0.000
Total Amount Paid x Total Number of Drugs	Unmatched	45,586	29,281	37.1		16.01	0.000
	Matched	45,586	39,970	12.8	66%	5.44	0.000
Total Amount Paid x Total Number of Alerts	Unmatched	16,659	10,170	36.6		15.81	0.000
	Matched	16,659	14,453	12.5	66%	5.27	0.000
Average Bias	Unmatched			**28.90**			
	Matched			**7.83**	**73%**		
Pseudo R2	Unmatched	0.108					
	Matched	0.008					

Sample Sizes: Study Group n=3,618
Unmatched Comparison Group n=3,801

Table A.2: Bias Reduction (Comparison #3)

Comparison #3 (Drug Change Level, All Intervention Types)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.7	79.4	-13		-5.06	0.000
	Matched	77.7	78.8	-8.3	36%	-3.17	0.002
(Age)^2	Unmatched	6,193	6,455	-14.8		-5.73	0.000
	Matched	6,193	6,325	-7.4	50%	-2.82	0.005
Race	Unmatched	32.4%	24.9%	16.5		6.47	0.000
(Non-White)	Matched	32.4%	30.8%	3.4	79%	1.18	0.237
Sex	Unmatched	75.8%	78.8%	-7.1		-2.79	0.005
(Female)	Matched	75.8%	77.0%	-2.8	60%	-1	0.319
Total Number of Drugs	Unmatched	27.2	20.4	57.6		22.39	0.000
	Matched	27.2	25.8	12	79%	4.46	0.000
Total Amount Paid	Unmatched	$1,460	$1,088	41.8		16.38	0.000
	Matched	$1,460	$1,358	11.5	73%	4.24	0.000
Total Number of Alerts	Unmatched	9.78	6.73	54.7		21.39	0.000
	Matched	9.78	9.16	11.1	80%	4	0.000
Number of Duplication Alerts	Unmatched	4.44	3.04	40.4		15.88	0.000
	Matched	4.44	4.06	10.9	73%	3.9	0.000
Number of Beers List Alerts	Unmatched	0.714	0.522	21		8.3	0.000
	Matched	0.714	0.677	4.1	81%	1.38	0.168
Number of PAL List Alerts	Unmatched	1.65	1.14	43.4		17.02	0.000
	Matched	1.65	1.58	5.9	86%	2.09	0.036
Number of Clinical Initiatives Alerts	Unmatched	2.84	1.89	56.3		21.98	0.000
	Matched	2.84	2.71	7.5	87%	2.7	0.007
Number of Consider Length Alerts	Unmatched	0.131	0.135	-1		-0.4	0.686
	Matched	0.131	0.124	1.7	-63%	0.59	0.557
(Number of Duplication Alerts)^2	Unmatched	32.7	20.1	25.8		10.18	0.000
	Matched	32.7	27.0	11.7	55%	4.27	0.000
(Number of Beers List Alerts)^2	Unmatched	1.46	0.98	15.4		6.19	0.000
	Matched	1.46	1.31	4.8	69%	1.58	0.113
(Number of PAL List Alerts)^2	Unmatched	4.24	2.60	31.7		12.66	0.000
	Matched	4.24	3.83	8	75%	2.7	0.007
(Number of Clinical Initiatives Alerts)^2	Unmatched	11.00	6.33	40.8		16.27	0.000
	Matched	11.00	9.96	9.1	78%	3.08	0.002
(Number of Consider Length Alerts)^2	Unmatched	0.209	0.187	2.4		0.96	0.338
	Matched	0.209	0.197	1.3	46%	0.43	0.665
Total Number of Alerts x Total Number of Drugs	Unmatched	314.1	187.8	43.1		17.09	0.000
	Matched	314.1	277.8	12.4	71%	4.36	0.000
Total Amount Paid x Total Number of Drugs	Unmatched	46,334	29,281	38.3		15.18	0.000
	Matched	46,334	40,659	12.7	67%	4.5	0.000
Total Amount Paid x Total Number of Alerts	Unmatched	17,115	10,170	38.5		15.35	0.000
	Matched	17,115	14,825	12.7	67%	4.46	0.000
Average Bias	Unmatched			**30.18**			
	Matched			**7.97**	**74%**		
Pseudo R2	Unmatched	0.108					
	Matched	0.008					

Sample Sizes: Study Group n=2,517
Unmatched Comparison Group n=3,8

Table A.3: Bias Reduction (Comparison #4)

Comparison #4 (Review Level, Retrospective-Only Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.3	78.3	-8.1		-2.88	0.004
	Matched	77.3	78.1	-6.5	20%	-2.88	0.004
(Age)^2	Unmatched	6,128	6,278	-8.5		-3.02	0.003
	Matched	6,128	6,223	-5.4	36%	-2.4	0.016
Race	Unmatched	31.3%	23.5%	17.6		6.16	0.000
(Non-White)	Matched	31.3%	29.6%	3.8	78%	1.58	0.114
Sex	Unmatched	74.7%	78.9%	-9.9		-3.48	0.000
(Female)	Matched	74.7%	75.6%	-2.2	78%	-0.9	0.371
Total Number of Drugs	Unmatched	28.4	28.9	-5.1		-1.82	0.069
	Matched	28.4	27.7	7.2	-42%	3.33	0.001
Total Amount Paid	Unmatched	$1,511	$1,527	-1.1		-0.36	0.716
	Matched	$1,511	$1,422	6.1	-443%	2.65	0.008
Total Number of Alerts	Unmatched	9.78	9.81	-0.6		-0.2	0.839
	Matched	9.78	9.38	7.3	-1192%	3.34	0.001
Number of Duplication Alerts	Unmatched	4.82	4.64	5		1.79	0.074
	Matched	4.82	4.54	7.8	-56%	3.57	0.000
Number of Beers List Alerts	Unmatched	0.715	0.778	-6.5		-2.34	0.019
	Matched	0.715	0.674	4.3	35%	1.93	0.054
Number of PAL List Alerts	Unmatched	1.48	1.58	-8.5		-3.02	0.003
	Matched	1.48	1.46	1.3	85%	0.56	0.577
Number of Clinical Initiatives Alerts	Unmatched	2.61	2.64	-1.5		-0.55	0.584
	Matched	2.61	2.55	3.5	-128%	1.58	0.115
Number of Consider Length Alerts	Unmatched	0.159	0.175	-3.3		-1.16	0.245
	Matched	0.159	0.153	1.3	59%	0.58	0.560
(Number of Duplication Alerts)^2	Unmatched	35.1	34.9	0.3		0.1	0.920
	Matched	35.1	30.4	8.4	-2968%	4.15	0.000
(Number of Beers List Alerts)^2	Unmatched	1.39	1.58	-5.8		-2.07	0.039
	Matched	1.39	1.22	4.9	16%	2.3	0.022
(Number of PAL List Alerts)^2	Unmatched	3.66	4.01	-6.3		-2.26	0.024
	Matched	3.66	3.41	4.4	31%	2.03	0.042
(Number of Clinical Initiatives Alerts)^2	Unmatched	9.64	10.01	-3.1		-1.1	0.272
	Matched	9.64	8.96	5.6	-83%	2.58	0.010
(Number of Consider Length Alerts)^2	Unmatched	0.244	0.254	-0.9		-0.33	0.742
	Matched	0.244	0.232	1.2	-24%	0.5	0.620
Total Number of Alerts x Total Number of Drugs	Unmatched	310.7	322.5	-3.9		-1.41	0.159
	Matched	310.7	288.7	7.3	-86%	3.47	0.001
Total Amount Paid x Total Number of Drugs	Unmatched	47,993	49,324	-1.7		-0.54	0.592
	Matched	47,993	43,069	6.1	-270%	2.7	0.007
Total Amount Paid x Total Number of Alerts	Unmatched	17,120	17,333	-0.7		-0.24	0.810
	Matched	17,120	15,145	6.8	-828%	3.02	0.003
Average Bias	Unmatched			**4.92**			
	Matched			**5.06**	**-3%**		
Pseudo R2	Unmatched	0.014					
	Matched	0.008					

Sample Sizes: Study Group n=3,638
Unmatched Comparison Group n=1,928

Table A.4: Bias Reduction (Comparison #5)

Comparison #5 (Recommendation Level, Retrospective-Only Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.3	78.3	-8.1		-2.55	0.011
	Matched	77.3	78.4	-8.8	-9%	-3.01	0.003
(Age)^2	Unmatched	6,124	6,278	-8.8		-2.78	0.005
	Matched	6,124	6,258	-7.7	13%	-2.6	0.009
Race	Unmatched	31.7%	23.5%	18.5		5.83	0.000
(Non-White)	Matched	31.7%	29.8%	4.2	77%	1.31	0.189
Sex	Unmatched	75.2%	78.9%	-8.7		-2.74	0.006
(Female)	Matched	75.2%	76.2%	-2.3	73%	-0.73	0.468
Total Number of Drugs	Unmatched	29.3	28.9	3.8		1.2	0.229
	Matched	29.3	28.2	10.1	-164%	3.43	0.001
Total Amount Paid	Unmatched	$1,553	$1,527	2.9		0.91	0.364
	Matched	$1,553	$1,460	10.2	-257%	3.57	0.000
Total Number of Alerts	Unmatched	10.33	9.81	9.5		3	0.003
	Matched	10.33	9.80	9.7	-2%	3.34	0.001
Number of Duplication Alerts	Unmatched	4.83	4.64	5.2		1.66	0.097
	Matched	4.83	4.51	9	-72%	3.13	0.002
Number of Beers List Alerts	Unmatched	0.759	0.778	-2		-0.62	0.533
	Matched	0.759	0.717	4.3	-116%	1.43	0.154
Number of PAL List Alerts	Unmatched	1.70	1.58	9.6		3.04	0.002
	Matched	1.70	1.65	4.1	57%	1.36	0.173
Number of Clinical Initiatives Alerts	Unmatched	2.90	2.64	15.2		4.79	0.000
	Matched	2.90	2.79	6.4	58%	2.17	0.030
Number of Consider Length Alerts	Unmatched	0.148	0.175	-5.9		-1.85	0.064
	Matched	0.148	0.141	1.6	73%	0.53	0.599
(Number of Duplication Alerts)^2	Unmatched	35.0	34.9	0.2		0.08	0.940
	Matched	35.0	30.0	9.2	-3767%	3.39	0.001
(Number of Beers List Alerts)^2	Unmatched	1.51	1.58	-2		-0.62	0.532
	Matched	1.51	1.34	5.1	-157%	1.75	0.081
(Number of PAL List Alerts)^2	Unmatched	4.42	4.01	7		2.22	0.027
	Matched	4.42	4.05	6.4	9%	2.14	0.032
(Number of Clinical Initiatives Alerts)^2	Unmatched	11.14	10.01	9.1		2.88	0.004
	Matched	11.14	10.18	7.8	15%	2.62	0.009
(Number of Consider Length Alerts)^2	Unmatched	0.224	0.254	-2.9		-0.93	0.353
	Matched	0.224	0.210	1.4	52%	0.47	0.635
Total Number of Alerts x Total Number of Drugs	Unmatched	337.0	322.5	4.7		1.49	0.137
	Matched	337.0	307.0	9.7	-106%	3.38	0.001
Total Amount Paid x Total Number of Drugs	Unmatched	50,319	49,324	2.1		0.66	0.509
	Matched	50,319	45,307	10.5	-404%	3.67	0.000
Total Amount Paid x Total Number of Alerts	Unmatched	18,254	17,333	4.8		1.51	0.132
	Matched	18,254	16,172	10.8	-126%	3.76	0.000
Average Bias	Unmatched			**6.55**			
	Matched			**6.97**	**-6%**		
Pseudo R2	Unmatched	0.021					
	Matched	0.009					

Sample Sizes: Study Group n=2,064
Unmatched Comparison Group n=1,928

Table A.5: Bias Reduction (Comparison #6)

Comparison #6 (Drug Change Level, Retrospective-Only Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.3	78.3	-7.8		-2.21	0.027
	Matched	77.3	78.3	-8.1	-5%	-2.3	0.022
(Age)^2	Unmatched	6,130	6,278	-8.5		-2.42	0.015
	Matched	6,130	6,250	-6.9	19%	-1.93	0.053
Race	Unmatched	31.1%	23.5%	17.2		4.93	0.000
(Non-White)	Matched	31.1%	28.9%	5	71%	1.28	0.202
Sex	Unmatched	75.6%	78.9%	-7.9		-2.27	0.023
(Female)	Matched	75.6%	76.1%	-1.4	83%	-0.35	0.724
Total Number of Drugs	Unmatched	29.6	28.9	7.2		2.05	0.040
	Matched	29.6	28.6	10.1	-40%	2.81	0.005
Total Amount Paid	Unmatched	$1,573	$1,527	5.1		1.46	0.144
	Matched	$1,573	$1,481	10.3	-100%	2.98	0.003
Total Number of Alerts	Unmatched	10.53	9.81	13.2		3.75	0.000
	Matched	10.53	10.03	9.2	31%	2.58	0.010
Number of Duplication Alerts	Unmatched	4.92	4.64	7.7		2.19	0.029
	Matched	4.92	4.61	8.4	-9%	2.38	0.018
Number of Beers List Alerts	Unmatched	0.749	0.778	-3		-0.86	0.391
	Matched	0.749	0.719	3.1	-2%	0.84	0.399
Number of PAL List Alerts	Unmatched	1.76	1.58	14.8		4.21	0.000
	Matched	1.76	1.70	4.8	68%	1.32	0.188
Number of Clinical Initiatives Alerts	Unmatched	2.97	2.64	19.2		5.45	0.000
	Matched	2.97	2.87	5.9	69%	1.67	0.095
Number of Consider Length Alerts	Unmatched	0.140	0.175	-7.5		-2.13	0.033
	Matched	0.140	0.131	2	73%	0.56	0.574
(Number of Duplication Alerts)^2	Unmatched	36.5	34.9	2.9		0.81	0.416
	Matched	36.5	31.6	8.9	-208%	2.61	0.009
(Number of Beers List Alerts)^2	Unmatched	1.49	1.58	-2.5		-0.7	0.482
	Matched	1.49	1.35	4.1	-68%	1.16	0.245
(Number of PAL List Alerts)^2	Unmatched	4.61	4.01	10.4		2.97	0.003
	Matched	4.61	4.21	6.8	34%	1.87	0.061
(Number of Clinical Initiatives Alerts)^2	Unmatched	11.58	10.01	12.7		3.62	0.000
	Matched	11.58	10.60	7.9	38%	2.22	0.027
(Number of Consider Length Alerts)^2	Unmatched	0.217	0.254	-3.7		-1.04	0.298
	Matched	0.217	0.199	1.8	51%	0.51	0.611
Total Number of Alerts x Total Number of Drugs	Unmatched	348.0	322.5	8.2		2.33	0.020
	Matched	348.0	317.9	9.6	-18%	2.71	0.007
Total Amount Paid x Total Number of Drugs	Unmatched	51,637	49,324	4.8		1.37	0.170
	Matched	51,637	46,456	10.8	-124%	3.07	0.002
Total Amount Paid x Total Number of Alerts	Unmatched	18,929	17,333	8.1		2.31	0.021
	Matched	18,929	16,788	10.9	-34%	3.07	0.002
Average Bias	Unmatched			**8.61**			
	Matched			**6.80**	**21%**		
Pseudo R2	Unmatched	0.025					
	Matched	0.01					

Sample Sizes: Study Group n=1,404
Unmatched Comparison Group n=1,928

Table A.6: Bias Reduction (Comparison #7)

Comparison #7 (Recommendation Level, Dual-Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.4	78.3	7.6		-1.93	0.053
	Matched	77.4	78.6	10	-32%	-2.34	0.019
(Age)^2	Unmatched	6,136	6,278	8.2		-2.09	0.037
	Matched	6,136	6,294	9.1	-12%	-2.12	0.034
Race	Unmatched	30.3%	23.5%	15.4		4	0.000
(Non-White)	Matched	30.3%	28.6%	3.9	75%	0.84	0.401
Sex	Unmatched	77.4%	78.9%	3.6		-0.93	0.350
(Female)	Matched	77.4%	79.2%	4.4	-21%	-0.98	0.326
Total Number of Drugs	Unmatched	30.8	28.9	18.2		4.65	0.000
	Matched	30.8	29.6	11.2	38%	2.58	0.010
Total Amount Paid	Unmatched	$1,648	$1,527	12.9		3.34	0.001
	Matched	$1,648	$1,558	9.6	26%	2.27	0.023
Total Number of Alerts	Unmatched	11.04	9.81	21.4		5.51	0.000
	Matched	11.04	10.52	8.9	58%	2.04	0.042
Number of Duplication Alerts	Unmatched	5.12	4.64	13		3.34	0.001
	Matched	5.12	4.85	7.3	44%	1.69	0.091
Number of Beers List Alerts	Unmatched	0.856	0.778	7.6		1.97	0.049
	Matched	0.856	0.788	6.6	13%	1.47	0.141
Number of PAL List Alerts	Unmatched	1.77	1.58	14.8		3.8	0.000
	Matched	1.77	1.71	4.3	71%	0.98	0.329
Number of Clinical Initiatives Alerts	Unmatched	3.14	2.64	28.1		7.22	0.000
	Matched	3.14	3.03	6.4	77%	1.45	0.147
Number of Consider Length Alerts	Unmatched	0.154	0.175	4.3		-1.11	0.266
	Matched	0.154	0.146	1.7	61%	0.38	0.702
(Number of Duplication Alerts)^2	Unmatched	40.0	34.9	8.4		2.16	0.031
	Matched	40.0	34.4	9.2	-10%	2.2	0.028
(Number of Beers List Alerts)^2	Unmatched	1.86	1.58	7.7		2	0.045
	Matched	1.86	1.60	7.3	6%	1.6	0.109
(Number of PAL List Alerts)^2	Unmatched	4.81	4.01	13.1		3.42	0.001
	Matched	4.81	4.33	7.8	41%	1.73	0.084
(Number of Clinical Initiatives Alerts)^2	Unmatched	13.14	10.01	23.1		6.06	0.000
	Matched	13.14	11.91	9.1	61%	1.99	0.047
(Number of Consider Length Alerts)^2	Unmatched	0.252	0.254	0.2		-0.05	0.960
	Matched	0.252	0.237	1.3	-573%	0.28	0.779
Total Number of Alerts x Total Number of Drugs	Unmatched	380.4	322.5	17.6		4.57	0.000
	Matched	380.4	346.1	10.4	41%	2.42	0.015
Total Amount Paid x Total Number of Drugs	Unmatched	56,100	49,324	13.6		3.51	0.000
	Matched	56,100	50,844	10.5	22%	2.44	0.015
Total Amount Paid x Total Number of Alerts	Unmatched	20,717	17,333	16.3		4.25	0.000
	Matched	20,717	18,506	10.7	35%	2.45	0.015
Average Bias	Unmatched			**12.75**			
	Matched			**7.48**	**41%**		
Pseudo R2	Unmatched	0.026					
	Matched	0.011					

Sample Sizes: Study Group n=986
Unmatched Comparison Group n=1,928

Table A.7: Bias Reduction (Comparison #8)

Comparison #8 (Drug Change Level, Dual-Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.2	78.3	-8.6		-1.94	0.052
	Matched	77.2	78.5	-10.5	-22%	-2.05	0.041
(Age)^2	Unmatched	6,119	6,278	-9		-2.05	0.041
	Matched	6,119	6,283	-9.4	-4%	-1.83	0.067
Race	Unmatched	30.2%	23.5%	15.1		3.46	0.001
(Non-White)	Matched	30.2%	28.9%	3	80%	0.53	0.595
Sex	Unmatched	77.7%	78.9%	-2.9		-0.65	0.513
(Female)	Matched	77.7%	79.6%	-4.6	-59%	-0.86	0.392
Total Number of Drugs	Unmatched	31.3	28.9	23		5.23	0.000
	Matched	31.3	30.2	10.7	53%	2.02	0.043
Total Amount Paid	Unmatched	$1,681	$1,527	16.1		3.72	0.000
	Matched	$1,681	$1,587	9.8	39%	1.93	0.054
Total Number of Alerts	Unmatched	11.43	9.81	28.2		6.43	0.000
	Matched	11.43	10.86	9.8	65%	1.86	0.063
Number of Duplication Alerts	Unmatched	5.27	4.64	16.9		3.82	0.000
	Matched	5.27	4.95	8.4	50%	1.63	0.104
Number of Beers List Alerts	Unmatched	0.923	0.778	13.7		3.18	0.001
	Matched	0.923	0.856	6.4	54%	1.15	0.250
Number of PAL List Alerts	Unmatched	1.84	1.58	20.6		4.66	0.000
	Matched	1.84	1.77	5.2	75%	0.99	0.322
Number of Clinical Initiatives Alerts	Unmatched	3.26	2.64	34.9		7.92	0.000
	Matched	3.26	3.15	6.4	82%	1.2	0.230
Number of Consider Length Alerts	Unmatched	0.141	0.175	-7		-1.59	0.113
	Matched	0.141	0.136	1.2	83%	0.23	0.820
(Number of Duplication Alerts)^2	Unmatched	41.8	34.9	11.3		2.58	0.010
	Matched	41.8	35.4	10.5	7%	2.12	0.034
(Number of Beers List Alerts)^2	Unmatched	2.09	1.58	13.2		3.15	0.002
	Matched	2.09	1.82	7	47%	1.23	0.220
(Number of PAL List Alerts)^2	Unmatched	5.00	4.01	16.4		3.81	0.000
	Matched	5.00	4.51	8.1	51%	1.49	0.136
(Number of Clinical Initiatives Alerts)^2	Unmatched	13.92	10.01	28.5		6.72	0.000
	Matched	13.92	12.75	8.6	70%	1.56	0.120
(Number of Consider Length Alerts)^2	Unmatched	0.246	0.254	-0.6		-0.15	0.879
	Matched	0.246	0.241	0.5	20%	0.09	0.929
Total Number of Alerts x Total Number of Drugs	Unmatched	400.1	322.5	23.3		5.38	0.000
	Matched	400.1	363.6	10.9	53%	2.09	0.037
Total Amount Paid x Total Number of Drugs	Unmatched	58,064	49,324	17.2		3.97	0.000
	Matched	58,064	52,646	10.7	38%	2.06	0.040
Total Amount Paid x Total Number of Alerts	Unmatched	21,635	17,333	20.5		4.78	0.000
	Matched	21,635	19,295	11.2	46%	2.15	0.032
Average Bias	Unmatched			**16.36**			
	Matched			**7.64**	**53%**		
Pseudo R2	Unmatched	0.036					
	Matched	0.012					

Sample Sizes: Study Group n=686
Unmatched Comparison Group n=1,928

Table A.8: Bias Reduction (Comparison #9)

