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Dear Blackburn,

Thank you for your time and interest in this project. I greatly appreciate the guidance and support you've given me over the years.

Patty

THE IMPACT OF A MEDICATION PROFILE RELEASE PROGRAM ON OUTPATIENT DRUG USE: AN EVALUATION OF SASKATCHEWAN'S PATIENT PROFILE RELEASE PROGRAM

A Thesis Submitted to the College of
Graduate Studies and Research
in Partial Fulfilment of the Requirements
for the Degree of
Master of Science in Pharmacy
in the College of Pharmacy and Nutrition
University of Saskatchewan
Saskatoon, Saskatchewan

By
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Spring 1996

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ABSTRACT

The Patient Profile Release Program was designed to promote optimal drug use in Saskatchewan by identifying individuals who are at risk for drug-related problems and communicating these drug use concerns to the physicians and pharmacists responsible for their care. During 1992, the PPRP had three components — the Extreme User, Polypharmacy and Polyprescriber Programs — which monitored for the use of high dosages of mood-modifying drugs and asthma medications, the use of multiple different drugs and the use of multiple prescribers, respectively. Similar programs have been implemented elsewhere; however, there is little objective evidence that these programs effectively influence physician prescribing practices and improve patient drug use.

The objectives of the present investigation were to describe the individuals who were identified by the PPRP in 1992, evaluate the impact of the PPRP on drug use by these patients and describe the use of mood-modifying drugs and asthma medications in the province of Saskatchewan. An historical cohort study with a 3.5 month follow-up period was used to evaluate the impact of the PPRP. The study population included all individuals who had a profile released under the Program during 1992. Profiles for the intervention group subjects were released at the time that they were identified whereas profile release for the comparison group subjects was delayed for at least two months after the index identification. Re-identification by the PPRP was the primary outcome of interest.

During 1992, 3124 individuals were identified by the PPRP, of which 2542 (81%) were eligible for inclusion in this study. 58.7%, 25.1% and 15.3% of the subjects were identified under the ExU, PPh and PPr Programs, respectively. The ExU and PPh subjects tended to be female and elderly. Women were also more likely than men to be identified under the PPr Program.

For all three Program components, the intervention group subjects were significantly less likely than comparison group subjects to be re-identified by the PPRP. This reduction in the likelihood of re-identification persisted even after controlling for

differences between the study groups with respect to age, sex, residence, coverage type, the numbers of pharmacies and prescribers during the pre-identification period, hospitalization during the follow-up period, the level of extreme use and the number of different drugs. A long-term descriptive analysis of the intervention group subjects demonstrated that re-identification continued during the 9 month post-intervention period. This finding highlights the need for ongoing feedback.

The findings of the present investigation indicate that the release of patient medication profiles under Saskatchewan's PPRP was associated with a reduction in the risk of re-identification during a short-term follow-up period. Since re-identification is a marker of changes in drug utilization, the findings indicate that profile release was associated with a decreases in the level of drug use, the number of different drugs and the number of different prescribers for individuals identified under the ExU, PPh and PPr Programs, respectively. Given the high threshold criteria for identification under the PPRP, the observed decreases in drug utilization reflect an improvement in the quality of patient drug use.

ACKNOWLEDGEMENTS

With sincere appreciation, I would like to express my gratitude to the following people:

Special thanks to Dr. Sylvia Wallace, my supervisor, for her guidance, encouragement and timely advice throughout my program.

To Dr. Nigel Rawson for his timely reviews and his constructive and insightful comments during the preparation of this thesis.

To Drs. Jim Blackburn and Ted Hawes, for their guidance and support.

To Dr. Bruce Reeder, my external examiner, for his time, interest and valuable editorial comments.

To the Saskatchewan Prescription Drug Services Branch, for generously providing the data on which this study was based, and in particular, to Margaret Baker for her valuable comments and suggestions, especially during the infancy of this project. And although this study is based on data provided by Saskatchewan Health, the interpretation and conclusions are solely those of the author and do not necessarily represent Saskatchewan Health or the Government of Saskatchewan.

To Health Canada, through the National Health Research and Development Program, and Parke-Davis Canada for their generous financial support of my graduate work. Thanks to the Saskatchewan Pharmaceutical Association and the Pepper family for their provision of the Alf Pepper Research Award.

To my fellow graduate students, past and present, for their friendship, understanding and support. And special thanks to Mary Rose, Michiko, Barb, Linie, Margaret, Karen, Kathy and Laurie whose continuing friendships are an additional reward to this endeavour.

To many friends for their good company and healthy diversions throughout my graduate program.

To Mom, Dad and my brother Paul for their encouragement and support in everything I do. Thanks for believing in me. And to my dog, Dreyfus, who never fails to make me laugh.

To my husband Doug who was a constant source of understanding, encouragement and support. Thanks for being there for me.

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LIST OF ABBREVIATIONS

AHFS	- American Hospital Formulary Service
ANOVA	- Analysis of Variance
Bens	- Beneficiaries
BZD	- Benzodiazepine
CI	- Confidence Interval
CME	- Continuing Medical Education
COPD	- Chronic Obstructive Pulmonary Disease
DDD	- Defined Daily Dose
EDS	- Exception Drug Status
ExU	- Extreme Use
HSN	- Health Services Number
HIRF	- Health Insurance Registration File
JCDU	- Joint Committee on Drug Utilization
NA	- Narcotic Analgesic
OR	- Odds Ratio
OTC	- Over-the-Counter Medication
PDSB	- Saskatchewan Prescription Drug Services Branch
PPh	- Polypharmacy
PPr	- Polyprescriber
PPRP	- Patient Profile Release Program
RR	- Relative Risk
RR_{MH}	- Relative Risk Derived from the Mantel-Haenszel Procedure
Rx	- Prescription
SAP	- Saskatchewan Assistance Plan
SD	- Standard Deviation
SE	- Standard Error
SPDP	- Saskatchewan Prescription Drug Plan

1.0 Introduction

Medications play an important role in society. In fact, drug therapies are the most commonly used treatments in medical practice (Soumerai and Lipton 1994). For example, it has been estimated that one-half to three-quarters of all physician visits result in the prescription of at least one medication (Rokstad et al. 1995; Soumerai et al. 1989; West et al. 1977). In the province of Saskatchewan, two thirds of residents eligible for coverage under the Saskatchewan Prescription Drug Plan received at least one outpatient prescription in 1989 (Quinn et al. 1992a). Widespread use of medications has also been described elsewhere in Canada (Aoki et al. 1983; Chaiton et al. 1976; Lexchin 1992; Tuominen 1988) and in other countries (Anderson 1980; Murdoch 1980; Hohmann et al. 1991).

One of the reasons that drugs have come to play such an important role in medical practice is that they provide an effective means of treating a wide variety of diseases. When used appropriately, many drugs are powerful therapeutic agents with unquestionable health benefits. The ability to cure infections with antibiotics, control high blood pressure with antihypertensives and relieve pain with analgesics are just a few examples of these benefits. Unfortunately, drugs also have the potential to produce many undesirable effects. Some adverse reactions are unpredictable and occur despite appropriate drug use. However, many adverse drug effects are both predictable and preventable (Lee and Bergman 1994). Inappropriate drug use increases the risk that these preventable adverse effects will occur and also decreases the likelihood that the beneficial effects of drugs will be realized.

Recognizing that many of the problems associated with drug use are preventable, various investigators and organizational or governmental bodies have

initiated programs aimed at improving drug utilization. One such strategy was the implementation of an educational profile release program to promote optimal drug use in the province of Saskatchewan. The present investigation was designed to evaluate the impact of Saskatchewan's Patient Profile Release Program on drug use by Saskatchewan residents.

1.1 Saskatchewan's Patient Profile Release Program

1.1.1 Background

Saskatchewan's Patient Profile Release Program (PPRP) was designed to promote rational drug use by helping physicians and pharmacists monitor their patients. The PPRP was an initiative of the Joint Committee on Drug Utilization (JCDU). This multidisciplinary committee was appointed by Saskatchewan's Minister of Health and has representation from the Saskatchewan Department of Health, the Colleges of Medicine and Pharmacy at the University of Saskatchewan and the regulatory bodies and professional associations of medicine, pharmacy and nursing. The mandate of the JCDU is to identify and analyze concerns related to drug utilization, recommend appropriate methods of dealing with such concerns and provide information that may be used in educational programs for health professionals and the public (Blackburn et al. 1990).

The PPRP was first implemented in 1979 as a result of concerns identified by the JCDU in its review of mood-modifying drug use in Saskatchewan (Joint Committee on Drug Utilization 1979). The format of the program has been modified several times since its inception. The first version focussed on high levels of drug use. Under this program, individuals who received quantities of mood-modifying drugs which exceeded the dosage criteria established by the JCDU were identified from computerized prescription claims on a quarterly basis. Medication profiles of these "extreme users" were sent to their attending physicians and primary dispensing

pharmacy. This version of the program operated until mid-1987, when changes in the way prescription claims were processed by the Saskatchewan Prescription Drug Plan (SPDP) made accurate determination of drug use on an individual patient basis impossible and resulted in discontinuation of the profile release program (Joint Committee on Drug Utilization 1991).

In 1989, further changes in the processing of prescription claims permitted the introduction of a small-scale manual version of the profile release program (Joint Committee on Drug Utilization 1991). This version continued to monitor for extreme use of mood-modifying drugs, but focussed only on those beneficiaries who received two or more prescriptions for the same drug from different physicians and pharmacies within a seven day period. An advantage of this manual program over the earlier version was that it allowed for a more timely release of profiles to prescribers and pharmacies (i.e. within days of identification of a potential concern rather than on a quarterly basis). An obvious disadvantage was that monitoring was limited to a highly select group of individuals.

In January 1992, the manual program was replaced by an expanded, computerized version of the profile release program. Computerization made it once again possible to monitor all Saskatchewan beneficiaries rather than limiting the review process to the small group of individuals monitored by the manual program. In addition, the monitoring process was expanded to include three types of potential drug use problems: extreme use of mood-modifying drugs and asthma medications, use of multiple medications and use of multiple prescribers. Medication profiles for individuals identified as exceeding program criteria were released to their physicians and pharmacies on a biweekly basis.

The most recent change to the PPRP occurred in October 1994, when the JCDU limited the monitoring process to extreme use of bronchodilators and lowered the dosage criteria for these drugs (Saskatchewan Health 1995). To accommodate the increased volume of profiles resulting from the lower dosage criteria, the JCDU temporarily suspended monitoring for extreme use of mood-modifying drugs and for the

use of multiple drugs and prescribers. Medication profiles for extreme users of bronchodilators are released to their physicians and pharmacies on a biweekly basis. In addition, a letter is sent to the patients informing them that their profiles have been released and encouraging them to consult with their physician and pharmacist.

The third version of the PPRP is the subject of the present investigation. Unless otherwise specified, all future references to the PPRP in this document refer to the version of the program which operated from January 1992 to September 1994.

1.1.2 Objective of the Program

The PPRP was designed to encourage the appropriate use of outpatient prescription medications by Saskatchewan residents. To fulfil this objective, the JCDU established drug utilization review criteria to identify individuals whose drug use patterns indicated that they may have been at increased risk for drug-related problems. Concerns about potential drug use problems in these individuals were communicated to the prescribing physicians and dispensing pharmacies using patient-specific feedback.

1.1.3 Components of the Program

During the period under review, the PPRP was comprised of three component programs which focussed on different areas of potentially inappropriate drug use. The ***Extreme User Program*** monitored the level of use of selected mood-modifying drugs and asthma medications. This program identified individuals whose apparent level of drug use exceeded 200% of the maximum dosage criteria established by the JCDU (Appendix A). The ***Polypharmacy Program*** focussed on the number of different medications and identified beneficiaries with prescription claims for more than 15 different drugs in a 90 day period. The ***Polyprescriber Program*** monitored the

number of different physicians, identifying individuals for whom medications claimed in the previous 90 day period were prescribed by more than six different physicians.

1.1.3.1 Extreme User Program — Mood-Modifying Drugs

The mood-modifying drugs monitored by the Extreme User Program included the benzodiazepine, barbiturate and miscellaneous anxiolytic, sedative and hypnotic agents, the narcotic analgesics and the major tranquilizers (Appendix A). When used appropriately, these drugs play an important role in medical practice. For example, benzodiazepines are highly efficacious anxiolytic and hypnotic agents, narcotic analgesics provide a very effective means of relieving moderate to severe pain and major tranquilizers effectively control psychotic disorders in many patients. However, each of these drug groups also has the potential to cause serious adverse effects, especially when used in high doses for prolonged periods of time.

The development of tolerance and physical dependence are widely recognized problems associated with benzodiazepine use. Tolerance occurs when a given dose of a drug produces a decreased effect (Gudex 1991). Studies have shown that the hypnotic effects of benzodiazepines may disappear after as little as two to three weeks of regular use (Kirkwood 1993; Shorr and Robin 1994). In addition, the effectiveness of benzodiazepines as anxiolytics has not been adequately studied beyond four months of continuous use (Gudex 1991; Hayes and Kirkwood 1993). The problem of physical dependence manifests as a withdrawal syndrome upon discontinuation of therapy. Withdrawal symptoms can occur with normal therapeutic doses and after treatment periods as short as three weeks; however, the risk of dependence and its associated withdrawal symptoms increases with high doses of benzodiazepines and with long-term use of these agents (especially more than 4 months of use) (Gudex 1991; Hayes and Kirkwood 1993). Given the problems of tolerance and dependence, current prescribing guidelines recommend that benzodiazepines be used on a short-term use

basis (Hayes and Kirkwood 1993; Rosser et al. 1981; Shorr and Robin 1994). Contrary to these recommendations, drug utilization data in Saskatchewan indicate that benzodiazepine users received an average of 4.7 prescriptions per user in 1989, suggesting that many patients use these drugs on a long-term basis (Quinn et al. 1992a).

The other mood-modifying drugs monitored by the Extreme User Program may also produce a variety of undesirable effects. Excessive sedation, rapid development of tolerance, a high potential for abuse and lethality in overdose are well known problems associated with barbiturate use (Hayes and Kirkwood 1993). Prolonged use of chloral hydrate or the narcotic analgesics may also produce tolerance, physical dependence and psychological dependence (AHFS 1992). In fact, tolerance to the hypnotic effects of chloral hydrate has been reported with as little as one week of use (Wincor 1988). Hydroxyzine has a low potential for dependence; however, the usefulness of this agent is limited by rather modest anxiolytic efficacy combined with significant anticholinergic effects, especially in the elderly (Hayes and Kirkwood 1993). As with the benzodiazepines, the efficacy of hydroxyzine as an anxiolytic has not been established during long-term administration (AHFS 1992).

Whereas the anxiolytic, sedative and hypnotic agents are generally indicated for short-term therapy, the major tranquilizers are sometimes indicated for long-term use in patients with psychoneurologic disorders. These drugs can cause a variety of adverse effects affecting many organ systems (Batey 1989). Of particular concern are the extrapyramidal reactions which commonly occur in patients treated with neuroleptic agents. Although extrapyramidal symptoms have been reported in patients using low doses of neuroleptics, the occurrence and severity of most of these symptoms are dose-related (AHFS 1992). Prolonged use of neuroleptics may also result in tardive dyskinesia, a potentially irreversible extrapyramidal reaction. The risk of developing tardive dyskinesia and the likelihood that it will become irreversible may increase with the duration of treatment and the cumulative dose of neuroleptic agents administered (AHFS 1992). Since there is no known treatment for tardive dyskinesia, antipsychotics should generally be used in the lowest possible dose, for the shortest length of time and

only in those patients who really need them (Batey 1989).

The Extreme User component of the PPRP was designed to identify individuals with apparently high levels of use of these mood-modifying drugs. Levels of use exceeding the extreme user dosage criteria may be appropriate in some patients. However, given the serious adverse effects which can occur with prolonged use of high doses of these agents, identification under the Extreme User Program should, at the very least, prompt a review of the patient's drug therapy.

For the most part, the dosage criteria established by the JCDU are consistent with the dosing recommendations of several drug reference books (AHFS 1992; CPS 1991; USPDI 1991). However, the dosage criteria established for the narcotic analgesics are somewhat lower than the recommended maximum doses in the reference texts. For example, the dosage range recommended by the CPS (1991) for the combination of acetaminophen, caffeine and codeine was 15 to 60 mg of codeine every 4 hours as needed. Whereas this dose range translates to a maximum of 360 mg codeine per day, the maximum dosage criterion established by the JCDU was 240 mg of codeine per day. However, it is important to note that narcotic analgesics are often indicated for acute pain and the dosing guidelines reflect the generally short-term nature of their use. In contrast, the apparent dosages calculated by the Extreme User Program were based on apparent use over a prolonged period (i.e. 90 days). The JCDU also established lower dosage criteria for elderly beneficiaries for most of the major and minor tranquilizers (Appendix A). These recommendations for the use of lower geriatric dosages are consistent with the dosing guidelines presented in the reference texts and with observations that elderly individuals may be at an increased risk for developing adverse reactions from these agents (Batey 1989; Gudex 1991; Shorr and Robin 1994).

1.1.3.2 Extreme User Program — Asthma Drugs

The JCDU's decision to begin monitoring the use of asthma medications in 1992 was a timely one. Over the past decade, there has been a fundamental shift in the treatment of asthma. This shift reflects a better understanding of the pathophysiology of the disease. Until recently, asthma was considered to be primarily a disease of airway constriction or bronchospasm (Kamada 1994; Kelly 1992). As a result, treatment strategies emphasized chronic bronchodilator therapy (Kelly 1992). Over the past few years, asthma has increasingly been recognized as primarily an inflammatory disease (Frew and Holgate 1993; Kelly 1992). The bronchoconstriction which is characteristic of asthma is thought to result from the underlying inflammation. Therefore, treatment strategies have begun to focus on reducing inflammation of the airways and bronchial hyperresponsiveness (Kamada 1994; Kelly 1992).

The Extreme User Program monitored three groups of drugs used to treat asthma: the β_2-agonist bronchodilators, the inhaled anticholinergic agents and the inhaled corticosteroids (Appendix A). Each of these drug groups has a role in the rational treatment of asthma. Detailed algorithms for the management of asthma have been published elsewhere (Frew and Holgate 1993; Kelly and Hill 1993). Briefly, the inhaled β_2-agonists are considered first line drugs for the treatment of patients with mild asthma characterized by symptoms which are infrequent or provoked only by exercise. Patients with symptoms which occur more than 1 or 2 times per week should be treated prophylactically with inhaled corticosteroids or sodium cromoglycate. In these individuals, the inhaled β_2-agonists should be used as required to relieve bronchospasm. The need for regular use of bronchodilators in asthmatic patients may be an indicator of inadequate anti-inflammatory treatment (Kelly and Hill 1993). The anticholinergic agents are less effective bronchodilators than the β_2-agonists. Nevertheless, ipratropium bromide can be useful for the treatment of bronchoconstriction associated with chronic obstructive pulmonary disease (COPD) and as an adjunct to the β_2-agonists for acute severe asthma (Kelly 1992). This drug may also be useful in the treatment of some

patients, particularly elderly individuals, with severe chronic asthma.

Although the clinical usefulness of the β_2-agonists and inhaled corticosteroids is well established, concerns have been raised about the long-term use of high dosages of these agents. Considerable controversy has been generated in recent years over the potential risks of long-term β_2-agonist use (Frew and Holgate 1993; Kamada 1994; Kelly 1992). In particular, asthma-related morbidity and mortality have been rising around the world (Kelly and Hill 1993; Sears et al. 1990) and there is concern that the β_2-agonists may be contributing to this trend. The findings of a number of studies support this concern. For example, regular use of fenoterol (4 times per day) has been shown to be associated with poorer control of asthma than intermittent (as needed) use of this agent (Sears et al. 1990). Other studies have also found that regular use of β_2-agonists can cause a decline in lung function and an increase in bronchial hyperresponsiveness (Kamada 1994). In addition, regular use of inhaled β_2-agonists has recently been shown to be associated with an increased risk of death or near death (Spitzer et al. 1992). In contrast, the findings of other studies suggest that long-term use of oral and inhaled β_2-agonists may be associated with improvements in asthma symptoms (Kelly 1992) and that concomitant administration of corticosteroids may protect patients from the adverse effects of high dose β_2-agonist therapy (Frew and Holgate 1993; Kamada 1994). Thus, the potential dangers of long-term regular use of β_2-agonists are still the subject of considerable debate. Nevertheless, regardless of whether the β_2-agonists are responsible for the increase in asthma morbidity and mortality or are simply markers of more severe disease, heavy use of these agents should signal that the likelihood of a major adverse event is markedly increased and that the patient's condition should be re-evaluated (Spitzer et al. 1992).

The inhaled corticosteroids are highly effective in reducing inflammation of the airways and bronchial hyperresponsiveness (Kelly 1992). As such, the use of these agents has become increasingly widespread over recent years. Although this trend can generally be considered positive, concerns have been raised about several dose-related adverse effects which may be caused by the inhaled glucocorticoids. Specifically,

inhaled corticosteroids may suppress growth in children, especially when used in high doses (Kamada 1994; Kelly 1992). In addition, doses of greater than 1000 or 1500 µg/day of beclomethasone dipropionate in adults (or greater than 400 µg/day in children) often result in adrenal suppression (Kamada 1994; Kelly 1992). Concerns have also been raised about the potential for long-term inhaled steroid use to produce osteoporosis (Kamada 1994).

Unlike the inhaled corticosteroids, ipratropium bromide is poorly absorbed across membranes and, therefore, has negligible systemic effects (Frew and Holgate 1993). Thus, adverse drug effects are not a major concern with the use of this agent. Nevertheless, the regular use of high doses of ipratropium bromide should prompt a review of the patient's medication regimen because it may indicate that the patient's asthma is poorly controlled or that the patient is using the drug improperly (e.g. poor inhaler technique).

The Extreme User Program was designed to identify individuals with high apparent levels of use of these asthma medications. Dosages exceeding the extreme user criteria do not necessarily indicate that drug use is inappropriate. However, extreme use of these agents, particularly the β_2-agonists and ipratropium bromide, may be indicative of poor asthma control and should signal the need for a further evaluation of the patient's condition.

1.1.3.3 Polypharmacy Program

The problem of polypharmacy is widely recognized as an important health issue. The term "polypharmacy" describes the use of multiple medications. There is no specific number of drugs that defines polypharmacy (Stewart and Cooper 1994). However, some authors have suggested that polypharmacy is "the prescription, administration or use of more medications than are clinically indicated in a patient" (Stewart and Cooper 1994). Others have suggested that polypharmacy occurs when a

medication regimen includes at least one unnecessary drug (Colley and Lucas 1993).

A variety of factors may to contribute to polypharmacy. For example, multiple symptoms and diseases within individual patients can lead to polypharmacy (Colley and Lucas 1993). Because the prevalence of symptoms and diseases tends to increase with age, polypharmacy is particularly common among the elderly (Colley and Lucas 1993; Stewart and Cooper 1994). For example, drug utilization studies in many different countries have shown that elderly individuals use from 3.1 to 7.9 medications at one time (Stewart and Cooper 1994).

Other factors which may contribute to polypharmacy include copious prescribing by physicians and the failure of physicians to discontinue medications when they are no longer needed (Beers et al. 1989; Colley and Lucas 1993). A general lack of guidelines for the discontinuation of drug therapy may also be contributing to the widespread prevalence of polypharmacy (Mant and Saunders 1990). The use of multiple medications may also result from the use of multiple physicians who may not be aware of each other's prescriptions (Beers et al. 1989; Meyer et al. 1991). Many other factors such as the sharing of medications, the failure to discontinue drugs as instructed, hoarding of old medications and self-treatment of illnesses are also important contributors to polypharmacy (Beers et al. 1989; Colley and Lucas 1993).

Polypharmacy can have important consequences both for individual patients and for the health care system. The use of multiple medications is associated with an increased risk of side effects and adverse drug reactions (Colley and Lucas 1993; Klein et al. 1984). In fact, the incidence of adverse drug effects has been shown to increase exponentially with increases in the number of medications (Colley and Lucas 1993; Stewart and Cooper 1994). Predictably, the incidence of drug interactions also increases as the number of concomitant medications increases (Stewart and Cooper 1994). Polypharmacy may also result in patient noncompliance since increases in the number of drugs and the complexity of medication regimens have been shown to increase the likelihood of noncompliance (Darnell et al. 1986; Stewart and Cooper 1994). In turn, noncompliance is an important cause of treatment failure and serious medical

complications (Colley and Lucas 1993). Given these serious consequences, polypharmacy can be a costly problem both in terms of direct drug costs and indirect costs resulting from treatment failures and adverse reactions.

The Polypharmacy component of the PPRP was designed to help physicians and pharmacists identify polypharmacy in their patients and to encourage them to review the patients' medication regimens, modifying therapy where appropriate. The criterion of more than 15 different drugs in a 90 day period is high, especially in light of reports of an increased risk of adverse drug reactions with much smaller numbers of drugs (Beers et al. 1989; Klein et al. 1984). This high threshold for identification was selected primarily for administrative reasons because the SPDP had only limited staffing resources to the operate the PPRP.

1.1.3.4 Polyprescriber Program

Patients sometimes see more than one physician. The use of multiple providers is appropriate in some circumstances, especially when the services of specialists are required in the diagnosis and management of patients with multiple disease states. Although the use of multiple physicians may be necessary for some patients, it may lead to a variety of drug-related problems. Meyer and colleagues (1991) found a significant correlation between the number of physicians and the number of drugs prescribed. The risk of problems resulting from therapeutic duplications, drug interactions and inappropriate drug-disease combinations may reasonably be expected to increase when numerous physicians are prescribing for the same patient but are unaware of each other's prescriptions.

As previously noted, the Polyprescriber component of the PPRP was designed to identify patients with prescriptions from more than 6 different physicians in a 90 day period. Health care providers receiving medication profiles for these patients may then use the information to review and coordinate the patients' drug regimens.

1.1.4 The Intervention

The PPRP is based on outpatient prescription claims submitted to the Saskatchewan Prescription Drug Plan. During the period under review, the Program operated on a biweekly basis, identifying beneficiaries whose drug use patterns exceeded the criteria established for the Extreme User, Polypharmacy and/or Polyprescriber Programs. Concerns about potential drug use problems in these individuals were communicated to the patients' prescribing physicians and dispensing pharmacies by using patient-specific feedback. This feedback consisted of medication profiles listing the prescriptions obtained by the patient and highlighting the criteria exceeded by the patient. The profiles did not provide specific recommendations for modifying the patients' medication regimens. Details of the monitoring process and the patient-specific feedback are provided in Section 3.2.

1.2 The Present Investigation

The aim of the present investigation was to examine the impact of Saskatchewan's PPRP on prescription drug use by patients identified under the Program. Specifically, the objectives of this investigation were three-fold:

1. to characterize the individuals identified by the PPRP during 1992, the first year of operation of the expanded version of the Program,

2. to evaluate the impact of the PPRP on drug use by Saskatchewan beneficiaries who were identified by the Program in 1992, and

3. to describe the utilization of mood-modifying drugs and asthma medications by the population of eligible Saskatchewan beneficiaries during the five year period 1989 to 1993.

2.0 Optimizing Drug Utilization

2.1 The Drug Utilization Process

Drug utilization has been defined as "the prescribing, dispensing, administering, and ingesting of drugs" (Serradell et al. 1987). Problems leading to inappropriate drug use may arise at each of these steps in the drug utilization process. Interventions designed to improve drug use may focus on the activities and responsibilities of patients, physicians, pharmacists or other caregivers. This literature review focuses on intervention programs, like Saskatchewan's Patient Profile Release Program, which were designed to promote optimal drug use by influencing outpatient prescribing practices. A comprehensive analysis of intervention programs focussing solely on pharmacist activities such as dispensing and counselling or on patient issues such as medication compliance was considered beyond the scope of this review.

Many different strategies have been employed in an effort to influence prescribing practices. These strategies may be broadly classified as regulatory, administrative or educational in nature. Regulatory approaches place restrictions on prescribing and usually have provisions for punitive actions against health care providers who fail to comply with the restrictions. For example, legislation in the United States requires that nursing homes be held liable to financial and administrative sanctions if the physicians caring for their patients prescribe antipsychotic drugs for inappropriate indications (Kane and Garrard 1994). Administrative strategies attempt to direct physicians' prescribing decisions by using measures such as formularies, financial incentives for "appropriate" prescribing patterns and requirements for special permission to prescribe certain drugs (Raisch 1990a). These regulatory and administrative strategies

may be considered coercive. In contrast, educational programs encourage physicians to change their prescribing practices of their own free will by providing them with information. This literature review is limited to interventions which use educational strategies to promote optimal prescribing. The term "educational" is used in a broad sense and includes approaches such as feedback and reminder systems.

2.2 Factors Influencing Prescribing

In 1969, the United States Task Force on Prescription Drugs defined rational prescribing as providing ". . . the right drug for the right patient in the right amount with due consideration of costs"(Lipton and Bird 1993). This simple definition describes a very complex decision-making process. Clearly, rational prescribing requires a consideration of the disease state, patient characteristics and drug attributes (including cost). However, the range of factors which influence prescribing decisions is not limited to these basic therapeutic considerations (Figure 2.1). In fact, the decision to prescribe a particular medication is the result of input from a number of sources including patients and their families, the pharmaceutical industry, professional colleagues, the academic literature and government regulators (Hemminki 1975; Lipton and Bird 1993; Miller 1973, 1974; Soumerai et al. 1989). Physician characteristics, organizational factors and psychosocial factors have also been shown to influence prescribing decisions (Figure 2.1) (Bradley 1992a; Eisenberg 1979; Hemminki 1975; Miller 1973; Raisch 1990a, 1990b; Schwartz et al. 1989).

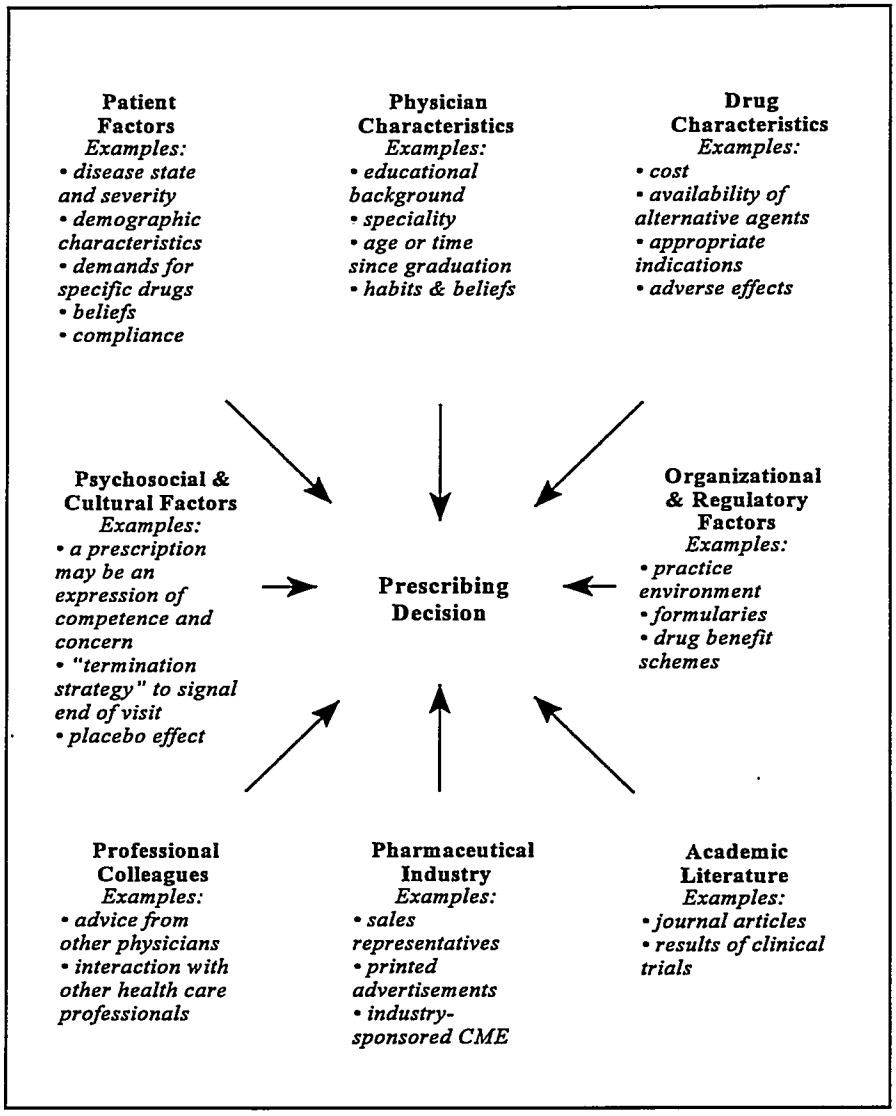

Figure 2.1: Factors Influencing Prescribing

References: Bradley 1992a; Eisenberg 1979; Hemminki 1975; Lipton and Bird 1993; Miller 1973, 1974; Raisch 1990a; Schwartz et al. 1989.

Some factors influence prescribing decisions in a positive manner. For example, advice from a knowledgeable colleague may result in an appropriate prescribing decision. However, other factors have a negative influence on prescribing. Factors which may contribute to inappropriate prescribing include the failure of practitioners to keep up with developments in pharmacology; an overreliance on clinical experience rather than scientific data; the influence of pharmaceutical companies; simple

errors of oversight or omission; inadequate knowledge of cost issues; demands by patients or their families for a particular drug; pressure from other health care workers (e.g. in the nursing home setting); physicians' need or desire to provide some treatment for problems with no clear medical solution; and, the use of a prescription as a "termination strategy" to signal the end of the visit (Bradley 1992b; Lipton and Bird 1993; Soumerai et al. 1989).

Given the complexity of the decision-making process and the many factors which may negatively influence prescribing, it should not be surprising that various forms of inappropriate prescribing have been documented (Gehlbach et al. 1984; Manning et al. 1986; Schaffner et al. 1978). Examples of inappropriate prescribing practices include the use of inappropriate dosages, therapeutic duplications or drug combinations which interact; the use of a drug in a patient who lacks an acceptable indication; the failure to prescribe an effective medication when needed; the use of essentially ineffective drugs; the use of expensive new medications rather than effective older drugs; and the failure to introduce new and effective agents into practice (Lipton and Bird 1993; Soumerai et al. 1989; West et al. 1977).

An understanding of the factors which contribute to inappropriate prescribing practices is important when designing programs aimed at encouraging rational prescribing. Different factors may contribute in varying degrees to different prescribing problems. For example, overpromotion by pharmaceutical sales representatives may result in the use of expensive new drugs when inexpensive, older medications are equally effective. Under such circumstances, the provision of objective educational information may positively influence prescribing practices. However, this type of intervention may be ineffective in modifying prescribing problems resulting from simple errors of oversight. Educational interventions which focus on the range of factors responsible for a particular prescribing problem will be more successful than interventions focussing solely on knowledge deficits.

2.3 Interventions Designed to Promote Rational Prescribing

Saskatchewan has not been alone in its efforts to promote optimal drug use by using education strategies. Educational drug use programs have been implemented elsewhere in Canada (Hlynka et al. 1981), the United States (Lipton and Bird 1993; Soumerai et al. 1989) and various other developed and developing countries (Gutierrez et al. 1994; Rokstad et al. 1995; Watson et al. 1975). Whereas Saskatchewan's Patient Profile Release Program attempts to modify outpatient drug use by providing patient-specific information to physicians and pharmacists, other programs have used a variety of different approaches ranging from mailed educational materials to face-to-face visits with prescribers.

2.3.1 Feedback Programs

Over the past decade, the provision of prescribing feedback has become a popular means of influencing physicians' practices. Feedback programs may focus on cost considerations, quality of care concerns or, ideally, a combination of the two. The feedback information is usually derived from a retrospective review of prescriptions written by specific groups of physicians (e.g. general practitioners in a geographic area) or dispensed to particular groups of patients (e.g. beneficiaries of a third party payment plan). Data sources for the retrospective review process include copies of prescriptions from participating physicians (Frazier et al. 1991; Rokstad et al. 1995; Manning et al. 1986), patient medical records (Putnam and Curry 1985), computerized prescription records from pharmacies (Hershey et al. 1986; Gehlbach et al. 1984; Holm 1990; Lassen and Kristensen 1992; Meyer et al. 1991; Tamai et al. 1987) and third party prescription claims databases (Groves 1985; Sandusky 1993).

The retrospective review process used by feedback programs may focus on the prescribing patterns of individual physicians (or groups of physicians) or on the drug

use patterns of individual patients. The scope of the review process varies for different programs. Simple reviews may entail only a basic description of each physician's prescribing practices (e.g. prescription counts for specific drugs or basic cost calculations). More extensive reviews may involve setting standards of care and identifying physicians whose prescribing patterns deviate from those standards. Retrospective reviews which focus on drug use by individual patients usually attempt to identify individuals who may be at risk for drug-related problems by applying explicit drug use criteria to prescription records.

There are two main forms of prescribing feedback. ***Prescriber-specific feedback*** highlights the prescribing practices of individual physicians, usually in relation to established standards of care or the practices of other physicians. Some programs provide feedback data for groups of physicians (e.g. within the same practice) rather than for individual prescribers. In contrast, ***patient-specific feedback*** highlights potential drug use problems in individual patients. Whereas prescriber-specific feedback is usually sent only to physicians, patient-specific feedback is sometimes sent to both the physicians and pharmacists caring for the patient. Both types of feedback rely on the assumption that notifying providers about potential drug use problems will prompt them to act accordingly.

2.3.1.1 Patient-Specific Feedback

Patient-specific feedback programs have become a popular means of encouraging rational drug use, especially since the United States Congress passed the Omnibus Budget Reconciliation Act in 1990 (OBRA'90). Under the OBRA'90 legislation, each state Medicaid program was required to implement a drug use review (DUR) program by January 1, 1993. One aspect of the mandated DUR program is a retrospective review of the drug therapy provided to Medicaid recipients. Patient-specific feedback is commonly used by these retrospective DUR programs as a means of

notifying health care providers about potential problems in patient drug use and encouraging them to modify the therapeutic regimen appropriately.

As the name implies, patient-specific feedback involves the provision of drug use information for individual patients to the health care providers responsible for their care. This drug use information may take on various forms, ranging from simple medication profiles listing only basic prescription information (such as the drug name, dosage, quantity, dispensing date and prescribing physician) to more detailed feedback highlighting potential drug use problems and providing specific recommendations for prescribing changes.

The retrospective DUR programs implemented by several state Medicaid programs have been described in the literature (Groves 1985; Guo et al. 1995; Holm and Helgeland 1993; LeGrady 1992; Sandusky 1993). With each of these programs, individuals who may be at risk for drug-induced illness are identified by applying explicit drug use criteria to computerized prescription claims data. A committee comprised of physicians and pharmacists then reviews the computer-generated profiles to decide which patients have potentially important drug use problems. Commonly targeted prescribing problems include overuse, underuse, drug interactions, contraindicated drug-disease combinations and adverse effects. Educational intervention letters are then sent to the physicians and pharmacists caring for the patients. The purpose of the intervention letters is to communicate the drug use concerns to the health care providers and to educate them about appropriate drug therapy. Most of the DUR programs request a reply from the health care providers, but do not require it. These Medicaid DUR programs are similar in many respects to the profile release programs operating in Saskatchewan (Blackburn et al. 1990; Joint Committee on Drug Utilization 1994) and British Columbia (Hlynka et al. 1981).

In both Canada and the United States, positive changes in physician prescribing practices and patient drug use patterns have been reported after the implementation of patient-specific DUR programs. Blackburn and colleagues (1990) described a 15% decrease in the number of extreme users of mood-modifying drugs and

a decline in the proportion of the population using these medications during the four year period after the implementation of Saskatchewan's Patient Profile Release Program. In British Columbia, investigators observed decreases in the proportion of eligible beneficiaries receiving sedative-hypnotic agents and the proportion of patients with high levels of sedative-hypnotic use during the two month period after a DUR program was implemented for B.C. Pharmacare recipients (Hlynka et al. 1981). Holm and Helgeland (1993) reported positive changes in the drug therapy of 68% of the South Dakota Medicaid patients for whom intervention letters were sent; the corresponding figure for the Florida Medicaid DUR program was 54% (Groves 1985). In Nebraska, LeGrady (1992) reported substantial cost savings during the five-year period after the initiation of a Medicaid DUR program. Unfortunately, the extent to which the DUR programs were responsible for the observed prescribing changes cannot be determined from the available literature because none of the studies used comparison groups to control for non-intervention factors which may influence drug utilization over time.

Unlike other studies of DUR programs, a comparison group was used in an investigation designed to evaluate the impact of the Alabama Medicaid DUR program (Guo et al. 1995). The researchers described significant cost-savings among prescribers who received DUR letters and patient medication profiles pertaining to the use of anti-ulcer agents. However, the investigators' method of selecting physicians for the comparison group brings into question the comparability of the study groups and, ultimately, the validity of the results. Specifically, the comparison group was comprised of physicians who had prescribed the target drugs during a one year study period but who had not received a DUR intervention letter. Presumably these physicians prescribed the anti-ulcer agents appropriately whereas intervention group physicians prescribed the drugs in a potentially inappropriate manner. Therefore, changes in the prescribing practices of the comparison group physicians should not be assumed to reflect the changes that would be expected for intervention group physicians in the absence of the DUR letters.

Although many DUR programs have been inadequately evaluated, there is

limited evidence from a number of controlled trials indicating that certain forms of patient-specific feedback may influence physician prescribing practices and improve patient drug use (Britton and Lurvey 1991; Kroenke and Pinholt 1990; Meyer et al. 1991; Tamai et al. 1987; Tierney et al. 1986). Kroenke and Pinholt (1990) designed a patient-specific feedback program aimed at reducing polypharmacy among individuals visiting an outpatient teaching clinic. Medical residents caring for elderly patients who were taking five or more different prescription medications were assigned to an intervention or control group. Patient medication profiles and non-mandatory recommendations for prescribing changes were provided to the intervention group physicians both verbally and in writing immediately before each patient's clinic visit. During the 6 month feedback period, physicians in the intervention group implemented 59% of the recommended prescribing changes compared with 12% in the control group. In addition, the mean number of medications used by intervention group patients decreased modestly from 5.9 to 5.4 drugs/patient ($p<0.001$); no such reduction was found in the control group. Interestingly, more than one-third of the instances of physicians' noncompliance with the recommended changes were due to patient factors including patients' refusal to accept the change. Perhaps the provision of patient brochures such as those used in other educational interventions (Avorn and Soumerai 1983) would have improved the effectiveness of this feedback program.

Another patient-specific feedback program focussing on polypharmacy was studied in the non-teaching environment (Meyer et al. 1991). Outpatients using 10 or more medications were randomized to control or intervention groups. Primary care providers for the patients in the intervention group received one of two types of feedback: (1) simple notification letters identifying the polypharmacy patients, stating the potential dangers of over-medication and suggesting reductions in the number of medications (without specifying which drugs should be discontinued), or (2) more intensive feedback including the simple notification letters plus patient-specific drug use information and specific recommendations for prescribing changes. During the one year follow-up period, the number of medications per patient decreased for all three study

groups. At 4 months of follow-up, the reductions for the two intervention groups (-2.5 drugs per patient) were significantly greater than the reductions in the control group (-1 drug per patient). Interestingly, the more intensive feedback intervention had no greater effect than the simple notification letters. During the remainder of the follow-up period, the difference between the intervention and control groups narrowed. By 12 months after the intervention, there was no significant difference between the study groups, indicating that the effects of a single feedback intervention may be temporary.

Tamai and coworkers (1987) focussed on a broader range of prescribing problems, including overuse, underuse, inappropriate dosing, drug duplication, inappropriate drug combinations and potential adverse drug reactions. During one month baseline and intervention periods, a clinical pharmacist reviewed the medication profiles for each patient who visited a general medicine teaching clinic. Immediately before each clinic session, the pharmacist provided computer-generated medication profiles to the experimental group physicians and alerted them to potential drug use problems, suggesting alternate therapy where appropriate. Medication changes for each patient were assessed at the end of their clinic visits. In the feedback group, the proportion of patients who continued to have drug use problems at the end of the clinic visit was only 9.4% during the intervention period compared with 49% during the pre-intervention period; the corresponding figures for the control group were 32% and 36%, respectively. In addition, intervention group subjects experienced a net reduction of 0.4 medications per patient during the feedback period compared with a net increase of 0.7 medications per patient during the pre-intervention period. Britton and Lurvey (1991) reported similar findings in their study of a comparable feedback program in a non-academic setting.

Patient-specific feedback may also improve physicians' preventive care practices (Tierney et al. 1986). Tierney and coworkers (1986) measured physicians' compliance with recommendations to perform 13 preventive care actions, 8 of which related to drugs. The monthly feedback reports provided to each intervention group physician listed all patients who had seen the physician in the previous month and who

had an indication for, but did not receive, one or more of the preventive care actions. During the 7 month intervention period, physicians in the feedback group performed a significantly greater proportion of preventive actions than control group physicians. It is important to note, however, that the impact of the feedback was not equal for all 13 preventive actions; in fact, compliance improved significantly for only three of the recommended actions.

Overall, the results of these studies indicate that patient-specific feedback programs which highlight potential drug use problems and provide general or specific recommendations for change may lead to modest improvements in physicians' prescribing practices. In contrast, simply providing physicians with lists of their patients' current medications appears to have little or no impact on prescribing practices (Johnson et al. 1976; Koepsell et al. 1983). Johnson and coworkers (1976) found that medication profiles inserted in outpatient medical records and updated monthly had no effect on either quantitative (e.g. numbers of prescriptions; expenditures) or qualitative (e.g. drug interactions; inadequate or excessive drug quantities) aspects of prescribing. In a similar controlled trial, Koepsell and colleagues (1983) found that medication profiles which were updated with each new prescription dispensed and placed in a prominent place in patients' medical records had no effect on the frequency of drug interactions or medication duplications. The nonspecific nature of the feedback used by Johnson et al. (1976) and Koepsell et al. (1983) was probably a major factor contributing to their negative results. That is, the medication profiles were provided for all intervention group patients rather than focussing on individuals with clearly identified drug use problems. In addition, the profiles neither alerted physicians to potential prescribing problems nor provided recommendations for prescribing changes.

The results reported by Kroenke and Pinholt (1990), Meyer et al. (1991), Tamai et al. (1987), Britton and Lurvey (1991) and Tierney et al. (1986) provide promising evidence that patient-specific feedback can have a modest impact on at least some prescribing decisions. However, the degree to which these results can be generalized to the state or provincial DUR programs is unclear because the controlled

trials differed from the DUR programs in terms of the setting, the source of the feedback and the format of the feedback. For example, all five of the controlled studies were conducted in single outpatient clinics and the feedback interventions were provided by clinicians working in the same clinic as the study physicians. In contrast, the feedback used by the state and provincial DUR programs is directed at physicians practising in a wide variety of settings. Furthermore, the feedback is sent to the health care providers from a remote source (i.e. a government agency). There is a clear need for further research to determine whether the patient-specific feedback used by such DUR programs is an effective means of influencing prescribing practices and improving patient outcomes.

Further studies must also be conducted to determine the optimal format of patient-specific feedback. Tamai et al. (1987), Kroenke and Pinholt (1990) and Britton and Lurvey (1991) used intensive forms of feedback which included verbal and written recommendations for prescribing changes in each patient. However, Meyer and colleagues (1991) reported that a simple notification mechanism with a general suggestion to reduce the number of medications in polypharmacy patients was as effective as more intensive feedback. This finding is important because simple notification systems would be easier to implement and maintain on an ongoing basis than programs which require a physician or pharmacist to review the drug profiles of each patient and suggest specific prescribing changes. Further studies should be conducted to investigate the relative effectiveness of simple notification letters and more intensive feedback mechanisms.

Finally, several other findings reported by these investigators raise some important questions. Specifically, Meyer and colleagues' (1991) finding that the effects of the feedback lasted for only a short time after the intervention is suggestive of a need for ongoing feedback. The duration of the feedback effect and the optimal frequency for the provision of patient-specific feedback are areas which require further study. Also interesting was the finding that physicians were more likely to comply with suggestions to simplify dosing schedules or substitute new medications for old ones than to

discontinue drugs without replacing them with other ones (Kroenke and Pinholt 1990). Future studies should be designed to determine the scope of prescribing problems that are amenable to patient-specific feedback interventions.

2.3.1.2 Prescriber-Specific Feedback

Prescriber-specific feedback programs have been designed with the aim of reducing costs, increasing generic prescribing or improving the quality of prescribing. Various forms of prescriber-specific feedback have been studied, ranging from simple prescription counts and cost summaries to more extensive prescribing information combined with educational packages or specific recommendations for change. Aggregate peer-comparison data are sometimes provided with the prescriber-specific feedback to encourage physicians to compare their individual prescribing practices with those of their peers (e.g. physicians in the same medical clinic or in the same geographical area).

The results of several controlled (Frazier et al. 1991) and randomized controlled trials (Gehlbach et al. 1984; Harris et al. 1985; Hershey et al. 1986) indicate that the provision of prescriber-specific feedback to physicians is an effective means of increasing generic prescribing and may also be effective in reducing prescribing costs. Relatively simple forms of prescribing feedback were used, including monthly or bimonthly prescription counts and prescribing cost summaries for selected drug groups (Frazier et al. 1991; Hershey et al. 1986) and monthly prescription counts for brand name and generic drugs (Gehlbach et al. 1984). In only one of these studies were physicians provided with peer-comparison data and specific recommendations for change (Frazier et al. 1991).

Improvements in generic prescribing were large and statistically significant. The impact of the feedback programs on prescribing costs was less impressive. Frazier and colleagues (1991) observed a non-significant trend toward lower costs per

prescription ($p=0.11$) and a shift among the feedback physicians toward prescribing a greater proportion lower-priced drugs. Harris and colleagues (1985) found that the cost per item increased by only 22.7% in the feedback group compared with a 33.0% increase in the control group. Hershey and coworkers (1986) reported that their feedback intervention was associated with significant reductions of 6.5% and 9.7% in the mean charges per prescription ($p<0.025$) and per patient ($p<0.10$), respectively. However, statistical significance in this study was achieved only in the ninth and final month of the feedback period. Nevertheless, if the modest reductions in prescribing costs observed by these investigators were in fact real, then the cost-savings may far outweigh the costs of the program because feedback interventions can be relatively inexpensive to implement. For example, Hershey and coworkers (1986) found a benefit-to-cost ratio of at least 50:1 when they compared the apparent cost savings with the costs of implementing and maintaining their feedback program.

Most of the evidence for the positive effects on generic prescribing and prescribing costs was derived from investigations conducted in academic settings (Frazier et al. 1991; Gehlbach et al. 1984; Hershey et al. 1986). However, the results reported by Harris et al. (1985) indicate that prescriber-specific feedback used in combination with small group discussions may also be a valuable means of influencing prescribing practices in community settings.

Presently, there is only limited information about the duration of the feedback effects. Prescribing changes were studied during feedback periods ranging from 5 to 18 months. Harris et al. (1985) and Gehlbach et al. (1984) observed a persistence of the improvements in generic prescribing practices for 12 to 18 months after the discontinuation of the feedback programs. However, the reductions in prescribing costs observed by Harris and coworkers (1985) during the feedback period were not maintained during the 18 month post-intervention period.

An interesting aspect of these studies was the apparent lack of an effect of the feedback on physicians' knowledge of prescribing costs. In both studies which examined this outcome, the feedback interventions had no meaningful effect on

physicians' knowledge of either actual drug prices (Hershey et al. 1986) or relative drug prices (Frazier et al. 1991). Yet, despite this lack of improvement in knowledge, the prescribing costs appeared to decrease. These findings suggest that feedback does not change prescribing practices by improving knowledge. Instead, the feedback may increase physicians' awareness of prescribing issues by highlighting areas for improvement. In addition, ongoing feedback reinforces positive prescribing changes, a factor which may be important for sustained improvements in behaviour. These proposed mechanisms for the effects of feedback are supported by an observation by Gehlbach and coworkers (1984) in which physicians reported becoming interested in monitoring their own practices and looking forward to "seeing how well they had done."

Investigations into the effects of feedback programs on the quality of prescribing have yielded mixed results. The findings of some studies suggest that feedback programs are effective in improving physician performance only when the participants have been involved in defining the review criteria on which the feedback is based. Putnam and Curry (1985) conducted a small randomized controlled trial to determine whether a prescriber-specific feedback program directed at family physicians would influence their management of common medical conditions and whether performance would improve to a greater extent when the study physicians were involved in the selection of diseases to be audited or the development of the optimal care criteria. Feedback data were generated from chart audits and presented to the intervention group physicians during a personal visit. During the 6 month post-intervention period, performance of the experimental physicians was better than the control group only for those conditions in which they had participated in setting the criteria. Selection of the conditions to be audited had no effect on performance. These findings are consistent with the results of a recent British study in which the prescribing of target drug groups improved only for those conditions in which the study physicians had participated in setting clinical standards for the review process (North of England Study of Standards and Performance in General Practice 1992). Neither receiving the standards set by other physicians nor receiving group feedback had any impact on prescribing practices in this

investigation.

