THE INFLUENCE OF PHARMACEUTICAL MARKETING ACTIVITY, PRACTICE CHARACTERISTICS AND PHYSICIAN PROFILE ON PHYSICIAN PRESCRIBING BEHAVIOUR

by

Kent E. M. Groves

Submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

at

Dalhousie University

Halifax, Nova Scotia

April 2006

Your file Votre référence
ISBN: 978-0-494-19602-1
Our file Notre référence
ISBN: 978-0-494-19602-1

DALHOUSIE UNIVERSITY

To comply with the Canadian Privacy Act the National Library of Canada has requested that the following pages be removed from this copy of the thesis:

Preliminary Pages

Examiners Signature Page (pii)

Dalhousie Library Copyright Agreement (piii)

Appendices

Copyright Releases (if applicable)

DEDICATION

This thesis is dedicated to my wife Brenda, daughter Bailey, son Jack, and so many wonderful friends and relations. If you don't enjoy the journey, the destination is of little consequence.

To my father, the late A. Roy M. Groves, thank you for the living years. To you I owe a debt of gratitude for 44 years of support and encouragement. Your intelligence, courage, sense of purpose, and strength of spirit is alive, and always present.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

The annual retail growth of prescription drugs continued in 2004 at a rate of 5.6% in volume and 8.9% in value. While it was the smallest increase since 1998(8), expenditures on prescriptions are now well past those for all services provided by physicians. The prescription drug category thus represents a significant expense, and one which is of concern to policy makers and health departments across the country.

While it is acknowledged as a significant and growing expense, management of this category presents significant political, organizational, ethical, logistical and budgetary challenges. One of the greatest hurdles is associated with the continuing medical education of physicians themselves, and keeping them up to date on drug related issues, options and considerations. To do this, one approach for government is to dedicate scarce resources to "academic detailers"; trained health professionals who attempt to update, educate physicians, given their knowledge on the risks and benefits of many of the drugs that exist on a given jurisdiction's formulary.

The analysis of a sample of 925 physicians in Nova Scotia (while considering advertising expenditures by drug category, physician demographics and prescribing behaviours) accommodated the development of insight into the profiles of the prescribing population, and the influence of marketing expenditures on prescribing. Using prescribing activity of cyclooxygenase-2 inhibitors (COX-2s) from their period of introduction in the province (mid 1999) to December 31, 2003, the profiles of volume COX-2 prescribers (profiles based on the absolute number of prescriptions written over a given period) and relative COX-2 prescribers (prescribing of COX-2s relative to COX-2s and non-selective non-steroidal anti-inflammatories(NS-NSAIDs)) were established. Additionally, this research established the parameters of a new model of "compressed adoption" which addresses the rapid uptake and almost immediate maturity in demand of a new category of drugs.

Journal advertising and pharmaceutical industry detailing were not correlated with increases in COX-2 prescribing, or prescribing in existing drug categories. Among physicians, individuals whose COX-2 prescribing volumes were in the upper or first quartile of the population of physicians during this period were more likely to be older than the median age of 49, male, active prescribers of drugs in other key categories, with rural practices. Conversely, individuals whose prescribing volumes of COX-2s relative to total COX-2/NSAID prescribing volumes in the upper or first quartile were more likely to be younger, female, with low levels of prescribing in other drug categories, practicing in an urban environment.

LIST OF ABBREVIATIONS USED

ACE: Angiotensin Converting Enzyme

ATC Codes: The ATC code is the anatomical therapeutic chemical classification code assigned by the WHO Collaborating Centre for Drug Statistics Methodology. The ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use. In the ATC classification system, the drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties(9).

Calcium: Calcium Channel Blocker

Cholesterol: Cholesterol Reducing Agents

COX-2: cyclooxygenase-2 inhibitors

DDD: Defined Daily Dose

DF: Degrees of Freedom – the number of independent pieces of information that go into the estmation of a parameter

DTC: Direct To Consumer

DIN: A Drug Identification Number is an eight digit numerical code preceded by the prefix DIN, which is assigned to each drug product marketed under or in accordance with the Canadian Food and Drugs Act and Food and Drug Regulations(10).

GP: General Practitioner

NOC: Notice of Compliance

NS – NSAID: Non-specific Non-Steroidal Anti Inflammatory

P Value: Probability value

PHRU: Population Health Research Unit, Dalhousie University

USP: Unique Selling Proposition

WHO: World Health Organization

ACKNOWLEDGEMENTS

I would like to thank IMS Health Canada for providing access to physican and drug level advertising and detailing data, and to the Population Health Research Unit at Dalhousie University for access to data and support with coding and conversion. Thanks in particular to Jill Casey and Mark Smith.

Secondly, I would like to thank Steven Zhao, whose statistical insight and SAS programming skills are second to none. Thank you for your support and sober second thought.

Finally, I would like to thank my committee for their support and guidance.

CHAPTER 1

INTRODUCTION

1.1 About the Study

Scientific research is typically a three-stage process. In stage one, a group of subjects (often a representative sample from a larger population) is selected for study. In the next stage, the researcher uses the information obtained from the sample of study subjects to generalize or draw a conclusion (association) about the larger population. Finally, these conclusions are in turn used to develop support for causation or scientific theory.

This thesis will in turn identify the relevance of the research, the literature supporting the hypotheses, the target population, research insights and relative support for the stated theories.

1.1.1 Research Relevance

Drug therapies are the most common treatments in medical practice, with more than 75% of all outpatient visits to a physician resulting in the writing of a prescription(11). Given this, the inappropriate or overuse of prescription drugs may lead to increased hospitalizations and unnecessary health expenditures. In the United States alone, over 100,000 hospitalized patients die each year from adverse drug reactions(12).

The relevance of this research is best summed up in a quote from Dr. Gerry Avorn, "Another reason the companies have been so singularly profitable is their capacity to induce demand on the part of physicians and patients. Marketing a drug

effectively can increase the number of people who want to use it and the amount that can be charged for it, well beyond its actual clinical benefit or economic value." (13), pg 227.

The retail growth of prescription drugs in 2004 was at a rate of 5.6% in volume and 8.9% in value, year over year. While it was the smallest increase since 1998(8), it still outpaced the growth in the other major health categories (physicians, facilities), as demonstrated by total spending in prescription drugs, which more than doubled from $7.6 billion in 1996 to $18.0 billion in 2004(14). The cost for prescription drugs thus represents a significant expense, one which is of concern to policy makers and health/finance departments across the country.

There are many variables that have contributed to this increase in prescription drug costs, including, the marketing/R&D activities of the pharmaceutical manufacturers and the prescribing practices of the physicians (increased drug utilization, changes in therapeutic choices). Research by Morgan has also suggested that the combined effect of federal price regulation, jurisdictional generic substitution policies, provincial price freezes and policies governing the coverage of drugs for seniors and the indigent population(15), are also having an impact on the growth of prescription drug spending in Canada. The issues related to the growing costs of pharmaceuticals thus may not be simply deemed to be a function of identification of alternatives and subsequent education of prescribers (physicians). The reality is that the prescribing process is complex, being driven by a number of variables unique to the physician, the patient and the prescribing environment.

In Nova Scotia, drugs are the second largest health expenditure, accounting for 17.8% of the total health budget, compared to 16.7% nationally(16). The impact of this

expense is in the Nova Scotia provincial pharmacare program, which grew 24% between 2000 and 2004(17), and is projected to increase by another 16.5% over the next fiscal period(2005). This type of increase is significant in any jurisdiction, but in a province that operates within an environment of single digit revenue increases, and whose focus is on maintaining a balanced budget(18), double digit increases in one area means that something has to be reduced elsewhere, just to maintain the balance.

Given the significance of this issue for the management of provincial financial integrity (while insuring adequate health coverage for its residents), this research is both timely and relevant. The greater the level of insight we can realize into the prescribing behaviour of physicians, the more likely it is that we can influence and direct their actions, such that they become more effective contributors to the fiscal solution, without compromising the health of their patients.

1.1.2 Objectives

The objective of this research was two-fold. The first objective was to develop "constituency specific insight" into the variables that influence physician prescribing behaviour in Nova Scotia. That is, the variables that influence prescribing activity in this province are not necessarily the same as those that influence prescribing in other constituencies (New Brunswick, Ontario, the US, etc). There are a number of influences on physician prescribing, among which pharmaceutical company's marketing activity plays a large role, as do a number of other variables associated with physicians and their practices, all of which may have a varying degree of impact the likelihood of them prescribing a particular drug.

The second objective was to gain greater insight into the fundamentals of innovation adoption, and specifically, determine if various physician profiles are more or less likely to prescribe new products from a newly introduced drug category. Evaluating the influence of individual physician, practice and patient variables through the use of multiple regression (factor analysis and stepwise logistic regression), provides insight into the nature of the relationship between two or more of the identified variables, and their expected covariance.

The attempt by this research to evaluate physician innovation and adoption relates to the innovation-decision process proposed by Rogers, who proposed the five stages through which an individual passes en route to adoption; knowledge, persuasion, decision, implementation and confirmation(19). Considering the adoption of new drugs, one of the critical stages is persuasion, defined as the point where an individual forms a favourable or unfavourable attitude toward the innovation. Within the social context of physicians, this stage typically involves the evaluation of the drug through trial. That is, the physician may provide drug samples to patients, or write prescriptions for a small number of patients to evaluate the drug prior to adoption (ie broader application to his/her patient population). This persuasion or trial period is thus critical to this research and its stated hypotheses.

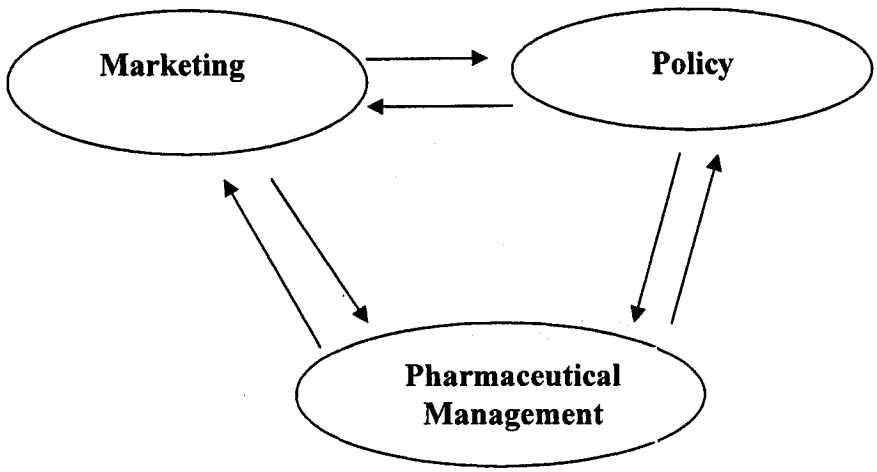
Of particular relevance here is the attempt to develop insight, not just into prescribing, but into the actual adoption of a new drug category, when its costs relative to the alternative are significant, yet its medical justification may be marginal.

1.1.3 Interdisciplinary Perspective

The nature of this PhD dissertation is interdisciplinary, which is to say that it provides research opportunities for topics that transcend the traditional departmental boundaries(20). To the layperson, this means that several related (in this case three), yet seldom integrated, disciplines are considered in the context of the research, the hypotheses and interpretation of the data. The three schools which contribute to this area of research are The School of Business, The School of Public Administration and the College of Pharmacy. The three disciplines against which the research and results from this dissertation are interpreted are marketing, policy and pharmaceutical (prescription drug) management, respectively. An intuitive relationship demonstrated in Figure 1-1.

While the literature review involved searches in all three disciplines, the challenge was one of focus and resisting the temptation of pursuing "literature creep". In many respects, this type of research parallels that which is ongoing in the field of health management globally, where the primary objective is knowledge transfer (research to application/implementation). The real question relates to our ability to ensure that valid insights identified by one discipline are effectively communicated to another discipline, where their relevance may have a greater impact. Thus, while the literature in all three of these areas is well-populated with studies, applications and theory, the challenge is to ensure that the research, analysis and interpretation all work together to present the most meaningful insights for each area, while supporting the primary objectives of the dissertation.

Figure 1.1: Marketing, Policy and Pharmaceutical Management Interrelationship



1.2 Marketing and the Pharmaceutical Industry

1.2.1 Influencing Physician Prescribing Behaviour

The literature on the influence of medical, non-medical, physician and non-physician variables on physician prescribing behaviour is extensive(21-37). While much has been done to understand this interrelationship, more work is required to understand the influence of individual variables, and more importantly, their influence on each other (covariance) in the prescribing process.

Within the literature, there are a number of models that have been proposed to provide a visual demonstration of variable interaction and degree of influence on the physician. Before we consider the models of physician influence, however, we need to understand the traditional and current marketing models used by the pharmaceutical industry in their development of marketing strategy to increase sales (writing of prescriptions) of prescription pharmaceuticals.

Historically, the marketing approach followed by the pharmaceutical industry globally, was to target its efforts toward the physician (Figure 1-2)(38). To a certain extent, this model still exists in markets where direct to consumer (DTC) advertising is not allowed. Despite this, there is an adjacency influence of DTC advertising on non-targeted populations (ie. DTC advertising in the United States has a spillover effect in Canada through print, broadcast and electronic media), and as such, the traditional model is less relevant.

As a result of the gradual reforms in the regulations on DTC advertising (in the United States) over the last 10 to 15 years, we have seen the evolution of a two pronged marketing approach. This new strategy consists of a continued focus on the physician, while targeting a complementary (and concurrent) message toward the patient (Figure 1-3), with the objective of educating and informing the end user, and peripherally, influencing (reinforcing) the physician's interpretation of the message(39). In markets like the United States, the two channels are acknowledged and pursued. In markets like Canada, however, where DTC advertising that combines the drug with the indication in the same message is not legal[1], its influence still exists (either through the adjacency effect, or indirectly through patient groups who may lobby to have particular drugs added to a jurisdictional formulary) albeit more subtle than the American approach. To this end, we must still consider the influence on consumers in our study of prescribing in Nova Scotia.

---

[1] In Canada, drugs may be advertised to consumers, but either the name of the drug appears with no medical condition mentioned, or the medical condition appears with no drug named(232).

Figure 1.2: Traditional Pharmaceutical Industry Marketing Strategy

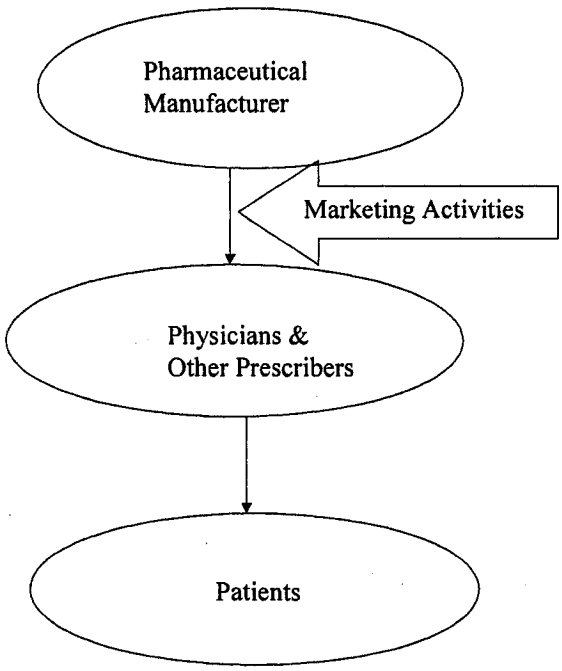
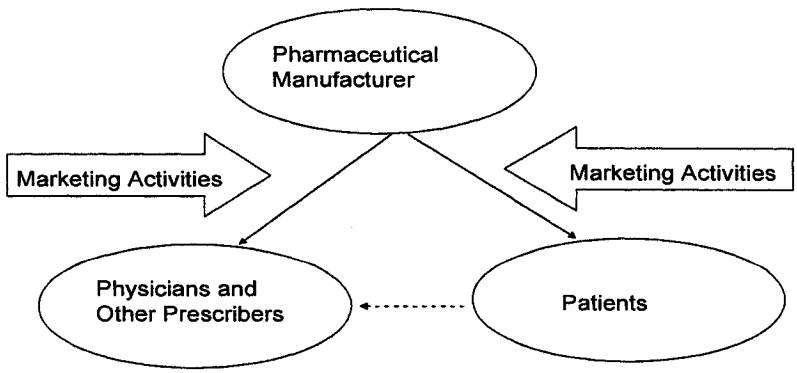


Figure 1.3: Pharmaceutical Industry Marketing Strategy in 2006

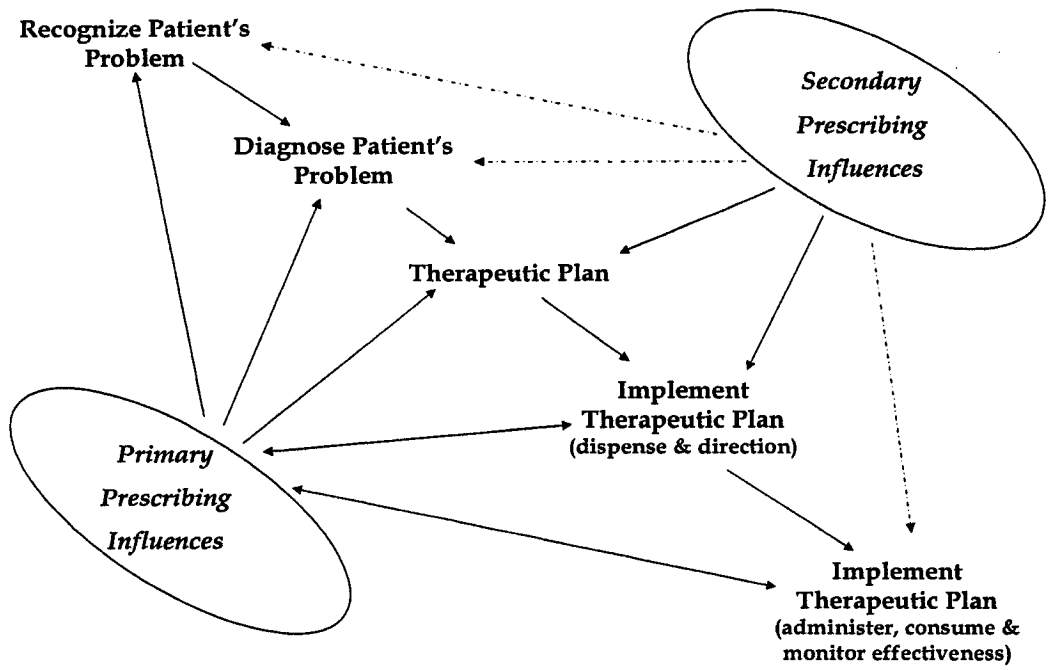


In addition to the targeted promotion we see in Figures 1-2 and 1-3, there is another level of consideration, as outlined in Figure 1-4. In this scenario, primary influences typically include physician specific factors, and secondary influences include non-physician characteristics such as those individuals or groups that may influence their decision.

Understanding the extent to which primary and secondary factors influence prescribing activity is critical, as these factors, to a greater or lesser extent, predicate the defined market size for a specific product. That is, the professional identification of a condition, association of that condition with a specific intervention, and the selection of one intervention over another, will be a direct artifact of the activities of the physician population, and more importantly, the success of the pharmaceutical company in reaching and influencing that group of prescribers. Although, as indicated above, extensive research has been done evaluating the factors that influence physician prescribing, there are a number of gaps in the literature, specifically in the areas relating to the interdependency between marketing activities and physician specific characteristics.

To this end, the question is, to what extent has the pharmaceutical marketing strategy changed, given the realities of the Nova Scotia (Canadian) marketplace, and to what extent does this new "marketing mix" influence prescribing. This study will consider the relationship between physician variables, patient variables and marketing effort in an attempt to evaluate the interdependencies between these variables, and the extent to which pharmaceutical marketing strategy has achieved its objective of getting physicians to write more prescriptions, or to write prescriptions for specific drugs.

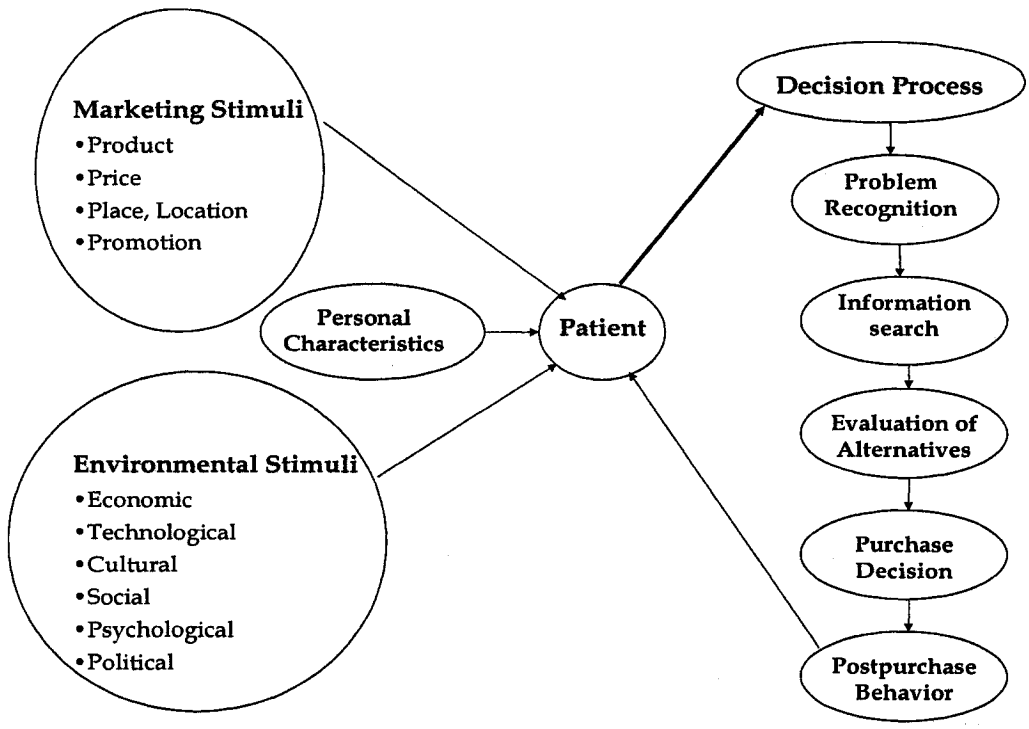
Figure 1.4: Flow of Influence Within the Medication Use System Model (Prescribers Decision Process) Adapted From Hepler(4)



While there are numerous factors that may influence a physician's prescribing behaviour, the factors that influence a patient's decision process (Figure 1-5) with respect to their pursuit of a pharmaceutical (more specifically, clinical) intervention for an identified condition must also be recognized and considered. While it is not the objective of this dissertation to develop hypotheses around patient influencing variables, it is important to acknowledge the influence of the patient decision making process, and its ultimate role in the development of product level marketing strategy. Within the context of health care consumers, we can see that the decision process involves recognition of a

problem which may lead to either evaluation of alternatives prior to visiting a physician, followed by a conscious decision to accept the physician's recommendation. This decision process is subsequently influenced by the influence of external stimuli as well as their own characteristics.

Figure 1.5: Patient Decision Making Process



The patient's role in influencing the physician is recognized, and as such tends to be approached using a strategy parallel to the traditional business to consumer marketing approach. While the model in Figure 1.5 is a construct based on the consumer decision making literature(6, 40-43), this direction of strategic evaluation involves another entire body of literature that is not directly related to the focus of this research, namely,

combining an appropriate marketing mix within the context of the existing external stimuli, to ultimately influence the consumer's (patient's) decision process. Typically, the approach taken by the pharmaceutical industry is to develop an overall marketing strategy that is both complementary to the activities targeted at the other audiences, and appropriately timed to ensure maximum synergy (integration) with promotional activities targeted at the other parties.

1.2.2 The Physician as a Consumer

We typically think of consumers as one of two types, those who buy for their own consumption, or those who buy for someone else. Marketers tend to position their messages to target one of these two types of consumers. Physicians, indeed many health care professionals, however, are unique in their "consumer/consumption" role. They are unique in that they are neither the consumer nor the purchaser. Although they may recommend (prescribe) a product, they are not necessarily concerned or influenced by the price of the product. Their reward for the "purchase" may be vicariously provided through seeing the health of a patient (in this case, the ultimate consumer) improve or, in some situations, through incentives from the manufacturer.

Given the unique nature of the physician as a consumer, the marketing strategies employed in the pharmaceutical industry are in sharp contrast to those used in other markets. The primary reason for this is that in the prescription drug market, the physician is the decision maker who identifies the product category, and selects a brand from the alternatives within that category on the patient's behalf. The most appropriate comparison between the physician as consumer, and other markets, is with that of an agency

relationship, where, in this case, the physician is the agent (38, 44-46) or advocate for the patient (47). While it is the physician who makes the decision, it is still the patient who uses the product, and ultimately takes responsibility for payment for the product.

Given their role as intermediaries and the key decision makers in the prescribing process, it is to be expected that physicians would become the target of the marketing activities associated with prescription drug. For years, they have been marketed to using any means available to the pharmaceutical industry (48, 49). The metric against which the industry measures the success of their marketing effort is the volume of drugs sold, or more specifically, the number of prescriptions written by the physician. The actual writing of a prescription is thus indicative of a physician's recognition that a product is the best alternative to address the patient's condition, or is at least a viable alternative, worthy of closer evaluation.

1.3 Policy and the Pharmaceutical Industry

While there are commonalities between the United States and Canada with respect to the evolution and development of the pharmaceutical industry, there are two areas where their paths diverge, namely, legalized DTC advertising, and health policy that relates to the pharmaceutical industry. DTC advertising was addressed earlier in this chapter, and will be addressed further in the literature review. The primary issues of policy relate to formulary approval, pricing and nature and extent of coverage for various sectors of the population. While it is not the intent of this study to address the impact of pharmaceutical marketing on policy, it is important to understand the relationship, as demonstrated in Figure 1-1, as ultimately, the evolution of the physician as an

adopter/prescriber will be evaluated with respect to his/her impact on health, and specifically, pharmaceutical policy.

In Canada, drugs are reviewed by the Therapeutics Product Directorate to assess their safety, efficacy and quality before being authorized for sale in Canada (50). Once a drug has met the submission requirements of the Therapeutics Product Directorate, and is approved for use in Canada, it in turn receives a Notice of Compliance (NOC). With this NOC in hand (and often before), and in conjunction with a number of other submission requirements, the pharmaceutical company, or its agent, will make an effort to have this drug listed on a provincial formulary, such that it is eligible for coverage under the respective provincial pharmacare programs(51). Currently, a submission is made by the pharmaceutical industry to the National Common Drug Review (CDR) housed at the Canadian Coordinating Office of Health Technology if it is a new drug entity, or to the Atlantic Common Drug Review (ACDR) for the Atlantic provinces, for all other types of submissions. Each province or drug plan participating in the CDR and/or ACDR will receive a listing recommendation. Following receipt of the listing recommendation, each province will either accept or reject the recommendation, and inform the pharmaceutical manufacturer of the benefit (pharmacare coverage) status of the drug in their province (52).

While each province ultimately makes its own decision with respect to whether or not a product will be listed on its formulary, common to all Canadian provinces is the requirement to have a NOC issued federally before it can be assigned benefit status provincially.

The pharmaceutical manufacturers are thus often in a position where they attempt to generate interest among health care practitioners and the public, thus gaining support for a drug (before the drug receives approval as a benefit under the pharmacare program), in an effort to pressure the policy makers (politicians and other decision makers) into moving the drug onto their respective provincial formularies.

CHAPTER 2

LITERATURE REVIEW

The introductory chapter of this thesis provided an overview into the history and development of pharmaceutical marketing strategy. Given this overview of who is influenced (and by whom), we have the framework within which the literature review can look specifically at the influencing prescribing variables as they relate to individuals or individual characteristics.

Considering the interdisciplinary nature of this dissertation, it was necessary to review the literature from a number of different disciplines (health, health management, pharmacy, marketing, business management, psychology, sociology), ultimately identifying the existing gaps and areas of thought that overlap, or cross over disciplinary boundaries. This process subsequently led to the development of the research statement, hypotheses and assumptions, as presented in Chapter 4.

The literature review itself has been divided into two parts. Chapter 2 considers the literature with respect to the nature of influence on prescribing, while Chapter 3 addresses theoretical development, interpretation and consideration, identifying and discussing the most relevant interdisciplinary theoretical considerations with respect to physician prescribing behaviour.

This portion of the literature review, Chapter 2, commences with an overview of the innovation diffusion and adoption literature, as much of our insight into the adoption of new technologies (prescribing new drug categories) comes from this area. Consequently, the final three chapters of this part of the literature review address the

macro influences of direct to physician and direct to consumer pharmaceutical marketing, followed by the influences of practice characteristics and physician profile.

2.1 Innovation Diffusion and Adoption

Given that, in the end, the question is really "To prescribe or not to prescribe", it is important to gain insight into the current thought on diffusion and adoption, and its role in understanding the issues related to influencing prescribing behaviour. This area of the literature review thus focuses on the adoption of new technologies in general, not specifically innovations associated with health care. While an extensive literature review on the topic of spreading and sustaining service innovations in health service delivery organizations was recently published by Greenhalgh (53), there is still additional insight into the adoption of technology in other disciplines, which we can relate back to health care, and more specifically, to the adoption of prescription drugs.

A review of the adoption of technology provides insight into key variables that may be directly involved in physician adoption, or more specifically, the variables likely to influence prescribing behaviour. This review thus provides a foundation into how one might consider the application and impact of various independent variables and their potential covariance.

The first step in any discussion on diffusion/adoption is to ensure an understanding of the stages and definitions associated with this process. Diffusion is defined as the process by which an *innovation* is *communicated* through certain *channels* over *time* among the members of a *social system* (19).

- The innovation is an idea, practice or object that is perceived as new by an individual or other unit of adoption.
- Communication is the process by which participants create and share information with one another in order to reach a mutual understanding.
- A communication channel is the means by which messages get from one participant to another.
- Time is an important element in diffusion, as it is involved in the process by which an individual passes from first knowledge to adoption or rejection, as well as the innovativeness, or speed by which an innovation is adopted relative to the other members of the social system.
- The social system is considered to be a set of interrelated units that are engaged in joint problem solving to accomplish a common goal.

Although initially there were a number of research traditions (schools or disciplines that considered adoption in their own specific context), by the late 1970s, all diffusion research traditions had effectively merged. Arising from the original research traditions were two primary disciplines which provided the foundation for this dissertation, namely; Marketing and Public Health and Medical Sociology. Interestingly, it was the latter, through a study commissioned by the (marketing research department of) Charles Pfizer Company, that really established our fundamental understanding of the diffusion and adoption of new drugs by physicians (54). While some elements of this diffusion model have been questioned (55), there are still a number of observations from Coleman et al's initial research that remain relevant. Considering that marketing

managers have long been concerned with how to launch a new product, their ultimate measure of success is through the rate or level of adoption among a target audience, and of course, retention of use among the adopting population.

Individuals (physicians) are not passive recipients of innovations. They seek them out, they experiment with them and evaluate them, they worry about them, they collaborate with peers and seek reinforcement, they modify them and attempt to adapt them to their specific circumstances, they challenge them and may even become emotionally attached to them. All of this may be done in isolation or with other members of their social system.

Within the context of this research, we need to recognize that the adopter is an actor who interacts purposefully and creatively with a complex innovation (53), and plays a critical role in the diffusion of innovations both within health service organizations, and the medical community at large. This being said, we need to gain a greater understanding of the influence of individual characteristics on adoption.

While all of the traditional variables associated with diffusion apply, probably two of the more important considerations, as proposed by Peay and Peay, are preparedness to prescribe the new drug, and presentation of particular circumstances which are appropriate for its use (56). While it is unlikely that the latter event can be predicted, an individual's preparedness to prescribe a "new" drug is an independent variable which may be predicted to a greater or lesser extent, depending on the physician, patient, and environmental information available.