Comparison #9 (Recommendation Level, Prospective-Only Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	79.7	80.5	-6.1		-1.25	0.212
	Matched	79.7	80.8	-8.9	-46%	-1.63	0.104
(Age)^2	Unmatched	6,496	6,638	-7.9		-1.63	0.104
	Matched	6,496	6,645	-8.3	-5%	-1.51	0.130
Race	Unmatched	39.8%	26.4%	28.7		6.16	0.000
(Non-White)	Matched	39.8%	36.6%	6.8	76%	1.1	0.272
Sex	Unmatched	74.3%	78.7%	-10.4		-2.21	0.027
(Female)	Matched	74.3%	76.4%	-5	52%	-0.83	0.409
Total Number of Drugs	Unmatched	12.5	11.7	18		3.58	0.000
	Matched	12.5	12.3	2.6	85%	0.5	0.617
Total Amount Paid	Unmatched	$740	$636	21.4		4.42	0.000
	Matched	$740	$707	6.8	68%	1.25	0.212
Total Number of Alerts	Unmatched	4.52	3.56	33.3		7	0.000
	Matched	4.52	4.26	8.9	73%	1.53	0.126
Number of Duplication Alerts	Unmatched	1.50	1.40	6		1.26	0.207
	Matched	1.50	1.39	6.3	-5%	1.09	0.275
Number of Beers List Alerts	Unmatched	0.257	0.258	-0.3		-0.05	0.958
	Matched	0.257	0.252	1	-287%	0.17	0.867
Number of PAL List Alerts	Unmatched	0.98	0.68	34.7		7.39	0.000
	Matched	0.98	0.92	6.4	82%	1.07	0.286
Number of Clinical Initiatives Alerts	Unmatched	1.70	1.12	50.9		10.58	0.000
	Matched	1.70	1.61	7.4	86%	1.29	0.198
Number of Consider Length Alerts	Unmatched	0.083	0.095	-3.7		-0.78	0.438
	Matched	0.083	0.077	1.6	57%	0.27	0.784
(Number of Duplication Alerts)^2	Unmatched	5.2	4.9	3.7		0.77	0.440
	Matched	5.2	4.6	6.5	-75%	1.19	0.234
(Number of Beers List Alerts)^2	Unmatched	0.35	0.36	-1.4		-0.28	0.780
	Matched	0.35	0.34	0.5	64%	0.09	0.932
(Number of PAL List Alerts)^2	Unmatched	1.74	1.14	24.8		5.57	0.000
	Matched	1.74	1.56	7.3	71%	1.15	0.252
(Number of Clinical Initiatives Alerts)^2	Unmatched	4.11	2.55	33.6		7.4	0.000
	Matched	4.11	3.70	8.9	74%	1.45	0.148
(Number of Consider Length Alerts)^2	Unmatched	0.114	0.119	-0.7		-0.16	0.873
	Matched	0.114	0.109	0.9	-29%	0.15	0.881
Total Number of Alerts x Total Number of Drugs	Unmatched	62.2	49.2	23.5		4.87	0.000
	Matched	62.2	58.5	6.6	72%	1.14	0.256
Total Amount Paid x Total Number of Drugs	Unmatched	10,140	8,651	17.2		3.59	0.000
	Matched	10,140	9,573	6.6	62%	1.17	0.241
Total Amount Paid x Total Number of Alerts	Unmatched	3,818	2,797	26.8		5.74	0.000
	Matched	3,818	3,507	8.2	70%	1.36	0.175
Average Bias	Unmatched			**17.66**			
	Matched			**5.78**	**67%**		
Pseudo R2	Unmatched	0.081					
	Matched	0.007					

Sample Sizes: Study Group n=568
Unmatched Comparison Group n=1,873

Table A.9: Bias Reduction (Comparison #10)

Comparison #10 (Drug Change Level, Prospective-Only Type Intervention)

Variables	Sample	Mean Treated	Mean Comparison	%bias	%reduction in bias	t-test t-value	t-test p>t
Age	Unmatched	77.6	80.5	-4.7		-0.84	0.399
	Matched	77.6	81.0	-8.9	-92%	-1.45	0.149
(Age)^2	Unmatched	6,175	6,638	-6.8		-1.23	0.217
	Matched	6,175	6,668	-8.5	-24%	-1.35	0.176
Race	Unmatched	32.2%	26.4%	29.2		5.64	0.000
(Non-White)	Matched	32.2%	37.5%	5.5	81%	0.77	0.440
Sex	Unmatched	75.1%	78.7%	-12.1		-2.32	0.021
(Female)	Matched	75.1%	76.1%	-6	50%	-0.87	0.386
Total Number of Drugs	Unmatched	26.9	11.7	19		3.36	0.001
	Matched	26.9	12.4	2.6	87%	0.43	0.669
Total Amount Paid	Unmatched	$1,442	$636	20.4		3.72	0.000
	Matched	$1,442	$693	8.6	58%	1.4	0.161
Total Number of Alerts	Unmatched	9.37	3.56	37		7.03	0.000
	Matched	9.37	4.33	10.8	71%	1.59	0.112
Number of Duplication Alerts	Unmatched	4.47	1.40	8.3		1.58	0.115
	Matched	4.47	1.42	7	17%	1.03	0.304
Number of Beers List Alerts	Unmatched	0.686	0.258	0.7		0.13	0.894
	Matched	0.686	0.255	1.3	-81%	0.19	0.848
Number of PAL List Alerts	Unmatched	1.47	0.68	36.7		7.06	0.000
	Matched	1.47	0.93	7.9	79%	1.12	0.262
Number of Clinical Initiatives Alerts	Unmatched	2.60	1.12	55.2		10.32	0.000
	Matched	2.60	1.64	9.9	82%	1.47	0.142
Number of Consider Length Alerts	Unmatched	0.150	0.095	-3.2		-0.6	0.548
	Matched	0.150	0.077	2.1	35%	0.31	0.759
(Number of Duplication Alerts)^2	Unmatched	32.4	4.9	7		1.31	0.190
	Matched	32.4	4.8	7.7	-10%	1.17	0.241
(Number of Beers List Alerts)^2	Unmatched	1.35	0.36	-0.6		-0.12	0.904
	Matched	1.35	0.35	0.6	1%	0.09	0.925
(Number of PAL List Alerts)^2	Unmatched	3.63	1.14	27.6		5.67	0.000
	Matched	3.63	1.61	8.4	70%	1.14	0.256
(Number of Clinical Initiatives Alerts)^2	Unmatched	9.62	2.55	38		7.69	0.000
	Matched	9.62	3.86	10.7	72%	1.48	0.140
(Number of Consider Length Alerts)^2	Unmatched	0.230	0.119	0.6		0.11	0.911
	Matched	0.230	0.115	1.2	-116%	0.16	0.873
Total Number of Alerts x Total Number of Drugs	Unmatched	293.7	49.2	26.6		4.99	0.000
	Matched	293.7	59.8	7.8	71%	1.15	0.252
Total Amount Paid x Total Number of Drugs	Unmatched	44,936	8,651	16.4		3.02	0.003
	Matched	44,936	9,370	8	51%	1.26	0.207
Total Amount Paid x Total Number of Alerts	Unmatched	16,183	2,797	28.5		5.5	0.000
	Matched	16,183	3,501	10.1	65%	1.46	0.145
Average Bias	Unmatched			**18.93**			
	Matched			**6.67**	**65%**		
Pseudo R2	Unmatched	0.085					
	Matched	0.01					

Sample Sizes: Study Group n=427
Unmatched Comparison Group n=1,873

APPENDIX B: DIFFERENCE IN DIFFERENCE RESULTS TABLES:

COMPARISONS 2-10

Table B.1: Difference in Difference Results (Comparison #2)

Comparison #2 (Recommendation Level, All Intervention Types)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,451	-32.11	-2.2%			
	Comparison	$1,347	59.83	4.4%	**-91.94**	**-6.3%**	**0.000**
Total number of drugs	Review	27.0	-0.18	-0.7%			
	Comparison	25.6	-0.37	-1.4%	**0.19**	**0.7%**	**0.340**
Number of PAL list alerts	Review	1.60	-0.53	-33.2%			
	Comparison	1.54	-0.18	-11.9%	**-0.35**	**-21.7%**	**0.000**
Number of Clinical Initiatives alerts	Review	2.78	-0.28	-10.2%			
	Comparison	2.65	-0.037	-1.4%	**-0.25**	**-8.9%**	**0.000**
Number of Beers List alerts	Review	0.71	-0.07	-9.5%			
	Comparison	0.67	-0.05	-7.3%	**-0.02**	**-2.6%**	**0.373**
Number of duplication alerts	Review	4.38	-0.19	-4.3%			
	Comparison	4.02	-0.12	-3.1%	**-0.07**	**-1.5%**	**0.415**
Number of Consider Length alerts	Review	0.14	0.00	-2.6%			
	Comparison	0.13	0.004	2.7%	**-0.01**	**-5.2%**	**0.565**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=3,618
Unmatched Comparison Group n=3

Table B.2: Difference in Difference Results (Comparison #3)

Comparison #3 (Drug Change Level, All Intervention Types)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,460	-64.82	-4.4%			
	Comparison	$1,358	49.33	3.6%	**-114.15**	**-7.8%**	**0.000**
Total number of drugs	Review	27.2	-0.50	-1.9%			
	Comparison	25.8	-0.41	-1.6%	**-0.09**	**-0.3%**	**0.701**
Number of PAL list alerts	Review	1.65	-0.65	-39.5%			
	Comparison	1.58	-0.21	-13.5%	**-0.44**	**-26.6%**	**0.000**
Number of Clinical Initiatives alerts	Review	2.84	-0.36	-12.8%			
	Comparison	2.71	-0.052	-1.9%	**-0.31**	**-10.9%**	**0.000**
Number of Beers List alerts	Review	0.71	-0.08	-11.5%			
	Comparison	0.68	-0.05	-7.6%	**-0.03**	**-4.2%**	**0.231**
Number of duplication alerts	Review	4.44	-0.28	-6.3%			
	Comparison	4.06	-0.18	-4.4%	**-0.10**	**-2.4%**	**0.292**
Number of Consider Length alerts	Review	0.13	0.00	-2.1%			
	Comparison	0.12	0.008	6.1%	**-0.01**	**-7.9%**	**0.484**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=2,517
Unmatched Comparison Group n=3

Table B.3: Difference in Difference Results (Comparison #4)

Comparison #4 (Review Level, Retrospective-Only Type Intervention)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,510	-3.91	-0.3%			
	Comparison	$1,422	58.48	4.1%	**-62.39**	**-4.1%**	**0.000**
Total number of drugs	Review	28.4	-0.65	-2.3%			
	Comparison	27.7	-0.61	-2.2%	**-0.03**	**-0.1%**	**0.861**
Number of PAL list alerts	Review	1.47	-0.40	-26.9%			
	Comparison	1.46	-0.13	-8.9%	**-0.27**	**-18.1%**	**0.000**
Number of Clinical Initiatives alerts	Review	2.61	-0.26	-9.9%			
	Comparison	2.55	0.044	1.7%	**-0.30**	**-11.6%**	**0.000**
Number of Beers List alerts	Review	0.72	-0.06	-8.5%			
	Comparison	0.67	-0.03	-4.6%	**-0.03**	**-4.2%**	**0.140**
Number of duplication alerts	Review	4.82	-0.42	-8.7%			
	Comparison	4.54	-0.09	-1.9%	**-0.33**	**-6.9%**	**0.000**
Number of Consider Length alerts	Review	0.16	-0.01	-7.2%			
	Comparison	0.15	-0.003	-2.2%	**-0.01**	**-5.2%**	**0.526**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=3,638
Unmatched Comparison Group n=1

Table B.4: Difference in Difference Results (Comparison #5)

Comparison #5 (Recommendation Level, Retrospective-Only Type Review)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,553	-36.01	-2.3%			
	Comparison	$1,460	55.56	3.8%	**-91.58**	**-5.9%**	**0.000**
Total number of drugs	Review	29.3	-0.57	-1.9%			
	Comparison	28.2	-0.61	-2.2%	**0.05**	**0.2%**	**0.860**
Number of PAL list alerts	Review	1.70	-0.56	-32.8%			
	Comparison	1.65	-0.20	-11.9%	**-0.36**	**-21.3%**	**0.000**
Number of Clinical Initiatives alerts	Review	2.90	-0.32	-11.0%			
	Comparison	2.79	-0.015	-0.5%	**-0.30**	**-10.4%**	**0.000**
Number of Beers List alerts	Review	0.76	-0.08	-10.9%			
	Comparison	0.72	-0.06	-8.5%	**-0.02**	**-2.8%**	**0.429**
Number of duplication alerts	Review	4.83	-0.30	-6.2%			
	Comparison	4.51	-0.13	-2.9%	**-0.17**	**-3.5%**	**0.138**
Number of Consider Length alerts	Review	0.15	0.00	-3.0%			
	Comparison	0.14	-0.004	-3.1%	**0.00**	**0.0%**	**1.000**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=2,064
Unmatched Comparison Group n=1

Table B.5: Difference in Difference Results (Comparison #6)

Comparison #6 (Drug Change Level, Retrospective-Only Type Intervention)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,573	-71.24	-4.5%			
	Comparison	$1,481	54.65	3.7%	**-125.89**	**-8.0%**	**0.000**
Total number of drugs	Review	29.6	-0.97	-3.3%			
	Comparison	28.6	-0.51	-1.8%	**-0.46**	**-1.6%**	**0.156**
Number of PAL list alerts	Review	1.76	-0.70	-39.8%			
	Comparison	1.70	-0.21	-12.3%	**-0.49**	**-27.9%**	**0.000**
Number of Clinical Initiatives alerts	Review	2.97	-0.40	-13.3%			
	Comparison	2.87	-0.030	-1.0%	**-0.37**	**-12.3%**	**0.005**
Number of Beers List alerts	Review	0.75	-0.09	-12.1%			
	Comparison	0.72	-0.06	-7.9%	**-0.03**	**-4.5%**	**0.314**
Number of duplication alerts	Review	4.92	-0.38	-7.8%			
	Comparison	4.61	-0.19	-4.1%	**-0.19**	**-3.9%**	**0.160**
Number of Consider Length alerts	Review	0.14	0.00	-3.6%			
	Comparison	0.13	0.004	3.3%	**-0.01**	**-6.6%**	**0.649**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=1,404
Unmatched Comparison Group n=1

Table B.6: Difference in Difference Results (Comparison #7)

Comparison #7 (Recommendation Level, Dual-Type Intervention)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,648	-50.20	-3.0%			
	Comparison	$1,558	-13.02	-0.8%	**-37.18**	**-2.3%**	**0.280**
Total number of drugs	Review	30.8	-0.53	-1.7%			
	Comparison	29.6	-1.33	-4.5%	**0.81**	**2.6%**	**0.052**
Number of PAL list alerts	Review	1.77	-0.60	-34.2%			
	Comparison	1.71	-0.25	-14.3%	**-0.36**	**-20.3%**	**0.000**
Number of Clinical Initiatives alerts	Review	3.14	-0.32	-10.3%			
	Comparison	3.03	-0.103	-3.4%	**-0.22**	**-7.0%**	**0.001**
Number of Beers List alerts	Review	0.86	-0.09	-10.5%			
	Comparison	0.79	-0.06	-7.9%	**-0.03**	**-3.3%**	**0.515**
Number of duplication alerts	Review	5.12	-0.26	-5.0%			
	Comparison	4.85	-0.37	-7.7%	**0.12**	**2.3%**	**0.503**
Number of Consider Length alerts	Review	0.15	-0.02	-12.5%			
	Comparison	0.15	-0.003	-2.1%	**-0.02**	**-10.5%**	**0.504**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=986
Unmatched Comparison Group n=1,9

Table B.7: Difference in Difference Results (Comparison #8)

Comparison #8 (Drug Change Level, Dual-Type Intervention)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$1,681	-95.41	-5.7%			
	Comparison	$1,587	-11.57	-0.7%	**-83.84**	**-5.0%**	**0.052**
Total number of drugs	Review	31.3	-1.06	-3.4%			
	Comparison	30.2	-1.47	-4.9%	**0.41**	**1.3%**	**0.419**
Number of PAL list alerts	Review	1.84	-0.69	-37.8%			
	Comparison	1.77	-0.22	-12.7%	**-0.47**	**-25.6%**	**0.000**
Number of Clinical Initiatives alerts	Review	3.26	-0.42	-12.8%			
	Comparison	3.15	-0.105	-3.3%	**-0.31**	**-9.6%**	**0.000**
Number of Beers List alerts	Review	0.92	-0.13	-13.9%			
	Comparison	0.86	-0.09	-10.2%	**-0.04**	**-4.4%**	**0.462**
Number of duplication alerts	Review	5.27	-0.42	-8.0%			
	Comparison	4.95	-0.44	-8.9%	**0.02**	**0.3%**	**0.940**
Number of Consider Length alerts	Review	0.14	-0.02	-12.4%			
	Comparison	0.14	0.004	3.2%	**-0.02**	**-15.5%**	**0.448**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=686
Unmatched Comparison Group n=1,9

Table B.8: Difference in Difference Results (Comparison #9)

Comparison #9 (Recommendation Level, Prospective-Only Type Intervention)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$740	13.49	1.8%			
	Comparison	$707	124.32	17.6%	**-110.83**	**-15.0%**	**0.000**
Total number of drugs	Review	12.5	1.82	14.6%			
	Comparison	12.3	1.66	13.5%	**0.16**	**1.3%**	**0.626**
Number of PAL list alerts	Review	0.98	-0.32	-32.2%			
	Comparison	0.92	-0.02	-1.7%	**-0.30**	**-30.6%**	**0.000**
Number of Clinical Initiatives alerts	Review	1.70	-0.09	-5.1%			
	Comparison	1.61	0.088	5.5%	**-0.17**	**-10.3%**	**0.005**
Number of Beers List alerts	Review	0.26	0.03	10.3%			
	Comparison	0.25	0.07	27.3%	**-0.04**	**-16.4%**	**0.263**
Number of duplication alerts	Review	1.50	0.32	21.2%			
	Comparison	1.39	0.35	25.4%	**-0.04**	**-2.3%**	**0.783**
Number of Consider Length alerts	Review	0.08	0.03	31.9%			
	Comparison	0.08	0.056	72.7%	**-0.03**	**-36.2%**	**0.226**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=568
Unmatched Comparison Group n=1,8

Table B.9: Difference in Difference Results (Comparison #10)

Comparison #10 (Drug Change Level, Prospective-Only Type Intervention)

Variable	Group	Pre-Period Mean	Mean Change	% change	Difference in Difference of Means	Difference in Difference of Means%	p-value
Total amount paid	Review	$733	5.44	0.7%			
	Comparison	$693	125.59	18.1%	**-120.15**	**-16.4%**	**0.000**
Total number of drugs	Review	12.5	1.93	15.4%			
	Comparison	12.4	1.78	14.4%	**0.15**	**1.2%**	**0.712**
Number of PAL list alerts	Review	1.00	-0.43	-42.6%			
	Comparison	0.93	-0.05	-5.3%	**-0.38**	**-37.7%**	**0.000**
Number of Clinical Initiatives alerts	Review	1.75	-0.17	-9.5%			
	Comparison	1.64	0.077	4.7%	**-0.24**	**-13.9%**	**0.001**
Number of Beers List alerts	Review	0.26	0.02	8.0%			
	Comparison	0.26	0.06	22.9%	**-0.04**	**-14.3%**	**0.398**
Number of duplication alerts	Review	1.55	0.27	17.7%			
	Comparison	1.42	0.36	25.3%	**-0.09**	**-5.6%**	**0.572**
Number of Consider Length alerts	Review	0.08	0.03	33.3%			
	Comparison	0.08	0.052	66.7%	**-0.02**	**-27.8%**	**0.419**

Notes: 1) Difference in Difference of Means is calculated by subtracting the Mean Change from the Comparison Group from the Mean Change of the Study Group 2) Difference in Difference of Means Percentage is calculated taking the Difference in Difference

Sample Sizes: Study Group n=427
Unmatched Comparison Group n=1,8

APPENDIX C: ASSESSMENT OF THE POLYPHARMACY INITIATIVE IN NURSING HOMES (PILOT PROJECT RESULTS)[70]

Assessment of the Polypharmacy Initiative in Nursing Homes

A Preliminary Analysis

By

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Executive Summary

Background, Methods, and Objectives

Beginning in March 2002, the Access II & III Programs initiated an effort to examine drug usage by elderly Medicaid enrollees in North Carolina nursing homes. The intervention consisted of a drug therapy management service provided by a pharmacist-physician team. The team 1) reviewed drug profiles and other medical records of Medicaid patients in nursing homes, 2) determined if a drug therapy problem existed, 3) recommended a change, and 4) followed up to determine if the change was implemented.

The overall aim was to determine if the team could save drug costs while simultaneously improving quality of pharmaceutical care available to elderly Medicaid recipients. The specific objectives of this report are to describe: 1) the frequency of each recommendation type, and 2) the drug cost impact of interventions performed by the team.

The analysis was done by assessing the baseline drug usage and costs, noting specific drug therapy change recommendations made and followed, and determining the resulting cost and quality impact.

Major Findings

- At baseline, Medicaid nursing home patients used, on average, 6.1 prescriptions per month (median = 6, standard deviation = 3.3, range = 1-18). The average cost of a single prescription for a 30 day supply of a drug was $54.81. The average cost per patient per month for prescription drugs was $336.68 (median cost = $269.19)
- The pharmacist-physician team made drug change recommendations for 37.7% (254/673) of all patients reviewed. There was considerable variability across nursing homes in the percentage of patients receiving change recommendations by the team.
- Of 408 drug change recommendations made by the consultant/pharmacist, 236 (57.8%) were acted upon (accepted or rejected) by the physician. A recommendation to discontinue a drug occurred in 124 or 30%, and another 69 (17%) involved a recommendation to change therapy from one drug to another.
- The baseline costs for one month of prescription drug usage across 12 nursing home sites was $226,588. The resultant cost after the reviews was $217,143, representing a 4.2% savings of $9,445 for the first month. An annualized gross annual savings of $113,340 would be achieved assuming these changes in drug therapy persisted for the entire year for all patients reviewed.
- Subtracting the $8,700 cost to hire pharmacist consultants and reimburse special physician consultant panels for their review services, the first year annual savings to costs ratio is estimated at 13 to 1.

Conclusions

- A program of review of Medicaid nursing home patients by pharmacist- physician consultants was cost-beneficial based solely on drug cost savings.
- Assuming that the drug use experiences of other NC Medicaid nursing home patients is similar to those in these homes, there is a need for a *different approach* to address drug therapy problems and save prescription drug costs among NC nursing home Medicaid patients.
- One viable approach involves having pharmacist-physician review teams make periodic visits to targeted nursing homes to perform both quality and cost of drug therapy reviews. Targeting patients in advance for specific review would appear to be a time- and cost-efficient strategy.

Assessment of Polypharmacy Initiative in Nursing Homes

A Preliminary Analysis

(Pilot Project)

BACKGROUND

Elderly persons are especially vulnerable to drug-related problems. Literature shows that drug-related morbidity and mortality are major problems in the elderly, and that the 2 major causes are therapeutic failure (i.e., inadequate drug therapy) and adverse drug reactions.[1-4] Two studies in particular have linked hospital readmissions in the elderly to drug related problems in 18%- 28% of the cases.[5,6] Compounding the problem is high prescription drug use; elders are at greater risk for experiencing sub-optimal drug therapy (i.e., polypharmacy, inappropriate use, or underutilization), which can lead to therapeutic failure or adverse drug reactions.[7-9]

Beginning in March, 2002, the Access II & III Programs initiated an effort to examine drug usage by elderly Medicaid enrollees in North Carolina nursing homes. This initiative was undertaken for three reasons. First, pharmacy costs in the Medicaid program are growing at an alarming and unprecedented rate. Second, elderly citizens use the most drugs per capita, and are most vulnerable to the adverse effects associated with inappropriate drug prescribing and prescription use. Finally, a review of current research suggested that pharmacy review programs coordinated by pharmacist-physician peer pairs can be effective in reducing inappropriate drug use in elderly patients.

The intervention consisted of a drug therapy management service provided by a pharmacist-physician team. Intervention activities consisted of: 1) reviewing drug profiles and other medical records of Medicaid patients in nursing homes, 2) determining if a drug therapy problem exists; if so, then 3) recommending a modification in the drug regimen, and 4) follow-up or results data collection. Pharmacists reviewed patients only after eliciting permission of the Department of Medical Assistance and the nursing homes as well as their Medical Directors and attending physicians. Confidentiality agreements were in place as a condition for enrollees and providers to participate in Medicaid, so patient confidentiality was maintained.

This is a preliminary report on the effectiveness of the first round of the pharmacist-physician initiative directed to addressing inappropriate drug use in the elderly nursing home population.