Although physician involvement in setting the review criteria may enhance the effectiveness of feedback programs, the results of two controlled trials suggest that such involvement may not be necessary (Manning et al. 1986; Rokstad et al. 1995). Rokstad and coworkers (1995) mailed prescriber-specific feedback, peer-comparison data and recommendations for the appropriate treatment of insomnia and acute cystitis to Norwegian general practitioners. Three months after the intervention, significant improvements in both the choice of therapeutic agents for the target conditions and the average number of defined daily doses (DDD) prescribed per patient were observed in the experimental group but not in the regional control group.

Positive findings were also reported by Manning and coworkers (1986). In this study, university faculty analyzed a sample of prescriptions written by the participating physicians in order to identify the learning needs for each prescriber. The most common prescribing problems were the use of improper dosages or inappropriate durations of therapy, the use of drugs with a high potential for adverse drug effects, the use of expensive drugs for which there are less costly alternatives and the use of medications in patients with an insufficient indication for drug therapy. Intervention group physicians were provided with prescriber-specific feedback data and educational packages targeted at each physician's prescribing problems. During the post-intervention period, significantly more of the recommended prescribing changes were made by the feedback group (30%) than the control group (3%).

Other feedback programs in Canada (Rosser et al. 1981), the United Sates (Gullion et al. 1983), and Europe (Damsgaard et al. 1992; Hamley et al. 1981) have also been reported to have a positive effect on prescribing. Unfortunately, the degree to which these feedback programs were responsible for the observed prescribing changes is unclear because comparison groups were not used to control for non-intervention factors which may influence prescribing. The fact that the intervention program described by Gullion and colleagues (1983) was later found to have no effect on prescribing when tested in a randomized controlled trial (Putnam and Curry 1989) highlights the

importance of conducting well-designed studies with adequate control or comparison groups.

Contrary to the positive prescribing changes described by Manning et al. (1985) and Rokstad et al. (1995), two groups of Danish researchers found that feedback had no effect on physicians' prescribing practices (Holm 1990; Lassen and Kristensen 1992). Holm (1990) studied the impact of mailed feedback on the outpatient prescribing practices of general practitioners. The intervention consisted of peer-comparison feedback describing the physicians' benzodiazepine prescribing practices plus printed information outlining the appropriate use of these agents. No significant differences in benzodiazepine prescribing were observed between the intervention and control groups during the one to two month post-intervention period.

Lassen and Kristensen (1992) provided general practitioners with three bimonthly peer-comparison feedback packages describing their overall prescribing levels for all drugs. No specific drug groups were targeted nor were there any recommendations for change. During the five month feedback period, there was no significant difference between the intervention and control groups with respect to their prescribing levels (measured as the number of DDD prescribed per patient per month).

Overall, the available evidence neither strongly supports nor refutes the hypothesis that prescriber-specific feedback is an effective means of improving the quality of prescribing. The findings reported by Putnam and Curry (1985) and by the North of England Study of Standards and Performance in General Practice (1992) are interesting in that they suggest that feedback programs influence physician performance only when the participants are involved in defining the standards of care on which the feedback is based. If this is indeed the case, then the utility of feedback mechanisms would be limited to settings in which it is feasible to consult with each individual physician about the clinical standards.

The findings reported by Manning et al. (1986) and Rokstad et al. (1995) suggest that physician involvement in the criteria setting process may not be necessary. Unfortunately, both of these studies were particularly susceptible to the Hawthorne

effect, a phenomenon which describes the effect that observation has on the behaviours of individuals who are being observed (i.e. study subjects may modify their behaviours because they aware that they are being monitored). In both of these investigations, the analyses of prescribing changes were based on information recorded by the participants specifically for the purposes of the study, i.e., copies of prescriptions written on special pressure-sensitive pads (Manning et al. 1986) or logs of patient, diagnostic and prescription information updated by the physician with each patient visit (Rokstad et al. 1995). Both data collection procedures would remind the physicians at the time of the patient visit that their prescribing decisions were being monitored. This increased awareness of being monitored may, in turn, have influenced their prescribing decisions. The Hawthorne effect would be expected to result in greater changes among the intervention group physicians because they were not only aware that they were being observed, but they also knew which types of prescribing decisions were being monitored. Therefore, it is unclear whether the observed improvements in prescribing were due to the Hawthorne effect or to the intervention.

The negative findings reported by Holm (1990) and Lassen and Kristensen (1992) also merit further comment. The apparent inability of these feedback programs to change prescribing practices may well represent the true state of affairs. However, there are several other possible explanations for the negative results. One factor which may have contributed to the negative findings is that both studies used *group feedback data* pertaining to the prescribing habits of all physicians in a given practice rather than *prescriber-specific feedback* describing the practices of each individual physician. Physicians may be more likely to change their prescribing habits when it is clear that their own prescribing (rather than that of the practice as a whole) is not consistent with current recommendations. Therefore, the group feedback may not have provided sufficient impetus for change. Another factor which may have contributed to the negative results reported by Lassen and Kristensen (1992) is that the feedback data pertained to the overall prescribing habits for all drugs rather than focussing on particular drug groups or specific prescribing problems. With such non-specific

feedback, physicians may not have known which aspects of their prescribing patterns required modification. Holm (1990) also reported that there was considerable variability in the prescribing levels during the one-week baseline and post-intervention monitoring periods. This variability may have reduced the power of the study to detect significant prescribing changes. In addition, relatively short intervention and follow-up periods may have contributed to the negative findings of both studies.

Finally, it is noteworthy that all four of the controlled studies which reported positive findings were performed using volunteers (Manning et al. 1986; North of England Study of Standards and Performance in General Practice 1992; Putnam and Curry 1985; Rokstad et al. 1995). Rokstad and colleagues (1995) had a participation rate of nearly 100% in the study regions, ensuring relatively good generalizability of the results, at least to other Norwegian general practitioners. In contrast, the investigation conducted by Manning and coworkers (1986) was characterized by a low participation rate and a high withdrawal rate; thus, the physicians who did complete the study were probably highly motivated to improve their prescribing practices. Interestingly, both groups of investigators who reported negative findings sent the feedback to physicians without first inviting them to participate (Holm 1990; Lassen and Kristensen 1992). Therefore, it is unclear whether feedback programs can positively influence the prescribing practices of physicians who may not be particularly motivated to change their behaviours.

2.3.2 Printed Educational Materials

The provision of printed information may be the most widely used of all educational interventions aimed at influencing physicians' prescribing practices. The types of printed materials commonly used in intervention programs include drug bulletins, newsletters, self-education packages, journal articles, guidelines and specially-designed brochures. Printed materials may be used alone or in combination with other

educational strategies. When used alone, the success of the intervention in changing physician behaviour relies on the assumption that exposing physicians to correct information will improve their knowledge about appropriate prescribing and that this improved knowledge will be incorporated into practice (Cohen et al. 1985; Soumerai et al. 1989).

There is evidence from several randomized controlled trials indicating that the provision of printed educational materials is an effective means of increasing practitioner knowledge (Cohen et al. 1985; Sadowsky and Kunzel 1991; Sibley et al. 1982). These studies focussed on physicians' knowledge of preventive prescribing practices (Cohen et al. 1985; Sadowsky and Kunzel 1991) and issues relating to the management of common conditions (Sibley et al. 1982). In addition to improving knowledge, printed materials have also been associated with improvements in physicians' intentions to perform some preventive actions (Cohen et al. 1985).

Although printed materials may improve knowledge and intentions, the results of well-controlled trials indicate that these materials have little or no impact on physicians' practices. Despite documented knowledge gains, Cohen et al. (1985) failed to find any significant improvement in physicians' overall compliance with recommended preventive actions during a 6 month follow-up period. Sibley and coworkers (1982) also found no significant improvement in physicians' overall documented quality of care during the 18 month period following the intervention. These negative findings are consistent with the results reported by Avorn and Soumerai (1983) and Schaffner et al. (1983). Working independently, these investigators found that mailed, illustrated, visually appealing brochures ("un-advertisements") had no impact on physicians' outpatient prescribing practices. More traditional drug bulletins also had no effect on prescribing practices (Avorn and Soumerai 1983).

Evans and coworkers (1986) went a step further than most studies of educational interventions and measured the impact of printed materials not only on physicians' practices but also on their patients' outcomes. In this investigation, mailed self-instruction packages relating to the diagnosis and management of hypertension were

found to have no impact on either the physicians' management of hypertension or their patients' blood pressure during a one year follow-up period. These findings confirm the results of a previous study in which self-instruction packages which were provided to medical residents had no effect on patients' blood pressures during a 7 month follow-up period (Dickinson et al. 1981).

In summary, although reading is the preferred method of continuing education for many physicians (Cohen et al. 1985; Evans et al. 1986), the balance of the evidence from well-controlled studies indicates that printed materials, when used alone, have little or no impact on physicians' practices or patient outcomes. Various types of potential prescribing problems were targeted, yet none were effectively modified by the printed materials. In addition, different types of printed materials were studied, including printed recommendations and supporting literature reviews (Cohen et al. 1985), self-instruction packages (Dickinson et al. 1981; Evans et al. 1986; Sibley et al. 1982), drug bulletins (Avorn and Soumerai 1983) and illustrated "unadvertisements" (Avorn and Soumerai 1983; Schaffner et al. 1983). None of these interventions successfully changed physician behaviour. Furthermore, studies which used volunteers were no more effective in changing behaviours than trials which sent unsolicited drug use information to physicians. Similarly negative findings have also been reported in the hospital setting (Soumerai and Avorn 1984).

There are several possible reasons for these negative findings. In the first place, physicians do not always read the materials which are provided to them. For example, Avorn and Soumerai (1983) reported that many physicians did not even recall seeing the materials that were mailed to them. Other investigators found that relatively few physicians read (Watson et al. 1975) or kept the educational materials (Schaffner et al. 1983). It follows that physicians will not be influenced to change their behaviours if they do not read the printed materials.

Some studies did, however, report knowledge gains among the participants, indicating that the physicians had read and understood the materials (Cohen et al. 1985; Sibley et al. 1982). Yet, despite these knowledge gains, physician performance did not

improve. One possible explanation for this discrepancy is that knowledge levels were measured shortly after the educational intervention whereas changes in performance were assessed over 6 to 18 month follow-up periods. It is possible that knowledge gains were transient and, therefore, had no lasting effects on physician behaviours.

Another possible explanation for the negative findings is that barriers in clinical practice may prevent physicians from changing their behaviours. This explanation is supported by several observations. Cohen and colleagues (1985) found a lack of significant correlations between knowledge, intentions and practice, indicating that knowledge and intentions are poor predictors of actions. Other investigators have also reported an inconsistent relationship between physicians' knowledge and their practices (Headrick et al. 1992). In addition, Manning and coworkers (1986) reported that physicians who participated in their study changed their prescribing behaviours in only half of the instances in which they had stated an intention to change. Thus, improvements in knowledge and intentions are not necessarily sufficient to change behaviours. This lack of a direct link between knowledge, intentions and prescribing practices should not be surprising given the wide array of factors which influence prescribing decisions (Figure 2.1) and the fact that many of the factors which contribute to inappropriate prescribing are not simply the result of knowledge deficits on the part of physicians.

It is important to note that the lack of an effect of printed materials on prescribing practices was demonstrated in trials in which these materials were used alone. These findings indicate that printed materials should not be relied upon by themselves as a means of changing prescribing practices. However, printed materials may be important components of other educational initiatives because they may predispose to behaviour change by improving physicians' knowledge, attitudes and intentions (Soumerai et al. 1989).

Finally, it is noteworthy that the negative results of the well-controlled trials cited above directly contrast with the positive findings of a number of uncontrolled studies which examined the effects of printed materials. For example, using pre- and

post-intervention measurements of drug utilization, Schaffner and coworkers (1978) found improved prescribing of antibiotics after two information letters and brief articles were sent to all physicians participating in the Tennessee Medicaid program. Positive prescribing changes have also been reported by Watson et al. (1975), Fendler et al. (1984) and Schectman et al. (1995); however, none of these studies had adequate comparison groups to control for other factors which may influence prescribing practices over time. In their review of educational strategies for improving prescribing, Soumerai and colleagues (1989) found that all the adequately controlled studies indicated that printed materials were ineffective in changing prescribing practices whereas all the uncontrolled studies reported positive effects. This discrepancy between the results of controlled and uncontrolled investigations highlights the importance of conducting carefully designed studies with adequate comparison groups to control for the many other factors such as marketing campaigns, media, regulatory policies and seasonal effects which can affect drug utilization levels over time (Soumerai and Lipton 1994). The finding of strong temporal trends in the prescribing practices of physicians *not* exposed to interventions (i.e. the control groups of many studies) (Klein et al. 1981; Schaffner et al. 1983; Reeder et al. 1991) further emphasizes the importance of including an adequate comparison group.

2.3.3 Reminders at the Time of Prescribing

Reminder systems have been designed to address prescribing errors caused by physician oversight rather than a lack of therapeutic knowledge. Typically, reminder systems are based on the information contained in patient medical records. These records may be scanned manually or by means of a computer in order to identify individuals who have an indication for a given procedure, laboratory test or treatment. The reminders generated by this review process are provided to the participating physicians at the time of patient visit or between visits. Reminders vary in format, but

most are designed with the aim of notifying physicians about clinical events and providing recommendations about the appropriate course of action.

Reminder systems are similar to patient-specific feedback programs in that both provide physicians with information pertaining to individual patients. The two types of programs differ, however, in the timing of the intervention in relation to the provision of patient care. Patient-specific feedback programs attempt to identify individuals who are at risk for drug-related problems by reviewing records of care that has already been provided to the patient (i.e. reviews are usually based on records of prescriptions which have been dispensed to the patient). Feedback is then sent to health care providers to notify them about potential drug-related problems that the patient may be experiencing. In contrast, reminder systems generally identify patients who may require a given clinical action. Patient-specific information is then provided to physicians in a prospective or concurrent manner such that prescribing decisions may be influenced at the time that care is provided.

Much of the research in the area of computerized reminder systems has been conducted by McDonald and colleagues in the outpatient clinics of a teaching hospital in the United States. Numerous controlled trials conducted by these investigators have consistently shown that physicians who received reminders at the time of the patient visit responded to a greater percentage of the clinical events than those physicians who were not provided with reminders (McDonald 1976a, 1976b; McDonald et al. 1980; McDonald et al. 1984; Tierney et al. 1986).

Several of the findings from these studies were interesting. Firstly, the investigators reported that physicians who received reminders did not maintain their improved practices when the reminders were discontinued (McDonald 1976b; McDonald et al. 1980). This lack of a carry-over effect suggests that little or no learning took place among the participating physicians. Secondly, subgroup analyses of individual clinical actions indicated that the reminders improved the response rates for only some of the clinical events (McDonald et al. 1984; Tierney et al. 1986). In particular, the reminders had little effect on physicians' compliance with newer clinical

practices which had not yet been widely accepted by physicians working in the clinic (McDonald et al. 1984). Another interesting finding related to the relationship between physicians' intentions and their actions. Specifically, intentions did not predict physician behaviour in the control group, a finding which is consistent with the observations of Cohen et al. (1985); however, intentions were significant predictors of the actions of physicians in the reminder group (McDonald et al. 1984). Based on these findings, the researchers concluded that reminders are "potent activators" of existing physician intentions, but they have little effect on the acceptance of new practices (McDonald et al. 1984). This conclusion is consistent with the lack of an educational or learning effect observed in previous studies (McDonald 1976b; McDonald et al. 1980).

Much of the research conducted by McDonald and coworkers focussed on the practices of medical residents or interns. These investigators did, however, provide evidence that reminders may also influence the behaviours of faculty physicians and nurse-clinicians (McDonald et al. 1984). Research conducted in a health maintenance organization also indicates that reminders may be effective in changing the behaviours of physicians who have completed their formal training (Barnett et al. 1978; Barnett et al. 1983). Barnett and coworkers (1978) described a computerized reminder system which was used to monitor the records of patients with positive streptococcal throat cultures. During the 32 month intervention period, there was a dramatic drop in the percentage of patients with positive throat cultures who were untreated after 10 days. Although there was no comparison group, the rise to baseline levels after discontinuation of the reminder system suggests that the program was at least partly responsible for the observed improvements in patient care. In a subsequent study, Barnett and coworkers (1983) found that computerized reminders were effective in improving the follow-up of potentially hypertensive patients (i.e. individuals who did not have repeat blood pressure measurements within the 6 month period following a newly elevated diastolic blood pressure measurement).

Another group of investigators studied the impact of generic chart reminders and patient-specific chart reminders on physicians' compliance with the National

Cholesterol Education Program (NCEP) guidelines for the identification and treatment of hyperlipidemia (Headrick et al. 1992). The generic reminder consisted of a two-page summary of the NCEP guidelines. The patient-specific reminder included the generic summary, the patient's most recent lipid levels and a list of specific recommendations for action. During the three month intervention period, modest improvements in physicians' compliance with the NCEP guidelines were observed for the control, generic reminder and patient-specific groups. The improvements in compliance for the two intervention groups did not differ from the control group. However, a larger sample size and a longer study period likely would have produced a statistically significant result.

In summary, the results of these studies indicate that reminders systems are an effective means of influencing physicians' practices in both academic and non-academic settings. Patient-specific reminders appear to be useful in addressing a variety of prescribing issues including the use of preventive regimens (McDonald et al. 1984; Tierney et al. 1986), the treatment of acute or chronic diseases which may be overlooked by physicians (Barnett et al. 1978; Barnett et al. 1983) and the identification and management of potential adverse drug reactions (McDonald 1976a, 1976b). As noted by Soumerai and colleagues (1989), it is not known whether such reminder systems could reduce unnecessary or inappropriate prescribing which results from factors such as inadequate knowledge, peer pressure or patient demands.

Soumerai and coworkers (1989) described reminder systems as "secretarial" in nature. This is an apt description because reminder systems help physicians recognize clinical events so that they may act accordingly. Reminders have little or no "educational" effect, as evidenced by the lack of a carry-over effect after discontinuation of the reminders and their lack of effectiveness in improving compliance with actions that physicians do not already intend to do.

2.3.4 Group Education Programs

Group education programs such as seminars, lectures, tutorials and workshops are among the most commonly used strategies for improving physician knowledge and practice. Most group education programs rely on traditional didactic learning to produce a change in physician behaviour (Soumerai et al. 1989). The educational content and format of these programs vary widely. Many group programs provide only general information on health care topics such as the diagnosis and management of a given disease. A minority of group programs specifically target the educational needs of the participants.

Given the popularity of group education strategies, surprisingly little research has been conducted to characterize the impact of these programs on physician behaviours and patient outcomes. Many of the evaluation studies which have been performed were designed only to assess the participants' satisfaction with the program or to test the ability of the program to transmit knowledge (Bertram and Brooks-Bertram 1977). There is reasonably good evidence that group education programs can improve knowledge and attitudes (Bertram and Brooks-Bertram 1977; Horder et al. 1986; Soumerai et al. 1989). However, the impact of these programs on physician practices and patient outcomes is much less clear.

The content and format of group education programs appear to influence the success with which they change behaviours. Highly-focussed, small-group tutorials have been shown to be an effective means of changing physicians' behaviours in two controlled trials conducted in academic settings (Inui et al. 1976; Klein et al. 1981). In both studies, the educational content of the tutorials was targeted at the specific learning needs of the participating physicians. The tutorials focussed on the treatment of urinary tract infections (Klein et al. 1981) and the management of hypertension (Inui et al. 1976). During a 5 month post-intervention period, Klein and coworkers (1981) observed significant improvements in physicians' choice of antibiotics. Inui and colleagues (1976) found significant improvements in the physicians' management of

hypertensive patients during a two month follow-up period. Furthermore, the proportion of patients who had controlled blood pressures by the end of the follow-up period was significantly greater for the experimental group than the control group. In addition, patients of the tutored physicians were shown to be more knowledgeable and compliant with their medication regimens than control patients.

Highly-focussed group education programs have also been reported to have an impact on the behaviour of physicians practising in non-academic settings (Gutierrez et al. 1994; Jennett et al. 1988). Jennett and colleagues (1988) identified the learning needs of their target audience and developed an educational program to address those needs. The intervention involved a small group discussion, mailed newsletters and two follow-up teleconferences focussing on the management of hypertension or the detection of colorectal and prostatic cancer. Six months after the intervention, physicians in both the cancer and cardiovascular education groups performed a significantly greater percentage of the recommended behaviours than those in the control group. The improvements in the cardiovascular education group persisted for at least 12 months after the intervention.

Gutierrez and coworkers (1994) developed an intensive educational program for Mexican physicians. The intervention consisted of five one-hour workshops focussing on the management of acute diarrhea. The group education sessions were supplemented with printed educational materials, a treatment algorithm and feedback pertaining to the prescribing patterns within the clinic. In addition, a peer review committee analyzed random samples of acute diarrhea cases on a weekly basis for a total of six months. The results were positive. The average proportion of cases treated appropriately more than doubled after the intervention and the improvement persisted for at least 18 months after that last peer review meeting. In contrast, the performance of the control physicians during the entire follow-up period remained virtually unchanged at the baseline level of slightly more than 30%.

The findings of both Gutierrez et al. (1994) and Jennett et al. (1988) lend reasonably strong support to the hypothesis that carefully-designed educational programs

can have a strong and persistent effect on the behaviours of physicians. As in the studies conducted by Inui et al. (1976) and Klein et al. (1981), these intervention programs focussed on the learning needs of the participating physicians. In addition, the programs provided participants with an opportunity to reflect on and discuss the educational issues. Both interventions also incorporated mechanisms to reinforce the educational messages [i.e. multiple workshop sessions and peer review (Gutierrez et al. 1994); mailed newsletters and teleconferences (Jennett et al. 1988)].

Evaluations more generalized group education programs, which were not targeted at the specific learning needs of the participants, have yielded mixed results. In Denmark, Friis and coworkers (1991) observed greater improvements in antibiotic prescribing in a study region which received group lectures than in the control regions which received only printed materials. Unfortunately, the timing of the intervention in relation to the baseline and post-intervention monitoring periods limits the conclusions that can be drawn from the findings. Specifically, the intervention took place at the beginning of 1987 and the post-intervention prescribing patterns were measured in March 1987. However, the baseline prescribing patterns were measured in March 1983, nearly four years before the intervention. Therefore, it is not known whether the observed differences between the groups in 1987 were already present before the intervention took place.

Rutz and coworkers (1990) also reported positive results in their study of a group education program in Gotland, Sweden. The intervention consisted of printed materials plus a two-part seminar program focussing on the diagnosis and management of depression. Compared with the rest of Sweden, psychotropic drug use in Gotland changed in a manner consistent with the expected effects of the educational program. However, the results should be interpreted cautiously because the baseline levels of drug use in Gotland differed from the rest of Sweden. In addition, there is a possibility that temporal factors may have influenced drug utilization patterns differently in different parts of the country. Therefore, it is unclear whether the differences between the drug use trends in Gotland and the rest of Sweden were due to the intervention or to factors

unrelated to the educational program.

In contrast with the positive results reported by Friis et al. (1991) and Rutz et al. (1990), several groups of investigators have failed to demonstrate a positive effect of group education programs on the prescribing behaviours of physicians (Ives et al. 1987, Pinkerton et al. 1980; Reeder et al. 1991). Ives and colleagues (1987) found that a group lecture pertaining to the appropriate use of oral cephalosporins had no impact on physicians' use of these agents. Pinkerton and coworkers (1980) found that physicians' knowledge of fluoride therapy for the prevention of dental caries improved after viewing an educational videotape. However, a chart review of patient records revealed that the physicians had failed to apply this knowledge to their patient care activities. This lack of an effect on physicians' practices despite documented knowledge gains echoes the findings of studies which evaluated the effects of printed educational materials (Cohen et al. 1985; Sibley et al. 1982).

Reeder and coworkers (1991) found that lectures and printed materials had a minimal effect on physicians' self-reported management of hyperlipidemia in Saskatchewan. A comparison of responses from pre- and post-education surveys indicated that both the regional controls and the intervention group physicians reported changes in their behaviours which were consistent with national hyperlipidemia guidelines. However, the changes in the intervention group were no greater than in the control group for most of the measures of interest. A factor which may have contributed to the apparent ineffectiveness of the educational program was the widespread media attention that had been focussed on the treatment of hyperlipidemia during the study period (Reeder et al. 1991). That is, the control group physicians were probably exposed through other communication channels to the same information as the intervention group. The method of measuring behaviour change may also have contributed to the negative findings since self-reported behaviours do not necessarily reflect actual performance (Hartlaub et al. 1993).

Other Canadian investigators have also reported negative findings. Putnam and Curry (1989) designed a one-day workshop aimed at developing criteria for the

treatment of hypertension. During the 18 month follow-up period, patients of family physicians who had participated in the workshop had no better blood pressure control than patients who saw control group physicians. Unfortunately, physicians' adherence to the treatment criteria was not reported. Therefore, it is not clear whether the lack of an effect on blood pressure control was the result of an inability of the criteria-setting process to change physicians' behaviours or whether the physicians' treatment practices had in fact improved but failed to produce a change in the patient outcome.

In summary, there is reasonably good evidence that carefully designed group education programs can be effective in changing physicians' behaviours (Gutierrez et al. 1994; Inui et al. 1976; Jennett et al. 1988; Klein et al. 1981). The results reported by Jennett et al. (1988) and Gutierrez et al. (1994) indicate that the impact on physicians' practices may persist for at least 12 to 18 months. It is noteworthy, however, that only two of these studies (Gutierrez et al. 1994; Klein et al. 1981) focussed specifically on prescribing practices whereas the others focussed on more general disease management issues.

All four of the "successful" programs incorporated many of the educational techniques which are considered important for changing behaviours, including the identification of the target physicians' learning needs; the definition of specific problems and learning objectives; the encouragement of two-sided communication and active learner involvement; the use of follow-up mechanisms to emphasize and reinforce the educational messages; and, the suggestion of practical alternatives to the discouraged behaviours (Soumerai and Avorn 1990; Stein 1981). In contrast, many of the group lectures and seminars which are still commonly used in continuing education programs provide only general therapeutic information without employing these educational techniques. There is much less compelling evidence that these "general" educational programs are effective in changing physicians' prescribing practices (Friis et al. 1991; Ives et al. 1987; Pinkerton et al. 1980; Reeder et al. 1991; Rutz et al. 1990). Furthermore, the evidence which does point to a positive effect was derived from studies which are of questionable methodological soundness.

As with other types of interventions, there is a lack of information about the ability of group education programs to improve patient health. Only two of the group education studies examined patient outcomes and they had contradictory results. Inui and coworkers (1976) observed improved blood pressure control among intervention group patients whereas Putnam and Curry (1989) found no such improvement. Methodological differences regarding the choice of study setting and participating physicians, the format and content of the educational programs, the method of estimating blood pressure control and the time frame for follow-up may have contributed to these disparate results. Thus, it is unclear whether group education initiatives are an effective means of improving patient health.

2.3.5 Face-to-Face Education

The face-to-face educational approach ("academic detailing") has received much attention in recent years. Academic detailing generally involves one or more visits to prescribers by a specially-trained physician or pharmacist. The purpose of the visits is to provide objective therapeutic information and advice pertaining to appropriate prescribing. These educational visits are often supplemented with printed materials. Some investigators have also provided prescribing feedback as part of the academic detailing intervention.

The strongest evidence for the effectiveness of face-to-face interventions comes from a carefully-designed randomized controlled trial (Avorn and Soumerai 1983). These investigators used prescription claims data from the Medicaid databases of four states to identify moderate to high prescribers of cephalexin, propoxyphene or cerebral and peripheral vasodilators. These target drug groups represented three different types of suboptimal prescribing: the use of expensive drugs when there are less costly, yet equally efficacious alternatives; the use of a marginally effective and potentially dangerous drug; and, the use of ineffective agents. Physicians were

randomized to one of three groups: mailed printed materials, face-to-face educational visits plus printed materials or no intervention (control group). Physicians in the face-to-face group were visited twice in their offices by specially-trained pharmacists who presented unbiased information about the target drugs, encouraged restrained use of these medications and provided suggestions for alternative therapeutic strategies. To address the perceived problem of patient demand, physicians in the face-to-face group were also given brochures for their patients. In the nine months during and after the intervention, the mean number of units prescribed for each drug was significantly lower in the "face-to-face" group than in the control group, with an overall reduction of 14% when all three drug groups were considered together ($p=0.0001$). In an economic analysis of this academic detailing intervention, Soumerai and Avorn (1986) demonstrated a benefit-to-cost ratio of approximately 2 to 1.

Other studies based on Medicaid records have also shown that face-to-face visits by physician counsellors are an effective means of improving physicians' prescribing practices (McConnell et al. 1982; Schaffner et al. 1983). These controlled trials focussed on the use of antibiotics which were contraindicated for use in office practice (Schaffner et al. 1983) or which were used for inappropriate indications (McConnell et al. 1982). Prescriber-specific feedback data were also presented the physicians participating in the study conducted by McConnell and coworkers (1982). During six month (McConnell et al. 1982) and one year (Schaffner et al. 1983) follow-up periods, both groups of investigators observed significant improvements in the prescribing practices of the visited physicians.

Several other groups of investigators have also reported that academic detailing programs resulted in improvements in the quality of prescribing (Peterson and Sugden 1995) or reductions in prescribing costs (Newton-Syms et al. 1992; Steele et al. 1989). Peterson and Sugden (1995) developed an educational program aimed at reducing the use of excessively high allopurinol doses among Australian general practitioners. Face-to-face visits by a pharmacist were supplemented with mailed printed educational materials and group prescribing feedback which highlighted

inappropriate drug use patterns in the study region. Significant prescribing improvements were observed in the intervention group during the six month follow-up period; no such change was found in the regional comparison group.

In the academic detailing program designed by Newton-Syms and colleagues (1992), the use of ibuprofen, an inexpensive yet efficacious NSAID, was encouraged as a cost-effective alternative to the more expensive NSAIDs. Follow-up analyses revealed an increase in the use of ibuprofen among the visited physicians compared with a slight reduction in ibuprofen prescribing among the control physicians during 5 month post-intervention period. Steele and coworkers (1989) also reported prescribing cost reductions associated an educational program involving the provision of prescribing feedback and weekly face-to-face visits to medical residents.

The studies cited thus far indicate that academic detailing is an effective means of addressing a variety of prescribing problems including the use of expensive agents for which there are less costly alternatives (Avorn and Soumerai 1983; Newton-Syms et al. 1992), the use of ineffective or marginally effective agents (Avorn and Soumerai 1983), the use of drugs for inappropriate indications (McConnell et al. 1982) and the use of drugs in a potentially unsafe manner (Schaffner et al. 1983; Peterson and Sugden 1995). One area in which the impact of academic detailing has been less impressive is in the use of benzodiazepine agents (Hartlaub et al. 1993; Ray et al. 1986). In a controlled trial, Ray and coworkers (1986) found that an academic detailing program aimed at frequent prescribers of diazepam had no effect on overall diazepam prescribing in the year after the intervention. The only positive finding was an 18% reduction in long-term diazepam prescribing relative to the control group; however, even this finding must be interpreted with caution, because the intervention and control groups had different baseline levels of prescribing and the investigators' method of controlling for these differences is questionable.

Hartlaub and coworkers (1993) also found that an educational program involving face-to-face visits and prescribing feedback had no impact on benzodiazepine use. During a six month follow-up period, the intervention and control groups had

similar proportions of patients receiving benzodiazepines after controlling for potential confounders. Several factors may have contributed to this negative finding. First, the outcome of interest (i.e. the proportion of patients receiving benzodiazepines) is a rather insensitive measure of prescribing changes. Looking only at whether an individual is taking a benzodiazepine during the study period is a conservative measure of prescribing change because withdrawing patients from long-term benzodiazepine use can be difficult and time-consuming. A meaningful change in this measure of prescribing may take more than six months to detect. As suggested by the investigators, the characteristics of the benzodiazepine class of drugs may also have contributed to the negative findings since these drugs are often used on a chronic basis and changes in chronic drug use may be more difficult to achieve than changes in acute drug use. In addition, reducing or discontinuing long-term benzodiazepine use can be difficult because it often triggers resistance from patients — a factor which would be expected to decrease the effectiveness of the intervention (Hartlaub et al. 1993).

In the investigations described in this section, face-to-face visits were conducted with individual prescribers in an effort to provide objective therapeutic information and thereby influence physician behaviour. Stross and Bole (1980) used a somewhat different approach. Physicians identified by their peers as being educationally influential were selected from communities assigned to the intervention group and were provided with an intensive educational experience including a clinical preceptorship in a university arthritis centre. After the intervention, the physicians returned to their home communities to disseminate what they had learned. This dissemination of information was done in a number of ways including informal communications which took place when the community physicians consulted with the influential physicians about specific patient problems. One year after the intervention, the experimental communities showed significant improvements in the use of corticosteroids and physical therapy; no such changes were seen in the control communities. The findings of this study are particularly interesting because intensive education of a small number of influential physicians was found to be associated with positive changes in disease management at

the community level.

In summary, face-to-face educational strategies have been shown to be an effective means of influencing the outpatient prescribing behaviours of physicians practising in community settings. This approach has also been reported to be effective in hospital settings (Soumerai et al. 1989) and nursing home environments (Ray et al. 1993, Avorn et al. 1992). Although academic detailing programs may be expensive to implement, evidence provided by Soumerai and Avorn (1986) indicates that this approach can be cost-effective.

As noted above, academic detailing programs have proven useful in addressing a variety of prescribing problems which may adversely affect the health of patients or increase costs to the health care system. Face-to-face strategies were not, however, particularly effective in modifying benzodiazepine prescribing practices (Hartlaub et al. 1993; Ray et al. 1986). This apparent inability to modify benzodiazepine prescribing is consistent with the negative findings reported by Holm (1990) in which feedback of benzodiazepine prescribing patterns had no impact on prescribing practices. Unfortunately, methodological aspects of each study may have contributed to the negative findings; therefore, it is not clear whether characteristics of the benzodiazepine drug class were responsible for the apparent lack of effectiveness, or whether the investigations simply failed to find an effect for reasons related to the study design.

Many of the investigations were conducted over relatively short periods of time. There is some evidence, however, indicating that the effects of academic detailing visits may persist for reasonably long periods after the intervention. McConnell et al. (1982) found significant improvements in prescribing for at least 6 months after the physicians were visited. Avorn and Soumerai (1983) described prescribing improvements during a 9 month period (5 months of which was after the last visit). Furthermore, a time series analysis conducted by Avorn and Soumerai (1983) indicated that the impact of the intervention had not diminished throughout the follow-up period. Finally, Ray and colleagues (1985) reported that the beneficial effects of the academic detailing program described by Schaffner et al. (1983) persisted for at least two years

after the visits by physician counsellors.

Some of the face-to-face educational programs provided individualized or group prescribing feedback (McConnell et al. 1982; Peterson and Sugden 1995); others did not (Avorn and Soumerai 1983; Newton-Syms et al. 1992; Schaffner et al. 1983). Both forms of academic detailing were effective in modifying prescribing practices. Whether the provision of feedback data has any incremental effect over the impact of the visits themselves is unclear.

Finally, academic detailing was well received by the target physicians. From 85% (Schaffner et al. 1983) to 100% (Hartlaub et al. 1993) of the targeted physicians consented to the visit. In addition, investigators reported that the physicians responded favourably to the visit (Avorn and Soumerai 1983; Schaffner et al. 1983). These findings indicate that academic detailing interventions can be successfully applied to a broad range of physicians. Furthermore, this educational approach need not be limited to volunteers as is the case with some other educational strategies such as group lectures.

2.3.6 Summary

A variety of educational interventions have been designed in an effort to influence physicians' prescribing practices. These interventions have met with varying degrees of success. The findings of a number of well-controlled studies indicate that printed materials may improve physicians' knowledge, attitudes and intentions. However, when used alone, these materials have little or no impact on prescribing practices.

Prescriber-specific feedback has been shown to be an effective means of increasing generic prescribing. This type of intervention may also produce modest reductions in prescribing costs, although further investigation is required to confirm this effect. Studies which have examined the impact of prescriber-specific feedback on the quality of prescribing have yielded mixed results. Further studies are needed to clarify

this issue.

There is reasonably good evidence that reminder systems can improve physicians' use of preventive regimens. Reminders may also alert physicians to potential adverse drug effects, acute conditions which require treatment or chronic diseases requiring follow-up. However, these interventions do not appear to improve physician knowledge and there is no evidence that reminders can effectively reduce inappropriate or unnecessary prescribing resulting from inadequate knowledge.

Several carefully-designed, highly-focussed group education programs have been shown to improve physicians' prescribing practices or their management of disease. These programs focussed specifically on the educational needs of the participants. However, many group education programs are less focussed and provide only general information about health care topics. These "general" programs have not been shown to improve physicians' practices.

A number of studies have also shown that face-to-face educational approaches are effective in addressing a variety of prescribing problems including the use of expensive drugs for which there are less costly alternatives, the use of ineffective agents and the use of drugs for inappropriate indications or in a potentially unsafe manner. Academic detailing programs have generally been well received and they appear to be an effective means of influencing physicians' prescribing practices in a variety of settings.

Finally, patient-specific feedback programs operating in medical clinics have been associated with modest improvements in a variety of potential prescribing problems including polypharmacy, inappropriate use of drugs and inadequate use of some preventive regimens. Patient-specific feedback is also used by many drug utilization review programs operating at the state or provincial level. Although some positive prescribing changes have been reported after the implementation of these DUR programs, none of the published studies used adequate comparison groups to control for non-intervention factors which may influence drug utilization over time. Thus, there is a lack of objective evidence for the effectiveness of these DUR programs in improving

physician prescribing practices and patient drug use. In evaluating the impact of Saskatchewan's PPRP, the present investigation will address this knowledge gap to some extent.

3.0 Methodology

3.1 Saskatchewan Health Services Databases

Saskatchewan is a western Canadian province which provides universal health care to nearly all of its approximately one million inhabitants. Health services are provided to residents through Saskatchewan Health, a government department comprised of numerous branches and agencies. Saskatchewan Health maintains large, computerized databases of health care information including physician services, outpatient drug use and hospitalizations (Malcolm et al. 1993). Although the data files were developed for administrative purposes, they are widely recognized as a valuable resource for research (Malcolm et al. 1993; Tennis et al. 1993; Thiessen et al. 1990; Tilson 1985).

An important feature of Saskatchewan's health care system is the assignment of a unique health services number (HSN) to all residents eligible for Saskatchewan Health coverage (Malcolm et al. 1993). This unique identifier allows individuals to be followed through time and permits the linkage of records in the various Saskatchewan Health databases. There are ten computerized databases which can be electronically linked (Malcolm et al. 1993). The following description is limited to the databases used in the present investigation.

3.1.1 Health Insurance Registration File

The Health Insurance Registration File (HIRF) contains identification and

demographic information for all residents who are eligible for Saskatchewan Health services (Rawson et al. 1992). Individuals whose health care is federally funded are excluded from the HIRF. This category, which accounts for approximately 1% of the Saskatchewan population, includes members of the Royal Canadian Mounted Police and the Canadian Forces and inmates of federal penitentiaries (Malcolm et al. 1993).

Each resident eligible for Saskatchewan Health benefits is assigned a unique health services number. Prior to 1991, the HSN was an eight-digit registration beneficiary number (RBN) which identified both the individual and the family unit. Although individuals could have more than one RBN in a lifetime, there was a mechanism to link old and new numbers for each person such that individuals could be traced through time (Malcolm et al. 1993). In 1991, the eight-digit number was replaced with a nine-digit unique lifetime HSN.

The HIRF contains the following information for each eligible beneficiary: name, health services number, sex, marital status, date of birth, health service coverage eligibility dates, date of death (if applicable), mailing address, five-digit residence code, an indicator for Registered Indian status and an indicator for recipients of the Saskatchewan Assistance Plan (Malcolm et al. 1993; Rawson et al. 1992). The HIRF is updated daily and all transactions for insured services are checked for the eligibility of the claimant and for the accuracy of identification and demographic information.

3.1.2 Prescription Drug Services Database

The Prescription Drug Services Branch (PDSB) of Saskatchewan Health administers the Saskatchewan Prescription Drug Plan which provides coverage for outpatient prescriptions for eligible beneficiaries. Individuals whose prescriptions are covered by other agencies, including Health and Welfare Canada – Indian Health Services, Workers' Compensation Board and Veterans Affairs Canada, are not eligible

for SPDP coverage. Also excluded are members of the Royal Canadian Mounted Police and the Canadian Forces because their prescription costs are covered by the federal government (Malcolm et al. 1993). In 1992-93 fiscal year, individuals excluded from SPDP coverage represented approximately 7% of Saskatchewan residents (Saskatchewan Health 1993b).

Any drug licensed for use in Canada may be prescribed in Saskatchewan, but, with few exceptions, only those drugs listed in the Saskatchewan Formulary are covered by the SPDP. The Formulary is updated semi-annually by the Minister of Health based on recommendations from the Saskatchewan Formulary Committee. In 1991, there were more than 2000 products listed in the Formulary (Rawson et al. 1992). Drugs are categorized into Formulary classes using the American Hospital Formulary Service (AHFS) classification system. In certain circumstances, Exception Drug Status (EDS) may be granted to provide coverage for some non-formulary drugs (Rawson et al. 1992).

The format of the SPDP has changed since its inception in 1975. From September 1975 to June 30, 1987, beneficiaries paid a fixed portion of the prescription cost and the pharmacy submitted a claim to the PDSB for the remainder of the cost. In June 1987, consumers paid a maximum charge of $3.95 per prescription. In July 1987, the SPDP changed from a fixed copayment program to a family-based deductible plus percentage copayment system. Under this new system, patients paid the full cost of prescriptions. Once the annual deductible was reached, consumers could submit prescription claims to the PDSB for reimbursement of 80% of the prescription costs in excess of the deductible. In January 1989, the SPDP automated its claims submission process with the installation of point-of-sale terminals in each pharmacy. Using the point-of-sale terminals, pharmacies submit prescriptions claims for eligible drugs directly to a central computer where the family's current deductible level is maintained. The central computer calculates the consumer's share of the prescription cost taking into account the current deductible level and percentage copayment.

The deductible level and copayment percentage changed several times

since the introduction of the deductible system in 1987 (Table 3.1). Most notable are the increases which took place in 1992 and 1993. With the increase in the deductible level in May 1993, the PDSB implemented a Special Support Program under which Saskatchewan beneficiaries may apply for reduced deductible and percentage copayment levels. Benefits under the Special Support Program are based on the annual family income and the annual drug costs (Saskatchewan Health 1993b).

Table 3.1: Changes in Deductible Levels from 1987 to the Present[¶]

Time Period	Deductible Level	Percentage Copayment[§]
July 1, 1987 to March 7, 1991	$125 annually per family unit $75 annually for senior families[‡] $50 annually for single seniors	20%
March 8, 1991 to May 18, 1992	$125 annually per family unit $75 annually for senior families[‡] $50 annually for single seniors	25%
May 19, 1992 to March 18, 1993	$190 semi-annually per family unit $75 semi-annually for senior families[‡] $50 semi-annually for single seniors	35%[†]
March 19, 1993 to present	$850 semi-annually per family unit[*]	35%

[¶] Reference: Saskatchewan Health 1993b.

[§] Percentage copayment applies to prescription costs above the deductible level.

[†] Percentage copayment decreased to 10% when family costs exceeded $375 in a semi-annual deductible period.

[‡] Senior families are those with at least one family member 65 years of age or older.

[*] Family Income Plan, Saskatchewan Income Plan and Guaranteed Income Supplement recipients have lower deductible levels.

Various forms of coverage are provided under the SPDP. Most residents have Regular coverage and are subject to the deductible system. A smaller number of individuals have Saskatchewan Assistance Plan (SAP) coverage and are exempted from the deductible plan. There are three types of SAP coverage. Beneficiaries with SAP–Plan 1 coverage receive selected drugs at no charge and pay a reduced charge (up to $2) for all other Formulary and EDS medications. Plan 1 beneficiaries who are less

than 18 years of age receive these medications free of charge. Upon application from a physician, SAP beneficiaries requiring multiple medications on a regular long-term basis may be eligible for Plan 2 coverage. Individuals with Plan 2 coverage receive all Formulary drugs, allergenic extracts, megavitamins and approved EDS products at no charge. The third category of SAP coverage, Plan 3, is provided to wards of the province and to residents who receive supplementary income assistance and live in approved homes licensed under *The Housing and Special-Care Homes Act* or *The Mental Health Act.* Plan 3 beneficiaries receive all Formulary and most non-formulary drugs at no charge (Saskatchewan Health 1993b).

In addition to the Regular and SAP coverage categories, certain individuals may be covered under the Saskatchewan Aids to Independent Living (SAIL) or the Palliative Care programs. Paraplegics, cystic fibrosis patients and chronic end-stage renal disease patients are eligible for SAIL coverage. SAIL recipients receive all Formulary and disease-related non-formulary drugs at no charge. The Palliative Care Program provides Formulary and EDS drugs free of charge to patients in the late stages of terminal illness.

Information contained in the SPDP database includes patient data (HSN, sex, year of birth, designation of special coverage status), drug data (AHFS drug classification, drug identification number, active ingredient number, generic and brand names, strength and dosage form, manufacturer of drug, date dispensed, quantity dispensed and "no-substitution" code), prescriber and pharmacy identification numbers and cost data (unit cost of drug material, dispensing fee and mark-up, total cost and consumer and drug plan shares of total cost) (Rawson et al. 1992). Complete drug data are available for the period September 1975 to June 1987 and from January 1989 to the present. During these periods, data were compiled on an individual patient basis. Incomplete drug data are available for the period July 1, 1987 to December 31, 1988. During this period, data were compiled by family unit (Malcolm et al. 1993).

3.1.3 Hospital Services Database

The Saskatchewan Urban Hospital and Rural Health Facilities Branches administer the Hospital Services Plan. Under this plan, Saskatchewan hospitals provide services free of charge to all members of the covered population (Rawson et al. 1992). In providing these services, the hospital services branches collect data on every hospital separation. Computerized data collection began in 1963 but the data are more easily accessible after 1970 (Rawson et al. 1992).

Data are collected from all general and rehabilitation hospitals in the province. The collected data include acute care inpatient separations, day surgery, long-term care separations for patients whose level of care[1] is assessed as level 2, 3 or 4 and who occupy a bed in a general hospital, active rehabilitation of patients in general hospitals, inpatient psychiatric separations for patients treated in general hospitals and out-of-province hospital separations involving members of the covered population (Malcolm et al. 1993; Rawson et al. 1992). Patient-specific information from hospital outpatient departments or psychiatric hospitals are not included in this database.

The information contained in the Hospital Services Database includes patient information (HSN, sex, residence code, year and month of birth), diagnostic and treatment data (before April 1987, up to two discharge diagnoses and one procedure code; after April 1987 up to three discharge diagnoses, three procedure codes and an accident code), service data (level of care codes), separation data (date of separation, length of stay, type of admission and separation), physician information (attending physician code, attending surgeon code) and hospital information (hospital identification code) (Malcolm et al. 1993; Rawson et al. 1992).

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[1] Levels of care are supervisory care (level 1), personal care (level 2), basic nursing care (level 3), extended care (level 4), rehabilitation care (level 5) and acute care (level 6).

3.2 Patient Profile Release Program — Monitoring Process

The Patient Profile Release Program is based on outpatient prescription claims submitted to the Saskatchewan Prescription Drug Plan. Therefore, the Program has the capacity to monitor all Saskatchewan residents who are eligible for SPDP coverage. As previously noted, this covered population represented approximately 93% of the total Saskatchewan population during the 1992-93 fiscal year (Saskatchewan Health 1993b). Individuals who were excluded from SPDP coverage were not monitored by the PPRP.

During the period under review, the PPRP computer program ran on a biweekly basis, monitoring all beneficiaries for whom a prescription claim was submitted during the previous two weeks (Figure 3.1). Beneficiaries who had been identified by the PPRP in the previous 90 day period or who had Palliative Care coverage were automatically excluded from the monitoring process (Joint Committee on Drug Utilization 1994). With each biweekly claims run, the computer program calculated (1) the apparent dosages of drugs monitored for extreme use (Appendix A), (2) the number of different drugs in the previous 90 day period[2], and (3) the number of different prescribers in the previous 90 day period. Ninety and 180 day periods were used for the calculation of mood-modifying and asthma drug dosages, respectively. An example of the apparent dosage calculation is provided in Appendix B. The computer program then generated a medication profile for each beneficiary who exceeded the Extreme User, Polypharmacy and/or Polyprescriber criteria. These profiles were reviewed by a SPDP pharmacist to identify situations in which profile release may be unnecessary or inappropriate (Appendix C).

Medication profiles were sent to the physicians and pharmacies identified on the patient's prescription claims for the previous 90 day period. The drug profile listed the beneficiary's name, address, health services number, age, sex and prescription

[2] Different brands and strengths of a given drug were counted only once.

information (i.e. drug, strength, quantity, dispensing date, prescribing physician and dispensing pharmacy) (Appendix D). All prescriptions claimed in the 90 day period prior to identification (or 180 day period for extreme users of asthma drugs) were included in the medication profile. The covering page of the profile highlighted the criteria exceeded by the patient, but did not provide any specific recommendations for change (Appendix D). A letter describing the program, a copy of the extreme user criteria and a response form were sent with the profile. The letter stressed that profile release does not necessarily imply that drug use is inappropriate, but that the apparent level of use warrants a review of the patient's regimen. The response form was sent with the profile to facilitate the voluntary provision of additional information to the SPDP.

Once individuals had been identified by the PPRP, their prescription records were flagged to prevent re-identification for the following 90 days. This period was chosen to give physicians and pharmacists an opportunity to review drug therapy and, if appropriate, modify the drug regimen. Beneficiaries who remained above the threshold criteria 90 days after the initial profile was released were eligible for re-identification and release of another profile.

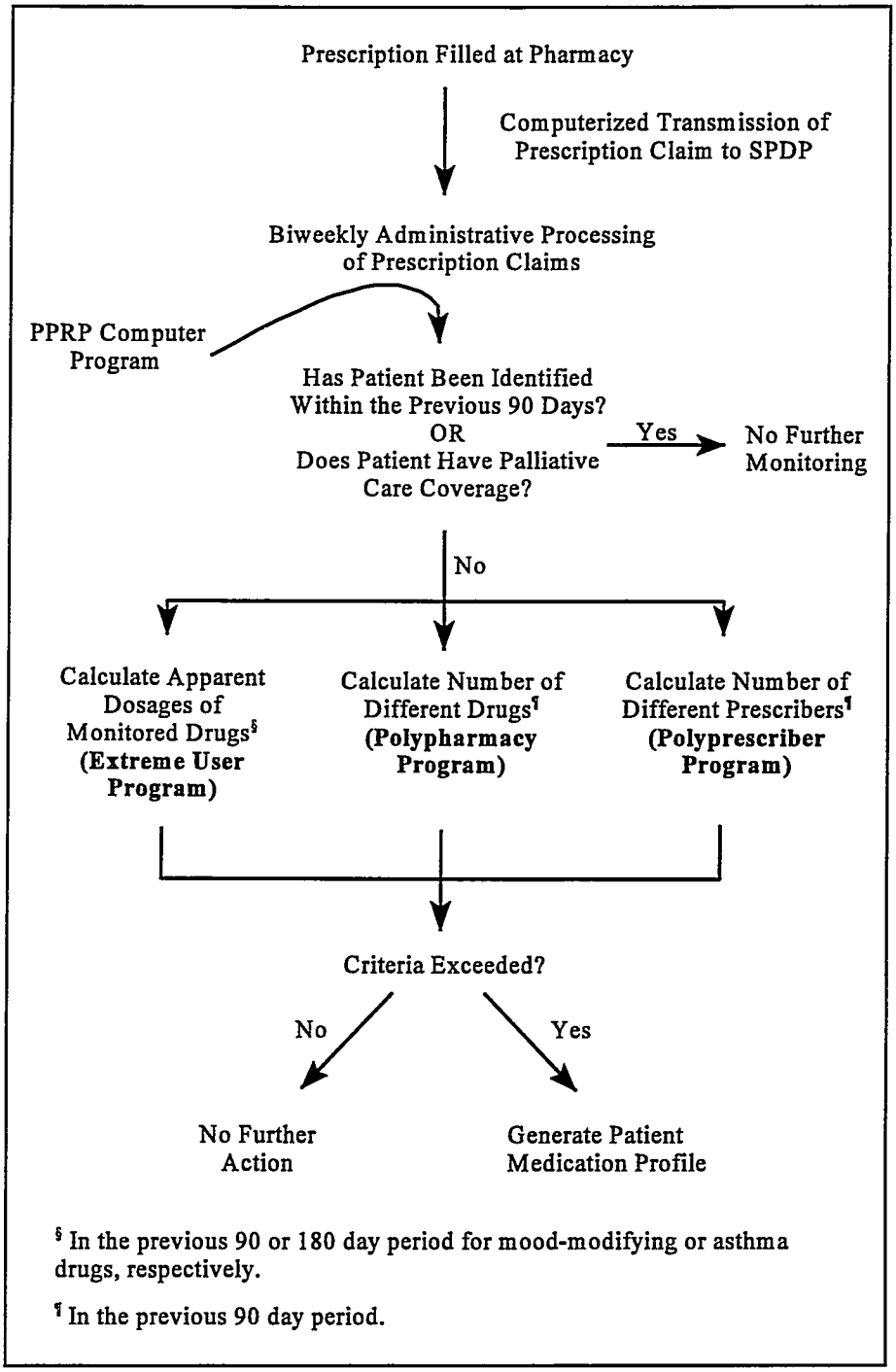

Figure 3.1: Patient Profile Release Program Monitoring Process

3.3 The Present Investigation

3.3.1 Objective

The present investigation was designed to examine the impact of the Patient Profile Release Program on outpatient prescription drug use. As noted in Section 1.3, the specific objectives of the study were to characterize the individuals identified by the PPRP during 1992, evaluate the impact of the PPRP on drug use by patients who were identified by the Program and describe the use of mood-modifying drugs and asthma medications in Saskatchewan during the period 1989 to 1993.

