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

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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.

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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).

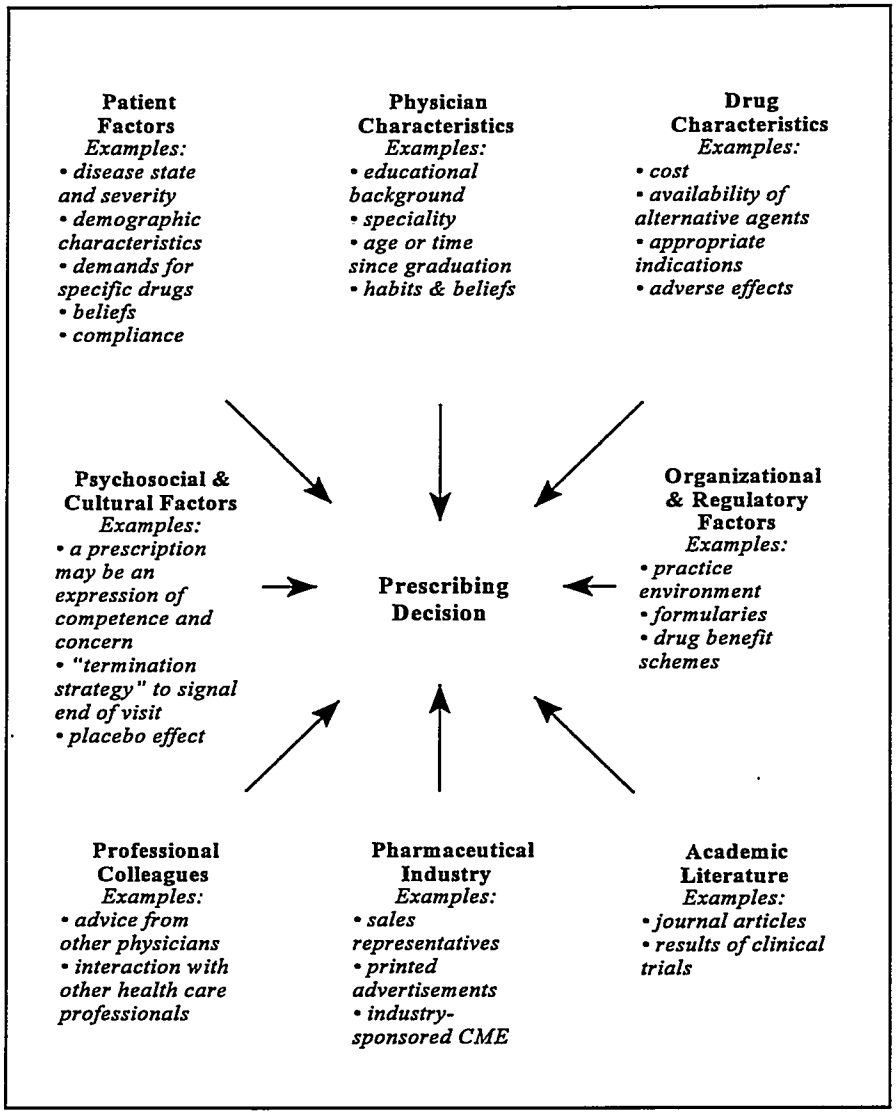

Figure 2.1: Factors Influencing Prescribing

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.