To appreciate the variables that may go on to influence physician adoption, one must revisit the innovation-decision process (19).Prior conditions required to create an

environment that will lead to the physician innovation-decision process taking place include:

- Previous practice
- Felt needs/problems
- Innovativeness
- Norms of the social system
- Presence of circumstances appropriate for trial

If these conditions are met, then it is more likely that an individual or group will seek out knowledge, be open to persuasion, decide to initiate trial, implement and evaluate, as described in the steps below:

1. Knowledge – Characteristics of the Decision Making Unit[2]
    a. Socio-economic characteristics
    b. Personality variables
    c. Communication behaviour
2. Persuasion – Perceived Characteristics of the Innovation
    a. Relative advantage
    b. Compatibility
    c. Complexity

---

[2] In this case, the decision making unit is typically the physician, but may also be considered the combination of the physician and the patient.

d. Trialability

e. Observability

3. Decision

    a. Adoption

    b. Rejection

4. Implementation

5. Confirmation

    a. Adoption – continued

    b. Adoption – discontinuance

    c. Rejection – continued

    d. Rejection – later adoption

When considering the traditional approach to adoption, one might determine that the characteristics of the adopter and the adoption environment are stable over time. Waarts et al, however, suggest that the driving factors in adopting innovations will change as the diffusion of the innovation within the market progresses (57). That is, while it is well known that different groups of adopters have different characteristics concerning the rate of innovation adoption (19), the factors explaining the adoption of innovations will not be stable over the diffusion process, but will change as larger numbers of individuals adopt the innovation. While this work was done on organizational adoption of Enterprise Resource Planning software, the insights realized are applicable to the issues of physician adoption, and support the notion of the existence of a broader mix

of variables likely to influence prescribing. Waarts went on to suggest that in the first stages of adoption of innovation by organizations, the most important stimulating factors are a combination of internal drives (personal characteristics), whereas subsequent adopters are more influenced by a mix of stimulating factors focusing on the practical issues(57).

This insight is particularly relevant, given the longitudinal nature of this research, and may account for variance in adoption profile over the period of the study. It is further supported by the actual marketing mix used by the industry itself, where their given combination of direct to consumer, journal and physician detailing changes with the nature and "perceived innovativeness" of the drug (58).

Another consideration in the adoption process relates to individual versus team decisions. Contrary to the traditional five steps associated with individual trial and adoption proposed by Rogers (19), Wozniak suggests that adoption and technical acquisition decisions are made jointly, and that the influences of the determinants of that decision differ with the timing of adoption and the channels of information dissemination (59). This suggests that the traditional steps may not occur successively, but that in effect different stages may need to be done concurrently to achieve maximum response. Despite this observation, his work concurs with earlier research with respect to differences between the individuals at various stages of adoption, as he indicates that adopters find information more useful in the early stages of adoption decision process than in the later stages. Again, this has implications on the traditional marketing model of trial followed by reinforcement.

While Wozniak questions the actual order of the traditional evaluation events, Olshavsky questions the individual's approach to innovation evaluation (60). The traditional marketing assumption has been that individuals faced with a new stimulus engage in some type of attribute by attribute evaluation, in which the interpretation of the innovation is a function of the elements or attributes of the stimulus. Olshavsky suggests that people may be more inclined to form an evaluation by placing the new stimulus into an existing category, thus simply giving the innovation the same evaluation that it gives other category members. Again, within the context of the traditional approach to innovation adoption, this suggests that all innovations are not adopted using an attribute approach as suggested in Rogers' step 2, " persuasion – perceived characteristics of the innovation". Unlike the traditional steps, Olshavsky suggests that there are four other processes influencing evaluation, namely, forming evaluative criteria, forming expectation about the innovation concept, assessing satisfaction with an old product, and comparing the new and the old products.

An intuitive consideration in adoption is that "adopters are more likely to adopt", and consequently, "prescribers are more likely to prescribe". With the exception of work by Dybdahl, health research in this area has been minimal, and his findings were inconclusive (61). Suggesting that prescribers are likely to prescribe relates to the acceptance of innovation(s) by the adopter after they have embraced it. Work by Shih and Venkatesh supports this logic, as they found that adopters with higher use-diffusion levels (that is, they use a newly adopted product more often and in a greater variety of ways), are not only more satisfied with the current innovation, but are more interested in adopting future innovations (62). Similarly, while suggestions that frequent users are

more interested in adopting future innovations, Marinova determined that innovation effort takes shape over time under two opposing forces: market knowledge diffusion (how will I use this product in the future) which propels innovation and satisfaction with past performance (I am content and am not interested in new applications or innovations) which hinders innovation (63). This in turn may impact adoption of "perceived similar" products within a product category (ie cyclooxygenase-2 inhibitors (COX-2s)) or between perceived similar product categories (ie non-selective non-steroidal anti-inflammatories (NS-NSAIDs) versus COX-2s).

While much of the original insight proposed by Rogers holds across a number of different applications, there are two areas that have been reconsidered that relate specifically to this research. The first area to reconsider relates to the classification of innovation, which typically involves assignment of the innovation into one of three classes (64): 1) continuous innovation where there is little change in the technology or the behaviour or consumers toward it, 2) dynamic continuous innovation where there is change in the technology, but little change required in the consumers' behaviour toward the product's use, and finally, 3) discontinuous innovation, where consumers must learn new or changed behaviour.

The second area relates to the theory that there is a clear difference between the personality of the innovators and the early adopters versus the remainder of the adopting population. While there may be some merit here, McDonald et al suggest that this variance is a function of behavioural variables (65), not the psychographic and demographic variables maintained by Rogers (19). In effect, behaviour predicts like-behaviour, which again supports the hypothesis that prescribers prescribe, and it becomes

more a function of their socially defined variables rather than their psychologically defined variables.

If behaviour predicts behaviour, preparedness to prescribe a new drug as proposed by Peay and Peay thus becomes a critical step in the process to actually prescribing (56). Considering behaviour, McDonald proposed that there may be a number of behavioural variables which influence the likelihood of prescribing. These may include, among others, individual prescribing habits, size of the practice, location of the practice, and the nature of their social groups. Despite McDonald's proposal of individual behavioural influence, there is still a body of literature that has looked at the variables associated with a prescribing population, and recognizes the role of collective behaviour on individual adoption (66), as well as the role of social networks on diffusion and adoption (67). Given this, we realize that there is still support for the influence of demographic variables as an individual's social and normative groups tend to be comprised of like people. To this end, both gender and age are also viable considerations as predictors of prescribing behaviour.

Considering the traditional approach to adoption of innovations in combination with much of the current area of thought, we realize that while the adoption or rejection of an innovation may be dependent on individual variables, it is more often than not the multiple interactions that arise in various settings that determine the success or failure of an innovation and its subsequent dissemination initiative. It is also important to recognize that different product markets may exhibit different adoption characteristics, thus impacting the extrapolation of insights between products and markets.

2.2 Influences on Physicians' Decision to Prescribe

The objective of the first chapter of this literature review was to identify critical areas of thought around diffusion and adoption, and to relate them to fundamental concepts of adopting new drugs and subsequently prescribing them. The second part of this literature review may be considered an analysis of how well the adoption variables have been interpreted, and subsequently applied.

At the level of strategic marketing development, the manufacturers must determine how to present "new" drugs to the target audiences. They recognize that the success of this new product is dependent on many variables, some that they can control (promotion, price, channels of distribution) and some that they can't control (regulation, scientific evaluation leading to publication, independent third party reviews). Additionally, the manufacturer recognizes that the success of its new drug depends on the nature of the physicians, and whether they will perceive the new product as a radically differentiated offering (discontinuous innovation) or as a minor variation of existing functionalities (dynamically continuous innovation), namely, the current opportunities for action that are afforded by existing products in the market (60, 68, 69).

While the objective of this research is not to evaluate product positioning strategy, it must consider the primary influences on a physicians' decision to prescribe, as they relate to the main categories of the marketing activities pursued by the pharmaceutical manufacturers. These primary influences are either a function of the environment in which the physicians practice, or they relate to the characteristics of the physicians themselves.

2.2.1 Pharmaceutical Marketing Activity

The relationship between a physician and a patient has some similarities to the relationship that exists between a variety of suppliers and customers in any given market. In consideration of this environment, marketing has shifted much of its dominant logic away from the exchange of tangible goods, toward the exchange of intangibles (specialized skills and knowledge) and processes (70). This, in effect, moves marketing toward a more inclusive dominant logic, one that integrates goods with services, and provides a broader foundation for the development of marketing thought. Work by Scharitzer and Kollarits in this area suggested that there is a significant relationship between the level of satisfaction expressed between physicians and pharmaceutical sales representatives and their subsequent prescribing behaviour (71). Thus, while the service centered view of marketing still plays a role in a physician's practice, the focus of this research is on diffusion and adoption, and the key variables that influence adoption in the prescribing environment.

This chapter addresses the issues around direct to physician and direct to patient (DTC) advertising, and its subsequent influence on prescribing behaviour. While it is not within the scope of this study to evaluate the influence of consumers on physician prescribing, this area of marketing activity is a significant element in the pharmaceutical marketing strategy pursued by the pharmaceutical industry in the United States, and is worthy of acknowledgement and discussion, given the tendency for policy diffusion between the two countries. Additionally, it quite possibly has an influence on Canadian consumers already (72), through passive overlap or active access to American television, internet and print media.

The search in this area involved mining the health related marketing/behaviour literature to identify studies that would provide specific insights into this research. To paraphrase David Revzan in his 1950 review of a collection of essays in marketing theory, this literature review served the purpose of ensuring that analysis leading to theory would not merely condone practice, but should rather seek to improve and direct such practice (73).

In addition to the literature relating to the influence of marketing activity targeted at physicians and consumers, we must also consider the general marketing approach pursued by the pharmaceutical industry.

2.2.1.1 Influence of Direct to Physician Marketing

It seems intuitive to suggest that the probability of prescribing a drug is a function of the marketing effort expended on that particular product. This marketing effort may be more specifically defined as corporate or academic detailing (the cost of maintaining a physical staff of individuals who visit physician's offices) and the associated cost of drug "trial samples", and other commercial sources of information targeted toward the physician for one drug, versus the other drugs in its category. It is worthwhile to note that the use and expense associated with free drug samples is a long standing industry practice (74), and is supported in the marketing literature as an excellent way to introduce new products, or dislodge a market leader (75). These two categories, detailing and product sampling are complimentary, and together they typically account for over 80% of the total drug promotional expenditure (58, 76).

Despite the fact that within the literature there is some disagreement on the impact that drug promotion has on adoption, there is little disputing the fact that if a particular promotional tactic (or strategy) does not work, the pharmaceutical industry would most likely discontinue its use. Hawkins and Hoch suggested that low involvement processing leads to poorer memory but greater belief (77).What this research suggests is that the less time an individual spends thinking about a given point or observation, the more likely they are to consider it true, while conversely, they may be less likely to remember it. This work is supported in part by Prosser et al who defined general practitioners as largely reactive recipients, rather than active searchers of new drug information, and in many instances relied heavily on the pharmaceutical industry as the major information source (78).

Given the pharmaceutical industry's approach to its market (brief, frequent visits), we now start to gain insight as to why physicians feel that they do not believe that they are influenced by the marketing activities of industry, even though research by Avorn, Guldal and others would tell us otherwise (79, 80). Watkins et al have even gone on to say that general practitioners who receive information and visits from the pharmaceutical industry are responsible for higher prescribing costs and prescribe in a less rational manner than their peers who function without direct pharmaceutical industry influence (81). Additionally, Muijrers et al found a negative relationship between prescribing according to evidence-based general practical guidelines and the frequency of visits by pharmaceutical sales representatives (82).

An extension of the physician's "perceived resilience or imperviousness" to advertising is the consensus among both high and low prescribing populations of

physicians that they like to prescribe drugs with which they are familiar, which means that there may be some reluctance to prescribe new medications(83). When considering the definition and application of the word familiar, we know that brand names have greater impact on choice in a search product where less total quality information on components is available (84). That is, when choosing between two similar products, the familiar brand name is often considered when less qualitative information is available against which to base the decision. This, in turn, can have a significant impact on usage (prescription) when that brand name is associated with pioneer or a "first-to-market" in-category product (85). Leffler suggested that brand loyalty may result from the high costs of acquiring new information or of learning by experience, and subsequently may generate persistence in prescribing patterns, thus influencing physician responsiveness to promotional efforts (86).

While physicians might believe that they are impervious to marketing, there is support for the relationship between physician satisfaction with their pharmaceutical sales representatives and their prescribing behaviour (71), as there is for the influence of drug company representatives through product information dissemination (87). Work by Watkins et al suggested that frequent contact with a drug representative was significantly associated with a greater willingness to prescribe new drugs and to agree to patients' requests for drugs that may not be clinically indicated (88). Additionally, promotional impact should not be limited to the perception that a manufacturer is simply communicating their message. Majumdar, et al demonstrated that while publication of new evidence may be associated with modest changes in individual practice, industry led

promotional activity appears to have a greater influence on the adoption of this new evidence (89).

Marketing success is not simply a function of the marketing or advertising dollars spent, but it is more a function of the message and the target audience. Kerr et al noted that the increase in COX-2 prescribing in Australia coincided with a period of energetic marketing to the medical profession, which promoted the message that the new COX-2s were "safer" than traditional NSAIDs (90). Additionally, retrospective work by Van den Bulte on the original study done by Coleman with respect to the medical community's understanding of tetracycline, suggests that it was through aggressive marketing efforts targeted at the physician population, and not social contagion, that this product gained in popularity and application (55).

It is interesting to note that surprisingly little is documented in the academic literature about the actual efficiency of marketing directly to physicians through detailing, and much of the evidence on the effectiveness of this form of promotion is anecdotal. Additionally, it is important that we temper the relationship between detailing and sampling, acknowledging that samples are often dropped off without an actual detail event.

Recent work by Mizik, however, has attempted to quantify this impact, and has subsequently determined that detailing and free drug samples have positive and statistically significant effects on the number of new prescriptions issued by a physician (albeit the magnitude of the effects are modest) (91). Interestingly, this impact is only significant when one considers the lagged effect, which has been shown to not simply dissipate in one year (Mizik chose a 6 month period), but in many cases, has a persistent

effect on product sales for more than 12 months (92). Gonul found that a certain level of detailing positively influences prescribing, but excessive detailing becomes counter-productive (93). Unlike Mizik's study, Gonul interpreted the feedback from a panel of physicians, rather than determining the correlation between units of samples and detail expenditure with changes in prescribing habits. While Gonul's work may have more limitations, given that the insights were gathered through panel data, it is supported by the work of Manchanda and Chintagunta, who demonstrated that there are optimal levels of marketing, after which incremental increases are negatively elastic (94). That is, the percentage increase in sales declines relative to a similar percentage increase in marketing expenditure.

Although we typically consider detailing from the pharmaceutical manufacturer's perspective, when pursued by governments and health management organizations it is referred to as academic detailing (counter detailing). While counter detailing has been shown to be a very effective technique to encourage adoption of clinical practice guidelines (95-97), it is not likely to achieve widespread use, as it is expensive, and, as noted by Mizik (91), physicians are not always receptive to this approach.

While the studies mentioned in this chapter address the positive impact of product detailing, the direct influence of free drug samples and journal advertising on prescribing (sales) of drugs, is often difficult to quantify, as their activity is not mutually exclusive. Work by Jones found no clear relationship between the extent of the advertising of a drug and the amount of prescribing by general practitioners (98). In fact, this research suggested that while advertising in journals is only one of many factors which influence general practitioners to prescribe, it is probably not a major influence. Interestingly, there

is very little work discussing the impact of drug samples, independent of the pharmaceutical representative. Only Schumock made an attempt to qualify this, and his results suggested that free samples influenced prescribing decisions, but the information disseminated by pharmaceutical sales representatives had no significant impact. It would seem that it is difficult to separate one from the other (99), and the covariance, or relationship between the two cannot be discounted.

Although it may be difficult to separate journal advertising from the marketing mix, and relate it back to response, it is an element of an organization's approach to market, and probably needs to be evaluated concurrently with the total marketing spending vs sales (prescriptions). While much of the literature focuses on the impact of marketing, it should be noted that if a drug is not promoted, it is unlikely that the physician will hear about it. Majumdar suggested that the publication of new evidence in peer-reviewed journals is associated with modest changes in clinical practice, but more active promotional strategies are required to accelerate the adoption of new evidence in routine clinical practice (89). The use of active promotional strategies was supported in earlier work by Hurwitz et al, who demonstrated that promotion outlays by market entrants contribute to expanding their market share, but price discounts have only a weak short-run effect on entrants' market share (100). Additionally, the predictable decline in promotional expenditure that is linked to an impending loss of patent status has been associated with a decline in prescriptions (101).

Considering the main elements of the pharmaceutical marketing mix, the literature tends to generally support the impact of all of the activities, but specifically acknowledges the role of detailing (be that academic or corporate) on the rate and volume

of prescribing. While there is much more work in the literature on this topic, this review provides insight into the key studies and general findings. Again, while it is within the scope of this research to consider the influence of actual promotional activities measured, relationships between physicians and their publics are not addressed here. That is, one must not forget the role of relationship marketing and the intricacies of the company-representative-physician relationship, and the role that it plays in both prescribing activity and brand loyalty.

2.2.1.2 Influence of Direct to Consumer Marketing

Although it is not within the scope of this research to measure the impact of DTC advertising on physician prescribing behaviour, it is well documented in the literature and worthy of discussion. While DTC advertising may be perceived as being a US phenomenon, the reality is that there is extensive overlap between the media and the images of US targeted DTC advertising on the Canadian consumer, and most likely on physician prescribing decisions made in Nova Scotia. One of the few studies that determined the impact of US DTC advertising found that in British Columbia, 87.4% of Vancouver patients in the study had actually seen prescription drug advertisements (72).

While there has been extensive research on this topic, physicians still hold true to the belief, as previously stated, they are not influenced by any form of targeted marketing activity (79, 102), be that pharmaceutical representative, patient, or journal advertisement. Despite this there has been much written about the marketing efficiency of DTC advertising, and its subsequent impact on prescribing behaviour through the medium of the patient, who makes a direct brand or product category request to their

physician (103). Even prior to the advent of DTC advertising, physicians indicated that one of the most common reasons for the use of many medications was patient demand (104).

The purpose of this chapter is thus to acknowledge that DTC advertising is an influence, and to address its measured impact on the patient. Given this, there is most likely a non-targeted impact in Nova Scotia, and while its degree of influence on physician prescribing decisions may be marginal, it is an area that may be worthy of additional research.

In 1997 the FDA in the United States loosened the regulations associated with DTC advertising, and I have chosen to consider the literature evaluating its impact since that time. This post-1997 period was selected, given that annual spending on direct-to-consumer advertising for prescription drugs tripled between 1996 and 2000, when it reached nearly $2.5 billion (76). Despite the increase from less than $500 million in 1995, DTC advertising still accounts for less than 15% of the total pharmaceutical marketing spending, with the majority of spending in this category continues to be targeted at the physician or the prescriber. Thus, while it may be a growing category, industry still recognizes that physician targeted activity has more impact.

Initially it was unclear what impact advertising targeted directly at the consumer would have. In 1998, shortly after the advertising regulations had changed, Peyrot et al did a random telephone survey of 440 central Maryland residents in an effort to determine prescription drug knowledge and drug requesting behaviour (105). Their study suggested that while DTC advertising had an effect on drug requesting, it was unclear whether requesting led to changes in prescribing behaviour. While this work did little to

determine the impact of DTC on prescribing, given that their sampled population was demographically representative of the US population, it did determine that a targeted message was reaching the appropriate audience. This work was supported in part by Mehta and Purvis, who determined that a broad range of individuals value DTC advertising, but they also determined that there was some variance among demographics (age, education, gender) with respect to comprehension, agreement with the message, and the expected impact of the message on the individual's anticipated exchange with their physician (106). Despite this, they still determined that older respondents are no more likely to insist on prescriptions than younger respondents.

Zachry et al took the approach of using a time series design on products advertised from January 1992 to December 1997 (107). Following the initial data reduction, they selected 19 specific agents that represented 13 national drug code directory classes. Their results suggested that the direct-to-consumer advertising expenditure was associated with physician diagnosing and physician prescribing only for certain drugs and drug classes. However, even when a statistically significant association was found, DTC advertising was deemed to account for only a modest amount of the variance associated with diagnosing and prescribing. Despite their results, the influence of DTC advertising, as determined by this study, is best summed up by their comment that the relationship between DTC advertising and physician prescribing and diagnosing is a complex process that is not well understood.

Vogel et al made an attempt, through literature review and the development of an economic model, to assess the probable effects of DTC advertising on the pharmaceutical industry in the United States (108). While their models suggest that DTC advertising

affects the price and quantity demanded of pharmaceutical products indirectly via its effect on changes in consumer demand, they gained little insight into the impact it has on prescribing trends, and recognize that more research is necessary to measure and clarify the impact.

One of the more thorough studies measuring the demand effect of DTC prescription drug promotion was carried out by Rosenthal et al for the Kaiser Family Foundation (39). Their approach was to measure the impact of DTC advertising on market share within a therapeutic class, as well as to measure its effect on an entire therapeutic class, which is effectively, a multi-stage budgeting structure.

They examined monthly data from August 1996 to December 1999 for five therapeutic classes, and data was collected on all the drugs in each class. While there are a number of approaches that can be used to measure the impact of promotional spending (simple flow, lag structure, depreciating stock following initial expenditure), they used the approach of simple flow. While an argument could be made supporting a lag design, their comparisons of results between all three demonstrated little difference. While their results varied between drug classes, their results suggest an average advertising elasticity of 0.1, where one would realize a 1% increase in sales following a 10% increase in DTC spending.

Again, as with previous studies, while DTC advertising was deemed important, it was not the primary driver of growth. Additionally, while their results are relatively stable at the class level, the influence of DTC advertising at the individual product level still remains quite uncertain.

Mintzes et al produced one of the few studies in which the researchers claim to conclusively link DTC advertising to increased prescribing (72). They surveyed a split population of physicians and their patients, with one study taking place in Vancouver, and the other in Sacramento. While patients in both markets reported seeing DTC advertising, Sacramento patients reported more advertising exposure and requested more advertised drugs than patients in Vancouver, but in both settings, patients with higher exposure to advertising requested more advertised drugs. Patients with higher self-reported exposure to advertising, had conditions that were potentially treatable by advertised drugs, and/or had greater reliance on advertising and subsequently requested more advertised medicines. The results of this study suggest that more advertising leads to more requests for advertised medicines, and ultimately more prescriptions. This study corroborates with work by Donohue et al whose research on the effects of DTC advertising suggested that not only was DTC advertising of antidepressants associated with an increase in the number of people diagnosed with depression, but it was also associated with an increase in the number who initiated medication therapy (109).

Once again, while it is not within the scope of this dissertation to measure the impact of DTC advertising on physician prescribing, we must recognize that there is a weight of evidence in the US that suggests there is a primary impact on the consumer, followed by a secondary influence on the physician. While this may not have as much of an impact in Canada, we need to be cognizant of its (potential) impact on prescribing behaviour.

2.2.2 Practice Characteristics (Clinical Profile)

This section of the literature review addresses the influence of the physician's practice (clinical profile) as it relates to the nature of their prescribing activity. It considers those elements of the practice that relate to patient demographics, the physical location of the practice and the nature of the practice (sole practitioner or multiple person clinic), and their subsequent influence on their prescribing behaviour.

2.2.2.1 Patient Profile and Demographics

While the previous studies have developed insight into the fact that DTC advertising actually reaches, and may have an impact on consumers, the issues that are addressed here are what types of consumers are influenced, and do consumer demographics lead to influence on prescribing decisions.

While there may be anecdotal evidence which suggests that patients influence prescribing decisions, Stevenson et al indicated that in interviews with 21 GPs in the Birmingham Health Authority, 100% of the respondents believed that they had experienced pressure for a prescription from patients, and they all indicated that they had prescribed when they would not have otherwise done so (110). Despite the small sample size and the qualitative nature of this study, the fact that all those interviewed supported the influence of patient pressure is important.

Britten et al considered the variables that influence patients with respect to their attitudes toward medicines and their expectations for a prescription (111). The study took place in South London, and surveyed 544 patients waiting in GPs offices. By virtue of

the geographic location of the study, the influence of DTC advertising was likely minimal, and thus it determined patients' expectations for a prescription as they were influenced by:

1. Demographic variables which included gender, age, marital status, period of time at the same address, age leaving school, ethnic group, employment status and prescription status (coverage).
2. Organizational variables which included day of the week and appointment status.
3. Illness variables including symptoms, reason for the visit and self medication.
4. Attitudes toward medicine, as measured by individuals' level of agreement with a variety of statements about medicines and their role in health and wellness.

While this study measured the influence of a variety of independent patient variables on prescription expectations, and it shows that attitudinal, demographic, organizational and illness variables are all significant precursors of expectations for a prescription, it doesn't measure the influence of the physician on patient expectations and behaviour. Despite this, the patient's expectations appear to still play a role in the prescribing decision, given a situation where a prescription is likely.

Unlike Britten, Skelly reported that research by Mamdani suggested that demographics, particularly age and household income, didn't play a role in patient expectations, but did appear to influence physician prescribing (112). This study determined that Ontario physicians practicing in low income neighbourhoods, are more likely to prescribe lower priced generic drugs for their elderly patients, regardless of the patients' drug coverage. This work is consistent with research by Soumerai and Avorn on

the impact of copay among lower income populations (113), and by Tamblyn et al on the impact of cost sharing among elderly persons and welfare recipients (114). In both studies, a demonstrated decrease in the use of essential drugs was established. None of the above studies, however, considered any physician variables, or the prescribing habits of the same physicians with patients outside the elderly or low-income cohort.

Work by Stewart in the Netherlands attempted to assess the effects of general practitioner and patient characteristics on prescribing behaviour (115). More specifically, he measured adherence to the global pharmacotherapeutic guidelines proposed by the WHO in 1987 (116) in combination with Barber's good prescribing guidelines (117). Stewart studied 251 general practitioners from 190 practices, with results that suggested adherence to prescribing guidelines (effectively, factors influencing prescribing behaviour) were influenced by two sets of variables, practice characteristics, and patient characteristics. More specifically, patient characteristics were either directly related to the patient, or were aggregated to a categorized patient level. Directly related variables of age and gender were shown to influence adherence to prescribing guidelines, while the aggregated variables mean costs, mean volume and different WHO anatomic therapeutic chemical classifications of drugs (effectively variance in drug selection for given conditions) were shown to influence prescribing. Interestingly, while patient variables were shown to influence prescribing, McKinlay suggests that patient attributes such as age, race, gender and socioeconomic status have no impact on diagnosis and test ordering (118), albeit this work did not consider whether or not this led to a change in prescribing behaviour.

The major limitation of Stewart's study is that, while inappropriate prescribing occurs, the scale and extent is not known. Furthermore, the focus of this research was specifically on adherence to guidelines (which are high-level), and not on the actual act of prescribing. As with Britten's and Mandami's work, we do not know what influence the physician had on the patient's expectations on prescribing outcome. This issue is of particular concern, given the work by Bradley which suggested that patient factors such as age, ethnicity, social class and education influence prescribing, but equally important were the doctor's prior knowledge of the patient, the doctor's feeling towards the patient, communication problems, and the doctor's desire to try to preserve the doctor-patient relationship (119). Additional work by Bradley (35), and McKinlay (120), while recognizing the many considerations, including medical, social, and logistic, that influence the decision to prescribe in general practice, support the reality of the act of prescribing as one that depends on a complex interaction of many disparate influences.

Work by Bennett focused on the variables that might influence the likelihood of switching a patient from one drug to another (121). Specifically, given the influence of NS-NSAIDs on gastrointestinal (GI) toxicity, her work focused on switching patients from NS-NSAIDs to COX-2s, and while it determined that a surprisingly low percentage (17%) of incumbent NS-NSAID users were switched to COX-2s during the period of the study, it did identify some switching influences. The results suggested that older, female patients were more likely to be switched from NS-NSAIDs to COX-2s. The weakness of this study, however, is twofold. Firstly, there is a perception that prescribers believe gender is an influencing variable associated with GI toxicity, and subsequently are more prone to switch females versus males. Additionally, the study only looked at switching

during the period from early introduction of the COX-2s (December 1999) to November 2001, a period during which prescribers may have not had all of the information desired to make prescribing decisions, and still hadn't formed their opinions (either on their own or through their peer groups) about the risks associated with the product.

Tamblyn et al suggested that a high proportion of elderly in a practice was associated with a greater likelihood of prescribing any new drug, but at the same time, there was a lower rate of new drug utilization among members of this cohort with multiple prescriptions (122). Again, while it may seem intuitive that patient's age might influence prescribing, this influence may simply be a function of their current drug regimen, and subsequently it is just as likely to influence more prescribing, as it is to influence less prescribing.

Another demographic variable, education, may have some influence on prescribing but this hasn't been tested. Mehta did, however, determine that individuals with advanced education are more acceptable to new approaches to health care, and most likely have insight and interest in new drugs (106), but it is unknown as to whether this converted into a change in prescribing.

In summary, while there is a large volume of research which supports the impact of patient demographics on physician prescribing, the results are inconsistent, and seem to reinforce the requirement that individual jurisdictional variables be taken into consideration. That is, extrapolations between similar populations in different geographic areas may be less representative than previously thought, and the inconsistency in influence simply reinforces the need for geographic (and geodemographic) specific analysis.

2.2.2.2 Location of Practice

Following patient demographics, the second practice consideration has to do with the population influence on the practice, that is, whether they are in a rural or urban setting. This location in turn may have an impact on a variety of factors ranging from the characteristics of the physicians and the patients, relative access to new information, continuing medical education and possibly extent of their contact with industry representatives.

Tamblyn's research indicated that new drug utilization was lower among generalists and specialists practicing in rural Quebec, and suggested that this may be a function of the characteristics of physicians who elect to practice in rural areas, their isolation from the influence of peers and colleagues, or possibly the reduced frequency of visits from pharmaceutical marketing representatives (122). One deficiency with this observation, however, relates to what is defined as rural and urban. Tamblyn indicated that Quebec uses "tarification" territories, which are classified as remote, rural and urban, to establish levels of physician remuneration. Unfortunately, these territories are not further defined by population density.

Stewart defined rural practices as those operating in an area with a population density of less than1500 addresses per square kilometer, and urban as those with more than 1500 addresses per square kilometer (115). While his work suggested that the location of the practice was significant with respect to adherence with prescribing best practices, he did not indicate the extent to which rural or urban practices were likely to prescribe.

Rural practitioners in Australia (obtained from a defined database of the rural workforce agency) felt that their remoteness and the remoteness of their patients had an influence on their prescribing activities (123). Cutts and Tett's work further suggested that of the 142 responding doctors practicing in rural Queensland (55% survey response rate), their propensity to prescribe a new drug was inversely proportional to the amount of monitoring required of the patient, following prescription. In general, rural physicians in this study had initiated fewer new medicines than their urban counterparts, but again we have a similar problem with the definition of rural. In another paper, Cutts and Tett suggested that the prescribing of recently marketed drugs was more likely by doctors practicing in less remote rural areas (124). Robust definitions of remote need to be applied in both of these situations, such that the responses may be consistently quantified. While the previous two studies demonstrated the variance between urban and rural practitioners with respect to prescribing "new" medicines, they did not really address the issue of the influence of rural vs urban on prescribing in general.

Another issue with respect to rural practitioners is their individual profiles, and those of their practices. Rural physicians tend to be older and more likely to be male than their urban counterparts (123, 125). Additionally, the patient profile of the rural practice tends to be more elderly than that of the urban practice. These variances may in turn have an effect on prescribing given the influence of patient age and physician gender as an influence on prescribing.

2.2.2.3 Nature of Practice

When considering the nature of the practice, there are really two areas of interest here, namely, the variety and frequency of occurrence of certain conditions, and whether the practice is a multiple person or single-handed (solo) operation. The latter relates to the opportunity the physician has to interact with other practitioners, and also addresses the influence of opinion leaders on prescribing behaviour. This is not to say that sole practitioners do not interact with their peers, but merely suggests that there is a greater opportunity for informal interaction among individuals working in the same clinic.