3.3.2 Study Design

An historical cohort design with a three and a half month follow-up period was used to assess the impact of the PPRP on short-term drug utilization by patients identified as exceeding Program criteria. The follow-up period was extended for up to nine months after profile release to characterize long-term re-identification rates. However, this long-term follow-up analysis was descriptive in nature due to the lack of an adequate comparison group. The cohort design was supplemented with a descriptive analysis involving the characterization of individuals identified by the PPRP in 1992 and the description of population drug utilization patterns during the period January 1, 1989 to December 31, 1993.

3.3.3 Data Sources

Demographic and drug use data for individuals identified by the PPRP were obtained from a computerized database maintained by the PDSB. This database is

updated with each biweekly run of the PPRP and contains information about each beneficiary identified by the Program (Table 3.2). The PPRP database is based on information in the SPDP database and is, therefore, subject to the same limitations. The PDSB provided the researcher with a pseudo-identified data set for this investigation. Strict confidentiality was maintained; the files provided for analysis did not contain any information which would permit identification of individual patients, prescribers or pharmacies. A summary of the data-cleaning process required to generate a data set that was suitable for analysis is outlined in Appendix E.

Table 3.2: Information Contained in the Patient Profile Release Program Database

Patient Identification	• Health Services Number (HSN) • Name
Demographic Data at the Time of Identification	• Age • Sex • Residence Code • Coverage Code
Data Pertaining to Identification by the Patient Profile Release Program	• Date Identified • Criteria Exceeded • Number of Pharmacies[§] • Number of Prescribers[§] • Indicator of Profile Release (yes/no)
Additional Information for Extreme Users	• Drug Linkage Group Exceeded • Monitored Drugs Used[¶] • Apparent Dosage[¶] • Percentage of Maximum Threshold Dosage[¶]
Additional Information for Polypharmacy Subjects	• Drugs Used by the Patient[§] • Number of Prescriptions for Each Drug[§]
Additional Information for Polyprescriber Subjects	• Prescriber Identification Numbers • Number of Prescriptions from Each Prescriber[§]

[§] In the 90 days prior to identification by the PPRP

[¶] In the 90 (or 180) days prior to identification for mood-modifying (or asthma) drug extreme use

Record linkage with two other Saskatchewan Health databases was necessary to obtain additional information about the beneficiaries identified by the PPRP during the study period. The Hospital Services Database provided 1992 hospital admission and discharge dates for the study subjects. Saskatchewan Health coverage dates for the study subjects were obtained through linkage with the HIRF. The databases were linked using beneficiaries' health services numbers. Both linkages were approved by Saskatchewan Health's Cross Agency Study Committee.

Drug utilization statistics for the province of Saskatchewan were obtained from annual drug use reports supplied by the PDSB. The drug use reports were based on SPDP records and were, therefore, limited to Formulary drugs that were dispensed to eligible beneficiaries and entered into the PDSB claims system. Prescriptions for non-formulary drugs covered under supplementary programs were also included in the reports. The annual drug use reports provided an age-sex breakdown of the prescriptions for and the users of eligible drugs during the period 1989 to 1993. Users were defined as beneficiaries with at least one claim for the drug in question during the calendar year.

The age-sex distributions of *eligible* Saskatchewan beneficiaries were obtained from the 1989 to 1993 annual Covered Population Reports (Saskatchewan Health 1989-1992, 1993a). These reports were derived from the HIRF database and were based on coverage data for the month of June for each year. These reports also provided an age-sex breakdown of eligible beneficiaries stratified by residence. The age-sex distribution of *active* beneficiaries was obtained from the PDSB Annual Statistical Report for the 1992-93 fiscal year (Saskatchewan Health 1993b). Active beneficiaries were defined as beneficiaries with at least one prescription claim for a drug eligible for coverage by the SPDP during the period of interest.

3.3.4 Study Subjects

The study population included all Saskatchewan residents eligible for SPDP coverage during the study period. Individuals who were not eligible for SPDP coverage were excluded from the study (Section 3.1.2). Specific inclusion and exclusion criteria for each phase of the study are detailed below in Section 3.3.5.

3.3.5 Data Collection and Analysis

3.3.5.1 Drug Utilization in Saskatchewan

The study population for this phase of the investigation included all Saskatchewan beneficiaries eligible for SPDP coverage during the study period. With the exception of the major tranquilizers, all drugs monitored by the PPRP were included in the analysis (Appendix A). Major tranquilizer utilization was not examined because subjects identified for extreme use of these drugs were excluded from the other phases of the investigation (Appendix E).

Three measures of drug utilization were calculated for each of the drugs and drug groups of interest:

Annual Prescription Rates: the average number of prescriptions for a monitored drug (or drug group) per 1000 eligible beneficiaries.

Annual User Rates: the average number of beneficiaries with at least one prescription for a study drug (or drug group) per 1000 eligible beneficiaries.

Annual Prescription per User Rates: the average number of prescriptions in a calendar year for the study drug (or drug group) among users of the drug(s).

Age- and sex-specific prescription, user and prescription per user rates were calculated for each of the study drugs and Formulary classes for the 1992 calendar year. To characterize drug utilization trends in Saskatchewan, the three measures of utilization were calculated for each of the study drugs for the five year period 1989 to 1993. The annual prescription and user rates were not age-sex adjusted because the age-sex distribution of the eligible population was nearly identical for each of the five years in the study period (Saskatchewan Health 1989-1992, 1993a). Thus, the observed trends in drug utilization could not have been attributed to changes in the age or sex distribution of eligible beneficiaries and standardization was, therefore, considered unnecessary. Age-sex adjustment of the rates was also considered undesirable because the actual utilization rates provide a better picture of what was happening in Saskatchewan than the artificial rates obtained through standardization.

3.3.5.2 Descriptive Statistics for the Patient Profile Release Program

The study population for this phase of the investigation included all beneficiaries for whom at least one medication profile was released by the PPRP during the 1992 calendar year. Records of individuals removed from the PPRP data files during the data cleaning process were excluded from the study (Appendix E).

Study subjects were stratified by the criteria exceeded: Extreme User, Polypharmacy or Polyprescriber. The demographic variables examined for each group included age, gender, residence and coverage type at the time of identification. The numbers of pharmacies and prescribers in the three months prior to identification, level of use (for extreme users) and the number of different drugs (for Polypharmacy subjects) were also studied. The descriptive data were obtained from the first profile released for each beneficiary. Coverage type was coded as Regular, SAP–Plan 1, SAP–Plan 2 or SAP–Plan 3. Residence codes were categorized into four groups as shown in Table 3.3.

Table 3.3: Definition of Residence Categories

Residence Category	Covered Population (1992)
Large Cities	
Saskatoon	184255
Regina	177557
Medium–Sized Cities	
Moose Jaw	34130
Prince Albert	33141
Battlefords[§]	17677
Yorkton	15520
Swift Current	15415
Small Cities	
Estevan	10536
Weyburn	9897
Lloydminster	7537
Melfort	6040
Humboldt	5177
Rural	<5000

[§] Battleford and North Battleford

Differences between the Extreme User, Polypharmacy and Polyprescriber groups were tested statistically using the Kruskal-Wallis test for continuous variables and the Chi-square test for categorical variables. The non-parametric Kruskal-Wallis test was used rather than the one-way fixed effects analysis of variance (ANOVA) because the assumptions of normality and homogeneous variance for the latter procedure were not fulfilled. Differences with a p-value of less than or equal to 0.05 were considered statistically significant. Pairwise comparisons were performed using multiple Wilcoxon Rank Sum tests for continuous variables and multiple Chi-square tests for categorical variables. The Bonferroni method was used to correct for the increased probability of a Type I error resulting from multiple statistical tests (Kleinbaum et al. 1988). Thus, to maintain an overall Type I error rate of 5%, differences between any two groups (i.e. ExU versus PPh, ExU versus PPr, PPh versus PPr) were considered significant only if the p-value from the Wilcoxon Rank Sum test or Chi-square test was less than or equal to 0.0167 (i.e. desired alpha divided by the

number of comparisons for each variable = 0.05/3).

Extreme users were further stratified based on the drug group for which dosage criteria were exceeded: asthma medications *versus* mood-modifying drugs. Subjects exceeding criteria for two or more drug groups were excluded from this analysis (n=13). Differences between the two groups with respect to the study variables were tested statistically using the Wilcoxon Rank Sum test for continuous variables and the Chi-square test for categorical variables. Fisher's exact test was used for categorical variables with expected cell frequencies of less than 5. Differences with a p-value of less than or equal 0.05 were considered statistically significant.

Age- and sex-specific identification rates were calculated to identify population subgroups that may have been at an increased risk for identification by the PPRP. The ***identification rate*** was defined as the proportion of active (or eligible) beneficiaries identified by the PPRP in 1992. Identification rates were also calculated for each of the four residence categories. The denominator for the residence-specific identification rates was the number of eligible beneficiaries rather than the number of active beneficiaries because the distribution of active beneficiaries stratified by residence was not available. To facilitate comparison of the residence categories, the identification rates were age-sex adjusted using the total Saskatchewan population of eligible beneficiaries in 1992 as the standard. The direct method of standardization was used (Hennekens and Buring 1987).

To provide some indication of which subgroups of drug users may have been at an increased risk of identification by the Extreme User Program, age-sex specific extreme user rates were calculated for each of the monitored drug groups. The ***extreme user rate*** was defined as the mean number of extreme users per 1000 users of the drug group in question.

3.3.5.3 Patient Profile Release Program Short-term Follow-up

The follow-up phase of the investigation focussed on a subgroup of individuals selected from the study population characterized in the descriptive phase outlined above (Section 3.3.5.2). Individuals who were first identified by the PPRP in January 1992 or between April 7 and September 8, 1992, inclusive, were eligible for this phase of the study. Subjects were excluded from the study if their first profile was not released to prescribers and pharmacies, or if SPDP coverage ceased at any point during the 112 day period follow-up period. Individuals identified after September 8, 1992 were also excluded because follow-up of these patients for the full 112 day post-identification period was not possible given the available data.

Study subjects were divided into two groups. The ***intervention group*** included subjects first identified between April 7 and September 8, 1992. Medication profiles for these individuals were released shortly after the index identification. The ***comparison group*** consisted of subjects first identified in January 1992. For administrative reasons, medication profiles for these individuals were not released by the PDSB until late March 1992. Profiles released late in the follow-up period were expected to have minimal or no impact on short-term outcomes. Therefore, the comparison group was used to approximate the outcome rates that would have been expected if no profiles had been released.

For each subject, data on the following baseline characteristics were obtained from the record of the first (i.e. index) identification: age, gender, type of SPDP coverage, residence code, number of prescribers and pharmacies in the 90 day period prior to the index identification, the drug group exceeded and the percentage of maximum threshold daily dose (for Extreme User subjects) and the number of different drugs in the 90 day period prior to the index identification (for Polypharmacy subjects). The number of days spent in hospital during the follow-up period was calculated from hospital admission and discharge data. For subjects who were re-identified by the PPRP during the study period, data on the following variables were obtained from the record of

the second identification: the criteria exceeded, the numbers of different prescribers and pharmacies, the percentage of maximum threshold daily dose (for Extreme User subjects) and the number of different drugs (for Polypharmacy subjects).

Because the Extreme User, Polypharmacy and Polyprescriber Programs focussed on different drug use problems, separate analyses were performed for individuals identified under each program. Baseline characteristics of the intervention and comparison groups were compared statistically using the Wilcoxon Rank Sum test for continuous variables and the Chi-square test for categorical variables. The Wilcoxon Rank Sum test, a non-parametric procedure, was used rather than the independent t-test because the assumption of normality for the latter test was violated by each of the continuous variables. Differences between the groups were considered statistically significant if the p-value for the test statistic was less than or equal to 0.05.

The primary outcome of interest was re-identification by the PPRP during the 112 day period following the index identification. The 112 day follow-up period, which took into account the 90 day post-identification period during which patients could not be re-identified by the PPRP, allowed each subject two opportunities to be re-identified. Re-identification was selected as the main outcome of interest because it was a readily available marker of changes in drug utilization patterns. That is, prevention of re-identification by the Extreme User, Polypharmacy or Polyprescriber Programs, required that the level of drug use, the number of different drugs or the number of different prescribers, respectively, fall below the threshold criteria for identification. Thus, the absence of re-identification during the follow-up period was considered a desirable outcome because it indicated that the utilization pattern had been modified at least to the extent that the subject no longer exceeded threshold criteria. Secondary outcomes of interest included changes in the numbers of prescribers and pharmacies, the level of drug use (for Extreme Use subjects) and the number of different drugs (for Polypharmacy subjects). Data on these secondary outcomes were available only for subjects who were re-identified during the follow-up period.

Analysis of the Re-identification Outcome Variable

Re-identification rates were calculated to estimate the cumulative incidence of re-identification among subjects in the intervention and comparison groups. The ***re-identification rate*** was defined as the proportion of subjects re-identified by the PPRP during the follow-up period. Re-identification rates for the study groups were compared statistically using the Chi-square test.

The magnitude of the association between profile release and re-identification was estimated by calculating crude and adjusted estimates of ***relative risk*** (RR). The RR is defined as the ratio of the incidence of the outcome in the exposed group divided by the incidence in the non-exposed group (Hennekens and Buring 1987). An RR equal to one indicates there is no association between the exposure and the outcome. An RR of greater than one indicates that exposed subjects have a greater risk of developing the outcome than non-exposed subjects and an RR of less than one that exposure is associated with a decreased risk of the outcome.

In the present investigation, exposure corresponded to profile release, which was represented by study group status. The intervention group was considered to be "exposed" to profile release, while the comparison group was considered "non-exposed". The outcome variable was defined as re-identification by the PPRP during the follow-up period. The crude (unadjusted) estimates of RR were calculated using the following formula (Hennekens and Buring 1987):

$$RR = \frac{a/(a+b)}{c/(c+d)} \qquad (3.1)$$

where a, b, c and d denote cell frequencies for a two-by-two table, as defined in Figure 3.2.

		Outcome		
		Yes	No	Total
Exposure	Yes	a	b	a + b
	No	c	d	c + d
	Total	a + c	b + d	T = a + b + c + d

Figure 3.2: Notation for a Two-by-Two Table

A confidence interval (CI) was calculated for each RR. A 95% CI which did not include the null value of one was considered to be an indication that the association between exposure and outcome was statistically significant at an α level of 5%. The CI was calculated using the Taylor series formula (Kleinbaum et al. 1982):

$$CI = RR \exp\left[\pm z_{1-\alpha/2} \sqrt{(1 - I_i)/a + (1 - I_c)/c} \right] \quad (3.2)$$

where

$z_{1-\alpha/2}$ = the critical value of the standard normal distribution for the chosen confidence level. For a 95% confidence interval, $\alpha = 0.05$ and $z_{0.975} = 1.96$,

I_i = incidence in the intervention group = a/(a + b), and

I_c = incidence in the comparison group = c/(c + d).

The Mantel-Haenszel method of stratified analysis was used to control for the effects of potential confounders on the association between study group status and re-identification. This method of analysis involves stratifying the confounding variable

into homogeneous categories, estimating the RR for the "exposure – outcome" association within each stratum and calculating a pooled summary estimate of relative risk (RR_{MH}). The RR_{MH}, a weighted average of the stratum-specific relative risk estimates, was calculated using the following formula (Hennekens and Buring 1987):

$$RR_{MH} = \frac{\Sigma a(c + d)/T}{\Sigma c(a + b)/T} \qquad (3.3)$$

where the numerator and denominator are summed over all of the strata.

The RR_{MH} provides an estimate of the magnitude of the association between the exposure and outcome that is adjusted for the effects of the confounding variable. For example, suppose that the RR_{MH} for the association between profile release and re-identification was 0.5 after controlling for the effects of gender. This RR_{MH} indicates, firstly, that intervention group subjects were half as likely as comparison group subjects to be re-identified and, secondly, that the observed association cannot be explained by differences between the two study groups with respect to gender.

The 95% CI for the RR_{MH} was calculated with the test-based formula (Hennekens and Buring 1987):

$$CI = RR_{MH}^{(1 \pm z/\chi)} \qquad (3.4)$$

where that χ is the square root of the Mantel-Haenszel chi-square statistic (χ^2_{MH}),

$$\chi^2_{MH} = \frac{\left[\Sigma a - \Sigma\left(\frac{(a + b)(a + c)}{T}\right)\right]^2}{\Sigma\left(\frac{(a + b)(c + d)(a + c)(b + d)}{T^2(T-1)}\right)} \qquad (3.5)$$

Summary RR_{MH} estimates were calculated only when the stratum-specific relative risks were similar. Assessment of the uniformity of the stratum-specific RRs involved both visual inspection of the risk estimates and statistical testing using the Breslow-Day Test for Homogeneity (Kleinbaum et al. 1982). Heterogeneity of the stratum-specific risk estimates means that there is an interaction between the stratified variable and the exposure, such that the effect of exposure on the outcome depends on the level of the interacting variable. When an interaction is present, it is inappropriate to summarize the stratum-specific RRs into a single risk estimate.

While stratified analysis is a valuable method of controlling for a small number of confounding variables, this procedure becomes rather cumbersome and inefficient as the number of strata increases. Therefore, multivariate logistic regression analysis was also employed to examine the association between profile release and re-identification and to evaluate the influence of the other independent variables on this outcome. The general form of the multiple logistic regression model is summarized by Equation 3.6 (Hosmer and Lemeshow 1989),

$$g(\mathbf{x}) = \ln \left\{ \frac{\pi(\mathbf{x})}{1 - \pi(\mathbf{x})} \right\} = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_p x_p \qquad (3.6)$$

where,

$\mathbf{x}$ = the collection of independent variables $(x_1, x_2, \ldots, x_p)$,

$\pi(\mathbf{x})$ = probability of the outcome given $\mathbf{x}$,

$g(\mathbf{x})$ = the natural logarithm of the odds of the outcome given $\mathbf{x}$,

β_0 = the intercept, and

$\beta_{1,2,\ldots,p}$ = the slope coefficients for $x_1, x_2, \ldots, x_p$.

For the present investigation, the outcome variable was re-identification during the follow-up period and $\pi(\mathbf{x})$ was the probability of re-identification given the collection of independent study variables. The independent variables considered for inclusion in the logistic model were age, gender, residence, coverage type, the number of

follow-up days spent in hospital and the numbers of prescriber and pharmacies in the 90 day period prior to the index identification. The level of extreme use and the drug group for which dosage criteria were exceeded were also included in the Extreme User regression analysis. The number of different drugs was included in the analysis of Polypharmacy subjects.

The slope coefficient β_1 represents the change in the logit for a change of one unit in the independent variable x_1. The slope coefficient was converted to an odds ratio (OR) by calculating its antilogarithm as follows:

$$OR = e^{\beta_1} \tag{3.7}$$

The confidence interval for the OR was calculated using the formula described by Equation 3.8:

$$CI = \exp[\beta_1 \pm z_{1-\alpha/2}\, SE(\beta_1)] \tag{3.8}$$

where

$z_{1-\alpha/2}$ = the critical value of the standard normal distribution for the chosen confidence level. For a 95% confidence interval, $\alpha = 0.05$ and $z_{0.975} = 1.96$; and,

$SE(\beta_1)$ = the standard error of β_1.

An odds ratio from a logistic regression model provides an estimate of the association between the independent variable and the response variable that is adjusted for the potential confounding effects of all the other variables in the model. For example, an OR of 2.0 for a dichotomous variable x_1 (coded as 1 and 0 for exposed and non-exposed, respectively), indicates that exposure to x_1 is associated with an increased risk of the outcome, and that this association cannot be explained by differences in the other variables included in the model.

Separate logistic regression models were fitted for the Extreme User, Polypharmacy and Polyprescriber Programs. The model-building process described by Hosmer and Lemeshow (1989) was used for the regression analysis in this investigation. This process involved five steps:

1. Univariate analyses were performed to examine the association between re-identification and each of the independent variables. These analyses involved univariate logistic regression supplemented with contingency tables for categorical variables and smoothed scatter plots for continuous variables.

2. A forward stepwise logistic regression with a liberal entry criterion ($p<0.25$) was then performed to identify variables that were potentially important predictors of re-identification in a multivariate model. A significance level of $p<0.25$ was chosen for this screening process because the conventional significance level of $p<0.05$ often fails to identify important variables (Hosmer and Lemeshow 1989). Variables which were not included in the model generated by the stepwise procedure were forced into the model under two conditions: (i) if they were moderately associated with the outcome in univariate analyses ($p<0.25$), or (ii) if they were considered to be potential confounders. The resulting model, which contained all potentially important predictors of re-identification and all potential confounders, was considered the ***"maximum model"***.

3. The importance of each variable in the maximum model was then examined more closely. This step involved consideration of two issues: the prediction of re-identification and the potential for confounding. Variables not contributing to the multivariate model in terms of prediction or confounding were eliminated from the maximum model.

To assess the statistical significance of the factors, the least significant variable

(i.e. the variable with the largest p value) was removed from the maximum model and the resulting "reduced" model was compared with the maximum model using the Likelihood Ratio Test (Hosmer and Lemeshow 1989). A non-significant result for the Likelihood Ratio Test ($p>0.05$) indicated that the variable in question was not a statistically significant predictor of re-identification in the multivariate model.

The importance of the variable as a confounder was assessed by comparing the regression coefficients of the variables in the model before and after the removal of the covariate. Substantial changes in the β values for the independent variables indicated that the factor in question was an important confounder of the association between re-identification and the variable(s) for which the regression coefficients changed. Determination of whether a change in the β value was substantial enough to indicate the presence of confounding required a judgement call. Hosmer and Lemeshow (1989) stated that any "biologically important" change in the estimated coefficient indicates that the covariate is a confounder.

The variable was removed from the model if it was neither a significant predictor nor a confounder. The next least significant variable in the resulting model was then examined in a similar manner. This cycle of removing variables and assessing their statistical significance and potential for confounding was repeated until no further variables could be eliminated from the model. The resulting model was considered the ***"main effects model"***.

4. Once the important variables had been identified, the assumption of linearity in the logit was examined for each of the continuous variables. This procedure involved dividing each continuous variable into categories (quartiles, if possible) and substituting the continuous-scaled variable in the main effects model with this newly formed categorical variable. The resulting β coefficients for the levels

of the categorical variable were plotted against the midpoints of the categories. A linear plot indicated that the assumption of linearity was fulfilled. Non-linearity required consideration of mathematical transformation or categorization of the variable.

5. The final step in the model-building process involved the examination of potential interactions among the main effects variables included in the model. Interactions were assessed by forming interaction terms, adding them to the main effects model individually and testing their statistical significance using the Likelihood Ratio Test. An interaction term for two variables is the product of the variables. For example, for a model containing three independent variables, x_1, x_2 and x_3, three interaction terms were examined: x_1x_2, x_1x_3 and x_2x_3. Interaction terms with a significant Likelihood Ratio Test ($p<0.05$) were considered for inclusion in the model.

Once a model containing the appropriate main effects variables and interaction terms was developed, the fit of the model was examined using various goodness-of-fit techniques. "Goodness-of-fit" refers to the effectiveness of a model in describing the outcome variable (Hosmer and Lemeshow 1989). A model is considered to fit well if the summary measures of the distance between the observed and fitted values of the response variable are small and if the contribution of each pair of observed and fitted values to the summary measures is small and unsystematic (Hosmer and Lemeshow 1989).

The Hosmer-Lemeshow goodness-of-fit Chi-square statistic was used to assess the overall fit of the model (Hosmer and Lemeshow 1989). This statistic is a summary measure of the distances between the observed and fitted values of the outcome. A small χ^2 statistic and corresponding large p-value indicates that the overall agreement between the observed and predicted values is good and that the overall fit of the model is good.

Regression diagnostic statistics were used to examine the fit of the model over the range of the covariate patterns. The term "covariate pattern" is used to "describe a single set of values for the covariates in a model" (Hosmer and Lemeshow 1989).[3] Three diagnostic statistics were examined for each covariate pattern. All three statistics measure the effect that deleting all subjects with a given covariate pattern has on the model. The first, $\Delta\chi_j^2$, is defined as the change in the value of the Pearson chi-square statistic that occurs when subjects with covariate pattern *j* are deleted from the model. The quantity ΔD_j measures the change in the value of the deviance that results from the deletion of subjects with covariate pattern *j*. The third diagnostic statistic was $\Delta\beta_j$ (also called "influence") is defined as the change in the estimated regression coefficients resulting from the deletion of subjects with covariate pattern *j* (Hosmer and Lemeshow 1989). Each of these statistics were plotted against the predicted probability (π) to identify covariate patterns which have a poor fit and/or a large influence.

With logistic regression analysis, it is possible to calculate the percentage of observed responses that are correctly predicted by the model. This figure provides an estimate of how well the model predicts the outcome, but it is not a good measure of the fit of the model because the expected error rate depends on the magnitude of the slope of the model, not necessarily on the fit (Hosmer and Lemeshow 1989). In addition, "classification is sensitive to the relative sizes of the two component groups and will always favour classification into the larger group, a fact that is also independent of the fit of the model" (Hosmer and Lemeshow 1989). Therefore, a classification table of predicted versus observed responses was not used to assess the fit of the logistic regression models in the present investigation.

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[3] To clarify the term "covariate pattern", consider a model which has four independent predictor variables: study group (intervention, comparison), age (<65, ≥65 years), sex (male, female) and level of drug use (high, low). All intervention group subjects who are males aged 65 years or older and have "high" levels of drug use have the same distinct covariate pattern.

Analysis of the Secondary Outcomes

As noted above, re-identification during the short-term follow-up period was the primary outcome of interest. To prevent re-identification by the PPRP, drug utilization had to fall below the threshold criteria. However, profile release may have resulted in changes in the level of extreme use, the number of different drugs or the number of prescribers which may have been clinically important, but which were not large enough to prevent re-identification by the Extreme User, Polypharmacy or Polyprescriber Programs, respectively. In such cases, limiting the investigation to the re-identification outcome would have failed to identify some clinically important effects. Therefore, the secondary outcomes were investigated to provide additional information about the impact of the PPRP.

Individuals who were re-identified by the PPRP during the short-term follow-up period were included in this analysis. Four outcomes were studied: the changes in the numbers of prescribers and pharmacies, the change in the level of extreme use (for Extreme User subjects) and the change in the number of different drugs (for Polypharmacy subjects). Analysis of these secondary outcomes was limited to the individuals who were re-identified by the Program because the PPRP database did not contain similar information for subjects who were not re-identified.

The secondary outcomes of interest were calculated as follows:

change in the # of prescribers	=	# of prescribers in the 90 day period prior to the 2nd identification	—	# of prescribers in the 90 day period prior to the 1st identification
change in the # of pharmacies	=	# of pharmacies in the 90 day period prior to the 2nd identification	—	# of pharmacies in the 90 day period prior to the 1st identification
change in the # of different drugs	=	# of different drugs in the 90 day period prior to the 2nd identification	—	# of different drugs in the 90 day period prior to the 1st identification

change in the level of extreme use	=	% of threshold dose in the 90 day[4] period prior to the 2nd identification	—	% of threshold dose in the 90 day[4] period prior to the 1st identification

Differences between the intervention and comparison groups with respect to these four variables were tested statistically using the independent t-test. Differences with a p value of less than or equal to 0.05 were considered statistically significant.

The outcomes were also measured as the proportion of re-identified subjects who had a decrease in the numbers of prescribers or pharmacies, the number of different drugs or the level of extreme use. The level of extreme use was considered to have decreased only if the level fell by 20 percentage points or more. This cut point of 20 was chosen because a change of less than 20 percentage points (e.g. a decrease in the percentage of maximum threshold dose from 260% to 250%) was not considered to be a meaningful decline in use. The remaining variables were considered to have decreased if the numbers of prescribers, pharmacies or drugs fell by one or more. Differences between the study groups with respect to the proportions of subjects with decreases in the variables of interest were tested statistically with the Chi-square test if the expected frequencies were 5 or more, or Fisher's test if this criterion was not fulfilled.

3.3.5.4 Patient Profile Release Program Long-term Follow-up

The short-term follow-up phase of the investigation was designed to estimate the impact of the PPRP by comparing the experience of an intervention group and a comparison group. As noted above, medication profiles for the intervention group subjects were released shortly after each patient's index identification. In contrast, profiles for the comparison group subjects were sent to prescribers and pharmacies 2 to 2.5 months after identification. Profiles released late in the follow-up period were

[4] 180 days for extreme use of asthma medications

expected to have little or no impact on re-identification rates. Therefore, by limiting the follow-up period to 112 days after the index identification, it was possible to use the comparison group to approximate the outcome rates that would have been expected if no profiles had been released. Beyond the 112 day follow-up period, there was an increased likelihood that patient outcomes for the comparison group were influenced by the release of their profiles. Therefore, comparison of the two study groups after the short-term follow-up period would provide a less reliable estimate of the impact of the PPRP.

The long-term follow-up phase of the investigation was designed to provide additional information about the experience of study subjects beyond the 112 day post-intervention period. This long-term follow-up analysis was limited to intervention group subjects. Subjects in the comparison group were excluded from this analysis because they represented neither individuals who did not have profiles released nor individuals whose profiles were released in a timely manner. Furthermore, because patients could start being re-identified by the PPRP 90 days after their initial identification, re-identification for comparison group subjects could occur within a month of the release of their profiles, and then not again for another 90 days. Therefore, creation of a meaningful summary description of the re-identification experience for these individuals was not possible.

In this phase of the investigation, study subjects were followed until December 31, 1992. Because the selection of intervention group subjects was based on identifications during the period April 7 to September 8, 1992 (Section 3.3.5.3), the follow-up period for individual patients ranged from 98 to 268 days. Re-identification for these subjects was described using the life table method described by Kahn and Sempos (1989). This analytic procedure provided an effective means of summarizing longitudinal data from individuals with differing lengths of follow-up.

For each subject, the follow-up period began on the day after they were first identified. The study period was divided into a number of intervals (Appendix I). The first interval, days 0 to 98, incorporated the 90 day post-identification period during

which the PPRP could not re-identify patients. Since the PPRP monitoring process operated on a biweekly basis, Day 98 of follow-up was the first date on which an individual could be re-identified. The remainder of the follow-up period was divided into 14 day intervals corresponding to the biweekly computer runs for the PPRP. The last interval, days 253 to 268, was 16 days long because the regular biweekly run scheduled for December 29 was delayed until December 31, 1992 to accommodate the year-end prescription claims.

Follow-up of individual study subjects ended for any of three reasons: (1) the patient was re-identified, (2) the patient was not re-identified by December 31, 1992, or (3) SPDP coverage ceased, e.g., due to death or a move out of the province. Individuals in the second and third categories were considered "censored". Subjects who were censored during a given interval were assumed to be eligible for re-identification until the end of the interval because any prescriptions obtained between day 1 of the interval and the censoring date were included in the biweekly claims on day 14.

A number of calculations were performed for the life table analysis. The probability of re-identification during the interval x to x + n for those individuals who were eligible for re-identification at the beginning of the interval was calculated as follows (Kahn and Sempos 1989):

$$ {}_nq_x = \frac{{}_nd_x}{O_x} \qquad (3.9) $$

where

x = time at the beginning of the interval,

n = length of the interval,

${}_nd_x$ = number re-identified during the interval x to x + n, and

O_x = number under observation at time x.

The probability of not being re-identified (i.e. surviving) during the interval x to x + n was calculated as:

$$ {}_{n}p_{x} = 1 - {}_{n}q_{x} \tag{3.10} $$

The probability, ${}_{N}P_{x}$, of surviving to the end of a period spanning multiple intervals (i.e. N denotes more than one interval of length n) was calculated as the product of the ${}_{n}p_{x}$ values for the intervals included in the period. For example, the probability of not being re-identified for at least 126 follow-up days was calculated as ${}_{126}P_{0} = ({}_{98}p_{0})({}_{112}p_{99})({}_{126}p_{113})$.

Ninety-five percent confidence intervals around ${}_{N}P_{x}$ were calculated using the following formula (Kahn and Sempos 1989):

$$ CI = {}_{N}P_{x} \pm z_{1-\alpha/2}\, SE({}_{N}P_{x}) \tag{3.11} $$

where

$z_{1-\alpha/2}$ = the critical value of the standard normal distribution for the chosen confidence level. For a 95% confidence interval, $\alpha = 0.05$ and $z_{0.975} = 1.96$; and,

$$ SE({}_{N}P_{x}) = {}_{N}P_{x}\sqrt{\sum_{i} \frac{{}_{n}q_{x}}{O_{x} - {}_{n}d_{x}}} $$

where i = the number of intervals in period N.

3.3.6 Statistical Analysis

Statistical analyses were conducted on the University of Saskatchewan VAX-VMS computer system using the SAS Version 6.08 statistical package. The logistic regression analysis was conducted using the BMDP Version 7.0 statistical package, but was supplemented with analyses in SAS.

4.0 Results

4.1 Drug Utilization in Saskatchewan

4.1.1 Study Population and Drug Utilization Data

Drug utilization data for the period 1989 to 1993 were obtained for all of the medications monitored by the Extreme User Program during its first year of operation (Appendix A). Use of the Major Tranquilizers (Formulary Class 28:16.08) was not studied because extreme users of these agents were excluded from the other phases of the investigation. The analysis included all prescriptions claimed on behalf of eligible beneficiaries during the study period. In June 1992, there were 949,986 beneficiaries eligible for coverage under the Saskatchewan Prescription Drug Plan (Saskatchewan Health 1992).

It is important to note that the drug utilization statistics were obtained from SPDP reports which were not designed specifically for this investigation. Ideally, utilization of the medications included in a given Patient Profile Release Program drug linkage group would have been examined together as a single group (Appendix A). However, the SPDP annual drug use reports provided prescription and user data only for individual drugs and for Formulary classes. Because most of the PPRP drug linkage groups included drugs from more than one Formulary class, or included only a few drugs in a given Formulary class, it was not possible to summarize drug utilization data for specific PPRP linkage groups. Instead, utilization figures for individual drugs or Formulary classes were examined separately. The drugs included in each Formulary class are listed in Appendix F.

The use of uneven age groups in the description of drug utilization patterns (Section 4.1.2) was also related to the format of the data source. The SPDP drug use reports presented age-specific utilization figures using a combination of five- and ten-year age categories. In this investigation, the description of drug utilization by age was limited to the age groups presented in the drug use reports.

4.1.2 Drug Utilization Patterns by Age and Sex – 1992

In 1992, the two most widely used mood-modifying drug groups were the Anxiolytic, Sedative and Hypnotic Benzodiazepines and the Opiate Agonist Narcotic Analgesics (Table 4.1). Salbutamol was the most extensively used of the monitored asthma medications.

Narcotic Analgesics

Narcotic analgesic (NA) agents were listed in two Formulary classes: Opiate Agonists (Class 28:08.08) and Opiate Partial Agonists (Class 28:08.12). The opiate agonists represented 98.3% of all prescriptions for Formulary NA agents and were used by nearly 4% of the study population in 1992. For every 1000 eligible beneficiaries, there was an average of 75.7 prescriptions for opiate agonists with an additional 1.3 prescriptions for pentazocine, the only drug listed as an opiate partial agonist (Table 4.1).

NA use was related to both age and sex. The proportion of the population with at least one prescription for an opiate agonist increased with age from 3.5 users per 1000 eligible beneficiaries less than 15 years of age to more than 80 users per 1000 beneficiaries aged 90 years or older (Figure 4.1). Overall prescription rates and user rates were 29.8% and 19.4% higher for females than males, respectively. The gender difference was observed for nearly all age groups, but was most pronounced among

Table 4.1: Utilization of Drugs Monitored by the Extreme User Program – 1992

Drug Group (Formulary Class)	Prescription Rate‡	User Rate¶	Prescription per User Rate§
Narcotic Analgesics			
Opiate Agonists (28:08.08)	75.7	38.3	2.0
Opiate Partial Agonists (28:08.12)	1.3	0.5	2.6
Anticonvulsants			
Phenobarbital (28:12.04)	14.7	2.6	5.6
Clonazepam/Nitrazepam (28:12.08)	19.0	3.8	5.0
Anxiolytics, Sedatives and Hypnotics (28:24.00)			
Barbiturates (28:24.04)	1.3	0.2	5.3
Benzodiazepines (28:24.08)	229.0	49.6	4.6
Miscellaneous (28:24.92)	36.4	15.2	2.4
Bronchodilators (12:12.00)			
Fenoterol	6.3	1.2	5.4
Salbutamol	144.3	37.2	3.9
Terbutaline	1.2	0.5	2.3
Inhaled Corticosteroids (68:04.00)			
Beclomethasone Dipropionate	28.1	19.2	3.0
Budesonide	3.6	1.5	2.5
Flunisolide	0.7	0.2	3.9
Anticholinergics (12:08.08)			
Ipratropium Bromide	16.1	3.3	4.9

‡ Prescription Rate = mean number of prescriptions per 1000 eligible beneficiaries.
¶ User Rate = mean number of users per 1000 eligible beneficiaries.
§ Prescription per User Rate = mean number of prescriptions per user per year.

beneficiaries 65 years of age or older (Figure 4.1).

An average of two NA prescriptions were claimed for each user in 1992 (Table 4.1). This relatively small prescription per user rate indicates that these agents tended to be used on a short-term basis. Prescription per user rates increased with age from an average of approximately 1 prescription per year for users less than 15 years old to more than 4 prescriptions per year for users aged 95 years or older (Figure 4.1). The average prescription per user rates were similar for males and females (i.e. 1.9 and 2.1, respectively).

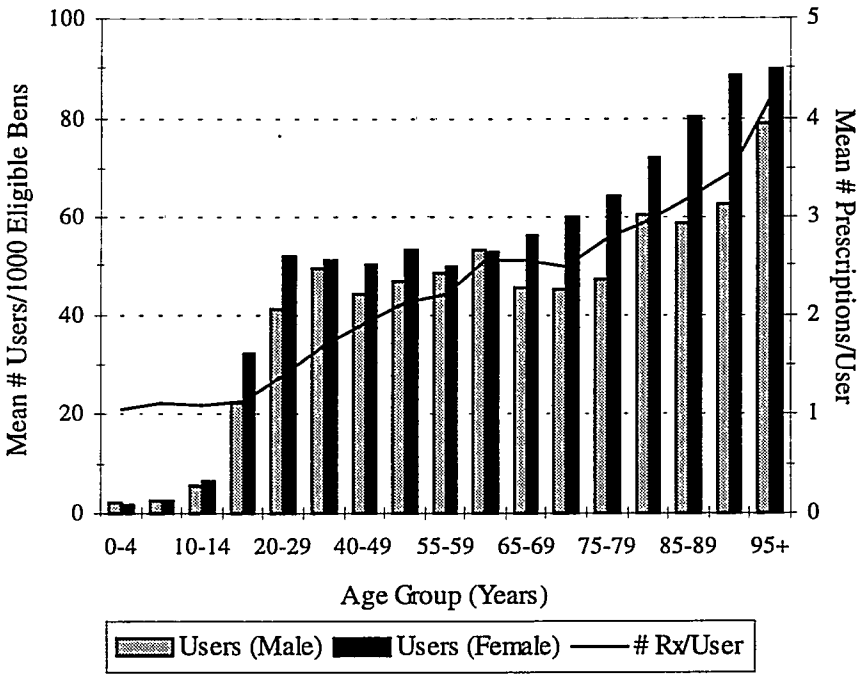

Figure 4.1: 1992 Drug Utilization by Age and Sex – Narcotic Analgesics (Formulary Class 28:08.08)

The combination product containing acetaminophen, caffeine and codeine was the most widely used narcotic analgesic agent, accounting for 73.3% of prescriptions for the opiate agonists in 1992 (Figure 4.2). Prescription, user and prescription per user rates for the individual NA agents are summarized in Appendix G. The age-sex distribution of utilization rates for acetaminophen/caffeine/codeine parallelled that of the NA group as a whole. The other agents were used less extensively and had more variable age-sex utilization patterns. Approximately 20% of the users of most NA agents were 65 years of age or older. However, some of the drugs indicated for the relief of moderate to severe pain were used more extensively in elderly beneficiaries than the other NA agents. In particular, 38.4%, 55.4% and 62.1% of hydromorphone, levorphanol tartrate and morphine users, respectively, were 65 years of age or older. Only one agent indicated for the relief of mild to moderate pain (propoxyphene) had a relatively high proportion of elderly users (47.9%).

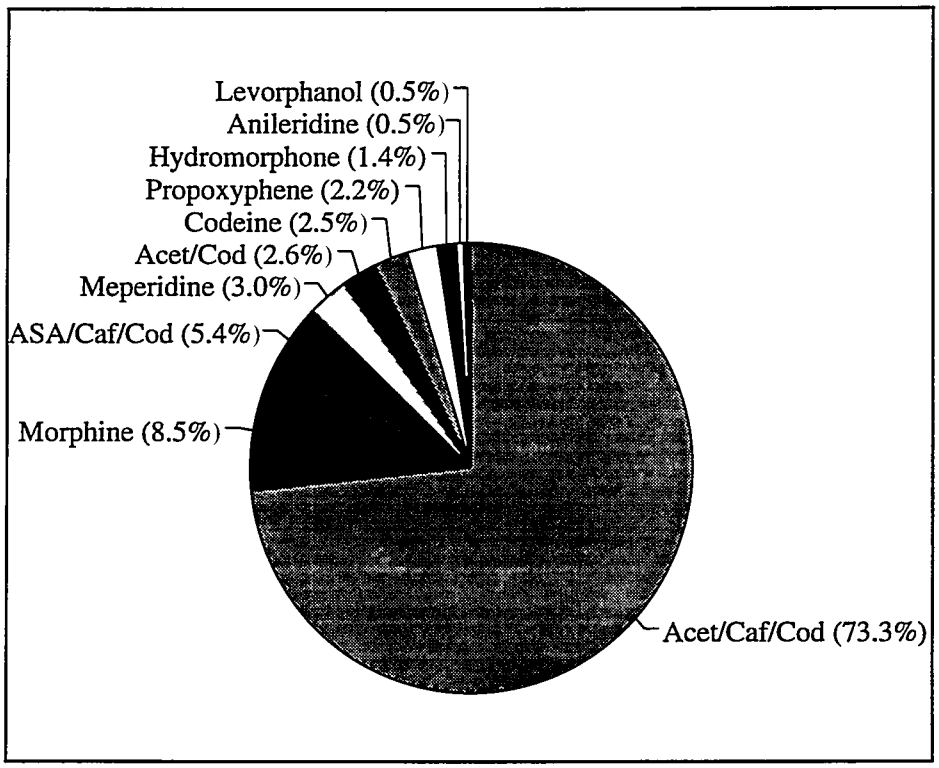

Figure 4.2: Percentage of Prescriptions for Opiate Agonist Narcotic Analgesics – 1992 (Abbreviations for combination products: Acet = Acetaminophen; Caf = Caffeine; Cod = Codeine)

Considerable variability was also observed in the prescription per user rates for the individual NA agents (Appendix G). Average annual prescription per user rates were highest for drugs indicated for the relief of severe pain (i.e. 4.2 and 3.7 prescriptions per year for users of morphine and levorphanol tartrate, respectively). Anileridine, hydromorphone, meperidine and pentazocine were indicated for moderate to severe pain and had somewhat lower prescription per user rates (range 1.9 to 3.0). Most of the agents indicated for the relief of mild to moderate pain had average prescription per user rates of less than two.

Benzodiazepines

The benzodiazepines (BZD) monitored by the PPRP were listed in two Formulary classes: Anticonvulsants (Class 28:12.08) and Anxiolytics, Sedatives and Hypnotics (Class 28:24.08). The Anticonvulsant BZD class included clonazepam and nitrazepam. The remaining BZD agents were listed in Class 28:24.08 (Appendix F).

The agents listed in the Anxiolytic, Sedative and Hypnotic class accounted for 92.3% of prescriptions for benzodiazepines. Average utilization rates in the study population were 229.0 prescriptions and 49.6 users per 1000 eligible beneficiaries (Table 4.1). The use of these agents increased with increasing age (Figure 4.3). When only beneficiaries 65 years of age or older were considered, the utilization figures rose to 807.3 prescriptions and 147.4 users per 1000 eligible beneficiaries. Thus, nearly 15% of elderly beneficiaries had at least one prescription for a BZD in 1992.

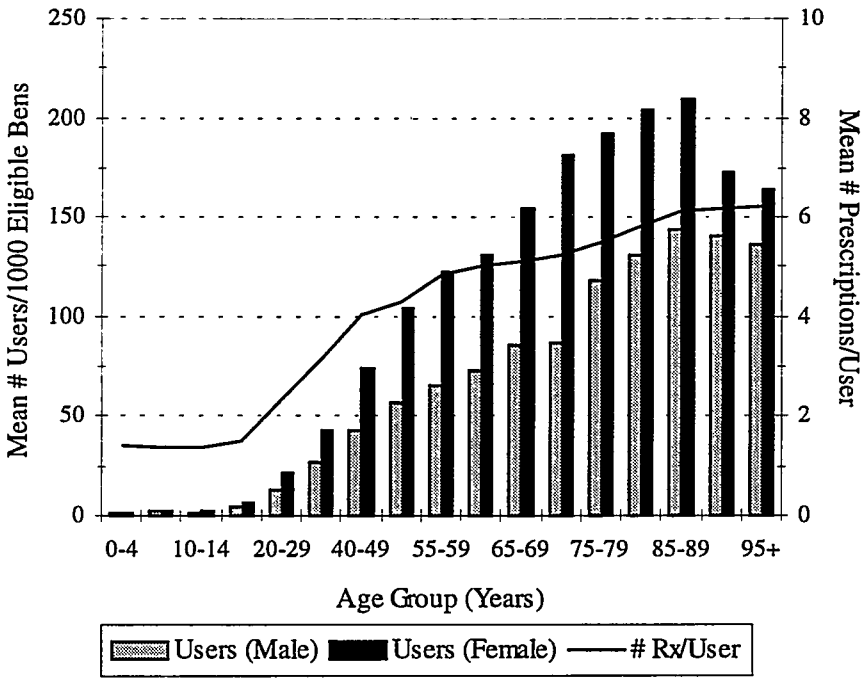

Figure 4.3: 1992 Drug Utilization by Age and Sex – Anxiolytic, Sedative and Hypnotic Benzodiazepines (Formulary Class 28:24.08)

A clear association between BZD use and gender was also observed. For every age group greater than 14 years, the proportion of eligible beneficiaries using Anxiolytic, Sedative and Hypnotic BZD agents was consistently greater for females than males. For every 1000 eligible female beneficiaries, there were 64.8 users and 306.0 prescriptions for BZD drugs; the corresponding figures for males were 34.3 users and 151.7 prescriptions.

An average of 4.6 BZD prescriptions were claimed for each user in 1992, suggesting that these agents tended to be used on a relatively long-term basis. Like the other measures of utilization, the number of BZD prescriptions per user increased with age from an average of 1.4 prescriptions per year for users less than 15 years of age to approximately 6.2 for users aged 90 years or older (Figure 4.3). There was little difference in the average number of BZD prescriptions claimed by male and female users in most age groups.

The most commonly prescribed BZDs were lorazepam, diazepam, triazolam and temazepam, together accounting for 67% of prescriptions for Anxiolytic, Sedative and Hypnotic BZD agents (Figure 4.4). Utilization figures for the individual BZD agents are summarized in Appendix G. The age-sex distributions for the individual BZDs had the same general pattern as that for the class as a whole. For each BZD, prescription and user rates were greater for females than males, with the most marked gender difference for clorazepate dipotassium (ratio of female to male user rates = 2.5) and the smallest difference for chlordiazepoxide (ratio of 1.1). User rates for each drug rose with increasing age until approximately 65 years of age. The use of diazepam and some of the shorter acting agents (lorazepam, oxazepam, temazepam and triazolam) continued to rise into old age, peaking between the ages 80 to 89 years. For the remaining BZDs, user rates increased only slightly or remained relatively constant after 65 years of age. Prescription per user rates ranged from a low of 3.3 for diazepam to 4.5 for oxazepam and did not appear to be related to the primary indication for use (i.e. sedative-hypnotic versus anxiolytic) (Appendix G).

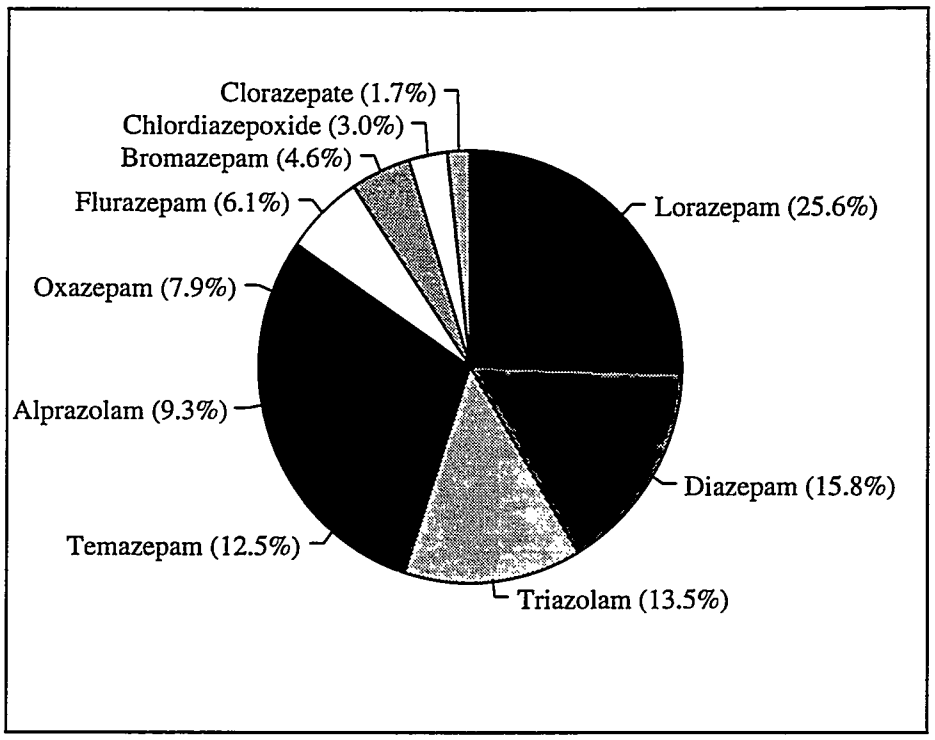

Figure 4.4: Percentage of Prescriptions for Anxiolytic, Sedative and Hypnotic Benzodiazepines (Formulary Class 28:24.08) – 1992

The age-sex utilization pattern of the Anticonvulsant BZDs was broadly similar to that of the Anxiolytic, Sedative and Hypnotic BZDs (Figure 4.5). As with the other BZD agents, the Anticonvulsant BZD utilization rates were higher among females than males and there was a clear association of increased use with increasing age (Figure 4.5). The main difference in the utilization patterns of the two BZD classes was the proportionately higher use of clonazepam and nitrazepam among children aged less than 14 years. This difference was likely a reflection of clonazepam and nitrazepam's indications for use in the prophylaxis of seizures, a disorder which often manifests in childhood.

The age distribution of the prescription per user rates for the Anticonvulsant BZDs was also markedly different from that observed for the other BZD agents. Children 14 years of age and younger had the highest number of prescriptions per user

for both nitrazepam and clonazepam (Figure 4.5). After age 50, the prescription per user rates for the Anticonvulsant BZDs were comparable to those observed in the Anxiolytic, Sedative and Hypnotic BZD group.