STUDY AIMS and OBJECTIVES

The overall aim of this intervention is to improve the overall quality of drug therapy while simultaneously improving the cost efficiency of current drug regimens. The specific objectives of this report are to:

1) describe the frequency of drug related problems encountered, recommendations made, and drug therapy changes that occurred as a result of the interventions
2) assess the drug cost impact of interventions performed by the team.

This pilot study report describes baseline patient drug regimens, recommendations made by the pharmacist-physician team, and results of those recommendations. The assessment of the resultant drug regimen changes was limited to their impact on drug costs. The effects of changes on patient outcomes such as an improvement (or reduction) in their health status or in use of health care services were not considered. A subsequent analysis is planned, which will include a longer follow-up period, as well as a concurrent assessment of a comparison group of patients in nursing homes without the pharmacist-physician team.

METHODS

Beginning in March of 2002, records were retrieved and examined for Medicaid recipients' prescription usage for 13 selected nursing homes served by physicians in the Access network. Patient drug profiles for each nursing home were then created. Algorithms were developed to screen patient records for signs of potential inappropriate and/or polypharmacy drug therapy problems such as therapeutic duplication, inappropriate drugs being used (based on the Beers drug list), multiple prescribers, and higher than normal drug usage. The consultant/ pharmacist verified the completeness of the patient database as well as the completeness of the drug profile for each patient during the first visit to the nursing home facility. Over-the-Counter (OTC) and "take-as-needed" (PRN) drugs were not considered in this analysis. The consultant/pharmacist reviewed and confirmed the patients' prescription regimen and then made recommendations to prescribers.

Five nursing homes in Cabarrus County utilized medical residents as part of the pharmacist-physician team. In these homes, recommendations were reviewed with ACCESS II and III Medical Directors. Subsequently, the pharmacist/consultant and medical directors met with attending physicians to discuss specific recommendations.

Based on those recommendations, the prescriber decided on one of three alternatives: (1) no change/recommendation rejected, (2) recommendation accepted, or (3) recommendation accepted with other changes. Consultant/pharmacists documented their process activities, including: which patients were reviewed, the type of recommendation made, whether or not the recommendations were accepted, and what drug therapy changes were made. Supplemental notes, records, and hard copies of the recommendation orders were maintained by participating pharmacist-physician pairs to verify the integrity of the databases and maintain consistency of data entry across nursing homes.

To assess cost impact, each specific drug recommendation was tracked and labeled as to whether or not it led to a *therapy change*, *discontinued drug* or *added drug* for each patient. For each drug change (addition or deletion), its cost impact was calculated by determining the average baseline drug cost per month and projecting these costs to the after period (one year). The baseline drug cost was determined by taking the average amount paid by Medicaid for a month's supply of each prescription identified by its unique drug name and dose (if available). The data source for determining costs was baseline Medicaid claims data for three months prior to the start of the intervention (i.e., November 1, 2001 to January 31, 2002) in the pilot nursing homes.

A payer perspective was used, recognizing the amount paid by Medicaid to pharmacies. While North Carolina Medicaid has a 6 prescription per patient per month benefit cap, many elderly patients had exceeded this cap under an exception procedure. Many patients without documented exemptions nevertheless received prescriptions but their drug claims (greater than 6) were paid directly by the nursing home. All such prescriptions were captured, and applied the average cost per prescription from non-exceptional drug claims.

Of the 13 pilot nursing homes, one home did not complete the intervention nor had data available by the end of the requested period, and was excluded from the results.

RESULTS

Baseline drug usage and costs (Table 1)

- At baseline, Medicaid nursing home patients used, on average, 6.1 prescriptions per month (median = 6, standard deviation = 3.3, range = 1-18).
- The cost of a single prescription drug used averaged $54.81 for a 30-day supply. The average cost per patient per month for prescription drugs was $336.68. The median cost per month was $269.19, indicating some outliers on the upper end when compared with the average. Baseline 30 days' supply costs ranged from $3.54 to $4,588 per patient.

Result of interventions

Analysis by patient (Table 2)

- Consultant/pharmacists reviewed 673 Medicaid patients in the assigned nursing homes. Across nursing homes, the number of patients reviewed ranged from 12 to 195.
- The pharmacist-physician team made some type of recommendation for change in drug therapy for 37.7% (254/673) of the patients reviewed. There was considerable variability across nursing homes. Patients with problems identified and recommendations made ranged from 5% to 100% across nursing homes. An additional 4 patients were prescribed drugs for a new indication independent of a specific recommendation from the consultant pharmacist. In all, 20 drugs were added to patients' regimens for new indications.

- A recommendation that resulted in a discontinued drug occurred in 94 (37%) of patient cases with identified drug therapy problems. Changed drugs (e.g, discontinue a current drug and add another in its place) occurred in an additional 60 (24%) of the patient cases. A result of some other type occurred in 40 (16%) of the patient cases. "No changes" (including "no action" or "not determined") occurred in 142 (56%) of the patient cases, and drugs were added in 18 (7%) patient cases. There was considerable variation across nursing homes.

Analysis by drug (Table 3)

- Of the 4,134 prescriptions reviewed, 408 (10%) had a recommendation for some type of change.
- There were 256 prescription changes to patients' drug therapy regimens. There were 408 consultant/pharmacist recommendations. Of these, 236 (58%) were acted upon (accepted or rejected) by the physician (20 other drugs were added for new indications). There were 124 (30%) recommendations to discontinue a drug, and another 69 (17%) were recommendations to change therapy by having a drug discontinued and another added. A result with another type of recommendation occurred in 43 (11%) cases.
- No change occurred in 172 (42%) of the prescriptions. Again, there was considerable variation across nursing homes.
- The drugs most frequently involved in drug discontinuation and change decisions were, in descending order of frequency, Prevacid, Prilosec, Celebrex, Zyprexa, and Norvasc. (Table 4)

Cost impact. (Tables 6, 7, and 8)

- The baseline costs for one month across all 12 nursing home sites that had complete data was $226,588 (Table 1) and the resultant costs after the reviews was $217,143. This was a 4.2% savings (or $9,445 less). Assuming the benefits persist for one year, an annualized gross annual savings of $113,335 would be achieved within the pilot nursing homes over one year.
- Subtracting the $8,700 cost for pharmacist consultants as well as for physician reviewers, the first year annual savings to costs ratio is estimated at 13 to 1.
- The average drug cost impact per patient reviewed was $14.03 ($9,445 saved/673 patients reviewed) for the first month. This cost difference was statistically significant at $p = 0.0001$ (paired T test results).
- The cost impact was also computed on a per prescription basis. As a result of the reviews, there were 124 prescriptions discontinued. There were also 69 prescriptions for which one drug was replaced with another. (Table 3) The average savings from a prescription discontinuation was $57.68. The average savings for the replacement of one drug with another was $33.23 for a month's supply.

DISCUSSION

Several points were notable in this review. First, there was considerable variation across nursing home settings in terms of the number and costs of prescriptions consumed by elderly residents. There was also considerable variation in the number of reviews conducted by consultants/pharmacists. In some cases, all of the patients in a home were reviewed, while in others (five nursing homes in Cabarrus County), only targeted patients (i.e., those flagged with possible drug therapy problems) were reviewed.

Findings showing that nursing home patients used a high number of drugs at high cost to Medicaid are consistent with what is generally known about elderly nursing home patients' drug use patterns nationally. The finding that patients used a median of 6 prescriptions per month indicates that most likely half of them must obtain drugs through an exceptional use procedure or have their medications covered directly by the nursing home itself.

Although the original intent of the pilot study was to focus only on patients previously identified as having exceptional drug therapy regimens as targets for review, pharmacist-physician reviewers chose to review all patients in the home at the majority of sites. This is one reason for the variability seen across nursing homes in the percentage of patients receiving change recommendations by the team. Across all settings, the pharmacist-physician team made drug change recommendations for 38% of all patients reviewed.

It was noteworthy that over half of the therapy recommendations made were acted upon within a relatively short time frame. Most of these involved a recommendation to discontinue a drug (30%) or to change therapy from one drug to another (17%). These findings, even if preliminary, support the conclusions of other researchers that drug therapy received by the elderly could be improved from a qualitative as well as a cost-effectiveness standpoint.

Additionally, these findings support the role of pharmacists working collaboratively with physicians in this activity. A recent Cochrane database review indicated that clinical pharmacists, working collaboratively with physicians, can be effective in addressing drug related problems among patients.[1] These studies imply that interventions of the type conducted in this pilot study have the potential for additional savings from reduced hospitalizations and other health care system costs.

It was not determined why the pilot program was more successful in some of the nursing homes than in others, especially recognizing that all have, by regulatory requirement, review and quality assurance systems in place as outlined in OBRA 87 regulations and updates. Some possibilities may be that, first, existing consultants typically audit for safety, compliance, quality, and legalities or liabilities/risk exposure but give less emphasis to cost effectiveness. In this pilot, however, a special emphasis was given to the potential for cost savings. Secondly, perhaps "another pair of eyes" provided by the pharmacist-physician team detected more problems or more opportunities for drug cost savings. Third, it may be that problems/opportunities were previously detected or noted in records by consulting pharmacists, but simply not acted upon because of the lack of follow-up.

LIMITATIONS

This preliminary report was limited to an assessment of the impact of the pharmacist consultant program after only one month of operation. Changes from baseline using documented recommendations made and followed were described, cost impact using baseline drug costs derived from claims data were assessed.

There are several limitations. First, assessments of changes were based only on the first round of interventions (i.e., one month). Over time, one might expect the pharmacist-physician team to become more familiar with, and more time efficient at these reviews. Documentation of reviews and interventions by pharmacist-physician consultant teams was, at times, incomplete. This assessment of cost impact to those interventions involving *drug discontinuations, changes* and *adds* is therefore limited. We are confident that we captured all recommendations made and followed, and that the cost savings realized were reasonable estimates. In a few cases, estimates of the cost savings impact were made because of incomplete data. For example, when a drug change was noted but details about the strength or daily dosage was missing, usual dosage criteria for the elderly were applied and a 30 days' supply in estimating the cost impact was assumed. Only the cost billed to Medicaid was considered. Any rebates received by Medicaid were not considered. For a few prescriptions (less than 10%), cost data was missing and was estimated using Medicaid reimbursement formulae.

The cost saving observed was annualized. In general, nursing home residents taking chronic medications do not frequently undergo drug regimen changes, and any economic benefits of a change in therapy would accrue over time. It is possible the drug regimens may change again sooner than one year or, conversely, the benefits may accrue for longer than one year. As to program costs, only the labor cost component of the intervention was considered. Startup costs and other indirect costs were not included.

The analysis did not include a formal assessment of the quality of drug therapy changes, nor of the impact on quality of health care. Since the screening criteria included drugs considered to be inappropriate for use in the elderly, as well as polypharmacy, the working assumption was that the "other pairs of eyes" examining patients' drug profiles would result in at least no change in quality of care, and would probably result in an improvement. Due to the short time period involved, the cost impact of changes in utilization of such services as emergency room visits or hospitalizations possibly related to drug therapy changes were not examined.

Finally, this preliminary assessment did not include a comparison group assessment involving nursing homes not involved in the demonstration. It is possible that the changes identified by pharmacists and physicians would have eventually been noted independently of this intervention. A planned follow-up and final assessment will address these issues more fully.

CONCLUSIONS

- Preliminary findings from this demonstration indicate that drug usage is high, and there exists a potential for reducing drug costs while maintaining or improving drug therapy for elderly nursing home residents in North Carolina. The frequency of drug

related problems among Medicaid patients varies considerably across nursing home settings.

- A program of review of Medicaid nursing home patients by pharmacist- physician consultants was cost-beneficial. Based on this preliminary analysis, the economic benefits appear to outweigh the investment of implementing this program by a ratio of 13 to 1 when monthly savings are annualized.
- Assuming that the drug use experiences of other Medicaid nursing home patients is similar to those in these homes, there is a need for a *different approach* to address drug therapy problems and save prescription drug costs among NC nursing home Medicaid patients.
- One viable approach involves having pharmacist-physician review teams make periodic visits to targeted nursing homes to perform both quality and cost of drug therapy reviews. Targeting patients in advance for specific review would appear to be a time and cost-efficient strategy.

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Table 1: Baseline drug costs of Medicaid recipients: analysis by patient

Baseline Drug Costs of Medicaid Recipients (Analysis by Patient)											
Nursing Home	Total Medicaid Residents Reviewed	Current Number of Prescriptions (Rx)	Number of Rx/Resident			Range of Rx/Resident		Estimated 30 Day Patient Drug Cost* ($)			
			Mean	Median	Standard Deviation	Min	Max	Baseline Total	Mean	Median	Standard Deviation
All Settings	673	4,134	6.1	6	3.3	1	18	$226,588	$337	$269	$353
Baptist	24	134	5.6	6	2.8	1	10	7,986	333	323	175
Britthaven	81	400	4.9	5	2.7	1	12	27,896	344	238	527
ClevelandPines	58	367	6.3	6	3.3	1	17	18,858	325	247	326
Huntersville	195	1,052	5.4	5	2.9	1	15	56,770	291	226	408
MaryGran	71	496	7.0	7	3.2	1	14	24,651	347	329	201
Southwood	29	234	8.1	7	3.8	2	18	11,699	403	350	228
WhiteOak	125	703	5.6	5	3.2	1	13	36,847	295	210	295
Avante	25	194	7.8	7	3.6	2	17	10,582	423	350	266
BrianCenter	15	122	8.1	7	3.5	2	16	6,510	434	419	191
FiveOaks	23	213	9.3	9	3.4	3	17	12,059	524	470	290
Transitional	15	144	9.6	10	3.1	3	15	7,602	507	528	165
Universal	12	75	6.3	6	3.4	2	14	5,128	427	403	234
Average Across Sites**	56	345	7	7	3	2	15	18,882	388	341	276

** Drug costs represent amount paid by Medicaid to suppliers. It includes pharmacy dispensing fees but excludes manufacturer rebates.*
*** Note this row determines averages using the # NH's as the denominator, whereas "all settings" uses averages across all patients. Same distinction exists for other tables.*

Table 2: Review activities and drug therapy recommendations made by pharmacists/physicians: analysis by patient

Review Activities and Drug Therapy Recommendations Made by RPh/MD (Analysis by Patient)															
	Total Medicaid Residents Reviewed	**Patients with Problem Identified (Recommendation Issued)**													
		All Patients with Problems Identified in their Drug Regimen		All Patients with a Result in the following categories****											
Nursing Home	Number	Number	% of pts review'd	Any Result: *(D/C, Therapy Change, Other or Add Drug) [N, % of all pts with problems]*		*Result: D/C [N, % of all pts with problems]*		*Result: Therapy Change* [N, % of all pts with problems]*		*Result: Other** [N, % of all pts with problems]*		*Result: Add Drug*** [N, % of all pts with problems]*		No Change	
All Settings	673	254	38%	163	64%	94	37%	60	24%	40	16%	18	7%	142	56%
Baptist	24	11	46	9	82	2	18	5	45	2	18	0	0	5	45
Britthaven	81	4	5	4	100	2	50	0	0	2	50	0	0	0	0
ClevelandPines	58	4	7	4	100	3	75	0	0	1	25	0	0	0	0
Huntersville	195	54	28	0	0	0	0	0	0	0	0	0	0	54	100
MaryGran	71	40	56	30	75	10	25	21	53	4	10	0	0	15	38
Southwood	29	22	76	14	64	9	41	1	7	6	27	0	0	18	82
WhiteOak	125	44	35	31	70	15	34	11	25	9	20	0	0	19	43
Avante	25	22	88	20	91	12	55	3	14	5	23	6	27	12	55
BrianCenter	15	9	60	9	100	7	78	6	67	3	33	0	0	0	0
FiveOaks	23	19	83	18	95	14	74	6	32	2	11	4	21	9	47
Transitional	15	13	87	12	92	10	77	4	31	3	23	4	31	7	54
Universal	12	12	100	12	100	10	83	3	25	3	25	4	33	3	25
Average Across Sites	56	21	56	14	81	8	51	5	25	3	22	2	9	12	41

* *A "Therapy Change" is the substitution of one drug entity for another.*

** *"Other" category results include: "Drug added" (as the result of a pharmacist/consultant recommendation), "Dosage Interval Changed", "Dose Changed", "Drug Decreased", or "Admin route change"*

*** *An "Add Drug" is one that is included as a result of treating a new indication and not as a result of a problem identified by the consultant/pharmacist. Therefore, these are not included in the baseline of Rx with problems identified.*

**** *Since there is often more than one Rx per patient, it is possible for any particular patient to have results in more than one category. Therefore, the totals will not equal 100.*

Table 3: Drug therapy recommendations made: analysis by Rx.

Drug Therapy Recommendations Made (Analysis by Rx)															
		RX with Problem Identified (Recommendation Issued)													
		All Rx with Problems Identified		All Rx with a Result in the following categories											
Nursing Home	Total Prescriptions Reviewed	Number	% of Rx review'd	Any Result: *(D/C, Therapy Change, Other or Add Drug) [N, % of all Rx with problems]*		Result: D/C *[N, % of all Rx with problems]*		Result: Therapy Change* *[N,% of all Rx with problems]*		Result: Other** *[N,% of all Rx with problems]*		Result: Add Drug*** *[N,% of all Rx with problems]*		No Change *[N, % of all Rx with problems]*	
All Settings	4,134	408	10%	256	63%	124	30%	69	17%	43	11%	20	8%	172	42%
Baptist	134	16	12	9	56	2	13	5	31	2	13	0	0	7	44
Britthaven	400	4	1	4	100	2	50	0	0	2	50	0	0	0	0
ClevelandPines	367	4	1	4	100	3	75	0	0	1	25	0	0	0	0
Huntersville	1,052	56	5	0	0	0	0	0	0	0	0	0	0	56	100
MaryGran	496	59	12	40	68	12	20	24	41	4	7	0	0	19	32
Southwood	234	43	18	19	44	12	28	1	2	6	14	0	0	24	56
WhiteOak	703	59	8	39	66	17	29	12	20	10	17	0	0	20	34
Avante	194	43	22	32	74	17	40	3	7	6	14	6	19	17	40
BrianCenter	122	22	18	22	100	10	45	9	41	3	14	0	0	0	0
FiveOaks	213	42	20	33	79	21	50	6	14	2	5	4	12	13	31
Transitional	144	38	26	29	76	15	39	6	16	4	11	4	14	13	34
Universal	75	22	29	25	114	13	59	3	14	3	14	6	24	3	14
Average Across Sites	345	34	14	21	73	10	37	6	16	4	15	2	6	14	32

* *A "Therapy Change" is the substitution of one drug entity for another.*

** *"Other" category results include: "Drug added" (as the result of a pharmacist/consultant recommendation), "Dosage Interval Changed", "Dose Changed", "Drug Decreased", or "Admin route change"*

*** *An "Add Drug" is one that is included as a result of treating a new indication and not as a result of a problem identified by the consultant/pharmacist. Therefore, these are not included in the baseline of Rx with problems identified.*
Example calculation: Any result=256=124+69+43+20. Any recommendation=408=124+69+43+172

Table 4: Drugs most commonly involved in therapy change recommendations

Top Prescriptions (by Rx Frequency)		
Drug First Name	Number of Prescriptions Encountered	Number of Recommendations Made
FUROSEMIDE	186	2
PREVACID	111	88
NORVASC	107	9
REMERON	99	3
ZOLOFT	96	2
POTASSIUM	90	1
COUMADIN	88	6
RANITIDINE	83	6
ARICEPT	72	0
ZYPREXA	71	11
RISPERDAL	69	7
NOVOLIN	68	2
LANOXIN	59	7
SYNTHROID	57	0
METOPROLOL	48	1
PAXIL	47	2
NEURONTIN	46	5
CELEBREX	45	13
DILANTIN	45	0
ISOSORBIDE	45	2

Top Prescriptions (by Frequency of Recommendations)		
Drug First Name	Number of Prescriptions Encountered	Number of Recommendations Made
PREVACID	111	88
PRILOSEC	20	18
CELEBREX	45	13
ZYPREXA	71	11
NORVASC	107	9
ACTOS	13	8
RISPERDAL	69	7
LANOXIN	59	7
PLAVIX	39	7
MEGESTROL	15	7
COUMADIN	88	6
RANITIDINE	83	6
LIPITOR	25	6
CATAPRES-TTS	17	6
ASPIRIN	7	6
NEURONTIN	46	5
LORAZEPAM	37	5
FOSAMAX	32	5
GLUCOTROL	26	5
ACCUPRIL	15	5

Table 5: Qualitative analysis of results of drug change recommendations—by type of action (*unit of analysis: pt drug-specific results)*

Qualitative Analysis of Prescription Specific Results					
Result Category	**Category Description**	**Total Results * (#)**	**Total Results (%)**	**Range Across Nursing Home Sites (%)**	
		All Sites	All Sites	Min	Max
All Results		428	100%	0%	98%
Drug Discontinued	The drug is removed from the regimen	124	29	0	46
Drug Changed	A therapeutic substitution	69	16	0	41
Drug Added	A direct result of a PharmD consultant recommendation	3	1	0	25
Add Drug/New Drug Prescribed	An addition not a direct result of a recommendation, but as a general result of a medical resident or MD carefully reviewing patient's overall regimen. Often for an untreated indication.	20	5	0	21
Dosage Interval Changed	The time at which the drug is administered is changed	1	0	0	0
Dose Changed	Usually, a dosage increase	10	2	0	7
Drug Decreased	Reduction in dosage	21	5	0	25
Administration Route, Technique or Compliance altered	Change in any of these characteristics	6	1	0	25
No Action/No Change	The recommendation is not relayed to the physician/no change to the regimen post-physician review	138	32	0	98
Not Determined	No response from the physician	34	8	0	21
Other	Any result not already categorized	2	0	0	5

** This number exceeds number of recommendations, due to the inclusion of Add Drugs in this list.*

Table 6: Projected cost savings of drug therapy changes -- analysis by patient

Nursing Home	Number of Residents with Recommendation	Number of Residents with at Least One Result (Other than No Change, No Action or Not Determined)	Baseline Rx Cost* (Entire Regimen, per Resident Reviewed, in Dollars)			Estimated Cost After Recommendations (Entire Regimen, per Resident Reviewed, in Dollars)			Estimated Cost Savings/Resident Reviewed (Entire Regimen, All Residents Reviewed, in Dollars)			
			Mean	Median	St. Dev.	Mean	Median	St. Dev.	Mean	Median**	St. Dev.	% of baseline costs (Mean)
All Settings	254	163	336	269	354	322	257	349	14	0	41	4.2
Baptist	11	9	333	323	175	312	322	157	20	0	43	6.1
Britthaven	4	4	344	238	527	343	238	527	1	0	8	0.4
Cleveland Pines	4	4	325	247	326	322	237	326	3	0	16	1.1
Huntersville	54	0	291	226	408	291	226	408	0	0	0	0.0
MaryGran	40	30	347	329	201	326	308	191	21	0	37	6.1
Southwood	22	14	403	350	228	384	315	219	20	0	40	4.9
WhiteOak	44	31	294	210	296	285	210	292	9	0	26	3.1
Avante	22	20	423	350	266	370	288	283	54	12	81	12.6
Brian Center	9	9	434	419	191	368	419	187	66	40	75	15.2
FiveOaks	19	18	524	470	290	458	407	259	67	56	78	12.7
Transitional	14	12	507	529	165	458	485	137	49	44	81	9.6
Universal	12	12	418	403	244	346	274	243	72	44	95	17.1
Average Across Sites	21	14	387	341	276	355	311	269	32	16	48	7.4

** Drugs added after problems were identified were not included in the costs or estimated savings, but are included in the result counts. Total for added Drugs across sites = $193 (n=20).*

*** Recall, a majority of the 673 patients reviewed had no drug changes, so it is reasonable to expect that the median is zero.*

Table 7: Projected annual cost savings of drug therapy changes (Analysis by Rx)

Projected Annual Cost Savings of Drug Therapy Changes (Analysis by Rx)								
Nursing Home	Results: D/C Rx	Results: Rx Therapy Change	Savings ($) from D/C *	Savings ($) from Therapy Change**	Gross Benefit (Cost)/Month ***	Gross Benefit (Cost)/Year	Consultant/ reviewer costs	Net Benefit (Cost) per Nursing Home / Year
All settings	124	69	$ 7,152	$ 2,293	$ 9,445	113,335	(8,700)	$ 104,635
Baptist	2	5	119	368	487	5,842	(460)	5,382
Britthaven	2	0	102	0	102	1,230	(320)	910
Cleveland Pines	3	0	201	0	201	2,407	(440)	1,967
Huntersville	0	0	0	0	0	0	(1,840)	(1,840)
Mary Gran	12	24	626	871	1,497	17,969	(520)	17,449
Southwood	12	1	548	29	577	6,926	(160)	6,766
White Oak	17	12	597	530	1,127	13,521	(1,060)	12,461
Avante	17	3	1,211	128	1,339	16,067	(780)	15,287
Brian Center	10	9	597	394	991	11,890	(780)	11,110
Five Oaks	21	6	1,373	161	1,534	18,409	(780)	17,629
Transitional	15	6	852	(120)	732	8,786	(780)	8,006
Universal	13	3	925	(67)	858	10,299	(780)	9,519
Averages across sites	10	6	596	191	787	9,446	(725)	8,721

* *Assuming recommendations were followed and drug was eliminated or added.*

** *Therapy change excludes added drugs not pursuant to a recommendation. Total cost for Add Drugs across sites was $192 (n=20).*

*** *Sum of savings from discontinuation (D/C) and from Therapy Change.*

Table 8: Program net cost impact: preliminary analysis

Program Net Cost Impact (Preliminary Analysis)									
Nursing Home	Patients Reviewed	Prescriptions Reviewed	Number of Problems Identified (Recommendations Made)***	Pharmacist Reviewer Labor (Hours)	Pharmacist Reviewer Labor Cost ($)	Estimated Physician Reviewer Labor Cost per Site ($)	Total Reviewer Cost ($) *(from Table 7)*	Net Benefit (Cost) per Nursing Home / Year *(from Table 7)*	Net Benefit (Cost) per Patient Reviewed /Year
All settings	673	4,134	428	165	$ 6,200	$ 2,500	$8,700	$ 104,635	$ 155
Baptist	24	134	16	12	460	0	460	5,382	224
Britthaven	81	400	4	8	320	0	320	910	11
Cleveland Pines	58	367	4	11	440	0	440	1,967	34
Huntersville	195	1,052	56	46	1,840	0	1,840	(1,840)	(9)
Mary Gran	71	496	59	13	520	0	520	17,449	246
Southwood	29	234	43	4	160	0	160	6,766	233
White Oak	125	703	59	27	1,060	0	1,060	12,461	100
Avante	25	194	49	7	280	500	780	15,287	611
Brian Center	15	122	22	7	280	500	780	11,110	741
Five Oaks	23	213	46	7	280	500	780	17,629	766
Transitional	15	144	42	7	280	500	780	8,006	534
Universal	12	75	28	7	280	500	780	9,519	793
Averages across sites	56	345	36	13	517	208	725	8,721	357

* Assumes $40/hour pharmacist consultant costs
** Attending physician response time in all sites was not factored nor paid for since this was determined to be part of their normal duties. Physician Consultation time in the five Cabarrus sites, however, was included.
*** Included the 20 Added Drugs.