While it may seem intuitive, the frequency of opportunities available to prescribe a new drug influences whether it can be adopted into practice and used. As Peay and Peay suggest, in order for the drug to be prescribed, the doctor must be prepared to use it, and the treatment situation must be appropriate for its use (56). Effectively, the presence of more patients likely to benefit from a specific drug in physician's practice increases the likelihood of drug trial.

While the increase in the number of situations available in which to prescribe a given drug influences the likelihood of trial, as the number of drugs introduced into a given patient's regimen increases, the likelihood of prescribing a new drug into the patient's mix decreases. Tamblyn suggests that one explanation may be a function of the physician's lack of confidence and understanding of co-morbidity and contraindications between multiple interventions (122). Interestingly, Redelmeier et al suggested that there is an inverse correlation between the presence of a chronic disease and the likelihood of treatment of an unrelated disorder (126). In other words, despite Tamblyn's finding, the explanation may not support the relationship, as Redelmeier suggests that in no case did

the presence of the chronic disease justify withholding an effective medical treatment. Studies by Howlett et al suggested that while effective medical treatment is not likely withheld, depending on physician specialty, there may be varying degrees of adoption of new interventions for specific conditions (in this case congestive heart failure) (127).

It is logical to surmise that the presence in a physician's patient population of health conditions for which a given drug is recommended will subsequently have an influence on trial of that drug. It is really the results and experience from this initial trial, however, that will have a significant effect on continued use (adoption), or conversely, discontinued use (relinquishment), of a drug. This was supported by Buban, who suggested that, in the case of new agents to treat cancer, one of the most significant influences on the adoption of paclitaxel was physician experience with paclitaxel to treat late-stage breast cancer (128). Buban also suggested that perceptions of the relative advantages of a new drug are formed through individual experience with the drug, and through their interactions with other practitioners.

While drug trial resulting from interaction was supported through early research by Coleman et al (129), the implications of this study were subsequently questioned by Van Den Bulte et al, who suggested that the social influence was overstated, and it was more than likely simply aggressive marketing which let to the rapid adoption of tetracycline (55). Despite this work by Van den Bulte, the fact that people act in accordance with a frame of reference produced by the groups to which they belong is a long-accepted premise, and is supported throughout the literature (130). Additionally, it is difficult to refute the impact of peers and individuals from the physician's normative social group, as supported by Ajzen's work on planned behaviour (7), which is discussed

at length in Chapter 4. It is also difficult to ignore the commentary and insight by individuals who feel that, while the key to effective health reform is through physician education, another real challenge is more around the process and approach to continuing medical education (131, 132).

Steffensen et al, determined that, while physicians in single-handed practices and those in partnerships both adopted new drugs, the median time for adoption (as defined by their first prescription) in partnership practices was 10 days (mean = 41) while in single handed practices it was 52 days (mean = 119) (133). With partnership practices adopting new drugs faster, Steffensen and his team concluded that the continuous professional stimulation and other social factors are responsible for the accelerated adoption. While this study certainly would support this conclusion, what we do not know is the influence or likelihood of a pharmaceutical representative visiting a solo versus partnership practice, and what the nature of cross-communication and sampling is in this type of environment. Despite the deficiency in Steffensen's approach, his findings were supported by Dybdahl who reduced the number of independent variables, and also found that larger practice size had a positive influence on adoption time, with partnership practices demonstrating the most rapid rate of new product adoption (61).

Much of the previous discussion has been around the research that has determined that there is a greater likelihood of formal and informal discussion (and peer pressure) around new products and their applications, which may in turn influence the rate of adoption. Conversely, it may also influence the rate of relinquishment or trial, if initial observations are less than favourable. Cranney et al surveyed 76 physicians in an attempt to determine why GPs do not implement evidence-based guidelines (134). While their

work suggested that single-handed GPs were enthusiastic about peer based continuing medical education, as it provided them with the peer interaction they lacked, this study was qualitative, lacked sample size and was not really representative. Interestingly, Peay and Peay suggested earlier that the inclination to innovate is not related to the number of other doctors with whom the doctor practices, but is more likely to be influenced by commercial advertising (56). Research by Prosser et al supported both the work of Peay et al and Cranney et al , and demonstrated that prescribing of new drugs is related to the mode of exposure to pharmacological information, the social influences on decision making, risk perception, frequency of pharmaceutical representative visits and individual experience with the drug (78, 135).

In Finland, a government sponsored program aimed at changing clinical practice to enhance rational prescribing has proven to be effective when using GPs as facilitators of their continuing medical education programs, and results at the local level have suggested that critical thinking and willingness to consider change of practice(s) has been achieved (136). This approach has been subsequently supported through research by Maue et al suggesting that implementation strategies that utilize well-respected physician champions in the practice sites may improve guideline compliance (137), and by Cutts et al who identified factors such as access to continuing medical education and specialists as having an influence on prescribing (although influence isn't necessarily adoption or rejection) (124).

While the arguments suggesting association through a clinical environment may or may not influence likelihood of adoption of innovations or evidence-based guidelines, there is no denying that there is a greater possibility of seeing or hearing about new

products if there is more than one individual in an office or peer group, or, if the physician regularly interacts with peers and opinion leaders through other associations. This interaction is also an opportunity for professional development, as suggested by Pearson et al in their study of interns, where every prescription charted has the opportunity for learning (138), and subsequently influencing their development as effective practitioners. This notion of practical application and trial to establish prescribing and therapeutic insight is supported by the steps in adoption, and was supported by Jones et al who found that the progression from first use to regular use is an important step in the drug innovation process (87). That is, early experience in using a new drug seems to strongly influence future use.

Previous experience with a drug which has had a positive or favourable outcome, may lead to a less than thorough investigation of the patient's condition prior to prescribing. Denig's in-depth interview with 61 general practitioners determined that fully 40% made recommendations out of habit, without undertaking any specific contemplation of the patient's condition (139). Schwartz et al also observed that prescribers asserted that their own clinical experience indicated that these drugs were actually the therapies of choice in the conditions presented, despite evidence from the research literature that this was not the case (104). So, even in the face of clinically supported preferred alternatives, physicians may remain with their previous prescribing patterns, as defined by habit and experience.

It is appropriate at this point to address the influence of peers in the same practice, as the collective experience should effectively complement the clinic's experience or knowledge base as a whole. Allery et al considered physician characteristics from the

perspective of changing their practice. In a study of 50 general practitioners, they found that organizational factors, education, and contact with professionals was influential in changing their clinical practices (140). The weakness of this study is that the aforementioned variables account for less than 50% of the changes in clinical behaviour. Additionally, the small sample size and the large number of independent variables make it difficult to confidently attach weight to the professional contact variable.

Landon et al suggested that physicians in solo and two person practices appear to have a more aggressive treatment style than those physicians in group practices (141). While the definition of aggressive is associated with the propensity to request tests or treatments, there is no indication that this activity is causal to prescribing. Additionally, this study is limited by the use of physician reported behaviour based on vignettes rather than measures of actual clinical decisions. A similar observation was made by O'Neill and Kuder who noted that being in a solo practice had a greater association with the propensity of a physician to ordering a service (tests) (142), but as with Landon, it was not indicated if this was associated with actual prescribing.

Ashworth et al considered the physician motivation to change within the context of general practitioners who had joined a general practice covering a geographic locality in south London, England (143). Within the context of the UKs Primary Care Commissioning Group structure, it appears that one of the lead motivators for change was related to a collectivist (team) perspective amongst GPs who are prepared to consider the prescribing implications for their fellow GPs.

While it seems intuitive that general practitioners that have access to an informal peer network may be more likely to prescribe (new interventions), the opposite of this

may also be true. That is, informal feedback from peers may result in a tendency to decrease their levels of prescribing. While the literature supports the latter, research by Watkins has suggested that there may be a greater tendency to prescribe among sole practitioners practicing in markets of low income with minimal academic detailing (81).This insight was supported in part by Peay and Peay who determined that the number of other doctors with whom the doctor practices was not a significant predictor of innovativeness (56).

Another consideration relative to the influence of peers on prescribing was proposed by Carthy et al, whose study population suggested that they didn't consult with their colleagues because they were either confident in their own decisions, or they didn't want to subject themselves to potential criticism (144). The weaknesses of this study, however, were a relatively small sample size of 17, and the general qualitative nature of the questioning.

Outside of the influence of colleagues in a practice environment is the issue of the influence of individuals in peer groups, colleagues operating in different clinics, markets or environments, as well as opinion leaders whose experience and insight is respected and deemed relevant. Soumerai, et al, suggests that working with opinion leaders and providing performance feedback can accelerate the adoption of some alternative acute myocardial infarction (AMI) therapies (145). This recommendation suggests that local physicians have the potential to be influenced by local peer/opinion leaders. The weakness of this study, however, was the inability to control a variety of other factors that may have led to the adoption of the alternative AMI therapies. Soumerai's proposal on the influence of local opinion leaders was supported by work by Sbarbaro (24). While

he suggested that the endorsement of national professional guidelines by local opinion leaders may have a positive influence on the impact of professional guidelines, it may also be effective to provide performance feedback comparing the physician's results to peers. While these observations were more of a commentary, again there may be intuitive value here.

Hepler reinforced the value of the opinion leader among health professionals by suggesting that physicians tend to value autonomy and be socially powerful. To this end, institutional pharmacists are well advised to seek out opinion leaders who have power and know how to use it. Having the support of such an individual can increase the ability to influence appropriate drug use (28).

2.2.3 Physician Profile

This final section of this portion of the literature review addresses a number of physician dependent variables including gender, age, training/background and experience. The objective of the literature review relating to these variables is to gain insight into what other considerations may be influencing prescribing behaviour, while recognizing that these variables may or may not act independent of the other considerations.

This area has always been recognized as playing a role in the likelihood of a physician prescribing a particular product, given a specific condition. An extensive review of physician influences by Hemminki categorized influencing variables into education, advertising, colleagues, regulations and control measures, societal and patient

demands and doctor characteristics (146). For purposes of this research, the key areas under consideration are gender, age, training and background, and experience.

2.2.3.1 Gender

While there is very little in the literature that considers the influence of gender on prescribing, there are also relatively few studies that have been conducted in the area of consumer behaviour on gender differences (147). Most research in this area tends to focus on the female (or collective) consumer because of their significant purchasing power, and in the case of some of the benchmark studies on consumer styles index and decision making, the influence of gender on the consumer decision making process isn't even weighted (148, 149). To this end, the research in this area is inconclusive, and often contradictory. Thus, while the challenge is to determine the influence of gender on prescribing, when considering the physician as a consumer, we must recognize that males and females want different products and they are likely to have different ways of thinking about obtaining them.

A review of the consumer behaviour literature (150-152) identifies men as being more independent, confident, competitive, externally motivated and more willing to take risks. A recent study of 358 male and female shoppers between the ages of 18 and 44 further suggests that men use more information and communication technology products than women and show a greater interest in these products (147). While the age profile is not truly reflective of the physician population in this study, this observation suggest that we may anticipate a greater propensity among male physicians to have an interest in new technology (new medications), and subsequently the prescribing of new drugs.

Tamblyn et al found that male general practitioners had higher rates of new drug use than females, but this trend was not significant after adjusting for other physician and practice characteristics such as year of graduation and the profile of the patients in their practice (122). This pattern, while not significant, relates to the work by Mitchell and Walsh that suggests that male physicians are more confident than female physicians in initiating new medical treatments (147).

Work by Steffensen et al concurs with Tamblyn's research, and suggests that there is an association between late adoption and the independent variables of female gender, smaller practice, low diagnostic activity per patient, and a general restrictive attitude toward pharmacotherapy (133). While this study was qualitative, and as such did not have the ability to test for these variables independently, it does suggest that the characteristics of the "light" prescriber tend to fit into the conservative physician typology.

Inman et al divided a sample of physicians involved in the UK's prescription event monitoring scheme into 6 segments, defined by the relative values of prescriptions of new drugs issued per patient over a 7 year period, commencing in 1984 (153).From an initial sample of over 28,000 physicians, they selected representative subsets from each segment. Their results suggest that female gender was strongly associated with the likelihood of not prescribing, or prescribing less than their male colleagues. While this is significant, given the low relative prescribing ratios, the logic here suggested that females may have more part-time practices, and spend more time with their patients. Subsequently, they have less of a propensity to test new drugs, and have less time to do so. The propensity to not prescribe was also supported through research by Duetz et al

who found that female physicians were more inclined to discontinue antihypertensive drug therapy than their male counterparts (154).

Thus, while we seem to have a trend, none of the studies have conclusively developed a relationship between gender and prescribing. Additionally, the research in this area did not appear to identify gender as a primary focus, but as an artifact that was identified following testing against some previously defined primary hypotheses.

2.2.3.1 Age

In consideration of the influence of age, sociologists, psychologists and marketers have done much to document the resistance to change common among the elderly (155). The combined observations from the literature are best summarized with the recognition that the older the consumer, the more negative the view toward technology, and the lower the use of various technologies (including new prescription drugs).

While Peay and Peay's work demonstrates a level of agreement with the consumer literature, and suggests that age was significant in predicting innovativeness in high risk therapy, it also suggested that the results were not stable when controlling for specialty or a specific drug (56). Despite this, they did suggest that older doctors are less innovative than younger ones. Hemminki summarized the influence of age with the suggestion that more appropriate prescribers were younger, more cosmopolitan and modern (146), albeit the definition of appropriate is subjective, and isn't necessarily reflective of the degree of adoption. This observation is supported by the work of Lacy et al who determined that older physicians prescribed proton pump inhibitors more often

than younger physicians for mild or intermittent gastroesophageal reflux disease, without really giving consideration to non-prescription solutions (156).

Steffensen et al's work supported the commonly held belief that rate of adoption is a function of physician characteristics, but also suggested that the rate of adoption may be influenced by the drug characteristics as well. Within this context, they identified several physician variables that may influence prescribing (gender was mentioned earlier) including age. In this case, physicians greater than 50 years old were more likely to be categorized as late prescribers (although the validity of these results may be questionable due to the small sample size). Freiman's work supported this proposal by demonstrating that the likelihood of prescribing a new drug decreases as the physician ages (157).

While Tamblyn didn't specifically measure for age, she did consider year of graduation from medical school (which may be considered as a relative age variable) (122). Given this, her results suggested that year of graduation had no influence on rates of adoption among general practitioners. Using a similar approach to Tamblyn, Helin-Salmivaara et al's work on the adoption of COX-2s, demonstrated that clinical experience of the physician, measured as the number of years since graduation, had no significant effect on adoption (158).

Interestingly, age, as an independent variable, appears to have some influence on prescribing, but when using date of graduation as a surrogate for age, we see that there appears to be no influence on prescribing. As such, this suggestion may be introducing a certain level of bias into our development of a "prescriber model". Perhaps one of these studies should revisit physician age to determine the correlation between age and date of graduation.

2.2.3.3 Training, Background and Experience

Hemminki's review of the literature on the influence of education on drug prescribing led her to conclude that education positively influences the quality of prescribing (146).Quality of prescribing, however, is subjective with respect to the level of prescribing, and as a result means little in our attempt to measure educational influence on prescribing. Work by Landon et al suggested that there is no evidence of a consistent practice style across general practitioners when presented with representative clinical scenarios (141). This was supported through research by Tamayo-Sarver et al with emergency physicians and the study of their prescribing practices for Opioids, which noted that while some physicians tended to interpret information provided in similar ways across conditions, they couldn't find any physician or practice characteristics that were significantly associated with physician responses (159).

In effect, Hemminki's review of the literature of the day (pre-1975) simply suggested that there was no significant difference in prescribing among doctors graduating from different medical schools. This observation is supported in part by Tamblyn, whose physician sample was representative of four medical schools in Quebec (122). While her results demonstrated no variance between the traditional schools, the school which uses a problem-oriented medical curriculum has demonstrated higher relative prescribing rates of new drugs versus the traditional curriculum format.

While Tamblyn has suggested that the type of educational format offered by the medical school may influence prescribing, she also demonstrated that specialists had higher relative rates of drug utilization then general practitioners. Helin-Salmivaara et al suggested this early adoption and more frequent utilization of drugs may relate to the

concept that prescribing a new drug may enhance reputation better than prescribing an older drug (158).

The dynamics of a physician's practice may be correlated to physician age and experience, and as such may be interchangeable. As their practice becomes more stable/predictable, and the physicians become more familiar with their patients and their specific conditions, the physicians may become more risk averse, and less inclined to try new drugs, or interventions that they do not have a regimen of experience with. Contrary to this logic, however, is the acknowledgment that familiarity may lead to the desire to try alternative products among that portion of a physician's patient population that has not responded to traditional treatments. Work by Armstrong et al (160) suggested that behaviour change follows a dramatic or conflictual clinical event (a product doesn't work), while Bennett et al (121)suggested that physicians with patient history (experience and knowledge of the patient's health and drug regimen over time) are more likely to switch patients to new drugs, particularly if they have the personal experience or insight into the results associated with previously prescribed interventions.

This latter body of research ties in with the notion that when a physician knows what works for them, they are less likely to actively consider all possible alternatives, and are likely to go with the familiar, given that the patients will not be greatly affected, one way or the other (144, 161, 162). Conversely, when, through their own trials, an intervention isn't working, they are more likely to seek out alternatives.

2.2.4 Summary

One of the challenges associated with the isolation of physician and patient characteristics is the fact that these variables do not function in isolation of each other, and tend to exhibit varying degrees of covariance. Additionally, influence may further be a function of non-measured variables such as practice geography, jurisdiction, beliefs and value or even sampling bias. Thus, while it is obvious from the literature that there are physician characteristics that influence prescribing, the challenge is determining which have the greatest influence and their weight of influence relative to the presence of other variables, and given sets of circumstances or prescribing situations.

While the nature of this challenge has been identified and pursued by many researchers, it was adequately summarized by Jones et al, following an analysis of general practitioner activities with respect to prescribing proton pump inhibitors (163). They made the observation that practice variables only explain a small proportion of the variance in prescribing, and that prescribing decisions are complex and idiosyncratic and will not be fully explained by easily identifiable general practitioner characteristics, or, as McKinlay at al suggested, variability in decision making is not entirely accounted for by strictly rational Bayesian inference (120).

CHAPTER 3

THEORETICAL DEVELOPMENT, INTERPRETATION AND CONSIDERATION

3.1 Introduction

The nature of the literature for this dissertation resulted in the development of two specific sections. Chapter 2 addressed the literature as it relates to adoption and diffusion, and the influences on a physician's decision to prescribe, namely, marketing, practice characteristics and physician profile. Chapter 3 expands on the theoretical considerations, and the recognition that all observations are constantly guided by some theories or hypotheses (tentative theories). These tentative theories ultimately lead to final theories either through confirmation/verification or refutation. To this end, this section of the literature search involved review of the literature on marketing, organizational, behavioural and consumer theory.

The major role of theory is to increase scientific understanding through systematized structures that provide the ability to both explain and predict phenomena. Theory in itself represents an interlacing of principles and ideas into a pattern that can be used to detect an underlying structure in the past and present, which, in turn, can be used to guide future human action. Theory, in fact, provides the groundwork for forecasting into the future with a view towards a more systematic understanding of what is true (73).

While the focus of this dissertation is on physicians and their prescribing activity, much of our expectation associated with how physicians will respond when presented with a specific set of cues (environmental, economic, social) is based on the study of

behavioural economics and consumer choice (namely, the process of consumer decision making). In the case of the physician, we must consider him or her from two perspectives, that of the consumer and more often, that of the intermediary or agent, where the patient is part of the end-user group. Within the context of the former, we need to consider applied behavioural literature with respect to consumer choice (164), recognizing that physicians, in their role as consumers, are influenced by many of the same variables that influence consumer choice. In their role as intermediaries, however, their influences may be more aligned with those of an organizational buyer (165), or agent, namely, an environment in which the chooser is not the user.

When considering the physician in the dual role of consumer and intermediary, we can look to agency theory (166), role theory (5, 167, 168), and the theory of planned behaviour (7, 169), to provide us with a greater insight into why we may expect physicians to respond a certain way, given a specific set of professional cues (particular diagnosis, patient expectations, practice norms). These latter two theories relate as much to the physician as an individual as they do to the physician in his/her role in a clinical environment, while the former refers to the physician:patient, physician:formulary relationship, namely, that of agent:principal.

Regardless of the role the physician occupies, they are still the target of extensive pharmaceutical marketing, and as such are considered within the context of advertising theory (170) and advertising elasticity.

Finally, while we need to consider physicians as individuals and subsequently consider the associated theories that give us insight into their specific actions, we must also consider the theory associated with the greater social order, namely, their network

and clinical environment. These influences are addressed within the context of diffusion/adoption theory. We can ultimately see a hierarchical model where role theory and the theory of planned behaviour influence the individual and the environment in which new products are adopted, and where diffusion-adoption theory attempts to recognize the influence and covariance of a number of influencing factors, ultimately leading to the adoption (prescribing) of a new drug category.

The next five sections will discuss the key theories as they relate to this research.

3.2 Agency Theory

Agency theory provides a framework for analyzing relationships between interdependent parties to identify problems that exist between the parties, as well as the mechanisms to solve any problems that may arise (166). Effectively, when one party (the principal) depends on another party (the agent) to perform some action on the principal's behalf, an agency relationship will arise. While there are many agency relationships that exist in pharmaceutical research, development, utilization and drug insurance/coverage environment (46), what singles out agency in health care is the joint product nature of the physician's role. That is, the nature and intensity of the relationship crucially depends upon the realization of the random variable "illness or condition", and the degree to which it is interpreted by the physician (44).

Within the scope of this research, the focus is really on two critical agency relationships, that of the physician (agent):patient (principal), and the pharmaceutical

manufacturer (principal):physician (agent). Having said this, the question associated with this theory is whose agent the physician is or should be.

In the context of the above definition, the manufacturer as principal obviously depends on the physician as the agent to select drugs from their specific offering. The patient, in their role as principal, depends on the physician, acting as the agent, to select or prescribe the appropriate drug. While these may be the two primary relationships considered in this research, it should also be noted that the physician's selection of drugs may be influenced by the provincial or private insurer's formulary, but within the context of this research, this is a secondary agency relationship.

Agency theory serves this research well, as in an agency relationship, the principal delegates decision-making authority to an agent to perform some action on the principal's behalf. To this end, it is appropriate to consider four assumptions surrounding the agency relationship (46), and then put them in the context of this research.

1. Principals and agents are motivated by self interest
2. Principals and agents function in conditions of incomplete information
3. Principals and agents differ in the amount of risk they are willing to assume
4. Outcomes of agents' actions are influenced by factors in the environment

Consider the above assumptions with respect to the manufacturer:physician relationship, where the manufacturer is the principal. The manufacturer is (1) motivated to sell its products and generate a profit, (2)while full disclosure is required, the manufacturer typically emphasizes only a limited amount of the available information related to the applications approved by Health Canada, and generally those which support

both the sale of that product to the physician and its safe use, (3)it believes in its products, and being at arm's length from the patient:physician relationship, is assuming less risk and (4) its success is often influenced by environmental factors over which it may have little control (adverse publicity, regulatory changes, formulary pre-authorization).

Conversely, consider the above assumptions with respect to the physician:patient relationship, where the patient is the principal. The patient (1) is obviously interested in the most effective, practical, least invasive and cost effective treatment, (2) may know something of their condition, but does not understand the pharmacokinetics or other properties of the prescription alternatives, and have little insight into the physician's rationale for the selection of one product over another, (3) is the individual to whom an intervention is being prescribed, and, all things being equal, is less inclined to take unnecessary risks, unless it is the only alternative, and finally, (4) the physician's recommendation or prescription is a function of many variables over which the patient has little control.

3.3 Theory of Planned Behaviour

While there are a number of mid level theories from social and behavioural science that might aid our understanding of physician behaviour as it relates to prescribing, one of the most appropriate, and oft considered when attempting to modify or influence physician prescribing (31, 171), is the theory of planned behaviour (7). This is a cognitive theory that suggests that behavioural intentions are influenced by attitudes, subjective norms and perceived behavioural control.

In broad terms, this theory supports the idea that intentions to perform behaviours of different kinds can be predicted with high accuracy from:

- attitudes toward the behaviour(the degree to which a physician has a favorable or unfavorable evaluation of the behaviour (prescribing))
- subjective norms(perceived social or professional pressure to perform or not perform the behaviour (prescribing))
- perceived behavioural control (the perceived ease or difficulty of performing the behaviour is assumed to reflect past experience, as well as anticipated future impediments and hurdles)

These intentions, together with perceptions of behavioural control, account for considerable variance in actual behaviour (7). With respect to an individual's ability to perform the intended behaviour, it is dependent to a certain degree on factors such as availability of the requisite opportunity and the resources to carry it out. Considering the likelihood of a physician's intention leading to behaviour, this refers to having patients with the appropriate set of symptoms and characteristics, availability of the drug (it is listed on the provincial formulary, or covered by the individuals' private insurer), and the physician having the appropriate motivation (a specific prescription is believed to be the right thing to do).

While the primary goal of the theory of planned behaviour is to explain human behaviour, it deals with the antecedents of attitudes, subjective norms and perceived behavioural control. These antecedents, in the final analysis, determine intentions and actions. Thus, at the most fundamental level, this theory suggests that behaviour is a

function of salient information or beliefs relevant to the behaviour. In many respects, the salient beliefs are analogous to a physician's evoked or choice set. Consider that while people can hold a great many beliefs about a given behaviour (ie prescribing), they can only attend to a relatively small number of these beliefs at any given moment. These salient beliefs are either behavioural, which influence attitudes toward the behaviour, normative, which constitute the determinants of subjective norms, or control beliefs, which provide the basis for perception of behavioural control.

The one element that may seem intuitive in this model, yet is not included, is the influence of past behaviour. While this is addressed by Ajzen with the explanation that, if all factors, be they internal of external to the individual, that determine a given behaviour are known, then the behaviour can be determined to the limits of measurement error. To this end, if the set of factors remained unchanged over time, then the behaviour would also remain stable and the notion that past behaviour is the best predictor of future behaviour would be met.

While this consideration is logical and may hold, the reality is that, as we know, all factors do not remain stable. Through our understanding of diffusion and adoption, we know different groups of adopters have different characteristics concerning the rate of innovation adoption (19). Additionally, as stated by Waarts et al, the factors explaining the adoption of innovations will not be stable over the diffusion process, but will change as larger numbers of individuals adopt the innovation (57). Again, prior behaviour may have an impact on later behaviour that is independent of the effects of beliefs, attitudes, subjective norms and intentions. Thus, while many of the variables influencing intentions may remain stable, we need to ensure that we evaluate and consider not just those static

elements of the equation, but also look at the individual and his or her influencing variables longitudinally, namely, what has the individual done in this situation when exposed to it previously.

Despite this consideration, the theory of planned behaviour fits the hypotheses of this study, lends itself well to our efforts to measure the likelihood of prescribing (namely diffusion and adoption), and is effective in contributing to our understanding of the relationship between a variety of independent variables and the health professional's behaviour.

3.4 Role Theory

In many respects, role theory serves as a bridge between agency theory and the theory of planned behaviour. Consider the foundations of the theory of planned behaviour which are based upon an individual's attitude toward the behaviour, a perceived behavioural control and subjective norms (7) and agency theory, which focuses on principal-agent relationships (166). In this predefined context, role theory thus permits better management/understanding of the dynamic aspects of the provider-client(agent-principal/physician-patient) interface, and greater focus on role performance, and the interpersonal dimensions of service quality (167). Additionally, when considering the physician as a manager, role theory provides further insight, arguing that interpretation of organizational context guides managers' perceptions of their role requirements. The application of role theory in the context of the relationships between physicians, patients and the pharmaceutical manufacturers is even clearer given the currently accepted definition of role theory, namely, "a science concerned with the study of behaviours that

are characteristic of persons within contexts and with processes that produce, explain or are affected by these behaviours"[3].

Considering that the roots of role theory are in social interaction, social penetration and social exchange theory (167), we would expect a strong relationship between the defined elements of role theory and the subjective (group/peer influenced) norms fundamental to the theory of planned behaviour. Within the context of role theory, the physician becomes the focal person who is influenced by the role set (characters who interact with the focal person, and have a stake in and hold expectations about the focal person's performance). This role set in turn develops beliefs and attitudes (role expectations) about what the physician should or should not do as part of their role. The physician's perception of the messages sent by the role set result in driving role behaviour, which is what they do in response to the messages they have received from their role set in combination with their own perception of their role (172).

Given this, the social exchange which occurs between the physician and the patient demonstrates certain patterns which are determined, to a large extent, by the role expectation and the actual role (role behaviour) each party adopts. That is, each party in a service encounter of this nature has learned a set of behaviours that are appropriate to that particular situation. These behaviours or "role scripts" define the boundaries within the social interactions, and how present and future encounters will evolve. Thus, while patients may have a clear expectation of their physician encounter, the degree to which

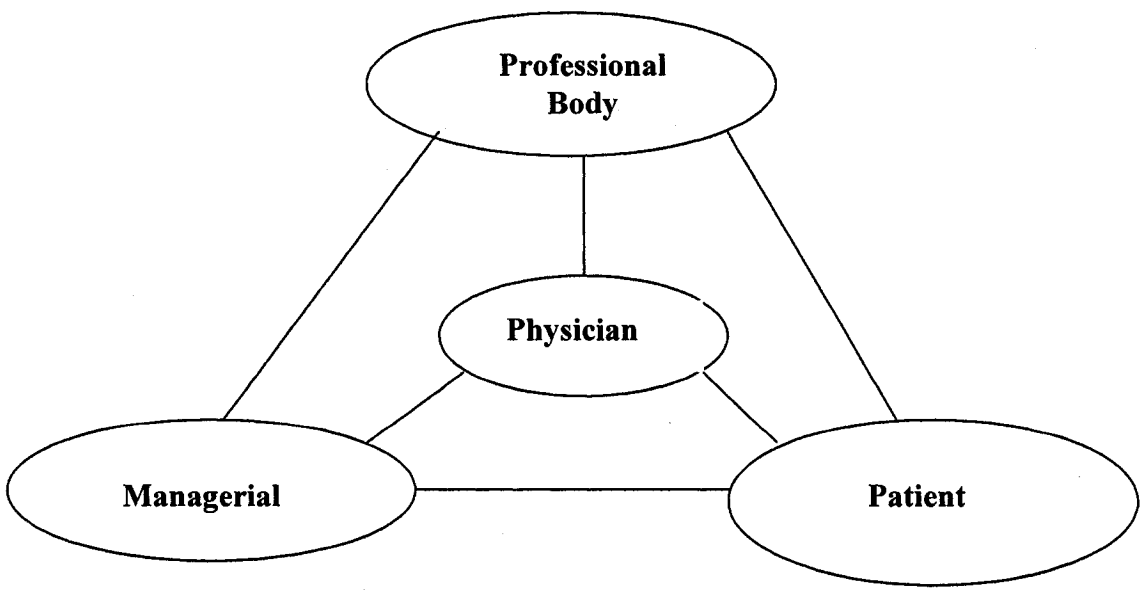
---

[3] Biddle, B., 1979, Role Theory: Expectations, Identities and Behaviours, 416p. New York, Academic Press

the physician and patient engage in a mutually beneficial and appropriate role script may determine the overall benefits of the encounter as perceived by the patient.

Rodham proposed the concept of the Status Triangle Dilemma, which, as demonstrated in Figure 3.1, is easily adapted to our situation (5). Given the context of this dissertation, health professionals (physicians) may be seen as being subjected to the expectations of their professional body or code of ethics, managerial expectations as directed by their governing health body or organization and by their patients, all of whom are trying to shape the physicians' perception regarding their role. Shivers-Blackwell had a similar insight, but rather, proposed that expectations of, and assumptions about the organization's structure, culture and senior management, exert pressures on managers (considering the physician as a manager) in order to make their behaviour congruent with organizational requirements (172).

Figure 3.1: The Physician Status Triangle Dilemma: Adapted from Rodham(5)



It is interesting to note that in Figure 3.1, the stakeholders and lines of influence are not all that different from some of the patient, policy, physician, pharmaceutical diagrams presented in Chapter 1.