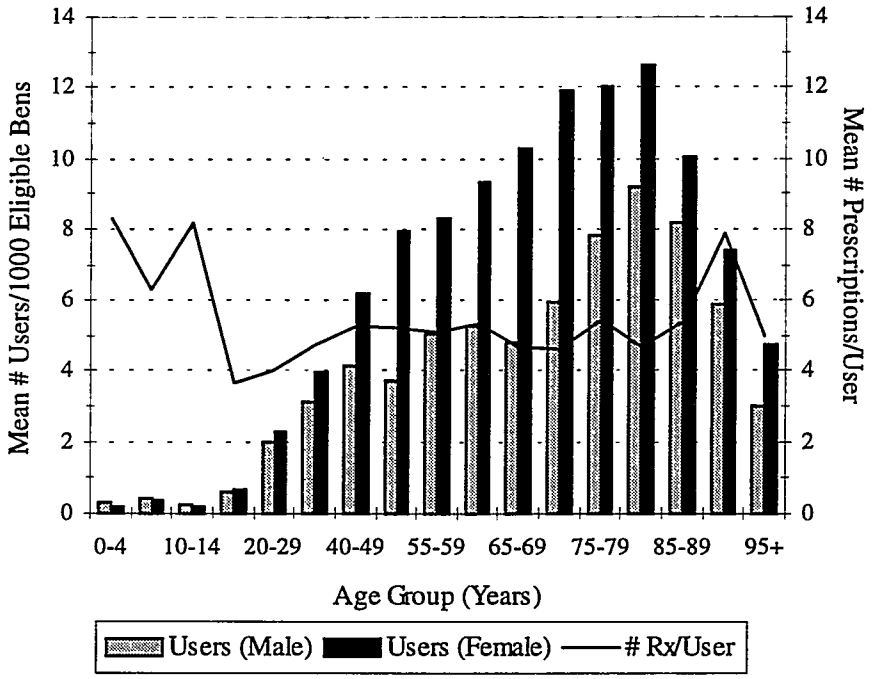

Figure 4.5: 1992 Drug Utilization by Age and Sex – Anticonvulsant Benzodiazepines (Formulary Class 28:12.08)

** Small numbers of users in the less than 20 year and greater than 89 year age groups contributed to the variability in the mean prescription per user rates in these age groups.

Barbiturates

The barbiturates listed in Anxiolytic, Sedative and Hypnotic Class 28:24.04 were used by small numbers of individuals. For every 1000 eligible beneficiaries, there were only 1.3 prescriptions for and 0.2 users of these drugs (Table 4.1). Secobarbital sodium was the most commonly prescribed sedative-hypnotic barbiturate, accounting for 42% of the prescriptions for drugs in this class (Figure 4.6).

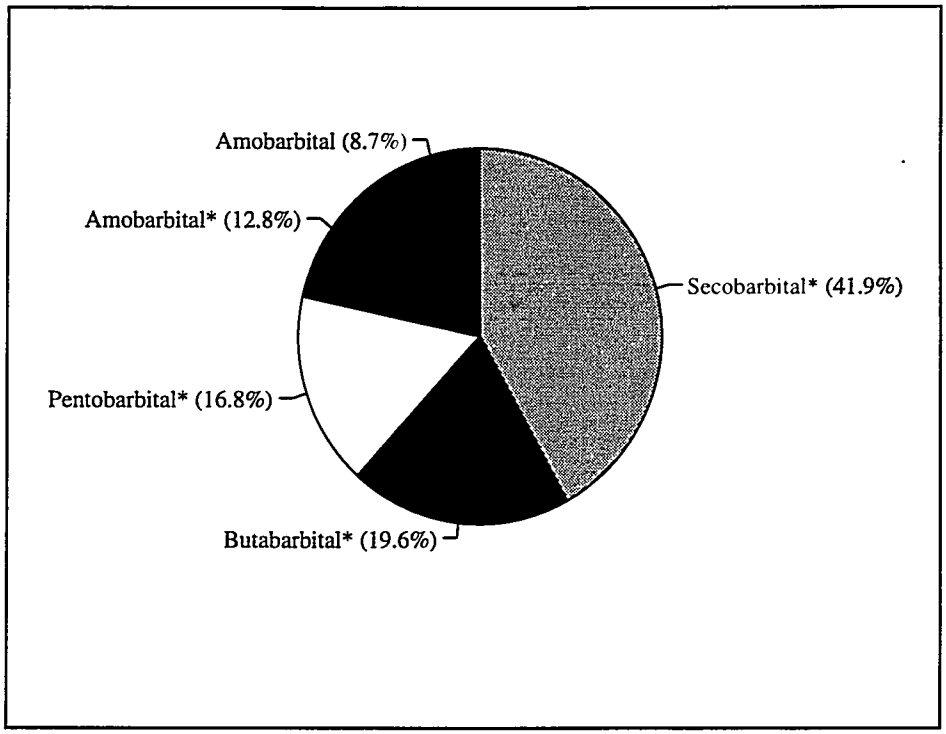

Figure 4.6: Percentage of Prescriptions for Anxiolytic, Sedative and Hypnotic Barbiturates (Formulary Class 28:24.04) – 1992 *Sodium Salt

Like the BZD agents, use of the barbiturates was greatest among females and the elderly (Figure 4.7). User rates for females were nearly twice as high those for males. When compared with the benzodiazepines, the barbiturates had an even greater predominance of elderly users: 64.0% of barbiturate users were 65 years of age or older compared with 43.7% of BZD users. The average number of prescriptions per barbiturate user was 5.3, somewhat higher than that of the BZDs. There was little difference in the average number of barbiturate prescriptions claimed by male and female users.

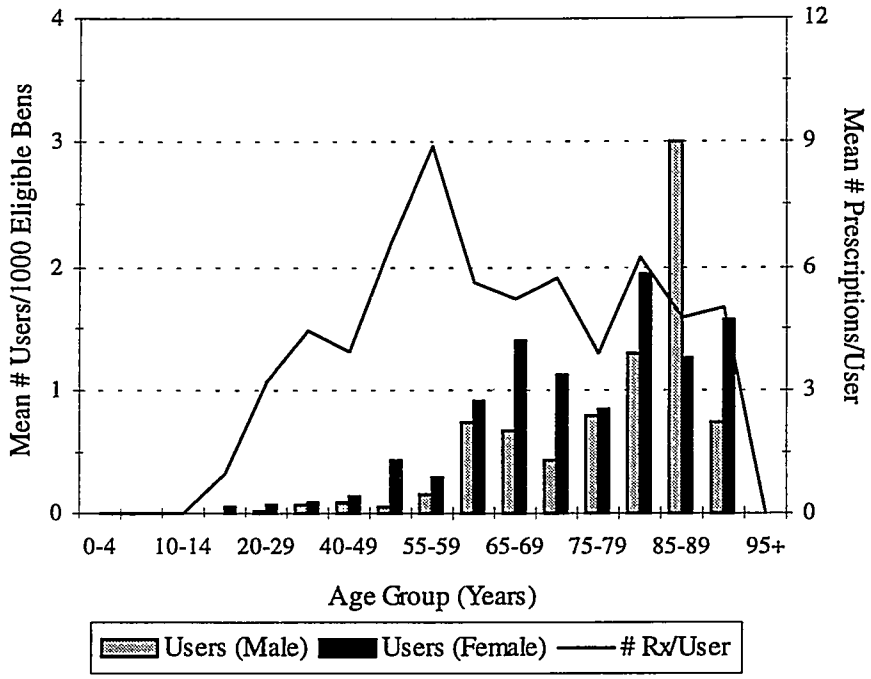

Figure 4.7: 1992 Drug Utilization by Age and Sex – Anxiolytic, Sedative and Hypnotic Barbiturates (Formulary Class 28:24.04)

** The small number of users in each age group contributed to the variability in the mean prescription per user rates.

Phenobarbital, an anticonvulsant agent listed in Formulary Class 28:12.04, was more widely used than the other barbiturates (Table 4.1). The age-sex utilization pattern for this drug differed in some respects from that of the other barbiturates. Like the sedative-hypnotic agents, phenobarbital prescription and user rates peaked among the very old (Figure 4.8). However, use among children and young adults relative to the other age groups was greater for phenobarbital than for the other barbiturates and the BZD agents. For example, 38.2% of phenobarbital users were less than 40 years old compared with only 8.1% of the barbiturate users and 17.9% of Anxiolytic, Sedative and Hypnotic BZD users. The relatively high use of phenobarbital among the young is likely a reflection of the use of this drug as an anticonvulsant. Unlike the other mood-modifying drugs, phenobarbital prescription and user rates were similar for males and females. The average number of prescriptions per phenobarbital user was 5.6. This measure showed little variation with either age (Figure 4.8) or sex.

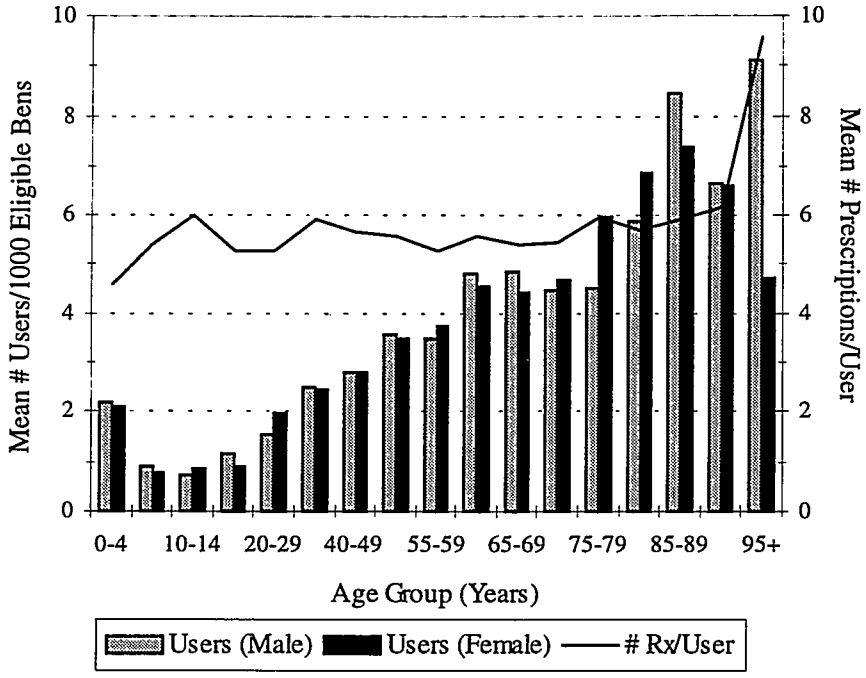

Figure 4.8: 1992 Drug Utilization by Age and Sex – Phenobarbital (Formulary Class 28:12.04)

Miscellaneous Anxiolytic, Sedative and Hypnotic Agents

Less widely used than the benzodiazepines, the Miscellaneous Anxiolytic, Sedative and Hypnotic drugs (Formulary Class 28:24.92) had prescription rates of 36.4 and user rates of 15.2 per 1000 eligible beneficiaries (Table 4.1). Hydroxyzine was the most widely used miscellaneous agent, accounting for nearly 59% of prescriptions for drugs in this class (Figure 4.9).

Use of these drugs was highest among elderly beneficiaries, particularly those greater than 80 years of age (Figure 4.10). Use was also higher for females than males. As with the BZD agents, prescription per user rates increased with age. However, the average number of prescriptions for each user was considerably lower for the miscellaneous agents than for the BZDs (2.4 versus 4.6 prescriptions per user,

respectively). A notable difference in the age-sex utilization patterns of the miscellaneous agents and the Anxiolytic, Sedative and Hypnotic BZD agents was the high use of the miscellaneous drugs in children and young adults relative to the other age groups. This difference was due almost entirely to hydroxyzine which accounted for 80.6% of the prescriptions for miscellaneous agents among individuals less than 40 years of age.

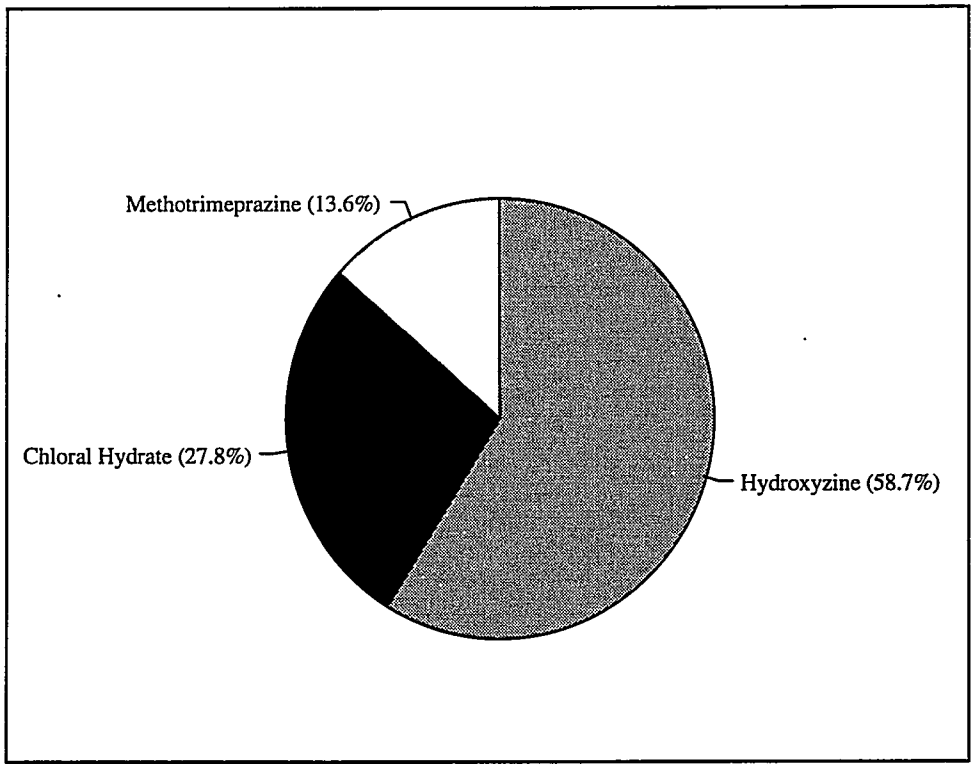

Figure 4.9: Percentage of Prescriptions for Miscellaneous Anxiolytic, Sedative and Hypnotic Agents (Formulary Class 28:24.92) – 1992

Although hydroxyzine was used more extensively in young individuals, the utilization patterns for the three drugs were similar in the elderly. For all three drugs, both prescription and user rates peaked among beneficiaries 90 years of age or older. User rates for all three agents were higher for females than males. Interestingly, the

three miscellaneous agents exhibited marked differences in the prescription per user rates, ranging from 1.8 for hydroxyzine to 6.1 for methotrimeprazine (Appendix G).

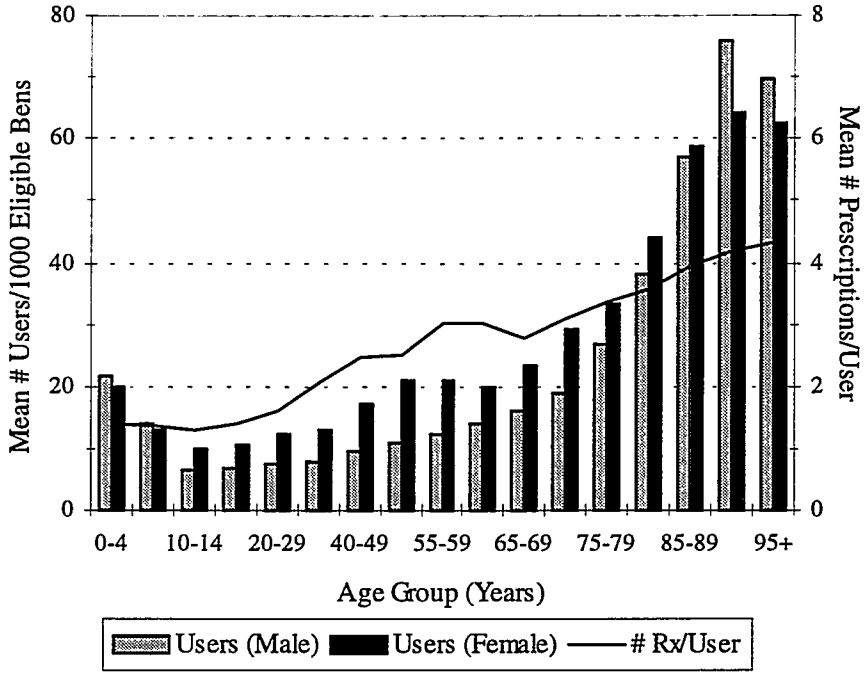

Figure 4.10: 1992 Drug Utilization by Age and Sex – Miscellaneous Anxiolytic, Sedative and Hypnotic Agents (Formulary Class 28:24.92)

Bronchodilators

Utilization data for fenoterol, salbutamol and terbutaline, the three bronchodilators monitored by the Extreme User Program in 1992, were examined individually (Table 4.1). These drugs were listed in Formulary Class 12:12.00 (Sympathomimetic Agents), however, use of the whole Formulary Class was not examined because many of the drugs included in the class were not monitored by the

PPRP (Appendix F).

Salbutamol was the most widely used bronchodilator, accounting for 95.0% of all prescriptions for the three drugs (Figure 4.11). Nearly 4% of the study population had at least one prescription for this drug. An average of 144.3 salbutamol prescriptions were claimed per 1000 eligible beneficiaries (Table 4.1).

The proportion of the population using salbutamol was greatest for children and the elderly (Figure 4.12). Prescription rates were much higher for the elderly than for any other age group, including children, because the average number of prescriptions claimed by salbutamol users increased with age. Overall prescription and user rates were 30.9% and 10.9% higher for males than females, respectively. However, male user rates exceeded female rates only for the age groups less than 15 years or greater than 59 years (Figure 4.12).

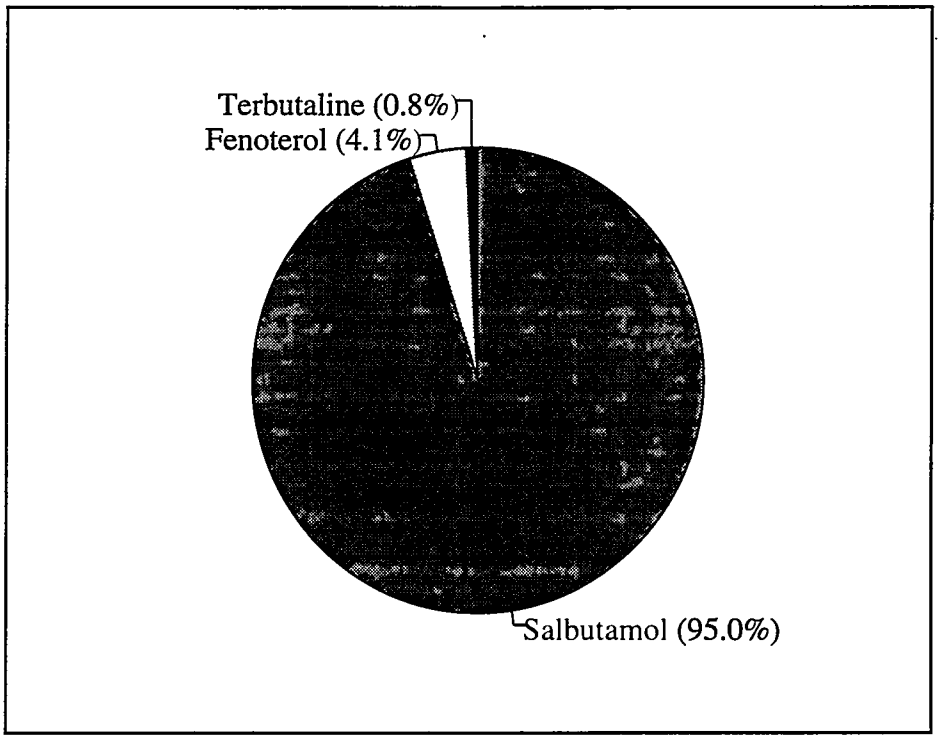

Figure 4.11: Percentage of Prescriptions for Bronchodilators (Formulary Class 12:12.00) – 1992

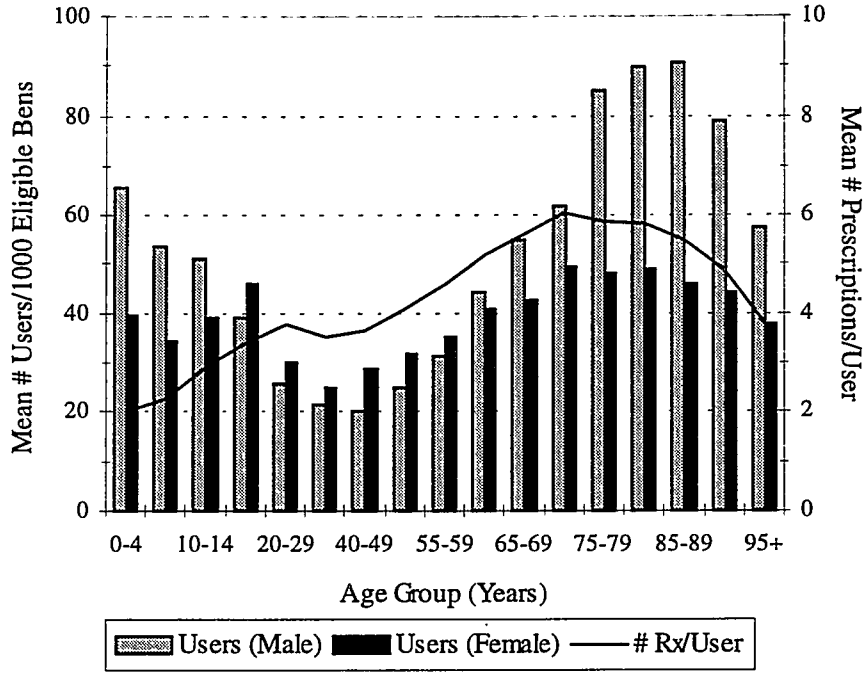

Figure 4.12: 1992 Drug Utilization by Age and Sex – Salbutamol

On average, 3.9 salbutamol prescriptions were claimed for each user in 1992. The prescription per user rate increased with age, from approximately 2 prescriptions for users less than 10 years old to nearly 6 prescriptions for users aged 70 to 84 years (Figure 4.12). Average prescription per user rates were higher for males than females (i.e. 4.2 versus 3.5, respectively).

Fenoterol was much less widely used than salbutamol (Table 4.1). Unlike salbutamol, the use of this drug was lowest among children and increased with age, peaking among beneficiaries aged 75 to 79 years (Figure 4.13). Overall prescription and user rates were 71.4% and 24.2% higher for males than females, but the gender difference was greatest among individuals 65 years of age or older (Figure 4.13).

The prescription per user rate for fenoterol was higher than for salbutamol (5.4 versus 3.9, respectively). This finding may reflect the greater use of this agent in seniors (Figure 4.13) because elderly users tend to receive more prescriptions for β_2-

agonists than younger patients. In addition, fenoterol may have been used in more severe asthmatics who have higher medication needs. The prescription per user rate increased through childhood but then remained relatively constant from age 20 to 74 years. The particularly high number of prescriptions per user (12 prescriptions) in the 95+ year age group was attributable to only one beneficiary (Figure 4.13). The prescription per user rates for males exceeded the female rates in nearly all age groups.

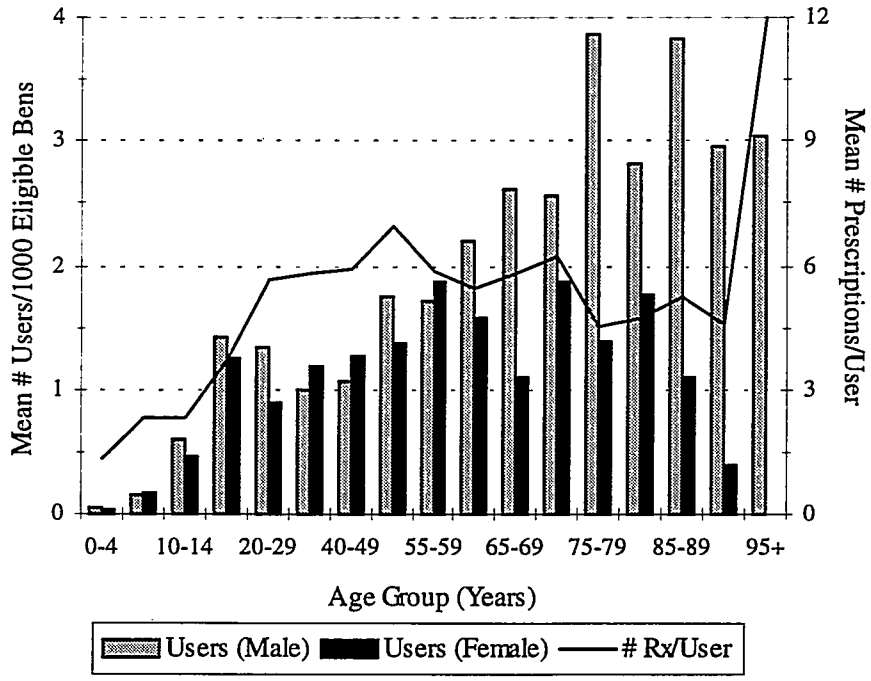

Figure 4.13: 1992 Drug Utilization by Age and Sex – Fenoterol
** The small number of users in most age groups contributed to the variability in the mean prescription per user rates.

Terbutaline was infrequently used by Saskatchewan beneficiaries (Table 4.1). The age-sex utilization pattern for terbutaline was more like that of salbutamol than fenoterol. User rates for male beneficiaries were higher for children and the elderly than for adults aged 20 to 49 years (Figure 4.14). The age pattern for female user rates was less clear. Unlike the other bronchodilators, the overall proportion of female

beneficiaries with at least one prescription for terbutaline was slightly greater than the proportion of male beneficiaries (i.e. female user rate of 0.60 compared to 0.49 for males). However, males had a greater average number of prescriptions per user than females (i.e. 2.7 versus 2.0, respectively). The average number of prescriptions per user was 2.3, which was considerably lower than that for salbutamol and fenoterol. This finding was not surprising, however, because the terbutaline aerosol container had twice as many doses as the fenoterol and salbutamol inhalers (CPS 1991).

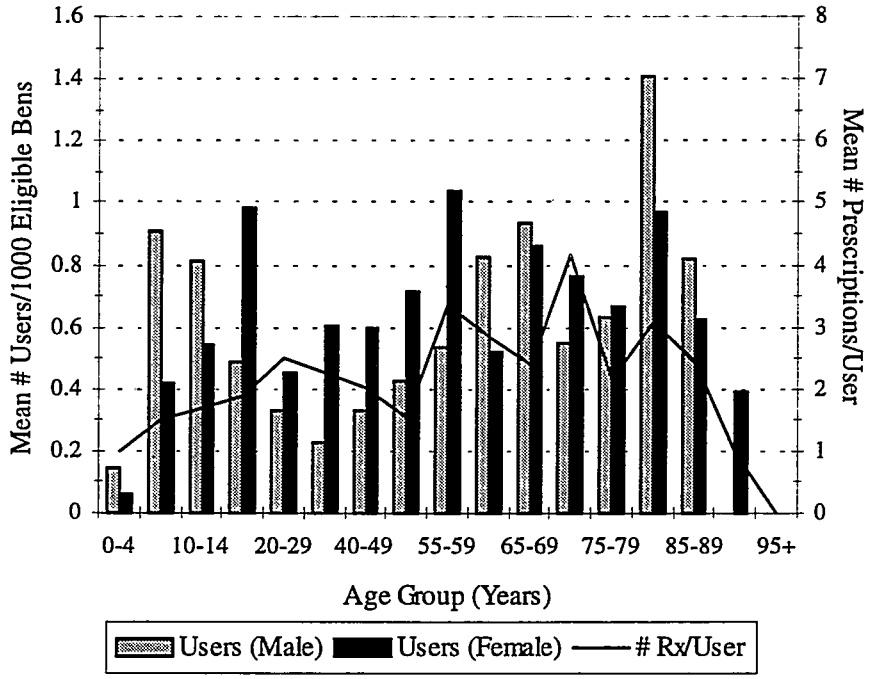

Figure 4.14: 1992 Drug Utilization by Age and Sex – Terbutaline
** The small number of users in each age group contributed to the variability in the mean prescription per user rates.

Inhaled Corticosteroids

The three inhaled corticosteroids monitored by the Extreme User Program were examined individually (Table 4.1). Utilization figures for the whole Formulary

Class 68:04.00 (Appendix F) were not studied because most of the drugs in the class were not monitored by the PPRP.

The inhaled corticosteroids were less extensively used than the bronchodilators. There were a total of 59,283 prescriptions for inhaled steroids in 1992 compared with 144,255 prescriptions for bronchodilators. A comparison of the two drug groups in terms of numbers of users was not possible because the discrete number of users for each drug group was not available.

Beclomethasone dipropionate accounted for 93.1% of all prescriptions for the inhaled steroids (Figure 4.15). The age-sex utilization pattern of this drug (Figure 4.16) was similar to that of salbutamol. Prescription and user rates peaked among beneficiaries in the 75 to 79 year age group, with a smaller peak among children aged 5 to 9 years. Overall utilization of beclomethasone dipropionate was similar for males and .

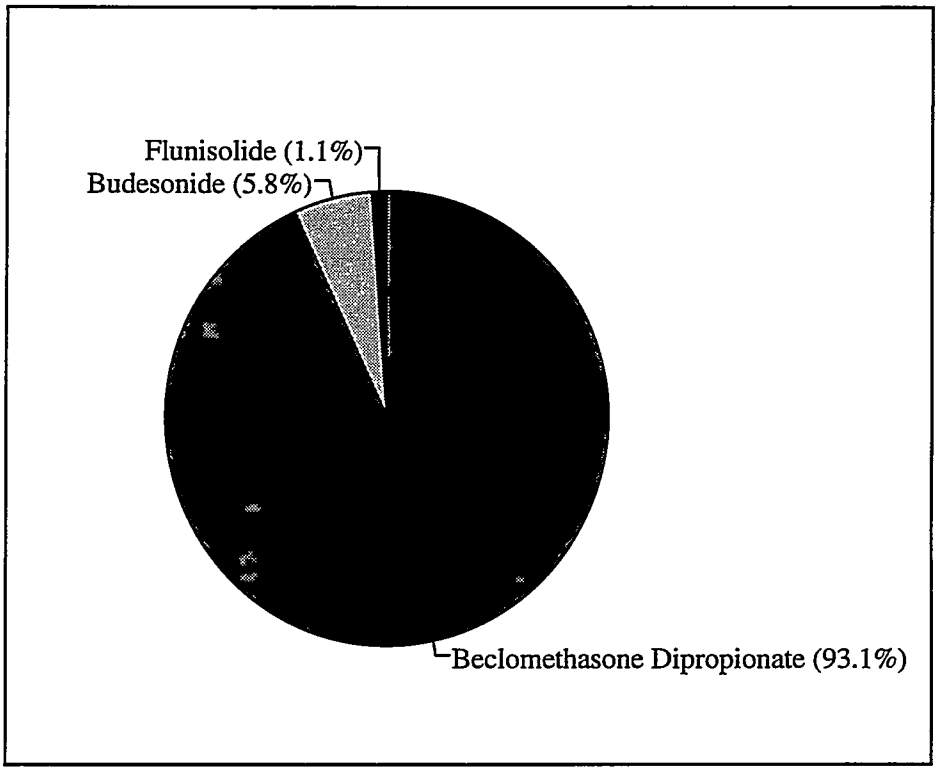

Figure 4.15: Percentage of Prescriptions for Inhaled Corticosteroids (Formulary Class 68:04.00) – 1992

females, with user rates of 19.9 and 18.6 users per 1000 eligible beneficiaries, respectively. As with salbutamol, male user rates exceeded female rates for beneficiaries less than 15 years of age and greater than 59 years of age.

An average of 3.0 beclomethasone dipropionate prescriptions were claimed for each user during the study period. Prescription per user rates tended to be greater for elderly users than for younger individuals (Figure 4.16). The average prescription per user rates were similar for males and females (i.e. 3.1 and 2.9, respectively).

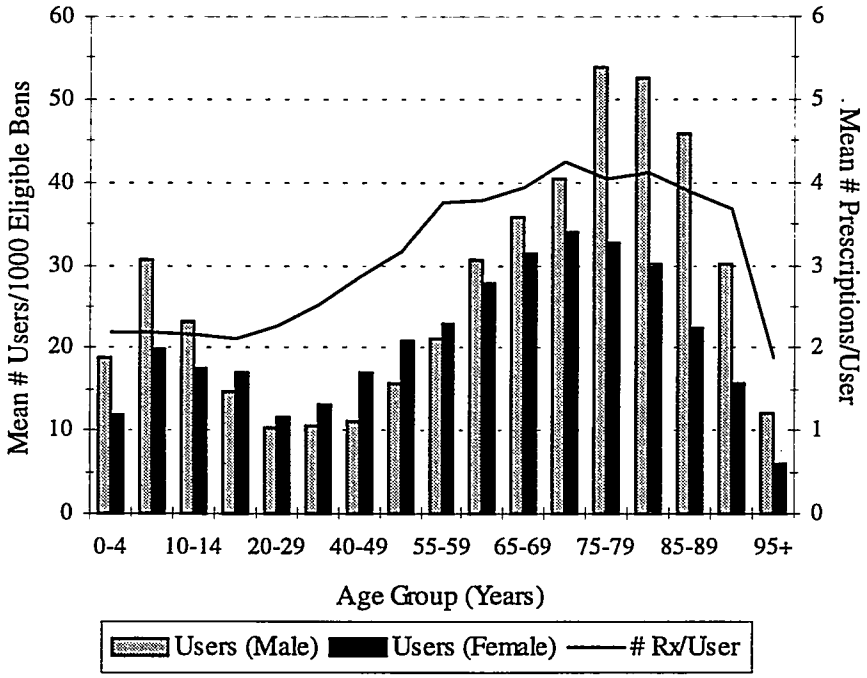

Figure 4.16: 1992 Drug Utilization by Age and Sex – Beclomethasone Dipropionate

The pattern of budesonide use was markedly different from the pattern of use for beclomethasone dipropionate. Budesonide user rates were highest in children aged 5 to 14 years (Figure 4.17). This preferential use of this agent in children may reflect budesonide's reduced risk of systemic adverse effects due to its greater topical-to-

systemic potency ratio (Kamada 1994).

Overall prescription and user rates were similar for males and females. The average number of budesonide prescriptions per user was 2.5. The prescription per user rates varied with age, but tended to be greater among elderly users than young users (Figure 4.17). Prescription per user rates were similar for males and females in most age groups.

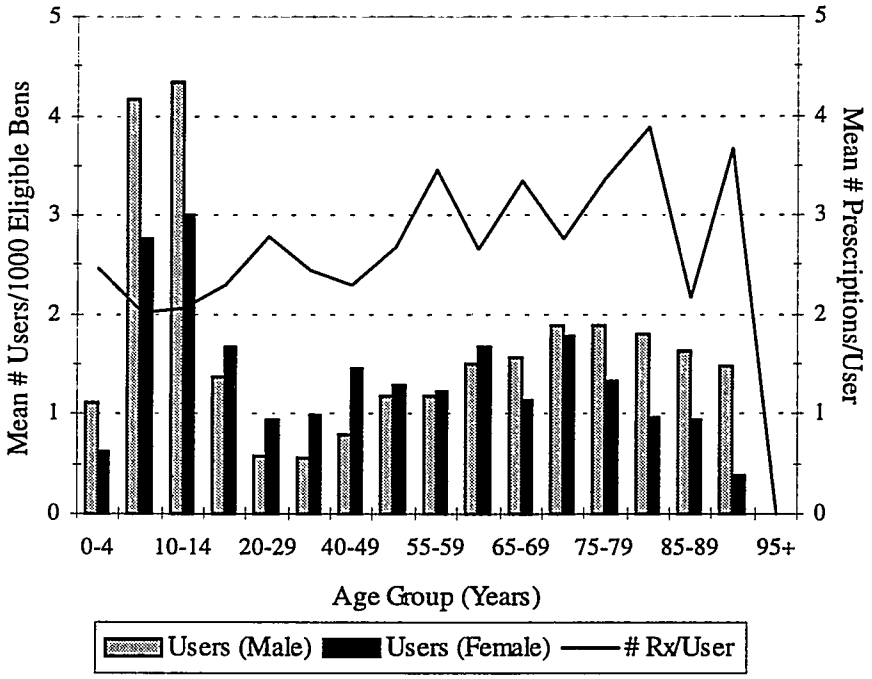

Figure 4.17: 1992 Drug Utilization by Age and Sex – Budesonide
** The small number of users in most age groups contributed to the variability in the mean prescription per user rates.

Flunisolide was used by only a small number of beneficiaries (Table 4.1). This drug appeared to be used preferentially in the elderly, with prescription and user rates peaking among beneficiaries 70 to 74 years of age (Figure 4.18). Like the other inhaled steroids, overall use of flunisolide was similar for males and females. The flunisolide prescription per user rates varied considerably with age (Figure 4.18), but, on

average, were higher for elderly users than for patients less than 65 years of age (i.e. 4.8 versus 3.3 prescriptions per user, respectively).

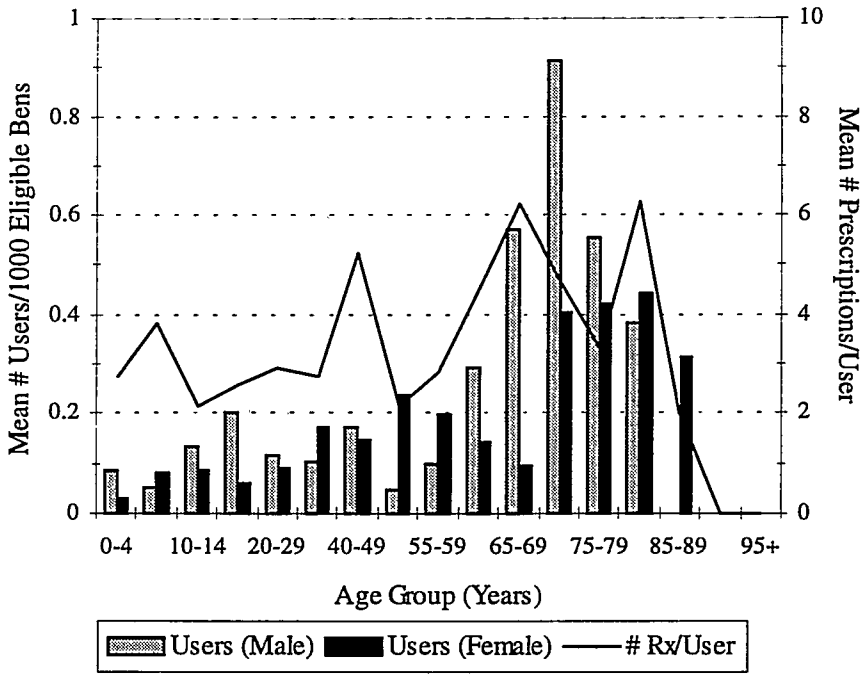

Figure 4.18: 1992 Drug Utilization by Age and Sex – Flunisolide
** The small number of users in each age group contributed to the variability in the mean prescription per user rates.

Anticholinergics

Ipratropium bromide was the only drug monitored for extreme use in this category. For each 1000 beneficiaries, there were 16.1 prescriptions for and 3.3 users of this drug in 1992 (Table 4.1). Ipratropium bromide was used primarily by elderly beneficiaries: 61.5% of users were 65 years of age or older. Prescription and user rates were 65.4% and 44.3% higher for males than females, respectively. The gender difference was particularly notable among the older age groups (Figure 4.19). The overall prescription per user rate was 4.9, but was much lower in young users than in the

elderly (Figure 4.19). Average prescription per user rates were slightly higher for males than females (5.2 and 4.5, respectively).

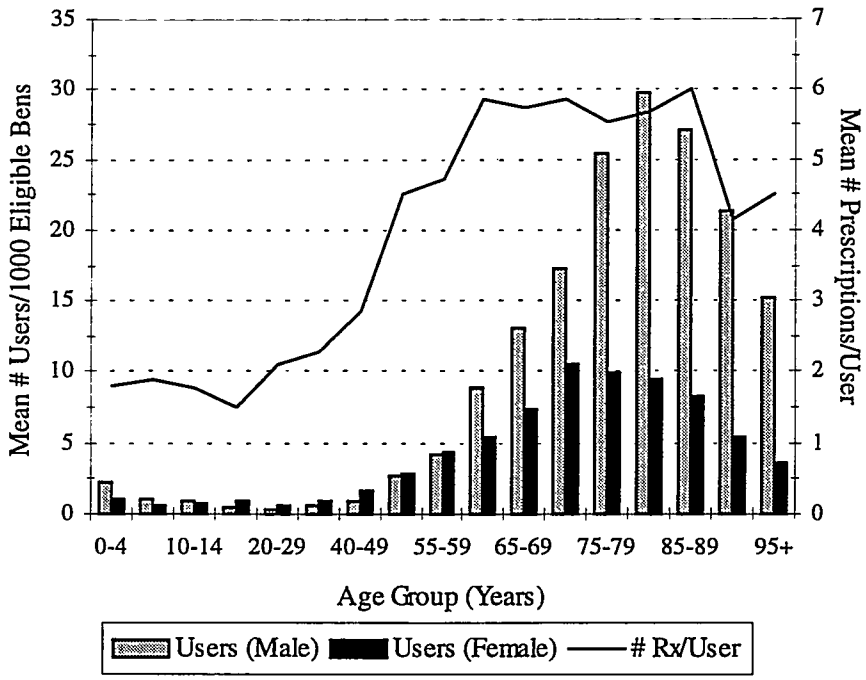

Figure 4.19: 1992 Drug Utilization by Age and Sex – Ipratropium Bromide

4.1.3 Five-Year Drug Utilization Trends – 1989 to 1993

The use of nearly all of the mood-modifying drug groups declined in Saskatchewan between 1989 and 1993 (Tables 4.2 and 4.3). Use of the Narcotic Analgesics (Formulary Class 28:08.08) and the Anxiolytic, Sedative and Hypnotic Benzodiazepines (Formulary Class 28:24.08) decreased to the greatest extent. The change in user rates was similar for both drug groups: 7.2 (15.8%) fewer NA users and 7.3 (13.3%) fewer BZD users per 1000 eligible beneficiaries. However, the fall in prescription rates was more dramatic for the BZD drugs than for the NA agents: 38.6 (15.3%) and 7.2 (8.5%) fewer prescriptions per 1000 eligible beneficiaries, respectively. The net decrease in overall benzodiazepine utilization was somewhat smaller, however, due to an increase in the use anticonvulsant BZD agents. Changes in the use of individual mood-modifying drugs are summarized in Appendix H.

Trends in asthma drug utilization between 1989 and 1993 were less consistent than for the mood-modifying drugs. Prescription rates for salbutamol and fenoterol, the two most widely used bronchodilators, fell during the study period (Table 4.2). In contrast, the use of ipratropium bromide and two of the three inhaled corticosteroids increased.

Narcotic Analgesics

The decline in overall NA utilization was not continuous throughout the study period (Tables 4.2 and 4.3). The fall in prescription and user rates was greatest from 1989 to 1990 and from 1991 to 1992. By 1993 the trend had reversed and prescription rates had increased slightly. The changes in NA utilization were similar for male and female beneficiaries in terms of both the pattern of change over time and the percentage change (i.e. prescription rates decreased by 7.2% and 9.8% for males and females, respectively). Despite decreases in NA prescription and user rates, the average number of prescriptions per user remained virtually unchanged throughout the study

Table 4.2: Trends in Drug Utilization – Prescription Rates for 1989 to 1993

Drug Group (Formulary Class)	Prescription Rate*					Change from 1989 to 1993*
	1989	1990	1991	1992	1993	
Narcotic Analgesics						
Opiate Agonists (28:08.08)	84.5	79.8	79.9	75.7	77.3	-7.2
Opiate Partial Agonists (28:08.12)	1.5	1.4	1.5	1.3	1.2	-0.3
Anticonvulsants						
Phenobarbital (28:12.04)	15.7	15.4	15.2	14.7	13.5	-2.2
Clonazepam/Nitrazepam (28:12.08)	10.8	13.4	14.6	19.1	19.4	+8.6
Anxiolytics, Sedatives and Hypnotics (28:24.00)						
Barbiturates (28:24.04)	2.1	1.8	1.7	1.3	1.1	-1.0
Benzodiazepines (28:24.08)	252.8	250.2	248.6	229.0	214.2	-38.6
Miscellaneous (28:24.92)	35.2	36.1	36.8	36.4	34.0	-1.2
Bronchodilators (12:12.00)						
Fenoterol	9.6	8.8	7.4	6.3	5.0	-4.6
Salbutamol	139.6	148.4	150.4	144.3	132.2	-7.4
Terbutaline	0.5	0.6	1.2	1.2	1.0	+0.5
Inhaled Corticosteroids (68:04.00)						
Beclomethasone Dipropionate	32.5	41.3	49.8	58.1	60.2	+27.7
Budesonide	0.3	1.2	2.3	3.6	4.3	+4.0
Flunisolide	0.6	0.8	0.8	0.7	0.6	0.0
Anticholinergics (12:08.08)						
Ipratropium Bromide	10.0	13.3	15.9	16.1	17.0	+7.0

*Mean number of prescriptions/1000 eligible beneficiaries

Table 4.3: Trends in Drug Utilization – User Rates for 1989 to 1993

Drug Group (Formulary Class)	User Rate*					Change from 1989 to 1993*
	1989	1990	1991	1992	1993	
Narcotic Analgesics						
Opiate Agonists (28:08.08)	45.6	42.0	41.4	38.3	38.4	-7.2
Opiate Partial Agonists (28:08.12)	0.7	0.5	0.6	0.5	0.5	-0.2
Anticonvulsants						
Phenobarbital (28:12.04)	3.3	3.0	2.9	2.6	2.4	-0.9
Clonazepam/Nitrazepam (28:12.08)	2.4	2.8	3.3	3.8	3.9	+1.5
Anxiolytics, Sedatives and Hypnotics (28:24.00)						
Barbiturates (28:24.04)	0.4	0.4	0.3	0.2	0.2	-0.2
Benzodiazepines (28:24.08)	54.7	53.0	52.8	49.6	47.4	-7.3
Miscellaneous (28:24.92)	14.9	15.3	15.3	15.2	14.2	-0.7
Bronchodilators (12:12.00)						
Fenoterol	1.6	1.4	1.4	1.2	1.0	-0.6
Salbutamol	29.6	33.1	37.0	37.2	37.5	+7.9
Terbutaline	0.2	0.3	0.5	0.5	0.5	+0.3
Inhaled Corticosteroids (68:04.00)						
Beclomethasone Dipropionate	8.6	11.8	16.1	19.2	21.6	+13.0
Budesonide	0.1	0.4	0.9	1.5	2.0	+1.9
Flunisolide	0.2	0.2	0.2	0.2	0.2	0.0
Anticholinergics (12:08.08)						
Ipratropium Bromide	2.4	3.0	3.3	3.3	3.8	+1.4

*Mean number of users/1000 eligible beneficiaries

period (i.e. 1.9 in 1989 and 2.0 in 1993). Thus, the decreased utilization of NA agents was due to a decrease in the number of users rather than a decrease in the number of prescriptions claimed by each user.

The decline in overall NA prescription and user rates was due primarily to decreases in the use of acetaminophen/caffeine/codeine and acetylsalicylic acid/ caffeine/codeine preparations (Appendix H). Although the use of most of the other NAs decreased slightly or remained the same, several NA agents had increased utilization rates in 1993 (Appendix H). Of these, morphine and hydromorphone had the greatest increases in prescription and user rates.

Benzodiazepines

In terms of the number of prescriptions, the decline in BZD use was greater than for any other drug group studied. The percentage change in prescription rates was similar for males and females (16.1% and 15.1%, respectively). However, the magnitude of change in terms of actual numbers of prescriptions per 1000 eligible beneficiaries was greater for females (minus 50.7 prescriptions) than for males (minus 27.3 prescriptions) due to the higher level use of these drugs among women.

When the BZD agents were stratified based on their recommended indications for use (Table 4.4), the decline in total BZD use was primarily attributable to a substantial decrease in sedative-hypnotic BZD use (Figure 4.20). Anxiolytic BZD use also decreased, although to a lesser degree, whereas anticonvulsant BZD use increased.

Changes in the use of only a few BZD agents were responsible for most of the observed changes in overall BZD use (Appendix H). Among the anxiolytic BZDs, lorazepam and alprazolam were the only drugs with increased utilization rates during the study period. Diazepam use decreased. Changes in the use of the other anxiolytic BZDs were small. By 1993, anxiolytic benzodiazepine use had shifted from the long half-life drugs such as diazepam to shorter acting agents such as lorazepam and alprazolam (Figure 4.21).

Table 4.4: Benzodiazepine Subgroups

Benzodiazepine Group	Drug
Anxiolytic Benzodiazepines	Alprazolam Bromazepam Chlordiazepoxide Clorazepate Dipotassium Diazepam Lorazepam Oxazepam
Sedative-Hypnotic Benzodiazepines	Flurazepam Temazepam Triazolam
Anticonvulsant Benzodiazepines	Clonazepam Nitrazepam

Reference: CPS (1994)

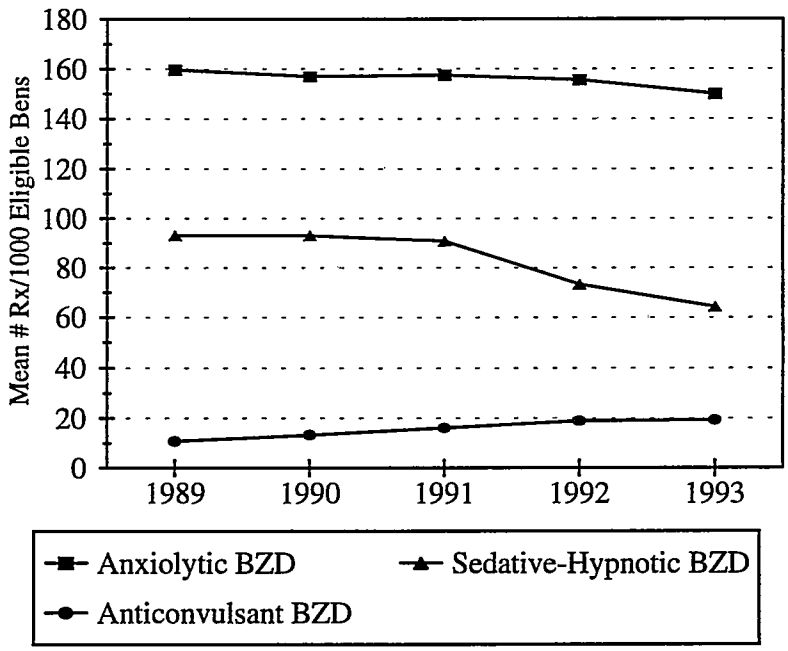

Figure 4.20: Trends in Benzodiazepine Utilization – 1989 to 1993

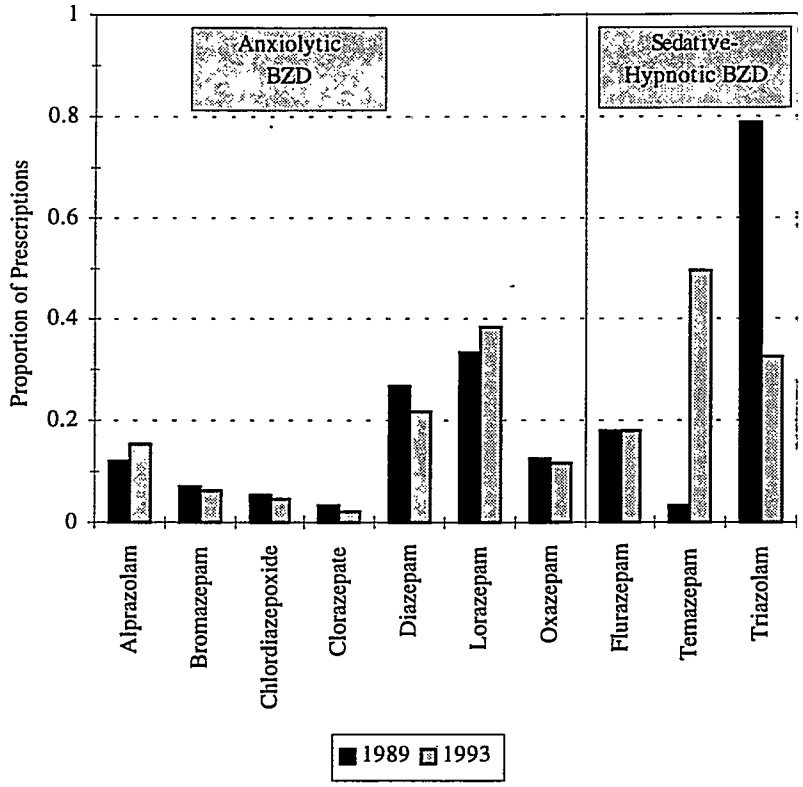

Figure 4.21: Proportion of Prescriptions for Anxiolytic and Sedative-Hypnotic Benzodiazepines – 1989 and 1993

A large decrease in triazolam use and a smaller decrease in the flurazepam use were responsible for the overall decline in the use of sedative-hypnotic BZDs. Although triazolam use fell throughout the study period, the drop was greatest from 1991 to 1992 (Appendix H). The decline in the use of triazolam and flurazepam was partially offset by an increase in temazepam use. By 1993, temazepam had replaced triazolam as the most widely prescribed sedative-hypnotic BZD on the Formulary (Figure 4.21). The increase in temazepam use was not surprising because it was first added to the Saskatchewan Formulary in 1989.