APPENDIX D: PUBLICATION OF EVALUATION #1[71]

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A Pharmacy Management Intervention for Optimizing Drug Therapy for Nursing Home Patients

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ABSTRACT

Background: A drug therapy management service was designed to reduce polypharmacy among Medicaid recipients. This service selectively focused on patients who were high users of prescription drugs and had potential drug therapy problems (PDTPs).

Objectives: This article reports the results of the first phase of the North Carolina Polypharmacy Initiative. The goals of this study were to determine: (1) the frequency with which recommendations were made by pharmacists in response to targeted profile alerts aimed at high-risk patients, (2) the frequency and type of drug therapy changes, and (3) the impact on drug-related quality and costs.

Methods: A before–after design was used. Nursing home patient profiles with PDTP alerts for specific drugs and drug categories were provided to consultant pharmacists. Targeted patients had received ≥18 prescription fills within 90 days. Pharmacists were compensated for performing and documenting targeted drug regimen reviews. Interventions of pharmacists and results after physician consultation are described, and cost impacts of changes in drug therapy are reported. Monetary results are shown in year-2002 US dollars.

Results: Prescription profiles were generated from Medicaid claims data and sent to consultant pharmacists for 9208 patients in 253 nursing homes. Pharmacists returned 7548 (82%) of all profiles sent to them. After excluding 1204 patients (13%) who were discharged or deceased, 6344 patients (69%) remained for analysis. At baseline, patients used a mean (SD) of 9.52 prescriptions per month, costing the North Carolina Medicaid program a mean (SD) of $502.96 (309.70). A mean of 1.58 recommendations were offered to prescribers. After physician consultation, ≥1 recommendation was implemented for 72% of patients with a change recommendation, 68% of whom experienced a switch to a lower-cost drug. Drug cost savings were a mean of $30.33/patient per month. Cost savings from 1 month alone covered the compensation paid to pharmacists for consultation efforts.

Conclusions: This supplemental program of medication reviews for targeted nursing home patients resulted in a reduction of polypharmacy and was beneficial based solely on drug cost savings. (*Am J Geriatr Pharmacother.* 2004;2:248–256) Copyright © 2004 Excerpta Medica, Inc.

Key words: nursing homes, pharmaceutical care, medication therapy management, drug use review, polypharmacy.

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INTRODUCTION

Older persons (ie, those aged ≥65 years) are especially vulnerable to drug-related problems. Drug-related morbidity and mortality have been identified as major problems in these patients; the 2 major causes are therapeutic failure (ie, inadequate drug therapy) and adverse drug reactions.[1–4] A study of 1492 nursing homes in 5 states showed that 33% of residents received ≥1 potentially inappropriate drug.[5] Two studies have linked hospital readmissions in older patients to drug-related problems in 18% to 28% of the cases.[6,7] Compounding the problem is high prescription drug use; older patients are at greater risk for experiencing suboptimal drug therapy (ie, polypharmacy, inappropriate use, or underutilization), which can lead to therapeutic failure or adverse drug reactions.[8–10] The risk of adverse drug reactions increases with the number of regularly scheduled medications.[11]

National attention has focused on the problem of rapidly rising costs of medications. Private insurers and state Medicaid programs have faced a double-digit rise in prescription drug costs per insured person over the past decade.[12–14] Within North Carolina, Medicaid costs approximately $7.4 billion per year.[15] The prescription drug component of North Carolina Medicaid costs about $1.2 billion per year,[16] rising at a rate of ~17% annually in recent years.[17] Of particular interest, older patients account for only 11% of enrollees[18] but 32% of all prescription drug costs.[12] If unnecessary medications are being prescribed, a reduction in their use could simultaneously enhance the quality of care while reducing costs.

We believe that initiatives targeting drug use, whether in the private or public sector, can be placed into 2 categories. The first involves efforts to optimize drug use, including drug profile review and consultations, clinical pharmacy management initiatives, and medication therapy management initiatives. The second involves efforts to optimize the choice of drug, including promotion of generic drugs, formularies or prior authorization policies, use of preferred drugs, and tiered copayment strategies. Both categories of initiatives can be incorporated into a single review to achieve mutual advantage.

Medication therapy management programs, sometimes referred to as cognitive services or pharmaceutical care services, have as their goal the improvement of patient outcomes by identifying and resolving drug-related problems.[15,19,20] Such programs have been developed and implemented for Medicaid medical insurance programs in Mississippi, Missouri, Iowa, Wisconsin, and Washington.[21–23] Some type of collaboration between pharmacists and physicians characterizes most of these programs. A medication therapy management component is contained within the recently passed Medicare Prescription Drug Improvement and Modernization Act of 2003, and is already part of some state senior care indigent prescription drug programs.[24]

Among residents of long-term care facilities, potential drug therapy problems (PDTPs) are magnified because of the typical resident's more frail state of health and greater use of prescription drugs. Several studies have noted the prevalence of drug-related problems in nursing home settings and that pharmacists are effective at reducing the number of drug-related problems.[25–27] Beginning in the 1970s, federal regulations required monthly drug regimen reviews to be conducted by consultant pharmacists.[28] Pharmacists are obliged to identify and report any irregularities and recommendations for action to the attending physician and director of nursing. Although these reviews have resulted in improved care since they were first mandated,[29] it would appear that there is further room for improvement.[5] Among the present-day concerns are that these regulations do not explicitly compensate reviewers for such services, nor do they explicitly focus on the cost-effectiveness of pharmaceuticals received by patients.

Given this background, a drug therapy management service was designed to reduce polypharmacy among Medicaid recipients. This service selectively focused on patients who were high users of prescription drugs and had potential PDTPs. The goals of the current study were to determine: (1) the frequency with which recommendations were made by pharmacists in response to targeted profile alerts aimed at high-risk patients, (2) the frequency and type of drug therapy changes, and (3) the impact on drug-related quality and costs.

MATERIALS AND METHODS

The North Carolina Polypharmacy Initiative was a collaborative demonstration program by AccessCare, Inc. (Morrisville, North Carolina), a component organization of the Community Care of North Carolina (CCNC) program. CCNC operates through collaborative agreements with local community organizations and physician group practices that work together to enhance the quality and to control costs of care for Medicaid recipients. AccessCare is one of the largest provider networks within CCNC, representing ~1500 physicians in 200 group practices, 14 counties, and 20 communities throughout the state at the time of the

study. The project involved the following statewide partners: the University of North Carolina School of Pharmacy, the North Carolina Long-Term Care Pharmacy Alliance, the North Carolina Medical Directors Association, and the North Carolina Health Care Facilities Association. This study received approval from the institutional review board at the University of North Carolina at Chapel Hill.

The 110 consulting pharmacists who participated in the study are members of the North Carolina Long-Term Care Pharmacy Alliance, a group that is broadly representative of pharmacists serving nursing homes throughout the state. The pharmacists were familiar with most of the patients in the facility and had working relationships with physicians providing care at each site, many of whom were members of the North Carolina Medical Directors Association. The nursing facilities participating in the study were members of the North Carolina Health Care Facilities Association, which encouraged participation by endorsing the program. A total of 253 nursing homes served by a participating consultant pharmacy organization took part in the study. All residents of the participating facilities who had ≥18 prescription fills in the previous 90-day period were enrolled. Even though nursing home residents take a mean of 6.69 regularly scheduled medications,[30] this level was selected because it yielded a manageable number of residents that could adequately be reviewed by consultants in the study period. The intended focus was on patients at highest risk for medication-related problems, or who had a potential for cost savings. In addition, information was collected regarding certain demographic factors (eg, sex, race, age).

This article reports the results of the first phase of the initiative.

Intervention Activities

The intervention consisted of a systematic pharmacist drug regimen review and consultation with prescribing physicians that was an additional supplement to the existing requisite Omnibus Budget Reconciliation Act of 1987 (OBRA 1987)[31] consultation programs in nursing homes. The overall goal of the intervention was to improve the quality of pharmaceutical care available to patients of nursing facilities while simultaneously decreasing aggregate drug costs. To aid in this intervention, AccessCare collaborated with the North Carolina Long-Term Care Pharmacy Alliance to develop an action plan and a proprietary Toolkit for consulting pharmacists. The Toolkit contained instructions for documenting consultations and explained the screening criteria used to select (flag) drugs for attention (see next subsection). Consultant pharmacists were introduced to the project during two 1-hour group meetings and 1 hour-long conference call in September and October 2002. Pharmacists were provided with the Toolkit and received individual training from the lead consultants in their organizations. Each consultant pharmacist was also provided with printed drug profiles of screened patients that contained computer-generated prompts for selected drugs and classes of drugs. The Toolkit and patient profile were developed to ensure consistency of interventions.

Because many different pharmacists were involved in this project, these 2 documents (Toolkit and patient profile) provided a guide and standard procedure for documenting interventions. The Toolkit criteria were used to prompt the pharmacist to review specific drug(s) or classes of drugs that had the potential to achieve cost savings as well as increase quality of care. The first criterion was receipt of a drug generally considered to be inappropriate for use in the elderly (ie, Beers drug list).[3] A second criterion was receipt of a drug on the CCNC Prescription Advantage List (PAL), which encourages substitution of less expensive drugs within a therapeutic class. For each of the 10 drug classes represented on the list, certain medications offered potential cost savings to the Medicaid program (PAL-1), whereas others either offered no clear cost advantage (PAL-2) or would incur significant costs (PAL-3). The third criterion was receipt of a drug on a list of clinical initiatives. This list was developed by the consultants participating in this project, and included 16 drugs and/or drug classes that have the potential for quality improvement and cost savings. The list was derived from North Carolina Medicaid's top 100 drugs by expenditures for fiscal year 2001, based on a data run of Medicaid claims data. Examples include the review of proton pump inhibitors for appropriate length of therapy and possible switch to a histamine$_2$-receptor blocker, and the evaluation of residents taking chronic sleep aids for a possible drug holiday or discontinuation. We also noted on profiles if there were therapeutic class duplications. Pharmacists conducted these targeted reviews during regularly scheduled visits to the home and employed their usual methods of communicating with physicians (eg, facsimile, telephone, written notes in the chart) to make recommendations as well as obtain results. Consultant pharmacist reviews occurred between October 2002 and March 2003. Pharmacists were compensated US $12.50 for

each comprehensive profile review for which results were clearly documented on the forms provided (ie, patient profile). Recommending changes in drug therapy was not required for compensation, only a complete review of a patient's drug regimen. Consultant pharmacists were asked to record both the result of the review (ie, the recommendation) and the result of the consultation with the prescribing physician (ie, the outcome) on a documentation form. Only one comprehensive review per patient was documented and compensated during this phase.

Statistical Analysis and Cost-Minimization/ Avoidance Analyses

Data Sources and Analysis Procedures

The data source for this study was pharmacist intervention documents submitted for payment. A 2-stage analysis was conducted. First, pharmacist-reported activities were analyzed to identify and resolve PDTPs using a before–after design with subjects serving as their own controls. The number of recommendations offered to prescribers was tabulated, as well as the percentage of those resulting in a drug therapy change after consultation with the prescribers. We measured before–after changes in the following: (1) the number of computer-flagged drug alerts, (2) the number of patients with drug therapy changes, and (3) the magnitude of these changes in terms of number of dispensed prescriptions and their costs (in year-2002 US dollars). We categorized patients by PDTP type (ie, Beers drug list, PAL-2 or PAL-3 drugs, and the clinical initiatives list of 16 prespecified drug/drug classes).

A cost-minimization analysis was used to examine the economic consequences of pharmacist activities, in terms of changes in drug fills and overall drug cost (before and after the intervention) and projected changes over the next 12 months. When a change in drug therapy occurred, the amount paid by Medicaid for the drug originally dispensed was compared with the amount that would be paid by Medicaid for the changed drug. The amount likely to have been paid was calculated by first comparing the changed drug with a drug of an identical name, strength, and dosage form in the claims database. It was possible to find a matching drug for >95% of all drugs with reported changes. In the remaining cases, the likely prescription cost was estimated by determining the average wholesale price per dosage unit minus 10% (the standard Medicaid reimbursement fee in North Carolina at the time of analysis) multiplied by the likely or reported dosage units the patient would have received in 1 month, plus a dispensing fee ($4.00 for brand name and $5.60 for generic drugs).[32] The future impact of drug therapy changes over time was projected using an intent-to-treat approach, with *intent* defined as a completed profile review.

After projecting the probable cost savings of the drug therapy changes using the method described here, this cost impact was annualized based on 3 major assumptions: (1) most drugs subject to change would be used to treat chronic conditions (this assumption is based on drug data returned by pharmacists); (2) savings per patient would dissipate over time at the rate of 15% per year until discharge due to usual changes in therapy; and (3) patients would leave nursing homes due to death or discharge at a rate of 3% per month (ie, 35% per year, the existing attrition rate of residents in North Carolina nursing homes as determined from claims analysis). Finally, the program costs of generating the profiles with PDTPs, and the cost of compensating the pharmacists $12.50 for each comprehensive profile review, were calculated. Because this analysis was done from the payer's perspective, the time required to train pharmacists or to allow physicians to act on the recommendation was not included. However, overhead payments to pharmacies for administrative duties were taken into account. Sensitivity analyses were also conducted to test the robustness of the findings.

To test statistical significance of any changes in drug use, the difference of proportions test for nominal level measures and the paired Student t test for interval level data were used. Findings were verified using equivalent nonparametric statistics (eg, Wilcoxon signed rank test). Statistical testing was performed using SAS Statistical Software, version 8.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Prescription profiles were generated from Medicaid claims data and sent to consultant pharmacists for 9208 patients in 253 nursing homes. Pharmacists returned 7548 (82%) of all profiles sent to them. After excluding 1204 patients (13%) who were discharged or deceased before the initial reviews, 6344 patients (69%) with flagged profile reviews remained for analysis. Of these, most (75%) were female and white (69%). The mean (SD) age was 76.8 (2.5) years (median, 79 years).

During the 3 months before intervention, these 6344 patients (all previously screened for having received ≥18 prescription fills) received a mean (SD) of 9.52 (3.29) prescriptions per month (median, 9.00). The upper 25th percentile of them had received ≥11 prescriptions per month, and the lower 25th percentile had received

≤7 prescriptions per month. The mean (SD) amount paid per month by North Carolina Medicaid for these prescriptions at baseline was $502.96 (309.70) per patient (median, $439.95). The 25th percentile was $314 and the 75th percentile was $612.

Using the patient profiles for review, pharmacists made a total of 6520 flagged drug therapy recommendations for 4136 patients, or a mean of 1.58 recommendations per patient with recommendations. Physicians concurred with 58% (3784/6520) of the pharmacist recommendations to change drug therapy. At least one recommendation for change in drug therapy was accepted and followed for 72% (2990/4136) of patients with such recommendations. Among patients with changes in drug therapy, 61% (1815/2990) had ≥1 change to a lower-cost drug.

Table I outlines the type of problems identified at baseline and the change after the intervention. As shown, for clinical initiatives and PAL-2 or PAL-3 flags, pharmacists made recommendations for change in approximately half the patients with PDTP alerts (51% [2470/4837], 49% [1625/3290], and 51% [685/1334], respectively), and the recommendations were subsequently endorsed by physicians and implemented approximately two thirds of the time (67% [1658/2470], 64% [1032/1625], and 67% [460/685], respectively). Recommendations were made and followed less often for Beers drugs. Among patients with Beers drug alerts, 20% of them (567/2814) were considered to have a PDTP resulting in a recommendation for change, and about half of these patients (54% [307/567]) had a resulting drug therapy change.

Next, the statistical significance of changes in the rate of PDTP occurrence before and after pharmacist intervention was examined. Presence or absence of a drug therapy change was used as a proxy of whether the problem remained or was resolved. Following pharmacist recommendations, there was a statistically significant reduction in PDTP occurrence ($P < 0.001$) for all 4 alert categories. Large sample sizes contributed to the levels of statistical significance observed.

Table II shows the number of drug therapy changes and the resultant cost savings for all 6344 patients receiving profile reviews. Although Beers alerts garnered a mean (SD) of 0.12 (0.34) Beers drug changes per patient with an alert, clinical initiative alerts had a mean (SD) of 0.63 (0.73) clinical initiative changes per patient as a result of pharmacist recommendations. Subsequently, the mean (SD) drug cost savings for Beers alerts and clinical initiative alerts were $2.49 (12.84) and $65.04 (63.51) per patient with those alerts, respectively. PAL-2 and PAL-3 list alerts resulted in a mean (SD) of 0.35 (0.55) and 0.36 (0.50) drug changes per patient, respectively, and mean (SD) savings of $18.04 (40.78) and $18.94 (38.89) per patient, respectively. Considering all patients and all prescriptions, the first phase of the initiative resulted in a mean 0.21 reduction in the number of prescriptions per month and a mean reduction of $30.33/patient per month in drug regimen costs for the 6344 nursing home residents receiving pharmacist profile reviews (**Table III**). In all cases, the differences were statistically significant (all, $P < 0.001$), again due in part to large sample sizes. Test results were validated using the

Table I. Drug therapy changes as a result of interventions (N = 6344).

PDTP Alert Type*	PDTP Alert and Recommendation for Change, No. (%) of Patients†	After Intervention: Patients with Changed Drug Therapy, No. (%) of Patients‡	After Intervention: Patients with No Change in Drug Therapy, No. (%) of Patients‡	P§
Beers (n = 2814)	567 (20)	307 (54)	260 (46)	<0.001
PAL-2 (n = 3290)	1625 (49)	1032 (64)	593 (37)	<0.001
PAL-3 (n = 1334)	685 (51)	460 (67)	225 (33)	<0.001
Clinical initiatives (n = 4837)	2470 (51)	1658 (67)	812 (33)	<0.001

PDTP = potential drug therapy problem; PAL = Prescription Advantage List (PAL-2 drugs had moderately higher costs at equivalent doses, and PAL-3 drugs had substantially higher costs).

*Patients may have been included in >1 alert category.

†Patients with a recommendation as a percentage of all patients with a PDTP alert of this type.

‡Expressed as a percentage of all patients with a PDTP alert and recommendation for change.

§Based on comparison of proportion of patients with PDTP alert before and after intervention, using difference of proportions test.

Table II. Per-patient drug cost savings from recommendations by potential drug therapy problem (PDTP) alert type (N = 6344).

PDTP Alert Type*	Drug Therapy Changes/Patient, Mean (SD), No.†	Change in Drug Therapy Cost/Patient, Mean (SD), Year-2002 US $†	P‡
Beers (n = 2814)	0.12 (0.34)	−2.49 (12.84)	<0.001
PAL-2 (n = 3290)	0.35 (0.55)	−18.04 (40.78)	<0.001
PAL-3 (n = 1334)	0.36 (0.50)	−18.94 (38.89)	<0.001
Clinical initiatives (n = 4837)	0.63 (0.73)	−65.04 (63.51)	<0.001

PAL = Prescription Advantage List (PAL-2 drugs had moderately higher costs at equivalent doses, and PAL-3 drugs had substantially higher costs).
*Patients may have been included in >1 alert category and may have received >1 alert per category.
†Number of drug therapy changes and cost shown per person, reflecting before–after changes in each respective alert category. Drug costs are amounts paid by Medicaid, exclusive of rebates.
‡Comparison of differences between before and after periods using the paired Student *t* test.

Table III. Active prescriptions and drug costs before and after pharmacy intervention (N = 6344).

	Before Intervention*		After Intervention†			
Measure	Mean (SD)	Median	Mean (SD)	Median	Mean Difference	P‡
Prescriptions filled, no.	9.52 (3.29)	9.00	9.31 (3.30)	8.00	−0.21	<0.001
Paid prescription claims, year-2002 US $§	502.96 (309.70)	439.95	472.63 (303.65)	409.30	−30.33	<0.001

*Based on 30-day period immediately preceding review period.
†Based on 30-day period immediately after review period.
‡Comparison of differences between before and after periods using the paired Student *t* test.
§Drug costs are amounts paid by Medicaid, exclusive of rebates.

Wilcoxon signed rank test to account for any abnormality. Results revealed nearly identical levels of statistical significance.

Applying the mean cost savings at 30 days of $30.33 per patient, multiplied by the number of patients (n = 6344), yielded a total savings of $192,414. Cost-minimization/avoidance analyses revealed that the first-year drug cost savings for the program involving the 6344 patients was estimated at $1.7 million. The cost of payments to pharmacist consultants was approximately $79,300 for 6344 comprehensive profile reviews. The administrative costs to generate the drug profiles sent to the consultant pharmacists included drug project manager time (0.5 full-time equivalent [FTE] for 1 year), programmer time (0.5 FTE for 1 year), document processing time, overhead payments to pharmacies for administrative duties ($20,000), and postage fees. Combined administrative costs amounted to approximately $65,000. Therefore, the total was $144,300 in overall program expenditures.