Rodham went on to propose four distinct role options, which were considered by the role incumbents to deal with the Status Triangle Dilemma (5). Despite the fact that her model was built around occupational health physicians, the typology of role options addresses the role dilemmas faced by physicians. The four role options proposed include medic, medic with managerial skills, manager with medical skills and manager. Rodham suggests that these options are not fixed, but are dynamic, such that the occupational health physician is able to move between the options, depending on the situation, other role expectations and his/her own role perception. This model is supported by Shivers-Blackwell who proposed the concept of the transformational leader as an individual who is likely to use personal resources including time, knowledge and experiences in multiple roles of coach, teacher and mentor, all dependent upon the situation (172). Again, this theory draws together the role perceptions proposed by agency theory for the principal and the agent, and the influence of the professional's environment, as well as their subjective evaluation of their own situation and role expectations.

A final consideration with respect to role theory is its relationship to what has been proposed by Vargo and Lusch as a new dominant logic for marketing (70). The authors propose that this new dominant logic is coming about as a result of an evolving environment in which service provision, rather than goods, is fundamental to economic exchange. While it is not within the scope of this research to evaluate the validity of this proposal, it is interesting to note that, within the context of service provider client

relationships (physician:patient, pharmaceutical manufacturer:physician) a role theoretical approach can enhance the perspectives of both parties and our approach to this new dominant logic, namely, interactive marketing exchanges(168). Thus, while we have considered the impact of role theory as a bridge between agency theory and theory of planned behaviour, further research is also likely to identify its role in diffusion/adoption as well as advertising theory.

3.5 Advertising Theory and the Physician as a Consumer

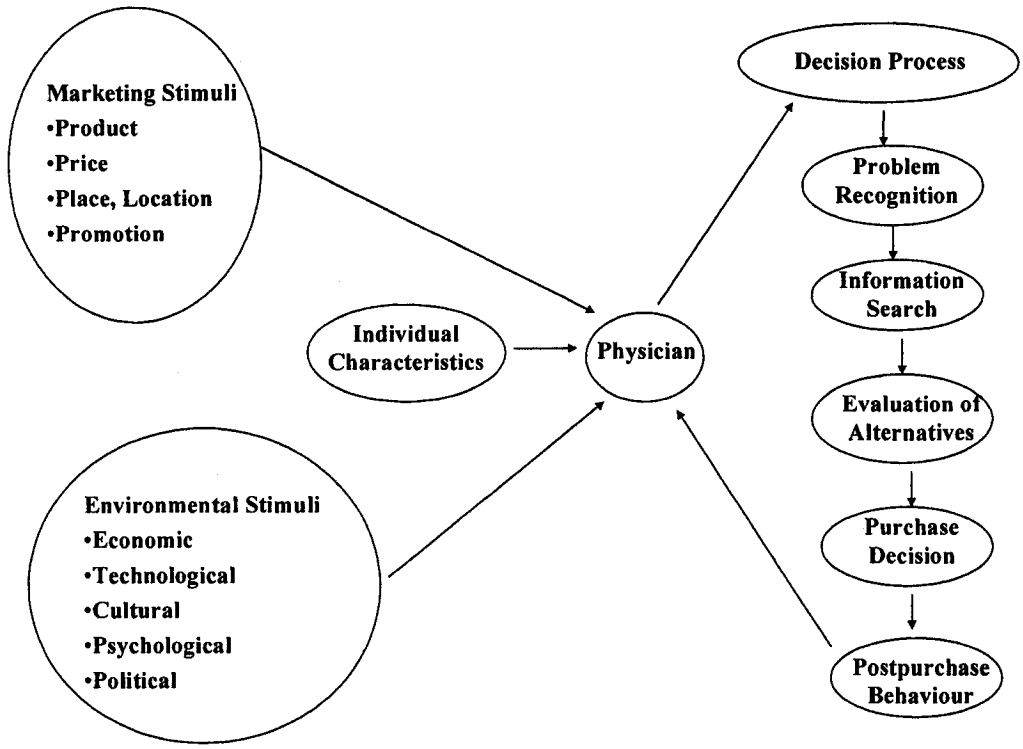
One of the main goals of advertising and marketing is to entice the consumer to purchase the product. In effect, advertising is an input for the consumer comprised of media schedules, message content and repetition, constituting the advertising strategy that triggers a consumer's response (173). While attention to the product and positive affect towards the product have face validity as dependent variables, the critical outcome is product selection or purchase, or in the case of this research, prescribing, as this is ultimately the metric against which pharmaceutical manufacturers measure success or failure.

Given the nature of the physician, from an advertising perspective, we must consider him or her in two separate contexts, that of the consumer and that of the intermediary or advocate, where the patient is part of the end-user group. As a consumer, a physician is faced with many of the same influences that an individual might be faced within a typical purchase decision involving a sought good, or any high involvement purchase decision (figure 3.2). While the flow of influence within the medication use system presented in Figure 1.4 presents a health professional model, there are similarities

and overlap between the consumer's and the physician's approach to health problem solving, worth of reinforcing with Figure 3.2. That is, physicians may thus be influenced in much the same way as any highly involved consumer who has the ability to assimilate information, and subsequently will undertake extensive cognitive processing or elaboration, an approach described by the elaboration likelihood model, proposed by Petty and Cacioppo(174). These influences include (but are not limited to) environmental stimuli, personal relationships, marketing stimuli, personal characteristics, impact of emotion on the decision making process and level of involvement (6, 164, 173, 175, 176).

In their role as intermediaries (agents), however, a physician's influences may be more aligned with those of an organizational buyer (46, 165), namely, an individual operating in an environment in which the chooser is not the user (38).

Figure 3.2:Physician (Consumer) Decision Making Process Adapted Kotler(6)



In their role as the consumer or the intermediary, physicians create and store a set of preferred brands against which they simplify routine decision making (42, 139). Nedungadi refers to the consumer's "consideration set" which is brought to mind on a particular choice occasion (164) which is analogous to the physicians' evoked set proposed by Denig (139). In both cases, memory organization shapes brand retrieval, determines the nature of the set, and thus influences brand choice. Retrieval of a brand from this consideration set then becomes a flexible process dependent upon internally generated and external retrieval cues. To this end, pharmaceutical companies will focus their marketing efforts on keeping their brand top of mind, as they know that in cluttered, fast-moving environments, typical of a physician's office or clinical setting, memory emerges as an important determinant of consumer belief (77). Additionally, awareness of

the names of one of the brands in a category will lead to repeated selection of that brand, even when it offers objectively determined lower quality (177).

Given this, the physician is often considered in the capacity of both the buyer and the consumer. One major exception to this model of the physician relates to their role in Canada, where the physician may be less inclined to consider price, as the Patented Medicine Pricing Review Board (PMPRB) regulates the maximum (non-excessive) price set for new and existing patented medicines (178). Subsequently, the marketing mix becomes focused on the product and the promotional elements (assuming that the product is on the respective jurisdictional formulary and it is relatively available). To this end, a firm which can influence the demand for its product by advertising will, in order to maximize it profits, select and assign the elements of its advertising budget (detailing, drug samples, journal advertising) such that the increase in gross revenue resulting from a one dollar increase in advertising expenditure is equal to the ordinary elasticity of demand for the product (170).

While the Dorfman-Steiner theorem developed the relationship between advertising expenditure and demand, Levy and Simon revisited the original proposition such that the determination of optimal price and advertising spend took into consideration the lag effect of advertising outside of the period during which it occurred (179). This approach has been supported in the literature, and is well recognized as a key contributor to marketing effectiveness (92, 180). Despite this recognition, it is important to acknowledge that while the period of time associated with the residual effect may be debated, the reality is that it most likely varies in its influence between products,

categories and industries. Thus, while we may acknowledge the role of advertising on adoption, there is little conclusive evidence of its additive effect over time.

3.6 Diffusion - Adoption Theory

In consideration of the theoretical basis for innovation leading to diffusion and adoption, we must establish the nature of the innovation of the products under consideration. This research is looking at the category of drugs known as the cyclooxygenase-2 inhibitors, selective non-steroidal anti-inflammatory drugs (COX-2s). Their primary USP (unique selling proposition) over the incumbent (non-selective non-steroidal anti-inflammatory drugs or NS-NSAIDs) was that the COX-2s were considered to have a better gastrointestinal safety profile, thus reducing risk of serious gastrointestinal tract bleeding when used as a prescribed intervention for the treatment of swelling and pain associated with arthritis and osteoarthritis (181, 182).

Given this profile of the COX-2s, the question arises as to the nature of this innovation. While innovations were originally thought to be exclusively discontinuous, Robertson suggested that there are, in fact, three types of innovations (64), namely:

1. Continuous innovations that have the least disruption/influence on established use patterns.
2. Dynamically continuous innovations that are more disruptive than continuous innovations, but still don't generally disrupt established patterns.
3. Discontinuous innovations that are associated with the introduction of a new product and the establishment of new behaviour patterns.

Within the context of these definitions, and subsequent to further discussion in the literature (183), the COX-2s are best categorized as dynamically continuous innovations. That is, while they are obviously different from the NS-NSAIDs, their use and application is unlikely to have any significant impact on established intervention patterns. This consideration is important as we recognize that given any innovation, the challenge ultimately becomes one of diffusion, and the creation of a theoretical model of diffusion will be influenced by a number of variables that will be different, given the categorization of the innovation.

A critical consideration with respect to communicating information related to the COX-2s to physicians, is recognizing that not all potential customers of an innovation will adopt it (19), and that despite the five classifications of adopters proposed by Rogers (Innovators, Early Adopters, Early Majority, Late Majority and Laggards), there may be more effective classifications worthy of consideration. It may be more appropriate that we categorize our population into four classes of innovation adopters as proposed by Foxall, initiators, imitators, later imitators and last adopters (184) or the three classes proposed by Assael; innovators, late adopters and non-adopters (185), or alternatively under the titles of adopters, postponers and rejectors as proposed by Gatignon and Robertson (186).

The three category classification of the population within the context of innovation adoption becomes particularly relevant. We realize that for most dynamically continuous innovations, not everyone will adopt, simply because the product will not be actually superior to existing alternatives, or not seemingly so in the mind of the physician, most likely because of the lack of measuring criteria (64). If we were

considering a product that was discontinuous in its classification, and was decidedly better than existing alternatives, such that ultimately most of a given population would adopt it, we may consider an entirely different set of influencing variables. This is not the situation when considering the COX-2s, and thus we need to consider the influence that different reasons for rejection may have on the likelihood of adoption. To this end, an innovation may be subject to any of the following rationales for rejection (60):

1. The basis of the category it evokes
2. It fails to meet or exceed a evaluative criteria
3. It may be difficult to form evaluative criteria or expectations
4. Formed expectations may be inaccurate
5. The target audience may be very satisfied with the present product
6. While the new product may be judged to be better, it may not be significantly better.

Additionally, within the universe of physicians under consideration, we are not trying to categorize the level of adoption, but more appropriately, we are simply trying to determine whether or not differences do exist between innovators and late adopters with respect to usage patterns, satisfaction patterns and product integration, adoption and usage.

To this end, while we are concerned with the process of adoption, we must also consider the reasons why an innovation may be rejected. We may consider a two-step theory or a two-step flow of communication, whereby advertising and targeted communication influence opinion leaders (step one), who in turn influence others (step

two), as proposed by Katz (187) .While this concept may appear dated, its value comes in realizing that mediating factors such as degree of socialization, proximity to peers, rural vs urban, do exist between product message and the act of adoption. This two step theory becomes particularly relevant in situations where significant risk is present (such as the prescribing of a new drug), and when the norms of the group (normative association) favor innovation. As Eddy suggested, uncertainty may result in an agent performing an activity that is consistent with what other agents are doing. The more uncertain it is that any particular action (prescription) is the best or worst option to pursue, the more likely it is that a physician will do what others are doing, believing that there is safety in numbers (188).

Thus, while we cannot begin to develop a predictive model that will arrive at an all encompassing theory of diffusion of innovations, this research will attempt to build a general model of diffusion of a dynamically continuous innovation, and discuss some of the key variables involved.

3.7 Theoretical Summary and Research Implications

Given the interdisciplinary nature of this research, it is appropriate for us to consider relevant theory from a number of different disciplines. Consequently, from each of the areas contributing to our theoretical understanding of physician prescribing behaviour, we have a number of different approaches to identification of variables, pursuant to the development of a predictive model. Table 3.1 lists the variable alternatives and provides a subjective indication under which theory they may be considered. That is, if considering one theoretical approach, the mix of independent

variables or sources of insight identified would be likely to have greater or lesser influence, given the theory under consideration.

Table 3.1

Relationship Between Independent Marketing and Physician Variables and Their Relative Influence in the Considered Theories

Variable	Agency Theory(46)	Role Theory(168)	Theory of Planned Behaviour(7)	Advertising Theory(173)	Diffusion-Adoption Theory(19)
Journal Advertising	High			High	Medium
Corporate Detailing	High			High	Medium
Physician Gender	Medium	High	High	Low	Medium
Physician Age	Medium	Medium	Medium	Low	Medium
Active Prescriber	Medium	High	High	Medium	High
Relative Prescribing Rates	Low	Medium	High	Medium	Medium
Practice Geographics	Low	Medium	Medium	Medium	Low

While this section of the literature review, dedicated to the review of related and relevant theory, has identified five key areas for consideration, there are hundreds of theoretical and sub-theoretical theses that may or may not relate to the nature of the relationship between physicians, patients and the pharmaceutical manufacturing industry as they relate to prescribing and the use of medicines. This having been said, the five identified are relevant, contextually overlap, and provide guidance to the key observations arising from the research in this area.

CHAPTER 4

RESEARCH STATEMENT, HYPOTHESES AND ASSUMPTIONS

4.1 Background

The initial work on the development of both this research statement and the hypotheses evolved from a number of assumptions. Those assumptions that were supported consistently by the literature were incorporated into the hypotheses, while those assumptions that had inconsistent findings are discussed in a separate section following the hypotheses.

While the data is discussed at length in Chapter 5, Data and Methodology, it is important to recognize that this research statement is a reflection of the variables available through the two data sources that provide the basis for this research. Thus, while there may be a number of other influencing factors (see figure 1.4), the three areas identified in the research statement, marketing activity, physician profile and practice characteristics can be tested using the data available.

4.2 Research Statement

"The likelihood of a physician prescribing from a new drug category to a sample of his/her patient population is affected by marketing activity, practice characteristics and physician profile."

4.3 Research Assumptions and Hypotheses

This chapter is divided into three parts; marketing activity, practice characteristics and physician profile.

4.3.1 Marketing Activity

One of the main goals of advertising and marketing is to entice the consumer to purchase the product. While attention to the product, and positive affect toward the product have face validity, the critical outcome is product selection or purchase, in combination with a reasonable "cost of acquisition". The first work on the theoretical underpinnings associated with the influence of marketing activity on sales was by Dorfman and Steiner in 1954 (170). In their paper, they suggested that a firm which can influence the demand for its product by advertising, will choose the advertising budget and price such that the increase in gross revenue resulting from a one dollar increase in advertising expenditure is equal to the ordinary elasticity of demand for the firm's product.

Their work went on to show that for a corporation with a profit-maximizing mandate, the optimal advertising expenditure to dollar sales ratio equaled the ratio of two elasticities, the elasticity of quantity demanded with respect to advertising efforts (ε_{qa}) and the elasticity of product demanded with respect to price (ε_{qp}), such that

$$\$\text{Advertising}/\$\text{ Sales} = \varepsilon_{qa} / \varepsilon_{qp}$$

The weakness of this theorem is that it is static, and suggests that advertising efforts last only for one time period. The carryover element, however, has been addressed by Levy and Simon (179) with their development of optimal advertising calculated over a lagged period vs the one-period, as proposed by Dorfman and Steiner, such that;

$$f'(A_t) = 1\text{-}bd$$

where A = advertising, b = a customer retention factor and d = the cost-of-capital discount factor.

Given the above, one can assume that any pharmaceutical manufacturer (often referred to in the literature as a "profit-maximizing monopolist") with a patent or a license on a specific drug is interested in maximizing its return on every dollar of advertising. To this end, I propose the following hypothesis with respect to marketing activity:

H1. The probability of prescribing a drug category is a function of the volume[4] of detailing and professional journal advertising targeted toward the physician for that specific drug category.

---

[4] In this case, the volume of detailing is measured by the total number of face to face "minutes" of detail time between pharmaceutical sales representatives for a given product, and physicians.

At an aggregate activity level, this hypotheses is supported by a large volume of research (55, 79, 87, 93, 97, 99, 153, 160, 189). Additional work supports the idea that individual detailing results in higher rates of prescribing (38, 91, 95, 96, 190, 191), and that if a drug is not aggressively promoted, it is less likely that the physician will hear about it (89, 98, 101).

While other commercial sources of information are critical (advertisements in trade and vertical journals, professional symposia, continuing medical education events), the research indicates that detailing plays a key role, and the extent of its impact is as much a function of the message as it is the nature of the relationship between the pharmaceutical sales representative and the health professional. While this is an entirely separate area of theoretical pursuit, namely, relational exchange (175), it is important to mention it here, and to recognize the impact it has on the process of adoption of innovations, and its subsequent role in the context of the evolution of marketing.

Marketing itself has moved from a goods-dominant view, in which tangible output and discrete transactions were objectives, to a service-dominant view, in which intangibility, exchange processes, and relationships are central to the process (70). This move toward the strength of the role of relationships, considered an organizational strength or asset, is affirmed by Hunt and Arnett in their discussion of Resource-Advantage theory, which suggests that a firm's relationships with its suppliers and consumers is an important basic resource that can lead to more advantageous positions in the marketplace and, in turn, superior financial performance (192) .Thus, while it is important that we recognize the theory behind the impact that detailing has on physicians,

it is not within the scope of this dissertation to pursue, but simply to incorporate the impact (measured return) that detailing has on drug adoption.

4.3.2 Practice Characteristics

Much of our consideration around the influence of a physician's practice (clinical environment) on their prescribing behaviour is a function of a set of activities or roles that are defined as potential behaviours to be performed in accordance with a specific job. To this end, for the purposes of aligning role theory with physician prescribing behaviour, we need to consider the physician in the role of a manager or professional, and the subsequent expectations (role pressures) that arise through peers, subordinates and customers (patients).

Role pressures are a function of the physician's perception of their role within the organization's context. These pressures influence the physician from both a psychological and evaluative perspective, and lead to either a conforming or non-conforming response. The proposal by Shivers-Blackwell suggests that leader/manager behaviour (the physician may serve in either capacity) may be classified as either transformational or transactional, and that this behaviour may in turn have a further impact on the decision process, as well as the individual's interpretation of respective directive (ie action of a patient with respect to adherence to a prescribed intervention) (172).

In addition, within the concept of role theory, the physician becomes the focal person who is influenced by the various characters that interact with them. This

influence ultimately leads to the development of beliefs and attitudes about what the physician should or should not do as part of their role (167).

While we may consider the mechanisms of role theory as a foundation for prescribing behaviour, the constituency, location and nature of their practice may also combine with a physician's perceived role in prescribing.

H2. The frequency of occurrence of opportunities available in which one may prescribe from a new drug category, will influence the consideration for and subsequent trial of a new product.

Logically, the presence of more patients in a physician's practice, likely to benefit from a specific drug, will increase the physician's likelihood of drug trial (56). Subsequent results and experience from initial trial will have a significant effect on continued use or conversely, discontinuation, of a drug (104, 128, 129, 139).

While an increased presence of a specific condition within a physician's patient population may have a positive influence on trial, as the proportion of individuals with more than one condition in a practice increases, a physician may be less inclined to try something that they have had little experience with and as a result would probably be less likely to prescribe new drugs (or new drug categories) (121). That is, the more likely it is that a patient has multiple disease states, the higher the chance of contraindication to the therapy or adverse events from drug interactions (122, 126). In this situation, the

physician may be inclined to postpone trial until they have seen post-market entry studies, or have received feedback from a peer group.

H3. Physicians with practices in urban settings are more likely to prescribe new drugs than are physicians operating in rural environments.

Physicians who choose to practice in rural areas may have different characteristics than those who practice in urban areas (87, 122-125). While these particular individual characteristics may influence their likelihood of prescribing, so to might their proximity to a greater peer network, or identified opinion leaders. Additionally, we might also surmise that patients who live in urban areas may be more accepting of change and new ideas, and thus more willing to accept interventions either in the form of a prescription or samples for new or trial products.

4.3.3 Physician Profile

Much of what a physician does is a function of three conceptually independent determinants of intention:

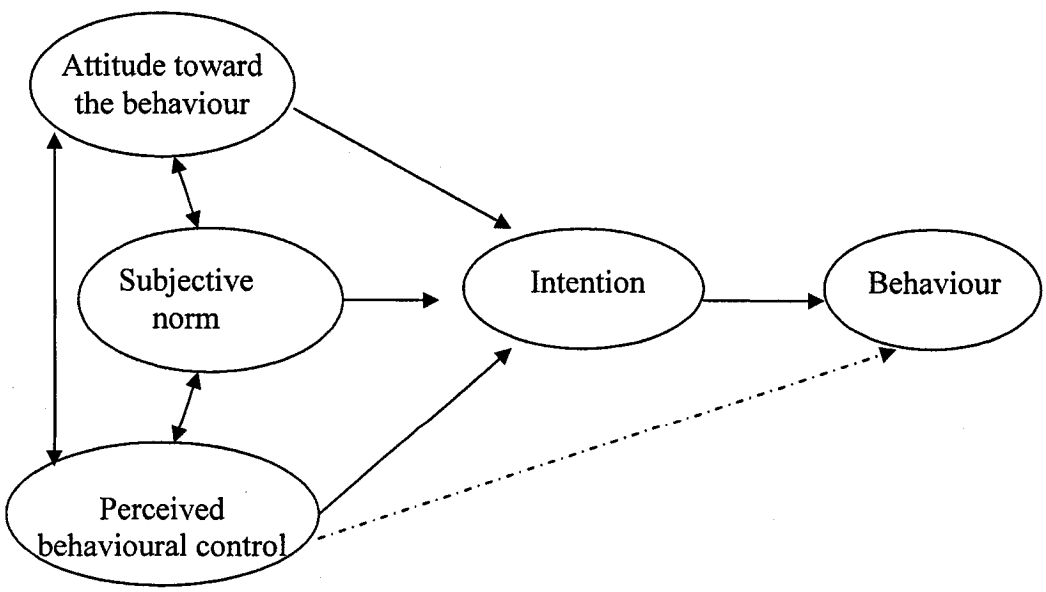
- ✓ Attitude toward the behaviour, namely, the degree to which a physician has a favorable or unfavorable evaluation of the behaviour (prescribing).
- ✓ Subjective norm, which refers to the perceived social (professional) pressure to perform or not perform the behaviour (prescribing).

- ✓ Perceived behavioural control, which refers to the perceived ease or difficulty of performing the behaviour and it is assumed to reflect past experience, as well as anticipated future impediments and hurdles.

Together these interact in the early stages of the theory of planned behaviour (7), which, at its most basic level, posits that behaviour is a function of salient information, or beliefs, relevant to the behaviour. The interrelationship of the above stated determinants subsequently leads to intention and behaviour, as demonstrated in Figure 4.1.

Thus, while we may consider the influence of a number of variables that may impact prescribing behaviour, we must acknowledge that the ultimate behaviour (prescribing a given drug) is a function of the impact these other variables have on the above stated determinants of intention. To this end, hypotheses 4 to 6, relating to physician's profiles, are proposed.

Figure 4.1: Theory of Planned Behaviour (7)



H4. Older physicians are less likely to prescribe from new product categories.

This hypothesis is based on the premise that while older physicians are more risk averse, they are also more confident in their diagnoses, and the continued use of specific product categories, particularly brands within those categories, whose results they have witnessed with their (and their peers) patient population. Consequently, not only are they less likely to prescribe new products, they are also less likely to prescribe from new product categories. While this may be a function of familiarity and risk aversion, it may also be a function of whether their medical training was problem-based or traditional (193).

This is consistent with the general literature which documents the resistance to change among the elderly in many areas including: resistance to relocation, resistance to changes in work situations, propensity to seek more information before acting, reluctance to adopt a new product, service or idea innovation (typically laggards or even non-adopters on the diffusion-adoption curve) and identification of an increasing disdain toward technology with age (155, 194).

In addition to the sociological and psychological documentation of the elderly person's resistance to change, the health literature also supports the decreased likelihood of adoption among older physicians in two areas. Firstly, as the dynamics of a physician's practice become more stable, and they become more familiar with their patients and their specific conditions, the physicians are less inclined to accommodate change (121, 160). It would also be true that another influencing variable, the peer group, would most likely fall into a comparable demographic, one that would also be less

inclined to change, and thus would not serve to introduce or reinforce new ideas. While this is an important consideration in adoption, when we consider the proposal by Olshavsky and Granbois, which suggests that for many purchases a decision process never occurs (41), but may simply result from conformity to group norms or imitation from others, alignment with a comparable peer group effectively removes a key influence for new ideas (ie "non-decisions" for new trial).

Secondly, when a physician knows what works for them, and they have composed their evoked set, they are less likely to actively consider all possible alternatives, and are likely to prescribe the familiar, given that the results will not be compromised with one choice over the other (42, 144, 161, 162). In many respects, the latter condition is as much a function of risk aversion as disinterest in new products, and the related decision rules used by the consumer (physician) are partially a function of their level of anxiety and self-confidence, as well as the level of perceived risk presented by the choice (40).

H5. Physicians with a history of active prescribing are more likely to prescribe from new product categories.

This hypothesis suggests that the physicians' early adoption of new drugs is a personal or environmental trait that is independent of drug groups, and suggests that there are effectively physician market segments that are likely to share specific characteristics. While this hypothesis is almost intuitive, there has been little work done in this area, with

the exception of Dybdahl et al, and their results were inconclusive, suggesting that the existence of the "early-drug adopting general practitioner" may be mistaken (61).

One interesting indication of the existence of this type of physician relates to the fact that physicians who are active prescribers are subsequently identified by the industry and as a result, are often invited to participate in pre and post-marketing clinical trials. By virtue of this involvement, they are more likely to prescribe these drugs that they test (72, 105, 110, 111, 195-198).

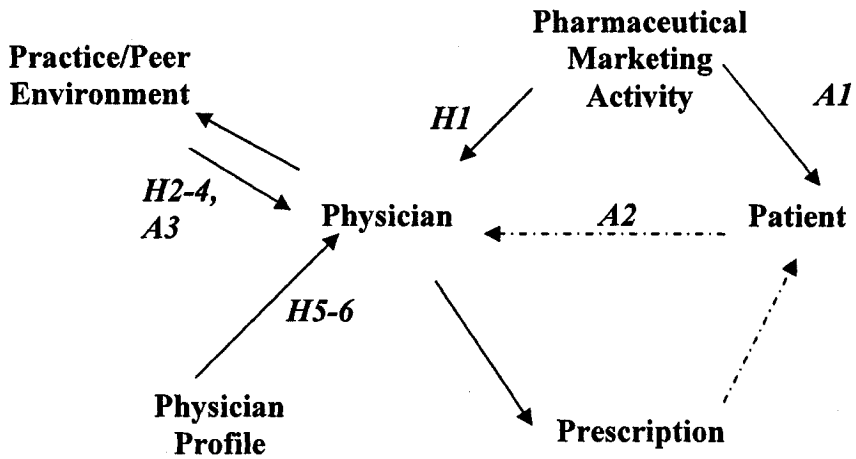
H6. *The probability of prescribing from a new drug category is greater among male than female physicians.*

This proposal is supported by the literature, but it is not as much a function of gender as it is the non-physician activities associated with gender, such as maternity leave leading to the desire to spend more time at home, and possibly resulting in a part-time career. While the suggestion is that male physicians are more confident in initiating new treatments than female physicians, this may be a function of the greater propensity toward part-time roles which, as proposed by Inman (153) subsequently results in less time to evaluate new drugs. Other research has found that while male general practitioners and specialists may have higher rates of new drug use than females, the results were either not significant after adjustment for other physician and practice characteristics (122), or were only significant in the presence of other influences such as a generally restrictive attitude toward pharmacotherapy or a tendency toward lower

diagnostic activity per patient (133). In actual practice, it is often the specialists who are the innovators, and they in turn influence the prescribing general practitioners.

These six hypotheses work together to address the major channels identified in the research statement as playing a key role in influencing physician prescribing behaviour, namely, marketing activity, practice characteristics and physician profile. Their relationship is presented in Figure 4.2.

Figure 4.2: Hypothesis and Assumption Relationship to Prescribing Influences



4.4 Assumptions

The assumptions are really hypotheses originally considered, but they were inconsistently supported by the literature or were supported by the literature and although relevant, were not within the scope of this research (or the data) to evaluate.

Assumption one was inconsistently supported in the literature. However, within specific market segments, or geographic constituencies, it may prove to have a significant impact on prescribing behaviour. As a result, it has not been included in the research hypotheses, but it still needs to be acknowledged, and is addressed at length in the literature review.

Assumptions 2 and 3 are adequately supported in the literature, and explain two key areas of prescribing behaviour influence. In the case of assumption 2, it was not within the scope of this study to measure this influence, and for assumption 3, this practice variable was not identifiable in the Nova Scotia health information data set we have available for analysis. Regardless, both are important and have been expanded upon in the literature review.

Assumption 1

The likelihood of a physician prescribing from a new drug category is a function of the demographics and geo-demographics of the patient.

Intuitively this makes sense, as one would expect that the patient's age and gender may be considered within the context of the clinically proven risk of a particular condition as it relates to age, gender and race. While the literature supports the notion that a patient is less likely to change their lifestyle as they age, a physician is not necessarily more likely to prescribe a drug in this situation (120). Gender, however, is known to have

an influence on medical treatment, some types of prescribing and certainly the outcome of drug treatment (121, 199, 200).

In addition to the patients' direct characteristics, this assumption considers the geography of the patient (where they live), education and household income. This assumption posits that individuals with advanced education are more accepting of new approaches and most likely have an interest and insight into new drugs. While there may be support for this (106), the reality is that these same individuals may be less inclined to accept new drugs for the same reasons. Finally, geodemographics, as related to household income as well as sociological and socioeconomic status, may have some influence on what the physician prescribes (201, 202). The end result could be as much a function of whether the individual has the ability to cover the costs of the prescription or the copay (114), as it is a function of the physician's inclination to pick one drug over another (112, 119).

Assumption 2

> *The probability of prescribing a drug is a function of the intensity of commercial marketing efforts targeted directly at the consumer.*

While there has been a large volume of research done on the influence of DTC advertising on prescribing (107), the majority of the work has focused on the concept that consumer awareness results in greater knowledge of conditions and intervention alternatives, which in turn leads to direct brand/product requests to physicians,

culminating in a prescription (108, 109, 203). While this dissertation is not attempting to evaluate this assumption, the topic has been addressed in the literature review, and has been identified as an area that requires further research in the study of Canadian physician prescribing influences.

Assumption 3

Physicians operating in multi-person practices are more likely to prescribe new drugs than are sole practitioners.

There is a greater likelihood of formal and informal discussion (and peer pressure) around new products and their applications when physicians operate in group practices (56, 131, 134, 136, 143). There may be social norms/habits in the team/peer group with which the individual must align their behaviour (67). Additionally, there may be formal or informal influences that support or discourage specific prescribing activity.

In addition to the social influence, there is increased opportunity to hear about new products if there is more than one individual in a physician's office or peer group that regularly interacts with peers and opinion leaders through other associations (137, 138, 145, 163).

CHAPTER 5

DATA AND METHODOLOGY

The purpose of this chapter is to describe the data and the approach to analysis used in this research.

5.1 Data

There are several types of data available in pharmacoepidemiologic research, this thesis is using two principal secondary data sources to address the research statement and proposed hypotheses. The sources of this data are the Nova Scotia Administrative Health Claims Data, provided through the Population Health Research Unit (PHRU) (204) and detail and journal advertising data provided by IMS Health Canada (IMS) (1).