The increase in anticonvulsant BZD prescription and user rates was due primarily to an increase in clonazepam use; there was virtually no change in the user

rates for nitrazepam.

The prescription per user rate for each of the benzodiazepines changed only slightly during the five year study period, suggesting that the observed decline in prescription rates was due primarily to decreases in the number of users rather than a decline in the average number of prescriptions claimed by each user. An exception was temazepam, for which the prescription per user rate increased from 2.0 in 1989 to 3.8 in 1993. Thus, the increase in temazepam utilization was a reflection of increases in both the number of users and the number of prescriptions each user received.

Barbiturates

By 1993, the use of the Anxiolytic, Sedative and Hypnotic Barbiturates (Formulary Class 28:24.04) fell to 50% of the 1989 utilization rates (Tables 4.2 and 4.3). Use decreased to a similar extent for both male and female beneficiaries. The average number of prescriptions per barbiturate user increased slightly from 4.8 prescriptions per user in 1989 to 5.2 in 1993, despite decreases in the prescription and user rates.

Phenobarbital prescription and user rates fell by 14.0% and 27.3%, respectively, during the five year period. The decline was slightly greater for females than males (16.7% and 10.6% decreases in prescription rates, respectively) but the pattern of change over time was similar for both sexes. As with the other barbiturates, the average number of phenobarbital prescriptions per user increased during the study period from 4.8 in 1989 to 5.6 in 1993, despite a decrease in overall utilization.

Miscellaneous Anxiolytic, Sedative and Hypnotic Agents

Use of the Miscellaneous Anxiolytic, Sedative and Hypnotic Agents in Formulary Class 28:24.92 decreased by less than 5% between 1989 and 1993 (Tables 4.2 and 4.3). A decrease in chloral hydrate use was responsible for the modest decline in overall utilization (Appendix H). Methotrimeprazine prescription and user rates

remained relatively constant throughout the study period. Hydroxyzine use initially increased, but then decreased by 1993 to levels near those in 1989. For all three drugs, the average number of prescriptions per user remained virtually unchanged during the study period.

Bronchodilators

Salbutamol was the most widely used bronchodilator throughout the five-year study period. Utilization rates for salbutamol fluctuated over the five year period (Figure 4.22). By 1993, there were 7.4 (5.3%) ***fewer*** prescriptions for and 7.9 (26.7%) ***more*** users of salbutamol per 1000 eligible beneficiaries than in 1989.

The average number of prescriptions claimed for each user fell steadily throughout the study period from 4.7 in 1989 to 3.5 in 1993. Prescription per user rates for both males and females fell by approximately 25%.

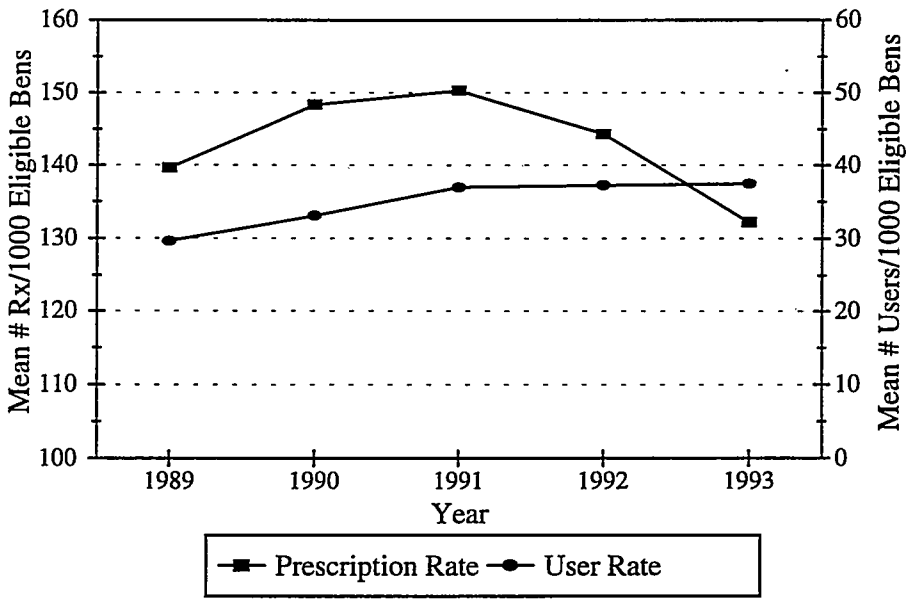

Figure 4.22: Trends in Salbutamol Utilization – 1989 to 1993

Both the prescription and user rates for fenoterol decreased steadily during the study period (Tables 4.2 and 4.3). The change in fenoterol use was similar for male and female beneficiaries. Like salbutamol, the average number of fenoterol prescriptions per user decreased by approximately 20% during the five-year period from 6.0 in 1989 to 4.8 in 1993.

Terbutaline use increased between 1989 and 1991, but then remained relatively constant from 1991 to 1993 (Tables 4.2 and 3.3). Like the other bronchodilators, prescription per user rates for this drug also decreased during the study period from 3.1 in 1989 to 2.2 in 1993. Changes in terbutaline use had little impact on overall bronchodilator utilization due to its low level of use.

Inhaled Corticosteroids

Beclomethasone dipropionate remained the most widely prescribed inhaled corticosteroid throughout the study period. The increase in the use of this drug was striking: the number of prescriptions per 1000 eligible beneficiaries nearly doubled and there were 2.5 times more users of this drug in 1993 compared to 1989 (Tables 4.2 and 4.3). The increase in the prescription rate was somewhat greater for females (+103.1%) than males (+71.9%), but the pattern of change over time was nearly identical for both sexes. Prescription and user rates for budesonide also increased throughout the study period but flunisolide use remained relatively unchanged (Tables 4.2 and 4.3). Despite increases in overall utilization, the average number of prescriptions per user per year decreased by 26.4% for beclomethasone dipropionate and by 13.4% for budesonide.

Anticholinergics

Ipratropium bromide use increased during the study period (Tables 4.2 and 4.3). This trend was apparent for both males and females. The prescription per user rate for ipratropium bromide increased only slightly from 4.2 in 1989 to 4.5 in 1993.

4.2 Descriptive Statistics for the Patient Profile Release Program

4.2.1 Study Subjects

A total of 3124 beneficiaries were identified by the Patient Profile Release Program at least once in 1992. Of these, 378 (12.1%) individuals were excluded from the study for the reasons outlined in Table 4.5. A more detailed explanation for the exclusions is presented in Appendix E. An additional 204 (6.5%) potential study subjects were excluded from the study because they had no profiles released in 1992. Profiles for these individuals were not sent to prescribers and pharmacies because manual review of the computer-generated profiles by SPDP pharmacists indicated that profile release was unnecessary or inappropriate. The supplemental review criteria used by the SPDP pharmacists are outlined in Appendix C.

Table 4.5: Beneficiaries Excluded from the Study

Number of beneficiaries identified by the Patient Profile Release Program in 1992:	3124
Beneficiaries excluded from the study:	
• *Polypharmacy count of less than 16 different drugs after exclusion of diagnostic agents*	69
• *Extreme User Program overestimation of apparent dose for asthma drugs*	73
• *Polyprescriber patients with fewer than 7 different prescribers after exclusion of incorrect prescriber codes*	7
• *Extreme use of major tranquilizers*	229
Number of potential study subjects with no profiles released in 1992:	204
Number of study subjects:	2542

4.2.2 Comparison of the Extreme User, Polypharmacy and Polyprescriber Programs

Of the 2542 study subjects with at least one profile released, 1492 (58.7%) were identified for Extreme Use (ExU), 638 (25.1%) for Polypharmacy (PPh) and 389 (15.3%) for exceeding Polyprescriber (PPr) criteria. An additional 23 (0.9%) subjects exceeded two sets of criteria: 9 with ExU and PPh, 1 with ExU and PPr and 13 with PPh and PPr. In the analysis, these 23 beneficiaries were counted once for each set of criteria exceeded.

The demographic characteristics of beneficiaries identified by each component of the Program are summarized in Table 4.6. Differences between the three groups were tested statistically using the Kruskal-Wallis test for continuous variables and the Chi-square test for categorical variables. The results of these tests indicated that statistically significant differences between the ExU, PPh and PPr subjects were present for all of the study variables: age, sex, residence, coverage type and the numbers of prescribers and pharmacies (Table 4.6).

Pairwise comparisons using multiple Wilcoxon Rank Sum tests or multiple Chi-square tests were performed to determine which groups differed from each other (i.e. ExU versus PPh, ExU versus PPr, PPh versus PPr). These tests demonstrated that all three groups were significantly different from each other for all of the study variables except sex ($p<0.0167$). With regard to gender, only the ExU and PPh groups were significantly different from each other.

Table 4.6: Characteristics of Beneficiaries Identified by the Patient Profile Release Program

Variable	Extreme Use (n=1502)	Polypharmacy (n=660)	Polyprescriber (n=403)	p-value
	Median (Range) (Mean ± SD)	*Median (Range) (Mean ± SD)*	*Median (Range) (Mean ± SD)*	
Age (years)	73 (10 – 97) *(69.4 ± 15.3)*	70 (1 – 99) *(66.1 ± 18.5)*	39 (0 – 98) *(41.7 ± 21.5)*	0.0001§
# of Pharmacies	1 (0 – 7) *(1.4 ± 0.7)*	1 (1 – 9) *(1.7 ± 1.1)*	3 (1 – 9) *(3.2 ± 1.7)*	0.0001§
# of Prescribers	1 (0 – 7) *(1.6 ± 0.9)*	3 (0 – 10) *(2.7 ± 1.5)*	7 (5 – 12) *(6.6 ± 0.8)*	0.0001§
	# (%)	*# (%)*	*# (%)*	
Sex				
Male	602 (40.1%)	213 (32.3%)	148 (36.7%)	0.002¶
Female	900 (59.9%)	447 (67.7%)	255 (63.3%)	
Residence				
Large Cities	464 (30.9%)	260 (39.4%)	267 (66.3%)	<0.001¶
Medium Cities	293 (19.5%)	97 (14.7%)	35 (8.7%)	
Small Cities	64 (4.3%)	23 (3.5%)	16 (4.0%)	
Rural	681 (45.3%)	280 (42.4%)	85 (21.1%)	
Coverage				
Regular	1394 (92.8%)	351 (53.2%)	243 (60.3%)	<0.001¶
SAP-Plan 1	62 (4.1%)	55 (8.3%)	111 (27.5%)	
SAP-Plan 2	18 (1.2%)	37 (5.6%)	18 (4.5%)	
SAP-Plan 3	28 (1.9%)	217 (32.9%)	31 (7.7%)	

§ Kruskal-Wallis Test (two-sided p-value)

¶ Chi-square Test (two-sided p-value)

Age

Beneficiaries with a profile released under the Extreme User or Polypharmacy Programs were considerably older than those exceeding Polyprescriber criteria (Table 4.6). Individuals 65 years of age or older accounted for 78.8% and 60.3% of ExU and PPh subjects, respectively, but represented only 16.9% of PPr subjects.

The high median ages for subjects in the ExU and PPh groups (73 years and 70 years, respectively) suggest that extreme use and polypharmacy were primarily

problems of the elderly. This is highlighted in the plots of the identification rates by age and sex for the two programs (Figures 4.23 and 4.24). Identification rates for both the ExU and PPh Programs increased with age. For the ExU Program, identification rates increased gradually until age 64 years and then increased sharply from 1.6 extreme users per 1000 active beneficiaries aged 55-64 years to 8.4 extreme users per 1000 active beneficiaries aged 65-74 years (Figures 4.23). PPh identification rates increased steadily with age and continued increasing even among the elderly (Figure 4.24). In contrast, there was no clear association between age and identification by the PPr Program (Figure 4.25).

Sex

Females accounted for the majority of individuals identified under all three programs, ranging from 59.9% of ExU subjects to 67.7% of PPh subjects. The proportion of females in the PPh group was significantly greater than in the ExU group ($p=0.001$), but neither group was significantly different from the PPr subjects ($p>0.0167$).

Women appeared to be at a greater risk for identification than men, since females represented only 56% of active beneficiaries in Saskatchewan in 1992, but accounted for more than 60% of subjects identified by the PPRP. Overall identification rates per 1000 active beneficiaries were greater for females than males for all three programs (Figures 4.23 to 4.25). However, the association between gender and identification by the PPh and ExU Programs varied with age. For the ExU Program, identification rates were greater for females than males only for the 45 to 74 year age range (Figure 4.23). Identification rates for the PPh Program were higher for women than for men in nearly every age group but the gender difference was most striking among beneficiaries 75 years of age or older (Figure 4.24). For the PPr Program, identification rates were slightly higher for females than males for nearly all age groups.

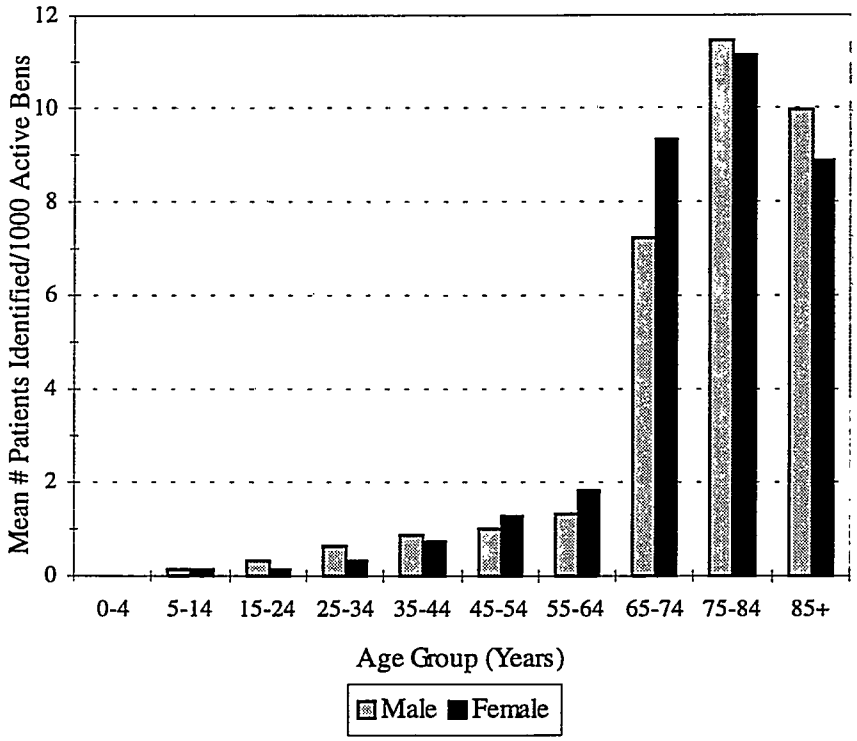

Figure 4.23: Identification Rates by Age and Sex – Extreme User Program

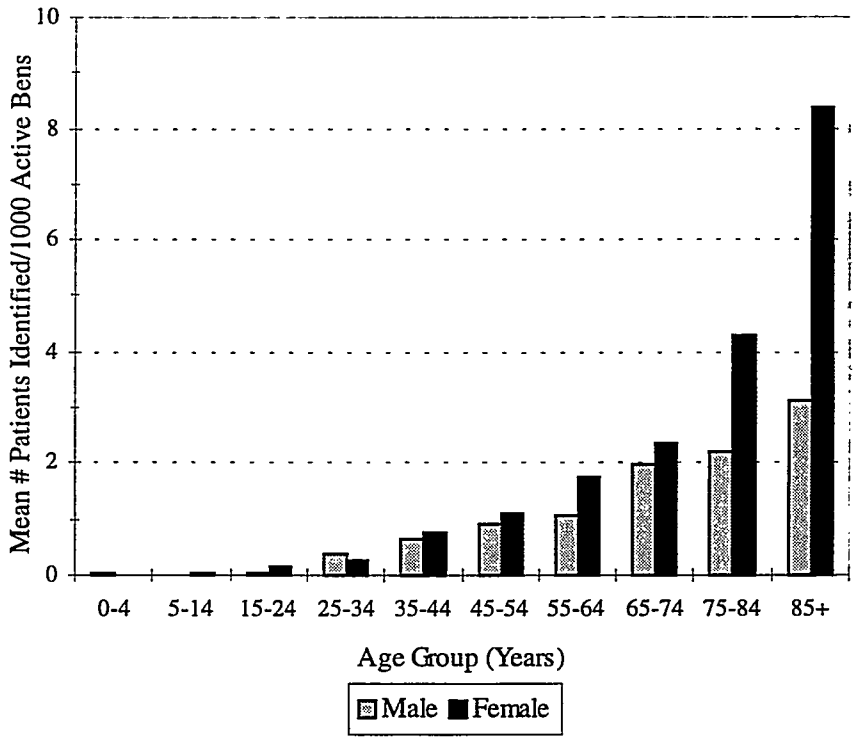

Figure 4.24: Identification Rates by Age and Sex – Polypharmacy Program

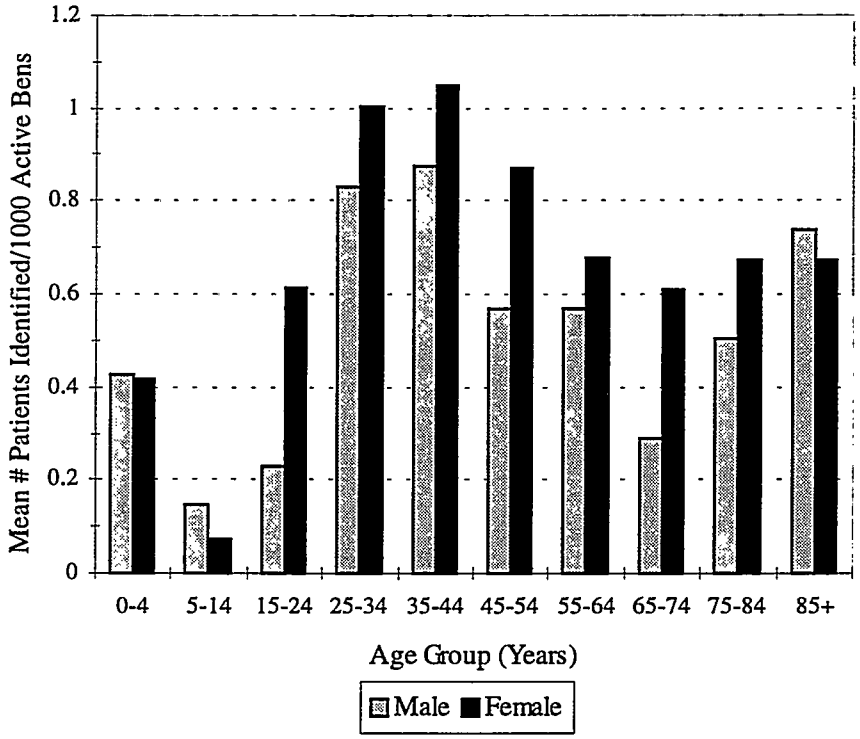

Figure 4.25: Identification Rates by Age and Sex – Polyprescriber Program

Residence

The ExU, PPh and PPr groups differed significantly from each other with respect to the distribution of subjects by residence category. In 1992, 38.1% of eligible beneficiaries had residence codes from large cities, 12.2% from medium-sized cities, 4.1% from small cities and 45.6% from rural areas. The distribution of PPh subjects by residence category was similar to that of the general population of eligible beneficiaries (Table 4.6). In contrast, the ExU group had a preponderance of subjects with residence codes from medium-sized cities (19.5%) with a correspondingly smaller proportion from large cities (30.9%). The distribution of PPr subjects differed even more markedly from the distribution of eligible beneficiaries: 66.3% of subjects had residence codes from large cities. These findings suggest that individuals from medium-sized cities may have been at a greater risk of identification for extreme use than individuals from other areas, whereas beneficiaries from large cities appear to have been at a much greater risk for identification by the PPr Program.

Age- and sex-standardized identification rates were calculated for each residence category to rule out the possibility that the apparent associations between residence category and the risk of identification by the ExU and PPr Programs were simply reflections of the different age-sex distributions for the four residence categories. The identification rates for each residence category were adjusted for age and sex using the total population of eligible Saskatchewan beneficiaries in 1992 as the standard. After age-sex standardization, the findings were no different than the unadjusted results (Figure 4.26). That is, the age-sex adjusted identification rates for the ExU Program were higher for beneficiaries residing in the medium-sized cities than for the other residence categories. Beneficiaries in large cities continued to have a higher PPr identification rate than beneficiaries in the other three residence categories.

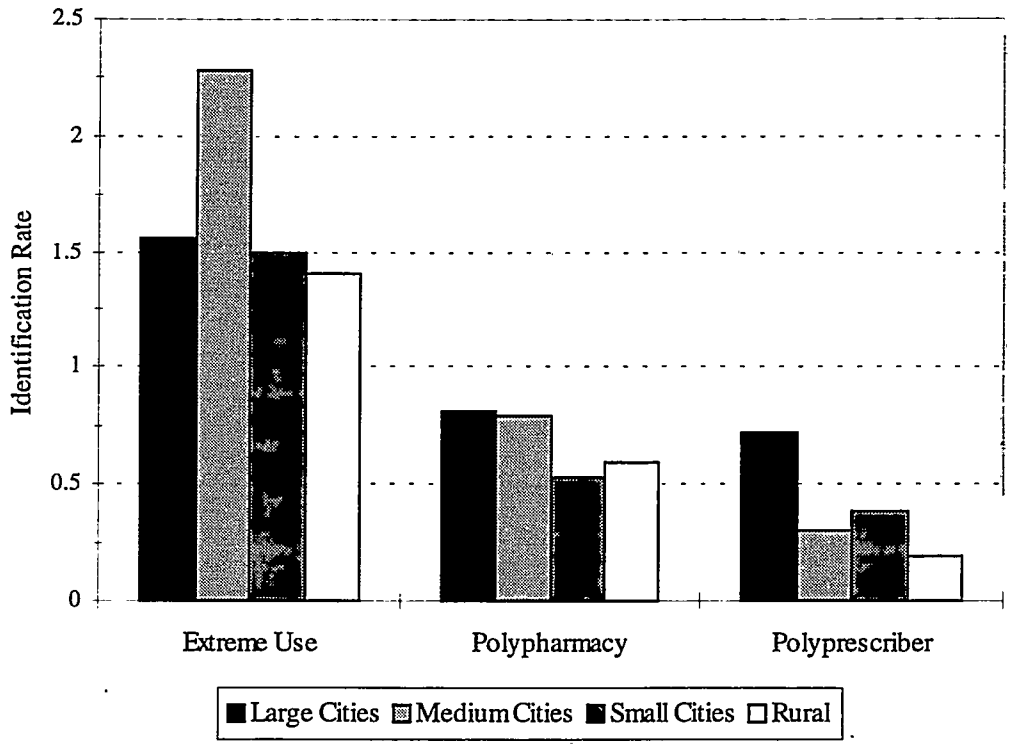

Figure 4.26: Age-Sex Adjusted Identification Rates by Residence Category
Identification rate = number of individuals identified per 1000 eligible beneficiaries.

Coverage

The ExU, PPh and PPr subjects differed significantly from each other with respect to type of SPDP coverage (Table 4.6). The percentage of ExU subjects with Regular coverage (92.8%) was similar to the percentage of active beneficiaries that had Regular coverage in the 1992-93 fiscal year (approximately 89%) (Saskatchewan Health 1993b). In contrast, only 60% of PPr subjects had Regular coverage while the remaining 40% had some form of Saskatchewan Assistance Plan coverage. Of the 160 PPr subjects with SAP coverage, 111 (69.4%) were Plan 1 beneficiaries.

The PPh Program had the smallest percentage of beneficiaries with Regular

coverage (53.2%). Of the 309 PPh subjects with SAP coverage, 217 (70.2%) were Plan 3 beneficiaries. The preponderance of Plan 3 beneficiaries among the PPh subjects can be explained, at least in part, by differences in the range of drugs covered for Plan 3 recipients compared to other beneficiaries. The drugs eligible for coverage for individuals with Regular, Plan 1 or Plan 2 coverage status included prescription drugs listed in the Saskatchewan Formulary and certain non-formulary prescription drugs covered by Exception Drug Status. For Plan 3 beneficiaries, most non-formulary prescription and over-the-counter drugs were also covered. Therefore, a broader range of drugs was included in the polypharmacy count for Plan 3 beneficiaries, making it easier for these individuals to be identified by the PPh Program.

Numbers of Pharmacies and Prescribers

Prescribers and pharmacies listed on prescription claims in the three months prior to identification were included in the "number of prescribers" and "number of pharmacies" variables. The number of prescribers recorded in the PPRP database included only physicians and dentists practising in Saskatchewan. Out-of-province prescribers and physicians identified only as "locum tenums" were excluded from the "number of prescribers" variable. Likewise, out-of-province pharmacies were excluded from the "number of pharmacies" variable. Therefore, some study subjects may have had more than the recorded number of prescribers or pharmacies. These exclusions explain why the average number of prescribers for PPr subjects was only 6.6 even though the criterion for identification by the Polyprescriber Program was 7 or more different prescribers. These exclusions also explain why the lower end of some of the ranges for the number of pharmacies and number of prescribers variables included zero (Table 4.6).

The three groups of subjects differed significantly from each other with respect to the number of prescribers and pharmacies. Eighty-five percent of ExU subjects had only one or two prescribers. The relatively small number of pharmacies

and prescribers for ExU patients suggests that the majority of extreme use was not the result of "drug shopping" by patients. In contrast, 50% of PPh subjects had at least three prescribers. The use of multiple physicians may have been a factor contributing to polypharmacy and/or a reflection of the multiple medical problems which can result in polypharmacy. PPr subjects had the most prescribers and pharmacies in the three months prior to identification (Table 4.6). Thus, PPr patients may have been at a particularly high risk of undesired drug effects due to the large number of health care practitioners involved in their care and the likelihood that none of the providers had a complete record of their drug use.

4.2.3 Extreme User Program

The vast majority (85%) of the subjects identified by the Extreme User Program exceeded dosage criteria for the Minor Tranquilizer drug group (Figure 4.27). Thirteen subjects exceeded criteria for more than one drug group: 6 with a combination of mood-modifying drug groups, 3 with a combination of asthma drug groups, and 4 with a combination of asthma and mood-modifying drug groups.

Drugs in the Minor Tranquilizer group accounted for 9 of the 10 agents most commonly involved in episodes of extreme use (Table 4.7). Temazepam was the drug most frequently implicated in extreme use, even though it was only the fourth most widely used benzodiazepine in 1992. Salbutamol was the asthma drug most commonly involved in episodes of extreme use.

Table 4.7: Ten Most Common Drugs Involved in Extreme Use

Drug	Number of Subjects*
Temazepam	705
Triazolam	488
Lorazepam	233
Nitrazepam	119
Flurazepam	117
Salbutamol	112
Diazepam	111
Oxazepam	84
Alprazolam	77
Chlordiazepoxide	57

*The sum of this column is greater than the total number of extreme users because some subjects used more than one drug.

Of the 1489 subjects identified for extreme use of a single drug group, 1345 (90.3%) exceeded mood-modifying drug criteria and 144 (9.7%) exceeded dosage criteria for asthma medications. Subjects identified for extreme use of asthma medications differed from mood-modifying drug extreme users in a number of respects (Table 4.8). In particular, extreme users of mood-modifying drugs were significantly older and had a higher level of extreme use (i.e. a higher percentage of maximum threshold dosage) than extreme users of asthma drugs ($p=0.0001$). In addition, females accounted for 62.5% of the mood-modifying extreme users, while only 38.2% of asthma drug extreme users were female ($p<0.001$). Interestingly, the preponderance of extreme users from medium-sized cities described in Figure 4.25 was observed only in the group of mood-modifying drug users; the residence distribution of asthma drug extreme users was similar to the distribution of eligible beneficiaries (Table 4.8).

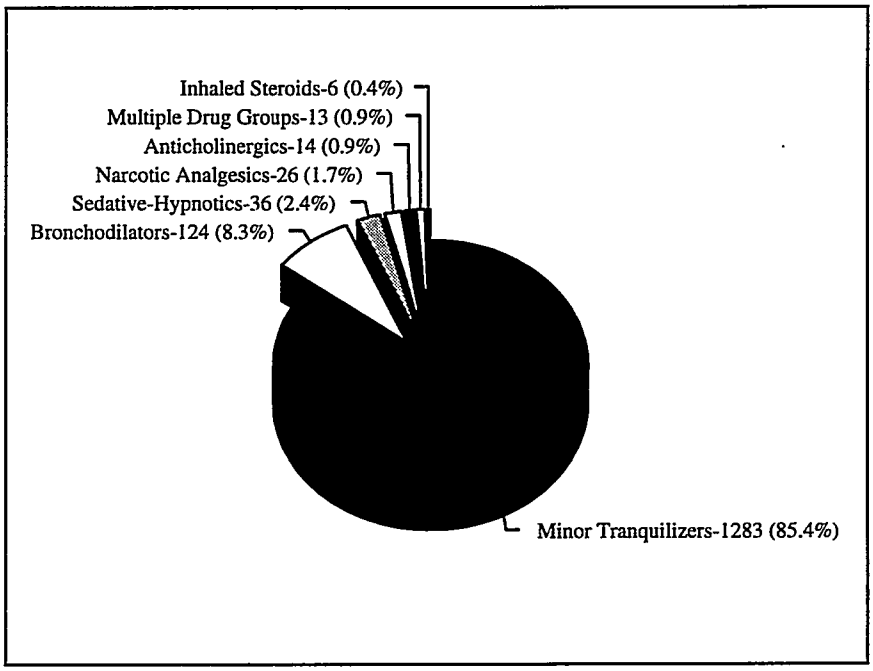

Figure 4.27: Extreme Use by Drug Group

Table 4.8: Comparison of Extreme Users of Mood-Modifying Drugs and Asthma Medications

Variable	Extreme Users of Asthma Drugs (n=144)	Extreme Users of Mood-Modifying Drugs (n=1345)	p-value
	Median (Range) *(Mean ± SD)*	*Median (Range)* *(Mean ± SD)*	
Age (years)	55 (10 - 89) *(51.5 ± 21.9)*	74 (12 - 97) *(71.4 ± 13.0)*	0.0001‡
Number of Pharmacies	1 (1 - 5) *(1.3 ± 0.7)*	1 (0 - 7) *(1.4 ± 0.7)*	0.6608‡
Number of Prescribers	1.5 (0 - 6) *(1.7 ± 0.9)*	1 (0 - 7) *(1.6 ± 0.9)*	0.2378‡
Percentage of Maximum Threshold Dosage	214.5 (200.5 - 542.5) *(231.9 ± 55.5)*	228.0 (200.6 - 800.9) *(249.5 ± 57.1)*	0.0001‡
	# (%)	# (%)	
Sex			
Male	89 (61.8%)	504 (37.5%)	
Female	55 (38.2%)	841 (62.5%)	<0.001§
Residence			
Large Cities	57 (39.6%)	405 (30.1%)	
Medium Cities	15 (10.4 %)	273 (20.3%)	
Small Cities	8 (5.6%)	56 (4.2%)	
Rural	64 (44.4%)	611 (45.4%)	0.012§
Coverage			
Regular	128 (88.9%)	1254 (93.2%)	
SAP-Plan 1	13 (9.0%)	49 (3.6%)	
SAP-Plan 2	3 (2.1%)	14 (1.0%)	
SAP-Plan 3	0 (0%)	28 (2.1%)	0.004†

‡Wilcoxon Rank Sum Test (two-sided p-value)
§Chi-square Test (two-sided p-value)
†Exact Test (two-sided p-value)

The age and sex differences between the two groups of extreme users were at least partly reflections of the age-sex utilization patterns of the mood-modifying and asthma drugs. With few exceptions, the drugs included in the mood-modifying category (i.e. narcotic analgesics, barbiturates, benzodiazepines and miscellaneous anxiolytic, sedative and hypnotic agents) were used primarily in middle-aged and elderly

beneficiaries. In addition, mood-modifying drug use was more prevalent in females than males. In contrast, most of the asthma medications were used extensively in children and young adults and the use of these drugs was somewhat more common in males than females.

The drug groups differed with respect to the rate of extreme use (Table 4.9). The extreme user rate was defined as the mean number of extreme users of a given drug group per 1000 users of the drug group. With the exception of the anticholinergic extreme user rates, the rates presented in Table 4.9 are approximations which slightly underestimate the true extreme user rates. The underestimation of the extreme user rate was the result of overestimation of the total number of users (i.e. the denominator of the rate). The total number of users was estimated by summing the users of all of the individual drugs or Formulary classes that were included in the PPRP drug linkage group. This procedure may have overestimated the total number of users because some beneficiaries may have used more than one drug (e.g. salbutamol and fenoterol) or drugs from more than one Formulary class (e.g. diazepam and hydroxyzine) and would, therefore, have been counted more than once.

The minor tranquilizer drug group had a higher rate of extreme use than any other monitored drug group (Table 4.9). For every 1000 users of minor tranquilizers, there was an average of 20.8 extreme users. The extreme user rate for the sedative-hypnotic group was also relatively high (i.e. 11.4 extreme users/1000 sedative-hypnotic users). In contrast, extreme use of the narcotic analgesics was infrequent, with less than one extreme user per 1000 NA users. The rate of extreme use was lower for the asthma medications than for most of the mood-modifying drugs. For the bronchodilators, there were fewer than four extreme users for every 1000 users.

The rate of extreme use for most of the drug groups was related to age and sex (Table 4.9). Interestingly, male users of minor tranquilizers had slightly higher rates of extreme use than females users, despite more common use of these agents among females beneficiaries. Thus, the predominance of female subjects in the mood-modifying study group was a reflection of the age-sex utilization pattern of these drugs

Table 4.9: Extreme User Rates by Drug Group, Age and Sex

Drug Group	Gender	Extreme User Rate (mean # extreme users/1000 users of the drug group)		
		Age <65 years	Age ≥65 years	Total
Narcotic Analgesics	Male	0.7	1.0	0.8
	Female	0.6	0.8	0.6
	Total	0.7	0.9	0.7
Minor Tranquilizers	Male	5.0	53.0	21.7
	Female	4.9	41.6	20.3
	Total	4.9	45.2	20.8
Sedative-Hypnotics	Male	10.0	9.7	9.8
	Female	13.8	11.4	12.4
	Total	12.1	10.8	11.4
Anticholinergics	Male	6.4	4.9	5.4
	Female	3.4	2.8	3.1
	Total	5.0	4.2	4.5
Bronchodilators	Male	3.3	6.0	3.9
	Female	2.6	3.1	2.7
	Total	3.0	4.7	3.4
Inhaled Corticosteroids	Male	0.3	0.4	0.3
	Female	0.3	0.4	0.3
	Total	0.3	0.4	0.3

rather than an indicator that female users were at a greater risk for extreme use than male users. Extreme user rates for the narcotic analgesics were also slightly higher for male users, but the association was reversed for the sedative-hypnotic group (Table 4.9).

Extreme use of the anticholinergic and bronchodilator drug groups was more common among male users than female users (Table 4.9). This finding, together with the observation that many of the monitored asthma drugs were used more extensively in males than females, explains the predominance of males in the asthma extreme user group. Extreme use of the inhaled steroids appeared to be unrelated to gender, although the number of subjects was small.

The influence of age on the rate of extreme use was most apparent for the minor tranquilizer group. The extreme user rate for elderly minor tranquilizer users was

more than nine times that observed in users less than 65 years of age. This difference in extreme user rates can be at least partly explained by the maximum dosage criteria established for the two age groups because the dosage criteria for most of the minor tranquilizer drugs were set at lower levels for elderly individuals (Appendix A). Thus, elderly beneficiaries using the same dosages of minor tranquilizers as younger individuals were more likely to be identified for extreme use. In contrast, the extreme user rate for the sedative-hypnotics was slightly lower in elderly users than in their younger counterparts. For the asthma drugs, higher extreme user rates were observed for elderly users of bronchodilators and inhaled steroids than for young users, but the opposite was true for ipratropium bromide.

4.2.4 Polypharmacy Program

The most common drugs claimed on behalf of Polypharmacy subjects in the three months prior to identification are listed in Table 4.10. Subjects were stratified by coverage because the type of coverage influenced the scope of drugs that were included in the PPh count. The distinction between the two groups of subjects is highlighted in Table 4.10. Among the Plan 3 subjects, four of the top 10 drugs were over-the-counter (OTC) preparations; with few exceptions, non-prescription drugs were not captured for beneficiaries with Regular, Plan 1 or Plan 2 coverage. When OTCs were excluded from the list of drugs prescribed to Plan 3 subjects, then seven of the 10 prescription drugs most commonly claimed by PPh subjects were the same for Plan 3 and Regular/Plan 1/Plan 2 subjects. The median number of different drugs claimed by PPh subjects in the 90 day period prior to the identification date was 16 (range 16 – 31). The number of different drugs for Plan 3 beneficiaries was not significantly different from that of the other subjects ($p>0.05$).

Table 4.10: Top Ten Drugs Prescribed to Polypharmacy Subjects – By Coverage Type

Regular, Plan 1 or Plan 2 Coverage (n=443)		Plan 3 Coverage (n=217)	
Top 10 Drugs	**Number of Subjects***	**Top 10 Drugs**	**Number of Subjects***
Furosemide	223	Acetaminophen[§]	126
Ranitidine	184	Furosemide	121
Potassium Chloride	148	Potassium Chloride	91
Cephalexin Monohydrate	139	Docusate[§]	74
Salbutamol	130	Bisacodyl[§]	65
Prednisone	125	Ranitidine	65
Amoxicillin	121	Cephalexin Monohydrate	57
Nitroglycerin	115	Acetylsalicylic Acid[§]	54
Acetaminophen/Caffeine/Codeine	113	Compound[¶]	54
Beclomethasone Dipropionate	107	Digoxin	53

*The sum of subjects for these columns is greater than the total number of study subjects because some patients used more than one of the drugs listed.

[§] Over-the-Counter Preparations

[¶] Extemporaneously Compound Prescription

4.3 Patient Profile Release Program Short-term Follow-up

4.3.1 Study Subjects

Of the 2542 subjects included in the descriptive analysis (Section 4.2), 1664 individuals were first identified by the Patient Profile Release Program in January 1992 or between April 7 and September 8, 1992, inclusive. Of these, 82 subjects were excluded from the follow-up analysis because their first profile was not released to prescribers and pharmacies. An additional 63 individuals were excluded because they were not eligible for SPDP coverage for the full 112 day follow-up period.

Of the 1519 subjects included in the follow-up analysis, 939 were identified for Extreme Use, 342 for Polypharmacy and 218 for exceeding Polyprescriber criteria. An additional 20 subjects exceeded criteria for two programs; these individuals were counted once for each set of criteria exceeded. The subjects were divided into intervention and comparison groups based on the date of their initial identification as shown in Figure 4.28. Separate analyses were conducted for the Extreme User, Polypharmacy and Polyprescriber Programs.

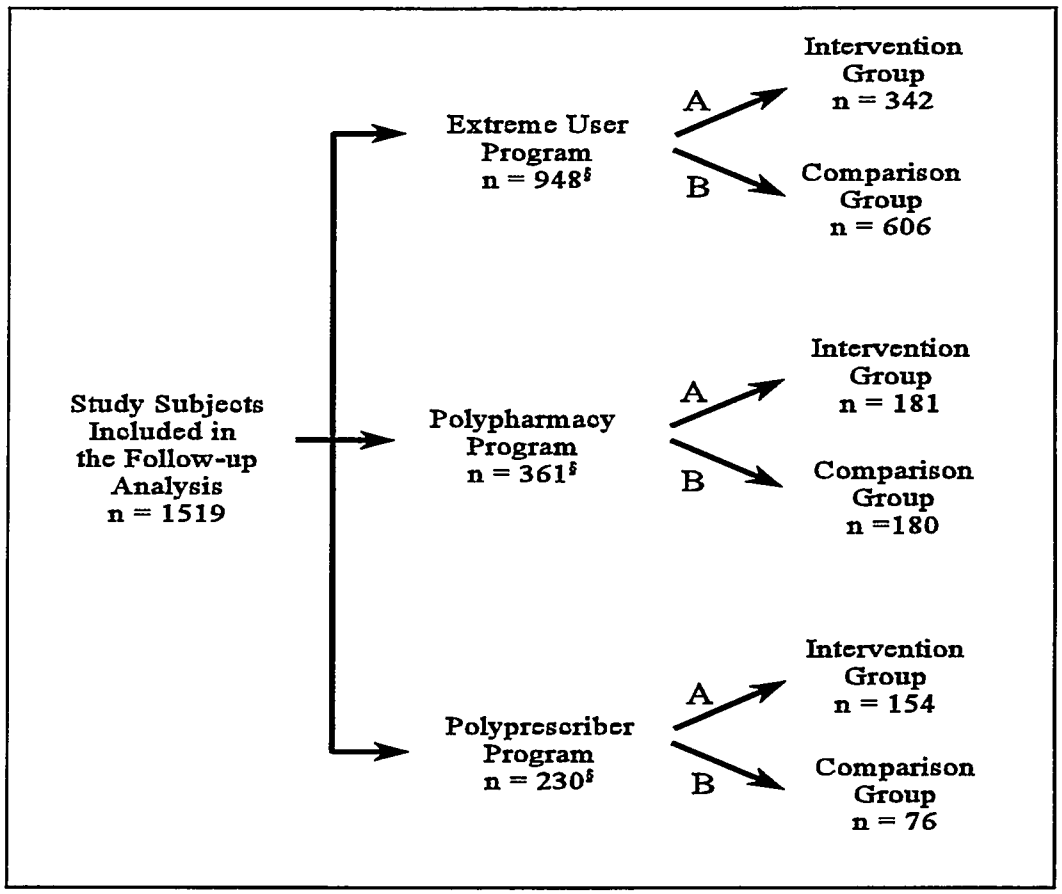

Figure 4.28: Allocation of Subjects to Study Groups

§Sum of Extreme User, Polypharmacy and Polyprescriber subjects is greater than 1519 because 20 individuals who were identified under more than one Program were counted once for each set of criteria exceeded.

A = first identified by the PPRP between April 7 and September 8, 1992.

B= first identified by the PPRP in January 1992.

4.3.2 Extreme User Program

Comparability of the Intervention and Comparison Groups

The intervention and comparison groups for the Extreme User component of the follow-up investigation had similar values for most of the baseline characteristics: age, gender, coverage type, number of pharmacies and prescribers in the 90 day period prior to identification and the number of follow-up days spent in hospital ($p>0.05$)(Table 4.11). However, the two groups differed with respect to residence and the level of extreme use. The intervention group had a greater proportion of subjects from small cities or rural areas while the majority of comparison group subjects were from large or medium-sized cities. In addition, subjects in the comparison group had significantly higher levels of extreme use, as measured by the percentage of the maximum threshold dosage criteria ($p=0.0001$). These differences were potentially important because both residence and the level of extreme use were considered possible confounders of the association between study group status and re-identification.

Crude and Adjusted Estimates of the Risk for Re-identification

The proportion of extreme users re-identified by the Patient Profile Release Program during the follow-up period was significantly lower for the intervention group (36.5%) than for the comparison group (56.8%)(Table 4.11). The crude relative risk (95% CI) for re-identification was 0.64 (0.55, 0.75), indicating that the intervention group subjects were 36% less likely than comparison group subjects to be re-identified during follow-up. This negative association between profile release and re-identification was statistically significant, as evidenced by the 95% CI which did not include the null value of one.

Table 4.11: Characteristics of Extreme User Intervention and Comparison Groups

Variable	Comparison Group (n=606)	Intervention Group (n=342)	p-value
	Median (Range) *Mean ± SD*	*Median (Range)* *Mean ± SD*	
Age (years)	73 (12 - 97) *69.9 ± 15.1*	72 (11 - 94) *69.1 ± 16.4*	0.8221§
Number of Pharmacies†	1 (1 - 7) *1.4 ± 0.8*	1 (1 - 6) *1.4 ± 0.7*	0.4106§
Number of Prescribers†	1 (1 - 5) *1.6 ± 0.9*	1 (0 - 7) *1.6 ± 0.9*	0.7806§
Number of Days in Hospital‡	0 (0 - 92) *2.6 ± 7.8*	0 (0 - 78) *3.5 ± 11.2*	0.6449§
Percentage of Maximum Threshold Daily Dose†	235.5 (201.0 - 1144.0) *272.3 ± 91.2*	226.7 (200.5 - 400.0) *230.8 ± 26.5*	0.0001§
	# (%)	*# (%)*	
Sex			
male	240 (39.6%)	137 (40.1%)	0.891¶
female	366 (60.4%)	205 (59.9%)	
Residence			
Large Cities	198 (32.7%)	94 (27.5%)	0.05¶
Medium-Sized Cities	130 (21.5%)	59 (17.3%)	
Small Cities	24 (4.0%)	15 (4.4%)	
Rural	254 (41.9%)	174 (50.9%)	
Coverage			
Regular	564 (93.1%)	313 (91.5%)	0.294¶
SAP Plan 1	20 (3.3%)	19 (5.6%)	
SAP Plan 2	10 (1.7%)	3 (0.9%)	
SAP Plan 3	12 (2.0%)	7 (2.0%)	
Number (%) Hospitalized‡	136 (22.4%)	70 (20.5%)	0.479¶
Number (%) Re-identified‡	344 (56.8%)	125 (36.5%)	<0.001¶

§ Wilcoxon Rank Sum Test (two-sided p-value)

¶ Chi-square Test (two-sided p-value)

† In the 90 day period prior to the index identification

‡ In the follow-up period

A Mantel-Haenszel stratified analysis was performed to control for the potential confounding effects of residence on the association between study group status and re-identification. The RR_{MH} (95% CI) was 0.65 (0.56, 0.75) after adjusting for the

effects of residence (stratified as large/medium-sized cities, small cities/rural). The similarity of the crude and adjusted estimates of RR indicates that residence was not a confounder of the association between profile release and re-identification in this investigation. A summary measure of relative risk adjusted for the level of extreme use was not calculated because the test for homogeneity indicated that the stratum-specific RR estimates were not uniform (p=0.014). Heterogeneity of the stratum-specific RRs implies that there was an interaction between study group status and the level of extreme use (i.e. the association between profile release and re-identification depended on the level of extreme use).

The Multivariate Logistic Regression Model

The findings of the crude and stratified analyses suggest that profile release by the Extreme User Program was associated with a decreased risk of re-identification, but that the magnitude of the association depended on the level of extreme use. A multivariate logistic regression analysis was conducted to clarify this association and to examine the influence of the other independent variables on re-identification. All the variables listed in Table 4.11 were included in the regression analysis, but only four were found to be significant predictors of re-identification in the multivariate model. The fitted model describing the association between re-identification and the independent study variables is summarized by Equation 4.1,

$$g(\mathbf{x}) = \ln\left\{\frac{\pi(\mathbf{x})}{1-\pi(\mathbf{x})}\right\} = \begin{aligned}&0.425 - 0.2364(\text{study group}) + 1.059(\text{level}) - 2.074(\text{hospitalization})\\&- 0.8943(\text{drug1}) - 0.5084(\text{drug2}) - 0.6902(\text{study group*level})\\&+ 1.471(\text{level*hospitalization})\end{aligned} \qquad (4.1)$$

where the independent variables are defined in Table 4.12 and asterisks designate interactions between variables. The terms $g(\mathbf{x})$ and $\pi(\mathbf{x})$ are defined as shown for Equation 3.6.

All four predictor variables were included in the model as categorical variables (Table 4.12). Continuous-scaled data were available for two of the variables: the level of extreme use and the number of follow-up days spent in hospital. However, modelling these factors as continuous variables was inappropriate because neither variable fulfilled the assumption of linearity in the logit which is a requirement of logistic regression (Hosmer and Lemeshow 1989). The level of extreme use was divided into two categories (Table 4.12). A cut point of 220% was chosen for this variable because individuals with a percentage of maximum threshold dose of ≥220% had a greater risk of re-identification than subjects below 220%. The risk of re-identification did not appear to increase any further with increases in the level of use above 220%. The number of hospital days was also categorized as a dichotomous variable (Table 4.12). The cut point of 1 day was chosen because even short stays in hospital (1 to 4 days) were associated with a decreased risk of re-identification when compared with subjects who were not hospitalized during the follow-up period.

Potential interactions between the four predictor variables were assessed by forming product terms and adding each term to the main effects model. The Likelihood Ratio test was used to assess the statistical significance of each interaction term. Two interactions terms, "study group*level" and "level*hospitalization", were statistically significant when added to the main effects model ($p<0.05$). Both interaction terms were included in the final model (Equation 4.1) because they were not only significant from a statistical point of view, but were also reasonable from a clinical point of view.

Table 4.12: Definition of Variables in the Logistic Regression Model for the Extreme User Program

Variable Name	Definition and Coding
Study Group	*Study Group:* 0 = Comparison Group 1 = Intervention Group
Level	*Level of Extreme Use in the Pre-identification Period:* 0 = percentage of threshold dose <220% 1 = percentage of threshold dose ≥220%
Hospitalization	*Number of Days in Hospital During the Follow-up Period:* 0 = Not hospitalized 1 = 1 or more days
Drug1 Drug2	*Design Variable Denoting the Drug Group Exceeded:* reference group = asthma drugs drug1= mood-modifying drugs drug2 = multiple drug groups
Study Group*Level	*Product Term for the Interaction between Study Group and Level*
Level*Hospitalization	*Product Term for the Interaction between Level and Hospitalization*

Assessing the Fit of the Logistic Regression Model

The effectiveness of the fitted model in describing the outcome variable was assessed by examining both the overall fit of the model and the fit over the range of covariate patterns. The Hosmer and Lemeshow goodness-of-fit chi-square statistic was small with a large p value ($\chi^2 = 2.937$ with 8 degrees of freedom; $p = 0.938$), indicating that the overall agreement between the observed and predicted values of the response variable was good. The results of this test were supported by the finding of a close agreement between the observed and predicted probabilities for nearly all of the covariate patterns. These findings indicate that the overall fit of the model was good.

Examination of the regression diagnostic statistics, ΔD and $\Delta\chi^2$, indicated

that the model fit reasonably well over the range of covariate patterns. The plots of ΔD versus the predicted probability (π) and $\Delta\chi^2$ versus π did not reveal any systematic deviation from the general form described by Hosmer and Lemeshow (1989). Several covariate patterns appeared to be moderate outliers with respect to the distribution of ΔD and $\Delta\chi^2$ since they were located some distance away from the rest of the points. However, it is noteworthy that the values of ΔD and $\Delta\chi^2$ for all of the covariate patterns were well below 4, the approximate 95th percentile of the χ^2 distribution with 1 degree of freedom. Therefore, it is questionable whether even these apparent outliers had a poor fit.

Of the three possible outliers, only one covariate pattern had a large influence on the values of the regression coefficients in the model. This highly influential covariate pattern consisted of comparison group subjects who had "high" levels of extreme use ($\geq$220%) of mood-modifying drugs and who were not hospitalized during the follow-up period. Given the large number of subjects with this covariate pattern (335 of the 948 study subjects), it is not surprising that this covariate pattern exerted a great deal of influence on the values of the regression coefficients in the model.

In summary, results of the goodness-of-fit techniques indicated that the overall fit of the model was good. The fit of the model across the range of covariate patterns was not perfect, but it was reasonably good. The lack of a perfect fit may be the result of the limited data that were available for the analysis. That is, information on other factors which may be expected to influence the risk of re-identification were not collected for this investigation. Examples of such factors include the conditions for which the drugs were prescribed, the severity of the illness and the prior history of drug use. Inclusion of such data in the multivariate model likely would have improved the fit further. Nevertheless, given the available information, the model defined in Equation 4.1 was considered to provide a good description of the association between re-identification and the independent variables and was, therefore, accepted as the final model.

Findings of the Multivariate Logistic Regression Analysis

The odds ratios and 95% confidence intervals for each of the variables in the logistic regression model are summarized in Table 4.13. Of primary interest is the relationship between study group and re-identification. The significance of the "study group*level" interaction term indicates that the effect of profile release on the risk of re-identification depended on the level of extreme use recorded at the index identification, confirming the findings of the stratified analyses. For subjects with "low" levels of extreme use (i.e. percentage of maximum threshold dosage = 200-219%), the OR (95% CI) for the study group variable was 0.79 (0.45, 1.38). The confidence interval, which includes the null value of one, indicates that profile release was not associated with a significant reduction in the risk of re-identification in this stratum. The corresponding OR (95% CI) for subjects with "high" levels of extreme use (≥220%) was 0.40 (0.28, 0.55). In this stratum, intervention group subjects were 60% less likely to be re-identified than subjects in the comparison group. Thus, the findings of the multivariate analysis indicate that, although profile release had little or no impact on re-identification of subjects whose levels of extreme use were only slightly above the threshold dosage (200-219%), it was associated with a reduction in the risk of re-identification among subjects with higher levels of extreme use (≥220%). Since the OR was statistically adjusted for the other variables in the model, this association cannot be explained by differences between the two study groups with respect to hospitalization or the drug group exceeded.