Considering only these costs, the cost-minimization ratio was 12:1. A partial sensitivity analysis for these estimates was also conducted. We varied the mean cost savings by 20%, and the dissipation rate of expected cost savings over the next months from 15% to 25%. Applying these assumptions produced a savings range of $218 to $335 per person, or $1.4 million to $2.1 million for the first patient sample of the initiative in the first year after reviews. The equivalent ratio ranged from 10:1 to 15:1.

DISCUSSION

These study findings present the impact of a single retrospective drug regimen review of targeted nursing

home patients. Considering only personnel costs and fees paid to consultant pharmacists, the program produced a cost-minimization ratio of 12:1. Furthermore, there were indications that interventions resulted in drug therapy that was of higher quality than before. These results confirm those of other investigators who reported the beneficial effect of drug therapy reviews in recently discharged hospital patients, ambulatory patients, and nursing home residents.[27,33–35] One study in particular showed that drug costs were substantially lower in a group that received pharmacist intervention versus a control group that did not.[36] Jameson et al[37] similarly demonstrated that when pharmacists evaluated drug regimens of high-risk ambulatory patients for drug-related problems such as those in this study (eg, therapeutic duplication, suboptimal drug selection, cost), the result was less-expensive drug regimens.

The current role for nursing home consulting pharmacists is based on OBRA 1987 and other federal regulations requiring that drug regimen reviews be conducted at least monthly by consultant pharmacists. As part of this demonstration project, consulting pharmacists were asked to do a focused review of targeted patients. The disease management program described herein reflects many of the elements of an enhanced drug regimen–review model. This model incorporates a pharmaceutical care plan. Within such a plan, the pharmacist works with other members of the health care team to implement and monitor patient drug therapy.[38] Based solely on casual observation and anecdotal reports, the authors feel that there were 2 keys to the success of this intervention. One was feedback and the financial incentive provided to pharmacists, and the second was the collaboration and enthusiastic support of the partners, particularly the consultant pharmacists and physicians serving Medicaid patients.

Computer-generated flags were found to be useful but imprecise instruments for identifying patients with suboptimal drug therapy or PDTPs. It was noted that pharmacists who reviewed targeted profiles did not make a recommendation for change in many cases, suggesting that at least some of the flags were false positives from their perspective. On the other hand, pharmacists made drug therapy recommendations for an additional 1762 patients for whom no drug profile or drug-problem flag was generated. The computer-generated flags used in this demonstration were based on claims data and were relatively easy to implement. For example, they were based largely on the existence of a drug on a patient's drug profile without respect to strength or dose form; they were therefore, by definition, relatively imprecise. One difficulty with computer-generated drug profiles was that flags were based on prescription claims data that were ~4 weeks old. At the time, this was simply the most current information available. However, as the results of our study suggest, these profiles produced positive results in terms of measurable improvements in drug therapy.

Several limitations to this study must be acknowledged. Before–after studies inherently contain several potential threats to internal validity, such as selection bias, imprecise natural history, and regression to the mean. It is possible, for example, that high-use patients may have naturally regressed toward more near-normal numbers of drugs used, or that drug therapy changes may have occurred without this targeted intervention. Furthermore, this study was not designed to distinguish the relative contribution of intervention components (eg, profile, Toolkit, financial reward, pharmacist motivations), and results must be observed in aggregate. Finally, this study was limited to a description of the impact of the intervention on drug therapy changes and costs.

CONCLUSIONS

Results from this study suggest that a focused program to encourage and compensate pharmacists for conducting focused reviews of drug therapy regimens of targeted high-risk patients in a supplementary fashion to usual (mandated) review activities can lower drug therapy costs, reduce polypharmacy, and maintain or enhance the quality of pharmaceuticals received. Further research is needed to investigate the sustainability and uptake of similar large programs, their effect on other (ie, non-drug) medical care utilization components, and additional dimensions of quality of care.

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APPENDIX E: PUBLICATION OF EVALUATION #2[72]

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Trygstad TK, Christensen D, Garmise J, Sullivan R, Wegner S. Pharmacist response to alerts generated from Medicaid pharmacy claims in a long-term care setting: results from the North Carolina polypharmacy initiative. J Manag Care Pharm. 2005 Sep;11(7):575-83.

ABSTRACT

OBJECTIVE: In response to burgeoning drug costs, North Carolina (NC) Medicaid encouraged pharmacists and prescribers to develop collaborative programs to reduce drug expenditures. One of these programs, the North Carolina Polypharmacy Initiative, was a focused drug therapy management intervention aimed at reducing polypharmacy in nursing homes. This intervention targeted patients with more than 18 prescription fills in 90 days, beginning in November 2002. These patients were believed to have a high likelihood of experiencing potential drug therapy problems (PDTPs). Consultant pharmacists were asked to utilize profiles displaying alerts generated from pharmacy claims to guide interventions in addition to usual-care drug regimen reviews. The pharmacists documented their reviews, recommendations, and resulting changes in drug therapy. Our objectives were to determine (1) the persistence of PDTP alerts following interventions by consultant pharmacists and (2) the impact of these interventions on patient drug costs from a payer perspective.

METHODS: A before-after study with comparison group design was used. Medicaid prescription claims data were compared for the 90-day periods prior to the intervention (June-August 2002) and following the intervention (March-June 2003). The 90-day postintervention period allowed for 2 to 3 follow-up prescriptions and reduced the drop-out rate. The 5 categories of potential problem alerts included potentially inappropriate medications (Beers criteria), substitution opportunity for a lower-cost drug, 16 drugs or drug classes with specific quality improvement opportunities (Clinical Initiatives list), therapeutic duplication, and length of drug therapy evaluation.

RESULTS: A total of 253 nursing homes, involving 110 consultant pharmacists and 6,344 patients, were in the intervention arm, with 5,160 patients (81.3%) remaining at the end of the follow-up period. At baseline, study-group patients used an average of 9.7 prescriptions per month, costing the NC Medicaid program $517 per patient per month (PPPM). There were 6,360 recommendations offered for 3,400 patients, or an average of 1.87 recommendations per patient. Physicians concurred with 59.8% (3,801 of 6,360) of all recommendations to change drug therapy, about half involving a switch to a lower-cost drug. Two of 5 alert categories had significant ($P < 0.01$) reductions in alert persistence: -10.8% for the study group versus -0.7% for the comparison group for the Clinical Initiatives list and -29.7% for the study group versus -14.1% in the comparison group for the drug substitution opportunity. Median drug costs per patient in the study group decreased by $12.14 (-0.92%), from $1,329.46 to $1,317.32, and increased in the comparison group by $44.98 (3.35%), from $1,341.25 to $1,386.23, creating a relative cost reduction of $57.12 per patient in the 3-month follow-up period, or $19.04 PPPM.

CONCLUSION: A supplemental program of medication reviews for nursing home patients targeted by high drug utilization resulted in a reduction in the persistence of PDTP alerts and was cost beneficial based solely on drug cost savings. This intervention may be a model for future medication therapy management services provided by prescription drug plans under Medicare Part D for patients in long-term-care settings and possibly ambulatory patients.

KEYWORDS: Nursing homes, Pharmaceutical care, Medication therapy management, Drug use review, Polypharmacy, Drug regimen review

J Manag Care Pharm. 2005;11(7):575-83

Note: An editorial on the subject of this article appears on pages 586-87 of this issue.

The passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) and the ensuing rollout of the outpatient drug benefit in January 2006 have focused attention on ensuring elderly patient access and cost-effective prescribing and use of drugs. Those responsible for Part D program administration within the Centers for Medicare and Medicaid Services (CMS) and prescription drug program sponsors share the formidable task of managing both the cost and quality of drug regimens for more than 40 million Medicare beneficiaries. Medicare will become the largest single payer of drug benefits in the United States, with a projected $70 billion in expenditures in 2006.[1]

The elderly have more chronic illnesses and use more prescription drugs than any other age segment, increasing the likelihood of adverse drug events, many of which are avoidable.[2-4] In an attempt to ameliorate the cost burden and ensure rationale and optimal drug use, Congress took the novel approach of requiring prescription drug plans (PDPs) and Medicare Advantage PDPs to offer a Medication Therapy Management Program (MTMP) as part of their drug benefit. Despite considerable variations in strategy and implementation, prior MTMP-like programs have demonstrated significant cost savings and reductions in drug therapy problems for other targeted patient populations.[5-7]

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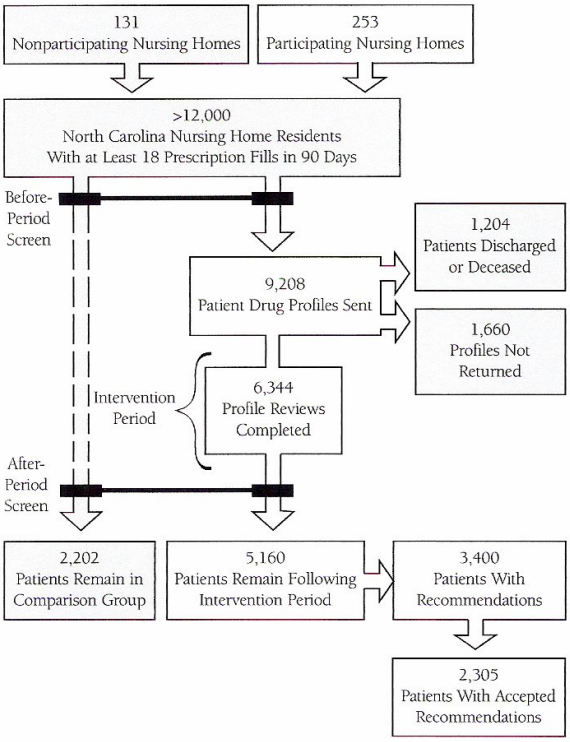
FIGURE 1 Inclusion Criteria and Cohort Development



Defining the nature and scope of MTMP services within Medicare Part D continues to be a dynamic and ongoing endeavor. A consortium of pharmacy trade and professional associations published a working definition in July 2004.[8] This definition was expanded by the American Pharmacists Association and the National Association of Chain Drug Stores in April 2005.[9] However, CMS's final rules pertaining to MTMP services remain broadly defined, leaving the operational details to PDP sponsors.[10]

MMA was not the first federal legislation to require pharmacist involvement in the drug-use process. Beginning in the 1970s, federal regulations imposed a requirement that monthly drug regimen reviews (DRRs) be conducted in long-term-care facilities by consultant pharmacists.[11] Subsequent Omnibus Reconciliation Act legislation (OBRA '87) required that this review be accomplished in collaboration with the attending physician. These regulations contained explicit requirements for reviewing therapy for targeted drugs and drug classes deemed to be overused in long-term-care settings. While such reviews have resulted in improved care since first mandated,[12] there is room for improvement, and a more holistic approach based upon the optimization of both the type and use of all drugs taken by Medicare Part D recipients seems prudent.[13]

Medicaid recipients are also subject to drug reviews through OBRA '90 regulations that require ongoing statewide drug utilization review (DUR) activities. These programs typically focus on drug use by ambulatory Medicaid recipients. The legislation compelled states to establish committees and systems to review patterns of drug use believed to be problematic but did not go as far as MMA to allow for explicit compensation of pharmacists as providers of care.

MMA legislation effectively shifts the burden of drug costs incurred by elderly Medicaid recipients from the state-federal program to the federal government. Prior to the passage of MMA, states were burdened with Medicaid drug expenditures that were ballooning at unsustainable rates despite the federal sharing of Medicaid costs. North Carolina (NC) Medicaid spent more than $1.2 billion on drugs in 2003, with the elderly accounting for 11% of recipients but 32% of all prescription drug costs.[14,15] In response to these trends, NC Medicaid introduced a program that combined the state-level, top-down administration characteristic of DUR activities with patient-level, pharmacist-driven activities typical of DRRs. This program was titled the North Carolina Polypharmacy (NCPP) Initiative.

Following a successful pilot study, the NCPP Initiative was launched in 253 nursing homes in North Carolina with emphasis on elderly Medicaid recipients. In addition to mandated DRRs, the initiative provided a targeted drug therapy management consultation provided by a pharmacist with the treating physician. In these targeted drug therapy management consultations, pharmacists were to (1) review a drug profile generated from Medicaid pharmacy claims with potential drug therapy problem (PDTP) alerts and medical records of Medicaid patients in nursing homes, (2) determine if a drug therapy problem existed, (3) recommend a change if needed, and (4) perform a follow-up to determine if the change was implemented.

The NCPP Initiative was organized as a collaborative activity that incorporated a physician primary care practice network (AccessCare of North Carolina), a pharmacy consultant coalition, and a network of nursing home medical directors. The nature of the NCPP Initiative and its organization was described in an earlier paper that reported the type and frequency of pharmacist interventions and estimated the cost impact of drug therapy changes by type of PDTP.[16] Intervention documents submitted by pharmacists were used as a single data source. For the 6,344 patients with reviews, pharmacists responded to approximately 20,000 drugs with alerts by making 6,520 recommendations, resulting in changes in drug therapy 58% of the time.[16] These changes were projected to save NC Medicaid $30.33 per patient per month (PPPM).[16]

FIGURE 2 Patient Profile Generated From Medicaid Pharmacy Claims—With Potential Drug Therapy Problem Alerts

Nursing Home Poly Pharmacy Project - Patient Profile **Patient Name** Medicaid ID Page 1 of 4 5/7/2003

Nursing Home Practice: Nursing Home Name and Number

Patient ID: XXXXXXX **Last Name:** XXXXXXX **First Name:** XXXXXXX

Gender: F **Age:** 82 **DOB:** XX/XX/XXXX **Avg # of Drugs/month:** 7.67 **Avg monthly drug $:** $625.85

Confidential - For record validation only. Not for inclusion in chart. Please return to

Fill Date	Drug Class	Medication	Amount Paid	Prescriber	PAL	Potential Therapeutic Duplication	Clinical Initiatives/Quality	Consider Length of treatment*	Beers List ≥ 65	Problem Type	Results Type	New Drug and Strength
7/30/02	ANALGESICS NARCOTIC	ULTRACET TABLET d	$164.96	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
8/16/02	ANTINAUSEANTS	METOCLOPRAMIDE 10MG TABLET	$11.81	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
6/5/02	ANTISPASMODIC-ANTICHOLINERGICS	HYOSCYAMINE 0.375MG TAB SA	$16.04	Prescriber Name					X	A B C D E F G	1 2 3 4 5 6	
8/7/02	ANTI-ULCER/OTHER GASTROINTESTINAL PREPS	NEXIUM 40MG CAPSULE	$131.32	Prescriber Name	PAL 3 Prefer Protonix		X			A B C D E F G	1 2 3 4 5 6	
8/9/02	BRONCHIAL DILATORS	ALBUTEROL .83MG/ML SOLUTION	$16.70	Prescriber Name	PAL 1					A B C D E F G	1 2 3 4 5 6	
8/29/02	DIURETICS	FUROSEMIDE 40MG TABLET d	$7.52	Prescriber Name						A B C D E F G	1 2 3 4 5 6	

*Please refer to toolkit for further explanation.

Problem Type (Circle all that apply)
A. Unnecessary Drug Therapy
B. More Cost Effective Drug Available
C. Wrong Dose or Strength
D. Drug has High Potential for ADRs
E. Needs Additional Therapy
F. Not a problem at this time
G. Other - Any other problem not listed above

Results Type (Circle all that apply)
1. Dose/Delivery Changed - Dosage or administration was changed
2. Drug Added - New drug was added for previously untreated indication.
3. Drug Change - Drug was changed from one to another.
4. Drug Discontinued - Drug was discontinued or was changed to PRN.
5. No Change - Physician Responded but did not make any changes.
6. Other - Any result not listed above.

Medication Superscripts
a. Recommended check for K+ need
b. Recommended use with Ca+ supplement.
c. Recommended check for Fe+ need
d. Recommended check for Stool Softener need
e. Recommend check for Folic Acid therapy.
f. Recommend check for supplemental calcium need..
g. TB test needed?
h. Does patient have BPH and HTN? Consider Cardura.
i. Consider dose reduction/excessive dose.

PAL Codes
PAL Code 1 - Preferred Drug
PAL Code 2 - No Preference
PAL Code 3 - Avoid
PA - Prior Authorization Required

In the present article, we reconcile the projected drug cost impact of pharmacist intervention activities with actual Medicaid claims data spanning a 6-month period. We describe the nature of PDTP alerts, drugs involved, recommendations, and actions taken after physician consultation. We also assess changes in drug therapy from a qualitative and economic perspective using a before-after study design with a comparison group.

Our working hypothesis was that a systematic program of pharmacist-directed DUR that supplements requisite OBRA '87 DRRs in nursing homes would produce drug therapy changes that maintain or improve the quality of care while decreasing drug costs. The specific objectives of the current study were to determine (1) the persistence of PDTP alerts following interventions by consultant pharmacists and (2) the impact of these interventions on patient drug costs from a payer perspective. This study received approval from the Institutional Review Board at the University of North Carolina at Chapel Hill.

Methods

Setting and Participants

Phase 1 of the NCPP Initiative was conducted by 110 pharmacists in 253 nursing homes, representing approximately 70% of all nursing homes in North Carolina (Figure 1). Participation in the intervention was solicited through the North Carolina Long Term Care Pharmacy Alliance, a representative group of pharmacists serving nursing homes throughout the state. Exempted were 13 homes that contracted with a single pharmacy provider and were involved in a separate, ongoing intervention project. All Medicaid residents of the participating facilities who had 18 or more prescription fills in the 90-day period prior to the start of the study were eligible for an on-site profile review by a consultant pharmacist. This time horizon was chosen to capture, on average, 3 monthly supplies of medications while limiting the dropout rate as much as possible.

Pharmacist Responsibilities

Participating pharmacists were introduced to the project, toolkit, and documentation form during two 1-hour group meetings and one 1-hour conference call. Other professional interactions took place throughout the course of the project, including informational meetings with geriatric associations, nursing home medical directors, and network physicians, as well as the use of telephone follow-ups. The toolkit contained instructions for documenting interventions and explained the screening criteria used to select (flag) drugs for attention.

Each consultant pharmacist was provided with drug profiles computer-generated from Medicaid pharmacy claims that displayed flags for patients and suggestions for modifications of drugs and classes of drugs. Pharmacists were asked to record both the result of the review (i.e., the intervention) and the result of the consultation with the prescribing physician (i.e., the outcome) on a documentation form (Figure 2). Recording the result of the intervention required awaiting the prescriber's response to the recommendation. Pharmacists were required to conduct these assessments during their regularly scheduled visits to each home. Consultant pharmacists employed their usual methods of communicating with physicians (fax, phone, or written notation in the medical record) to make recommendations and to learn the outcome of the change recommendation. We categorized the drug therapy flags as (1) unnecessary drug therapy, (2) more cost-effective drug available, (3) wrong dose/delivery, (4) potential for adverse drug reaction, (5) needs additional therapy, and (6) other problem. We coded intervention results as (1) dose/delivery changed, (2) drug added, (3) drug changed (from one to another), (4) drug discontinued, (5) no change, and (6) other intervention.

If an intervention resulted in a drug therapy change of any type, the new drug, dose, and quantity were noted. Drug, dose, and quantity were also reported for each new drug added for previously untreated indications. Pharmacists were compensated $12.50 for each comprehensive profile review for which results were clearly documented on the forms provided (i.e., the patient profile). This compensation amount was based on our estimate of the additional time required for these focused reviews above and beyond normal review activities and a customary rate of pay of $50 per hour. Pharmacists were compensated regardless of problem determination and/or the offering of a recommendation.

Drug Profiles and PDTP Alert Criteria

Patient drug profiles were generated from Medicaid claims data and contained, for each listed drug, a space for all alert categories, marked with the appropriate flag/alert if a PDTP was determined by matching claims data with drug lists generated from alert categories. The profiles were a compilation of all drugs for which a claim was paid in the 90 days prior to generation, regardless of the presence of an alert. The first alert criterion was receipt of a drug widely considered to be inappropriate for use in the elderly (Beers drug list).[17] In order to engender participation and maximize the quality of the PDTP alerts, program administrators also elicited input from local physicians and consultant pharmacists. Thus, the second criterion was receipt of a drug on the Community Care of North Carolina Prescription Advantage List (PAL), which encourages substitution of less expensive drugs within a therapeutic class. This voluntary preferred drug list was conceived and is maintained by a committee of practicing physicians in North Carolina specifically for NC Medicaid. There are 3 categories of PAL drug alerts. PAL-3 drugs are considered to incur "significant cost" to the Medicaid program (e.g., Nexium, Prilosec, Zestril, Prinivil, as of November 2002), while PAL-2 drugs offered "no clear cost advantage" (e.g., Prevacid, Aciphex, Accupril, Monopril, Lotensin, Altace, as of November 2002), and PAL-1 drugs offer "significant cost savings" to the Medicaid program (e.g., Protonix, lisinopril, enalapril, captopril, as of November 2002). The third criterion was the appearance of a drug on a "Clinical Initiatives" list. The Clinical Initiatives list was developed by consultant pharmacists participating in the NCPP Initiative and included 16 drugs and/or drug classes (e.g., COX-inhibitors, statin drugs, sleep aids, low-sedating antihistamines) that had the potential for quality improvement and cost savings. Program administrators offered 2 additional alerts: therapeutic duplication and a "consider length of therapy" alert that was derived from classes of drugs considered appropriate only for short-term use (e.g., antibiotics, injectable enoxaparin).

Research Design

We first evaluated pharmacist action and reporting by reconciling the response to alerts with downstream prescribing activity using the Medicaid dispensed prescription claims database. Using a before-after, study-comparison-group design, we compared prescription use during the 3 months before intervention (June-August 2002) with a period of equal length at the end of Phase 1 (March-June 2003). Second, we assessed whether or not PDTP alerts were reduced during the follow-up period compared with usual-care controls (nonrandomized comparison group). Third, we describe the economic consequences of pharmacist activities in terms of changes in drug cost using pharmacy paid claims data.

Study-group patients were Medicaid recipients residing in participating nursing homes who received a completed profile review by a consultant pharmacist. The comparison group consisted of patients in nursing homes not responding to the invitation for inclusion in Phase 1 of the intervention. Inclusion of patients in comparison-group homes was determined by criteria identical to study-group patients (i.e., more than 18 prescription fills in 90 days, Figure 1). Several of the nursing homes in the comparison group became participants in later phases of the project, but only after the 6-month study window in this

TABLE 1 Baseline Characteristics of Continuously Enrolled Patients by Treatment Group

Characteristic	Study Group (n = 5,160)	Study Group (With Recommendation*) (n = 3,400)	Study Group† (With Acceptance) (n = 2,305)	Comparison Group (n = 2,202)
Sex, no. (%)				
Male	1,289 (24.98)	820 (24.12)	533 (23.99)	484 (21.98)
Female	3,871 (75.02)	2,580 (75.88)	1,752 (76.01)	1,718 (78.02)
Race, no. (%)				
White	3,533‡ (68.47)	2,325‡ (68.38)	1,588‡ (68.89)	1,667 (75.70)
Other	1,627 (31.53)	1,075 (31.62)	717 (31.11)	535 (24.30)
Age, years, mean ± SD	77.57 ± 12.72	77.63 ± 12.42	77.67 ± 12.44	78.65 ± 12.46
(median)	(80.0)	(80.0)	(80.0)	(81.0)
No. of prescription fills, 3 month period, mean ± SD	29.04 ± 9.92	29.86 ± 10.27	30.19 ± 10.53	28.18 ± 10.74
(median)	(27.0)	(28.0)	(28.0)	(26.0)
Amount of paid claim ($), 3-month period, mean ± SD	$1,549.89 ± 1,652.49	$586.91 ± 919.17	$1,610.02‡ ± 926.77	$1,543.67 ± 921.98
(median)	($1,329.46)	($1,392.14)	($1,427.13)	($1,341.25)

Note: Difference of proportions tests were used to determine differences in sex and race. T-testing was used to determine differences in age, number of prescription fills, and amount of paid claims.