Another source of insight into the analysis involved a self-directed survey targeted at a small convenience sample of 9 physicians. Their responses to a physician survey served as a "litmus test" for the research statement, hypotheses, and results. While the intent of this survey was not to establish quantitative support, the comments and response were insightful, and have been addressed, where appropriate, in Chapter 7, Discussion and Conclusions. A sample of the survey, and a summary of the participant's comments, is found in Appendix 5.1.

5.1.1 Nova Scotia Seniors Pharmacare Administrative Health Claims Data

In a time of health care reform, spending constraints and an expanding world of therapies and technologies, the need for effective and efficient support services for

population-based research has never been greater (205). In Nova Scotia, this need was addressed through the creation of the Population Health Research Unit, established within Dalhousie University's Department of Community Health and Epidemiology in 1993, to meet the growing need for data and research support in population health, health services utilization and their interrelationships (http://www.phru.dal.ca/). Medicare, pharmacare, vital statistics and hospital admission and separation files can be linked using encrypted unique identifiers, creating a comprehensive data system, which provides excellent opportunities for research in the health and social sciences. The Province of Nova Scotia has supplied PHRU with complete medicare, pharmacare and hospital files for eligible beneficiaries in a format suitable for research purposes. Additionally, PHRU has also been supplied with worker's compensation records and has access to a variety of other data sources including clinical databases and large scale population surveys.

The databases housed at PHRU contain information on mortality (vital statistics database), health services utilization, including physician billings (physician services database) and hospitalizations (from Nova Scotia and Canadian Institute for Health Information (CIHI) databases), and include a record of all prescriptions dispensed to eligible seniors over 65 years, registered in the Pharmacare Program in Nova Scotia (pharmacare database). This includes drug type, quantity dispensed, date dispensed, cost of the prescription, and the physician who prescribed the medication.

The data extracted specifically for this research includes the Nova Scotia Pharmacare data, Medicare data, Geocode (Patient)/Demographic data and Physician profile data. There are a number of relational independent variables in these data sets, which provide greater predictive power in the development of a model and related

profiles. Further details on the PHRU research data repository and the method of extraction are summarized in Appendix 5.2.

The pharmacare data were extracted for the period from January 1, 1999 to December 31, 2003. Records were retained if the Drug Identification Numbers (DINs) matched those provided in the original data query for four drug categories (Cholesterol Reducing Drugs, Antihypertensives, COX-2s, Calcium Channel Blockers) or, in the case of non-specific non-steroidal anti-inflammatories (NS-NSAIDs) fell within their defined World Health Organization Anatomical Therapeutic Class (ATC). Details of the WHO-ATC codes and their respective product names are provided in Appendix 5.3. The study population (patients) was determined as a unique list of individuals who had received at least one prescription, any time between January 1, 1999 and December 31, 2003, from the selected ATC categories.

The population of physicians was selected as any type of physician (general practitioner or specialist) who had practiced for at least 48 months during the period of the study (identified by their MSI date of opt-in). Selecting only those physicians who had practiced for 60 months was considered unreasonable, subsequently, 48 months was considered (80% of the study period) as the minimum "active" period for inclusion in the study sample. The 48 month selection criteria accommodated temporary absences from practice for such activities as sabbaticals or maternity/paternity leaves, but would be unlikely to impact their actual exposure to new drugs, the related promotional activity, or more importantly, their approach to adoption and innovation of new technologies.

Physician billings data were extracted for all individuals identified in the study population for the calendar years 1999-2003. This data was inclusive meaning that an

individual that may have issued only one prescription during the period would be included in all years (1999 – 2003) of the study. Unique physician identifications (IDs) were determined from each physician and pharmacare year file. These IDs were used to create physician demographic files.

5.1.2 IMS Health Canada Data

IMS Health Canada is an independent pharmaceutical market research company, which publishes a variety of promotional activity reports for pharmaceutical products (1). For purposes of this study, the data used comes out of IMS's self-titled Canadian Promotion Audit. This audit provides information on manufacturer and therapeutic class with respect to the number of details per product, the length of time per detail, and the estimated cost per product detail for the current month, rolling two-months, year-to-date, and for the previous 12 months. Expenditures for detailing were estimated by product, based on the average minutes reported for promoting a product, and the estimated average expenses for pharmaceutical representatives.

In addition to detail expenditures (costs associated with pharmaceutical representatives visiting physicians), this data set also provides a summary of journal advertisements by pharmaceutical company, journal expenditures and number of pages per product and therapeutic class, as well as a ranking of leading products, therapeutic classes and companies by journal expenditure. Journal advertising costs represented universal census figures rather than sample estimates. The cost of a journal advertisement was estimated by first applying a basic advertisement price and then adjusting upward or downward according to its design and printing characteristics. The

price was based on a one-time black-and-white advertisement, and adjustments were made according to rates and charges found in *Standard Rate and Data*, an industry publication. The journals, and their respective circulation numbers, used in this analysis, are listed in Appendix 5.4.

Given the objective of determining the extent of the relationship between marketing activities and prescribing, the original request to IMS generated a list of brand names within the five product categories on which this research was focused. An additional field in this file was populated with all of the Drug Identification Numbers (DIN)s listed with Health Canada Drug Product Database (206). A table containing the five product categories, brand names and DINs is provided in Appendix 5.5.

The IMS data provided the names of the drugs against which marketing activity is currently being performed, but did not include the brand names associated with generic products and their corresponding DINs, and as a result, prescribing information for these products was not obtained. There are a large number of generic products in the NS-NSAID category that are prescribed, but their DINs aren't tracked or monitored by the IMS Health Canada database. Given that much of the analysis involved comparison of COX-2 prescribing with NS-NSAID prescribing, total NS-NSAID prescribing for both IMS-tracked and non-tracked products was required. The data obtained from PHRU thus included all available NS-NSAID ATC codes, which provided the complete universe of prescription NS-NSAIDs written during the study period, and reimbursed by Nova Scotia Pharmacare.

Among the physician study population using only IMS supplied NS-NSAID DINs, the average number of prescriptions per month during the study period was 1.41.

This number increased to 4.01 with the inclusion of all Nova Scotia pharmacare listed NS-NSAIDs (generic and other) available for prescription. Despite the increase in total NS-NSAID prescribing following inclusion of the generic data, there is still the limitation that this data does not address over the counter NS-NSAIDs that patients may have purchased on their own, received as samples or were reimbursed through private health plans. Details of the NS-NSAID WHO ATC codes are in Appendix 5.3.

5.1.3 Data Linkage

The IMS data was used primarily to explore the relationship between prescribing and marketing activity. To this end, the link between these two data sets was established at the ATC level as presented in Appendix 5.3. This link accommodated the bivariate and multivariate evaluation of the relationship between the analysis of six IMS reported marketing variables; advertising page numbers, advertising cost, advertising circulation, total minutes of detailing, detailing cost and number of details.

5.2 Data Preparation

As previously indicated, there are several databases that are being linked (merged) to evaluate the proposed hypotheses and research statement. Prior to merging, the data was cleaned and subjected to transformations that provided measurable independent variables. This chapter expands on the data cleaning, transformation and the final variable names.

Following is an outline of the steps for data merger, bivariate analysis, and the file names associated with each step.

Data Merge steps:

1. Bring all of the pharmacare data together.
2. Clean the doctor data files.
3. Merge the pharmacare data generated in step 1, with the cleaned doctor data generated in step 2.
4. Using a one to many merge using doctor id, append all demographic data to the pharmacare data from doctors who have practiced at least 48 months
5. Aggregated data generated in 3 doctor levels:
    - Doctors who have practiced at least 48 months,
    - Doctors from and including November 1999 to and including November 2001 (25 months),
    - Doctors from and including December 2001 to and including December 2003 (25 months).
6. Produce the bivariate analysis, define dependent variables and generate different profiles from the data generated in the previous step.
7. Merge the pharmacare data and marketing activity data using key of drug, prescribing year and month.
    - The dependent variable was total prescription in particular drug category for a given year and month.

In the initial analysis of the merged data sets, there was a potential universe of 3,067 physician records (provided in the PHRU physician demographic data from 1999 to 2003). As is often the case with compiled data sets, however, there were many fields that were incomplete. Records with missing birth dates, gender, specialty and graduate year were deleted, which resulted in a study universe of 1206 physicians with fully populated independent variable data fields. A summary of the loss of physician variables by record is detailed in Table 5.1.While a more detailed analysis of the removal of physicians by field is really a function of the sequence of deletion, the following equation provides some insight into the size of the missing data by field. Starting sample (3067) – physicians with missing specialty (55) – physicians with missing date of birth (79) – physicians with missing opt-in date (554) – physicians with more than one specialty (270) – physicians with more than one county (100) – physicians who have practiced for less than 48 months (803) = 1206.

Table 5.1:

Profile Comparison between the Nova Scotia Physician Universe (N = 3067) and the Research Sample (N = 1206)

Variable	Original Data	After Deleting Those Without Date of Birth, Specialty, and Starting Year	Doctors Practicing for >48 months*
Population (N)	3067	2379	1206
General Practice	63%	69%	69%
Gender Female	29%	30%	28%
Doctor Average Age	45	48	49
Practice – Urban	48%	53%	47%

* Profile of the actual data which was used for the primary research and analysis.

The SAS program used to aggregate this data cleaned each year's doctor data first, and then merged the data together to find all of the doctors that had practiced in at least 48 months of the study period. The algorithm took the approach of identifying all physicians who had "opted in" to the pharmacare program prior to 1999[5] and were still in the program at the end of the study period, December 31, 2003. After cleaning and merging, the total physician population left in the analysis was 1,206.

In addition to the removal of observations that were incomplete, the confounding influence of individuals who had reported being both specialists and general practitioners, as well as those who reported practicing in both the defined rural and urban areas of the province, needed to be addressed. Whereas a confounder is defined as a variable that may be related to the outcome of the analysis, and may have a distribution different from the groups being compared (207, 208), the concern here is that removal of the individuals for either of these reasons may influence the results. While removal of the doctors having identified themselves as both a specialist and a general practitioner removed one confounding effect, there was concern that their removal may result in a further bias on the data. Table 5.1, however, illustrates that the pre and post removal profile remained relatively unchanged.

There were also a number of doctors who indicated that they practiced in multiple counties, and, while this is not uncommon, they were eliminated to reduce potential

---

[5] While Opted In is the variable that indicates physician eligibility for payment under the pharmacare program, it was used in this study to identify those individuals who were actively seeing patients prior to the start of the study period, and were still seeing patients following the end of the study period.

confounding effects between rural and city practices, and to obtain clearer insights into the prescribing activities between city and rural practices.

At this point, it is appropriate to address the challenges associated with the separation of rural from urban, and its respective interpretation by physicians. The data available from PHRU is coded against all 18 Nova Scotia counties, as well as the municipalities of Halifax, Dartmouth and Sydney. The Government of Canada defines rural as referring to individuals living outside centres with a population of 1,000 AND outside areas with a population of 400 persons per square kilometer (209). The challenge with the incorporation of this definition into this analysis is two fold. Firstly, physicians, while they may work within a previously defined non-rural area, may have a significant percentage of their patient base that comes from a defined rural area. Similarly, a subsequently defined "rural" physician may have patients that come from a defined non-rural area. The lack of distinction between rural and urban was supported by the physician convenience survey which also addressed the overlap between city and rural populations. Thus, while the approach may be somewhat subjective, given the nature of the PHRU data, and for purposes of this study, all physicians who indicated that they practiced in the municipalities of Dartmouth, Halifax or Sydney, were considered urban, and those practicing in all other areas were coded rural.

While one may be concerned with the confounding influence of inappropriately reported variables, as stated earlier, one should also consider the impact that their removal may have on the representative nature of the sample population. Again, Table 5.1 demonstrates the profile of the available physician universe prior to and following cleaning and removal of incomplete data fields.

5.3 Data Transformation

5.3.1 Variable Labels

From the aggregated datasets, the following variables were derived:

- Physicians were assigned the label of genp (general practitioner) where if genp = 1, the physician was a general practitioner, or genp = 0, the physician was a specialist. One of the limitations of this step relates to the prescribing volume of specialists. While some specialists rarely prescribe outpatient medications (anesthetists), others are likely to have a smaller or narrower defined prescribing universe, as defined by the nature of their practice.

- The derived variable of medcdn was assigned for doctors who graduated from Canadian medical schools. The number of USA graduates was small, so they are in the other country category. Thus, if doctors have not graduated from Canadian Schools (if med_sch = 'Canada', then medcdn = 1) they graduated from foreign medical schools (medcdn = 0)

- As previously indicated, doctors who practice in the municipalities of Halifax, Dartmouth and Sydney are defined as practicing in "city", all others are defined as practicing in "rural". The limitation of this variable relates to physicians who may have the appropriate city code but are on the border of the regional municipality, and as a consequence, are closer to a rural population than they are to an urban population. Conversely, physicians practicing in smaller metropolitan centres such as Truro, Amherst, New Glasgow and Yarmouth may effectively have an urban practice, but the reporting nature of the data identifies their county, and as a

result, they are assigned the general geographic label associated with the majority of the physicians in their area.

- Physicians identified as female were assigned "1", and those identified as male were assigned "0".
- Birthplace was defined by the numeric code assigned to each physician in the original file. This field is highly correlated to medical school but it has many missing values (approximately 20% of the final universe). Based on analysis of the original codes, the variable was assigned as Nova Scotia (cnnova), Canada other than Nova Scotia (cnothr), or anywhere outside Canada (othrcntry).
- Doctor age (dage) has been calculated as the period from their birth date up to mid year of 2003. Doctors with age less than 29 were deleted due to partial presence during the study period, and those greater than 83 were assigned to the 100^{th} percentile.
- Duration of practice (lentime) is defined as the period since graduation up to the year 2003. Although this is not 100% accurate, it is relative, and provides a different perspective on the simple variable of age. Many individuals go back to school after being in the work force, take maternity leaves, or follow other pursuits, and as such, their age is not always directly related to their years in practice.

As mentioned earlier, doctors had to be present in at least 48 of the 60 months of the study period, or they were removed. Again, this may introduce some bias for individuals taking maternity or paternity leaves, sabbaticals or related and being out of

practice for more than 12 months, but the variance in the data between the two universes, as presented in Table 5.1, is small. There were also defined interaction (cross-tabulation) terms which included comparisons between general practitioner and specialist versus city and rural which created the derived variables of citygenp and ruralgenp, citysp and ruralsp. Additionally, there was a comparison between physician gender and general practitioner which created the derived variables of femgenp, femsp, malgenp and malsp. Given the interaction between these variables as presented in Appendix 5.6, the creation of the identified representative derived variables served to develop more effective predictors of the target variables (prescribing). As an example, where a city practitioner and a general practitioner may not be significant, the city-general practitioner variable provided another way to consider the independent variables, and the subsequent construction of the multiple regression equations presented in Chapter 7.2. A complete listing of variable names and labels is provided in Appendix 5.6.

Following the cleaning of the physician demographic data, this dataset was combined with the pharmacare data through the Doctor ID link. This "new" database had additional independent variables of:

- Prescription date, which was derived from the prescription year, month and day.
- DIN or drug ID number which was used to categorize individual prescriptions into the categories of cholesterol lowering agents, NS-NSAIDS, COX-2 Inhibitors, Calcium Channel Blockers and Angiotensin Converting Enzyme (ACE) Inhibitors.
- WHO-ATC or anatomical therapeutic category.

The combined physician demographic/pharmacare dataset accommodated the determination of aggregate quantity of drugs prescribed by physician by prescribing date. Following transformation, this data was combined with the Canadian drug marketing data provided by IMS by drug, month and year, with advertising and detailing expense maintained as the main marketing influencing factors.

The five drug categories were then transferred into five indepedent variables. Three of the drug categories (cholesterol lowering agents, calcium channel blockers and ACE inhibitors) were put into a single category called other drugs. They were still retained as individual variables, in the correlation procedure, but were aggregated for the stepwise analysis. This approach accommodated the evaluation of the collective co-existence of these categories with COX-2s and NS-NSAIDs.

While there were a number of drug categories considered, the five categories used in this study were selected for a number of reasons. With the exception of NS-NSAIDS, they all had products in the 2003 top 25 most prescribed drugs in Canada, and together accounted for 28% (7/25) of all of the drugs in that list (Table 5.2). Additionally, these drug categories were in the top 10 therapeutic classes in Canada with respect to prescribing, with cardiovasculars (ACE Inhibitors and Calcium Channel Blockers) holding the top prescribing class in both 2003 and 2004 (Table 5.3). Finally, given that the data from PHRU is comprised of patients with an age 65 and over, it was appropriate to select drug categories whose products addressed the conditions more prevalent in an older population cohort.

Table 5.2:

Canadian Prescription Drug Ranking(1)

Rank 2004	Rank 2003	Product	Drug Category
1	1	Lipitor	Cholesterol Lowering Agent
3	3	Altace	ACE Inhibitor
4	6	Norvasc	Calcium Channel Blocker
14	16	Celebrex	Cox-2 Inhibitor
17	19	Adalat XL	Calcium Channel Blocker
20	10	Vioxx	Cox-2 Inhibitor
28	25	Vasotec	ACE Inhibitor

Table 5.3:

Canadian Top 10 Prescribed Therapeutic Classes, 2004(1)

Therapeutic Class	Rank 2003	Rank 2004	% Change Over 2003
Cardiovasculars	1	1	+7.7
Cholesterol Agents	7	6	+15.5
Anti-Arthritis	7	8	+0.7
Total Market			+5.6

5.4 Methodology

5.4.1 Methodological Considerations

While there are a number of approaches that may be used in the analysis of this data, it is important to recognize that the primary research objective is to develop a descriptive model of the prescribing physician. As a subfield of the science of data-mining, modeling has evolved through the study and practice of machine learning, database analysis and related management, pattern recognition and of course classical statistics, and is based upon techniques used for classification and regression modeling (210).

When considering the model of prescribing (prescription) drugs, one can easily draw parallels to the model of selection of any frequently purchased consumer good. For practical purposes, this process of selection may be considered in the context of adoption, or the evolution of a physician from a non-prescriber to a prescriber. This approach supports the definition of a good decision-maker, as one who gives appropriate weight to clinically relevant patient attributes (118), and their dynamic nature over time.

We also need to consider the actual process by which consumers (remember that physicians, in their role as prescribers, are consumers of information relative to their selection of prescription drugs) make decisions, namely, the decision making, experiential and behavioural influences (176), the aspects of behavioural learning theory (shaping, extinction and reinforcement) (211), as well as the influence of classical conditioning, which continues to be a target of theoretical inquiry from a consumer behavioural perspective (212).

One of the earliest methods developed for classification (predictive) modeling, is simple regression analysis. This approach effectively involves the analysis of a number of individual (independent) variables with respect to their relationship to a forecast or dependent variable. While this approach doesn't measure multicollinearity (covariance) between the predictive or independent variables, it provides an indication as to which variables may be most likely to appear in a multivariate analysis. To this end, this process becomes exploratory, providing insight as to which variables one may expect to be a component in the "multiple influence" decision making process.

Thus, while the actual decision process would account for a percentage of individual physician-patient prescription decisions, it would ultimately be influenced by a number of other variables as well. To this end, the literature supports the premise that an equal (and possibly greater) weight of the decision process would be a function of the interrelationship or the simultaneous influence of a number of variables (11, 21, 23, 99, 119, 137, 144).

This, then, takes us into the next stage of analysis, namely, the multivariate component. The foundation of multivariate analysis is the variate, namely, a linear combination of variables with empirically determined weights. The end result of this approach is the creation of a single value (composite measure) that represents the combination of all of the variables available, a value that achieves the best predictive power for the dependent or forecast variable (213).

These interrelationships tend to be a function of the influence of marketing activity, physician characteristics and practice characteristics, and their subsequent impact on often unrecognized biases, and long-held social preferences. The research

statement proposed in Chapter 4.2 addresses these three key areas (with the exception of specific consumer/patient related variables), in an attempt to quantify the relationship between known influences and the physician prescribing decision.

Understanding or applying weights to these influencing variables provides us with the wherewithal to establish confidence intervals around given parameters, and falsify the a-priori null-hypotheses, or, what we would expect the physician to do. The challenge faced in this approach relates to the clinical judgment of physicians in choosing an "appropriate" and "feasible" mode of dealing with clinical problems. This is an issue that plays a significant role in many of the identified and documented variations in clinical judgment and prescribing behaviour.

Given this, a consideration in understanding the physician decision making process is to give appropriate weight to clinically relevant patient attributes during the process of making a patient management decision. While this approach is analogous to evidence based medicine (EBM), it is often constrained by deficient EBM skills, limited access to evidence, lack of time, patient demand for treatment despite lack of evidence for effectiveness, relevance to general practice, and a variety of cognitive, environmental, local contextual and patient factors (214-216). Thus, for any number of reasons, EBM is not always adopted, with resulting intervention decisions based on any number of other influences.

While patient attributes may play a role in both the physician prescribing process, as well as their propensity to adopt "best practices", there are a number of other extraneous clinical, physician and market/environment characteristics which should not influence physician decision making, but have been demonstrated throughout the

literature as playing some role (11, 217). The challenge in any analysis, however, is to determine when an individual's activity is a function of the identified, known, quantified variables and when it is dependent on other, possibly unidentified influences.

5.4.2 Methodological Approach

Data from any source presents the researcher with a number of analytical approaches to consider. The actual process of data analysis involves the partitioning, identification and measurement of fluctuation in a set of variables, either among themselves, or, as the approach taken in this study, between a dependent (forecast) variable and a population of independent variables. When considering a single physician (data point), it has been demonstrated that there are any number of independent variables likely to have some degree of influence on their prescribing activity (Literature Review, Chapter 2). While this has been supported through consideration of the individual physician feedback in the convenience sample (Appendix 5.1), it should be acknowledged that physician perspective and prescribing triggers are dynamic and difficult to generalize. Additionally, any set of variables, as demonstrated through multivariate analysis, and the variates themselves, is further subject to different weights and relevance, given different physicians, different environments, resources and patient populations.

Given the data, the hypotheses were developed based on the variables that were available (See Appendix 5.6 for a complete listing of the variables and their definitions), and subsequently, each hypothesis was developed to support the research statement. The research statement is thus supported by a combination of simple and multiple variates.

Their defined influence on physician activity in turn supports (or refutes) agency theory, role theory, theory of planned behaviour, advertising theory, and diffusion-adoption theory.

The nature of the physician work environment is such that they either operate in single-handed (solo) practices, or in a clinical environment with other physicians. Additionally, they are typically influenced by their peers and opinion leaders through their daily activities. To this end, early consideration was given to the use of hierarchical linear models, with the intent of evaluating groups of physicians within nested or clustered entities (218). Unfortunately, the data available did not provide any indication as to the nature of the size of the physicians' practice, and as such, this approach was ruled out. Time series analysis was also considered, as this approach takes into account possible internal structure in the data, namely, that data points taken over time may demonstrate trends or seasonal variations that should be taken into account. While this time series analysis is effective to evaluate policy and educational interventions (219), these activities were not recorded over the period of this study, and subsequently ruled out this approach. This would serve as an area of future analysis, and should be considered to evaluate the influence of educational interventions, policy (prior authorization, changes in co-pay) or even targeted public relations activities.

The two primary approaches (discussed earlier) involved in hypotheses testing were simple regression which involves the identification of a "predictive" independent variable, and measures their relationship to a dependent variable and multiple regression, which identifies two or more independent variables and measures their relationship to a

dependent variable. The final step in the analysis involved the actual creation of the predictive model.

Model selection is the process of adding and/or removing variables from a model until one finds the model or algorithm that is relatively the best predictor, given the independent variables available. The approach used in this analysis was stepwise estimation, which involved entering the independent variables into the discriminant function, one at a time, on the basis of their individual predictive power. This approach chooses the single best discriminating variable, which is subsequently paired with each of the other independent variables one at a time. The variable that is best able to improve the power of the function in combination with the first variable is chosen. The third, fourth and n^{th} subsequent variables are chosen (and possible removed if they are determined to no longer contribute) in the same manner, until additional variables are deemed to offer no further significant contribution toward discrimination. For this analysis, the stepwise logistic regression model uses the significance level of $p \leq 0.05$ for retention in the model.

5.4.3 Dependent and Independent Variables

While the discussion around the methodological approach to this point has addressed the analysis of the data, it is important to also address the nature of the dependent and independent variables used in the analysis. Independent variables are those elements provided through the secondary data that serve to establish the predictive model(s), and may be defined as causal to the dependent variable. The dependent variable

is the defined forecast, that is, given *actions a, b* and *c* we can more accurately predict outcome *d.*

The independent variables used in this analysis are identified and defined in Appendix 6.6, while the dependent variables were related to the prescribing activity associated with the COX-2s. There is further discussion around the dependent variables in Chapter 6, Analysis and Results.

As previously stated in Chapter 1.3, while each province ultimately makes its own decision with respect to whether or not a product will be listed on its formulary, common to all Canadian provinces is the requirement to have a Notice of Compliance (NOC) issued federally before it can be provincially assigned benefit status. The NOC is issued once Health Canada approves a drug, and at this point, physicians are able to prescribe it and it is available to patients. Outpatient prescription drugs are not covered by the Canada Health Act, however, and patients must pay for drugs themselves unless the drug is covered by a private drug plan or a federal, provincial or territorial drug plan.

The Common Drug Review (CDR) process, administered by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA), is a single process for reviewing new drugs and providing formulary listing recommendations to participating publicly-funded federal, provincial and territorial (F/P/T) drug benefit plans in Canada[6]. Each of the drug benefit plans that participate in CDR make their own formulary listing and benefit coverage decisions based, in part, on the recommendations from the Canadian Expert Drug Advisory Agency (CEDAC) (220).

---

[6] All jurisdictions with the exception of Quebec participate in this program.

In the case of the COX-2s, the first NOC was issued for Celecoxhib (Celebrex®) on April 14, 1999 (2), and subsequently, provinces assigned the products to their formulary on their own schedule. See Table 5.4 for the dates of issuance for other COX-2 NOCs.

Table 5.4:

Notice of Compliance Issuance Dates for the COX-2s(2)

Common Name	Brand Name	Date of Issuance
Celebrex®	Celecoxhib	1999-04-14
Vioxx®	Rofecoxhib	1999-10-25
Mobicox®	Meloxicam	2000-10-24
Bextra®	Valdecoxhib	2002-12-11

The fact that the dates for which the COX-2s were issued their NOC were all after January 1, 1999, provided an excellent opportunity to evaluate the adoption of a new drug category, and not simply new brands of the same chemical entity or new chemical entities within the same drug category. The time period covered by the data used in this study (January 1, 1999 to December 31, 2003), affords the researcher the opportunity to evaluate both drug adoption, continuance and even discontinuance or relinquishment.

The advantage of looking at an entire category of (new) drugs, rather than an individual drug within the category, resulted from the acknowledgement of the difficulty often faced in separating a brand from a category. Testament to this has been demonstrated by the challenge Pfizer has faced separating negative publicity surrounding

Vioxx® from their product, Celebrex®. Additionally, it is important to recognize that the promotion of one brand within a category often results in a spillover influence on the other brands in the category (177, 221, 222), and the influence of media coverage and general market "hype" around the product category becomes difficult to assign to individual brands within the category.

Another reason for the selection of "prescribing activity around the COX-2 category" as the dependent variable, relates to the approach that the manufacturers (Pfizer and Merck) took in the positioning of this product in the marketplace. This product category was (and continues to be) positioned directly against the NS-NSAIDs through statements such as:

> "CELEBREX works to relieve arthritis pain by targeting a certain enzyme in the body. An enzyme is a protein that causes chemical changes in other substances in the body. The enzyme that CELEBREX targets is called COX-2. The COX-2 enzyme plays a key role in causing both pain and inflammation.
>
> The body also makes an enzyme called COX-1. This enzyme helps protect the lining of the stomach. Most pain relievers work by blocking the actions of both the COX-1 and COX-2. CELEBREX is different because, when taken at suggested doses, it targets the COX-2 enzyme, but not the COX-1. For this reason, doctors refer to CELEBREX as a COX-2–specific inhibitor."[7]

---

[7] What Makes Celebrex Different, http://www.celebrex.com/about/default.asp, accessed November 17, 2005.

The effectiveness of this marketing approach was addressed by Dai, et al, who identified that the increase in COX-2 inhibitor use among patients in whom NS-NSAIDs could be used, accounted for more than 63% of the growth in COX-2 inhibitors used during the period 1999 to 2002 (223). This increase is presented numerically for Canadian office based physicians in Table 5.5 (graphically in Figure 5.1) and for Nova Scotia physicians in Table 5.6 (graphically in Figure 5.2).