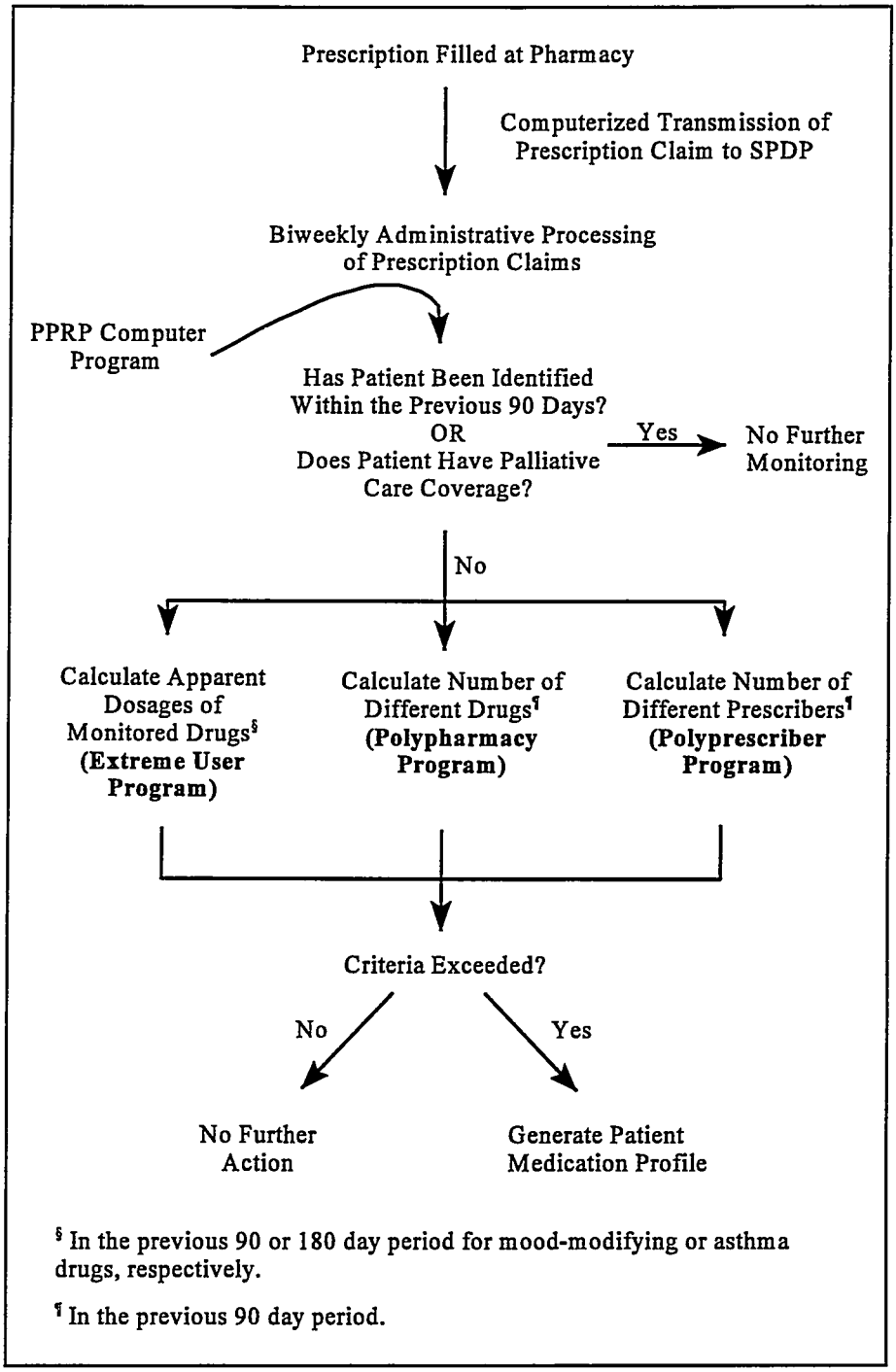
During the period under review, the PPRP computer program ran on a biweekly basis, monitoring all beneficiaries for whom a prescription claim was submitted during the previous two weeks (Figure 3.1). Beneficiaries who had been identified by the PPRP in the previous 90 day period or who had Palliative 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.



§ In the previous 90 or 180 day period for mood-modifying or asthma drugs, respectively.

¶ In the previous 90 day period.

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).