Table 4.13: Logistic Regression Model Describing Re-identification Among Extreme User Subjects

Variable	β[§]	SE(β)[¶]	Odds Ratio	95% Confidence Interval	p-value
constant	0.425	0.289	—	—	—
study group	-0.236	0.285	*if level <220%:* 0.79 *if level ≥220%:* 0.40	(0.45, 1.38) (0.28, 0.55)	0.4066
level	1.059	0.232	*if studygrp = 0 & hosp = no:* 2.88 *if studygrp = 0 & hosp = yes:* 12.55 *if studygrp = 1 & hosp = no:* 1.45 *if studygrp = 1 & hosp = yes:* 6.30	(1.83, 4.55) (4.14, 38.10) (0.87, 2.39) (1.99, 19.96)	<0.0001
hospitalization	-2.074	0.544	*if level <220%:* 0.13 *if level ≥220%:* 0.55	(0.04, 0.67) (0.38, 0.79)	<0.0001
drug1 drug2	-0.894 -0.508	0.259 0.763	0.41 0.60	(0.25, 0.68) (0.14, 2.69)	0.0016
study group*level	-0.690	0.332	0.50	(0.26, 0.96)	0.0382
level*hosp	1.471	0.576	4.36	(1.41, 13.5)	0.0038

[§] β is the slope coefficient for the independent variables.
[¶] SE(β) is the standard error of the regression coefficient.

Hospitalization during the follow-up period was also associated with a reduction in the risk of re-identification, although its impact was less marked for subjects with "high" levels of extreme use (OR = 0.55) than for subjects with "low" levels of extreme use (OR = 0.13) (Table 4.13). A possible explanation for this negative association relates to the fact that medications administered in hospital were not recorded in the SPDP database and, therefore, were not captured by the PPRP. In addition, hospitalized individuals may not have renewed their outpatient prescriptions

during their stay in hospital. Given these two factors, the apparent daily dosages calculated during the follow-up period may have been based on smaller quantities of drug for hospitalized patients than for non-hospitalized individuals even if their actual drug use was similar. Following this line of reasoning, individuals who were hospitalized during the follow-up period would have been less likely to be re-identified than non-hospitalized subjects with similar levels of actual consumption.

The observed interaction between hospitalization and the level of extreme use is consistent with this reasoning. For individuals whose level of extreme use at the index identification was just slightly above the threshold level, even a small disruption in the apparent dosage calculation may have been sufficient to avoid re-identification. For subjects with "high" levels of extreme use, hospitalization would have had to produce a much larger disruption in the apparent dosage calculation if it were to influence re-identification. Thus, hospitalization would be expected to have a greater impact on re-identification among subjects with "low" levels of extreme use than among subjects with higher levels of use.

The level of extreme use recorded at the index identification was also a highly significant predictor of re-identification in the multivariate model. The interaction of this variable with both hospitalization and study group status necessitated the calculation of four odds ratios (Table 4.13). For subjects who were hospitalized for one or more days during the follow-up period, the odds ratios (95% CI) for the subjects with "high" levels of extreme use relative to those with "low" levels of extreme use were 6.30 (1.99, 19.96) and 12.55 (4.14, 38.10) for the intervention and comparison groups, respectively. Among non-hospitalized subjects, the corresponding odds ratios (95% CI) were 1.45 (0.87, 2.39) and 2.88 (1.83, 4.55). In all but one of the four strata, subjects with "high" levels of extreme use had a significantly greater risk of re-identification than subjects with "low" levels of extreme use. A general association in this direction was expected because the magnitude of change required to prevent re-identification by the Extreme User Program was related to the level of extreme use during the pre-identification period. That is, for subjects with pre-identification levels of

use that were slightly above the threshold level, only small decreases in the apparent dosages would have been needed to avoid re-identification. In contrast, much larger decreases would have been required to prevent re-identification of subjects with "high" pre-identification levels of extreme use, making it more difficult for these individuals to avoid re-identification.

Finally, the drug group for which extreme user criteria were exceeded was also a significant predictor of re-identification in the multivariate model. The OR (95% CI) for the mood-modifying drug group compared with the reference group of asthma drug extreme users was 0.41 (0.25, 0.68) (Table 4.13). Thus, subjects who exceeded dosage criteria for mood-modifying drugs were nearly 60% less likely than asthma drug extreme users to be re-identified during the follow-up period. The odds of re-identification for subjects who exceeded criteria for multiple drug groups were not significantly different from the reference group (Table 4.13).

Six variables – age, sex, residence, coverage type and the numbers of prescribers and pharmacies in the three months prior to identification – were not significantly associated with re-identification in the multivariate model ($p>0.05$). Modelling age and the numbers of prescribers and pharmacies as categorical rather than continuous variables also did not improve the model. Removal of each of the six variables from the multivariate model did not result in meaningful changes in the β coefficients and odds ratios for the remaining variables; therefore, inclusion of these variables was not necessary to control for confounding.

4.3.3 Polypharmacy Program

Comparability of the Intervention and Comparison Groups

The intervention and comparison groups for the Polypharmacy component of the follow-up investigation were similar in most respects (Table 4.14). There were no significant differences between the groups with respect to age, sex, residence, the numbers of prescribers and pharmacies and the number of follow-up days spent in hospital ($p>0.05$). Nevertheless, there were some important differences. In the 90 day period prior to the index identification, the comparison group had prescription claims for a greater number of different drugs than the intervention group ($p=0.0001$). The two groups also differed with respect to the distribution of subjects by SPDP coverage type ($p<0.001$). The majority of individuals (58.0%) in the intervention group had Regular coverage and, therefore, were subject to the deductible system. In contrast, only 37.2% of comparison group subjects had Regular coverage, while 62.8% were covered under the Saskatchewan Assistance Plan and were exempted from the deductible system. The dissimilarity of the two groups with respect to the number of different drugs and the type of coverage was important because both variables were considered potential confounders of the association between profile release and re-identification.

Table 4.14: Characteristics of Polypharmacy Intervention and Comparison Groups

Variable	Comparison Group (n=180)	Intervention Group (n=181)	p-value
	Median (Range) *Mean ± SD*	*Median (Range)* *Mean ± SD*	
Age (years)	68.5 (1 - 98) *64.9 ± 19.8*	70 (11 - 98) *66.3 ± 17.7*	0.6958§
Number of Pharmacies†	1 (1 - 9) *1.8 ± 1.4*	1 (1 - 6) *1.7 ± 1.0*	0.9890§
Number of Prescribers†	3 (1 - 10) *2.8 ± 1.8*	2 (0 - 7) *2.6 ± 1.4*	0.4367§
Number of Days in Hospital‡	0 (0 - 110) *4.6 ± 12.0*	0 (0 - 59) *5.1 ± 10.0*	0.2058§
Number of Different Drugs†	17 (16 - 31) *17.7 ± 2.5*	16 (16 - 21) *16.4 ± 0.8*	0.0001§
	# (%)	*# (%)*	
Sex			
male	53 (29.4%)	48 (26.5%)	0.536¶
female	127 (70.6%)	133 (73.5%)	
Residence			
Large Cities	76 (42.2%)	74 (40.9%)	0.836¶
Medium-Sized Cities	28 (15.6%)	24 (13.3%)	
Small Cities	6 (3.3%)	5 (2.8%)	
Rural	70 (38.9%)	78 (43.1%)	
Coverage			
Regular	67 (37.2%)	105 (58.0%)	<0.001¶
SAP Plan 1	23 (12.8%)	4 (2.2%)	
SAP Plan 2	15 (8.3%)	12 (6.6%)	
SAP Plan 3	75 (41.7%)	60 (33.1%)	
Number (%) Hospitalized‡	56 (31.1%)	67 (37.0%)	0.237¶
Number (%) Re-identified‡	70 (38.9%)	28 (15.5%)	<0.001¶

§ Wilcoxon Rank Sum Test (two-sided p-value)

¶ Chi-square Test (two-sided p-value)

† In the 90 day period prior to the index identification

‡ In the follow-up period

Crude and Adjusted Estimates of the Risk for Re-identification

During the 112 day follow-up period, re-identification of subjects occurred

less frequently for the intervention group (15.5%) than the comparison group (38.9%) ($p<0.001$). The crude RR (95% CI) of re-identification was 0.40 (0.27, 0.59), indicating that intervention group subjects were 60% less likely than comparison group subjects to be re-identified by the PPRP.

Mantel-Haenszel stratified analyses were performed to control for the potential confounding effects of coverage type and the number of different drugs on the association between study group status and re-identification. The RR_{MH} (95% CI) was 0.44 (0.31, 0.64) after adjusting for the effect of coverage (stratified as Regular or SAP). The similarity of the crude and adjusted risk estimates implies that the type of coverage was not an important confounder of the association between study group status and re-identification in this investigation. The RR_{MH} (95% CI) adjusted for the effect of the number of different drugs (stratified as 16, 17-18 and ≥19 different drugs) was 0.50 (0.34, 0.75). This RR_{MH} was somewhat different from the crude RR of 0.40, indicating that the number of different drugs confounded the association between profile release and re-identification in this study. Nevertheless, even after adjusting for the confounding effects of this variable, intervention group subjects were still only half as likely to be re-identified than comparison group subjects.

The Multivariate Logistic Regression Model

The strong negative association between intervention group status and re-identification suggests that profile release had an positive impact on short-term re-identification rates. Further analyses using multivariate logistic regression were performed to clarify the association between profile release and re-identification and to examine the influence of the other independent variables on this outcome. All of the independent variables listed in Table 4.14 were considered for inclusion in the multivariate model. Three variables – age, number of prescribers and number of pharmacies – were not included in the final model because they were neither significant predictors of re-identification nor important confounders in the multivariate model. The

fitted model describing the association between re-identification and the independent variables is summarized by Equation 4.2,

$$g(\mathbf{x}) = \ln\left\{\frac{\pi(\mathbf{x})}{1-\pi(\mathbf{x})}\right\} = \begin{array}{l} -7.091 - 0.9825(\text{study group}) + 0.3267(\text{drugs}) \\ +0.9327\ (\text{hospital days}) + 0.7394(\text{sex}) + 1.612(\text{covcode1}) \\ +0.5713(\text{covcode2}) - 0.7075(\text{residence}) \end{array} \quad (4.2)$$

where the independent variables are defined in Table 4.15 and the terms $g(\mathbf{x})$ and $\pi(\mathbf{x})$ are defined as shown for Equation 3.6.

With the exception of the number of different drugs, all of the predictor variables were modelled as categorical variables (Table 4.15). Continuous-scaled data were available for the hospital days variable. However, it was inappropriate to model this factor as a continuous variable because the data did not fulfil the assumption of linearity in the logit. Instead, the number of hospital days was dichotomized as 0 – 4 versus 5 or more days. The cut point of 5 days was chosen because the odds ratio for re-identification for subjects with short stays in hospital (1 to 4 days) was similar to that for subjects not hospitalized during the follow-up period whereas subjects spending more than 5 follow-up days in hospital had a greater risk of re-identification.

The four categories of residence and coverage were collapsed into two and three groups, respectively (Table 4.15). The small cities and rural categories were combined because there was a trend toward decreased risk for both categories when compared with the large cities group. Subjects from medium-sized cities and large cities had a similar risk of re-identification and were combined as the reference group. For the coverage variable, subjects with Regular coverage or SAP–Plan 1 coverage had a similar risk of re-identification and were, therefore, combined as the reference group. SAP–Plan 2 and SAP–Plan 3 beneficiaries had a tendency toward an increased risk of re-identification when compared to Regular beneficiaries, but the magnitudes of the associations were different; therefore, these two groups were considered separately.

Table 4.15: Definition of Variables in the Logistic Regression Model for the Polypharmacy Program

Variable Name	Definition and Coding
Study Group	*Study Group:* 0 = Comparison Group 1 = Intervention Group
Drugs	*Number of Different Drugs in the 90 Day Period Prior to Identification:* (continuous variable; range 16-31)
Hospital Days	*Number of Days in Hospital During the Follow-up Period:* 0 = Less than 5 days 1 = 5 or more days
Sex	*Gender* 0 = male 1 = female
Covcode1 Covcode2	*Design Variables for SPDP Coverage Type:* referent = Regular/SAP-Plan 1 covcode1 = 1 (SAP-Plan 2) covcode2 = 1 (SAP-Plan 3)
Residence	*Residence* 0 = large & medium-sized cities 1 = small cities & rural

Potential interactions between the predictor variables were assessed by forming interaction terms and testing the significance of these terms when added to the main effects model (Equation 4.2). None of the interaction terms studied were statistically significant (Likelihood Ratio Test $p>0.05$); therefore, none were included in the final model.

Assessing the Fit of the Logistic Regression Model

The fitted model (Equation 4.2) described the response variable reasonably well. The Hosmer-Lemeshow goodness-of-fit chi-square statistic indicated that the

overall agreement between the observed and fitted values was good, which means that the overall fit of the model was good (χ^2=1.295 with 8 degrees of freedom; p=0.996).

Examination of the regression diagnostic statistics, ΔD and $\Delta\chi^2$, indicated that the model fit reasonably well over the range of covariate patterns. The plots of ΔD and $\Delta\chi^2$ against the predicted probability (π) did not reveal any systematic deviation from the general form described by Hosmer and Lemeshow (1989). However, several of the 119 covariate patterns were obvious outliers in both plots. Two of these outliers, which accounted for only one subject each, did not have a large influence statistic ($\Delta\beta$). Thus, the inclusion of these two "poorly fit" individuals in the analysis had little impact on the β values of the variables in the model and, therefore, had little impact on the conclusions that will be drawn from the ORs derived from the model.

The third outlier did have a relatively large influence on the regression coefficients of variables in the fitted model. This influential covariate pattern, which represented only 7 of the 361 study subjects, consisted of female comparison group subjects with Plan 3 coverage, rural residence codes, 17 different drugs at baseline and 0 – 4 follow-up days spent in hospital. There was nothing particularly unusual about this covariate pattern which would explain the relatively poor fit and high influence for these 7 study subjects. Interestingly, when these 7 individuals were excluded from the analysis, the regression coefficients in the model changed by up to 25%; however, there were no meaningful changes in the conclusions about the significant predictors in the model and the relative magnitude of the associations.

In summary, the findings of the assessment of fit techniques indicated that the overall fit of the model was good. The fit of the model over the entire range of covariate patterns was not perfect, but it was reasonably good. As discussed in the results of the regression analysis for the Extreme User Program, the lack of a perfect fit may be the result of the limited data that were available for the analysis. The inclusion of other information in the analysis, such as the conditions for which the medications were prescribed, the prior history of drug use, the severity of illness and other socio-demongraphic factors, may have improved the fit of the model. However, given the

available information, the model defined in Equation 4.2 provided a good description of the association between re-identification and the independent variables and was, therefore, accepted as the final model.

Findings of the Multivariate Logistic Regression Analysis

The estimated odds ratios and 95% confidence intervals for the variables in the multivariate model are summarized in Table 4.16. Each variable was a statistically significant predictor of re-identification in the multivariate model ($p<0.05$). Of particular interest is the odds ratio for the study group variable. The OR (95% CI) of 0.37 (0.21, 0.67) for this variable indicates that subjects in the intervention group were approximately one-third as likely to be re-identified as their counterparts in the comparison group. Thus, profile release under the Polypharmacy Program was associated with a reduced risk of re-identification by the PPRP. Since the odds ratio was adjusted for the effects of the other variables in the model, the observed association between profile release and re-identification cannot be explained by differences between the two study groups with respect to these variables.

Table 4.16: Logistic Regression Model Describing Re-identification Among Polypharmacy Subjects

Variable	β[§]	SE(β)[¶]	Odds Ratio	95% Confidence Interval	p-value
constant	-7.091	1.44			
study group	-0.983	0.294	0.37	(0.21, 0.67)	0.0007
drugs	0.327	0.081	1.39	(1.18, 1.62)	<0.0001
hospital days	0.933	0.306	2.54	(1.39, 4.64)	0.0023
sex	0.739	0.331	2.09	(1.09, 4.02)	0.0209
covcode1	1.612	0.495	5.01	(1.90, 13.23)	}
covcode2	0.571	0.292	1.77	(1.00, 3.15)	} 0.0022
residence	-0.708	0.293	0.49	(0.28, 0.88)	0.0138

[§] β is the slope coefficient for the independent variables.
[¶] SE(β) is the standard error of the regression coefficient.

The number of different drugs claimed in the 90 day period prior to the index identification was also a highly significant predictor of re-identification (Table 4.16). The number of drugs claimed by Polypharmacy subjects ranged from 16 to 31. Within this range, an increase of one drug was associated with a 39% increase in the risk of re-identification. For example, the odds of re-identification for a subject with 21 different drugs in the three months prior to the index identification was 5.1 times higher than for subjects with 16 different drugs. This finding was not surprising because the magnitude of change required to avoid re-identification depended on the number of drugs claimed prior to identification. For example, only one drug would have to be discontinued from a medication regimen with 16 different drugs for a given patient to fall below the threshold level for re-identification by the Polypharmacy Program. In contrast, prevention of re-identification for a patient with 21 different drugs would require discontinuation of at least six drugs.

The time spent in hospital during the follow-up period was also an important predictor of re-identification for Polypharmacy subjects (Table 4.16). Subjects spending 5 or more follow-up days in hospital were 2.5 times more likely to be re-identified than subjects in the reference category of 0 to 4 days ($p=0.0023$). This finding of an increased risk of re-identification for hospitalized Polypharmacy subjects contrasts with the strong negative association between hospitalization and re-identification for Extreme User subjects. A possible explanation for the positive association between hospitalization and re-identification for Polypharmacy patients is that prolonged hospitalization may be a marker for more severe illness. If PPh patients who were hospitalized for 5 or more days were sicker than subjects with no admissions or only short hospitalizations, then discontinuation of medications in these sicker, hospitalized patients may have been more difficult than in their healthier counterparts, resulting a greater risk of re-identification. Another factor which may have contributed to the positive association is the initiation of new medications which sometimes occurs during hospitalization. These new medications may be added to the regimen or may be intended to replace drugs already being used. In either case, apparent drug use during

the follow-up period would remain high because medications claimed before or after hospitalization would be included in the count of the different drugs, even if some drugs were replaced or discontinued in hospital.

Demographic variables significantly associated with re-identification in the multivariate model were gender and residence (Table 4.16). The OR (95% CI) for females compared to males was 2.08 (1.09, 4.02). Thus, not only were females more likely to be identified by the Polypharmacy Program (Figure 4.24), but, once identified, they were twice as likely as their male counterparts to be re-identified during the follow-up period. With regard to residence, subjects from large or medium-sized cities were twice as likely as residents of small cities or rural areas to be re-identified by the Program.

Finally, SPDP coverage type was a significant predictor of re-identification. Individuals with Regular coverage or SAP–Plan 1 coverage had a similar risk of re-identification and were grouped together as the reference category. The OR (95% CI) for the SAP–Plan 2 coverage category was 5.01 (1.90, 13.23), indicating that Plan 2 beneficiaries were five times more likely to be re-identified than the reference group. The wide confidence interval is a reflection of the relatively small number of Plan 2 subjects (n=27) on which this estimate was based. The odds ratio (95% CI) for SAP–Plan 3 beneficiaries was 1.77 (1.00, 3.15). The lower limit of the confidence interval indicates that the apparent increase in risk for Plan 3 beneficiaries was of borderline statistical significance.

The variables not included in the model – age, number of prescribers and number of pharmacies – were not associated with re-identification in univariate analyses. Inclusion of these variables in the multivariate model as either continuous or categorical variables did not improve the model. Also, since the addition of these variables to the model did not result in meaningful changes in the regression coefficients and odds ratios of the other variables in the model (Table 4.16), their inclusion in the model was not necessary to control for confounding. Thus, inclusion of age and the number of prescribers and pharmacies in the multivariate model was neither necessary

from a predictive point of view nor for control of confounding.

4.3.4 Polyprescriber Program

Comparability of the Intervention and Comparison Groups

The comparison and intervention groups for the Polyprescriber component of the investigation had similar values for most of the baseline characteristics (Table 4.17). Nevertheless, some differences between the two groups were observed. In particular, subjects in the intervention group had significantly fewer prescribers and pharmacies in the 90 day period prior to identification than subjects in the comparison group (Table 4.17). Differences in these two variables were potentially important because the numbers of prescribers and pharmacies were considered possible confounders of the association between study group status and re-identification.

Crude and Adjusted Estimates of the Risk for Re-identification

Re-identification of Polyprescriber subjects was significantly less common for the intervention group (3.9%) than for the comparison group (19.7%) ($p<0.001$). The crude RR (95% CI) for re-identification was 0.20 (0.08, 0.49), indicating that intervention group subjects were only one-fifth as likely as comparison group subjects to be re-identified by the PPRP during the follow-up period.

Table 4.17: Characteristics of Polyprescriber Intervention and Comparison Groups

Variable	Comparison Group (n=76)	Intervention Group (n=154)	p-value
	Median (Range) *Mean ± SD*	*Median (Range)* *Mean ± SD*	
Age (years)	38 (0 - 98) *41.2 ± 21.2*	38 (0 - 96) *39.7 ± 22.5*	0.6865§
Number of Pharmacies†	3.5 (1 - 9) *3.8 ± 2.0*	3 (1 - 8) *3.2 ± 1.5*	0.0270¶
Number of Days in Hospital‡	0 (0 - 43) *4.3 ± 9.7*	0 (0 - 46) *3.7 ± 8.6*	0.9641§
Number of Different Prescribers†	7 (7 - 12) *7.6 ± 1.0*	7 (7 - 9) *7.1 ± 0.3*	0.0001¶
	# (%)	*# (%)*	
Sex			
male	26 (34.2%)	57 (37.0%)	0.677¶
female	50 (65.8%)	97 (63.0%)	
Residence			
Large Cities	55 (72.4%)	106 (68.8%)	0.083¶
Medium-Sized Cities	9 (11.8%)	9 (5.8%)	
Small Cities	4 (5.3%)	5 (3.2%)	
Rural	8 (10.5%)	34 (22.1%)	
Coverage			
Regular	42 (55.3%)	95 (61.7%)	0.656¶
SAP Plan 1	23 (30.3%)	42 (27.3%)	
SAP Plan 2	3 (3.9%)	7 (4.5%)	
SAP Plan 3	8 (10.5%)	10 (6.5%)	
Number (%) Hospitalized‡	23 (30.3%)	48 (31.2%)	0.889¶
Number (%) Re-identified‡	15 (19.7%)	6 (3.9%)	<0.001¶

§ Wilcoxon Rank Sum Test (two-sided p-value)

¶ Chi-square Test (two-sided p-value)

† In the 90 day period prior to the index identification

‡ In the follow-up period

Stratified analyses were conducted to control for the potential confounding effects of the numbers of pharmacies and prescribers. The RR_{MH} (95% CI) adjusted for the effect of the number of pharmacies (stratified as 1-2, 3-4 or ≥5 pharmacies) was 0.23 (0.11, 0.50). The RR_{MH} adjusted for the effect of the number of different prescribers

(stratified as 7 versus 8 physicians) was also 0.23 with a 95% CI of (0.08, 0.67). The similarity of the crude and adjusted RR estimates implies that neither the number of pharmacies nor the number of prescribers were important confounders of the association between profile release and re-identification in this investigation. Thus, the lower risk of re-identification observed for the intervention group cannot be explained by differences between the study groups with respect to these two variables.

Before proceeding to the results of the regression analysis, one further comment should be made about the stratified analysis that was performed to control for the effects of the number of prescribers. Although the test for homogeneity of the stratum-specific RRs indicated a lack of significant interaction ($p>0.05$), visual inspection of the RRs for the strata suggested that intervention group status may have been associated with a greater reduction in the risk of re-identification for subjects with 8 or more prescribers compared with subjects with 7 prescribers. This potential interaction was studied in more detail in the logistic regression analysis described below.

The Multivariate Logistic Regression Model

The findings of the simple and stratified analyses suggest that intervention group status was associated with a decreased risk of re-identification for Polyprescriber patients. Multivariate logistic regression analysis was performed to clarify this association and to examine the influence of the other study variables on this outcome. All the independent variables listed in Table 4.17 were considered for inclusion in the multivariate model. The fitted model describing the association between re-identification and the independent study variables is summarized by Equation 4.3,

$$g(\mathbf{x}) = \ln\left\{\frac{\pi(\mathbf{x})}{1-\pi(\mathbf{x})}\right\} = \begin{array}{l} -3.191 - 1.823(\text{study group}) + 1.410(\text{prescribers}) \\ +1.856(\text{hospitalization}) + 1.813(\text{covcode1}) + 0.626(\text{covcode2}) \\ +1.188(\text{residence}) \end{array} \qquad (4.3)$$

where the independent variables are defined in Table 4.18 and the terms $g(\mathbf{x})$ and $\pi(\mathbf{x})$ are defined as shown for Equation 3.6.

All of the variables included in Equation 4.3 were modelled as categorical variables (Table 4.18). Continuous-scaled data were available for the number of prescribers and the hospitalization variables. However, it was inappropriate to model these factors as continuous variables because the data did not fulfil the assumption of linearity in the logit. Given the limited range (7 to 12) and the skewed nature of the distribution of prescribers (i.e. 190 of 230 subjects had 7 physicians), this variable was dichotomized as 7 versus 8 or more prescribers. The hospitalization variable had a greater range (0 to 46 days), but also had a highly skewed distribution with 69% of subjects not hospitalized during the follow-up period. Because individuals with even short stays in hospital (i.e. 1 to 4 days) had a significantly greater risk of re-identification than those who were not hospitalized, this variable was categorized as 0 versus ≥ 1 hospital days. As with the regression analysis for the Polypharmacy Program, the four categories of residence and coverage were collapsed into two and three groups, respectively (Table 4.18).

In the assessment of potential interactions among the main effects variables, only one interaction term, "study group*prescribers", was found to be significant when added to the main effects model ($p=0.04$). The significance of this interaction term indicates that the effect of intervention group status on re-identification depended on the number of physicians recorded at the index identification. The regression coefficients and standard errors [$SE(\beta)$] for the model containing the main effects variables plus the "study group*prescribers" interaction term are summarized in Table 4.19. Of particular interest is the extremely large β and $SE(\beta)$ for the interaction term. The magnitude of these statistics indicates that the model is unstable, resulting in unreliable estimates of the odds ratios for the variables involved in the interaction. For example, among subjects with 7 different physicians, the OR (95% CI) for the intervention group was 0.27 (0.07, 1.06). The corresponding OR for subjects with 8 or more prescribers was

1.58×10^{-33} with an extraordinarily large confidence interval ($e^{\pm 1.28 \text{ billion}}$). The unrealistically small odds ratio and large confidence interval for the study group variable are reflections of the instability introduced into the multivariate model with the addition of the "study group*physicians" interaction term. This instability can be explained by the small number of intervention group subjects with 8 or more prescribers (n = 11). Thus, although the analyses suggested that profile release may have had a greater effect on re-identification among subjects with 8 or more physicians than among subjects with 7 prescribers, the available data were insufficient to test this hypothesis adequately. Therefore, given the available data, the main effects model (Equation 4.3) was considered to be the model which best described the association between re-identification and the independent variables.

Table 4.18: Definition of Variables for the Logistic Regression Model for the Polyprescriber Program

Variable Name	Definition and Coding
Study Group	*Study Group:* 0 = Comparison Group 1 = Intervention Group
Prescribers	*Number of Different Prescribers in the 90 Day Period Prior to Identification:* 0 = 7 prescribers 1 = 8 or more prescribers
Hospitalization	*Number of Days in Hospital During the Follow-up Period:* 0 = 0 days 1 = 1 or more days
Covcode1 Covcode2	*Design Variables for SPDP Coverage Type:* referent = Regular/SAP Plan 1 covcode1 = 1 (SAP Plan 2) covcode2 = 1 (SAP Plan 3)
Residence	*Residence* 0 = large & medium-sized cities 1 = small cities & rural

Table 4.19: Estimated Regression Coefficients and Standard Errors for the Polyprescriber Logistic Regression Model Containing an Interaction Term

Variable	β[§]	SE(β)[¶]	p-value
constant	-3.589	0.691	
study group	-1.309	0.694	0.0642
prescribers	1.999	0.735	0.0038
hospitalization	2.011	0.592	0.0003
covcode1	2.029	0.958	}
covcode2	0.730	0.822	} 0.1113
residence	1.144	0.679	0.0949
study group*prescribers	-74.22	6.56×10^8	0.0402

[§] β is the regression coefficient for the independent variable.
[¶] SE(β) is the standard error of the regression coefficient.

Assessing the Fit of the Logistic Regression Model

The fitted model (Equation 4.3) described the outcome variable reasonably well. The Hosmer-Lemeshow goodness of fit chi-square statistic indicated that the overall fit of the model was good (χ^2=5.862 with 8 degrees of freedom; p=0.663). The results of the Hosmer-Lemeshow test were supported by the finding of a close agreement between the observed and predicted probabilities for most of the covariate patterns.

Examination of the regression diagnostic statistics, ΔD and $\Delta\chi^2$, indicated that the model explained the response variable reasonably well over the range of covariate patterns. The plots of ΔD versus π and $\Delta\chi^2$ versus π did not reveal any systematic deviation from the general form described by Hosmer and Lemeshow (1989). Several covariate patterns were obvious outliers in both plots. One of these outliers did not have a large influence statistic, but two of the covariate patterns did have a relatively large influence on the regression coefficients of variables in the fitted model. These two covariate patterns represented 30 of the 230 study subjects. There was nothing particularly unusual about these covariate patterns which would explain the relatively poor fit and high influence for the 30 study subjects. When these 30 individuals were excluded from the analysis, the regression coefficients for the study group,

hospitalization and physicians variables changed by up to 50%, but all three variables continued to be significant predictors of re-identification.

In summary, the goodness-of-fit techniques suggested that the overall fit of the model was good and that the fit across the range of covariate patterns was reasonably good. Given the available information, the model summarized by Equation 4.3 was considered to provide a good description of the association between re-identification and the independent variables and was, therefore, accepted as the final model.

Findings of the Multivariate Logistic Regression Analysis

The estimated odds ratios and 95% confidence intervals for the variables in the final model are summarized in Table 4.20. Study group status, the number of prescribers and the number of follow-up days spent in hospital were significant predictors of re-identification in the multivariate model. Coverage and residence were not significant predictors of re-identification ($p>0.05$), but were included in the model to control for confounding. Three of the study variables — age, sex and the number of pharmacies — were not included in the final model.

Re-identification during the follow-up period was strongly associated with study group status. The odds ratio (95% CI) for the study group variable was 0.16 (0.05, 0.54) indicating that subjects in the intervention group were approximately one-sixth as likely as comparison group subjects to be re-identified by the PPRP, after controlling for the other variables in the model. Therefore, as with the Extreme User and Polypharmacy Programs, profile release under the Polyprescriber Program appeared to be associated with a reduction in the short-term risk of re-identification.

Table 4.20: Logistic Regression Model Describing Re-identification Among Polyprescriber Subjects

Variable	β[§]	SE(β)[¶]	Odds Ratio	95% Confidence Interval	p-value
constant	-3.191	0.595			
study group	-1.823	0.612	0.16	(0.05, 0.54)	0.0018
prescribers	1.410	0.611	4.10	(1.23, 13.7)	0.0198
hospitalization	1.856	0.561	6.40	(2.12, 19.3)	0.0005
covcode1	1.183	0.921	6.13	(1.00, 37.6)	}
covcode2	0.626	0.805	1.87	(0.38, 9.13)	} 0.1552
residence	1.188	0.668	3.28	(0.88, 12.2)	0.0784

[§] β is the slope coefficient for the independent variable.
[¶] SE(β) is the standard error of the regression coefficient.

The number of different prescribers in the 90 day period prior to the index identification was also an important predictor of re-identification. Subjects with 8 or more different prescribers had 4.1 times greater risk of re-identification than subjects with 7 different prescribers (Table 4.20). A strong association in this direction was expected because re-identification by the Polyprescriber Program depended on the number of different prescribers in the follow-up period which, for most individuals, would be closely related to the number of prescribers in the pre-intervention period.

Hospitalization during the follow-up period was another important predictor of re-identification in the multivariate model (Table 4.20). The OR (95% CI) for the hospitalization variable was 6.40 (2.12, 19.3). Thus, subjects spending 1 or more follow-up days in hospital were more than six times as likely as non-hospitalized individuals to be re-identified. A possible explanation for this finding is that individuals who were hospitalized may have had more extensive or severe medical problems than those who were not hospitalized. Reducing the number of physicians seen by a given patient may be more difficult for subjects with more extensive medical problems. Another factor which may have contributed to the observed association is that individuals may begin seeing new physicians while in hospital. Outpatient prescriptions ordered by these additional physicians would be included in the polyprescriber count for the PPRP.

As noted above, residence and coverage (covcode1 and covcode2) were

included in the multivariate model to provide for control of confounding. The removal of coverage from the model resulted in a decrease in the magnitude of the OR for the study group variable and an increase in the OR for the hospitalization variable. Thus, coverage was a negative confounder of the effect of study group and a positive confounder of the effect of hospitalization on the risk of re-identification. Deleting coverage from the model had little effect on the odds ratio for the number of prescribers variable. Removal of residence from the model resulted in a decrease in the magnitude of the association between the number of prescribers and re-identification, but had little impact on the odds ratios for study group and hospitalization.

Age, sex and the number of pharmacies were not significant predictors of re-identification either in univariate analyses or in the multivariate model ($p>0.05$). Furthermore, adding age and the number of pharmacies to the model as categorical variables did not significantly improve the prediction of the outcome. Also, since the addition of these variables to the model did not result substantial changes in the regression coefficients of the other variables in the model, it was not necessary to include them in the model to control for confounding. Given the lack of a significant association between re-identification and these variables, together with the lack of confounding by these variables, age, sex and the number of pharmacies were excluded from the final model.

4.3.5 Secondary Outcomes for Subjects who were Re-identified

Four secondary outcomes were examined for subjects who were re-identified by the PPRP during the 112 day follow-up period. These secondary outcomes included the changes in the numbers of different prescribers and pharmacies, the change in the level of extreme use (for Extreme User subjects) and the change in the number of different drugs (for Polypharmacy subjects).

Extreme User Program

In the Extreme User component of the investigation, 344 (56.8%) comparison group subjects and 125 (36.5%) intervention group subjects were re-identified by the PPRP during the follow-up period. The two study groups had similar numbers of prescribers and pharmacies at baseline but differed with respect to the baseline level of extreme use, as measured by the percentage of maximum threshold dosage (Table 4.21)

Table 4.21: Extreme User Subjects who were Re-identified by the Patient Profile Release Program

Variable	Comparison Group (n = 344)	Intervention Group (n = 125)	p-value
Baseline Characteristics [median (range)]:			
Percentage of Threshold Dose†	250.0 (201.5 - 1144.0)	226.7 (200.5 - 300.0)	0.0001§
Number of Prescribers†	1 (1 - 5)	1 (0 - 5)	0.7827§
Number of Pharmacies†	1 (1 - 7)	1 (1 - 4)	0.9047§
Mean Change (±SD)‡ in:			
Percentage of Threshold Dose¶	-8.5 ± 61.3	+20.4 ± 67.7	<0.0001¶
Number of Prescribers	0.0 ± 0.8	-0.2 ± 1.1	0.1538¶
Number of Pharmacies	0.0 ± 0.6	0.0 ± 0.7	0.4941¶

¶ Estimates of the change in the level of extreme use were based on 340 and 123 subjects in the comparison and intervention groups, respectively.
§ Wilcoxon Rank Sum Test (two-sided p-value)
¶ Independent T-Test (two-sided p-value)
† In the 90 day period prior to the index identification
‡ SD = Standard Deviation

The mean changes in the numbers of pharmacies and prescribers were similar for the intervention and comparison groups; however, there was a significant difference in the average change in the level of extreme use (Table 4.21). The comparison group had an overall decline of 8.5 percentage points in the level of extreme

use, while the intervention group had an average increase of 20.4 percentage points ($p<0.0001$). This difference can be explained in part by the fact that individuals in the comparison group had higher baseline levels of extreme use than the intervention group subjects. When the subjects were stratified into three groups based on level of extreme use at the index identification, the differences between the two groups within each stratum were less marked (Table 4.22). Nevertheless, some differences still existed. In the lowest stratum (200-224%), the level of extreme use increased for both groups, but the average increase was greater for the intervention group (+48.7 percentage points) than the comparison group (+19.5). In the highest stratum, the level of use decreased for both groups, but the reduction was somewhat greater for the comparison group than the intervention group (Table 4.22).

Table 4.22: Results of the Stratified Analysis for the Change in the Level of Extreme Use

Strata[§]	Study Group	Number of Subjects	Mean Change in the Percentage of Maximum Threshold Dose (± SD)[†]	p-value[‡]
200 - 224%	Comparison Intervention	58 46	+19.5 ± 29.2 +48.7 ± 96.7	0.0532
225 - 249%	Comparison Intervention	109 56	+9.9 ± 27.9 +8.3 ± 25.4	0.7149
≥ 250%	Comparison Intervention	173 21	-29.6 ± 75.5 -9.5 ± 44.8	0.0843

[§] Strata are based on the percentage of maximum threshold dose
[†] SD = Standard Deviation
[‡] Independent T-Test (two-sided p-value)

When the change in the level of extreme use was measured as the proportion of subjects with a decrease of at least 20 percentage points in the percent of maximum threshold dosage, 30% and 11.4% of comparison and intervention group subjects, respectively, had experienced a decrease in utilization ($p<0.001$). However, when subjects were stratified as shown in Table 4.22, the proportions of intervention and study group subjects with a decrease in the level of use was nearly identical within each

stratum.

There were no significant differences between the two study groups with respect to the proportions of subjects with a decrease in the number of prescribers or pharmacies. Overall, 41 (11.9%) and 15 (12.0%) of subjects from the comparison and intervention groups, respectively, had a decrease in the number of pharmacies. The corresponding figures for the number of prescribers were 72 (20.9%) and 27 (21.6%).

Polypharmacy Program

During the follow-up period for the Polypharmacy subjects, 70 (38.9%) and 28 (15.5%) of subjects in the comparison and intervention groups, respectively, were re-identified by the PPRP. At baseline, the numbers of prescribers and pharmacies were similar for both study groups (Table 4.23). However, the baseline number of different drugs was significantly greater for the comparison group than the intervention group (Table 4.23).

Table 4.23: Polypharmacy Subjects who were Re-identified by the Patient Profile Release Program

Variable	Comparison Group (n = 70)	Intervention Group (n = 28)	p-value
Baseline Characteristics [median (range)]:			
Number of Different Drugs†	18 (16 - 31)	16 (16 - 19)	0.0001§
Number of Prescribers†	3 (1 - 9)	2 (1 - 7)	0.8427§
Number of Pharmacies†	1 (1 - 4)	1 (1 - 5)	0.2031§
Mean Change (±SD)‡ in:			
Number of Different Drugs ♮	+0.3 ± 4.4	+0.9 ± 2.0	0.3736¶
Number of Prescribers	-0.2 ± 1.0	+0.3 ± 1.7	0.1566¶
Number of Pharmacies	0.0 ± 0.7	0.0 ± 0.8	0.9647¶

♮ Estimates of the change in the number of different drugs were based on 65 and 26 subjects in the comparison and intervention groups, respectively.
§ Wilcoxon Rank Sum Test (two-sided p-value)
¶ Independent T-Test (two-sided p-value)
† In the 90 day period prior to the index identification
‡ SD = Standard Deviation

There were no significant differences between the two study groups with respect to the mean changes in the numbers of different drugs, prescribers or pharmacies among the subjects who were re-identified (Table 4.23). The lack of a significant difference between the two groups persisted when the data were stratified based on the number of different drugs at baseline (i.e. 16 versus ≥17 different drugs).

The proportions of subjects with decreases in the numbers of prescribers or pharmacies were nearly identical for the intervention and comparison groups, but this was not the case for the number of different drugs variable. Overall, 27 (41.5%) and 6 (23.1%) of comparison group and intervention group subjects, respectively, had a decrease of at least one in the number of different drugs. This apparently large difference between the two groups was of only borderline statistical significance (p=0.098) due to the relatively small number of subjects. The observed difference between the two groups was partly the result of confounding by the number of different drugs at baseline. Of the 65 comparison group subjects who were re-identified for Polypharmacy, 17 (26.2%) had 16 different drugs at the index identification and, therefore, could not have experienced a decrease in the number of different drugs and still have been re-identified. Of the remaining 48 (73.8%) comparison group subjects who were re-identified and had 17 or more different drugs at baseline, 27 (56.3%) had a decrease in the number of drugs. Of the 26 intervention group subjects who were re-identified for Polypharmacy, only 9 (34.6%) had 17 or more different drugs and, of these, 6 (66.7%) had a decrease in the number of different drugs. Thus, among subjects with 17 or more different drugs, there was no significant difference in the proportions of intervention and comparison group subjects with a decrease in the number of different drugs (p=0.72).

Polyprescriber Program

In the Polyprescriber component of the investigation, 15 (19.7%) comparison group subjects and 6 (3.9%) intervention group subjects were re-identified

by the PPRP during the follow-up period. Subjects in the comparison group had a significantly greater number of different prescribers at baseline, but there was no difference between the two study groups with respect to the number of pharmacies (Table 4.24)

Table 4.24: Polyprescriber Subjects who were Re-identified by the Patient Profile Release Program

Variable	Comparison Group (n = 15)	Intervention Group (n = 6)	p-value
Baseline Characteristics [median (range)]:			
Number of Prescribers†	8 (7 - 12)	7 (7 - 7)	0.0104§
Number of Pharmacies†	4 (1 - 8)	4 (1 - 6)	0.9371§
Mean Change (±SD)‡ in:			
Number of Prescribers ♮	-0.9 ± 1.4	+0.2 ± 0.8	0.1080¶
Number of Pharmacies	+0.1 ± 1.4	-0.2 ± 1.3	0.8848¶

♮ Estimates of the change in the number of prescribers were based on 13 and 5 subjects in the comparison and intervention groups, respectively.
§ Wilcoxon Rank Sum Test (two-sided p-value)
¶ Independent T-Test (two-sided p-value)
† In the 90 day period prior to the index identification
‡ SD = Standard Deviation

The difference in the average change in the number of prescribers for the two study groups was of borderline significance, but likely would have reached statistical significance had the number of subjects been larger (Table 4.24). The mean change in the number of pharmacies was similar for both study groups.

There was also no significant difference between the two groups with regard to the proportions of subjects with a decrease in the numbers of pharmacies: 1 (16.7%) and 5 (33.3%) of intervention and comparison groups had a decrease in the number of pharmacies (p=0.623). None of the intervention group subjects and 7 (53.8%) comparison group subjects had a decrease in the number of prescribers (p=0.101). It was not possible to do a stratified analysis to control for the confounding effects of the number of different prescribers because all intervention group subjects had 7 prescribers

at baseline. The small number of Polyprescriber subjects who were re-identified limits the conclusions that can be drawn about the impact of profile release on the secondary outcomes.

4.4 Patient Profile Release Program Long-term Follow-up

4.4.1 Study Subjects

The long-term follow-up phase of the investigation focussed on the 674 intervention group subjects who were included in the short-term follow-up analysis described above in Section 4.3. Three of these individuals were identified for exceeding the criteria for more than one component of the PPRP; these subjects were counted once for each set of criteria exceeded. Therefore, the study groups for the Extreme User, Polypharmacy and Polyprescriber Programs consisted of 342, 181 and 154 subjects, respectively.

Study subjects were followed from the date of their initial identification until the end of 1992. Actual lengths of follow-up for individual patients ranged from 98 to 268 days, depending on the date of the index identification. Re-identification was the outcome of interest. The probability of surviving (i.e. not being re-identified) throughout the follow-up period is shown in Figure 4.29. Because the ExU, PPh and PPr Programs focussed on different drug use problems, separate survival curves were prepared for patients identified under each program. These survival curves are based on data contained in the life tables presented in Appendix I.

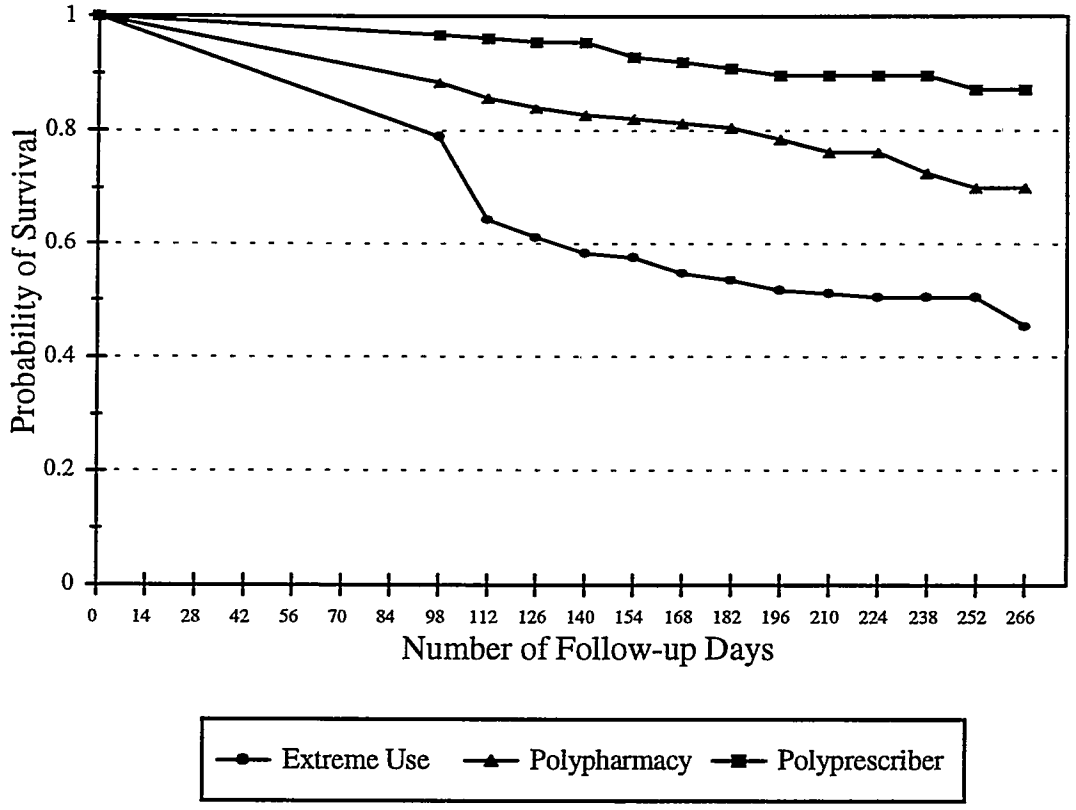

Figure 4.29: Survival Curves for Patients Identified Under the Extreme User, Polypharmacy and Polyprescriber Programs
("Survival" indicates not being identified.)

4.4.2 Extreme User Program

Re-identification of extreme users occurred most frequently during the short-term follow-up period — the 112 day period after the index identification (Figure 4.29). As noted above in Section 4.3.2, 36.5% of extreme users in the intervention group were re-identified by the end of the short-term follow-up period (Table 4.11). Analyses of the long-term follow-up data indicated that re-identification continued throughout the follow-up period, but at a reduced rate (Figure 4.29). The probability of ***not*** being re-

identified by the end of the 268 day follow-up period was 0.454 (95% CI =0.370, 0.538) (Appendix I). Therefore, if all intervention group patients had been followed for at least 268 days after the index identification, an estimated 54.6% of them would have been re-identified. These figures indicate that more than half of the extreme users for whom medication profiles were released exceeded PPRP criteria within 9 months after their profiles were sent to their physicians and pharmacies. This relatively high risk of re-identification after profile release is suggestive of a need for ongoing feedback.

4.4.3 Polypharmacy Program

Re-identification was less common for the Polypharmacy subjects than the extreme users. Approximately 15% of PPh subjects were re-identified during the short-term follow-up period, leaving approximately 85% of subjects who had not been re-identified within 3.5 months of their initial identification (Table 4.14; Figure 4.29). Re-identification during the long-term follow-up period took place at a relatively constant rate (Figure 4.29). The estimated probability of surviving to the end of the long-term follow-up period was 0.701 (95% CI = 0.607, 0.794) (Appendix I). Therefore, if all of the PPh subjects had been followed for the 9 month post-intervention period, an estimated 30% would have been re-identified for exceeding PPRP criteria again. As with the Extreme User Program, these findings are suggestive of a need for ongoing feedback to maintain improvements in drug use.

4.4.4 Polyprescriber Program

Throughout the follow-up period, re-identification was much less common for the Polyprescriber subjects than for the Extreme User or Polypharmacy subjects (Figure 4.29). Only 3.9% of PPr subjects were re-identified during the short-term follow-up phase. This figure rose to approximately 13% by the end of the 268 day follow-up period.

5.0 Discussion

The present investigation was conducted to study three aspects of drug use in the province of Saskatchewan. The initial phase of the study involved a description of the use of mood-modifying drugs and asthma medications in nearly the whole Saskatchewan population. The second phase focussed on individuals who were identified by the Patient Profile Release Program during 1992. The drug use patterns of these individuals indicated that they were at risk for drug-related problems resulting from extreme use, polypharmacy or the use of multiple prescribers. In the final phase of the investigation, follow-up data were analyzed to evaluate the short-term impact of the PPRP on patient drug use. This short-term follow-up study was supplemented with a descriptive analysis of longer-term re-identification rates.

5.1 Drug Utilization in Saskatchewan

5.1.1 Mood-Modifying Drugs

Drug utilization studies have described widespread use of sedatives and hypnotics in several countries (Rawson and D'Arcy 1991; van der Waals et al. 1993). Canada is no exception. In the 1978 Canada Health Survey, 6.1% of respondents aged 15 years or older reported using sedative or hypnotic agents in the previous 48 hours (Rawson and D'Arcy 1991). In the Health Promotion Survey of 1985, the overall rate of sedative-hypnotic use in the previous 12 months was 11.9% (Rawson and D'Arcy 1991).

The Anxiolytic, Sedative and Hypnotic Benzodiazepines (Formulary Class

28:24.08) were the most widely used mood-modifying drugs in Saskatchewan during 1992. Five percent of eligible beneficiaries received at least one prescription for these drugs. Narcotic analgesic agents were the next most frequently used mood-modifying drugs — nearly 4% of the population had at least one prescription for these medications. The miscellaneous anxiolytic, sedative and hypnotic agents were used by only 1.5% of the eligible population. Use of the barbiturates was infrequent during the study period.

It is difficult to compare the use of mood-modifying drugs in Saskatchewan with the results of other drug utilization studies due to differences in the source of drug use data, the drugs of interest, the units of measurement and the time periods studied. Nevertheless, the findings of previous investigations suggest that the use of mood-modifying drugs in Saskatchewan may be lower than in other regions of Canada (Blackburn et al. 1990; Rawson and D'Arcy 1991).

With the exception of phenobarbital, all of the mood-modifying drugs studied in the present investigation were used more extensively in females than males. The gender difference was greatest for the anxiolytic, sedative and hypnotic BZDs — the proportion of females using these drugs was 89% greater than the proportion of males. For the barbiturates, anticonvulsant BZDs and miscellaneous agents, user rates were approximately 50 to 75% greater for females than males. These findings echo the results of numerous drug utilization studies which have consistently shown that females are more likely to use sedatives and hypnotics than males (Rawson and D'Arcy 1991; Swartz et al. 1991; van der Waals et al. 1993). Interestingly, the average number of prescriptions claimed per user was similar for male and female beneficiaries for all of the drug groups. Therefore, although women were more likely than men to use mood-modifying drugs, they did not tend to use more of the drug (assuming that the average quantity of drug per prescription was similar for both sexes).

Anxiety and insomnia occur more commonly in women than men (Hayes and Kirkwood 1993; Kirkwood 1993). Therefore, gender differences in the distribution of these conditions may explain, to some extent, the increased use of anxiolytics, sedatives and hypnotics among women. It has also been suggested that a greater use of

health services by females may contribute to the increased use of psychotropic drugs among women (Swartz et al. 1991). In Saskatchewan, 93% of women saw a physician at least once in 1989-90 compared with 82% of men (Quinn et al. 1992a). However, even in studies which have controlled for gender differences in health service utilization, females were still more likely to use benzodiazepines than males, although the difference was less marked (Swartz et al. 1991; van der Waals et al. 1993). Other reasons put forth to explain the increased use of sedatives and hypnotics by women include differences in the perception of symptoms and assessment of severity by men and women, a greater willingness on the part of women to discuss symptoms and disease, and a possibility that the male-dominated medical community expects a greater proportion of females to require these medications (Rawson and D'Arcy 1991). The observation that men consume more alcohol than women has also led to the suggestion that females are more likely to use drugs whereas males are more likely to use alcohol in times of stress and anxiety (Rawson and D'Arcy 1991).