Table 5.5:

Comparison of Total COX-2 and NS-NSAID Prescribing By Canadian Office Based Physicians Between 1999 and 2003. (Adapted from IMS Health Canada, (3))

	Estimated Annual NS-NSAID and COX-2 Prescribing ('000s of Prescriptions in Canadian Retail Pharmacies)				
	1999	2000	2001	2002	2003
COX-2	1,907	6,282	7,724	7,430	7,673
Year/Year % Change	NA	229.4%	23.0%	-3.8%	3.3%
NS-NSAID	8,292	6,503	5,804	5,734	5,715
Year/Year % Change	NA	-21.6%	-10.7%	-1.2%	-0.3%
TOTAL	10,199	12,785	13,529	13,165	13,389
Year/Year % Change	NA	+25.4%	+5.8%	-2.7%	1.7%

NA-Not Available

Figure 5.1: Five Year Trend Analysis of COX-2 and NS-NSAID Prescribing Activity Among Canadian Office Based Physicians (Adapted from IMS Health Canada(3))

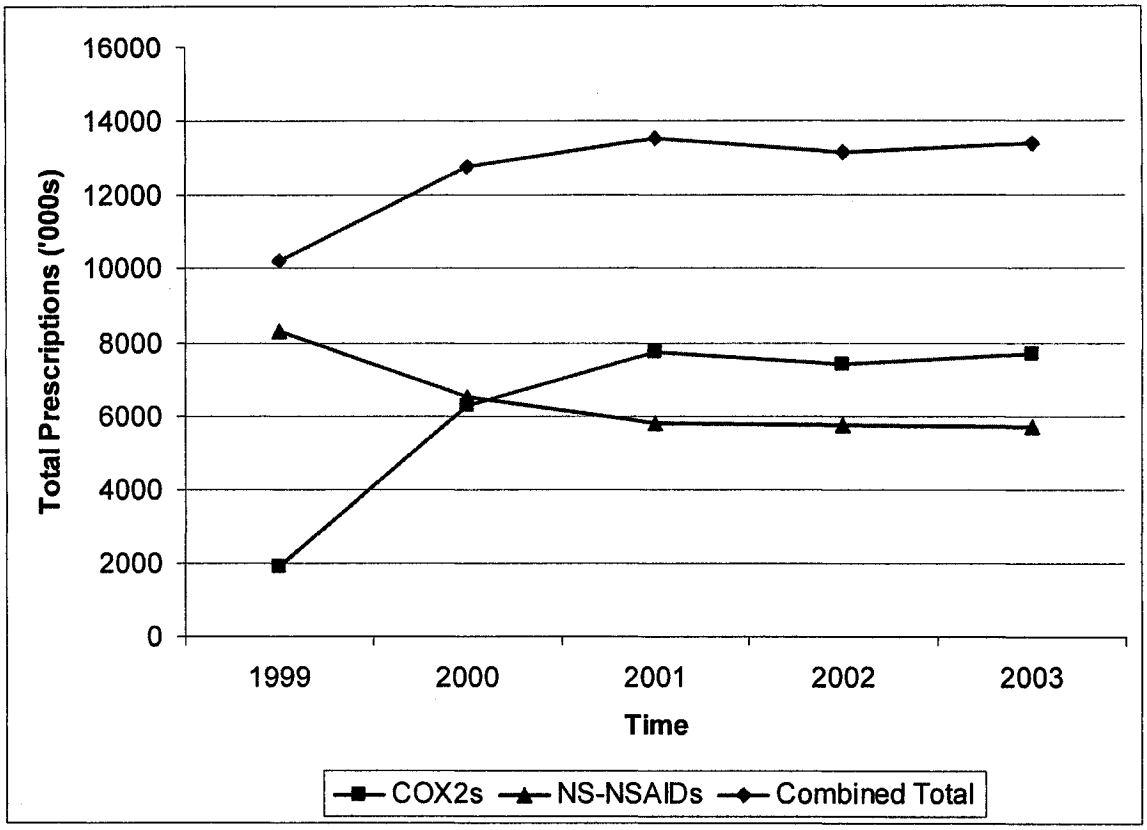


Table 5.6:

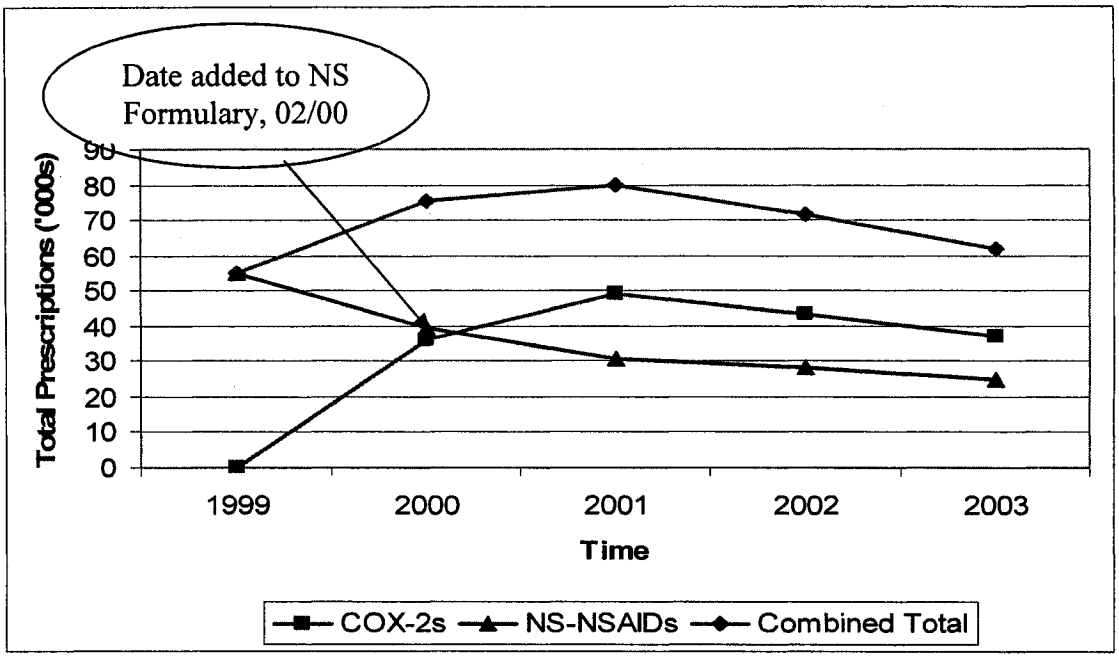
Comparison of Total COX-2[8] and NS-NSAID Prescribing by Nova Scotia Physicians Between 1999 and 2003 (Nova Scotia Seniors With Pharmacare Benefits)

	Actual Annual NS-NSAID and COX-2 Prescribing ('000s of Prescriptions)				
	1999	2000	2001	2002	2003
COX-2	0.1	36.1	49.2	43.3	37.2
Year/Year % Change	NA	NA	+36.3%	-12.0%	-6.1%
NS-NSAID	55.0	39.3	30.7	28.4	24.8
Year/Year % Change	NA	-28.5%	-21.9%	-7.5%	-12.7%
TOTAL	55.1	75.4	79.9	71.7	62.0
Year/Year % Change	NA	+36.6%	+6.0%	-10.3%	-13.5%

NA-Not Available

[8] The IMS COX-2 Category includes Meloxicam (Canadian Trade Name Mobicox), technically a COX2-NSAID hybrid, it has COX-2 properties, and is marketed as a COX-2 Tables 6-5 and 6-6 presents a relative comparison of COX-2 vs NS-NSAID use between 1999 and 2003.

Figure 5.2: Five Year Trend Analysis of COX-2 and NS-NSAID Prescribing Activity Among Nova Scotia Office Based Physicians(Source – PHRU data, recorded prescriptions in both categories for pharmacare covered drugs)



Given this approach to market, it is important to see the conditions against which the COX-2s are prescribed relative to the NS-NSAIDs. Tables 5.7 and 5.8 provide a summary of the estimated number of drug uses (actual prescriptions) for NS-NSAIDs and COX-2s as recommended by Canadian office based physicians.

While it is expected that there should be some variance between these drug categories and their respective applications, it is interesting to note that the top three disease categories for COX-2s, between 2001 and 2003, were the same as the top three disease categories for NS-NSAIDs during the same period, accounting for approximately 75% and 66% of drug category prescribing, respectively.

Table 5.7:

Estimated Number of COX-2 Prescriptions by Canadian Office Based Physicians by Condition Between 2001 and 2003(3)

WHO ICD9 Major Disease State Categories	2001		2002		2003	
	Drug Use*	% of Total	Drug Use*	% of Total	Drug Use*	% of Total
Musculoskeletal Disorders	3,017	37.6	2,884	37.4	3,026	38.2
Osteoarthritis	1,707	21.3	1,763	22.9	1,622	20.5
Injury and Poisoning	1,311	16.3	1,035	13.4	1,177	14.9
Other**	1,993	24.8	2,020	26.3	2,092	26.4
Total	**8,029**	**100.0**	**7,701**	**100.0**	**7,917**	**100.0**

* numbers are in '000's

**Other includes prescriptions for disorders of synovium and tendon, as well as endocrine, nutritional, metabolic and immunity disorders

Table 5.8:

Estimated Number of NS-NSAID Prescriptions by Canadian Office Based Physicians by Condition Between 2001 and 2003(3)

WHO ICD9 Major Disease State Categories	2001		2002		2003	
	Drug* Use	% of Total	Drug* Use	% of Total	Drug* Use	% of Total
Musculoskeletal Disorders	1,706	35.4	1,679	34.9	1,777	36.4
Injury and Poisoning	1,186	24.6	1,108	23.0	1,116	22.8
Osteoarthritis	345	7.2	486	10.1	427	8.7
Other	1,581	32.8	1,543	32.0	1,567	32.1
Total	**4,819**	**100.0**	**4,815**	**100.0**	**4,886**	**100.0**

* numbers are in '000's

Considering the similarity between the conditions for which these two drug categories are prescribed, NS-NSAID prescribing was considered an accurate surrogate for the presence of conditions among the physician's patient population that would be suitable for COX-2 prescribing. This comparison provides further support for the use of COX-2 prescribing activity as the dependent variable.

CHAPTER 6

ANALYSIS AND RESULTS

6.1 Background

The purpose of this chapter is to discuss the approach to analysis and present the results. The significance and interpretation of these results is covered in chapter 7, Discussion.

The research statement for this dissertation proposed: "The likelihood of a physician prescribing from a new drug category to a sample of his/her patient population is affected by marketing activity, practice characteristics and physician profile". The data discussed in Chapter 5 was used to test the related hypotheses, ultimately providing useful insight into the research statement and support (or not) for the hypotheses.

The approach, which involved evaluation of prescribing activity within the COX-2 category of drugs, was taken given the unique opportunity presented by the introduction of this category of drugs to the marketplace in 1999. Consider the following:

a) Seldom do we have a completely new category of drugs populated with more than one brand introduced into the marketplace in a very narrow period of time.
b) All elements of the marketing mix (product, price, place (accessibility) and promotion) had an impact on individual brand activity, but also had within category, cross brand selection influence that, given the approach to analysis, doesn't present a bias on the results.
c) The volume of negative media (external to the controllable elements of the marketing environment) associated with the COX-2s was marginal during the timeframe for which the data was analysed. That is, the influence of adverse public relations did not

really start to influence the trial and adoption of these products, until after the study period for this data ended (December 31, 2003). While there had been evidence of heart attack and stroke risks reported through the media and the professional literature as early as March 2000 (224, 225), it was not until September, 2004 when Merck voluntarily discontinued the sales of Vioxx®. Thus, the time period for which this analysis was targeted was not influenced by the removal of one prescription product from the market or the subsequent impact that action might have had on the category.

d) With the exception of claimed decreased cardiovascular risk associated with Celebrex® over Vioxx®, the primary unique selling proposition (USP) for these two drugs was similar, namely, reduced risk of gastrointestinal (GI) bleeding and related disorders. Thus, in many respects, physicians may have viewed these products as interchangeable. In fact, following the removal of Vioxx® from the market, within one week, over 58% of patients in the United States receiving Vioxx® had been switched to Celebrex® or Bextra®(226).

e) Inadequately controlled studies often exaggerate the effectiveness of a given intervention, and their success is often due to the attribution of pre-existing trends (clinical inertia) in practice patterns (11). Again, the unique nature of the introduction of COX-2s eliminates this "clinical inertia bias", providing a rare opportunity to evaluate uptake and adoption of a new drug category.

Given the above, of critical note is the fact that this data provides one with an opportunity to evaluate an isolated introduction of a product category over an approximate five year (really 50 months, given the NOC timeline) period. A product

category whose likelihood of adoption and trial aren't influenced by negative consumer or public media, and have a perceived unique selling proposition that made their marketing message "interesting" to physicians struggling with a patient population who genuinely stood to benefit from the stated features of these products. To many physicians, their patients were either not responding to the alternatives (NS-NSAIDs), or the discomfort associated with gastrointestinal (GI) side effects was greater than the discomfort associated with the actual condition for which the NS-NSAIDs were prescribed.

Considering the nature of the secondary data available, the number of variables that could be evaluated was limited. To this end, while the research demonstrates a number of bivariate and multivariate influences on prescribing, there are, as presented in the literature, and summarized in the literature review, a number of other variables which also have an influence on prescribing, and undoubtedly have covariate or confounding influences on each other. This having been said, an argument can be made for parsimony, that is, increased model strength through the creation of a predictive algorithm with a smaller number of independent (individual) variables.

6.2 The Analysis

Following cleaning and preparation of the data (as discussed in Chapter 5.2), there were effectively three different approaches to analysis that were considered, namely;

- the patient as the unit of analysis
- each prescribing event as the unit of analysis
- the physician as the unit of analysis

The patient as the unit of analysis was ruled out, as this practice tends to violate the assumptions of independence, namely, the prescribing behaviours associated with individual patients are likely to be correlated within each physician's practice. This issue is further exacerbated given the relationship between physicians and prescribing in multi-physician practices.

The second approach considered focused on the actual prescription as the unit of analysis, where each prescribing event subsequently builds the profile of a physician unit[9] (217). That is, the demographics and physician related activities were considered for each prescribing event, which totaled 1,674,000 unique observations over five years. While this approach provided some general insights into the data, it did not support efforts to develop an understanding of the profile of individual physician demographic segments, namely, those likely to try and ultimately adopt new products. Additionally, the insights were limited given the lack of independence and the lack to independent variables.

Ultimately, given the focus on adoption and trial of a new drug category, the approach taken in this research involved identifying the prescribing patterns, and then selecting and profiling the physicians within various segments of prescribing activity. To this end, the unit of analysis was set to the actual physician, which then accommodated the evaluation of physician prescribing activities, and the subsequent influence of demographic, marketing and practice characteristics on this individual unit of analysis, the physician.

---

[9] A unit is considered the action (prescription, intervention, etc,) of the physician at a set period in time given the immediate influence of related variables (age, patient, environment, schedule, etc).

6.2.1 Total (Volume) and Relative Prescribing

With the physician established as the unit of analysis, there were really two ways to approach the analysis of the data. The first approach considered prescribing activity from a "Total" (volume) perspective, and the second considered prescribing from a "Relative" perspective. For purposes of this research, total prescribing looks at the volume of a drug category prescribed during a set period of time (average number of prescriptions written for a specific drug category per month), whereas relative prescribing considers adoption as a substitution for existing drugs and controls for relative levels of prescribing behaviour among physicians. The latter presents prescribing volume (in the case of COX-2s, adoption) relative to the "demographics" of the practice, while the former simply looks at the total volume of prescribing. Despite their individual strengths and weaknesses, both perspectives provided unique insights that would be overlooked if a researcher was to select one approach over the other.

While relative prescribing provides a more representative approach to evaluating physician trial and adoption, total prescribing may be more relevant in a number of situations, such as:

- Markets where there is an inadequate supply of physicians. In this situation, by virtue of their practice demands, they may have less time to evaluate each patient.
- Practices where the physician's patient load is well above average.
- Situations where there is pressure on the physician to see as many patients as possible, and often, to the patient, the writing of a prescription signals the end of the appointment.

The comparison between relative and total prescribing becomes more interesting in light of the responses to the physician survey (Appendix 5.1.2). They indicated a broad range in the number of patients they saw on a weekly basis (25 to >200) and they also had a broad range in their perceptions of what would constitute an average patient load.

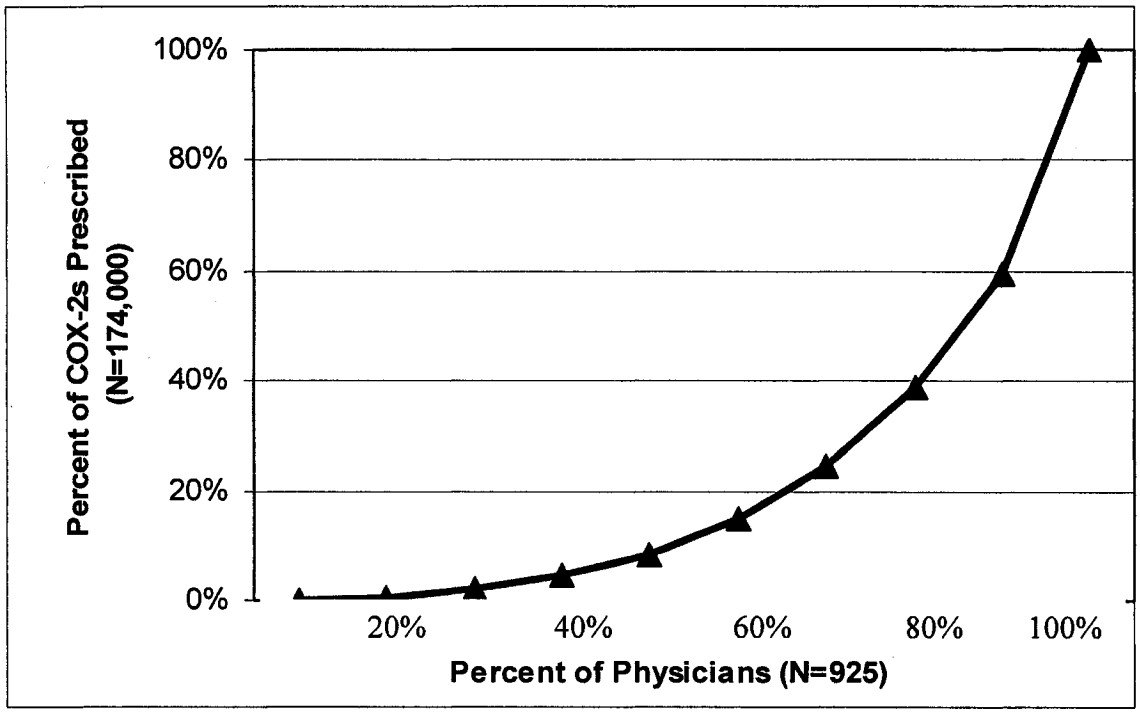
6.2.2 Dependent Variables

Considering the fundamentals of bivariate and multivariate analysis, the challenge is to select the appropriate dependent (forecast) variable, against which selected independent variables combine to predict the likelihood of a response. Considering the question addressed through the research statement, namely, what is the likelihood of a physician prescribing from a new drug category, the challenge was not just to identify those individuals who are prescribing from the new category, but more appropriately, to segment those individuals into various levels of prescribing, establishing segmented cohorts against which to develop a definition of adoption.

An initial approach to analysis was to establish "likelihood of prescribing a COX-2", as the dependent variable. While this didn't address the question of adoption, it served to develop a profile of those individuals more likely to prescribe COX-2s than not. Physician distribution against COX-2 monthly prescribing averages is presented in Figure 6.1. While this analysis provides insight into the variables that may have an influence on categorical (COX-2s and NS-NSAIDs) prescribing, it doesn't necessarily give us insight into adoption. That is, writing COX-2 prescriptions doesn't necessarily infer adoption, particularly if the number of prescriptions, as a percentage of the total prescriptions written for an appropriate condition, is small. The question of adoption is best answered

by looking at COX-2 prescribing relative to the presence of appropriate conditions for which the drug may be prescribed, the total volume of drugs prescribed by the physician or more specifically, the volume of the drug prescribed relative to the viable alternatives.

Figure 6.1:
Distribution of Total COX-2 Prescribing for Nova Scotia Seniors with Pharmacare Benefits Within the Physician Population Prescribing a COX-2 (1999 – 2003)



This latter issue is addressed through the creation of the derived variable, volume of COX-2s prescribed / volume of COX-2s prescribed plus volume of NS-NSAIDs prescribed. This gives a relative comparison of COX-2 prescribing activity, in situations where the patient conditions exist for which these drugs may be deemed appropriate by the physician. As was stated in Chapter 5, the top three disease categories for which COX-2s were prescribed, were the same as the top three disease categories for which NS-

NSAIDs were prescribed (during the same period). These conditions accounted for approximately 75% and 66% of COX-2 and NS-NSAID drug category prescribing, respectively (3). This supports the assumption that the presence of NS-NSAID prescribing is a valid surrogate for the presence of patients in a practice who have conditions for which COX-2s may be considered (and ultimately prescribed).

Figure 6.2 presents the distribution of physicians against the ratio of (COX-2/COX-2 + NS-NSAIDs). Individuals with a low value (<0.5) prescribe a small number of COX-2s relative to the total combined category (ie NS-NSAID prescribing is much greater than COX-2 prescribing). Conversely, individuals with a high value (>0.5) prescribe a large number of COX-2s relative to the total combined category (ie COX-2 prescribing is much greater than NS-NSAID prescribing). At either end of this prescribing distribution, note the high percentages of physicians who have not prescribed any COX-2s (relative value = 0) as well as the high percentage of physician who have prescribed only COX-2s (relative value = 1). Figure 6.3 presents the incremental and cumulative frequency distribution of physicians against this same ratio.

Figure 6.2:

Distribution of Physicians Prescribing COX-2s(N = 925) Against the Relative Prescribing Scale: Prescriptions for COX-2s/Prescriptions for COX-2s plus NS-NSAIDs Among Nova Scotia Senior Pharmacare Beneficiaries From 1999 and 2003

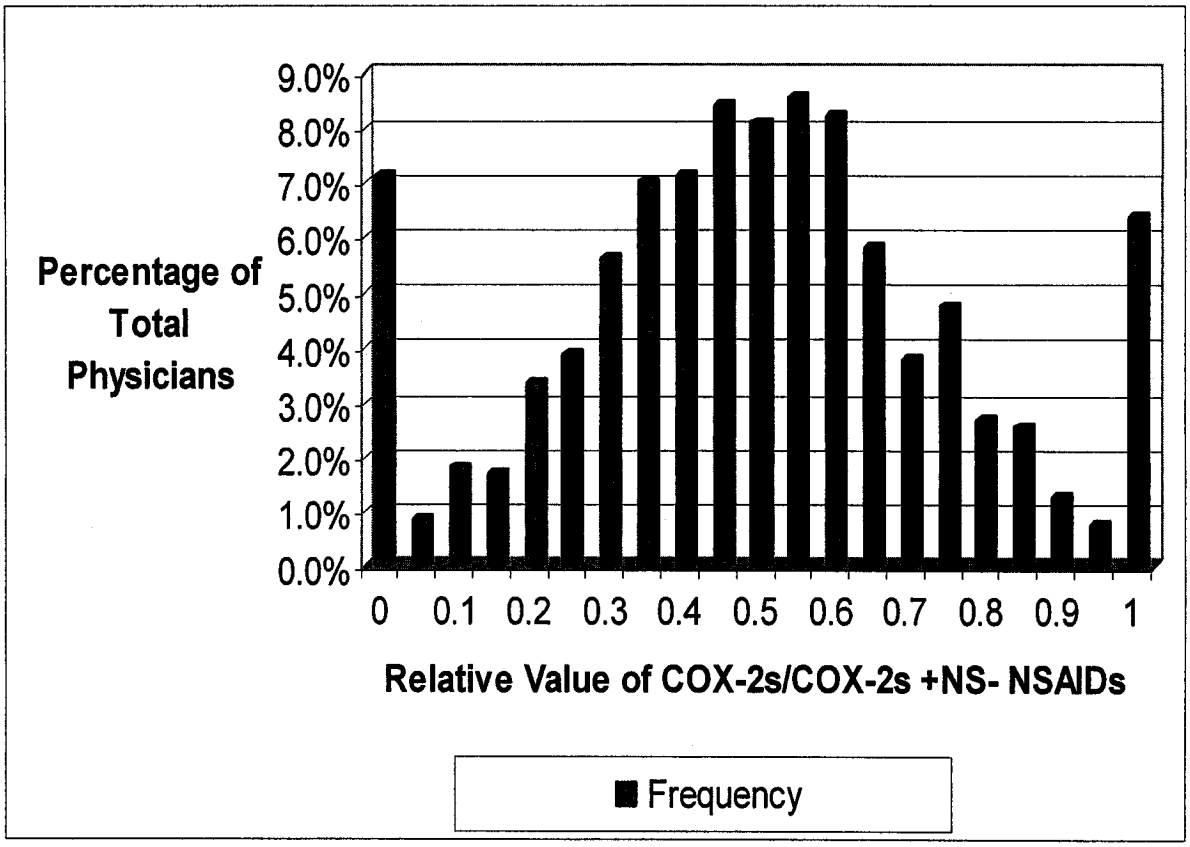
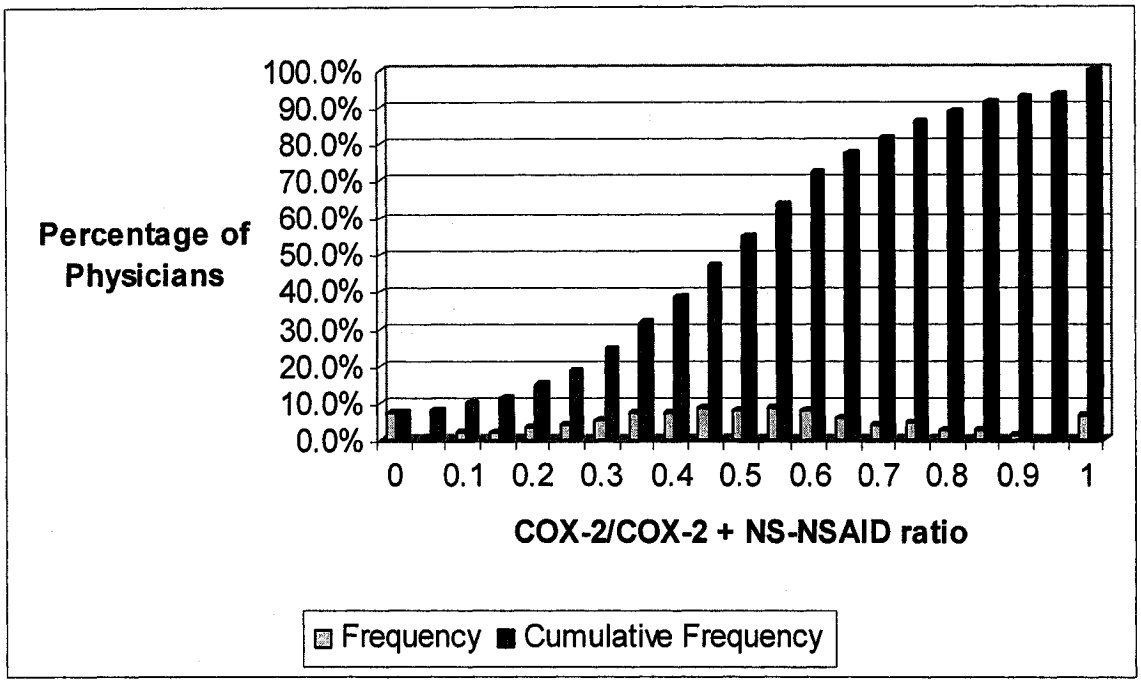


Figure 6.3:

Incremental and Cumulative Frequency Distribution of Physicians (N = 1206) Against the Relative Prescription Scale: Prescriptions for COX-2s/Prescriptions for COX-2s plus NS-NSAIDs Among Nova Scotia Senior Pharmacare Beneficiaries From 1999 and 2003



Creation of this relative variable accommodated the inclusion of independent prescribing variables in the model, in combination with key physician demographic variables. Simply using total prescribing of a given drug category suppressed all other independent variables.

To summarize, there were effectively two primary dependent variables used in the bivariate procedure to provide insight into the significance of the independent variables and their predictive power in identifying (and attempting to create a profile of) COX-2 prescribers. They were "Likelihood to prescribe a COX-2" and "Likelihood of having a relative value of prescribing COX-2s/COX-2s + NS-NSAIDs".

6.3 Physician Sample Selection And Profiles

While the focus of this research centered on the likelihood of a physician prescribing from the COX-2 category, the first stage of the analysis involved identifying the correct sample from the physician universe. While the original data file provided 3067 physicians, cleaning, elimination of duplicate records, and selection according to the criteria outlined in the previous chapter, resulted in a final universe of 1206 physicians (see Chapter 5.2).

This sample population of 1206 physicians provided the foundation for all of the analysis, while within this sample there were only 925 who either prescribed an NS-NSAID or a COX-2 during the study period. Table 6.1 provides a profile of the general demographics and what this sample of physicians looked like, and Appendix 6.1 expands on the demographic sub-segments of the phyisician profiles. Additional non-binary demographic information not included in Table 6.1:

- Graduation Year; mean = 1979
- Doctor's Age (up to 2003, see Chapter 6.3.1); mean = 49.9
- Years In Practice; mean = 23.8

Table 6.1:

Summary of Physician Demographics in the Study Sample

Variable Description		Frequency	Percent
General Practice:	GP	835	69.2
Practice Locale:	City	567	47.0
Doctor Gender:	Male	863	71.6
Medical School:	Canadian	947	78.5
City General Practice:	Yes	347	28.8
Rural General Practice:	Yes	488	40.5
City Specialist:	Yes	220	18.2
Rural Specialist:	Yes	151	12.5
Female GP:	Yes	270	22.4
Female Specialist:	Yes	73	6.0
Male GP:	Yes	565	46.9
Male Specialist:	Yes	298	24.7

6.4 Hypothesis Testing

The coefficient of correlation describes the degree of relationship between a dependent and an independent variable, where a correlation coefficient of zero means there is no relationship between the two variables and a value of 1 suggests a perfect relationship. While the Pearson product-moment correlation coefficient if appropriate for uniform or normally distributed variables, Spearman is appropriate for situations that present a combination of bivariate normal (prescribing and gender, prescribing and locale) as well as those that differ from the bivariate normal(prescribing of one drug relative to other drugs, prescribing and age). Given this, Spearman was used for this analysis, with values of $p \leq 0.05$ considered significant.

The testing in this research really involved two concurrent steps. The first step, bivariate analysis, involved the evaluation of all of the independent variables against a dependent variable, identifying those variables that support the hypothesis or reject it. This was effectively an exploratory stage to gain insight into the data and those variables that may ultimately play a role in the development of a predictive algorithm in the final step of the analysis. This final step was multivariate in nature, looking to combine those variables that provided the greatest predictive power or support for the dependent variable. Testing of hypotheses H2 to H6 was performed using the dependent variables discussed in Chapter 6.2.2.

6.4.1 Influence of Detailing and Advertising

H1: The probability of prescribing a drug category is a function of the volume of detailing and professional journal advertising targeted toward the physician for that specific drug category.

In testing this hypothesis, the influence of advertising was considered as both a direct month to month measure, as well as a lag measure, that is, results in month N+1, N+2, and N+3 were compared to advertising activity in month N. Unlike the other hypotheses, this really relates to the relationship between marketing activity and prescribing, and subsequently can be evaluated from two perspectives, the relationship between marketing and the writing of a prescription or the relationship between marketing and the total pills prescribed. For reasons discussed in Chapter 5.3.2, the dependent variable used was the total number of prescriptions written in a drug category

in a given month (sumdrug). The independent variables that were available for this analysis were:

- Detailing (per drug)
    - Minutes of Detailing
    - Cost of Detailing
    - Number of Details
- Advertising (per drug)
    - Number of Pages of Advertising
    - Total Advertising Circulation
    - Total Cost of Advertising

Their source and support is outlined in Chapter 5.1.2; IMS Health Canada Data. The variables which were selected for the analysis were number of details, number of pages of advertising and total advertising circulation. All detail values are actually derived from the number of details, and the total cost of advertising is a function of advertising pages and circulation.

While the objective was to evaluate the relationship between marketing and prescribing activity for the COX-2 product category, ACE Inhibitors were also evaluated in an effort to determine the impact that marketing has on prescribing activity for an established category of drugs. While all three of these categories contain a mix of both brand name, and generic products, ACE inhibitors were selected over Calcium Channel Blockers and Cholesterol Reducing Drugs, as they represent the largest therapeutic class of drugs in Canada (cardiovasculars) (1). The actual levels of detail expenditures and advertising expenditures are presented in Figures 6.4 and 6.5.

Given that sales typically only increase following the launch of a new product, the effects of advertising and sales need to be considered over a period of time that extends beyond the initial introduction period. To this end, trendlines were calculated for each of the independent marketing variables, as well as for the dependent variable, the number of prescriptions written.

To construct the trendline, a binomial line equation was calculated for each variable. This equation was then populated with the actual IMS/PHRU data for each month, and a value of the line equation was calculated, which presented the actual value for this period. Subsequently, the deviation from the trend was then calculated for each variable for each month. The line equations(trendline values) were then subtracted from the actual values which provided the absolute deviation from the trend. The deviation from trend for the independent variables was regressed against the deviation from trend for the number of prescriptions written in both the month they occurred as well as against the 1, 2 and 3 month lag period. This provided a measure of the relationship between variations in the monthly marketing activity relative to the monthly prescribing activity.

Following evaluation of the relationship between individual marketing variables and the prescribing of COX-2s and ACE inhibitors, a factor analysis was performed on the original 6 independent marketing variables to determine if these elements function separately, or if they may be more effectively grouped into smaller sets of evaluation (factors or variates). The extraction method, using principle component analysis, yielded two factors for both the COX-2s and the ACE Inhibitors. These factors (Factor 1 developed from the detailing variables and Factor 2 was developed from the advertising

variables) were regressed against the same dependent variables (number of prescriptions) to measure the extent of their relationship with prescribing.

In both the month to month and lag comparisons for COX-2s, the period evaluated for both detailing and advertising was 48 months, starting with January 2000 data. This sample period was selected given that the first major product in this category, Celebrex®, received its Notice of Compliance (NOC) in April, 1999 and Vioxx®, the second major product in this category, received its NOC in October, 1999 (See Table 5.1). Thus, while there was most likely some detailing and advertising occurring before the drug was listed as a benefit on the Nova Scotia Seniors Pharmacare program, the 48 month period started with the analysis of the data from January, 2000.

For the month to month and lag analyses of COX-2s, there was no significance at the $p \leq 0.05$ level for the three independent variables and the two derived factors against the dependent variable, average monthly number of prescriptions. Table 6.2 presents the results of the correlation procedure analysis.