** Study group (with recommendation) = those patients having a recommendation resulting from pharmacist consultation, regardless of outcome.*

† Study group (with acceptance) = those patients having a recommendation and a change in therapy as a result of a recommendation provided by a pharmacist.

‡ Denotes significantly different from comparison group at P<0.01.

analysis. For study-group patients, we linked prescription drug use elicited through claims data to pharmacist-reported interventions (or lack thereof) on patient profiles. We examined 2 study subgroups: (1) patients whose drug use received pharmacist recommendations and (2) patients for whom recommendations were accepted.

Studies in the long-term-care arena are often burdened by a high attrition rate. Using a combination of claims data and pharmacist report, we estimated an annual nursing home resident attrition rate of 36% due to death or discharge in North Carolina. Since we were not able to verify dropout from prescription claims with certainty, only residents having claims in the last 35 days of the 90-day follow-up period were included in both the study and comparison groups.

Statistical testing was performed using SAS statistical software, version 8.2 (1999-2001, SAS Institute Inc., Cary, NC). We used nonparametric statistical testing to account for possible skewness in the data.

Results

Prescription profiles were generated and sent to consultant pharmacists for 9,208 patients. Pharmacists returned 7,548 (82%) of all profiles sent to them (Figure 1). After excluding 1,204 patients (13%) who were discharged or deceased, 6,344 patients were subjected to profile reviews. This number diminished to 5,160 patients who remained in the Medicaid population throughout the follow-up period, constituting an 18% dropout rate over 6 months due to death or discharge. This is consistent with historical dropout rates for Medicaid recipients. Remaining patients had received an average of 9.7 prescription fills (median 9) per month during the 3-month period prior to profile generation. Exclusive of manufacturer rebates, the average PPPM drug cost to NC Medicaid was $517, with a median of $443.

The comparison group consisted of 2,202 patients selected in the same manner as study-group patients (having 18 or more prescription fills in a 90-day period). We compared study and comparison groups based on age, gender, race, baseline prescription use, and dropout rates (Table 1). The groups differed with respect to race, with a lower proportion of whites in study nursing homes versus comparison-group homes (69% vs. 76%, respectively, $P < 0.01$). At baseline, drug usage and costs were similar for study and comparison-group patients with one exception: the study subgroup with changes resulting from recommendations had higher baseline prescription costs. Dropout rates from the original cohorts were also similar across the groups (at 18% to 19%).

Among study group patients, the most common PDTP alert was for a drug with a potential therapeutic duplication with an average of 5.11 alerts (Table 2). Therapeutic duplication alerts were common because a single potential duplication triggered at least 2 alerts. Clinical Initiative alerts averaged 2.77 alerts per patient. This was followed by PAL-2 or PAL-3 drugs (1.58 per patient) and Beers list drugs (0.78 per patient). A total of 6,360 interventions were offered for 3,400 patients in the study group, an average of 1.87 per patient with intervention. Based on pharmacist reporting, physicians concurred with 59.8% (3,801 of 6,360) of all interventions to change drug therapy (Table 3). Pharmacist suggestion for a more cost-effective drug was the most popular recommendation (3,327) with the greatest frequency of success (2,088, 62.8%). A recommendation for a

TABLE 2 Comparison of Potential Drug Problem Alert Rates Before and After a Single Retrospective Intervention

Alert Type	No. of Alerts Per Patient Before (3 months)	After (3 months)	Difference (%)
Beers List§			
Study	0.78	0.70	-0.08 (-10.8)
Study (w/recommendation*)	0.82	0.72	-0.10 (-12.2)
Study (w/acceptance†)	0.83	0.71	-0.12 (-14.5)
Comparison	0.83	0.74	-0.09 (-10.8)
PAL List (2 or 3)‖			
Study	1.58	1.11	-0.47‡ (-29.7)
Study (w/recommendation*)	1.76	1.16	-0.60‡ (-34.1)
Study (w/acceptance†)	1.82	1.10	-0.72‡ (-39.6)
Comparison	1.63	1.40	-0.23 (-14.1)
Clinical Initiatives List¶			
Study	2.77	2.47	-0.30‡ (-10.8)
Study (w/recommendation*)	3.00	2.67	-0.33‡ (-11.0)
Study (w/acceptance†)	3.09	2.68	-0.41‡ (-13.3)
Comparison	2.73	2.71	-0.02 (-0.7)
Consider Duration Flag#			
Study	0.16	0.15	-0.01 (-6.3)
Study (w/recommendation*)	0.15	0.15	0.00 (0.0)
Study (w/acceptance†)	0.14	0.14	0.00 (0.0)
Comparison	0.18	0.15	-0.03 (16.7)
Therapeutic Duplication**			
Study	5.11	4.63	-0.48 (-9.4)
Study (w/recommendation*)	5.15	4.78	-0.37 (-7.2)
Study (w/acceptance†)	5.22	4.75	-0.47 (-9.0)
Comparison	5.00	4.56	-0.44 (-8.8)

Note: The Wilcoxon 2-sample test was used to assess differences in alert rates between the comparison group and study.
Sample sizes:
Study group: n=5,160
Study group with recommendations: n=3,400
Study group with accepted recommendations: n=2,305
Comparison group: n=2,202
* *Study group (with recommendation)=those patients having a recommendation resulting from pharmacist consultation, regardless of outcome.*
† *Study group (with acceptance)=those patients having a recommendation and a change in therapy as a result of a recommendation provided by a pharmacist.*
‡ *Denotes significantly different from comparison group at P <0.01.*
§ *The Beers List is a list of drugs generally considered to be inappropriate in the elderly.*[17]
‖ *PAL = Prescription Advantage List, a categorization of drug alerts proposed by practicing physicians in North Carolina. PAL 3 drugs are considered to "incur significant cost." PAL 2 drugs are considered to offer "no clear cost advantage." PAL 1 drugs are considered to offer "significant cost savings." The rates of PAL 2 and 3 drug alerts are shown in this table.*
¶ *Clinical Initiatives List refers to potential drug therapy problem alerts proposed by consultant pharmacists in North Carolina.*
\# *Consider Duration alerts were derived from classes of drugs considered appropriate only for short-term use.*
** *Therapeutic Duplication alerts were generated based upon duplications within hierarchical drug class codings.*

TABLE 3 Frequency of Recommendation by Type With Resultant Success* (n=3,400)

Recommendation Type	Frequency	Success, No. (%)
Wrong dose or strength	545	444 (81.5)
More cost-effective drug available	3,327	2,088 (62.8)
Drug has potential for ADRs	632	328 (51.9)
Needs additional therapy	167	69 (41.3)
Other (not specified)	432	146 (33.8)
Total	6,360	3,801 (59.8)

* *Recommendations were considered successful when a change in therapy occurred subsequent to a recommendation by the clinical pharmacist.*
ADRs=adverse drug reactions.

different dose garnered the highest rate of success (444 of 545, 81.5%). For Clinical Initiatives and PAL-2 or PAL-3 flags, pharmacists made interventions for change in 46.2% (2,271 of 4,916) of patients; physicians endorsed 60.2% (1,939 of 3,222) of the recommendations. Beers drugs and "consider length" (of drug therapy) categories garnered considerably fewer recommendations.

We next examined persistence of computer-generated alerts in the drugs received by patients before and after intervention. Our working hypothesis was that, if the intervention program was successful, there should be a decrease in the number of PDTP alerts on subsequent patient drug profiles using the same computer-screening process employed in the before-intervention period. We found statistically significant declines in the number of alerts per patient for both PAL and Clinical Initiatives flags ($P<0.01$) for all study groups (-29.7% and -10.8%, respectively) compared with the comparison group (-14.1% and -0.7%, respectively) using the Wilcoxon 2-sample test (Table 2). As expected, even greater declines in alert rates were observed in the study subgroup that received intervention (-34.1% and -11.0%) and in the subgroup that had drug therapy changes as a result of dispensing pharmacist recommendations (-39.6% and -13.3%). When compared with baseline drug use, all flag categories in all study groups had statistically significant reductions ($P<0.01$; Wilcoxon signed rank test), with the exception of the "consider length" (of drug therapy) flag.

Finally, we examined before-after changes in the amount paid for prescriptions (Table 4). Median drug costs per patient in the intervention group decreased by $12.14 (-0.92%) from $1,329.46 to $1,317.32 and increased in the comparison group by $44.98 (3.35%) from $1,341.25 to $1,386.23, creating a relative cost reduction of $57.12 per patient in the 3-month follow-up period, or $19.04 PPPM. Even larger reductions in drug costs were observed in the study subgroups with (1) documented profile reviews and with recommendations for change, where a median decline of $25.83 per patient was observed and (2) in the subgroup for which drug therapy changes occurred as a result of the recommendations, where a decline of $61.68 per patient was observed.

Discussion

The results indicate that the addition of PDTP alerts to usual-care DRRs was associated with more changes in drug therapy and a reduction in computer-generated drug therapy alerts during the follow-up period. Among drug problem alert categories, we found statistically significant differences between the study group and the comparison group in alert persistence for Clinical Initiatives and PAL drugs. These 2 categories were constructed by physician and pharmacist leaders, suggesting that practitioner involvement with a centralized DUR process aids in program response. Beers list and therapeutic duplication alerts decreased in all study groups and in the comparison

group, but persistence was not statistically different between study and comparison groups. This finding is consistent with the role of DRRs as outlined in OBRA '87.[11] These types of drugs and drug problems are explicitly mentioned as part of the guidelines for conducting customary mandated DRRs.

Residents in comparison homes were not subject to drug profile reviews with PDTP alerts generated from pharmacy claims as part of the NCPP Initiative. However, residents in both study and comparison homes were subject to requirements based on OBRA '87 and screening guidelines for the overuse of particular prescription drugs. This may explain the reduction in both groups. A *JMCP* article published in April 2005 demonstrated significant reductions in the use of Beers list drugs associated with an intervention involving letters to prescribers, pharmacist phone consultations, and written literature disseminated in a predominantly ambulatory population of Medicare + Choice (now Medicare Advantage) recipients.[18] It would seem prudent, given previous success, to attempt to replicate the NCCP Initiative in an ambulatory Medicare setting. Notably, few recommendations were made pursuant to the "consider length" (of therapy) flag category in all study and comparison groups. This length of therapy category generated only 205 alerts in total and did not contain drugs such as benzodiazepines or psychotropic medications customarily scrutinized for length of therapy during regularly scheduled DRRs.

This analysis of prescription claims data supports previous findings with regard to drug cost savings resulting from the NCPP Initiative as well as its pilot project. The NCPP Pilot Project was found to have generated an approximate 4% reduction in drug costs.[19] A previously published article utilizing primary data from pharmacist reports found that the NCPP Initiative produced savings of $30.33 PPPM savings in the month immediately following the intervention.[16] The resulting cost minimization ratio was determined to be 12:1.[16]

In the present study, we utilized Medicaid claims data to reconcile documented pharmacist interventions and to determine the downstream effects of those interventions. We also added a comparison group to further strengthen its internal validity. Using the results from Medicaid claims data in conjunction with comparison group findings, we observed a savings of $19.04 ($P$=0.06) PPPM for all patients receiving profile reviews, $23.60 for patients receiving interventions (P <0.01), and $35.55 ($P$ <0.01) for patients having at least 1 accepted intervention. The 3-month PPPM difference between the study group and comparison group of $57.12 remains substantial and justifies the implementation of the Polypharmacy Initiative on the basis of drug cost savings alone.

Previous projections based upon the first month immediately following the interventions did not allow us to consider the persistence of the intervention effect. An intervention may not have been carried out for reasons unknown to the consultant pharmacist. The intervention decision may have been reversed by the physician after the pharmacist documented acceptance in the report. Pharmacists may also have underreported new drugs found on the nursing home medical record but not appearing on the drug profile generated from Medicaid pharmacy claims due to lag time from profile receipt to regularly scheduled DRR activities. We noted an average difference of $15 per month between claims analysis and pharmacist-reported drug cost data ($516.63 in claims analysis versus $502.96 in pharmacist-reported data) in baseline costs between these studies. This difference illustrates the importance of reconciling pharmacist intervention reporting with administrative claims. Using both data sources, as we did in the present study, is advantageous since we can tie observed medication-level interventions derived from pharmacist reporting with actual costs incurred from claims data to validate pharmacist action.

The NCPP Initiative combines population-level, drug-specific surveillance of DUR programs with patient-level, comprehensive reviews characteristic of DRR activities. Alerts were generated by the payer, in this case NC Medicaid, and were provided to prescribing physicians to encourage change in targeted drugs and drug classes. In line with usual care in long-term-care settings, pharmacists were free to review and recommend therapy changes for any drug in a patient's profile for any problem they discovered. Beginning in 2006, Medicare PDP sponsors will take on a DUR role with differing approaches to MTMP under the MMA. Standard DUR approaches have offered little evidence, to date, of effectively improving patient outcomes for state Medicaid recipients despite the large budget outlays to these programs.[20-23] However, targeted, population-specific interventions such as the NCPP Initiative have shown some success.[24-26] Focused reviews based upon patient-specific

TABLE 4 Total Amount Paid for Prescriptions in the Before and After Periods

	Before Period (3 Months) (Median)	After Period (3 Months) (Median)	Difference (%)	*P* Value
Study group (n=5,160)	$1,329.46	$1,317.32	-$12.14 (-0.92)	0.06
Study group (n=3,400) (w/recommendation*)	$1,392.14	$1,366.31	-$25.83 (-1.86)	<0.01
Study group (n=2,305) (w/acceptance†)	$1,427.13	$1,365.45	-$61.68 (-4.32)	<0.01
Comparison group (n=2,202)	$1,341.25	$1,386.23	$44.98 (3.35)	n/a

Note: the Wilcoxon 2-sample test was used to assess differences in total amount of paid claims between the comparison and study groups.

* *Study group (with recommendation) = those patients having a recommendation resulting from pharmacist consultation, regardless of outcome.*

† *Study group (with acceptance) = those patients having a recommendation and a change in therapy as a result of a recommendation provided by a pharmacist.*

n/a = not applicable.

profiles generated from administrative pharmacy claims, in combination with collaborative activities that individualize care,[27] such as DRRs, may be a better strategy for PDPs to adopt through the MTMP service requirement.

This strategy is not limited to the long-term-care setting and may in fact be more effective in an ambulatory setting where less frequent review of drug use profiles takes place. The strategy is generally applicable to any group of beneficiaries that use online adjudication for processing pharmacy claims.

Limitations

It was not possible to draw a true random sample of patients, nursing homes, or pharmacist consultants due to the intermingling of providers. Our comparison group was not, by design, a randomized sample of patients. Due to clustering effects, it is difficult to construct a truly randomized patient-level sample within a nursing home because physicians often provide care to patients in more than one nursing home. Additionally, groups of pharmacists are often clustered through consulting organizations serving multiple nursing homes, and multiple nursing homes often operate under a common ownership structure. Fortunately, baseline demographic characteristics and prescription drug costs between the study group and the comparison group were remarkably similar ($516.63 in the study group versus $514.56 in the comparison group).

The study group, its subgroups, and the comparison group did not differ statistically with respect to gender, age, or number of prescriptions filled at baseline. There was a statistically significant difference with respect to race, with the study group and its subgroups having a greater proportion of nonwhite participants. We do not suspect that this difference confounded the results. Whatever unmeasured population differences existed, we believe our use of before-after comparisons within groups and the relatively large sample sizes enhance the validity of study results. We assume that contamination effects arising from sharing of pharmacist consultant firms between study and comparison facilities was trivial. While some pharmacist consulting firms served several different nursing homes, no individual pharmacist provided consulting services to both study and comparison group homes. Pharmacist turnover was not a problem since the time period was relatively short. To the extent that contamination effects were present, they would serve to diminish observed between-group differences. We do not know the effect of repeated interventions, the effects of continually evolving PDTP alerts criteria,[28] or intervention persistence beyond 6 months.

We cannot confidently project the long-term impact of these interventions. Our 3-month follow-up period reflected a balance in our approach. On the one hand, we wanted at least two 1-month follow-up periods to ensure that drug therapy changes were reflected in claims data and persisted. On the other hand, a longer follow-up period of 6 to 12 months would have incurred problems of patient attrition within the nursing homes, given the statewide average attrition rate of 36% per year. Yet another factor was the strong desire by the sponsor to finish the analysis of Phase 1 as soon as possible for public policy planning and budgeting purposes.

Using administrative claims data to measure differences in drug costs is not without limitations. Drugs may have been filled without submission of a claim, or nursing homes may have paid for products such as over-the-counter medications out of a separate budget. However, this study takes a payer perspective, and paid claims are the most meaningful measurement from this perspective. Administrative claims are also poor stand-alone proxies for measuring changes in quality, particularly in such areas as adverse effects or health status. On the other hand, the very large sample sizes involved in our study suggest that our findings are real and replicable.

As with any nonrandomized observational study, regression toward the mean must be considered. We chose our comparison group in the same way we chose study group patients; hence, both should have equally incurred this regression effect, and it is, in essence, neutralized for purposes of differential analysis.

Using a payer perspective, we assessed the impact of all drug claims not just those drugs flagged in profiles from preintervention screening. It is likely that our broader focus diluted our findings toward the null. Yet we found important drug cost differences on a PPPM basis.

Conclusions

A program of supplemental pharmacist review targeting patients with high drug use and the potential for multiple drug therapy problems was successful in generating changes in drug therapy. We believe that involving pharmacists and physicians in the creation of PDTP alerts was crucial to widespread adoption. The changes in drug therapy that resulted from a single (compensated) pharmacist retrospective review significantly reduced the number of PDTP alerts at follow-up. Currently, regulations governing DRRs do not explicitly focus on cost-effectiveness or cost reductions of pharmaceuticals received by patients, nor do they explicitly compensate reviewers for such services. Results from this study suggest that a program to encourage and compensate pharmacists for conducting focused reviews of drug therapy regimens for targeted high-risk patients as a supplement to usual mandated review activities can lower drug therapy costs and maintain or enhance the quality of drug therapy. Interventions by pharmacists were economically beneficial when labor costs and savings in drug costs are considered. Elements of this program can be applied to both ambulatory and long-term-care settings.

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Author Trygstad served as principal author of the study. Study concept and design were contributed by Trygstad, Christensen, Wegner, and author Robert Sullivan. Analysis and interpretation of data were contributed by Trygstad, Christensen, and Sullivan. Drafting of the manuscript was primarily the work of Trygstad, and its critical revision was the work of all authors. Statistical expertise was contributed by Trygstad and Christensen.

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APPENDIX F: PHASE 1 CONSULTANT PHARMACIST TOOLKIT, VERSION 1.0

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CONSULTANT PHARMACIST

TOOL KIT

FOR

IMPLEMENTATION OF THE

ACCESS II and III/ CONSULTANT PHARMACIST

Nursing Home POLY-PHARMACY PROJECT

OCTOBER 2002

Developed by AccessCare, Inc. Morrisville, NC

Table of Contents

Appendices

**For any questions related to this document, please call 1-877-570-0001. Address medical questions to Dr. Steve Wegner and all others to Jennifer Thorpe, PharmD.*

Chapter 1:
Nursing Home Polypharmacy Project Overview
(For background on Access II and III and AccessCare, see Appendix E)

Aim:

- To minimize medication related costs and improve quality through a pharmacist-physician consultation program directed at nursing home patients.

Rationale:

- NC Medicaid drug program costs have been increasing in excess of 17% per year.
- NC Medicaid program administrators have targeted a cost reduction of $29M for the next year.
- A medication therapy management program is seen as a potentially viable way to help achieve this cost reduction target while improving or maintaining quality of care.
- The program's success depends on the active cooperation of pharmacists and physicians.

How the project will work:

- AccessCare will screen NH patients for potential drug therapy problems and opportunity for cost savings.
- AccessCare will electronically generate profiles of flagged patients.
- Profiles will be sent to NH dispensing pharmacy organization who will in turn forward them to consultant pharmacists.
- The task of the consultant pharmacists will be to review each flagged profile for potential drug therapy problems or cost savings potential, make clinical recommendations, and follow-up to determine if a change was made.
- Reviews will be done as part of the monthly drug regimen review (DRR) process.
- Consultant pharmacists will document patients reviewed, problems detected, and results.
- Pharmacists will be paid $12.50 per patient profile reviewed.
- **It is critically important to document problem interventions and results on the forms provided as this is the primary method for measuring the success of the program.**

Chapter 2:
How to Complete the Intervention Form

Consultant Pharmacist's Guide to the Nursing Home Poly-pharmacy Initiative (understanding and using the forms, recording and reporting results)*

**** EXISTING PATIENT PROFILE FORM ****

Pre-populated with Medicaid claims data. AccessCare has screened each patient's prescription claims and flagged those which fell into 1 or more of the following categories:

I. FLAGGED COLUMN HEADINGS:

PAL – Prescription Advantage List. This is a *voluntary* list developed by a group of physicians that ranks drugs within 10 different therapeutic categories according to cost (1 being least expensive, 3 most expensive). If a patient is taking a drug in one of these categories, the PAL number will appear. If it is a 1, that's good! If it is a 2 or 3, the number one choice(s) will also appear to suggest that, if clinically appropriate for the patient, try to change to the #1 choice.

Potential Therapeutic Duplication – This is identified by using the Therapeutic Classification field provided by claims data. These classes are very broad, and many combinations of drugs may not involve a true duplication. However, use clinical judgment when determining whether it is really a duplication or not.

Clinical Initiatives/Quality Indicators – This represents ~20 drugs or groups of drugs for which significant money can be saved without compromising patient care, derived from the top 100 drugs by Medicaid expenditures. Representatives of several LTC pharmacies (the Committee) reviewed the data for potential cost savings opportunities. If a patient is taking one or more of these drugs, this column will be marked with an X. The exact drugs and drug groups, as well as a description of the two-tiered approach to achieving savings, are discussed in detail at the end of this document.

Consider Length of Treatment – This column targets drugs that patients are commonly prescribed for a short period of time, but are left on indefinitely. These will also be marked with an X. The drugs that will be flagged are: Bactroban cream & ointment, antibiotic and/or steroid eye drops/ointments, and low molecular weight heparins. Please evaluate whether it is still necessary for the patient to be taking this medication.

Beers' List – Drugs which are inappropriate for use in elderly, nursing home patients are identified here. Be aware of some contradictions here. Some drugs that are Beer's List drugs may be most appropriately replaced by a more expensive drug flagged in the above columns. Again, use your clinical judgment to determine the most appropriate patient-specific therapy that addresses both cost and quality.

* Restricted for use in the NC AccessCare Nursing Home Polypharmacy intervention project. Created 10/10/02

Medication Superscripts:
A superscript appearing next to a drug indicates that there is a quality check associated with it. Descriptions are listed at the end of the document. Drugs that are targeted and their corresponding quality checks are as follows:

a. Diuretics – "Recommend check for K+ need". This is a reminder that you check those patients on loops and thiazides are receiving supplemental K+ if needed, and those on potassium-sparing diuretics are not.

b. Fosamax, Actonel – "Recommend use with Ca+ supplement"

c. Hematinics – "Recommend check for Fe+ need". Applies to those patients on Epogen and Procrit who should be taking supplemental Fe+, and also to ensure that those on Fe+ supplements are not receiving excessive doses and are having Hct & Hgb measured as necessary.

d. Narcotic Analgesics – "Recommend check for stool softener need".

e. Methotrexate – "Recommend check for folic acid therapy".

f. Corticosteroids – "Recommend check for supplemental Ca+ need". Applies to those on chronic steroids. You will need to verify with the chart if this is a concern.

g. Remicade – "TB test needed?"

h. Flomax – "Does patient have BPH and HTN? Consider Cardura".

i. Atypical antipsychotics – "Consider dose reduction/excessive dose".