The use of mood-modifying drugs was most common among elderly individuals in Saskatchewan. For all of the drug groups studied, the proportion of the population using these drugs increased with age. Numerous other investigators have made similar observations (North et al. 1992; Rawson and D'Arcy 1991; Swartz et al. 1991; van der Waals et al. 1993). Nearly 15% of Saskatchewan beneficiaries 65 years of age or older had at least one prescription for an anxiolytic, sedative or hypnotic BZD agent in 1992; the sex-specific user rates were 18.2% and 10.3% for elderly females and males, respectively. These prevalence figures are consistent with several estimates of sedative-hypnotic use among elderly individuals living in European countries (van der Waals et al. 1993; North et al. 1992).

Many investigators have raised concerns about the widespread use of sedative-hypnotic agents in elderly individuals (Busto et al. 1989; Huston 1992; North et al. 1992; Swartz et al. 1991). Seniors may be more sensitive to the cognitive and psychomotor effects of benzodiazepines (Gudex 1991; Huston 1992; Shorr and Robin 1994). In addition, the use of long half-life benzodiazepines has been associated with an

increased risk of hip fracture in elderly patients (Ray et al. 1989). The drug utilization data for Saskatchewan are suggestive of a preferential use of short- or intermediate-acting agents in the elderly — 68.5% of benzodiazepine prescriptions claimed by non-seniors were for short-acting agents whereas short-acting agents accounted for 78% of the benzodiazepine prescriptions claimed by elderly patients. Nevertheless, long-acting agents still represented a substantial proportion of benzodiazepine prescriptions dispensed to elderly patients, placing these individuals at an increased risk for adverse effects. Furthermore, the finding that more than 18% of elderly females and 10% of elderly males in Saskatchewan received at least one prescription for a benzodiazepine raises questions about the appropriateness of the use of these agents in the province.

During 1992, the average number of prescriptions claimed by users of mood-modifying drugs ranged from a low of 2.0 prescriptions for narcotic analgesic users to a high of 5.6 prescriptions for phenobarbital users (Table 4.1). The relatively small number of prescriptions per user for the narcotic analgesics indicates that these drugs tended to be used on a short-term basis, a finding which is consistent with their indication for use as pain relievers. In contrast, the average rates of 4.6 to 5.6 prescriptions per year for benzodiazepine and barbiturate users indicate that these drugs tended to be used on a longer-term basis. Frequent long-term use of these agents has also been described elsewhere in Canada, the United States and Europe (Busto et al. 1989; Gudex 1991; Huston 1992; North et al. 1992; Shorr and Robin 1994; van der Waals et al. 1993). Given the problems of physical and psychological dependence associated with prolonged use of sedatives and hypnotics and the lack of evidence for the long-term effectiveness of these agents, the relatively high prescription per user rates observed in this investigation raise concerns about the appropriateness of the use of these agents in Saskatchewan.

Changes in the Use of Mood-Modifying Drugs Over Time

Prior drug utilization studies have shown that the overall use of mood-modifying drugs in Saskatchewan declined between 1977 and 1985 (Blackburn et al. 1990; Joint Committee on Drug Utilization 1984). This decrease in overall use was primarily attributable to a decline in the use of minor tranquilizers. The findings of the present investigation indicate that the use of mood-modifying drugs continued to decrease throughout the period 1989 to 1993 (Tables 4.2 and 4.3). The decline was greatest for the narcotic analgesics and the benzodiazepines. The prescription rates for the narcotic analgesics fell by 8.5% during the five year period; prescription rates for the anxiolytic, sedative and hypnotic BZDs declined by 15.3%. The observed decreases in prescription rates were attributable to a decline in the proportion of the population using these agents (Table 4.3). The average number of prescriptions claimed by each user remained relatively constant throughout the period.

The decline in overall benzodiazepine use was due primarily to a decrease in the use of the hypnotic BZDs (Figure 4.20). Use of the anxiolytic BZDs declined to a lesser extent. The decrease in hypnotic use largely reflected a drop in the use of triazolam. Use of this agent fell throughout the five year period, but the decrease was greatest from 1991 to 1992. Media attention surrounding the withdrawal of triazolam from the market in the United Kingdom in October 1991 (North et al. 1992) may have accelerated the decline in triazolam use in Saskatchewan during 1992.

It is unlikely that the decreased use of benzodiazepines reflects a decrease in the prevalence of insomnia or anxiety because a recent review of physicians claims data in Saskatchewan indicated that the overall prevalence of these conditions remained relatively constant between 1983 and 1991 (Joint Committee on Drug Utilization 1993). Instead, the decreased use of benzodiazepines may reflect an increased awareness of the potential problems associated with these agents, a possible shift to non-drug therapy, increased treatment of the underlying causes of anxiety and insomnia with other drugs or the use of non-Formulary or OTC agents (Joint Committee on Drug Utilization 1993).

Previous studies have documented a shift from long to short-acting benzodiazepines in Saskatchewan during the period 1977 to 1986 (Joint Committee on Drug Utilization 1983, 1993). This shift in utilization patterns continued between 1989 and 1993 (Figure 4.21). A similar observation was made by Busto and coworkers (1989) in their study of benzodiazepine use in Canada during the period 1978 to 1987. Wysowski and Baum (1991) also observed a shift from long to short-acting agents in the United States during the period 1978 to 1989. The rapidly-eliminated benzodiazepines have some advantages over the long-acting agents because they do not tend to accumulate in the body and, therefore, have a lower risk of adverse effects such as drowsiness and oversedation, especially in elderly individuals (Busto et al. 1989). However, it is important to recognize that the short-acting agents are not without risk — rebound insomnia and anxiety are more common with these agents (Joint Committee on Drug Utilization 1993). Furthermore, withdrawal reactions resulting from the abrupt discontinuation of benzodiazepines tends to be more frequent and severe with the rapidly-eliminated agents (Busto et al. 1989; Joint Committee on Drug Utilization 1993).

Overall, the decreased use of mood-modifying drugs and the shift from long to short-acting benzodiazepines may be considered positive trends. Unfortunately, the observation that the average number of prescriptions per user remained relatively constant throughout the five year period suggests that the frequent long-term use of anxiolytic, sedative and hypnotic agents has not decreased with time.

5.1.2 Asthma Drugs

Three types of asthma medications were monitored by the Extreme User Program during 1992: the β_2-agonist bronchodilators, inhaled corticosteroids and inhaled anticholinergic agents. In Saskatchewan, prescriptions for these drugs represented approximately 80% of all prescriptions dispensed for medications

commonly used to treat asthma. The methylxanthine bronchodilators and sodium cromoglycate, drugs which were not monitored by the PPRP, accounted for 12.4% and 7.1% of the prescriptions, respectively.

The overall utilization patterns of the β_2-agonist and inhaled corticosteroid drug groups largely reflect the use of salbutamol and beclomethasone dipropionate. These two drugs accounted for 95% and 93% of the prescriptions for the β_2-agonists and inhaled corticosteroids, respectively. During the study period, ipratropium bromide was the only inhaled anticholinergic agent listed in the Saskatchewan Formulary.

The β_2-agonists and inhaled corticosteroids are widely used in the treatment of asthma and COPD. In Saskatchewan, 3.7% of eligible beneficiaries received at least one prescription for salbutamol and 1.9% received at least one prescription for beclomethasone dipropionate during 1992. Ipratropium bromide was less widely used — only 0.3% of the eligible population received prescriptions for this agent. These figures are generally consistent with estimates of the prevalence of asthma and COPD in North American populations. In surveys of Saskatchewan residents, the prevalence of self-reported asthma was 6.4% among children (Dales et al. 1994) and 3.8% among adults (Senthilselvan et al. 1993). Elsewhere in Canada, estimates based on physician diagnostic claims and population-based surveys have placed the prevalence of asthma at approximately 2.5% of the population (Manfreda et al. 1989, 1993). In the United States, asthma has an estimated prevalence of 3 to 7% of the population (Dodge and Burrows 1980; Parker et al. 1989; Turkeltaub and Gergen 1991; Weiss and Speizer 1993). COPD has an estimated prevalence of approximately 1.5% to 2.5% of the population (Manfreda et al. 1989, 1993).

In Saskatchewan, the age-sex utilization patterns of salbutamol, beclomethasone dipropionate and ipratropium bromide reflect both the epidemiology of asthma and COPD and the respective roles of the three drug groups in the treatment of these diseases (Figures 4.12, 4.16 and 4.19). The prevalence of asthma is high in childhood, decreases in adolescence and young adulthood and then begins increasing again, peaking in middle or old age (Dodge and Burrows 1980; Manfreda et al. 1993;

Parker et al. 1989; Turkeltaub and Gergen 1991; Weiss and Speizer 1993). In contrast, the prevalence of COPD is low in children and increases dramatically with age (Higgens 1984; Lebowitz 1989; Stratton 1993). The β_2-agonists are useful in the treatment of both asthma and COPD. Among individuals less than 60 years of age, the age distribution of salbutamol use (Figure 4.12) largely reflects the age distribution of asthma. Beclomethasone dipropionate, which is indicated primarily for the treatment of asthma, has a similar utilization pattern (Figure 4.16). The increased use of both of these agents among individuals 60 years of age or older is a reflection of the increased prevalence of both asthma and COPD in this age group. In contrast, ipratropium bromide plays a less important role in the treatment of asthma, but it is a valuable bronchodilator in the management of COPD. The utilization pattern of this agent more closely reflects the age distribution of COPD (Figure 4.19).

The utilization patterns for salbutamol, beclomethasone dipropionate and ipratropium bromide were similar in terms of gender. For all three drugs, the user rates were greater for males than females among individuals aged less than 15 years; females predominated in the 15 to 59 year age range; and, use was much higher among males than females aged 60 years or older. These differences in the utilization patterns for males and females are consistent with the epidemiology of asthma and COPD (Manfreda et al. 1989, 1993; Weiss and Speizer 1993).

Patients using salbutamol received an average of 3.9 prescriptions per user during 1992. The corresponding prescription per user rates for ipratropium bromide and beclomethasone dipropionate were 4.9 and 3.0, respectively. For all three drugs, the average number of prescriptions claimed by each user increased with age. Among patients less than 40 years of age, the prescription per user rates for salbutamol, beclomethasone dipropionate and ipratropium bromide were 3.0, 2.3 and 1.9, respectively. These figures indicate that the drugs tended to be used on an intermittent basis in many younger patients. Intermittent use of the β_2-agonists and ipratropium bromide is consistent with the current guidelines for the management of asthma (Frew and Holgate 1993; Kelly and Hill 1993; McManus and Birkett 1993).

After 40 years of age, the average prescription per user rates increased for the bronchodilators, peaking at approximately 6 prescriptions per user in the elderly age groups (Figure 4.12 and 4.19). The tendency toward regular use of these agents among older beneficiaries may simply be a reflection of their use in the treatment of COPD, since regularly scheduled use of salbutamol and ipratropium bromide is appropriate for this condition (Canadian Thoracic Society Workshop Group 1992; Ferguson and Cherniack 1993). On the other hand, the high prescription per user rates may instead represent regular use of these agents among older asthmatics. In asthmatic patients, regular use of these agents is less desirable and may, in fact, be an indicator of poorly controlled asthma (Kelly and Hill 1993). Since the SPDP drug use statistics do not include information about the indication for therapy, it was not possible to determine the extent to which the relatively large numbers of prescriptions per patient in this age group represent appropriate treatment for COPD or potentially inappropriate treatment for asthma.

The relatively low prescription per user rates for the inhaled steroids, particularly among individuals less than 40 years of age, is troubling (Figure 4.16). In patients with moderate to severe asthma characterized by more than 1 or 2 episodes per week, prophylactic agents should be used on a regular basis to reduce inflammation of the airways and decrease bronchial hyperresponsiveness (Frew and Holgate 1993; Kelly and Hill 1993). However, the low prescription per user rates for the inhaled corticosteroids indicate that many of the patients using these agents were using them on an intermittent basis. This finding signals a need for further drug utilization studies to determine the appropriateness of inhaled steroid use in individual patients.

The utilization patterns of asthma medications have been studied in many other countries including the United Kingdom (Jones 1995; Roberts and Bateman 1994), Australia (McManus and Birkett 1993), the United States (Gerstman et al. 1989), the Scandinavian nations (Hallas and Hansen 1993; Klaukka et al. 1991; Larsson et al. 1993) and Hong Kong (Kumana et al. 1989). Differences in the source of drug utilization statistics, the unit of measurement, the age groups studied and the drugs

included in the analyses limit the direct comparisons that can be made about the drug use figures in different countries. Nevertheless, some general comparisons can be made.

Roberts and Bateman (1994) described the use of inhaled bronchodilators and inhaled corticosteroids in the United Kingdom during 1992-93. The age distributions for the users of these anti-asthmatic agents in the UK bore a striking similarity to the utilization patterns of salbutamol and beclomethasone dipropionate in Saskatchewan (Figures 4.12 and 4.16), both in terms of the proportion of the population using these drugs and the average number of items per patient.

Studies based on patient-specific drug use information in Denmark and the UK have shown that a substantial proportion of asthmatic patients using the β_2-agonists on a regular basis were not using concomitant prophylactic agents as is generally recommended in current prescribing guidelines (Hallas and Hansen 1993; Jones 1995). In Saskatchewan, 3.7% of eligible beneficiaries received prescriptions for salbutamol during 1992; only 1.9% and 0.7% received prescriptions for beclomethasone dipropionate and sodium cromoglycate, respectively, indicating that a considerable proportion of salbutamol users were not receiving concomitant prophylactic therapy. The use of β_2-agonists without prophylactic therapy is appropriate in asthmatic patients with infrequent attacks or episodes triggered only by exercise or in patients with COPD (Frew and Holgate 1993; Kelly and Hill 1993). However, regular use of the β_2-agonists in patients with asthma is generally considered to be an indication for the use of inhaled anti-inflammatory agents (Kelly and Hill 1993). The drug utilization statistics used in the present investigation were provided in aggregate form rather than on an individual patient basis. Therefore, it was not possible to determine the extent to which individual asthmatic patients were using β_2-agonists on a regular basis without prescriptions for inhaled steroids. Given the importance of the anti-inflammatory agents in the rational treatment of asthma, this is an issue that deserves further investigation.

Changes in the Use of Asthma Drugs Over Time

In Saskatchewan, the total number of prescriptions for the three monitored drug groups rose by 14% between 1989 and 1993, from 193.1 to 220.3 prescriptions per 1000 eligible beneficiaries. This increase in the overall prescription rate cannot be explained by changes in the age and sex composition of the eligible population because the age-sex distribution of the population changed only slightly during the five year study period (Saskatchewan Health 1989-1992, 1993a). Furthermore, the increased use of asthma medications by Saskatchewan beneficiaries is consistent with reports of increasing use in several other developed countries including the United States (Gerstman et al. 1989), Australia (McManus and Birkett 1993) and Scandinavia (Klaukka et al. 1991). This widespread increase in the use of anti-asthmatic agents may be a reflection of an increased prevalence or severity of asthma and COPD (Gerstman et al. 1989; Klaukka et al. 1991; Manfreda et al. 1993), more intensive treatment of a stable number of patients (Hallas and Hansen 1993) or an increased proportion of asthmatic and COPD patients that are being treated with these agents (Klaukka et al. 1991).

Changes in the utilization patterns for the individual asthma medications were generally consistent with recent changes in the approach to the management of this disease. Until recently, asthma was thought to be primarily a disease of airway constriction or bronchospasm (Kamada 1994; Kelly 1992). Accordingly, treatment strategies emphasized chronic bronchodilator therapy (Kelly 1992). However, research conducted over the past ten or fifteen years has highlighted the importance of inflammation in the pathogenesis of asthma. This better understanding of the pathophysiology of the disease has resulted in a shift in treatment strategies. Current guidelines emphasize the importance of using prophylactic agents to decrease inflammation of the airways and reduce bronchial hyperresponsiveness (Kamada 1994; Kelly 1992; McManus and Birkett 1993).

The proportion of the population using salbutamol increased from 3.0% in 1989 to 3.8% in 1993 (Table 4.3). However, the average number of prescriptions per

salbutamol user declined steadily throughout the study period from 4.7 to 3.5 prescriptions per user. Data provided by the SPDP indicated that the average number of units (e.g. tablets, inhalers) dispensed per prescription was similar in 1989 and 1993 for most salbutamol dosage forms. Therefore, these figures indicate that more individuals were using salbutamol, but that these patients were, on average, using less of the drug. This finding is consistent with a shift from regular to intermittent (as needed) use of the β_2-agonists, as recommended in the current prescribing guidelines.

The overall use of the inhaled corticosteroids increased steadily throughout the five year study period. The proportion of the population using beclomethasone dipropionate more than doubled between 1989 and 1993 (Table 4.3). The proportion of the population using budesonide rose by 20-fold during the five year period (Table 4.3). The dramatic increase in budesonide use was not surprising because this drug was first listed in the Saskatchewan Formulary in 1989. The increased use of inhaled steroids by a greater proportion of the population reflects an increased emphasis on treating the inflammatory component of asthma.

During the five year study period, the prescriptions per user rate for beclomethasone dipropionate fell by 26% from an average of 3.8 to 2.8 prescriptions per user. However, this decrease in the prescription per user rates was accompanied by a shift from low dose to high dose formulations. In 1989, the high dose formulations (250 µg/puff inhaler; 200 µg/dose aerosol capsules and disks) accounted for 17.6% of the prescriptions for this drug. By 1993, 47.1% of the prescriptions were for high dose formulations. Thus, a greater proportion of beclomethasone dipropionate users were receiving higher doses of the drug despite receiving fewer prescriptions per year.

Ipratropium bromide use increased throughout the five year period. This increase was apparent in all three measures of utilization — the prescription rate, user rates and the average number of prescriptions claimed per user. These findings indicate that a greater proportion of the population was using ipratropium bromide and that these patients were using more of the drug (in terms of the number of prescriptions).

In summary, the observed changes in the use of asthma medications reflect a

shift in treatment strategies which is consistent with the current guidelines for the management of asthma. Furthermore, the ratio of the number of users of beclomethasone dipropionate to number of users of salbutamol rose from 0.29 in 1989 to 0.58 in 1993, indicating that fewer patients were using β_2-agonists without concomitant prophylactic therapy.

5.2 Patient Profile Release Program

5.2.1 Characterization of Individuals Identified by the Program

The expanded, computerized version of Saskatchewan's Patient Profile Release Program was implemented on January 1, 1992. During the first year of operation, 2542 individuals were identified by the Program and met the criteria for inclusion in the present investigation (Table 4.5). All of these individuals had drug use patterns which indicated that they were at risk for drug-related problems resulting from the use of high dosages of selected drugs, multiple medications or prescriptions written by multiple providers.

The 2542 individuals included in the study represented only 0.3% of the beneficiaries eligible for coverage under the Saskatchewan Prescription Drug Plan. This relatively small figure does not necessarily indicate that extreme use, polypharmacy and the use of multiple prescribers is rare in Saskatchewan. Instead, the small proportion of eligible beneficiaries identified by the PPRP is a reflection of the high threshold criteria established by the JCDU; i.e., the Program identified only those individuals who received quantities of mood-modifying drugs or asthma medications which exceeded 200% of the maximum dosage criteria (Appendix A) or who received prescriptions for more than 15 different drugs or from more than 6 different prescribers in a 90 day period. The criteria for identification were set at these high levels in an effort to limit the number of patients identified by the Program because the SPDP had only limited

staffing resources to operate the PPRP. However, it is important to recognize that problems associated with high levels of drug use, polypharmacy and the use of multiple physicians may occur at levels well below the criteria set for the Program. Thus, the 2542 subjects included in this investigation represented the patients at greatest risk for these drug-related problems.

Most individuals identified by the PPRP exceeded Extreme User criteria (58.7%); 25.1% and 15.3% were identified under the Polypharmacy and Polyprescriber components of the Program, respectively. Subjects identified under each Program component differed from each other and from the general population of eligible beneficiaries in several respects.

5.2.1.1 Extreme User Program

During 1992, 1502 individuals were identified by the ExU Program. Of these, 85% exceeded the dosage criteria for the Minor Tranquilizer drug group (Figure 4.27). Therefore, the characteristics of the extreme user group as a whole largely reflect the characteristics of the minor tranquilizer extreme users.

Extreme users tended to be elderly. The median ages for extreme users of mood-modifying drugs and asthma medications were 74 years and 55 years, respectively (Table 4.8). Whereas seniors represented only 18.7% of active beneficiaries, they accounted for nearly 79% of the extreme users. The preponderance of elderly subjects is a reflection of both the types of drugs monitored by the ExU Program and the dosage criteria established for these drugs. The proportion of eligible beneficiaries using mood-modifying drugs increased with age (Figures 4.1, 4.3, 4.5, 4.7, 4.8, 4.10). The same was true for ipratropium bromide (Figure 4.19). For the bronchodilators and the inhaled steroids, the user rates peaked in children and in the elderly (Figure 4.12, 4.16). Thus, the relatively high rate of extreme use among elderly beneficiaries is attributable, in part, to the more widespread use of monitored drugs by older individuals.

Reflecting the skewed age distribution for the ExU group, nearly 5% of the elderly minor tranquilizer users were identified for extreme use in 1992 compared with only 0.5% of minor tranquilizer users aged less than 65 years (Table 4.9). This ten-fold difference in extreme user rates can be at least partly explained by the maximum dosage criteria established for the two age groups. Specifically, the dosage criteria for most of the minor tranquilizer drugs were set at lower levels for individuals 65 years of age or older (Appendix A). Thus, elderly beneficiaries using the same dosages of minor tranquilizers as younger individuals were more likely to be identified for extreme use. Elderly users of bronchodilators were also more likely to exceed extreme user criteria than younger individuals (Table 4.9). However, in this case, the dosage criteria were set at the same level for the two age groups.

The finding that nearly 5% of elderly minor tranquilizer users were identified by the ExU Program is an important one. These individuals received quantities of minor tranquilizers over a three month period which exceeded **twice** the maximum established dose for this age group. Thus, the absolute level of drug use in these individuals was high. For example, temazepam and triazolam were the two drugs most commonly involved in instances of extreme use. To be identified for extreme use of these drugs, elderly individuals had to receive quantities exceeding 30 mg/day for temazepam or 0.5 mg/day of triazolam. Given the increased potential for adverse effects in elderly individuals and the lack of evidence for the long-term effectiveness of these agents (Gudex 1991; Shorr and Robin 1994), a reduction in the dose or, ideally, discontinuation of the minor tranquilizer would be a desirable outcome for many of these patients.

Other demographic variables associated with identification by the ExU Program were gender and residence. Identification for extreme use was somewhat more common for women than men. Overall rates of extreme use (per 1000 active beneficiaries) were 2.4 for females and 2.0 for males. The predominance of females is not surprising because the use of the mood-modifying drugs (especially the minor tranquilizers) was more common among women than men. However, despite the more

widespread use of these medications among women, females users of the drugs were no more likely than male users to be identified for extreme use (Table 4.9). In fact, among elderly minor tranquilizer users, males were considerably more likely to exceed the extreme user criteria (5.3%) than females (4.2%). A notable exception was the non-benzodiazepine sedative-hypnotic drug group, for which female users were approximately 25% more likely than male users to be identified for extreme use.

When the analysis was confined to extreme users of asthma medications, there was a preponderance of male subjects (61.8%) (Table 4.8). This finding is the result of a combination of two factors: more common use of anti-asthmatic agents by males and an increased incidence of extreme use among male users of these drugs (Table 4.9). There are several possible reasons for the greater rate of extreme use among male patients. The increased rate of extreme use may simply reflect the increased prevalence of COPD among males and the need for regular administration of relatively high doses of the β_2-agonist and anticholinergic bronchodilators in some COPD patients (Canadian Thoracic Society Workshop Group 1992; Ferguson and Cherniack 1993). On the other hand, the preponderance of males in the group of asthma drug extreme users may indicate that asthma is less well controlled in males than females. Unfortunately, it was not possible to investigate these hypotheses due to the lack of diagnostic information in the SPDP prescription drug database.

The regional variation in rates of extreme use was interesting. After adjusting for age and sex differences in the four residence categories, the rate of extreme use (per 1000 eligible beneficiaries) was approximately 50% higher for residents of medium-sized cities than for subjects residing in large cities, small cities or rural areas (Figure 4.26). This finding was consistent with the results of a recent study of drug use in Saskatchewan (Quinn et al. 1992b). Quinn and colleagues (1992b) observed considerable regional variation in the use of some central nervous system medications. In particular, the use of anxiolytics and sedatives was higher in the cities of Swift Current and North Battleford than in the rest of the province. Thus, the increased rate of extreme use for residents of medium-sized cities likely reflects the greater use of

anxiolytic and sedative agents in Swift Current and North Battleford since both of these communities were included in this residence category (Table 3.3).

For the most part, extreme use was not the result of drug shopping on the part of individual patients. Approximately 85% of extreme users had prescriptions from only one or two physicians in the three months prior to identification. Similar findings were reported by Blackburn and coworkers (1990) in their examination of the first version of the Patient Profile Release Program in Saskatchewan and by Hlynka and colleagues (1981) in their evaluation of a similar program which focussed on barbiturate use in British Columbia.

Using the available drug utilization data, it was possible to estimate the rates of extreme use among users of the monitored drugs (Table 4.9). The overall rates of extreme use were fairly low: less than 1% of users of most of the monitored drug groups were identified for extreme use. The minor tranquilizer users had the highest rate of extreme use (2.1%). As previously noted, problems resulting from prolonged use of high dosages of the monitored medications can occur at levels well below the threshold levels for identification. Therefore, the relatively low rates of extreme use observed in the present investigation do not provide a good estimation of the extent to which Saskatchewan beneficiaries use mood-modifying drugs and asthma medications at potentially inappropriate dosages.

5.2.1.2 Polypharmacy Program

Polypharmacy is an important health problem because it is associated with an increased risk of adverse drug reactions, drug interactions and patient noncompliance (Colley and Lucas 1993; Klein et al. 1984; Stewart and Cooper 1994). The Polypharmacy component of the PPRP was designed to identify individuals who were at risk for drug-related problems resulting from the use of multiple medications. During 1992, the PPh Program identified 660 beneficiaries who had prescription claims for

more than 15 different drugs in a 90 day period. Because an increased risk of adverse drug reactions has been observed with much smaller numbers of drugs (Beers et al. 1989; Klein et al. 1984), the individuals identified by the PPh Program were at a particularly high risk of drug-related problems.

There was a disproportionate number of females and the elderly in the PPh group. Figure 4.24 clearly shows that the rate of identification by the PPh Program increased with age and was greater for women than men in most age groups. Nearly 68% of the PPh subjects were female; 60% were 65 years of age or older. These findings are consistent with the results of numerous drug utilization studies. Elderly individuals have consistently been shown to use more medications than younger persons (Dixon 1978; Murdoch 1980; Skoll et al. 1979; Tuominen 1988). Drug utilization studies in many countries have shown that elderly beneficiaries use from 3.1 to 7.9 medications at one time (Stewart and Cooper 1994). In Saskatchewan, nearly 81% of eligible beneficiaries over the age of 65 years received at least one prescription during 1989 whereas only 63% of younger beneficiaries received one or more prescriptions (Quinn et al. 1992a). In addition, these elderly patients received an average of 18.4 prescriptions per patient during the year compared with an average of 6.0 prescriptions for non-seniors (Quinn et al. 1992a). The increased use of drugs and increased incidence of polypharmacy with advancing age is not surprising since the prevalence of symptoms and diseases tends to increase with age (Colley and Lucas 1993; Stewart and Cooper 1994).

Drug utilization studies have also shown that females are more likely to use drugs than males and that they tend to use more drugs than males (Akoi et al. 1983; Chaiton et al. 1976). In Saskatchewan, 73% of females and only 59% of males received at least one prescription drug during 1989 (Quinn et al. 1992a). Furthermore, female patients received an average of 8.7 prescriptions during the year compared with 7.6 prescriptions for male patients. Thus, the preponderance of females in the PPh group was not surprising.

Another interesting, but not unexpected, finding was the large proportion of

PPh subjects with SAP–Plan 3 coverage. During the 1992-93 fiscal year, approximately 89% of active Saskatchewan beneficiaries had Regular coverage; approximately 11% had SAP coverage and were exempt from the deductible system. In contrast, only 53% of the PPh subjects had Regular coverage and nearly 33% had SAP–Plan 3 coverage. An important difference between Plan 3 coverage and other forms of SPDP coverage is that Plan 3 beneficiaries received all Formulary and most non-formulary drugs (including over-the-counter preparations) at no charge (Saskatchewan Health 1993b). In contrast, for beneficiaries with Regular, SAP–Plan 1 or SAP–Plan 2 coverage, only those drugs listed in the Saskatchewan Formulary or approved under the Exception Drug Status Program were eligible for coverage. With few exceptions, non-formulary drugs were not covered for these individuals. Therefore, because a broader range of drugs was included in the polypharmacy count for Plan 3 beneficiaries, it was easier for them to be identified by the PPh Program.

Finally, PPh subjects had a median of three different prescribers during the 90 day period prior to identification. The use of multiple prescribers by PPh patients may simply be a reflection of multiple symptoms and diseases which often result in polypharmacy. However, the use of multiple physicians who may not be aware of each other's prescriptions may also contribute to polypharmacy (Beers et al. 1989; Meyer et al. 1991). Therefore, the observed tendency toward the use of multiple prescribers by PPh subjects may also be contributing to their use of multiple medications. Thus, the PPRP may be especially useful in providing physicians with a more complete record of their patients' drug use, thereby facilitating the identification and resolution of medication problems such as drug interactions and therapeutic duplications.

5.2.1.3 Polyprescriber Program

The Polyprescriber component of the PPRP was designed to identify beneficiaries who received prescriptions from multiple different prescribers. During

1992, 403 individuals were identified for having 7 or more prescribers in a 90 day period.

Unlike the ExU and PPh Programs, identification rates for the PPr subjects varied only slightly with age. The identification rate for the PPr Program ranged from a low of 0.1 per 1000 active beneficiaries aged 5 to 14 years of age to a high of 1.0 per 1000 active beneficiaries aged 35 to 44 years.

Females were somewhat more likely than males to be identified for exceeding PPr criteria (Figure 4.25); however, the absolute difference in identification rates was not large (i.e. 0.5 and 0.7 per 1000 active beneficiaries for males and females, respectively). The slightly increased rate of identification by females may be related to observations that women are more likely to visit physicians than men (Quinn et al. 1992a) and that females tend to use more medications than males.

Interestingly, residents of large cities were 2 to 3.5 times more likely to be identified under the PPr Program than individuals from medium or small cities and rural areas (Figure 4.26). These differences were apparent even after adjusting for the differences in the age-sex distributions of the residence categories. This finding is likely a reflection of the increased access to a greater number and variety of doctors in large cities.

Another interesting finding was the large proportion of PPr subjects who had SAP coverage. SAP beneficiaries accounted for 40% of patients identified for exceeding PPr criteria. On average, SAP recipients may have poorer health than Regular beneficiaries due to their lower socioeconomic status. Therefore, these individuals may have an increased need for medical services. This may explain the increased likelihood of identification under the PPr Program for SAP beneficiaries.

By definition, PPr subjects had 7 or more prescribers in the 90 day period. As noted above, the use of multiple physicians who may not be aware of each other's prescriptions may result in the use of multiple different medications (Beers et al. 1989; Meyer et al. 1991), which in turn may result in a variety of drug-related problems such as adverse drug effects, drug interactions and noncompliance. The number of

prescribers used by PPr patients ranged from 7 to 12. Furthermore, these individuals tended to fill their prescriptions at a multiple pharmacies (median = 3). Therefore, it is highly unlikely that any one health care provider had a complete record of each patient's medication regimen. In this regard, the Profile Release Program may be particularly useful as a means of informing health care providers about drugs prescribed by other physicians. Physicians and pharmacists receiving medication profiles may then use the information to review and coordinate the patients' therapeutic regimens.

5.2.1.4 Summary

The descriptive phase of the present investigation provided some valuable insights into the types of individuals who were identified by the Patient Profile Release Program. In turn, this information may be used as a basis for designing educational initiatives to further reduce the incidence of drug-related problems associated with extreme use, polypharmacy and the use of multiple prescribers.

The relatively high rate of extreme use among elderly users of minor tranquilizers (approximately 5%) is an area of concern. As discussed in greater detail below, the release of patient medication profiles under the PPRP appeared to address this problem to some extent. Specifically, the Program appeared to reduce the risk of re-identification for the majority of extreme users, indicating that the dosages used by many of these individuals were reduced at least to levels below the threshold criteria. Additional interventions aimed at educating physicians about the importance of using reduced benzodiazepine dosages in elderly beneficiaries may also be warranted. The finding that the vast majority of cases of extreme use occurred in patients who had only one or two prescribers is also suggestive of a need for physician education about the potential dangers of high dosages of the monitored drugs.

The observation that patients from medium-sized cities had an increased rate of extreme use was an interesting and potentially important finding. Further

investigation should be conducted to determine whether the regional variation can be explained by differences in the distribution or severity of disease. If certain prescribing practices are found to be less appropriate in the medium-sized cities than in other regions, educational initiatives should be implemented to address the problems.

The finding that polypharmacy occurred with increased frequency among the elderly, especially among female elderly beneficiaries, is consistent with the results of other drug utilization studies. Although the age-sex pattern of polypharmacy was not surprising, the findings do point to a need for increased vigilance on the part of health care providers to reduce the incidence of polypharmacy and its associated problems. This is particularly true for elderly beneficiaries, who represented 60% of the instances of polypharmacy.

Finally, the observation that most polypharmacy subjects filled their prescriptions at multiple pharmacies highlights the need for increased patient education about the benefits of using a single pharmacy. Some patients have a justifiable need for more than one physician. However, by filling prescriptions at one pharmacy, these patients may reduce the likelihood of undesirable drug effects because the pharmacist can work with the physicians to monitor drug use.

5.2.2 Impact of the Patient Profile Release Program

An important objective of the present investigation was to estimate the impact of the Patient Profile Release Program on outpatient prescription drug use. This was accomplished by following intervention and comparison groups for a three and a half month period. Both study groups consisted of individuals who were identified as exceeding PPRP criteria during 1992. Medication profiles for subjects in the intervention group were sent to their physicians and pharmacies shortly after they were identified by the Program. Profile release for individuals in the comparison group was delayed for at least two months after the index identification. Thus, for short-term

outcomes, the comparison group provided a means of approximating the outcome rates that would have been expected if no profiles had been released.

5.2.2.1 Effect of Profile Release on Re-identification

The PPRP was designed in an effort to encourage rational drug use by helping physicians and pharmacists monitor their patients. The Program identified individuals with an increased risk of drug-related problems and communicated these concerns to the physicians and pharmacies responsible for their care. The patient medication profiles were designed to prompt health care providers to review the patients' drug use and modify their medication regimens where appropriate. Because the PPRP criteria were high, an appropriate response to the intervention for most patients identified under the Extreme User, Polypharmacy or Polyprescriber Programs would have been to decrease the level of use of mood-modifying or asthma medications, reduce the number of different drugs or decrease the number of prescribers, respectively. Reductions to levels below the threshold criteria would have prevented patients from being re-identified by the PPRP.

A simple comparison of the re-identification rates for the intervention and comparison groups suggests that profile release was, indeed, associated with a lower risk of re-identification. For the Extreme User Program, 56.8% of the comparison group subjects and only 36.5% of the intervention group subjects were re-identified during the follow-up period (Table 4.11). The corresponding figures for the comparison and intervention groups were 38.9% and 15.5%, respectively, for the Polypharmacy Program (Table 4.14) and 19.7% and 3.9%, respectively, for the Polyprescriber Program (Table 4.17). For each of the three programs, the differences in the re-identification rates for the intervention and comparison groups were statistically significant ($p<0.001$).

For the Polypharmacy and Polyprescriber Programs, the results of the multivariate logistic regression analysis confirmed the findings of this simple

comparative analysis. Among Polypharmacy patients, the intervention group subjects were approximately one-third as likely to be re-identified during the follow-up period as their counterparts in the comparison group [OR (95% CI) = 0.37 (0.21, 0.67)]. As previously noted, the OR derived from the logistic regression analysis provided an estimate of the association between intervention group status and the outcome variable after controlling for the effects of the other variables in the model. Therefore, the observed negative association between profile release and re-identification could not be explained by differences between the two study groups with respect to any of the other variables in the logistic model, including gender, coverage type, residence, the number of different drugs or hospitalization status. Three additional variables — age, the number of pharmacies and the number of prescribers — were excluded from the model because they neither predicted the outcome nor confounded the relationship between study group status and re-identification. Thus, the relationship between profile release and re-identification also cannot be explained by these factors.

For the Polyprescriber Program, the intervention group subjects were one-sixth as likely to be re-identified as comparison group subjects [OR (95% CI) = 0.16 (0.05, 0.54)]. As with the Polypharmacy Program, the negative association between profile release and re-identification could not be explained by differences between the study groups with respect to the variables included in the model (i.e. coverage, residence, number of prescribers and hospitalization) or the variables excluded from the model due to a lack of predictive power and the absence of confounding (i.e. age, gender and number of pharmacies).

The relationship between profile release and re-identification was less straightforward for the Extreme User Program. Among individuals with a baseline level of extreme use ranging from 200% to 219% of the maximum dosage criteria, profile release had no apparent effect on the risk of re-identification, as evidenced by the odds ratio of 0.79 with a 95% confidence interval (0.45, 1.38) which crossed the null value of one. However, among patients with a baseline level of extreme use of 220% or more, the intervention was associated with a significantly decreased risk of re-identification

[OR (95% CI) = 0.40 (0.28, 0.55)]. Sixty-five percent of the intervention group subjects fell into this category. Interestingly, the magnitude of the association between profile release and re-identification was similar to that observed for the Polypharmacy Program. Again, the observed association could not be explained by either the variables included in the model (i.e. level of extreme use, hospitalization during the follow-up period and drug group exceeded) or the study variables excluded from the model (i.e. age, sex, residence, coverage type and the number of pharmacies or prescribers).

The apparent lack of an association between profile release and re-identification among extreme users whose baseline level of use was at the lower end of the scale (i.e. 200 to 219%) merits further comment. It is important to remember that the apparent dosages calculated by the ExU Program were estimates of actual drug consumption. Depending on the timing of prescription fills, these estimates may have been higher or lower than the actual levels of drug use. Therefore, the estimates of patient drug use likely fluctuated around the true dosage. For patients whose actual level of use was approximately 200% of the maximum dosage criteria, minor fluctuations in prescription claims may have resulted in identification for extreme use, and further fluctuations during the follow-up period may have prevented re-identification. Therefore, even if profile release resulted in post-identification levels of drug use which were lower in the intervention group than in the comparison group, this difference may not have been reflected in the re-identification rates for the two study groups.

Overall, these results indicate that intervention group status was associated with a significant reduction in the short-term risk of re-identification for most individuals. These findings are consistent with the hypothesis that the release of patient medication profiles reduces the likelihood of re-identification by the Program, presumably by prompting health care providers to review and modify their patients' medication regimens appropriately. However, there are several alternate explanations for these findings.

This study was designed to investigate the effects of a program which was already operating at the time the study began. Therefore, it was not possible to

randomize subjects into intervention and comparison groups, thereby ensuring a high degree of comparability of the study groups. Using multivariate regression techniques and the information available in the PPRP data files, it was possible to control for the effects of the various demographic variables (i.e. age, sex, residence and type of SPDP coverage) as well as the numbers of pharmacies or physicians in the 90 day period prior to the index identification, hospitalization during the follow-up period, the number of different drugs (for PPh subjects), the level of extreme use and the drug group exceeded (for ExU subjects). However, the study groups may have differed with respect to other potentially important variables which, in turn, may have confounded the association between profile release and re-identification.

Firstly, the data files used for this investigation contained only limited sociodemographic information and no clinical data such as the diagnosis, severity of illness and possible reasons for the subjects' extreme patterns of drug use. If the study groups differed with respect to these factors, then the apparent association between study group status and re-identification may, in fact, have been a reflection of these differences rather than an indicator that profile release influenced the outcome. Because the intervention and comparison groups for each program component were similar in many respects including age and sex, two factors correlated with the distribution of many diseases (Tables 4.11, 4.14 and 4.17), it is unlikely that the groups differed significantly in the distribution of disease or the severity of illness. Nevertheless, this possibility cannot be dismissed and the lack of clinical information is clearly a limitation of this investigation.

Secondly, the subjects in the intervention and comparison groups were identified at different times in relation to the implementation of the Program. Specifically, subjects included in the intervention group were first identified by the PPRP between April 7 and September 8, 1992. Because these individuals were not identified when the Program was first implemented, the extreme drug use patterns resulting in their index identifications may be regarded as either recent or intermittent phenomena. In contrast, the comparison group subjects were identified during January

1992, the first month of operation of the PPRP. It is possible that the drug use patterns for these individuals were at levels exceeding PPRP criteria for many months before the implementation of the Program. If this was the case, then the comparison group subjects may have been less likely to fall below the threshold criteria for re-identification during the follow-up period. This would tend to overestimate the apparent effectiveness of the PPRP. Unfortunately, it was not possible to confirm or refute this possibility because records of patient drug use prior to their contact with the PPRP were not included in the PPRP database (i.e., the data files on which this investigation was based). However, it was possible to control for the effects of the level of extreme use, the number of different drugs and the number of different prescribers for the Extreme User, Polypharmacy and Polyprescriber subjects, respectively. Since individuals who exceeded PPRP criteria for longer periods of time may have had higher baseline levels of extreme use or larger numbers of different drugs or prescribers, controlling for the effects of these variables may have controlled to some extent for potential differences prior drug use patterns.

Finally, the intervention and comparison groups were followed during different calendar periods. Therefore, the comparison group may not have provided sufficient control for some non-intervention factors which may influence drug utilization patterns over time. Nevertheless, the consistency of the intervention effect for all three components of the Program, each of which focussed on different prescribing problems, provides a measure of confidence that the observed associations between profile release and re-identification were not simply manifestations of a single temporal factor. For example, a widely cited article demonstrating an association between the regular use of inhaled β_2-agonists and an increased risk of death or near death among Saskatchewan beneficiaries was first published in February 1992 (Spitzer et al. 1992). Given its timing, this article may have influenced the re-identification rates for asthma drug users in the intervention group to a greater extent than in the comparison group, thereby confounding the association between profile release and re-identification for these patients. However, the publication of this article would not be expected to influence the

outcomes of extreme users of mood-modifying drugs or those individuals identified under the PPh or PPr Programs.

One factor which could have influenced the results for all three Program components was the increase in the deductible level in May 1992 (Table 3.1). To investigate this possibility, supplementary logistic regression analyses were conducted using only those subjects who had SAP coverage. These SAP beneficiaries were exempt from the deductible system and, therefore, should not have been affected by the changes in the deductible level. For all three Program components, intervention group status continued to be associated with a highly significant reduction in the likelihood of re-identification. These findings suggest that the observed associations between profile release and re-identification were not simply reflections of the change in the deductible level.

Thus, although the findings of the present investigation are subject to some limitations, they do provide reasonably good evidence that profile release under the PPRP significantly reduced the risk of re-identification by the Program. This finding is positive because it indicates that patients' short term drug utilization patterns decreased at least to levels below the threshold criteria. Furthermore, because the investigation focussed only on prescription drug use, these changes in patient drug use reflect a change in physician prescribing practices.

In the final phase of the investigation, intervention group subjects were followed for up to 9 months after their initial identification. The results of these analyses indicated that re-identification of some subjects continued throughout the follow-up period. Although the probability of re-identification during the entire follow-up period was only 13% for PPr subjects, nearly 55% of ExU and 30% of PPh subjects were re-identified by the end of the 9 month post-intervention period. These findings highlight the importance of ongoing feedback in maintaining the improvements in physicians' prescribing practices and patient drug use patterns.

5.2.2.2 Effect of Non-Intervention Variables on Re-identification

Using multivariate analytic techniques, it was possible to estimate not only the impact of the intervention on re-identification, but also the effects of other variables on this outcome of interest. Various demographic factors — age, sex, residence and type of SPDP coverage — were included in the analysis. Other study variables included the number of prescribers and pharmacies in the 90 day period prior to the index identification, the time spent in hospital during the follow-up period, the number of different drugs, the level of extreme use and the drug group exceeded. The effect of each of these variables on re-identification varied for the three components of the PPRP.

As previously noted, patient age was clearly associated with the likelihood of ***initial*** identification under the Extreme User and Polypharmacy Programs (Figures 4.23 and 4.24). However, follow-up analyses indicated that age had no impact on the risk of ***re-identification*** during the 112 day post-intervention period. This was true for all three components of the Program. Thus, once identified by the ExU, PPh or PPr Programs, the likelihood being re-identified did not vary with age.

Like age, gender was not associated with re-identification for the ExU and PPr subjects. In contrast, female Polypharmacy subjects were twice as likely to be re-identified as their male counterparts. Given the lack of clinical information for the study subjects, possible reasons for this interesting finding can only be speculated upon. It is possible that gender differences in the distribution of disease may have resulted in greater difficulty changing the medication regimens of female subjects. However, an examination of the drug use patterns for male and female Polypharmacy subjects indicates that this is an unlikely explanation because 15 of the top 20 drugs were identical for males and females. This similarity in drug use patterns suggests that the male and female PPh subjects had a similar distribution of disease. Other possible explanations for the findings are that physicians may have been less inclined to change the medication regimens of female patients or that women were more resistant to their physicians suggestions for medication changes.

The other demographic variables — residence and coverage type — also had an inconsistent effect on re-identification. Residence was dichotomized as large/medium- sized cities versus small cities/rural (Table 3.3). Neither residence category had an excess risk of re-identification for the ExU subjects. However, among Polyprescriber subjects, there was a non-significant trend toward an increased risk of re-identification for individuals from small cities or rural areas (p=0.078) (Table 4.20). An opposite effect was observed in the Polypharmacy group: subjects with residence codes in the category of large/medium-sized cities were twice as likely to be re-identified by the PPRP as their counterparts residing in small cities or rural areas (p=0.014). Possible reasons for the differing effects of residence are unclear.

Coverage type had no significant effect on the likelihood of re-identification for the ExU and PPr subjects. However, coverage was a significant predictor of re-identification for the Polypharmacy Program. PPh subjects with SAP–Plan 2 coverage were five times more likely to be re-identified than individuals with Regular or SAP–Plan 1 coverage [OR (95% CI) = 5.01 (1.90, 13.23)]. As noted in Section 3.2.2, Plan 2 coverage was provided to Saskatchewan Assistance Plan recipients who required several prescription medications on a regular long-term basis (Saskatchewan Health 1993b). Because all PPh subjects had prescription claims for at least 16 different drugs in a 90 day period, the criterion of multiple regular medications for Plan 2 coverage does not distinguish these individuals from the other PPh subjects and, therefore, does not explain the observed increase in the risk of re-identification. However, the fact that Plan 2 patients received prescriptions for Formulary drugs free of charge while Regular and Plan 1 beneficiaries paid at least a nominal fee for each prescription may have contributed to the apparent higher risk of re-identification for Plan 2 subjects.

Polypharmacy subjects with SAP–Plan 3 coverage were 77% more likely to be re-identified than individuals with Regular or SAP–Plan 1 coverage [OR (95% CI) =1.77 (1.00, 3.15)]. The lower limit of the confidence interval indicates that the apparent increase in risk for Plan 3 beneficiaries was of borderline statistical significance. Although the statistical significance of the association was questionable,

the finding of a moderately increased risk of re-identification for Plan 3 beneficiaries compared with Regular/Plan 1 beneficiaries is reasonable from a practical point of view. As previously noted, Plan 3 coverage was available to wards of the province and to residents receiving supplemental income assistance and living in approved homes licensed under *The Housing and Special-Care Homes Act* or *The Mental Health Act* (Saskatchewan Health 1993b). Since many Plan 3 beneficiaries live in special care homes, medication decisions for these individuals may have been influenced not only by the physician, patient and pharmacist, but also by nursing staff. This may have increased the difficulty with which medication regimens could be changed. In addition, the scope of medications eligible for SPDP coverage differed for Plan 3 and Regular/Plan 1 beneficiaries. Most non-formulary prescription and over-the-counter (OTC) drugs were covered for Plan 3 beneficiaries but were not covered for individuals with Regular or Plan 1 coverage. If OTC drugs were re-ordered more freely than prescription drugs, then Plan 3 beneficiaries would have been more easily re-identified than Regular/Plan 1 beneficiaries.

Among the Extreme User and Polypharmacy subjects, neither the number of prescribers nor the number of pharmacies in the 90 day period prior to the index identification had any impact on the likelihood of re-identification. Initially, this finding was surprising. Re-identification was expected to be more common among patients who had multiple physicians and pharmacies because it is unlikely that any one health care provider had a complete list of their medication regimens. This was not the case. An examination of some simple descriptive statistics helps to explain this unexpected finding. Approximately 85% of the extreme users had only one or two prescribers and 93% had only one or two pharmacies at the time that they were identified. For Polypharmacy subjects, 51% had only one or two prescribers and 83% had only one or two pharmacies. The very fact that these individuals were identified by the ExU and PPh Programs indicates that their patterns of drug use were not simply caused by multiple prescribers who were unaware of each other's prescriptions. In light of this observation, it should not be surprising that the use of multiple pharmacies and

physicians was not an important predictor of re-identification for ExU and PPh subjects.

For all three components of the PPRP, hospitalization during the follow-up period influenced the likelihood of re-identification by the Program. Among the extreme users, hospitalization for one or more days during the follow-up period was associated with a significantly decreased risk of re-identification. This effect was greater for patients whose levels of extreme use were less than 220% of the maximum dosage criteria [OR (95% CI) = 0.13 (0.04, 0.67)] than for patients with levels of use exceeding 220% [OR (95% CI) = 0.55 (0.38, 0.79)]. This negative association was anticipated because medications administered in hospital were not recorded in the SPDP database and, therefore, were not captured by the PPRP. In addition, hospitalized individuals may not have renewed their outpatient prescriptions during their stay in hospital, further decreasing the likelihood of re-identification. As noted in Section 4.3.2, the smaller effect of hospitalization on re-identification for extreme users with "high" levels of use (≥220%) is consistent with this explanation. For individuals whose baseline level of extreme use was just slightly above the threshold level, even a small disruption in the apparent dosage calculation during the follow-up period may have been sufficient to avoid re-identification. However, for subjects with "high" levels of extreme use, hospitalization would have to produce a much larger disruption in the apparent dosage calculation if it were to influence re-identification.

Hospitalization had an opposite effect on re-identification for Polypharmacy and Polyprescriber subjects. For the PPh Program, patients who were hospitalized for 1 to 4 days during follow-up had a similar risk of re-identification as those who were not hospitalized. However, hospitalization for 5 or more days was associated with a significantly greater risk of re-identification [OR (95% CI) = 2.54 (1.39, 4.64)] (Table 4.16). If PPh patients who were hospitalized for 5 or more days were sicker than subjects with no admissions or only short hospitalizations, then discontinuation of medications in these sicker, hospitalized patients may have been more difficult than in their healthier counterparts, resulting a greater risk of re-identification. Furthermore, the initiation of new medications which often occurs during hospitalization may have

contributed to the increased rates of re-identification for PPh subjects. In a study of the effect of acute hospitalization on the use of medications by elderly patients, Beers and colleagues (1989) found that 40% of all admission medications were discontinued by discharge and 45% of all discharge medications were newly started during hospitalization. Assuming that hospitalization has a similar effect on Saskatchewan beneficiaries, the number of drugs used by hospitalized PPh subjects would remain high because medications claimed before and after hospitalization would be included in the count of the different drugs.

For the Polyprescriber Program, hospitalization for 1 or more days during the follow-up period was associated with a significantly greater risk of re-identification [OR (95% CI) = 6.40 (2.12, 19.3)] (Table 4.20). A possible explanation for this finding is that individuals who were hospitalized may have had more extensive or severe medical problems than those who were not hospitalized. Therefore, these individuals may have had a legitimate need for multiple prescribers. Another factor which may have contributed to the observed association is that patients may begin seeing new physicians while in hospital. Outpatient prescriptions ordered by these additional physicians would be included in the polyprescriber count, increasing the likelihood of re-identification by the PPRP.

For all three programs, the likelihood of re-identification was associated with the baseline levels of criteria exceeded by the study subjects. Among extreme users, the level of drug use recorded at the index identification was a highly significant predictor of re-identification. The interaction of this variable with both hospitalization and study group status necessitated the calculation of four odds ratios (Table 4.13). In all but one of the four strata, subjects with "high" levels of extreme use (i.e. ≥220%) had a significantly greater risk of re-identification than subjects with "low" levels of extreme use (i.e. 200-219%). In the fourth stratum, which consisted of non-hospitalized intervention group subjects, there was a non-significant trend toward an increased risk for subjects with high levels of extreme use. As noted Section 4.3.2, a general association in this direction was expected because the magnitude of change required to

prevent re-identification by the ExU Program was related to the level of extreme use during the pre-identification period. In a similar manner, the numbers of different prescribers and drugs in the 90 day period prior to the index identification were important predictors of re-identification for the Polyprescriber and Polypharmacy subjects, respectively.