Figure 6.4:

Canadian Monthly Detailing Expenditures for ACE Inhibitors, COX-2s and NS-NSAIDs From 1999 and 2003

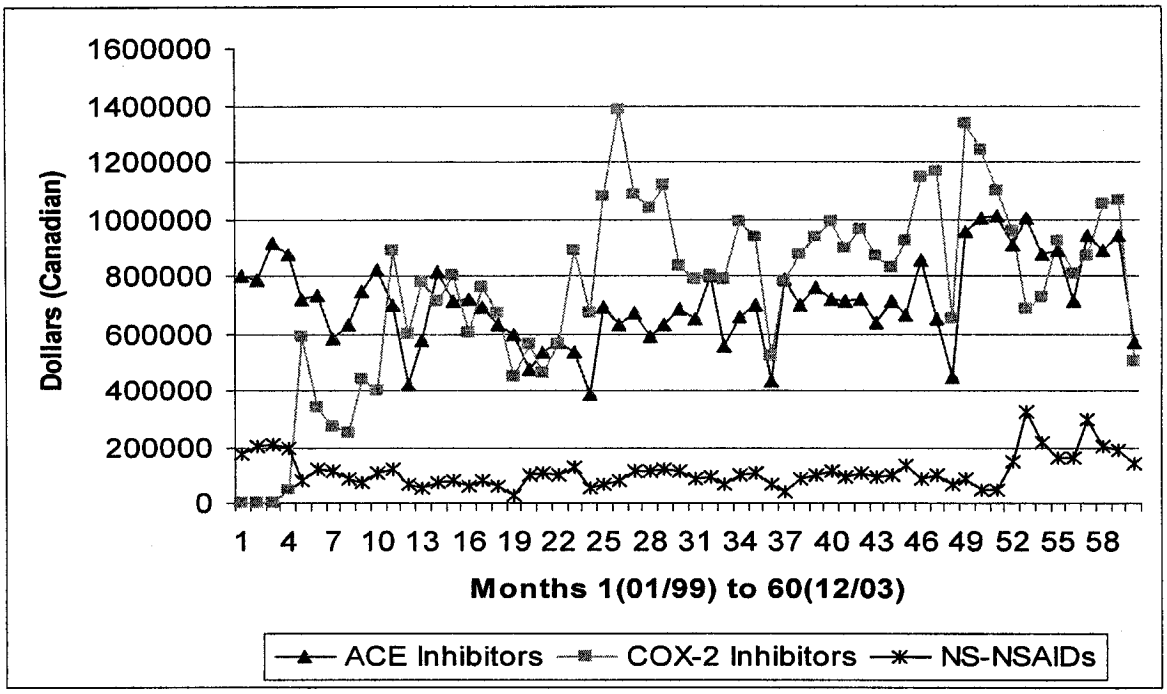


Figure 6.5:

Canadian Monthly Advertising Expenditures for ACE Inhibitors, COX-2s and NS-NSAIDs From 1999 and 2003

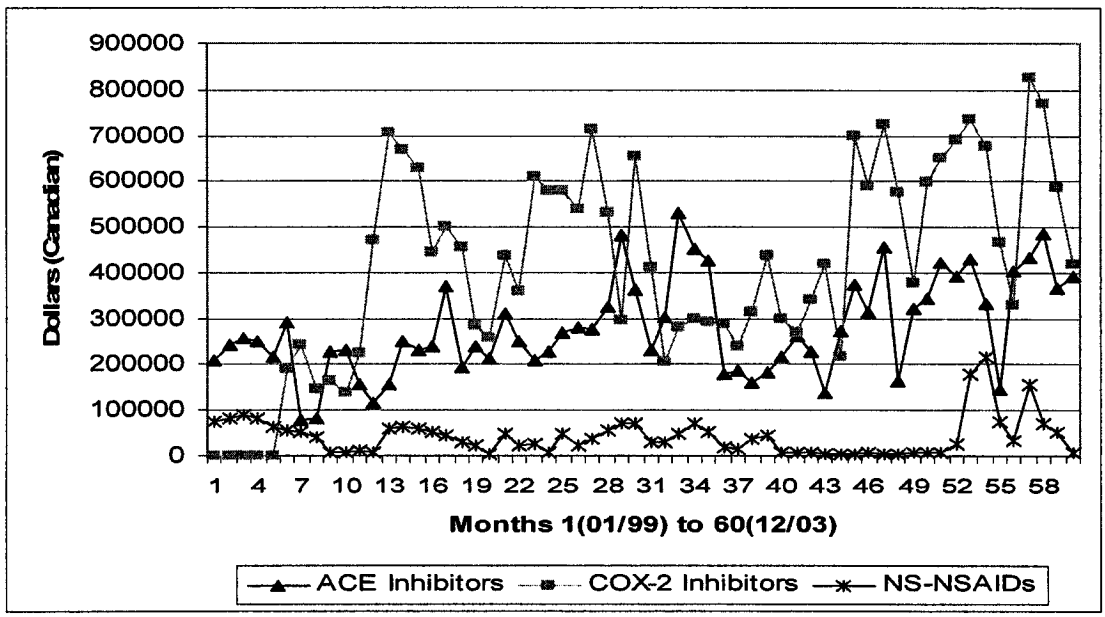


Table 6.2:

Correlation Analysis for IMS Canadian Marketing Activity and COX-2 Prescribing*

	Month To Month N = 48 (months)		One Month Lag N = 47		Two Month Lag N = 46		Three Month Lag N = 45	
	Corr**	p Value	Corr**	p Value	Corr**	p Value	Corr**	p Value
Advertising Circulation	-0.019	0.900	0.000	1.000	0.062	0.683	0.216	0.155
Advertising Page Numbers	-0.052	0.727	-0.027	0.859	0.027	0.856	0.174	0.254
Number of Details	-0.254	0.081	-0.136	0.362	-0.161	0.284	0.162	0.287
Factor 1 - Detailing	0.040	0.788	0.144	0.336	0.175	0.245	-0.161	0.292
Factor 2 - Advertising	0.031	0.832	0.146	0.328	-0.029	0.846	-0.147	0.337

* The correlation analysis was performed using the IMS national estimates relative to the actual Nova Scotia prescribing values, and assumes that the expenditures (detailing and advertising) in Nova Scotia are proportional to the national averages.

**Correlation Coefficient

Following the same trendline approach for the creation of representative independent variables, the ACE Inhibitors were also evaluated in an effort to measure the impact that marketing activity has on prescribing activity for established categories of drugs. Again, correlation was evaluated on a month to month and a 1, 2 and 3 month lag basis, and the period represented 48, 47, 46 and 45 months, respectively.

For the month to month and lag analyses of the dependent variable of quantities of ACE Inhibitors prescribed, as with the COX-2s, there was no significance at the $p \leq 0.05$

level for the three independent variables, and the 2 factors arising from principle component analysis that were considered. Table 6.3 presents the results of the correlation procedure analysis.

Table 6.3:

Correlation Analysis for IMS Canadian Marketing Activity and ACE Inhibitor Prescribing* for Nova Scotia Senior Pharmacare Beneficiaries

	Month To Month N = 48 (months)		One Month Lag N = 47		Two Month Lag N = 46		Three Month Lag N = 45	
	Corr**	p Value	Corr**	p Value	Corr**	p Value	Corr**	p Value
Advertising Circulation	0.077	0.604	0.133	0.372	-0.059	0.696	-0.157	0.304
Advertising Page Numbers	-0.058	0.693	0.108	0.470	-0.141	0.352	-0.021	0.889
Number of Details	0.016	0.914	0.144	0.334	0.186	0.217	0.144	0.347
Factor 1 - Detailing	-0.013	933	-0.017	0.908	0.053	0.728	0.146	0.339
Factor 2 - Advertising	-0.267	0.067	-0.158	0.288	-0.160	0.288	0.146	0.362

* The correlation analysis was performed using the IMS national estimates relative to the actual Nova Scotia prescribing values, and assumes that the expenditures (detailing and advertising) in Nova Scotia are proportional to the national averages.

**Correlation Coefficient

6.4.2 Hypotheses H2 to H6

H2: The frequency of occurrence of opportunities available in which one may prescribe from a new drug category, will influence the consideration for and subsequent trial of a new product.

H3: Physicians with practices in urban settings are more likely to prescribe new drugs than are physicians operating in rural environments.

H4: Older physicians are less likely to prescribe from new product categories

H5: Physicians with a history of active prescribing, are more likely to prescribe from new product categories.

H6: The probability of prescribing from a new drug category is greater among male than female physicians.

Determination of support for hypotheses H2 – H6 was attempted using univariate analysis, against the dependent variables summarized in Chapter 6.2.2.

6.4.2.1 Total (Volume) Prescribing: Hypotheses H2 to H6

This analysis was refined to further explore the profiles of individuals classified as "high prescribers", and to provide insight into the influence of the independent variables on total prescribing. Considering the average number of COX-2 prescriptions per month over the period of the study led to the creation of two dependent variables, namely, the upper quartile of total COX-2 prescribers ($\geq$ 5.69 COX-2 prescriptions per month) and the lower quartile of total COX-2 prescribers($\leq$0.167 COX-2 prescriptions per month). The universe against which the quartiles were defined was 925 physicians

(originally 1206 less those individuals who neither prescribed COX-2s or NS-NSAIDs) and included individuals who prescribed NS-NSAIDs only (n=65), COX-2s only (n=60) and both (n=800), and the distribution of this population is presented in Figure 6.1.

The independent variables, their relative Spearman Correlation Coefficients and associated p values are presented in Appendix 6.2, while the key observations from the bivariate analysis are presented below:

- Male physicians were more likely to comprise the first quartile of COX-2 prescribers than their female counterparts
- Older physicians are more likely to comprise the first quartile of COX-2 prescribers than younger physicians
- Individuals who have had more time in practice and are classified as older graduates (above the mean) are more likely to comprise the first quartile of COX-2 prescribers than individuals with less time in practice or who have graduated more recently
- Physicians with rural practices are more likely to comprise the first quartile of COX-2 prescribers than physicians with urban practices.
- General practitioners are more likely to comprise the first quartile of COX-2 prescribers than specialists.
- Physicians who prescribe any of the other four categories of drugs in this study are more likely to comprise the first quartile of COX-2 prescribers

While Appendix 6.2 provides the relative Spearman Correlation Coefficients and associated p values for the 16 independent variables, it is interesting to note the difference between the profile of individuals who are in the upper quartile of prescribers

and those who are in the lower quartile of prescribers. Table 6.4 presents the extent of the variance in the demographics between the upper and lower quartiles of the physician population.

Table 6.4:

Comparison of Upper Quartile and Lower Quartile Total COX-2 Prescribers Within the Nova Scotia Physician Study Sample (N = 1206) Between 1999 and 2003

	Upper Quartile	**Lower Quartile***	**T-Test For Significance *p value***
Physician Gender Female	11%	38%	<0.0001♣
Doctor age up to mid 2003 (years)	51.4	49.0	0.0014♣
Year of Graduation	1977.6	1980.2	0.0011♣
Doctor Type: general practice	98%	76%	0.0007♣
Medical school: Canadian	79%	81%	0.4223
Practice County: city	21%	51%	0.0001♣
Years of Practice	25.4	22.8	0.0011♣
Average Monthly NS-NSAID Prescriptions	10.6	1.8	<0.0001♣
Average Monthly Cholesterol Lowering Prescriptions	31.8	6.2	<0.0001♣
Average Monthly ACE Inhibitor Prescriptions	42	7.5	<0.0001♣
Average Monthly Calcium Channel Blocker Prescriptions	35.0	6.5	<0.0001♣
Average combined monthly cholesterol lowering, ACE and calcium channel blocker prescriptions	108.9	20.3	<0.0001♣
Birth Place: Nova Scotia	30%	27%	0.4510
Birth Place: Other Canadian Province	22%	28%	0.0497
Birth Place: Other Country	26%	25%	0.8220
Birth Place: Canada	52%	56%	0.2877♣

*All values presented are the mean values for each segment and characteristic, unless otherwise stated.

♣ all values are significant at the 95% confidence level

6.4.2.2 Relative Prescribing: Hypotheses H2 to H6

This analysis was refined to further explore the profiles of individuals classified as "high relative prescribers", and to provide insight into the influence of the independent variables on relative prescribing. Considering the monthly relative value of COX-2 prescribing (relative value calculated by dividing total monthly COX-2 prescriptions into the combined monthly total of COX-2 and NS-NSAID prescriptions) led to the creation of two dependent variables, namely, the upper quartile of relative COX-2 prescribers ($\geq$ 0.656) and the lower quartile of relative COX-2 prescribers($\leq$0.333). The universe against which these high relative prescribers was selected, consisted of the same 925 physicians used to analyse the total COX-2 prescribers, and the distribution of this population is presented in Figure 6.2.

Considering the relative prescribing variable of COX-2s/COX-2s + NS-NSAIDs, the profile of individuals likely to be in the upper quartile of this relative scale was established, and subsequently set the criteria for bivariate analysis of the correlation between the independent variables and this new, "upper" relative prescribing variable.

This approach provided insight into the influence of the independent variables on relative prescribing within relative category of COX-2s to COX2s plus NS-NSAIDs. The independent variables, their relative Spearman Correlation Coefficients and associated p values are presented in Appendix 6.3, while the key observations from the analysis are presented below:

- Female physicians were more likely to comprise the first relative quartile of COX-2 prescribers than their male counterparts

- Younger physicians are more likely to comprise the first relative quartile of COX-2 prescribers than older physicians
- Individuals who have less time in practice and are classified as younger graduates (below the mean) are more likely to comprise the first relative quartile of COX-2 prescribers than individuals with more time in practice or who graduated earlier than the mean
- Physicians with urban practices are more likely to comprise the first relative quartile of COX-2 prescribers than are physicians with rural practices
- Physicians with low NS-NSAID and high COX-2 prescribing are more likely to comprise the first relative quartile of COX-2 prescribers, but the prescribing patterns of the other three categories of drugs appear to be unrelated to this result

While Appendix 6.3 provides the relative Spearman Correlation Coefficients and associated p values for the 16 independent variables, it is interesting to note the difference between the profile of individuals who are in the upper relative quartile of prescribers and those who are in the lower relative quartile of prescribers. While a characteristic may be significant as defined by a p value ≤ 0.05, Table 6.5 presents the variance in the demographics between the first and fourth quartiles of the physician population.

Table 6.5:

Comparison of Upper Quartile and Lower Quartile Relative COX-2 Prescribers Within the Nova Scotia Physician Study Sample (N = 925) Between 1999 and 2003

	Upper Quartile	Lower Quartile*	T-Test For Significance *p value*
Physician Gender Female	36%	30%	0.0698
Doctor age up to mid 2003 (years)	48.1	50.1	0.0109♣
Year of Graduation	1981.3	1979.0	0.0049♣
Doctor Type: general practice	68%	86%	<0.0001♣
Medical school: Canadian	82%	80%	0.4876
Practice County: city	58%	38%	<0.0001♣
Years of Practice	21.7	24.0	0.0049♣
Average Monthly NS-NSAID Prescriptions	0.99	5	<0.0001♣
Average Monthly Cholesterol Lowering Prescriptions	7.5	14.4	<0.0001♣
Average Monthly ACE Inhibitor Prescriptions	9.5	18.4	<0.0001♣
Average Monthly COX-2 Prescriptions	3.07	3.96	<0.0001♣
Average Monthly Calcium Channel Blocker Prescriptions	8.2	15.5	<0.0001♣
Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	25.3	48.3	0.4510
Birth Place: Nova Scotia	24%	29%	0.1334
Birth Place: Other Canadian Province	31%	25%	0.1161
Birth Place: Other Country	29%	24%	0.1226
Birth Place: Canada	55%	55%	0.9661

*All values presented are the mean values for each segment and characteristic.

♣ All values are significant at the 95% confidence level

6.4.2.3 Gender and Age "Within" Category Analysis

Given that the overall analysis involved establishment of the relationship between the physician universe (N = 1206) and either total COX-2 prescribing or relative COX-2 prescribing, there is some question as to the "within demographic" influence of the various independent variables on prescribing activity. To this end, further exploratory analysis was performed using the total prescribing model, in an attempt to gain insight into variances in prescribing activity within the following physician segments:

- Younger (< 49 years) physicians
- Older (> 49 years) physicians
- Female physicians
- Male physicians

The total prescribing model was used in this analysis to determine if the influencing factors (independent variables where $p \leq 0.05$) as previously presented in Appendix 6.2, were similar. The results from the analysis within the age profiles are presented in Appendices 6.4 and 6.5. The similarity of results between younger and older physicians, and those presented for the population as a whole suggest that there is little difference between the two age cohorts. The following observations from the analysis are similar to those outlined in Chapter 6.4.2.1:

- Males were more likely to comprise the first quartile of total COX-2 prescribers
- Physicians with rural practices were more likely to comprise the first quartile of total COX-2 prescribers than physicians with rural practices
- General practitioners are more likely to comprise the first quartile of total COX-2 prescribers than specialists

- And physicians who prescribe any of the other four categories of drugs in this study are more likely to comprise the first quartile of total COX-2 prescribers.

The results from the analysis within the gender profiles are presented in Appendices 6.6 and 6.7. The similarity between the independent variables in the male and female physician populations would suggest that while gender may have an influence on COX-2 prescribing, with the exception of the level prescribing activity in any of the other four categories of drugs in this study, the within gender influences are not significant.

6.4.2.4 Analysis of Adoption

To this point the analysis has focused on total COX-2 prescribing and relative COX-2 prescribing within the physician universe, over the 60 month period of the study. Given that one of the objectives of this research was to expand on our understanding of diffusion and adoption as it relates to prescription drugs, two approaches were taken to differentiate between these groups of individuals.

In the first approach, adoption and diffusion were considered within the context of early and late prescribers. Table 6.6 presents the total universe of physicians in this study, and their prescribing activities associated with COX-2s and NS-NSAIDs. In this table, November 1999 was taken as the starting point (while first prescriptions didn't occur until February 2000, November was the point at which the two major brands in the COX-2 category had received their NOC). Individual profiles were then determined for physicians prescribing in the first 25 months (early prescribers) as well as for physicians prescribing in the latter 25 months (late prescribers).

Table 6.6:

COX-2 and NS-NSAID Prescribing Activity Within the Nova Scotia Physician Study Sample (N = 1206) Between November, 1999 and November, 2003 For Nova Scotia Seniors With Pharmacare Benefits*

	11/1999 to 10/2001	11/2001 to 10/2003	11/1999 to 10/2003
NS-NSAIDS Only	68	57	65
COX-2s Only	87	84	60
NS-NSAIDS & COX-2s	720	705	800
Subtotal NS-NSAIDS and/or COX-2s	875	846	925
Neither	324	366	281

The profiles of total prescribers and relative prescribers were established against the dependent variable, likelihood of prescribing COX-2s. Total prescribers are profiled in Appendices 6.8 and 6.9. Appendix 6.8 considered the independent variables (See Appendix 5.6), their relative Spearman Correlation Coefficients, and associated p values for the early and late prescribers of COX-2s. Appendix 6.9 compared the variance between upper quartile and lower quartile of total COX-2 prescribers.

The alternative to the analysis of the total COX-2 prescribing individuals, involved creation of the derived variable of COX-2 prescribing relative to total prescribing in the combined categories of COX-2 and NS-NSAIDs. Appendix 6.10 presents the same independent variables used above, their relative Spearman Correlation Coefficients and associated p values for the early and late relative prescriber profiles of COX-2s. Appendix 6.11 presents the extent of the variance among individuals who are

in the upper relative quartile of COX-2 prescribers, compared with those who are in the lower relative quartile of COX-2 prescribers.

While the first approach defined adoption as the likelihood of prescribing in the first 25 months a drug was available versus the second 25 months, the second approach required the creation of a narrower definition of adoption, followed by the analysis of the physician universe corresponding to that definition (ie those individuals who met the adoption criteria). Profiles of these individuals were subsequently created to determine the variance between the two populations.

For purposes of this analysis, the study group within the total Nova Scotia physician universe was selected from that group of physicians who averaged 8 or more prescriptions of NS-NSAIDs and/or COX-2s over the 60 month period of the study (N = 296). Adoption within this group was defined as that point where the ratio of COX-2s to COX-2s plus NS-NSAIDs was ≥ 0.333 for at least a 3 month period. That is, if the physician's total NS-NSAID/COX-2 prescriptions in a given month totaled 9, 3 or more of them had to be COX-2s for 3 or more consecutive months, before the individual was considered an adopter.

For purposes of analysis, the 296 physicians who met the selection criteria were divided into 3 segments; segment 1 (N = 143) adopted in 3 months, segment 2 (N = 44) adopted in 4, 5, 6 or 7 months, and segment 3 (N = 109) adopted in greater than 7 months. Physicians in segment 1 were defined as immediate adopters, and physicians in segment 3 were defined as later adopters. Their profiles are presented in Appendix 6.12.

6.5 Total (Volume) COX-2 Prescribers and Relative COX-2 Prescribers

Having presented the results from the bivariate analysis of the physician population for both total and relative COX-2 prescribers, this chapter will compare these two groups.

Table 6.7, which presents a cross-tabulation of the population of relative COX-2 prescribers with total COX-2 prescribers, illustrates the uniqueness of the two categories of physicians. Here we can see that over the period of the study, the percentage of physicians who were classified as both upper quartile relative COX-2 prescribers and upper quartile total COX-2 prescribers was small, representing just 4.65% (N = 43) of the total sample of 925 physicians. This number was virtually unchanged when considering the same relationship in what has previously been defined as the early prescribing period, the 25 months from November 1, 1999 to November 30, 2001 (Table 6.8). Here we see the percentage of physicians who were classified as both upper quartile relative COX-2 prescribers, and upper quartile total COX-2 prescribers as 5.03% (N = 44) of the total sample of 875 physicians. Finally, when considering the final evaluation period, covering the 25 months from December 1, 2001 to December 31, 2003 (Table 6.9), we see the percentage of physicians who were classified as both upper quartile relative COX-2 prescribers, and upper quartile total COX-2 prescribers as 4.50% (N = 38) of the total sample of 846 physicians.

Table 6.7:

Cross Tabulation of Physicians in the First Quartile of Relative COX-2 Prescribers and Total COX-2 Prescribers for Nova Scotia Senior Pharmacare Beneficiaries from Jan 1999 to Dec 2003

		Relative Prescribing Activity		Total
		Lower 75%	Top 25%	
Prescribing Volume	Lower 75%	506	185	691
	Top 25%	191	43	234
Total		697	228	925

Table 6.8:

Cross Tabulation of "Early Prescriber"* Physicians in the First Quartile of Relative COX-2 Prescribers and Total COX-2 Prescribers for Nova Scotia Senior Pharmacare Beneficiaries from November 1, 1999 to November 30, 2001

		Relative Prescribing Activity		Total
		Lower 75%	Top 25%	
Prescribing Volume	Lower 75%	483	174	657
	Top 25%	174	44	218
Total		657	218	875

* In this table, early prescribers were classified as those individuals who prescribed COX-2s in the period identified (first 25 months after NOC)

Table 6.9:

Cross Tabulation of "Late Prescriber"* Physicians in the First and Fourth Quartiles of Relative COX-2 Prescribers and Total COX-2 Prescribers for Nova Scotia Senior Pharmacare Beneficiaries from December 1, 2001 to December 31, 2003

		Relative Prescribing Activity		Total
		Lower 75%	Top 25%	
Prescribing Volume	Lower 75%	449	176	625
	Top 25%	183	38	221
Total		632	214	846

* In this table, late prescribers were classified as those individuals who prescribed COX-2s in the period identified (months 26 to 50 after NOC)

While Tables 6.7 to 6.9 give us an indication of the lack of commonality (overlap) between upper quartile relative and total prescribers, Tables 6.10 presents the actual demographic differences between the two groups.

Table 6.10:

Comparison of First Quartile Total COX-2 Prescribers and First Quartile Relative COX-2 Prescribers for Nova Scotia Senior Pharmacare Beneficiaries Over the Period of January 1999 to December 2003

	First Quartile Relative COX-2s	First Quartile Total COX-2s*	T-Test For Significance *p value*
Physician Gender Female	36%	11%	0.0002♣
Doctor age up to mid 2003 (years)	48.1	51.4	0.2100
Year of Graduation	1981.3	1977.6	0.1836
Doctor Type: general practice	68%	98%	<0.0001♣
Medical school: Canadian	82%	79%	0.0759
Practice County: city	58%	21%	<0.0001♣
Years of Practice	21.7	25.4	0.1836
Average Monthly NS-NSAID Prescriptions	0.99	10.6	<0.0001♣
Average Monthly Cholesterol Lowering Prescriptions	7.5	31.8	<0.0001♣
Average Monthly ACE Inhibitor Prescriptions	9.5	42	<0.0001♣
Average Monthly Calcium Channel Blocker Prescriptions	8.2	35.0	<0.0001♣
Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	25.3	108.9	<0.0001♣
Birth Place: Nova Scotia	24%	30%	0.0015♣
Birth Place: Other Canadian Province	31%	22%	0.0500♣
Birth Place: Other Country	29%	26%	0.0321♣
Birth Place: Canada	55%	52%	0.2824

*All values presented are the mean values for each segment and characteristic, unless otherwise stated.

♣ All values are significant at the 95% confidence level

6.6 Multivariate Analysis and Modeling

While the bivariate analysis served to explore the data, while providing insight into key independent variables, this stage of the research attempted to establish support for the hypotheses through the creation of models that identify prescribing physicians, given the variables available. Model selection is the process of either adding or removing variables from a regression equation, until you find one that is the best of the available alternatives for the data. While there are three primary approaches used in the creation of a model (backward, forward and stepwise), stepwise selection was the approach used in this study. Stepwise combines the backward elimination (removes variables one at a time from the model as those variables fail to meet specified significance criteria) and forward selection methods to add variables to the model or remove variables from the model as they meet (or fail to meet) specified significance levels.

6.6.1 Variable Selection

The first step in the multivariate regression analysis was to take the study universe which consisted of 925 physicians (originally 1206 less those individuals who prescribed neither COX-2s or NS-NSAIDs) and included individuals who prescribed NS-NSAIDs only (n=65), COX-2s only (n=60) and both (n=800), and split it into calibration and validation sets using a 60:40 ratio. The former provides the foundation against which the model is constructed (calibrated), while the latter provides a sample against which the model may be tested (validated). Appendix 6.3 shows the output from this analysis.

The stepwise regression was performed using three different target (dependent) variables; best (the upper quartile in the total COX-2 prescribing category) and rbest (the

upper quartile in the COX-2/COX-2 + NS-NSAID relative prescribing category, and immediate adopters. With this third target variable, the universe of physicians consisted of those averaging 8 or more COX-2s and/or NS-NSAIDs prescriptions per month, and the dependent variable (immediate adopters) was defined as those physicians with COX-2 prescriptions ≥ 0.333 of the total of COX-2s plus NS-NSAIDs for each month in the first three months of availability.

6.6.1.1 Total Prescribing

The first approach taken in the stepwise analysis used the upper quartile of total COX-2 prescribers as the dependent variable. In the first analysis, all of the independent variables that have been used throughout the study were included in the variable selection procedure. The variables are entered into the regression equation if their p value ≤ 0.05, the significance level for entry into the model. Table 6.11 presents the p and Chi-Square values. The first effect entered is avrgothr3 (the average combined monthly prescribing volume of Calcium Channel Blockers, ACE Inhibitors and Cholesterol Lowering Agents), producing a concordant[10] value of 95.1%. The final three effects entered into the equation, average monthly prescriptions of NS-NSAIDs, relative monthly COX-2

---

[10] Concordance is a measure of the association of predicted probabilities and observed responses used to assess the quality of a logistic model. The procedure gives the percentage of concordant, discordant, and tied observations, as well as the number of observations with different values of the response or target variable. A pair of observations with different responses is considered concordant if the observation with the larger ordered value of response has a lower predicted event probability than the observation with the smaller ordered value of response. Practically, a model with higher values for the concordant index has better predictive ability that a model with lower values. Concordant values are thus reflective of the contribution of the associated independent variables in predicting the dependent or response variable(233).

prescribing over the average monthly prescribing of COX-2s, Calcium Channel Blockers, ACE Inhibitors, and Cholesterol Lowering Agents and general practitioner increased the concordant value to 97%.

Given the strength of the first effect entered (Average monthly total ACE inhibitors, calcium channel blockers and cholesterol lower agents), stepwise was performed a second time, suppressing all drug related variables, in an attempt to develop an equation with a greater demographic representation. The dependent variable remains the upper quartile of COX-2 total prescribers. The effects entered and their resulting concordant values are presented in Table 6.12.

Table 6.11:

Analysis of Effects Not in the Model Using the Upper Quartile of Total COX-2 Prescribers as the Dependent Variable *

Effect	DF	Chi-Square	p Value
Physician gender	1	35.3	<0.0001
Physician age	1	10.2	<0.0014
Year of graduation	1	9.5	<0.0020
General practitioner	1	38.9	<0.0001
City practice	1	31.4	<0.0001
Length of time in practice	1	9.5	<0.0020
Average monthly total ACE inhibitors, calcium channel blaocers and cholesterol lower agents	1	284.6	<0.0001
Average monthly prescriptions of NS-NSAIDs	1	261.1	<0.0001
Monthly COX-2 prescriptions relative to monthly total of COX-2s, ACE inhibitors, calcium channel blaocers and cholesterol lower agents	1	8.5	<0.0036
City based general practitioner	1	7.3	<0.0070
Rural based general practitioner	1	52.8	<0.0001
City based specialist	1	23.8	<0.0001
Rural based specialist	1	11.7	<0.0006
Female general practitioner	1	28.7	<0.0001
Female specialist	1	4.7	<0.0300
Male general practitioner	1	91.7	<0.0001
Male specialist	1	32.4	<0.0001

*This presents a table of the effects prior to the creation of the regression model.

Table 6.12:

Summary of Entry and Influence of Effects into the Predictive Model for the First Quartile COX-2 Prescribing Volume

Effect	Percent Concordance	Chi-Square	C Statistic[11]	Odds Ratio	95 % Confidence Limits Lower	Upper
Male general practitioner	50.8	91.7	0.73	5.467	3.018	9.903
Rural general practitioner	66.4	21.7	0.781	2.917	1.798	4.734
Year of graduation	80.1	10.7	0.804	0.963	0.943	0.984
General Practitioner	80.5	4.7	0.808	7.451	1.731	59.517

6.6.1.2 Relative Prescribing

The second approach taken in the stepwise analysis used the relative prescribing variable of COX-2s/COX-2s + NS-NSAIDs, as the dependent variable, and, as with the bivariate analysis, further refined the target profile to individuals likely to be in the upper quartile of this relative scale (> than 0.6563). Using the same approach as the model created above, which used total COX-2 prescribers as the dependent variable, the first analysis within the relative prescribing category used all of the independent variables that have been used throughout the study in the variable selection procedure. The variables with a p value ≤ 0.05, and their respective Chi-Square values are presented in Table 6.13.

---

[11] The **c statistic** is a measure of the discriminative power of the logistic equation. It varies from 0.5 (the point at which the model's predictions are no better than chance) to 1.0 (the model always assigns higher probabilities to correct cases than to incorrect cases for any pair involving dependent=0 and dependent=1). Thus c is the percent of all possible pairs of cases in which the model assigns a higher probability to a correct case than to an incorrect case.

Table 6.13:

Analysis of Effects Not in the Model Using the Upper Quartile of the COX-2/COX-2 plus NS-NSAID Ratio as the Dependent Variable*

Effect	DF	Chi-Square	p Value
Physician age	1	8.3	0.0040
Year of graduation	1	7.8	0.0051
General practitioner	1	19.0	<0.0001
City based practice	1	7.8	0.0052
Length of time in practice	1	7.8	0.0051
Monthly COX-2 prescriptions relative to monthly total of COX-2s, ACE inhibitors, calcium channel blaocers and cholesterol lower agents	1	82.6	<0.0001
Born outside of Canada	1	6.5	0.0110
Rural based general practitioenr	1	17.3	<0.0001
City based specialist	1	9.8	0.0018
Rural based specialist	1	7.6	0.0060
Male general practitioner	1	16.9	<0.0001
Male specialist	1	14.6	0.0001

*This presents a table of the effects prior to the creation of the regression model

The variables are entered into the regression equation based on their relative strength. The first variable entered, the relative value of COX-2 prescribing over COX-2s plus Calcium Channel Blockers, ACE Inhibitors and Cholesterol Reducing Agents, produced a concordant value of 69.2%. The final two effects entered into the equation, physician age and rural based general practitioner, increased the concordant value to 72.8%. Given the strength of the first variable entered, stepwise was performed a second time, suppressing cox2othr3, in an attempt to develop a profile with a greater demographic representation. This time, the first effect entered into the equation was

genp, producing a concordant value of 26.1%. The final two effects entered into the equation, physician age and city based general practitioner increased the concordant value to 66.4%. The effects entered and their resulting concordant values are presented in Table 6.14.