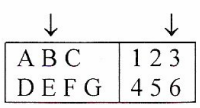
In general, superscripts encourage the use of additional therapy. However, the additional therapy tends to be very cost effective. Since we are interested in both cost *and* quality, due attention should be given to the superscripts to maximize patient outcomes.

II. RECORDING YOUR INTERVENTIONS

"Problem Type" and **"Result Type"**

- This is ESSENTIAL INFORMATION for tracking the success of this program.
- You will find definitions of the A,B,C.. and 1,2,3.. codes on the bottom of the form.
- If more than one Problem or Result is associated with a particular drug, Choose the SINGLE BEST CODE FOR EACH DRUG.
- If you record a result of 2 or 3 (Drug Added or Drug Change), please also record in the last column the name and strength of the newly prescribed drug.
- REMEMBER, payment will NOT BE MADE to you or your company for the patient encounter unless ALL drugs in a given patient's regimen have a corresponding problem and result code circled. Notice that there is a code for "no change" indicating the drug is appropriate at the time of intervention.

Example: Patient is taking Prevacid 30mg QD and you recommend Protonix 40mg QD:
Circle Problem Type B Circle Recommendation Type 3



III. DRUGS NOT FLAGGED BY ACCESSCARE/NOT IDENTIFIED BY ACCESSCARE

- You will note that not all drugs listed on the profiles are flagged. These FLAGS ARE ONLY ADVISORY and the DRUG LIST MAY BE OUTDATED.

- It is VERY IMPORTANT that you ADD DRUGS TO THE FORM not found in our claims search, AND that you DELETE ANY DRUGS not currently found on the patient's MAR by DRAWING A LINE through the drug row. There is space near the end of the form for you to record any ADDITIONAL DRUGS the patient is currently taking.

  Example 1. Lipitor 10mg (Fill date 10/1) shows up on one row and Lipitor 20mg (Fill date 11/1) shows up on another row. This type of duplication will be common. Cross out which ever drug is not listed in the MAR and intervene on the drug the patient is currently taking.

  Example 2. Lovenox 80mg (Fill date 9/1) shows up on the claims-generated report, but the patient is no longer taking it and it is not on the MAR. CROSS IT OUT, and **do not** circle an intervention code.

- If there is a problem for ANY DRUG, LISTED OR NOT, FLAGGED OR NOT, code it in the usual way on the form. Even if a drug has not been "flagged" on the form, if you see a problem with it, please intervene!

  LAST STEP for this form: Complete the last page and sign it.

****NEW PATIENT/PROSPECTIVE INTERVENTION FORM ****

(blank form, Appendix A)

Use it to record *both*:

- **newly admitted patients** since printing of the reports and
- any **prospective interventions** made on new or established patients. Prospective intervention is a source of big savings, so this is a good way to document and get "credit" for it.

Ideally, there will be one form for each home so you can enter multiple patients on it. AGAIN, PLEASE PROVIDE ALL THE INFORMATION REQUESTED. PLEASE PRINT.

RETURN ALL FORMS TO YOUR DISPENSING PHARMACY ORGANIZATION'S CENTRAL OFFICE FOR FURTHER PROCESSING.

Attention Consultant Pharmacy Central Office: Forward to your project coordinator / contact person and mail completed forms to AccessCare, Inc., 3500 Gateway Centre Blvd. Suite 130, Morrisville, NC 27560-8501 Attn: NH Polypharmacy Project, PHONE 919-380-9962.

Chapter 3:
CLINICAL INITIATIVES/QUALITY INDICATORS, abbreviated version

(Please refer to Appendix B for a complete description.)

ATYPICAL ANTIPSYCHOTICS: Switch to a more cost effective agent if possible. Determine if a change to a different class of medication or a reduction in dose would be indicated as per CMS guidelines (www.cms.gov). Target polytherapy with antipsychotics for specific review.

PROTON-PUMP INHIBITORS (PPI's): Review length of therapy and make recommendation for potential D/C or switch to a more cost effective H2.

COX2 INHIBITORS (e.g. Celebrex/Vioxx, Relafen): Review residents who have a COX2 as a first-line therapy for possible switch to nabumetone or other agent. Review length of therapy. Consider D/C or change to less costly agent.

LIPID LOWERING AGENTS (Statins): Focus on patients whom may no longer clinically benefit from lipid lowering. Mevacor (Lovastatin) is available generically at a substantial savings compared to other agents in this class.

REMERON TABS TO SOL-TABS: Conversion to the Sol-Tab would save significant dollars without negative impact.

ANTI-DEPRESSANTS (SSRI): Consider change to more cost effective agent. Evaluate residents on **Prozac Once Weekly** for conversion to fluoxetine.

H2RAs: Review residents for appropriateness and length of therapy, possible dosage reduction or D/C. Refer to prepared consult forms for further explanation.

PAIN MANAGEMENT (Oxycontin, Duragesic, propoxyphene/apap): Determine appropriateness of therapy and possible switch to another agent, such as Oramorph SA, morphine sulfate ER.

SLEEP AIDS (Ambien): Convert patients from Ambien to Temazepam 7.5mg as appropriate. (lower cost alternative). Review chronic sedative-hypnotic use for possible d/c or drug holiday.

NON-SEDATING ANTIHISTAMINES: Assess rationale for continued use, length of therapy and recommend dosage reduction or discontinuation or changing dose to "as needed".

MEGACE: Evaluate length of therapy and clinical efficacy for possible discontinuation. See attached sheet for specific guidelines.

OXANDRIN: Evaluate other causes associated with weight loss to assess continued need for therapy.

ACETYLCHOLINESTERASE INHIBITORS: Evaluate whether patient is clinically benefiting from medication.

URINARY INCONTINENCE PRODUCTS: Consider change from extended release to immediate release product. If lack of efficacy, should consider a D/C of therapy.

NEURONTIN: Evaluate the effectiveness and either suggest appropriate titration of dose or if no improvement in pain syndrome scores, ask prescriber to consider D/C therapy.

ACE INHIBITORS: Conversion of ACE inhibitors to enalapril will save significant healthcare dollars while providing comparable efficacy.

****Attention Consultants***: Please remove this page and take with you for reference when you do the reviews.

Chapter 4:
Common Questions & Answers

Q: Where, when, and how often will I get these Patient medication forms?
A: You will receive your "kit" including forms to review and instructions starting in October, 2002. You will receive them from your nursing home dispensing pharmacy location. It has not been yet decided when you will receive a new set of forms.

Q: What do I do with the forms at the end of my visit to the nursing home?
A: After you have *recorded **all** results to your interventions,* submit them to **your company's main office** who will then express/priority/overnight to AccessCare in Morrisville, NC.

Q: I recommended a change to a patient's drug regimen, but I don't know if that change will be accepted/made. How do I document that on the form?
A: You must find out what happens to your recommendations! Regulations allow for approximately 30 days for follow-up on pharmacist recommendations Even if no change is made, we still want you to document your intervention (see result codes). If there is a physician that is not responding to you and is slowing your progress, please let AccessCare know ASAP. *(Contact Dr. Wegner at AccessCare 919-380-9962 or email him at swegner@ncaccesscare.org).*

Q: Which long term care patients are eligible to participate in this program?
A: Only "Medicaid" covered "nursing facility" level (i.e. ICF or SNF level) patients are eligible to participate. Patients covered by other payor sources such as Medicare-A or private are not covered by the program. In addition, assisted living level of care (i.e. rest home or adult care home level) is not covered by the program at this time.

Q: I have encountered a new Medicaid patient for which there is no form. I have a couple of recommendations for change. How do I document this encounter?
A: Your kit will have at least one blank New Patient/Prospective Intervention Form. Make copies of this and use it to record the nursing home, patient, drug, and drug change involved.

Q: I have identified a case of suboptimal therapy and have action based on a blanket authority granted to me for patients in this home. Should I document anything differently?
A: No, just be sure to circle "collaborative agreement" on the last page of the form.

Q: What if the dispensing pharmacy identifies a case of suboptimal therapy while filling an Rx for a patient the first time?
A: We want to know about it, as it counts as an intervention. It's probably best to provide them with extra copies of the New Patient/Prospective Intervention Form for this purpose. It's OK to send in 2 forms for interventions on the same patient during the same month by different pharmacists. We can combine them.

Q: What if the patient is no longer in the home when I visit the home?
A: We need to know that. Make that notation on the form and return it along with the others.

Q: What if the patient is no longer taking a drug listed on the profile?
A: We need to know that too. Draw a line through the drug entry.

Nursing Home PolyPharmacy Project - Patient Profile John Doe XXXXXX 10/29/2002

Nursing Home Practice: Nursing Home Name

Patient ID: XXXXXXXX Last Name: XXXXXXXXX First Name: XXXXXXXXX

Gender: F Age: 75 DOB: 2/22/27 Avg # of Drugs/month: 17.33 Avg monthly drug $: $1,048.82

Confidential - For record validation only. Not for inclusion in chart. Please return to AccessCare

Fill Date	Drug Class	Medication	Amount Paid	Prescriber	PAL	Potential Therapeutic Duplication	Clinical Initiatives/ Quality Indicators*	Consider Length of treatment*	Beers List ≥ 65	Problem Type	Results Type	New Drug and Strength
8/6/02	ALDOSTERONE ANTAGONISTS	SPIRONOLACTONE 25MG TABLET	$14.42	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
7/9/02	ANALGESICS, NARCOTIC	PROPOXY-NAPAP 100-650 TAB *d*	$9.00	Prescriber Name			X		X	A B C D E F G	1 2 3 4 5 6	
8/19/02	ANARACTICS - TRANQUILIZERS	LORAZEPAM 0.5MG TABLET	$11.23	Prescriber Name		X			If exceeds 3 mg daily	A B C D E F G	1 2 3 4 5 6	
7/9/02	ANARACTICS - TRANQUILIZERS	LORAZEPAM 1MG TABLET	$14.44	Prescriber Name		X			If exceeds 3 mg daily	A B C D E F G	1 2 3 4 5 6	
6/21/02	ANARACTICS - TRANQUILIZERS	ZYPREXA 2.5MG TABLET *i*	$144.04	Prescriber Name		X				A B C D E F G	1 2 3 4 5 6	
7/10/02	ANARACTICS - TRANQUILIZERS	ZYPREXA 2.5MG TABLET *i*	$144.04	Prescriber Name		X				A B C D E F G	1 2 3 4 5 6	

*Please refer to toolkit for further explanation.

Problem Type (Circle all that apply)
A. Unnecessary Drug Therapy
B. More Cost Effective Drug Available
C. Wrong Dose or Strength
D. Drug has High Potential for ADRs
E. Needs Additional Therapy
F. Not a problem at this time
G. Other - Any other problem not listed above

Results Type (Circle all that apply)
1. Dose/Delivery Changed - Dosage or administration was changed
2. Drug Added - New drug was added for previously untreated indication.
3. Drug Change - Drug was changed from one to another.
4. Drug Discontinued - Drug was discontinued or was changed to PRN.
5. No Change - Physician Responded but did not make any changes.
6. Other - Any result not listed above.

Medication Superscripts
a. Recommended check for K+ need
b. Recommended use with Ca+ supplement.
c. Recommended check for FE+ need
d. Recommended check for Stool Softener need
e. Recommend check for Folic Acid therapy.
f. Recommend check for supplemental calcium need..
g. TB test needed?
h. Does patient have BPH and HTN? Consider Cardura.
i. Consider dose reduction/excessive dose.

PAL Codes
PAL Code 1 - Preferred Drug
PAL Code 2 - No Preference
PAL Code 3 - Avoid
PA - Prior Authorization Required

Nursing Home PolyPharmacy Project - Patient Profile XXXXXXXXXXX XXXXXXXXXXX Page 2 of 7 10/29/2012

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Fill Date	Drug Class	Medication	Amount Paid	Prescriber	PAL	Potential Therapeutic Duplication	Clinical Initiatives/ Quality Indicators*	Consider Length of treatment*	Beers List ≥ 65	Problem Type	Results Type	New Drug and Strength
6/19/02	ANARACTICS - TRANQUILIZERS	ZYPREXA 5MG TABLET *i*	$334.81	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
8/2/02	ANARACTICS - TRANQUILIZERS	ZYPREXA 5MG TABLET *i*	$334.81	Prescriber Name		X				A B C D E F G	1 2 3 4 5 6	
6/21/02	ANTICOAGULANTS	COUMADIN 10MG TABLET	$16.59	Prescriber Name		X				A B C D E F G	1 2 3 4 5 6	
8/5/02	ANTICOAGULANTS	COUMADIN 10MG TABLET	$35.47	Prescriber Name						A B C D E F G	1 2 3 4 5 6	
8/22/02	ANTICOAGULANTS	WARFARIN SODIUM 5MG TABLET	$31.39	Prescriber Name		X				A B C D E F G	1 2 3 4 5 6	
8/22/02	ANTICOAGULANTS	WARFARIN SODIUM 7.5MG TAB	$18.21	Prescriber Name		X				A B C D E F G	1 2 3 4 5 6	
7/2/02	ANTIHISTAMINES	PROMETHAZINE 25MG/ML AMPUL	$33.49	Prescriber Name					X	A B C D E F G	1 2 3 4 5 6	

*Please refer to toolkit for further explanation.

Problem Type (Circle all that apply)
A. Unnecessary Drug Therapy
B. More Cost Effective Drug Available
C. Wrong Dose or Strength
D. Drug has High Potential for ADRs
E. Needs Additional Therapy
F. Not a problem at this time
G. Other - Any other problem not listed above

Results Type (Circle all that apply)
1. Dose/Delivery Changed - Dosage or administration was changed
2. Drug Added - New drug was added for previously untreated indication.
3. Drug Change - Drug was changed from one to another.
4. Drug Discontinued - Drug was discontinued or was changed to PRN.
5. No Change - Physician Responded but did not make any changes.
6. Other - Any result not listed above.

Medication Superscripts
a. Recommended check for K+ need
b. Recommended use with Ca+ supplement.
c. Recommended check for FE+ need
d. Recommended check for Stool Softener need
e. Recommend check for Folic Acid therapy.
f. Recommend check for supplemental calcium need..
g. TB test needed?
h. Does patient have BPH and HTN? Consider Cardura.
i. Consider dose reduction/excessive dose.

PAL Codes
PAL Code 1 - Preferred Drug
PAL Code 2 - No Preference
PAL Code 3 - Avoid
PA - Prior Authorization Required

Confidential - For record validation only. Not for inclusion in chart. Please return to AccessCare

Fill Date	Drug Class	Medication	Amount Paid	Prescriber	PAL	Potential Therapeutic Duplication	Clinical Initiatives/ Quality Indicators*	Consider Length of Treatment*	Beers List ≥65	Problem Type	Results Type	New Drug and Strength

Prescriptions Not Identified by Access

Start Date	Drug Class	Medication	Strength	NDC #	Prescriber	Comments or Problems Identified	Problem Type	Results Type	New Drug and Strength
							A B C D E F G	1 2 3 4 5 6	
							A B C D E F G	1 2 3 4 5 6	
							A B C D E F G	1 2 3 4 5 6	
							A B C D E F G	1 2 3 4 5 6	

For Office Use Only

Data Entered By ____ Date _____

Checked By ____ Date _____

Prospective Intervention YES NO
If yes, please document only on NewPatient Prospective Intervention Form.

Initial Chart review performed by: (Circle one) RPH MD RPH/MD(Combo)

Prescriber was contacted: (Circle one) 1) Written Consult - Written note in chart was only action.
2) Collaborative Agreement - Change made via prior agreement protocol
3) In Person - Direct physician contact
4) Mail /Phone/Fax - Recommendation faxed, phoned, mailed, or emailed.

Review performed by: _____ _____ _____
(Print Name) (Sign Name) (Date)

*Please refer to toolkit for further explanation.

Problem Type (Circle all that apply)
A. Unnecessary Drug Therapy
B. More Cost Effective Drug Available
C. Wrong Dose or Strength
D. Drug has High Potential for ADRs
E. Needs Additional Therapy
F. Not a problem at this time
G. Other - Any other problem not listed above

Results Type (Circle all that apply)
1. Dose/Delivery Changed - Dosage or administration was changed
2. Drug Added - New drug was added for previously untreated indication.
3. Drug Change - Drug was changed from one to another.
4. Drug Discontinued - Drug was discontinued or was changed to PRN.
5. No Change - Physician Responded but did not make any changes.
6. Other - Any result not listed above.

Medication Superscripts
a. Recommended check for K+ need
b. Recommended use with Ca+ supplement.
c. Recommended check for FE+ need
d. Recommended check for Stool Softener need
e. Recommend check for Folic Acid therapy.
f. Recommend check for supplemental calcium need..
g. TB test needed?
h. Does patient have BPH and HTN? Consider Cardura.
i. Consider dose reduction/excessive dose.

PAL Codes
PAL Code 1 - Preferred Drug
PAL Code 2 - No Preference
PAL Code 3 - Avoid
PA - Prior Authorization Required

Appendix B

Nursing Home PolyPharmacy Project

New Patient/Prospective Intervention Form

Nursing Home _____

Please note below only those drugs for which there was a change from the original order. Please PRINT.

Pharmacist name (print) _____ Signature: _____ Review date: _____ Company: _____

Patient name + Medicaid #	Original Drug Prescribed (& strength)	Original Rx Qty or mo. supply	Problem Type (circle only one)	Result Type (circle only one)	Changed Drug & Strength	New Rx Qty or mo. supply	Mark with an X if Prospective Intervention
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			
			A B C D E F G	1 2 3 4 5 6			

Problem Type (circle all that apply above)
A. Unnecessary Drug Therapy
B. More Cost Effective Drug Available
C. Wrong Dose or Strength
D. Drug has High Potential for ADRs
E. Needs Additional Therapy
F. Not a problem at this time
G. Other-Any other problem not listed above.

Result Codes (circle all that apply above)
1. Dose/Route Changed- Dosage or administration was changed.
2. Drug Added- New drug was added for previously untreated indication.
3. Drug Change- Drug was changed from one to another for an existing indication
4. Drug Discontinued- Drug was d/c or was changed to PRN.
5. No Change
6. Other-Any other result not listed above.

For Office Use Only
Data Entered By_____ **Date** _____
Checked By _____ **Date** _____

Appendix C

CLINICAL INITIATIVES/QUALITY INDICATORS

Tier 1

Pharmaceuticals to target for immediate cost savings

- Therapeutic Interchange of equally effective, more cost beneficial agents
- Generic substitution

Tier 2

Individual resident focus by internal and external consultant pharmacists.

- Assess appropriateness of therapy-possible alternative
- Review effectiveness of therapy-possible alternative or D/C
- Assess length of therapy-possible switch to different agent or D/C
- Review for possible less costly alternative therapy-recommend switch
- Assess for potential D/C-recommend D/C
- Assess for potential change to OTC product-recommend change
- Academic detailing to physicians and facilities regarding appropriate prescribing first-line agents.

The value of LTC clinical pharmacists in assessing the most appropriate therapies, monitoring outcomes and successful market share movement is proven and documented.

ATYPICAL ANTIPSYCHOTICS

Due to the very individual response to these agents and varied diagnoses, there is no direct interchange that would not have the potential to jeopardize resident care.

1) Review residents with true psych diagnoses for effectiveness of current therapy.
2) Review residents on these agents with a diagnosis of dementia. Assess targeted behaviors, effectiveness of current therapy, duration of therapy and current dose to determine if a switch to a more cost effective agent, change to a different class of medication or a reduction in dose would be indicated. See CMS guidelines (www.cms.gov).
3) Target polytherapy with antipsychotics for specific review.

PROTON-PUMP INHIBITORS (PPI's)

1) PPI's are often prescribed as first-line therapy without documented failure on less costly H2 antagonists. Consultants will review residents for potential switch to more cost effective H2. Evaluate as to whether patient has had an adequate trial of an H2 antagonist.
2) Review length of therapy and make recommendation for potential D/C or switch to a more cost effective H2

COX2 INHIBITORS (Celebrex/Vioxx, Relafen included)

Celebrex and Vioxx represent a widely prescribed and very costly therapy. Recent changes in drug labeling have removed the claim these agents cause fewer GI side effects. Often prescribed as a first-line therapy, there are many alternatives that could and should be tried first. The recent introduction of generic Relafen (nabumetone) further expands the list of suitable substitutes for the more costly therapies. It is important to note that of all populations the residents served by LTC are at greater risk for adverse reactions to standard NSAID's and would be more appropriately managed by the COX2 inhibitors.

1) Review residents who have a COX2 as a first-line therapy for possible switch to nabumetone or other agent. Recommended starting dose is 1000 mg as a single dose with or without food. Some patients may obtain more symptomatic relief from 1500 to 2000 mg/day. Nabumetone can be given either once or twice daily. Dosages > 2000 mg/day have not been studied. Use the lowest effective dose for chronic treatment. Patients at risk may be tried on 500mg/day initially.
2) Review length of therapy. Possible discontinuation or change to less costly agent.
3) Educate physicians and facilities on significant cost differential between COX2 and other classes.
4) Patients whom do require treatment with a COX2, consider converting to Celebrex (if not sulfa allergic). Also, review dose of medications to make sure they are appropriate for the geriatric population.

Vioxx
OA: The recommended starting dose is 12.5 mg once daily. Some patients may receive additional benefit by increasing the dose to 25 mg once daily. The maximum recommended daily dose is 25 mg.
RA: Recommended dose is 25 mg once daily. The maximum recommended daily dose is 25 mg.

Celebrex:
OA: Recommended dosage is 200 mg/day administered as a single dose
RA: Recommended dosage is 100 to 200 mg twice/day.

Bextra:
OA/Adult RA: 10 mg once daily

LIPID LOWERING AGENTS (Statins)
Consultants will review residents who have been on statin therapy to determine if continuation of therapy is appropriate. Specifically focus on patients whom may no longer clinically benefit from lipid lowering therapy (i.e. patients with advanced Alzheimer's Dz or metastatic Ca). Therapies may be D/C'ed or dosages reduced.

Be aware that some studies have documented benefit in patients >70 yo with multiple risk factors (age is a risk factor as well as HTN, cigarette smoking, CAD, PVD, family Hx CAD, diabetes, AAA). Heart Protection Study (*Lancet, Vol. 360, July 6, 2002) included 5806 patients >/= 70 yo which had a clinically and statistically significant redcuction in vascular event.*

Some evidence is now available that Lipitor can be dosed on an "every-other-day" regimen and still meet therapeutic goals.

Mevacor (lovastatin) is available generically at a substantial savings compared to other agents in this class. Mevacor (lovastatin) is less potent (29 % to 31 % reduction in LDL at 20 to 40 mg dose and 40% reduction at 80 mg dose) compared to Zocor and Lipitor but lipid lower goals can be achieved in mild to moderate levels of hyperlipidemia.

Mevacor (lovastatin) is contraindicated in severe renal impairment and is primarily metabolized by the Cytochrome 3A4 isoenzyme system.

Mevacor (lovastatin) is indicated for both primary and secondary prevention of coronary events. Please refer to the Statin conversion table at the end of this document to convert other statins to equipotent doses of lovastatin.

Mevacor (lovastatin) should be dosed with the evening meal to enhance bioavailability.

REMERON TABS TO SOL-TABS

Remeron tablets are more costly than the equivalent Sol-Tab formulation. Conversion to the Sol-Tab would save significant dollars without negative impact to the residents. Actually, this dosage form provides a more flexible profile for administration to elderly residents.

ANTI-DEPRESSANTS (SSRIs)

There are multiple agents available in this category with similar profiles. Also, Prozac is now available generically. Under-recognition and under-treatment of depression is a significant issue in the institutionalized elderly. Clinical pharmacists can educate and direct physicians to the most clinically suitable and cost effective choices.