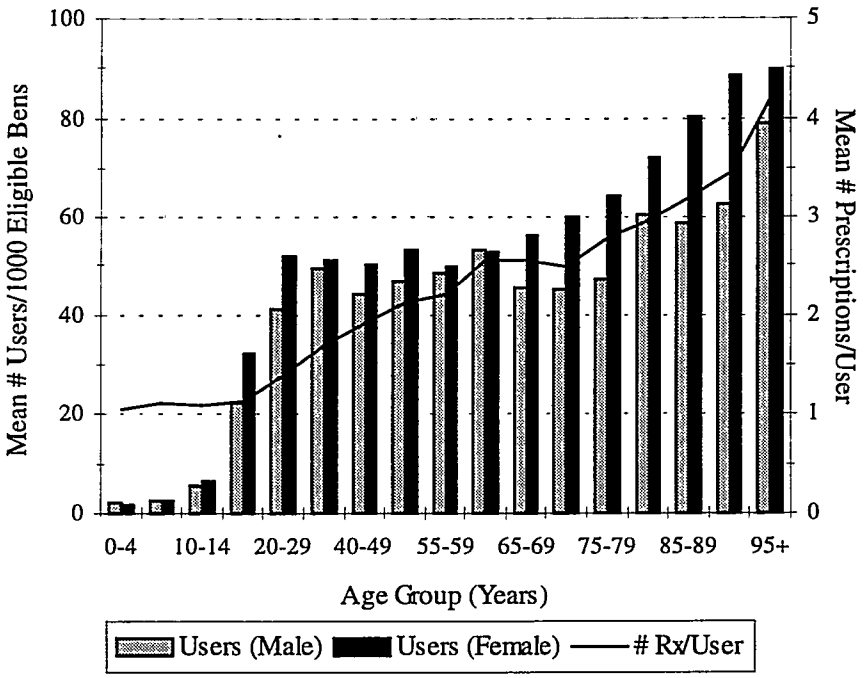

Figure 4.1: 1992 Drug Utilization by Age and Sex – Narcotic Analgesics (Formulary Class 28:08.08)

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%).

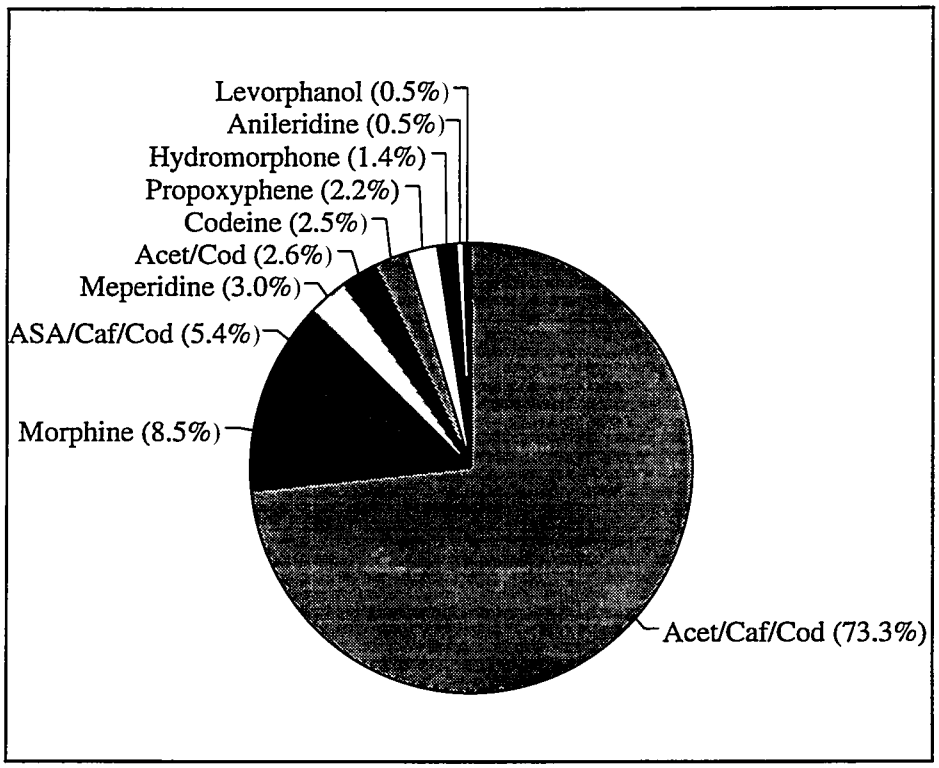

Figure 4.2: Percentage of Prescriptions for Opiate Agonist Narcotic Analgesics – 1992 (Abbreviations for combination products: Acet = Acetaminophen; Caf = Caffeine; Cod = Codeine)

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.