Finally, the drug group exceeded by extreme users was also a significant predictor of re-identification in the multivariate model. The OR (95% CI) for extreme users of mood-modifying drugs was 0.41 (0.25, 0.68). Thus, subjects who exceeded dosage criteria for mood-modifying drugs were nearly 60% less likely than asthma drug extreme users to be re-identified during the follow-up period. The higher risk of re-identification observed for asthma drug extreme users relative to the mood-modifying group may be a reflection of the difficulty in managing poorly controlled asthmatics with high medication requirements. However, this finding may also be an artifact of the PPRP dosage calculation because asthma drug dosages were calculated over a 180 day period while mood-modifying drug dosages were calculated over a 90 day period. Therefore, changes made to asthma drug regimens during the 112 day follow-up period would have been "diluted" by the inclusion of approximately 2.5 months of pre-identification drug use in the apparent dosage calculations.

5.2.2.3 Effect of Profile Release on Secondary Outcomes

To a certain extent, re-identification by the PPRP is an insensitive marker of changes in patient drug utilization. For example, even if the level of extreme use of an intervention group patient fell from 300% at baseline to 210% during the follow-up period, this patient would still be re-identified. Therefore, focussing solely on re-identification as the outcome of interest may fail to identify some changes in patient drug use which are clinically important, but which are not sufficient to prevent re-identification. To address this limitation, patients who were re-identified during the

follow-up period were subjected to a supplementary analysis of four secondary outcomes. These outcomes of interest included changes in the level of extreme use, the number of different drugs and the numbers of prescribers and pharmacies.

It was hypothesized that profile release under the PPRP may lead to reductions in one or more of these variables. Analyses of the follow-up data indicated that this was not the case. For all three components of the PPRP, there were no important differences between the intervention and comparison groups with respect to the proportion of re-identified patients who experienced a decrease in the number of different pharmacies or prescribers, the number of different drugs (for the PPh Program) or the level of extreme use (for the ExU Program). Interestingly, for ExU subjects who were re-identified, the average level of use actually increased for the intervention group compared with an overall decrease in the comparison group. This difference was only partly explained by differences between the two groups with respect to the baseline level of extreme use (Table 4.22).

5.2.3 Comparison with Other Interventions Designed to Promote Rational Prescribing

Saskatchewan's Patient Profile Release Program is one of many intervention programs designed to influence physicians' prescribing decisions and improve patient drug use. Like other programs implemented elsewhere in Canada (Hlynka et al. 1981) and the United States (Groves 1985; Guo et al. 1995; Holm and Helgeland 1993; LeGrady 1992; Sandusky 1993), Saskatchewan's PPRP uses patient-specific feedback to communicate concerns about potential drug use problems in individual patients to the physicians and pharmacists responsible for their care.

As discussed in Chapter 2, evidence from several small-scale controlled trials indicates that certain forms of patient-specific feedback may produce modest improvements in physicians' prescribing practices and patients' drug use patterns

(Britton and Lurvey 1991; Kroenke and Pinholt 1990; Meyer et al. 1991; Tamai et al. 1987; Tierney et al. 1986). However, the generalizability of these findings to the large-scale DUR programs such as Saskatchewan's PPRP is questionable because the controlled trials differed from the DUR programs in terms of the source and format of the feedback, the practice setting, the method of delivery of the feedback (i.e. verbal versus written) and the use of specific recommendations for prescribing changes.

Improved prescribing practices or reduced prescribing costs have been reported after the implementation of some patient-specific DUR programs (Blackburn et al. 1990; Groves 1985; Hlynka et al. 1981; Holm and Helgeland 1993; LeGrady 1992). Unfortunately, the uncontrolled nature of these studies limits the conclusions that may be drawn about the degree to which the DUR programs were responsible for the observed prescribing changes. There is remarkably little objective evidence from well-controlled studies which indicates that these programs effectively influence physician prescribing practices and improve patient drug use (Lipton and Bird 1993; Soumerai and Lipton 1994). The findings of the present investigation address this knowledge gap to some extent. This study provided reasonably good evidence that the release of patient medication profiles under Saskatchewan's PPRP reduced the short-term risk of re-identification by the Program. As previously noted, this reduction in re-identification rates indicates that patient drug utilization patterns decreased at least to the extent that they no longer exceeded Program criteria. Since the study focussed only on prescription drug use, the results provide an indirect estimate of changes in physicians' prescribing practices.

As noted in Chapter 2, several other types of educational interventions have shown promise as strategies for influencing physician prescribing practices. Prescriber-specific feedback effectively increased generic prescribing in several studies (Frazier et al. 1991; Gehlbach et al. 1984; Harris et al. 1985). This type of feedback may also reduce prescribing costs (Frazier et al. 1991; Harris et al. 1985; Hershey et al. 1986); however, further studies will be needed to confirm this effect because the observed cost reductions were modest and of borderline statistical significance.

Presently, it is unclear whether prescriber-specific feedback influences the quality of prescribing — some studies reported improvements in prescribing practices (Manning et al. 1986; North of England Study of Standards and Performance in General Practice 1992; Putnam and Curry 1985; Rokstad et al. 1995); others reported no change (Holm 1990; Lassen and Kristensen 1992). Many factors, including differences in the format of the feedback, the target drugs, the selection of participants, the methods of data collection and the length of follow-up may have contributed to these disparate results. There is a clear need for further investigation of the impact of prescriber-specific feedback on the quality of prescribing. If the findings reported Manning et al. (1986) and Rokstad et al. (1995) are confirmed, this type of intervention may represent an effective strategy for dealing with a variety of prescribing problems.

Reminder systems have been shown to reduce prescribing problems resulting from physician oversight (Barnett et al. 1978; Barnett et al. 1983; McDonald 1976a, 1976b; McDonald et al. 1980; McDonald et al. 1984; Tierney et al. 1986). However, studies indicate that reminders have little or no educational effect in the sense that the improvements in physicians' practices do not persist after the reminders are discontinued (Barnett et al. 1978; McDonald 1976b; McDonald et al. 1980). Furthermore, reminders do not appear to influence physicians' use of clinical practices that they are not already predisposed to do. Nevertheless, reminders are effective for the purpose for which they were designed — they help to eliminate oversights in medical practice and thereby help physicians to act on their intentions.

Group education strategies are widely used in efforts to improve physician knowledge and practices. Several studies have shown that highly-focussed group education programs which specifically target the learning needs of the participants can be effective in improving the quality of prescribing or the general management of disease (Gutierrez et al. 1994; Inui et al. 1976; Jennett et al. 1988; Klein et al. 1981). However, the evidence for the effectiveness of less focussed group education programs is much less convincing (Friis et al. 1991; Rutz et al. 1990). The findings reported by Jennett et al. (1988) and Gutierrez et al. (1994) suggest that the positive effects of

targeted education programs may persist for at least 12 to 18 months. Further studies will be needed to clarify various issues relating to the duration of the prescribing improvements, the need for and optimal frequency of ongoing contact with the participating physicians and the scope of prescribing problems amenable to group education strategies.

Finally, face-to-face education of prescribers has been successful in addressing a variety of prescribing problems including the use of expensive agents for which there are less costly alternatives, the use of ineffective or marginally effective agents, the use of drugs for inappropriate indications and the use of drugs in a potentially unsafe manner (Avorn and Soumerai 1983; McConnell et al. 1982; Newton-Syms et al. 1992; Peterson and Sugden 1995; Schaffner et al. 1983). The results of some studies indicate that the effects of face-to-face visits on physician prescribing practices may persist for reasonably long periods of time (Avorn and Soumerai 1983; Ray et al. 1985; Schaffner et al. 1983). Although there is some evidence that these programs can be cost-effective (Soumerai and Avorn 1986), this issue requires further investigation since academic detailing programs can be expensive to implement and maintain.

It is difficult to estimate the relative effectiveness of different types of interventions because the studies differed with respect to many variables including the selection of participants, the choice of practice settings, the targeted prescribing problems and the outcomes of interest. However, the particular type of change being encouraged may be an important factor influencing the success of a given intervention. For example, reminders help to eliminate errors of oversight but are not useful in convincing physicians to change their practices. Patient-specific feedback is well-suited to prescribing problems which can occur in individual patients, e.g., drug interactions, polypharmacy, potentially inappropriate dosages, therapeutic duplications and the use of multiple prescribers. These types of prescribing problems may be less amenable to the more general educational approaches such as group education programs or academic detailing. In contrast, face-to-face visits and targeted group education strategies may be more effective in changing overall prescribing practices (e.g. encouraging increased use

of a target drug for specific disease states or discouraging the use of a given drug). The effectiveness of patient-specific programs in modifying these more general prescribing practices is unclear.

Patient-specific feedback programs have certain advantages over other educational interventions. Several investigators have stressed the importance of reinforcing educational messages in producing lasting behaviour changes (Horder et al. 1986; Kane and Garrard 1994; Soumerai and Lipton 1994). Patient-specific DUR programs generally have the capability to provide ongoing monitoring of patient drug use problems and to communicate concerns about the drug use problems to health care providers on a regular basis. In contrast, regularly visiting prescribers or scheduling periodic group meetings to reinforce educational messages may be neither practical nor cost-effective. As noted above, patient-specific feedback interventions can also be designed to focus on a variety of prescribing problems which may be less effectively addressed by other educational approaches. Furthermore, because the feedback highlights potential problems in individual patients, the information provided to physicians and pharmacists is clearly relevant to their practices. In contrast, physicians who are provided with more general prescribing information by other types of intervention programs may not be able to readily identify specific patients for whom the prescribing changes should be implemented.

Saskatchewan's PPRP shares these advantages and has some advantages of its own. The Program is based on prescription claims submitted to the Saskatchewan Prescription Drug Plan. Therefore, it provides an efficient and relatively inexpensive means of monitoring outpatient drug use in nearly the whole Saskatchewan population. Furthermore, because the monitoring process reviews prescription claims every two weeks, potential drug use problems can be identified and communicated to health care providers on a timely basis.

An important factor contributing to the success of an educational intervention is the use of a credible and respected source of information (Horder et al. 1986; Soumerai and Lipton 1994). The PPRP was an initiative of the JCDU. As noted

in the Introduction section, this multidisciplinary committee has representation from the Colleges of Medicine and Pharmacy at the University of Saskatchewan and from the regulatory bodies and professional associations of medicine, pharmacy and nursing. Input from these sources, combined with the non-regulatory nature of the intervention, may enhance the acceptability of the PPRP to physicians and pharmacists.

Several aspects of the patient-specific feedback used by the PPRP are also noteworthy. Firstly, the feedback intervention consists of a patient medication profile, a general letter describing the program and a voluntary response form. Attached to the profile is a summary sheet which clearly identifies the potential drug use problem. Highlighting the criteria exceeded by the patient may enhance the effectiveness of the Program since studies have shown that simply providing physicians with lists of their current medications has little or no impact on prescribing practices (Johnson et al. 1976; Koepsell et al. 1983). In addition, the medication profile lists all prescriptions claimed by the patient during the previous three month period (six months for extreme users of asthma medications) and, therefore, provides physicians and pharmacists with information about drugs prescribed and dispensed to the patient by other health care providers. Using this information, the physicians and pharmacists can identify their role in the development of the drug use problem and in its resolution. Furthermore, the medication profiles may facilitate communication between health care providers by informing them about other physicians and pharmacists caring for the patient.

Because the potential problems in patient drug use are communicated to physicians and pharmacies by mail, the PPRP can reach health care providers across the province. This is a particular advantage for regions like Saskatchewan in which the population is dispersed over a relatively large geographical area. Strategies such as academic detailing or group education programs which rely on personal contact may be impractical and less cost-effective for addressing drug use problems on a province-wide basis.

Although the PPRP has may positive qualities, it is important to recognize that the Program also has a number of limitations. As noted above, the use of SPDP

claims data provides an efficient means of monitoring a large number of individuals. However, the use of prescription claims data is also the source of several limitations. In particular, the Prescription Drug Services database contains no clinical information such as the diagnosis, the presence of concomitant illnesses and the severity of disease. Therefore, the PPRP may identify some patients for whom special clinical circumstances justify their extreme drug use patterns. If a large proportion of the extreme drug use patterns were easily explained by clinical information unavailable to the PPRP, then the Program would be perceived by health care providers as a nuisance. During the period under review, the lack of clinical information was probably not a major limitation of the PPRP because the threshold criteria for the Extreme User, Polypharmacy and Polyprescriber Programs were very high. Thus, the drug use patterns of patients identified for exceeding these criteria at the very least warranted a review of the drug therapy.

A second limitation arising from the use of SPDP claims data is that the monitoring process is, for the most part, limited to drugs listed in the Saskatchewan Formulary. This is not a major drawback since more than 2000 drug products were listed in the Formulary in 1992 (Saskatchewan Health 1993b). Furthermore, it has been estimated that Formulary drugs represent more than 90% of the prescriptions dispensed in the province (Blackburn et al. 1990). Nevertheless, it is important to recognize that medications not eligible for SPDP coverage cannot be monitored by the Program.

Thirdly, identification under the PPRP is based on apparent drug use. Because consumption of medications is estimated from prescription claims, it is not known with certainty that the patients actually took the medications. This limitation is common to all DUR programs that are based on prescription claims. The use of monitoring periods of 90 days (or 180 days for extreme use of asthma medications) addresses this problem to some extent because individuals who have received quantities of a drug over a three to six month period which exceed PPRP criteria likely consumed the most of the medications.

Overall, the PPRP appeared to improve patient drug use at least to the extent

that many of the intervention group subjects were not re-identified during the short-term follow-up period. Further improvements in drug use may have occurred if additional educational techniques had been used in the development of this program. When designing educational initiatives, it is important to identify and address the factors contributing to the prescribing practices which require modification (Epstein 1991; Soumerai and Lipton 1994). Furthermore, health care providers must be convinced about the need for change (Horder et al. 1986). Although the PPRP targeted legitimate drug use problems with a potential for adverse consequences (i.e. extreme use, polypharmacy and the use of multiple prescribers), the Program did little to educate health care providers about the potential consequences of these drug use problems. Nor did the Program address the specific factors which may have contributed to the drug use problems. For example, why were extreme users of salbutamol receiving more than six inhalers per month and is it possible to provide physicians and pharmacists with information or tools to reduce the patients' salbutamol consumption and prevent the extreme use from recurring? Multifaceted approaches which combine *predisposing* factors (to increase awareness, improve knowledge and change attitudes), *enabling* elements (to help health care providers overcome barriers and change their practices) and *reinforcing* factors (to establish lasting behaviour changes) may be more effective than single interventions in improving physicians' practices (Davis et al. 1992; Horder et al. 1986; Soumerai and Lipton 1994). The addition of predisposing and enabling elements to the PPRP may have further increased the effectiveness of the Program.

5.3 Limitations of the Present Investigation

A major objective of the present investigation was to estimate the impact of the PPRP on patient drug utilization. Ideally, this would have been accomplished by measuring patients' drug use during the post-intervention period and comparing it with their drug use patterns during the pre-intervention period. Unfortunately, this was not

possible because the PPRP database contained no information about the post-intervention drug use patterns of patients who were not re-identified by the Program. Therefore, changes in patient drug use were measured indirectly by determining whether study subjects were re-identified during the follow-up period. Re-identification indicated that the patients' drug use continued to exceed PPRP criteria. The absence of re-identification indicated that the apparent use of drugs fell below the threshold criteria for the Extreme User, Polypharmacy and Polyprescriber Programs.

Within the constraints of the available data, re-identification was the best marker of changes in patient drug use. However, it is important to recognize that this outcome measure was a rather insensitive indicator of changes in drug utilization. This lack of sensitivity manifests in two ways. As noted previously, focussing on re-identification may have resulted in the failure to identify changes in drug use which were potentially important from a clinical perspective but which were not sufficiently large to prevent re-identification, e.g., a decline in the apparent level of extreme use from 300% to 210% of the maximum dosage criteria. The analysis of secondary outcomes among subjects who were re-identified was conducted to address this limitation. Secondly, it was not possible to quantify the degree to which drug use improved. For example, by focussing on re-identification, it was not possible to distinguish between a decrease in the level of extreme use from 220% to 175% and a decrease from 220% to 75%. Clearly, the latter change would be more desirable from a clinical perspective.

It may also be argued that the use of re-identification as an outcome measure simply focussed on changes in the *quantity* of drug use but did not necessarily address issues related to the *quality* of prescribing. This was not considered a major limitation because the criteria for identification under the Extreme User, Polypharmacy and Polyprescriber Programs very high; therefore, decreases in patient drug use to levels below the threshold criteria may reasonably be considered improvements in the quality of drug use for most individuals.

As previously noted, the PPRP database is based on information contained in the Prescription Drug Services data files and is, therefore, subject to the same

limitations. A thorough discussion of the limitations of the Saskatchewan Health databases has been presented elsewhere (Rawson et al. 1992). Only the limitations which relate specifically to this project will be discussed. The Prescription Drug Services database is based on claims submitted to the SPDP and, therefore, only contains information about Formulary drugs and certain medications covered under supplementary programs. For the most part, the data files contain no information about the use of non-formulary drugs, over-the-counter medications or drugs administered in hospital. Therefore, it was not possible to determine if patients were switched to non-formulary drugs. A switch to non-formulary medications may have prevented re-identification, but would not necessarily represent an improvement in drug use. In addition, the Prescription Drug Services database contains only limited sociodemographic information and no clinical information such as the diagnosis, severity of illness and concomitant diseases. Additional information pertaining to these variables may have helped to further explain variations between the study groups with respect to the likelihood of re-identification.

Another limitation of the present investigation is that outcomes were measured over a relatively short period of time. As previously noted, it was necessary to limit the follow-up period to 112 days because medication profiles were eventually released for the comparison group subjects. Beyond this 112 day period, profile release was expected to influence the outcomes of the comparison group subjects, resulting in a less reliable estimate of the impact of the intervention on re-identification by the Program. The long-term follow-up analyses addressed this limitation to some extent by describing the re-identification experience of the intervention group subjects over a nine month post-intervention period. Nevertheless, the inability to compare the intervention and comparison group subjects beyond the three and a half month follow-up period limits the conclusions that may be drawn about the impact of the PPRP over the longer term.

The very fact that profiles were released for the comparison group subjects may also be considered a limitation of the study. The comparative analyses were

conducted under the assumption that the release of medication profiles two or two and a half months into the 112 day follow-up period had little or no impact on the short-term re-identification rates of the comparison group. This was a reasonable assumption because re-identification was based on drug use during a 90 day period (or a 180 day period for extreme use of asthma medications), therefore, the majority of drug use on which re-identification was based occurred prior to profile release. Nevertheless, even if profile release did influence the short-term outcomes of comparison group subjects, the effect simply would have been to underestimate the impact of the intervention.

Other limitations related to the selection and follow-up of comparison group subjects have been discussed previously. Specifically, the comparison group was followed during a different calendar period than the intervention group and, therefore, provides questionable control for temporal factors which may influence drug utilization over time. In addition, the comparison group subjects were identified during the first month of operation of the PPRP. Therefore, these individuals may have had patterns of drug use which exceeded the PPRP criteria well before the Program started. In contrast, intervention group subjects were first identified after the program had been operating for at least three months. Therefore, the drug use problems in these individuals were likely new or intermittent. Thus, it is possible that potential differences between the study groups with respect to the duration of drug use problems may have confounded the association between profile release and re-identification.

Although the comparison group was not ideal, it did provide good control for regression toward the mean, a problem which commonly occurs in studies in which subjects are selected on the basis of exceeding a predetermined threshold level (Soumerai and Lipton 1994). In the present investigation, subjects in both the intervention and comparison groups were identified for exceeding the same criteria. Therefore, regression toward the mean probably occurred in both groups. The importance of an adequate comparison group to control for this phenomenon has been stressed by others (Soumerai and Lipton 1994) and is further emphasized by the findings of the present investigation. Specifically, comparison group subjects for the Extreme

User, Polypharmacy and Polyprescriber Programs had short-term re-identification rates of only 56.8%, 38.9% and 19.7%, respectively. In the absence of these comparison groups, similar re-identification rates in the intervention groups may have been interpreted as a positive effect when, in fact, no such conclusion would have been justified. In this regard, the present investigation is a major improvement over previous evaluations of DUR programs since most of the published studies have not used comparison groups to control for regression toward the mean and other factors which may influence drug utilization over time.

6.0 Conclusions and Future Directions

One of the objectives of the present investigation was to describe the use of mood-modifying drugs and asthma medications in the province of Saskatchewan. Both groups of drugs were widely used. Five percent of the eligible population had at least one prescription for an anxiolytic, sedative or hypnotic benzodiazepine, the most commonly used of the mood-modifying drugs. Salbutamol was the most widely used asthma medication — 3.7% of eligible beneficiaries used this drug in 1992. The age-sex patterns of use for these drugs were generally consistent with the findings of other studies.

The purpose of the drug utilization phase of the investigation was to quantify drug use in the province and to describe the changes in drug use over the five year period 1989 to 1993. An evaluation of the appropriateness of drug use was not possible due to limitations of the data source with respect to the lack of clinical information and the aggregate format of the drug use reports. Nevertheless, some of the observed trends in drug use are suggestive of improvements in the use of these agents. Specifically, the decreased use of mood-modifying drugs and the shift from long-acting benzodiazepines to more rapidly eliminated benzodiazepines may be considered positive changes. Possible improvements in the use of asthma medications include a decrease in the average number of β_2-agonist prescriptions per user and a substantial increase in the use of inhaled corticosteroids.

Unfortunately, some of the findings also raise questions about the appropriateness of the use of some mood-modifying drugs and anti-asthmatic agents. In particular, 18.2% and 10.3% of elderly women and men, respectively, had at least one prescription for a benzodiazepine in 1992. Furthermore, approximately 5% of these

elderly patients had apparent levels of benzodiazepine use which exceeded the dosage criteria for extreme use. In addition, the relatively high prescription per user rates for anxiolytic, sedative and hypnotic agents indicate that these drugs tend to be used on a long-term basis in Saskatchewan. Since the prescription per user rates remained relatively constant throughout the five year study period, there is no indication that the duration of sedative-hypnotic use is on the decline. Given the potential risks of benzodiazepine use, especially in elderly patients, and the lack of evidence for the long-term effectiveness of these agents, the findings of this study merit further investigation.

With respect to asthma medications, two findings suggest that the inhaled corticosteroids may be under-utilized: the user rate for salbutamol was nearly double that of beclomethasone dipropionate; and, the prescription per user rates for the inhaled steroids were relatively low, especially among children and young adults. Given the importance of inhaled corticosteroids in the rational treatment of asthma, this issue should be investigated further.

The second objective of this investigation was to describe the patients identified by the PPRP. The characteristics of these individuals were heavily influenced by the criteria for which they were identified. Extreme use was most common among females and the elderly, a finding which reflects both the age-sex distribution for the use of minor tranquilizers and the establishment of lower maximum dosage criteria for elderly users of these drugs. Polypharmacy was also most common among females and the elderly, a finding which is consistent with the observations of numerous drug utilization studies. Identification under the PPr Program was slightly more common for females than males. This finding may be related to the tendency towards an increased use of health services by females.

The third objective of the present investigation was to evaluate the impact of the PPRP on patient drug use. The results of this study provide reasonably good evidence that the release of patient medication profiles under the PPRP had a positive impact on the short-term drug use patterns of patients. As with most studies of educational interventions, further investigation will be needed to determine if the

apparent improvements in drug use translate to improved patient health.

Because the analyses focussed on prescription drug use, the positive changes in patient drug utilization largely reflect a change in physicians' prescribing practices for these patients. However, it is unclear to what extent these prescribing changes are generalizable to the physicians' overall practices. For example, did the physicians who received medication profiles for elderly extreme users of minor tranquilizers begin prescribing lower doses for all of their elderly benzodiazepine users? The extent to which the PPRP influenced overall prescribing practices requires further investigation.

The observed reductions in re-identification rates for subjects identified under the Extreme User, Polypharmacy and Polyprescriber Programs suggests that patient-specific feedback may be an effective means of addressing a variety of prescribing problems. However, the generalizability of these results may be limited by the very high criteria used to identify patients under the PPRP. Whether patient-specific feedback is effective in addressing drug use problems which are less obvious is another area requiring further study.

The positive effects of profile release were observed during a three and a half month period. During this short-term follow-up period, 36.5%, 15.5% and 3.9% of Extreme User, Polypharmacy and Polyprescriber subjects in the intervention groups had been re-identified by the PPRP. Within nine months after profile release, the estimated re-identification rates had risen to 55%, 30% and 13%, respectively, suggesting a need for ongoing feedback. The duration of the feedback effect and the optimal frequency for the release of patient profiles should be addressed in future studies.

Lastly, few studies have compared different types of interventions. Further investigations should be conducted to determine the relative effectiveness of different interventions in influencing physicians' prescribing practices and improving patient drug use. These studies should also address issues related to the cost-effectiveness of different educational approaches for a variety of prescribing problems.

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APPENDIX A

Extreme Use Criteria

A. Mood Modifying Drugs

Drug Group	Daily Use Exceeding (over a three month period) <65 years of age	≥65 years of age
Analgesics		
Acetaminophen/Codeine	240 mg	240 mg
Anileridine	200 mg	200 mg
Acetylsalicylic Acid/Codeine	240 mg	240 mg
Codeine	240 mg	240 mg
Hydromorphone	24 mg	24 mg
Levorphanol Tartrate	15 mg	15 mg
Meperidine Hydrochloride	400 mg	400 mg
Morphine (injection)	60 mg	60 mg
Morphine (oral and rectal)	120 mg	120 mg
Pentazocine	300 mg	300 mg
Propoxyphene (HCl equivalent)	195 mg	195 mg
Minor Tranquilizers		
Alprazolam	3 mg	2 mg
Bromazepam	30 mg	12 mg
Chlordiazepoxide	60 mg	30 mg
Clonazepam	10 mg	10 mg
Clorazepate Dipotassium	30 mg	15 mg
Diazepam	40 mg	20 mg
Flurazepam Hydrochloride	30 mg	30 mg
Hydroxyzine	200 mg	100 mg
Lorazepam	10 mg	4 mg
Nitrazepam	10 mg	5 mg
Oxazepam	120 mg	60 mg
Temazepam	30 mg	15 mg
Triazolam	0.5 mg	0.25 mg

Drug Group	Daily Use Exceeding (over a three month period) <65 years of age	≥65 years of age
Phenobarbital	300 mg	300 mg
Sedative-Hypnotics		
Amobarbital	200 mg	200 mg
Amobarbital Sodium	200 mg	200 mg
Butabarbital Sodium	200 mg	200 mg
Chloral Hydrate	1000 mg	1000 mg
Pentobarbital Sodium	100 mg	100 mg
Secobarbital Sodium	100 mg	100 mg
Major Tranquilizers		
Chlorpromazine	900 mg	600 mg
Chlorprothixene	600 mg	300 mg
Flupenthixol Decanoate	80 mg/month	80 mg/month
Flupenthixol Dihydrochloride	12 mg	12 mg
Fluphenazine Hydrochloride	20 mg	10 mg
Fluphenazine Decanoate	200 mg/month	100 mg/month
Fluphenazine Enanthate	200 mg/month	100 mg/month
Fluspirilene	80 mg/month	80 mg/month
Haloperidol	32 mg	12 mg
Haloperidol Decanoate	300 mg/month	100 mg/month
Loxapine	250 mg	100 mg
Mesoridazine	300 mg	300 mg
Methotrimeprazine	200 mg	200 mg
Pericyazine	60 mg	30 mg
Perphenazine	36 mg	36 mg
Pimozide	24 mg	16 mg
Pipotiazine Palmitate	250 mg/month	150 mg/month
Prochloperazine (oral)	150 mg	75 mg
Prochloperazine (inj. & rectal)	100 mg	50 mg
Thioridazine	800 mg	600 mg
Thiothixene	60 mg	30 mg
Trifluoperazine	40 mg	30 mg

B. Asthma Drugs

Drug	Dosage Form	Maximum Daily Dose (all ages)
Bronchodilators		
Fenoterol	tablets	15 mg
	inhaler	2 units/month
	inhalation solution	10 mL
Salbutamol	oral	32 mg
	200 ug rotacap & disk	800 ug
	400 ug rotacap & disk	1600 ug
	inhaler	3 units/month
	inhalation solution	4 mL
	nebules	8 nebules
Terbutaline	tablets	15 mg
	aerosol	1 unit/month
Anticholinergics		
Ipratropium Bromide	inhaler	2 units/month
	inhalation solution	8 mL
Inhaled Steriods		
Beclomethasone dipropionate	100 ug rotacap & disk	400 ug
	200 ug rotacap & disk	2000 ug
	50 ug inhaler	2 units/month
	250 ug inhaler	2 units/month
Budesonide	50 ug inhaler	2 units/month
	100 ug turbuhaler	2 units/month
	200 ug inhaler	4 units/month
	200 ug turbuhaler	2 units/month
Flunisolide	inhaler	3 units/month

Example Calculation of an Apparent Daily Dosage

In the previous 90 days, Patient A (female, aged 50 years) has had prescriptions for diazepam and lorazepam, two drugs monitored under the Extreme User component of the Patient Profile Release Program. Both drugs are listed in the same drug linkage group (Minor Tranquilizers)[1].

Monitored Drugs	Strength	Quantity[2]	Strength x Quantity
Diazepam	2 mg	400	800 mg
	10 mg	400	4000 mg
Lorazepam	2 mg	450	900 mg

Apparent Dosage Calculation:

$$\text{Apparent Dose} = \frac{\Sigma\ (\text{Strength x Quantity})}{90 \text{ days}}$$

$$\text{Diazepam} = \frac{4000 \text{ mg} + 800 \text{ mg}}{90 \text{ days}} = \frac{4800}{90} = 53.33 \text{ mg/day}$$

$$= 133\% \text{ of maximum dose}^3$$

$$\text{Lorazepam} = \frac{900 \text{ mg}}{90 \text{ days}} = 10 \text{ mg/day}$$

$$= 100\% \text{ of maximum dose}^3$$

Total Percentage of the Maximum Threshold
Dose for the Minor Tranquilizer Drug Group = 133% + 100% = 233%

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[1] The agents included in each drug linkage group are listed in Appendix A.

[2] The quantity is determined from prescriptions claimed in the 90 day period prior to the calculation of the apparent dose. A 180 day period is used for the calculation of asthma drug apparent dosages. The quantity equals the total number of units for each strength of the monitored drug.

[3] The maximum threshold dosages are 40 mg/day for diazepam and 10 mg/day for lorazepam (Appendix A). For drugs in the same linkage group, the percentages (of the maximum doses) are summed to provide an estimate of use for the drug group as a whole. Percentages for drugs from different linkage groups are not summed.

APPENDIX C

Pharmacist Review of Computer-Generated Medication Profiles

During the period under review, the Patient Profile Release Program automatically generated a drug profile for each beneficiary who exceeded the criteria established for the Extreme User, Polypharmacy and/or Polyprescriber Programs. The computer-generated profiles were then reviewed by a SPDP pharmacist to identify situations in which profile release may have been unnecessary or inappropriate. Circumstances under which medication profiles were <u>not</u> sent to prescribers and pharmacies include the following (Joint Committee on Drug Utilization 1994):

- obvious stockpiling,
- use of nitrazepam or clonazepam as an anticonvulsant (e.g. use in children or in patients receiving other anticonvulsants),
- extreme use of narcotics in patients whose record of drug use suggests cancer treatment,
- extreme users aged 65 or 66 years when it appears that the physician has not yet reduced the patient's dose to the levels recommended for elderly individuals,
- extreme users of asthma medications where the quantity of drug appeared to be entered into the computer system incorrectly (e.g. when the quantity of an inhaler was entered as 200 doses rather than 1 inhaler), and
- patients for whom a physician or pharmacist has provided some clinical information indicating that drug use is appropriate.

APPENDIX D

Sample Covering Page for the Patient Medication Profile

SASKATCHEWAN HEALTH	PRESCRIPTION DRUG SERVICES BRANCH	
Patient Profile for CONFIDENTIAL	Patient Name Address	HSN: Age: 66 years Sex: Male

Extreme User Summary

Index Date (date on which patient was identified as exceeding criteria): Jul 12,1992
Generic Usage Period: Apr 14, 1992 to Jul 12, 1992

Minor Tranquilizers	Patient Apparent Dose	Percentage of Maximum Dose Criteria
Alprazolam Tablet	4.28 mg/day	= 214% of Max
		Total = 214%

Sample Patient Medication Profile

SASKATCHEWAN HEALTH — PRESCRIPTION DRUG SERVICES BRANCH

Patient Profile for CONFIDENTIAL
Patient Name
Address
HSN:
Age: 66 years
Sex: Male

PRESCRIPTIONS PROCESSED BETWEEN APR 14, 1992 TO JUL 12, 1992

Drug	Quantity	Prescriber	Pharmacy
Jul 12, 1992 Salbutamol Ventolin Inhaler Aerosol	2	Physician Name Address	Pharmacy Name Address
Jul 12, 1992 Alprazolam Apo-Alpraz 0.5mg Tablet	220	Physician Name Address	Pharmacy Name Address
Jun 17, 1992 Glyburide Diabeta 2.5mg Tablet	34	Physician Name Address	Pharmacy Name Address
May 25, 1992 Alprazolam Apo-Alpraz 0.5mg Tablet	200	Physician Name Address	Pharmacy Name Address
May 25, 1992 Salbutamol Ventolin Inhaler Aerosol	2	Physician Name Address	Pharmacy Name Address
Apr 25, 1992 Alprazolam Apo-Alpraz 0.5mg Tablet	200	Physician Name Address	Pharmacy Name Address
Apr 16, 1992 Glyburide Diabeta 2.5mg Tablet	34	Physician Name Address	Pharmacy Name Address
Apr 16, 1992 Alprazolam Apo-Alpraz 0.25mg Tablet	300	Physician Name Address	Pharmacy Name Address

APPENDIX E

Data Cleaning Process

The present investigation was based on data derived from administrative databases not specifically designed for this investigation. Various manipulations of the Patient Profile Release Program (PPRP) data files were necessary to create a data set that was appropriate for analysis. This appendix summarizes the modifications to the PPRP database:

(i) Midway through 1992, the Polypharmacy Program was modified to exclude diagnostic agents such as blood glucose monitoring strips (Formulary Class 36:00) from the count of different drugs. Records for individuals identified by the Polypharmacy Program prior to this change were selected from the data files and the number of different drugs was re-calculated after manual exclusion of the diagnostic agents. Beneficiaries no longer exceeding the Polypharmacy criterion of 16 or more different drugs were excluded from the study. A total of 69 individuals were excluded from the study for this reason. An additional 43 beneficiaries had Polypharmacy counts of less than 16, but these individuals had also been identified for exceeding other criteria during the study period. Therefore, these 43 individuals were included in the study, but the records pertaining to the Polypharmacy identification were excluded from the analysis.

(ii) For some asthma medications, the SPDP claims system permitted the entry of either the number of units (e.g. tablets, disks for inhalation, inhalers) or the number of doses (e.g. 120 doses for a package of 15 salbutamol disks) as the prescription quantity. Since the formulas for the apparent dosage calculations for the Extreme User Program were based on the number of ***units*** claimed during the monitoring period, calculations based on the number of ***doses*** resulted in an overestimation of the apparent dosage. Beneficiaries for whom the prescription

quantity was entered as the number of doses were identified and apparent dosages were re-calculated. Individuals no longer exceeding extreme use criteria were excluded from the study. A total of 73 beneficiaries were excluded for this reason. Two additional subjects failed to meet the extreme use criteria, but had also been identified for exceeding other criteria during the study period. These 2 individuals were included in the study, but the records pertaining to the episodes of extreme use of asthma drugs were excluded from the analysis.

(iii) The formulas for the apparent dosage calculations for some of the depot formulations of major tranquilizers were incorrect. Because the overall estimate of major tranquilizer use was based on all dosage forms, including depot formulations, all subjects identified for extreme use of these drugs were excluded from the study. A total of 229 individuals were excluded for this reason. An additional 9 beneficiaries exceeded major tranquilizer dosage criteria, but were also identified for exceeding other criteria during the study period. These 9 individuals were included in the investigation, but the records pertaining to the episode of extreme use of major tranquilizers were excluded from the analysis.

(iv) The number of different prescribers was overestimated for a small number of beneficiaries identified by the Polyprescriber Program. Some pharmacies had entered zero as the prescriber number for insulin claims submitted to the SPDP, presumably because insulin does not require a prescription. This prescriber number was incorrectly included in the count of different prescribers. Records of these beneficiaries were selected, the incorrect prescriber number was manually excluded and the count of prescribers was re-calculated. Seven subjects no longer exceeded the Polyprescriber criterion and were excluded from the study.

APPENDIX F

Formulary Classes of Drugs Monitored by the Patient Profile Release Program

Opiate Agonists (Narcotic Analgesics) - 28:08.00

Acetaminophen/Caffeine/Codeine
Acetaminophen/Codeine
Anileridine Hydrochloride
Acetylsalicylic Acid/Caffeine/Codeine
Codeine Phosphate
Hydromorphone Hydrochloride
Levorphanol Tartrate
Meperidine Hydrochloride
Morphine
Oxymorphone Hydrochloride*
Propoxyphene

Opiate Partial Agonists - 28:08.12

Pentazocine

Anticonvulsants (Barbiturates) - 28:12.04

Phenobarbital
Primidone*

Anticonvulsants (Benzodiazepines) - 28:12.08

Clonazepam
Nitrazepam

Anxiolytics, Sedatives and Hypnotics (Barbiturates) - 28:24.04

Amobarbital
Amobarbital Sodium
Butabarbital Sodium
Pentobarbital Sodium
Secobarbital Sodium

Miscellaneous Anxiolytics, Sedatives and Hypnotics - 28:24.92

Chloral Hydrate
Hydroxyzine
Methotrimeprazine

Anxiolytics, Sedatives and Hypnotics (Benzodiazepines) - 28:24.08

Alprazolam
Bromazepam
Chlordiazepoxide
Clorazepate Dipotassium
Diazepam
Flurazepam Hydrochloride
Lorazepam
Oxazepam
Temazepam
Triazolam

Antimuscarinics/Antispasmodics - 12:08.08

Ipratropium Bromide[§]

Sympathomimetic (Adrenergic) Agents - 12:12.00

Epinephrine Hydrochloride*
Fenoterol Hydrobromide
Metaproterenol Sulphate*
Procaterol Hydrochloride Hemihydrate*
Ritodrine Hydrochloride*
Salbutamol
Terbutaline

Adrenal Corticosteroids - 68:04.00[¶]

Beclomethasone Dipropionate
Budesonide
Flunisolide
Triamcinolone Acetonide*

*Not monitored by the Patient Profile Release Program.

[§] Ipratropium Bromide is the only drug in this class that is used for asthma.

[¶] Only the corticosteroids with inhalation dosage forms are listed.

Utilization of Mood-Modifying Drugs – 1992

Drug Group (Formulary Class)	Prescription Rate[§]	User Rate[¶]	Prescription per User Rate[‡]
Opiate Agonists (28:08.08)			
Acetaminophen/Caffeine/Codeine	54.76	31.73	1.73
Acetaminophen/Codeine	1.94	1.00	1.95
Anileridine	0.39	0.16	2.48
Acetylsalicylic Acid/Caffeine/Codeine	4.03	2.58	1.56
Codeine	1.89	1.28	1.48
Hydromorphone	1.05	0.35	3.00
Levorphanol Tartrate	0.39	0.11	3.68
Meperidine Hydrochloride	2.25	1.20	1.88
Morphine	6.38	1.53	4.16
Propoxyphene	1.66	0.62	2.65
Opiate Partial Agonists (28:08.12)			
Pentazocine	1.29	0.49	2.64
Anticonvulsants (Barbiturates) (28:12.04)			
Phenobarbital	14.69	2.63	5.58
Anxiolytics, Sedatives and Hypnotics - Barbiturates (28:24:04)			
Amobarbital	0.11	0.01	5.94
Amobarbital Sodium	0.17	0.04	4.24
Butabarbital Sodium	0.25	0.04	5.71
Pentobarbital Sodium	0.22	0.04	5.28
Secobarbital Sodium	0.54	0.11	5.03

[§] Mean number of prescriptions per 1000 eligible beneficiaires
[¶] Mean number of users per 1000 eligible beneficiaires
[‡] Mean number of prescriptions per user

Utilization of Mood-Modifying Drugs – 1992

Drug Group (Formulary Class)	Prescription Rate[§]	User Rate[¶]	Prescription per User Rate[‡]
Anxiolytic, Sedative and Hypnotic Benzodiazepines (28:24.08)			
Alprazolam	21.40	5.83	3.67
Bromazepam	10.64	2.53	4.20
Chlordiazepoxide	6.86	1.78	3.85
Clorazepate Dipotassium	3.87	0.92	4.20
Diazepam	36.17	11.05	3.27
Flurazepam	13.87	3.37	4.12
Lorazepam	58.64	14.72	3.98
Oxazepam	18.07	4.03	4.49
Temazepam	28.67	8.13	3.53
Triazolam	30.86	7.94	3.89
Anticonvulsants - Benzodiazepines (28:12.08)			
Clonazepam	13.90	2.63	5.29
Nitrazepam	5.11	1.22	4.19
Miscellaneous Anxiolytic, Sedative and Hypnotic Agents (28:24.92)			
Chloral Hydrate	10.00	3.08	3.25
Hydroxyzine	21.15	11.50	1.84
Methotrimeprazine	4.88	0.80	6.12

[§] Mean number of prescriptions per 1000 eligible beneficiaires
[¶] Mean number of users per 1000 eligible beneficiaires
[‡] Mean number of prescriptions per user

Trends in Prescription Rates for Mood-Modifying Drugs – 1989 to 1993

Drug Group (Formulary Class)	Prescription Rate[§]					Change from 1989 to 1993[§]
	1989	1990	1991	1992	1993	
Opiate Agonists (28:08.08)						
Acet/Caffeine/Codeine	61.95	58.16	58.06	54.76	55.11	-6.84
Acetaminophen/Codeine	2.59	2.17	1.96	1.94	1.96	-0.63
Anileridine	0.45	0.45	0.46	0.39	0.37	-0.08
ASA/Caffeine/Codeine	7.68	6.04	5.12	4.03	3.16	-4.52
Codeine	1.92	1.95	2.12	1.89	1.91	-0.01
Hydromorphone	0.19	0.21	0.59	1.05	1.36	1.17
Levorphanol Tartrate	0.65	0.55	0.49	0.39	0.49	-0.16
Meperidine Hydrochloride	2.21	2.35	2.10	2.25	2.63	0.42
Morphine	4.00	4.97	6.00	6.38	7.60	3.60
Propoxyphene	1.95	1.90	1.83	1.66	1.40	-0.55
Opiate Partial Agonists (28:08.12)						
Pentazocine	1.50	1.37	1.47	1.29	1.15	-0.35
Anticonvulsants (Barbiturates) (28:12.04)						
Phenobarbital	15.67	15.44	15.25	14.69	13.51	-2.16
Anxiolytics, Sedatives and Hypnotics - Barbiturates (28:24:04)						
Amobarbital	0.16	0.13	0.13	0.11	0.07	-0.09
Amobarbital Sodium	0.36	0.31	0.26	0.17	0.11	-0.25
Butabarbital Sodium	0.32	0.30	0.28	0.25	0.22	-0.10
Pentobarbital Sodium	0.33	0.26	0.27	0.22	0.19	-0.14
Secobarbital Sodium	0.93	0.76	0.68	0.54	0.49	-0.44

[§]Mean number of prescriptions per 1000 eligible beneficiaries

Trends in Prescription Rates for Mood-Modifying Drugs – 1989 to 1993

Drug Group (Formulary Class)	Prescription Rate[§]					Change from 1989 to 1993[§]
	1989	1990	1991	1992	1993	
Benzodiazepines (28:24.08)						
Anxiolytics						
Alprazolam	19.04	20.45	21.79	21.40	22.89	3.85
Bromazepam	11.09	11.39	10.95	10.64	9.66	-1.43
Chlordiazepoxide	8.91	8.03	7.29	6.86	6.58	-2.33
Clorazepate Dipotassium	5.26	4.87	4.36	3.87	3.39	-1.87
Diazepam	42.49	40.32	39.51	36.17	32.66	-9.83
Lorazepam	53.00	53.42	55.49	58.64	57.52	4.52
Oxazepam	19.77	18.56	18.21	18.07	17.18	-2.59
Sedative-Hypnotics						
Flurazepam	16.88	15.60	14.23	13.87	11.55	-5.33
Temazepam	2.96	10.20	15.39	28.67	31.91	28.95
Triazolam	73.40	67.37	61.34	30.86	20.85	-52.55
Anticonvulsants - Benzodiazepines (28:12.08)						
Clonazepam	7.32	9.37	11.97	13.90	14.71	7.39
Nitrazepam	3.46	4.01	4.26	5.11	4.71	1.25
Miscellaneous Anxiolytic, Sedative and Hypnotic Agents (28:24.92)						
Chloral Hydrate	10.70	10.00	10.06	10.00	9.17	-1.53
Hydroxyzine	19.31	20.98	21.44	21.15	19.73	0.42
Methotrimeprazine	5.07	5.02	5.15	4.88	4.79	-0.28

[§]Mean number of prescriptions per 1000 eligible beneficiaries

Trends in User Rates for Mood-Modifying Drugs – 1989 to 1993

Drug Group (Formulary Class)	Users Rate[$]					Change from 1989 to 1993
	1989	1990	1991	1992	1993	
Opiate Agonists (28:08.08)						
Acetaminophen/Caffeine/Codeine	36.68	34.25	33.97	31.73	32.06	-4.62
Acetaminophen/Codeine	1.33	1.09	0.98	1.00	1.00	-0.33
Anileridine	0.17	0.20	0.15	0.16	0.15	-0.02
Acetylsalicylic Acid/Caffeine/Codeine	5.53	4.18	3.47	2.58	2.03	-3.50
Codeine	1.24	1.28	1.53	1.28	1.31	0.07
Hydromorphone	0.06	0.08	0.20	0.35	0.45	0.39
Levorphanol Tartrate	0.19	0.15	0.13	0.11	0.12	-0.07
Meperidine Hydrochloride	1.19	1.24	1.20	1.20	1.36	0.17
Morphine	0.99	1.22	1.41	1.53	1.78	0.79
Propoxyphene	0.74	0.71	0.70	0.62	0.54	-0.20
Opiate Partial Agonists (28:08.12)						
Pentazocine	0.66	0.54	0.60	0.49	0.47	-0.19
Anticonvulsants (Barbiturates) (28:12.04)						
Phenobarbital	3.26	3.00	2.87	2.63	2.43	-0.83
Anxiolytics, Sedatives and Hypnotics - Barbiturates (28:24:04)						
Amobarbital	0.04	0.03	0.03	0.20	0.01	-0.03
Amobarbital Sodium	0.07	0.06	0.05	0.04	0.02	-0.05
Butabarbital Sodium	0.08	0.06	0.06	0.04	0.04	-0.04
Pentobarbital Sodium	0.05	0.05	0.04	0.04	0.03	-0.02
Secobarbital Sodium	0.20	0.16	0.12	0.11	0.10	-0.10

[$] Mean number of users per 1000 eligible beneficiaries

Trends in User Rates for Mood-Modifying Drugs – 1989 to 1993

Drug Group (Formulary Class)	User Rate[§]					Change from
	1989	1990	1991	1992	1993	1989 to 1993
Benzodiazepines (28:24.08)						
Anxiolytics						
Alprazolam	5.47	5.73	6.11	5.83	6.43	0.96
Bromazepam	2.95	2.87	2.64	2.53	2.24	-0.71
Chlordiazepoxide	2.51	2.16	1.95	1.78	1.78	-0.73
Clorazepate Dipotassium	1.26	1.19	1.02	0.92	0.74	-0.52
Diazepam	12.53	11.78	11.84	11.05	10.20	-2.33
Lorazepam	13.71	13.55	14.11	14.73	14.65	0.94
Oxazepam	4.63	4.24	4.10	4.03	3.89	-0.74
Sedative-Hypnotics						
Flurazepam	4.34	3.74	3.40	3.37	2.65	-1.69
Temazepam	1.46	3.69	5.00	8.13	8.42	6.96
Triazolam	17.37	15.39	13.72	7.94	5.00	-12.37
Anticonvulsants - Benzodiazepines (28:12.08)						
Clonazepam	1.46	1.85	2.27	2.63	2.89	1.43
Nitrazepam	0.99	0.97	1.03	1.22	1.06	0.07
Miscellaneous Anxiolytic, Sedative and Hypnotic Agents (28:24.92)						
Chloral Hydrate	3.22	2.87	2.89	3.08	2.63	-0.59
Hydroxyzine	11.11	11.84	11.82	11.50	10.96	-0.15
Methotrimeprazine	0.85	0.83	0.80	0.80	0.81	-0.04

[§] Mean number of users per 1000 eligible beneficiaries

Life Table for the Long-term Follow-up of Extreme User Subjects

Time Interval	Number of Subjects at Beginning of Interval	Number of Subjects Re-identified During Interval	Number of Subjects Censored During Interval	Probability of Re-identification During Interval[§]	Probability of Surviving[‡] During Interval[§]	Probability of Surviving[‡] to End of Interval	95% Confidence Interval
0-98	342	72	0	0.211	0.789	0.789	0.746, 0.833
99-112	270	50	1	0.185	0.815	0.643	0.593, 0.694
113-126	219	11	15	0.050	0.950	0.611	0.559, 0.663
127-140	193	9	22	0.047	0.953	0.582	0.530, 0.635
141-154	162	2	13	0.012	0.988	0.575	0.522, 0.628
155-168	147	7	7	0.048	0.952	0.548	0.494, 0.602
169-182	133	3	13	0.023	0.977	0.536	0.481, 0.590
183-196	117	4	19	0.034	0.966	0.517	0.462, 0.573
197-210	94	1	21	0.011	0.989	0.512	0.456, 0.568
211-224	72	1	11	0.014	0.986	0.505	0.448, 0.562
225-238	60	0	21	0.000	1.000	0.505	0.448, 0.562
239-252	39	0	19	0.000	1.000	0.505	0.448, 0.562
253-268	20	2	18	0.100	0.900	0.454	0.370, 0.538

[‡] Survival indicates not being re-identified.

[§] For those individuals eligible for re-identification at the beginning of the interval.

Life Table for the Long-term Follow-up of Polypharmacy Subjects

Time Interval	Number of Subjects at Beginning of Interval	Number of Subjects Re-identified During Interval	Number of Subjects Censored During Interval	Probability of Re-identification During Interval[§]	Probability of Surviving[‡] During Interval[§]	Probability of Surviving[‡] to End of Interval	95% Confidence Interval
0-98	181	21	0	0.116	0.884	0.884	0.837, 0.931
99-112	160	5	0	0.031	0.969	0.856	0.805, 0.907
113-126	155	3	14	0.019	0.981	0.840	0.786, 0.893
127-140	138	2	11	0.014	0.986	0.828	0.772, 0.883
141-154	125	1	13	0.008	0.992	0.821	0.765, 0.877
155-168	111	1	12	0.009	0.991	0.814	0.756, 0.871
169-182	98	1	17	0.010	0.990	0.805	0.746, 0.865
183-196	80	2	7	0.025	0.975	0.785	0.721, 0.849
197-210	71	2	13	0.028	0.972	0.763	0.694, 0.832
211-224	56	0	15	0.000	1.000	0.763	0.694, 0.832
225-238	41	2	10	0.049	0.951	0.726	0.643, 0.809
239-252	29	1	17	0.034	0.966	0.701	0.607, 0.794
253-268	11	0	11	0.000	1.000	0.701	0.607, 0.794

[‡] Survival indicates not being re-identified.

[§] For those individuals eligible for re-identification at the beginning of the interval.

Life Table for the Long-term Follow-up of Polyprescriber Subjects

Time Interval	Number of Subjects at Beginning of Interval	Number of Subjects Re-identified During Interval	Number of Subjects Censored During Interval	Probability of Re-identification During Interval[§]	Probability of Surviving[‡] During Interval[§]	Probability of Surviving[‡] to End of Interval	95% Confidence Interval
0-98	154	5	0	0.032	0.968	0.968	0.940, 0.996
99-112	149	1	0	0.007	0.993	0.961	0.930, 0.992
113-126	148	1	18	0.007	0.993	0.955	0.922, 0.987
127-140	129	0	15	0.000	1.000	0.955	0.922, 0.987
141-154	114	3	11	0.026	0.974	0.929	0.887, 0.972
155-168	100	1	13	0.010	0.990	0.920	0.874, 0.966
169-182	86	1	13	0.012	0.988	0.909	0.860, 0.959
183-196	72	1	10	0.014	0.986	0.897	0.842, 0.952
197-210	61	0	6	0.000	1.000	0.897	0.842, 0.952
211-224	55	0	11	0.000	1.000	0.897	0.842, 0.952
225-238	44	0	7	0.000	1.000	0.897	0.842, 0.952
239-252	37	1	16	0.027	0.973	0.873	0.801, 0.944
253-268	20	0	20	0.000	1.000	0.873	0.801, 0.944

[‡] Survival indicates not being re-identified.

[§] For those individuals eligible for re-identification at the beginning of the interval.