1) Residents will be evaluated for effectiveness of therapy. Recommendations for change to more cost effective agent will be made when appropriate.
2) Evaluate residents on Prozac Once Weekly to see if appropriate to convert to fluoxetine. Also, consider the fact that some patients may do just as well on "every-other day" dosing of fluoxetine.

H2 ANTAGONISTS

1) Consultants will review residents for appropriateness and length of therapy, possible dosage reduction or discontinuation indicated.
2) Educate physicians and facilities regarding cost effective choices for first-line prescribing.
3) Some H-2 Blockers should be adjusted in renal impairment. Further cost savings can be achieved by adjusting ranitidine based on renal function.

Renal impairment (Ccr < 50 mL/min): 150 mg orally every 24 hours. The frequency of dosing may be increased to every 12 hours or further with caution.

PAIN MANAGEMENT (Oxycontin, Duragesic, propoxyphene/apap)

Management of pain is highly individual. Effective pain control, quality of life issues and resident dignity must all be considered when choosing pharmaceutical agents. There are options that can be equally effective and lower in cost.

Tier 1

A potential alternative to both Oxycontin and Duragesic is generic MS Contin (Oramorph SA, morphine sulfate ER). Based on the individualized aspect of this therapy, even a modest switch to Oramorph has potential for significant savings. The committee feels as many as 30% of Oxycontin prescriptions have the potential to be changed. Duragesic will be more individual and be reviewed in the Tier 2 process.

Propoxyphene/apap is a drug that has questionable benefit over acetaminophen alone. As well, propoxyphene is an inappropriate drug for use in the elderly due to the side effect profile. LTC targets this drug already for interchange to another entity. More dedicated resources and education could further increase the savings already realized by this initiative.

Tier 2

1) Assess effectiveness of therapy, diagnosis and usage (PRNs) to determine if alternative therapy or discontinuation is indicated.
2) Educate facility on non-pharmacologic interventions related to pain control.
3) Work with facilities to assess resident pain and choose/recommend appropriate agents.
4) Assess residents on Duragesic to determine appropriateness of therapy and potential switch to another agent, specifically those who have not had a trial on an oral first-line therapy.
5) Be cautious with using Morphine in patients with poor renal function as active metabolites may accumulate and result in oversedation.
6) Educate physicians and facilities regarding appropriate agents for initial prescribing.

SLEEP AIDS (Ambien)

The committee feels an appropriate switch for our resident population would be in most cases temazepam 7.5mg, an underutilized shorter-acting sedative with minimal effect on REM sleep that does not form long-acting metabolites and may minimize potential hang-over.

Tier 1

Convert patients from Ambien to Temazepam 7.5mg as appropriate

Tier 2

1) Pharmacists will evaluate continued need for sleep aids and recommend reduction in dosage or possibly discontinuation.
2) Education of facility staff regarding non-pharmacologic approach to insomnia.

NON-SEDATING ANTIHISTAMINES

Second generation antihistamines tend to be used frequently in the elderly for indefinite periods of time. Some use is for seasonal or episodic needs, yet the resident remains on

therapy without significant assessment for continued need.

1) Assess length of therapy and recommend dosage reduction or discontinuation or changing dose to "as needed". Note: Claritin, Allegra and Clarinex have recommended dose adjustment in renal impairment.
   Claritin:

   Hepatic/Renal function impairment (GFR < 30 mL/min):
   Adults and children >= 6 years of age: 10 mg every other day as starting dose

   Clarinex:

   Adults and children >= 12 years of age: The recommended dose is 5 mg once daily. In patients with liver or renal impairment, a starting dose of one 5 mg tablet every other day is recommended based on pharmacokinetic data.

   Allegra:

   Renal function impairment:
   Adults and children >= 12 years of age: 60 mg once daily as a starting dose.
2) Educate physicians and facilities on shorter duration orders for these agents.
3) Assess for potential switch to OTC antihistamine (consider the risk of anticholinergic side effects when doing this!).

MEGACE

Many elderly long-term care residents are placed on Megace or Megestrol for weight loss. However, the literature support for use of this medication in this situation is very limited. **Megace** is a progestin indicated for cachexia associated with AIDS wasting syndrome often used in elderly patients with unexplained weight loss. In clinical trials doses of 400mg to 800mg were clinically effective.

In elderly patients, with unexplained weight loss, studies indicate that 12 weeks of therapy is adequate to evaluate efficacy.

Please assess length of therapy, weight prior to Megace and current weight to assess continued efficacy. Also assess other potential causes of weight loss including side effects from other medications, functional decline, acute clinical or mental status changes, dentition and other factors.

In most cases, any weight gain is related to fluid volume expansion. This medication, whether in brand name or generic is very costly.

1) Consultant pharmacists evaluate length of therapy and clinical efficacy to consider possible discontinuation. If patients have been on therapy for > 3 months without any change in weight or with continued weight loss, consider discontinuing therapy.

2) Educate prescribers on the cost of this medication and limited support for clinical effectiveness.

OXANDRIN

Oxandrin (oxandrolone) is an anabolic steroid used as adjunctive therapy to promote weight gain in patients who fail to gain or maintain weight. Efficacy is dependent on adequate protein intake to promote subsequent metabolism.

Oxandrin is expensive and therapy should be limited to 2 to 4 weeks. Please evaluate other causes associated with weight loss to assess continued efficacy.

ACETYLCHOLINESTERASE INHIBITORS

The clinical effectiveness of this class of medication in a group of patients with Alzheimer's Dementia and Vascular Dementia may be good. However, generally these patients need to be caught in an early phase of the dementia to benefit most. Also, there is some information that these medications may help control behaviors associated with dementia and reduce the need for psychoactive medications. Keep in mind that in some patients, discontinuation may lead to rapid decline, especially in terms of behaviors. At most, this class of medications slows the inevitable decline in cognitive function and may initially, mildly improve cognitive behavior. However, it is often the case that patients with very advanced dementia wind up on this class of medication long past any clinical benefit.

1) Consultant pharmacists may conduct a MMSE to evaluate patient's overall cognitive function and follow this while patient is on medication. If MMSE continues to worsen drastically OR is extremely low (*Cutoff recommendation should be as high as 17/30 or as low as 10/30*), consider discontinuation.

2) Evaluate patients for very advanced cases (end-stage) of dementia and evaluate whether patient is clinically benefiting from medication.

URINARY INCONTINENCE PRODUCTS

Urge incontinence is prevalent, especially in elderly females. Patients are typically placed on a long-acting product, before using a trial of a less expensive, generically available immediate release product.

The efficacy of the extended release products is similar to the immediate release products, however, it is prudent for the consultant to monitor for potential anticholinergic side effects. Additionally, these products should show efficacy within the first four weeks of therapy.

1) Assess for medication/reversible causes of incontinence.
2) Consider change of extended release product to immediate release product. Monitor for potential increased incidence of anticholinergic side effects.
3) Monitor for efficacy – lack of efficacy should consider a D/C of therapy.
4) Educate physicians and facilities on significant cost differential between oxybutnin IR and oxybutnin XR, and tolterodine IR and tolterodine LA.

NEURONTIN

If Neurontin is being used for seizure prophylaxis/treatment, do not address. However, Neurontin is often used as adjunctive therapy in many different pain syndromes, most commonly neuropathy. Often this medication is started for pain control and either titrated incorrectly (high enough doses never obtained) OR never reassessed for effectiveness. Consultant Pharmacists should evaluate the effectiveness of Neurontin and either suggest appropriate titration of dose (most studies indicate at least 300mg TID must be obtained to relieve pain and many studies go as high as 1200mg TID or higher) or if adequate trial has been given without improvement in pain syndrome scores (neuropathic pain), ask prescriber to consider discontinuation of therapy.

ACE INHIBITORS

There are multiple agents in this category with similar profiles. Despite minor variations, ACE inhibitors tend to exhibit a "class effect" in treatment. Conversion of ACE inhibitor therapy in PAL 2 or 3 to enalapril will save significant healthcare dollars, while providing comparable efficacy. This conversion should be considered when appropriate. Consultants should monitor BP's after conversion to enalapril. Of course, monitoring of renal function and potassium is also recommended.

ACE Inhibitor Equivalent Dosing

Drug	Brand Name	Dose
Benzapril	Lotensin	10mg
Enalapril	**Vasotec**	**5mg**
Fosinopril	Monopril	10mg
Lisinopril	Prinivil, Zestril	10mg
Moexipril	Univasc	7.5mg
Quinapril	Accupril	10mg
Ramipril	Altace	2.5mg
Trandolapril	Mavik	1mg

Characteristics Of The Various Statins

	Lovastatin (Mevacor)	**Pravastatin** (Pravachol)	**Simvastatin** (Zocor)	**Fluvastatin** (Lescol)	**Atorvastatin** (Lipitor)
Potency: Average Decrease m LDL-Chol.	20 mg: 29% 40 mg: 31% 80 mg: 40%-48%	10 mg: 19% 20 mg: 24% 40 mg: 34% 80 mg: 40%	10 mg: 28% 20 mg: 35% 40 mg: 40% 80 mg: 48%	20 mg: 17% 40 mg: 23% 80 mg: 33%	10 mg: 38% 20 mg: 46% 40 mg: 51% 80 mg: 54%
Renal Function	Use lower does for severe renal impairment (creatimine clearance <30mL/min).	Use lower doses for moderate to severe renal impairment (reduce initial dose for creatimine clearance <60mL/min).	Use lower doses for severe renal impairment (reduce initial dose to 5 mg daily).	No dose adjustment necessary for reduced renal function.	No dose adjustment necessary for reduced renal function
Liver Function Monitoring	LFT's at baseline. Also, at 6 and 12 weeks after start of therapy or elevation of dose. Then every 6 months thereafter.	LFT's at baseline. Also, prior to elevation of dose, and when otherwise clinically indicated.	LFT's at baseline. Also, every 6 months for the first year of treatment or until 1 year after the last elevation in dose. Patients titrated to 80 mg should receive an additional test at 3 months	LFT's at baseline. Also, at 12 weeks after initiation or elevation of dose.	LFT's at baseline. Also, at 12 weeks following both the initiation of therapy and dose elevation. Check every 6 months thereafter
Drug Interactions	Metabolized by CYP3A4 enzyme system. Watch for interactions with other drugs metabolized by this enzyme including: erythromycin, clarithromycin, ketoconazole, verapamil, diltiazem, nefazodone, fluvoxamine, cyclosporine, grapefruit juice, etc.	Not significantly metabolized by cytochrome P250 and may be less likely to be involved in drug interactions	Metabolized by CYP3A4 enzyme system, Watch for interactions with other drugs metabolized by this enzyme including: erythromycin, clarithromycin, ketoconazole, verapamil, diltiazem, nefazodone, fluvoxamine, cyclosporine, grapefruit juice, etc.	Metabolized by CYP2C9 enzyme systems and may be less likely to be involved in drug interactions. Fluvastatin can increase levels of cyclosporine and phenytoin. Rifampin can lower fluvastatin levels.	Metabolized by CYP3A4 enzyme system, but less than lovastatin and simvastatin. Some drugs metabolized by CYP3A4 include: erythromycin, clarithromycin, ketoconazole, verapamil, nefazodone, fluvoxamine, cyclosporine, grapefruit juice, etc.
Food Interactions	Take with dinner	Take without regard to meals	Take without regard to meals	Take without regard to meals	Take without regard to meals
Clinical Benefit	Reduces coronary events, but hasn't been shown to improve survival.	Reduces overall mortality and death due to coronary heart disease	Reduces overall mortality and death due to coronary heart disease	Slows CHD progression but hasn't shown to reduce clinical events or improve survival.	There's preliminary evidence of improved outcomes in patients with CHD

Users of this document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Adapted from *The Pharmacists Letter 2002 by Therapeutic Research Center, www.pharmacistletter.com*

Appendix D

October 14, 2002

Dear Medical Director:

As a member of the Carolina Access II & III Community Care Projects, I would like to introduce you to a new Medicaid program, a PolyPharmacy Initiative, in which your participation will be instrumental. Carolina Access II & III currently is responsible for 235,000 enrollees and is an enhanced care management program in select communities that is working in partnership with the State to better manage the care of the Medicaid population. I am the Medical Director for AccessCare which is entirely owned and managed by physicians and is one of the Access II & III programs. Our primary objective in Access II & III is to build community-based health care systems that are able to impact access, quality, utilization, and cost objectives. In the past three years, we have successfully set up processes, developed and implemented programs focusing on Medicaid recipients with specific diagnoses, such as Asthma and Diabetes. As you may well know, the State of North Carolina faces more deficits next year. It is important that all providers – long-term care facilities, managers, nurses, doctors and pharmacists work together to be as cost effective as possible so that providers and recipients do not face further cuts.

AccessCare is one of the Access II & III programs, and is acting on behalf of these programs and Carolina Access to help lead the PolyPharmacy Initiative. We will be expanding our pilot nursing home initiative, conducted last summer, from thirteen (13) local nursing homes to all nursing homes Statewide. Our approach included a team comprised of the attending physician/medical director and a clinical pharmacist reviewing, together, a patient's prescription regimen. The pilot program was very successful, saving over one hundred thousand dollars in just 13 facilities. Expanding the program statewide has the potential for saving several millions of dollars.

The statewide initiative will be accomplished through a partnership with the Long-Term Care Pharmacists of North Carolina in an approach similar to the pilot. Medicaid recipients that meet specified criteria will be screened for potential review by the PolyPharmacy team. Our overall goal of the nursing home PolyPharmacy Initiative is to improve the quality of care by reviewing drug regimens and to make appropriate recommendations in a consultative manner. Equipped with prescription regimen information concerning your Medicaid nursing home residents, clinical pharmacists will closely review the respective patient charts with a special concern toward cost effectiveness. They will then recommend any changes in prescriptions to attending physicians, who make the final prescription decisions. Patient health information will be treated with the utmost confidence, as is current standard procedure for long-term care pharmacists. State surveyors will also be informed of the details of this initiative.

Any changes will be captured in the data and an analysis of the results will be conducted by Dr. Dale Christensen at the University of North Carolina, School of Pharmacy. We are confident, especially as a result of the pilot study last summer, that there will be significant opportunities for improved cost effective care. We are also confident that there will be no reduction in quality of care, and in actuality, as a result of this special review of your residents' prescription regimens, there will be an overall improvement in quality.

Your willingness to partner and collaborate in the PolyPharmacy initiative with the Access II & III local physician leadership, North Carolina Association of Pharmacists, North Carolina Long Term Care Pharmacy Alliance and the State is most appreciated. Your time commitment should be minimal, however, please try to respond quickly to Consultant Pharmacists and their requests. Your sincere

efforts with this project should help the State's ability to retain its rather unrestricted approach to the prescription writing process. Success to date in the Access II & III program is due to strong community and physician leadership and the willingness of Medicaid providers to work in concert with the State's goals and objectives.

Thanks for being part of an on-going effort to better serve the Medicaid recipients in our communities.

Sincerely,

Steven Wegner, MD
Access II and III

Appendix E

Project Background

In the fall of 2001, the long term care pharmacy alliance (LTCPA) began discussions with N.C. Medicaid to evaluate proactive ways to improve the quality of patient care and decrease medication-related expenditures. During this same time period, LTCPA, via a connection from the NC Association of Pharmacists (NCAP), collaborated with AccessCare, Inc to conduct a pilot "Poly-pharmacy Initiative" study with 13 participating nursing homes. Preliminary results indicated a 13:1 benefit-to-cost ratio by having consultant pharmacists perform specific clinical/quality interventions. Meanwhile, in the summer of 2002, LTCPA continued to negotiate with the leadership at NC Medicaid to consider alternative cost-saving interventions that would save the Medicaid department money and avoid an additional Medicaid dispensing fee cuts for LTC pharmacies. Visionary leadership in the department recognized the value in having consultant pharmacists collaborate with physicians to improve quality of care and reduce medication-related expenditures. Subsequently, this led to expansion of the Poly-pharmacy Initiative statewide study to include nearly all nursing homes.

This initiative is important for every consultant pharmacist in NC! It begins in October 2002 and funding is committed through September 2003. No other State Medicaid department has supported this type of initiative in the long term care setting! The real challenge is ahead of us because each consultant pharmacist will be held accountable for implementing the Poly-pharmacy initiatives in the nursing facilities he serves. Periodic assessments will be done to measure the progress of the program. Progress reports will be forwarded to the administrative leadership at NC Medicaid. Successful implementation of this project will facilitate future, constructive negotiations with Medicaid to reimburse consultant pharmacists for their clinical initiatives and minimize their focus on reduction of dispensing fees.

AccessCare, Inc. will be coordinating this project. AccessCare is a network of primary care physicians committed to providing the highest quality medical care for the Medicaid population of North Carolina.

Since April 1991, a growing number of NC Medicaid recipients have received services within the framework of Carolina ACCESS, a primary care coordination program currently functioning in 99 counties. Carolina ACCESS was developed in an effort to create a more efficient and effective health care system for Medicaid enrollees. Specifically, Carolina ACCESS set out to enhance access to primary care and to improve the coordination of medical services for the underserved. The program emphasizes a working partnership between the state and local communities, with primary care providers playing a pivotal role in program development and operation. In addition, under Carolina ACCESS, recipients are assured access to a continuity of care through assignment to a primary care provider.

Access II & III are demonstration programs established in 1998 that builds on Carolina ACCESS. Access II & III assist local providers in developing managed care delivery systems that coordinate a continuum of health care with processes to influence cost and quality. The program is administered by the North Carolina Office of Research, Demonstration, and Rural Health Development and is sponsored by the Division of Medical Assistance (DMA) and the North Carolina Foundation for Alternative Health Programs, Inc.

AccessCare is one of eleven demonstration projects within the ever growing Access II & III programs in the state. A not-for-profit organization, AccessCare was designed to improve access to medical services, maintain quality of care, and reduce costs for the Medicaid population. Established in July 1998, AccessCare seeks to expand and improve access to care for the Medicaid population of North Carolina through a statewide network of 30 primary care practices with about 340 primary care physicians, and over 100,000 Medicaid enrollees. Together, Access II & III programs are comprised of over 150 primary care practices with about 1,400 primary care physicians, and over 235,000 Medicaid enrollees. Steve Wegner, M.D., J.D. is the Executive Director of AccessCare, Inc.

AccessCare focuses on four areas to accomplish its mission:

1. Employment of Local Care Managers who work closely with provider practices, enrollees, and local community organizations

2. Ongoing development of infrastructure solutions (e.g., web-based case management systems, hand-held computers with drug reference information) which offer providers an effective vehicle to collect and receive data and track clinical resources

3. Utilization of accredited nurse triage services which use standardized and approved protocols to give appropriate medical advice to clients in an effort to avoid unnecessary admissions or emergency room visits

4. A cohesive system-wide education effort to help patients understand and carefully select the best place to receive care based on their presenting complaint

2002 Projects

- Enhancements to the Case Manager Web Application, also including CAP and ABCD Programs for several Access II & III sites.
- Refocused on providing immediate case management and improved cost effective care to high risk, high volume or problematic diagnosis related members.
- Launched a Prescription Advantage List (PAL) - prescription reference data integrated through the widely popular physician application, ePocrates that is now available on hand-held PDA devices.
- Conducted pilot PolyPharmacy Initiative study with 13 participating nursing homes. Preliminary results indicate a 13:1 benefit-to-cost ratio.
- **Expanded PolyPharmacy Initiative study statewide to include nearly all nursing homes, with exclusions for a few based on unique criteria.**

Appendix F

Prescription Advantage List (PAL)*

(The number 1 alternative will also be listed on the existing patient intervention form.)

Drug Class	#1	#2	#3
PPIs	Protonox	Prevacid Aciphex	Nexium Prilosec
H2RAs	ranitidine famotidine		Zantac Pepcid Tagamet, cimetidine Axid, nizatidine
SSRIs	fluoxetine	Celexa Paxil, Paxil CR Zoloft Fluvoxamine Lexapro	Prozac Prozac Weekly
Statins	lovastatin	Lescol, Lescol XL Pravachol	Lipitor Mevacor Zocor
Non-Sedating Antihistamines	Zyrtec Allegra		Clarinex Claritin Claritin Reditabs
ACE Inhibitors	captopril enalapril lisinopril	Lotensin Monopril Univasc, Aceon Accupril, Altace Mavik	Capoten Vasotec Prinivil Zestril
Fluoroquinolones	Noroxin Maxaquin	Cipro Levaquin Tequin	Avelox
Macrolides	Generic erythromycin products, E.E.S., Erythrocin Ery-tab, E-mycin	Zithromax Biaxin XL Ery-Ped Eryc P.C.E.	Biaxin Dynabac
Inhaled Beta Agonists	albuterol Combivent MDI	Serevent Serevent Diskus Maxair Autohaler Foradil	Xopenex , Proventil Proventil HFA Ventolin Ventolin HFA AccuNeb Alupent, Maxair DuoNeb
Inhaled Corticosteroids	Pulmicort Turbuhaler Flovent 220mcg Advair	Pulmicort Respules Flovent 110mcg Aerobid, Aerobid-M Flovent Rotadisk 100 & 250mcg, Azmacort	Qvar, Flovent 44mcg, Flovent Rotadisk 50mcg

* The Prescription Advantage List is a *voluntary* list developed by a group of physicians that ranks drugs within 10 different therapeutic categories according to cost (1 being least expensive, 3 most expensive).

APPENDIX G: REPRINT PERMISSIONS

Evaluation #1, The American Journal of Geriatric Pharmacotherapy

Troy Trygstad
2210 Kerr Hall
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March 31, 2006

Gail Gallo, Manager, Reprints and Permissions, AGJP

Dear Gail:

I am completing a doctoral dissertation at The University of North Carolina entitled "An Analysis of the Nursing Home Polypharmacy Initiative". I would like your permission to reprint in my dissertation excerpts from the following:

Christensen D, Trygstad T, Sullivan R, Garmise J, Wegner SE. A pharmacy management intervention for optimizing drug therapy for nursing home patients. Am J Geriatr Pharmacother. 2004 Dec;2(4):248-56.

The excerpts to be reproduced will be included as an Appendix.

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Sincerely,

Troy Trygstad PharmD MBA PhD Candidate

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Gail Gallo, Manager, Reprints and Permissions, The American Journal of Geriatric Pharmacotherapy

Date: April 3, 2006

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Evaluation #2, The Journal of Managed Care Pharmacy

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March 31, 2006

Tamara Faggen, Managing Editor, Journal of Managed Care Pharmacy

Dear Tamara:

I am completing a doctoral dissertation at The University of North Carolina entitled "An Analysis of the Nursing Home Polypharmacy Initiative". I would like your permission to reprint in my dissertation excerpts from the following:

Trygstad T, Christensen D, Garmise J, Sullivan R, Wegner S. Pharmacist response to alerts generated from Medicaid pharmacy claims in a long-term care setting: results from the North Carolina polypharmacy initiative. *J Manag Care Pharm.* 2005;11(7)575-83.

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Troy Trygstad PharmD MBA PhD Candidate

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Tamara Faggen

Tamara Faggen, Managing Editor, Journal of Managed Care Pharmacy

Date: 3/31/06

Troy Trygstad
106 Kenilworth Place
Chapel Hill, NC 27516

March 31, 2006

John Bristol, Vice President, Finance and Operations, AccessCare of North Carolina

Dear John:

I am completing a doctoral dissertation at The University of North Carolina entitled "An Analysis of the North Carolina Nursing Home Polypharmacy Initiative". I would like your permission to reprint in my dissertation excerpts from the following:

The North Carolina Nursing Home Polypharmacy Toolkit, Version 1.

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Sincerely,

Troy Trygstad PharmD MBA PhD Candidate

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USE REQUESTED ABOVE:

John J Bristol

John Bristol, Vice President, Finance and Operations

Date: 4/4/06

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