Table 6.14:

Summary of Entry and Influence of Effects into the Predictive Model Using the Upper Quartile of the COX-2/COX-2 plus NS-NSAID Ratio as the Dependent Variable, and all Available Independent (Excluding Drug Related) Variables

Effect	Percent Concordance	Chi-Square	C Statistic	Odds Ratio	95 % Confidence Limits Lower	Upper
General practitioner	26.1	19.0	0.583	0.222	0.129	0.381
Physician age	63.9	13.2	0.648	0.957	0.936	0.979
City based general practitioner	66.4	8.4	0.669	1.992	1.244	3.190

6.6.1.3 Immediate Adopters

While the previous attempts at stepwise regression considered models using the upper quartile of either total prescribers or relative prescribers as the dependent variable, this final regression considered the defined "immediate adopter" segment of physicians as the dependent variable. While this variable may be defined a number of different ways, for purposes of this study it was considered to be those physicians who prescribed an average of 8 or more COX-2s and/of NSAIDs per month for the study period AND,

prescribed COX-2s to a level ≥ 33% of this total for a 3 month period, commencing at the point when the drug was commercially available.

As with the other two approaches, all of the independent variables that have been used throughout the study were included in the variable selection procedure. The variables are entered into the regression equation if their p value ≤ 0.05, the significance level for entry into the model. Within the above universe, the only variables that proved significant were the average number of COX-2s written per month(avrgcox2) and the average number of NS-NSAIDs written per month(avrgnsaids). Despite this, four effects entered into the preliminary regression, but the first two, avrgcox2 and avrgnsaids produced a concordant value of 82.1%. The remaining two effects, length of time in practice and non-Canadian country of birth increased the concordant value to 83.0%.

Given the strength of the first two effects entered, stepwise was performed a second time, suppressing the two drug related variables in an attempt to develop an equation with greater demographic representation. In this attempt, there were no effects entered into the equation. Even changing the criteria for admission to p≤0.15 did not change the results.

6.6.2 Regression Model Development

The stepwise variable selection process is an effective approach to identify the key influencing variables that should be used in the construction of the regression equation. This equation is critical, as it is used to develop the model which will segment the physician sample (n=925) into segments (bins) of individuals ranging from those most likely to prescribe down to those least likely to prescribe.

This regression equation and model presents the equation output and r-values for the model created using the variables selected from the stepwise procedure. The model is created using two of the three target (dependent) variables as the stepwise selection process, best (the top performing quartile in the total COX-2 prescribing category) and rbest (the top performing quartile) in the COX-2/COX-2 + NS-NSAID relative prescribing category. The target variable, immediate adopters, produced no significant results.

6.6.2.1 Total Prescribing

In the first total prescribing model, the dependent variable is "best" which is defined as the first quartile of the monthly average COX-2 prescribers. The independent variables are monthly average ACE inhibitors, cholesterol reducing agents and calcium channel blockers prescribing incidents, monthly NS-NSAID prescribing incidents, the ratio of total COX-2 monthly average incidents relative to COX-2s plus all other drugs' average incidents, as well as all doctor demographic variables. This regression is dominated by other drugs' monthly incidents, has an R-Square of 0.5221, and a percent concordant value of 97.0%. With the exception of a minor contribution by general practice, demographics plays no role in this model. The output from this analysis is summarized in Appendix 6.13.

In the second total prescribing model using the first quartile of the monthly average COX-2 prescribing incidents as the dependent variable, the independent variables are the same as above, but don't include monthly average ace inhibitor, cholesterol lowering agents, calcium channel blockers or NS-NSAID prescribing

incidents. This regression has greater demographic input, with an R-Square of 0.2476, and a percent concordant value of 82.8%. The odds ratio estimates from this analysis are summarized in Table 6.15.

Table 6.15:

Analysis of Maximum Likelihood Estimates Using All Doctor Demographic and COX-2/COX-2 + NS-NSAID Independent Variables and "best" as the Dependent Variable

Effect	Odds Ratio	95 % Confidence Limits	
		Lower	Upper
General practitioner	7.380	1.918	59.364
Rural based general practice	3.102	1.882	5.113
Year of graduation	0.956	0.935	0.978
Male general practitioner	6.236	3.384	11.492
Born in Nova Scotia	1.534	1.032	2.472

6.6.2.2 Relative Prescribing

The first two models presented in 6.6.2.1 provide an approach to identifying and segmenting the physician universe based on the construction of a model using total COX-2 prescribing as the dependent variable. The next two models consider the dependant variable of rbest, which is defined as the first quartile of the ratio of monthly COX-2 prescribing incidents/COX-2 prescribing incidents + NS-NSAID prescribing incidents.

In the first model, the independent variables are monthly average other drug prescribing incidents, the ratio of COX-2 monthly average incidents relative to COX-2s plus all other drugs' average incidents, as well as all doctor demographic variables. This regression is dominated by the variable defined as the ratio of COX-2s to COX-s + all

other drugs , it has an R-Square of 0.1479, and a percent concordant value of 72.8%. The output for this analysis is summarized in Appendix 6.14. In the second model for relative prescribing, the independent variables are demographics relating to the physician. This regression has an R-Square of 0.0687, and a percent concordant value of 66.4%. The odds ratio estimates for this analysis are summarized in Table 6.16.

Table 6.16:

Analysis of Maximum Likelihood Estimates Using All Doctor Demographics as Independent Variables and "rbest" as the Dependent Variable

Effect	Odds Ratio	95 % Confidence Limits	
		Lower	Upper
General practitioner	0.222	0.129	0.381
Physician age	0.957	0.936	0.979
City based general practitioner	01.992	1.244	3.190

CHAPTER 7

DISCUSSION

The purpose of this section is to evaluate the results of this research in the context of the hypotheses, the research statement and the proposed theoretical considerations.

7.1 General Observations

The objective of this research was to further our understanding of physician prescribing behaviour, and to gain insight into the factors that influence the adoption of new interventions, in this case, a new category of prescription drugs, the COX-2s. While this work provided insight into physician prescribing behaviour, it further contributed to our understanding of physician prescribing populations and their respective prescribing sub-segments, within the physician universe. More specifically, this research provided insights into the profiles of high volume prescribers and high relative prescribers, and it presented new perspectives on the process of diffusion and adoption of new drugs among the prescribing population, relative to the social, environmental and marketing realities of the early 2000s.

This research also presents support for a diffusion/adoption cycle that is highly compressed, containing few of the elements of the historical adoption models proposed by Rogers and Coleman (19, 54). This perspective on the diffusion of new technologies within specific populations stands to influence aspects of government policy with respect to continuing medical education and the approach to academic detailing. This research also changes the way we look at the marketing strategy for new products within a given population of physicians, and our subsequent expectations around adoption and

implementation. Finally, it reinforces some of evolving thought around marketing and social theory as it relates to drug prescribing and physician behaviour.

Three approaches to the analysis were pursued in an effort to gain insight into the profiles of physicians, as defined by their approach to prescribing. Establishment of the three profiles resulted in:

- Evaluation of that segment of the physician population with a large average monthly volume of COX-2 prescriptions written.
- Evaluation of that segment of the physician population with a high proportion of COX-2s written, relative to the total products written in the general NS-NSAID/COX-2 category.
- Evaluation of that segment of the physician population with an average of 8 or more COX-2s and/or NS-NSAIDs prescribed per month, where an amount equal to 33% or higher of the total prescriptions were COX-2s for at least 3 consecutive months (adopters).

Figures 6.1 through 6.3 present the distribution of the 925 physicians used in this study relative to their COX-2/NS-NSAID prescribing activity. Figure 6.1 demonstrates that the greatest volume of COX-2s, are prescribed by a small percentage of the physician population. This analysis subsequently led to the development of a dependent variable based on the profile of the upper quartile of prescribers, that is, individuals who averaged 5.7 prescriptions or more per month. (The mean value of COX-2 prescriptions written per month among the 925 physicians sampled was 3.88)

In Figure 6.2 and 6.3 we see the incremental and cumulative distribution of physicians against the relative scale of COX-2 prescriptions divided by COX-2 plus NS-

NSAID prescriptions, respectively. With the exception of the two extremes (no COX-2s, 7.03% and no NS-NSAIDs, 6.49%), the remainder of the sample (N=860) is representative of a normal distribution across the relative prescribing scale, from >0.0 to <1.0, with a mean of 0.492 and a median of 0.50.

These distribution analyses of the physician population provide distinctly unique views of physicians who are high volume prescribers, as well as those who are more likely to prescribe new drugs relative to the alternatives. Further analyses of the profiles of these sub-segments of the physician population provided insight into the demographics and profile of the study population.

The final element of this research was to determine the presence of an adoption curve, and to establish criteria for differentiation between the profile of early adopters and late(r) adopters.

7.2 Hypotheses – Discussion and Observation

Regression analysis (linear or multiple) serves three major purposes, namely, description, control and prediction. While much of this research established correlation between dependent and independent variables, it is necessary to acknowledge that correlation does not imply causality. Regardless of the strength of the statistical relationship between the variables, a cause and effect pattern is not necessarily implied by the regression model. Furthermore, even when a strong statistical relationship reflects causal conditions, it is important to recognize that the causal conditions may act in the opposite direction from the hypothesis.

To this end, bivariate analysis of each independent variable against the dependent variable of COX-2 prescribing provided preliminary insight into which variables are likely to have the greatest influence in profiling the prescribing population, while multivariate analysis considered the interaction of the independent variables (covariance).

As stated earlier, the hypotheses were considered within the physician segments of total prescribing, relative prescribing and immediate adoption. The upper quartile of total COX-2 prescribers, and the upper quartile of the ratio of COX-2 prescribers/COX-2 plus NS-NSAID prescribers are the two dependent variables for total and relative prescribing, respectively. The dependent variable among prescribers averaging eight or more COX-2s and/or NS-NSAIDs per month was immediate adopters, namely, those who adopted within three months.

The multivariate analysis for both relative and total prescribing was done twice: once incorporating the influence of the average drug prescribing variables per month, and once in which these variables were suppressed. Given the strength of the variables representing actual drug prescribing activity, when suppressed, the resulting analysis demonstrated a measure of the influence of the non-prescribing variables.

These analyses led to the creation of the following multiple regression (model) equations of the prescribers as a sub or 2^{nd} stage model. That is, the profile (of prescribing physicians) within a given population (of physicians);

Y_{TD} - Total Prescribers Including Prescription Drug Variables

Y_{TWD} - Total Prescribers Excluding (Without) Prescription Drug Variables

Y_{RD} - Relative Prescribers Including Prescription Drug Variables

Y_{RWD} - Relative Prescribers Excluding (Without) Prescription Drug Variables

These equations, their independent elements and predictive capability are discussed further within the context of each hypothesis.

7.2.1 Hypothesis 1

The probability of prescribing a drug category is a function of the volume of detailing and professional journal advertising targeted toward the physician for that specific drug category. Hypothesis 1 is rejected within both relative and total groups of prescribers.

This hypothesis was tested by considering two types of marketing activities, prescription drug detailing and professional journal advertising. Within each activity, there were three parameters measured. The analysis, discussed in Chapter 6.4.1, evaluated the influence of prescription drug detailing and professional journal advertising on physician prescribing of an existing drug category (ACE Inhibitors) and a new drug category (COX-2s). Figures 6.4 and 6.5 illustrate the expenditures in detailing and advertising by drug category by month.

As discussed in Chapter 6.4.1, these two marketing activities were sub-divided into three separate activities (tactics). For the bivariate analysis, of the six sub-variables available, the three considered in this analysis were the number of details per month, total monthly advertisement circulation and number of advertisement pages purchased. The correlation of these three independent variables to prescribing is presented in Table 6.2 for the month in which the activity was performed, as well as for periods one, two and three months after the marketing expenditure took place. There was no significant

correlation between COX-2 prescribing and any of the marketing activities ($p \leq 0.05$) considered.

While these results may seem counterintuitive, consider the early increase in prescribing of COX-2s, followed by a period of decline in volume. There was a 36.6% net increase in prescribing in the combined NS-NSAID/COX-2 category in 2000, the first full year[12] COX-2s were available for prescribing in Nova Scotia (see Table 5.6). Furthermore, in Nova Scotia, for the three years following 2000, COX-2 prescriptions declined to 37,200 in 2003 from a peak of 49,200 in 2001 (-24.4%), and the decline in the combined NS-NSAID/COX-2 category was 17.8% during the same period. Interestingly, advertising and detailing expenditures for both of these product categories during the same period remained relatively constant (Figures 6.4 and 6.5)

Conversely, national growth in all prescription drugs during this same period averaged 7.2% per annum (8). To this end, the average annual increase in the combined category for the first four years that the COX-2s were available was 3.1%, well below the national average of 7.2% reported by IMS for all prescription drugs. This further reinforces the observed lack of any relationship between marketing activity and prescribing.

Work in Australia by Kerr et al supports this observation, where he found that the combined category increased about 20% in the year immediately following introduction (90) Thus, while one might expect adoption of a new drug in response to advertising (and a variety of other factors), an increase of these proportions over the actual replacement

---

[12] While there was marginal prescribing in January 2000, analysis of PHRU data indicates that February was the first full month the drugs were broadly prescribed.

rate can have a significant impact on drug insurance programs, and their respective budgets.

While this lack of a correlation between COX-2 prescribing relative to COX-2 journal advertising and detailing may seem counter-intuitive, the influence of these same marketing activities on an existing product (ACE Inhibitors) demonstrated a similar relationship. Again, for the bivariate analysis, of the six sub-variables available, the three considered in this analysis were the number of details per month, total monthly advertisement circulation and number of advertisement pages purchased. The correlation of these three independent variables to prescribing is presented in Table 6.3 for the month in which the activity was performed, as well as for periods 1, 2 and 3 months after the marketing expenditure took place. There was no significant correlation between ACE Inhibitor prescribing and any of the marketing activities ($p \leq 0.05$) considered.

The majority of the physicians consulted in the convenience survey maintained that the decision to prescribe from a category was based on their own objective analysis of the alternatives available, given the needs of their patients. They did, however, agree that detailing and commercial marketing influenced their activities, but felt that its influence was limited to the selection of brands within a category (ie Vioxx® versus Celebrex®), rather than the actual selection of the category itself.

As was previously discussed, following evaluation of the relationship between individual marketing variables and the prescribing of COX-2s and ACE inhibitors, a factor analysis was performed on the original six independent marketing variables to determine if these elements function separately, or if they may be more effectively grouped into smaller sets of evaluation (factors or variates). The extraction method, using

principle component analysis, yielded two factors or components for both the COX-2s the ACE Inhibitors.

With both the COX-s and the ACE inhibitors, factor 1 consisted of detail cost, detail minutes and number of details, and factor 2 consisted of advertising cost, advertising circulation and advertising page numbers. The results from both analyses, as presented in Tables 6.2 and 6.3, demonstrated that neither of the derived factors was correlated with the number of prescriptions written monthly.

While we see no support for Hypothesis 1 in these results, it reinforces the fact that that marketing activities alone do not explain all of the prescribing activity in new drug categories.

7.2.2 Hypothesis 2

The frequency of occurrence of opportunities in which one may prescribe from a new drug category, will influence the consideration for and subsequent trial of a new product. Hypothesis 2 is supported among total prescribers and rejected among relative prescribers.

The inference in this hypothesis is that the greater the exposure a physician has to opportunities in which to prescribe a drug, the more likely it is that they will try a relevant intervention from a new drug category, as opposed to using the same products they have always used. As stated in Chapter 6.2.2, presence of an NS-NSAID prescribing regimen was considered indicative of the presence of conditions in a physician's practice for which COX-2s may be prescribed. Support for this hypothesis

would then be demonstrated by high levels of absolute and relative COX-2 prescribing by physicians, who had demonstrated high levels of NS-NSAID prescribing.

Appendix 6.2 demonstrates a high correlation between monthly NS-NSAID prescriptions and the upper quartile of total COX-2 prescribers, which supports this hypothesis among total COX -2 prescribers. Additionally, the average number of NS-NSAID prescriptions per month in the upper quartile of total COX-2 prescribers was 10.6, compared with 1.8 in the lower quartile of COX-2 prescribers (Table 6.4). When considering NS-NSAID prescribing among the upper quartile of relative COX-2 prescribers, however, average NS-NSAID prescriptions per month were less than 1, compared to the average of 5 demonstrated in the lower quartile of relative prescribers of COX-2s (Table 6.4). This suggests that the likelihood of being a high relative COX-2 prescriber, was greater if total prescriptions in the combined NS-NSAID/COX-2 category was small.

The multiple regression analysis carried out with the upper quartile of total prescribers(Y_T) and the upper quartile or relative prescribers(Y_R) as the dependent variables. This led to the development of the four regression equations defined in Chapter 7.2, Y_{TD}, Y_{TWD}, Y_{RD}, and Y_{RWD}.

In the first multiple regression equation for both categories, all independent variables, including the prescribing drug variables, were available for selection, and the resulting equations for both Y_{TD} and Y_{RD} demonstrated the influence of the physican's prescribing activity on the likelihood of being either a high relative or high total COX-2 prescriber. For total prescribers, $Y_{TD} = ß_0 + ß_1$ (average combined monthly cholesterol lowering, ACE inhibitor and calcium channel blocking prescriptions) + $ß_2$ (average monthly NS-NSAID prescriptions) + $ß_3$ (monthly COX-2 prescriptions relative to monthly total of COX-

2s, ACE inhibitors, calcium channel blockers and cholesterol lower agents prescribed) + β_4 (general practitioner) + ε, where the adjusted R-square value for Y_{TD} was 0.7644 and the concordant value was 97.0. The high concordance for Y_{TD} combined with the fact that the only non-prescribing variable in the equation raised the concordant value incrementally from 96.7 to 97.0, supports the relationship between the presence of prescribing and the occurrence of situations in which a drug may be prescribed, but does not explain the variance.

For relative prescribers, $Y_{RD} = \beta_0 + \beta_1$(monthly COX-2 prescriptions relative to monthly total of COX-2s, ACE inhibitors, calcium channel blockers and cholesterol lower agent prescriptions) + β_2 (general practitioner) + β_3 (physician age) + β_4 (city based general practitioner) + ε, where the adjusted R-Square value for Y_{RD} was 0.2219 and the concordant value was 73.0, suggesting that the variables in this equation may account for approximately 73.0% of the prescribing activity of a new drug category. The three non-prescribing variables raised the concordant value incrementally from 69.6 to 73.0.

While these results demonstrate a strong correlation between NS-NSAID and COX-2 prescribing among the total COX-s prescribers (supports H2), this relationship is not significant within the category of high relative COX-2s prescribers. Given the low average prescribing of NS-NSAIDs among this group (1 vs 10.6), the lack of a relationship is most likely a function of the lack of opportunity to prescribe in the category.

These results were supported by the comments from the surveyed physicians, who generally agreed with the hypothesis, and further indicated that if a patient has a condition that is relatively common, and the existing regimen of drugs isn't working, they

may be more inclined to try a new intervention (drug). The presence of the condition in the patient group thus plays a key role in prescribing the new intervention (COX-2s) across all demographics.

7.2.3 Hypothesis 3

Physicians with practices in urban settings are more likely to prescribe new drugs than are physicians operating in rural environments. Hypothesis 3 is rejected among total prescribers and supported among relative prescribers.

This hypothesis was proposed in an effort to acknowledge and evaluate the variance in the demographics of physicians who live and work in urban and rural environments. To this end, it attempts to recognize the potential influence of these differences on prescribing practices. The challenge with this hypothesis, as discussed in Chapter 6, relates to the definitions of urban and rural, and the inconsistencies in assigning a rural or urban label to the physicians in this database. Despite this, while it is likely that a small number of "urban" practices have been overlooked by selecting only those physicians practicing in Halifax, Dartmouth or Sydney, there may also be, by definition, a small number of rural practices within these defined areas, which have been assigned an urban label.

Despite the potential for incremental overlap between the rural and urban physician, the results provide us with insight into the prescribing habits of these two geographic cohorts. The data supports the greater likelihood of physicians in rural settings prescribing at the upper quartile level of total COX-2s (Appendix 6.2), where 79% of the upper quartile prescribers operate in a rural practice and only 49% of the

physicians in the lower quartile of prescribers are considered to have a rural practice (Table 6.4). While these results demonstrate a strong correlation between total COX-2 prescribing and operating a rural practice, when considering relative prescribers of COX-2s, we see the opposite. High relative prescribers are more likely to have an urban practice, with 58% of the physicians in the upper quartile operating an urban practice and only 38% of the physicians in the lower quartile operating an urban practice (Table 6.5). Again, as discussed in Chapter 6.4.2.3, these urban-rural trends remained when prescribing practices between gender, and among younger and older physicians were compared.

The multivariate analysis supported both of these observations. When the drug prescribing variables were suppressed, in Y_{TWD}, we see the presence of rural general practioners, where $Y_{TWD} = ß_0 + ß_1$ (general practitioner)$+ ß_2$ (rural based general practitioner) + $ß_3$ (year of graduation) + $ß_4$ (male general practitioner) + $ß_5$ (born in Nova Scotia) + ε, with an adjusted R-square value of 0.3348 and the concordant value was 81.1, suggesting that, given the independent variables in our analysis, the selected variables explain approximately 81.1% of the prescribing activity of a new drug category.

Similarly, in Y_{RWD}, where the drug prescribing variables are suppressed, we see the presence of city based general practitioners, where $Y_{RWD} = ß_0 + ß_1$ (general practitioner) + $ß_2$ (physician age) + $ß_3$ (city based general practitioner) + ε, with an adjusted R-Square of 0.1031 and a concordant value of 66.9.

Thus, while rural physicians may be more likely to be larger volume prescribers of the COX-2s, it is the urban physicians who, given the option, appear more likely to select COX-2s over NS-NSAIDs. While it was expected that new drugs would be

prescribed at a greater level in urban environments, this was anticipated to be a function of greater exposure to corporate detailing and promotional efforts, as well as potentially greater access to peers and opinion leaders. While the majority of the physicians participating in the convenience survey disagreed with this hypothesis, there were still individuals who felt it was true, given the potentially greater exposure to corporate detailing. In summary, while rural physicians are likely to be the higher volume prescribers of new products, urban physicians are likely to be the higher relative prescribers of new products.

7.2.4 Hypothesis 4

Older physicians are less likely to prescribe from new product categories. Hypothesis 4 is rejected among total prescribers and supported among relative prescribers.

There were three variables that provided an opportunity to measure the relationship between age and prescribing practices. These included the actual age of the physician (age was calculated as the physician's age at the mid-point of 2003), the date of graduation and their length of time in practice.

Again, physician age was considered for both the relative level of prescribing and the total level of prescribing. Among total prescribers of COX-2s, older physicians were more likely to prescribe at the upper quartile level. This was supported with significant correlations by both length of time in practice and physician age (Appendix 6.2). Despite the significance of these two variables, the actual difference between the upper and lower quartile was only 2.4 years in age and 2.6 years for length of time in practice (Table 6.4).

When considering relative prescribers, younger physicians were more likely to prescribe at the upper quartile level. This was supported by significant correlations for both length of time in practice and physician age (Appendix 6.2). The actual difference between the upper and lower quartiles was only 2 years in age and 2.3 years for length of time in practice (Table 6.5). Further analysis of the two groups (older physicians, >49 and younger physicians < 49) demonstrated no appreciable difference in prescribing habits or demographics between the two groups (Chapter 6.4.2.3).

The multivariate analysis supported both of these observations. When the drug prescribing variables were suppressed, in Y_{TWD}, we see the presence of year of graduation, which is an age influenced variable, where $Y_{TWD} = \beta_0 + \beta_1$ (general practitioner)+ β_2 (rural based general practitioner) + β_3 (Year of graduation) + β_4 (male general practitioner) + β_5 (born in Nova Scotia) + ε, with an adjusted R-square value of 0.3348 and the concordant value was 81.1.

Similarly, in Y_{RWD}, where the drug prescribing variables are suppressed, we see the presence of physician age, where $Y_{RWD} = \beta_0 + \beta_1$ (general practitioner) + β_2 (physician age) + β_3 (city based general practitioner) + ε, with an adjusted R-Square of 0.1031 and a concordant value of 66.9.

While both the bivariate and multivariate analysis suggest that younger physicians are more inclined to be among the upper relative quartile of COX-2 prescribers, and older physicians are more likely to prescribe a larger quantity of a new product, the physicians in the convenience survey indicated that they expected that older physicians would be less inclined to adopt new products, feeling that they would be more inclined to go with the "tried and true".

7.2.5 Hypothesis 5

Physicians with a history of active prescribing, are more likely to prescribe from new product categories. Hypothesis 5 is supported among total prescribers and rejected among relative prescribers.

This hypothesis proposes that physicians, who are regular prescribers from a number of different drug categories, would be more inclined to prescribe from a new drug category. Classification as an active prescriber really becomes a function of the way a physician approaches a patient's condition. That is, would they be more inclined to recommend some element of lifestyle change, possibly associated with a prescription or would they be more inclined to write a prescription, possibly associated with some recommendation for a lifestyle change. This latter group would comprise the segment referred to as active prescribers.

For purposes of this study, an active prescriber is thus an individual whose relative or total COX-2 prescribing activity is highly correlated with prescribing activity in the other four drug categories. The likelihood of prescribing in the upper quartile of total COX-2 prescribers was highly correlated with prescribing in all of the four other categories (Appendix 6.2). The actual average number of prescriptions written per month in the categories of cholesterol lowering agents, calcium channel blockers and ACE inhibitors was 108.9 in the upper quartile of total prescribers and 20.3 in the lower quartile of prescribers (Table 6.4).

Conversely, among relative prescribers, NS-NSAIDs and COX-2s were negatively and positively correlated (as one would expect given the nature of the relative equation), respectively, but the other three drug categories were not significant

(Appendix 6.3), that is, relative adoption is not a function of total prescribing. Comparison of the actual quantity of drugs prescribed between the upper and lower quartiles demonstrated lower prescribing rates in all categories among the upper quartile of relative prescribers.

In the multivariate analysis, for total prescribers, $Y_{TD} = \beta_0 + \beta_1$ (average combined monthly cholesterol lowering, ACE inhibitor and calcium channel blocking prescriptions) + β_2 (average monthly NS-NSAID prescriptions) + β_3 (monthly COX-2 prescriptions relative to monthly total of COX-2s, ACE inhibitors, calcium channel blockers and cholesterol lower agents prescribed) + β_4 (general practitioner) + ε, where the adjusted R-square value for Y_{TD} was 0.7644 and the concordant value was 97.0. The high concordance for Y_{TD} combined with the fact that the only non-prescribing variable in the equation raised the concordant value incrementally from 96.7 to 97.0, supports the stated hypothesis. That is, the relationship between a physician's demonstrated prescribing activity (active prescriber) and the likelihood of them being an upper quartile prescriber of a new drug.

For relative prescribers, $Y_{RD} = \beta_0 + \beta_1$ (monthly COX-2 prescriptions relative to monthly total of COX-2s, ACE inhibitors, calcium channel blockers and cholesterol lower agent prescriptions) + β_2 (general practitioner) + β_3 (physician age) + β_4 (city based general practitioner) + ε, where the adjusted R-Square value for Y_{RD} was 0.2219 and the concordant value was 73.0, suggesting that the variables in this equation can account for approximately 73.0% of the prescribing activity of a new drug category. The absence of total NS-NSAID prescribing variables in this equation supports the bivariate analysis which indicates that high relative prescribers are less likely to have an active prescribing history.

While the physicians surveyed had mixed comments with respect to this hypothesis, they generally felt it made sense. What we see here is a strong relationship between prescribing volume of all drugs and total COX-2 prescribers, and, within relative prescribers, no apparent relationship between prescribing volume and relative prescribing of COX-2s. Interestingly, physicians who tend to prescribe fewer drugs (less active), are more inclined to have a higher relative rate of prescribing new drugs. In this case, we see support for the hypothesis with both total prescribing and relative prescribing.

7.2.6 Hypothesis 6

The probability of prescribing from a new drug category is greater among male than female physicians. Hypothesis 6 is supported among total prescribers and rejected among relative prescribers.

The physicians surveyed were unanimous in their disagreement with this hypothesis, but the results from the analysis suggest otherwise. Their opposition to the hypothesis was interesting, considering the high correlation between male physicians and the likelihood of prescribing at the upper quartile level of total COX-2s (Appendix 6.2). In terms of actual numbers, 89% of physicians prescribing in the upper quartile of total COX-2s were male, while only 62% of the physicians prescribing in the lower quartile were male (Table 6.4). The multivariate analysis supported the observations among total prescribers. With the drug prescribing variables suppressed, in Y_{TWD} we see the presence of male general practitioners, where $Y_{TWD} = ß_0 + ß_1$ (general practitioner) + $ß_2$ (rural based general practitioner) + $ß_3$ (year of graduation) + $ß_4$ (male general practitioner) + $ß_5$ (born in Nova Scotia) + ε, with an adjusted R-square value of 0.3348 and the concordant value was 81.1.

When considering the relationship between gender and the relative prescribing levels of COX-2s, gender again is significant, but this time it is correlated with female physicians (Appendix 6.3), with 36% of the physicians in the upper quartile of relative COX-2 prescribers female, and only 30% in the lower quartile female (Table 6.5). Interestingly, among relative prescribers, where the drug prescribing variables are suppressed, we see $Y_{RWD} = ß_0 + ß_1$ (general practitioner) + $ß_2$ (physician age) + $ß_3$ (city general practitioner) + ε, with an adjusted R-Square of 0.1031 and a concordant value of 66.9. Gender is not significant in the multivariate analysis with relative prescribing as the dependent variable.

In a comparison of the profile of female and male physicians among those in the upper quartile, age is significant only in the female population (older is more inclined to prescribe at the upper quartile level), and a rural based practice combined with prescribing other drugs is significant in both genders(Chapter 6.4.2.3). The results of this analysis demonstrate a strong relationship between total COX-2 prescribing and male physicians, while female physicians are more likely to have a high relative level of COX-2 prescribing, which partially supports H6.

7.2.7 Summary of Hypotheses

While there are varying degrees of support for each hypothesis, the final analysis, with the exception of H1, really becomes a function of how one wishes to consider the actual act of adoption. That is, do we consider it from the perspective of the average number of prescriptions written for a given product in a given month or, from the perspective of a ratio of the number of prescriptions written relative to a common

denominator such as total patient visits, other drugs prescribed, or the presence of specific conditions among the patient population, to name but a few of the denominator alternatives. Finally, should we consider the variables that influence prescribing within a unique population. The third consideration, given the above hypotheses, is to categorize a sub-segment of the physician population, defined as adopters, and determine the validity of the hypotheses as it relates to this cohort of the physician population.

While the choice of approach is really dependent of the objectives of the study, this research provides the opportunity to consider prescribing of new drug categories from three perspectives, namely, prescribing, prescribers and active prescribers. Within the category of prescribing, we are really considering those individuals with high levels of COX-2 prescribing relative to the alternatives. Here we are likely to see younger female physicians with urban practices who have low levels of NS-NSAID prescribing (a patient base for whom the new product would be less relevant), and low levels of the other three categories of drugs analysed.

Considering this research from the perspective of the prescribers, the profile of those individuals expected to be among the upper quartile of total COX-2 prescribing are older male physicians in rural practices, actively prescribing NS-NSAIDs (a patient base with conditions for which the new product would be relevant), as well as the other three categories of drugs analysed.

Within this universe of the upper quartile of total prescribers, a sample of 252 physicians who have averaged 8 or more prescriptions of NS-NSAIDS and/or COX-2s since the start of the study period, have been categorized as adopters. This group was selected to evaluate the validity of the traditional model of adoption. Using the profile of

immediate adopters[13] as the dependent variable, none of the independent variables, with the exception of average NS-NSAID prescribing, demonstrated any significance in the remainder of this sample classified as later adopters (N= 109). Furthermore, among individuals who have a higher average prescribing rate (8 or more), with the exception of a lower rate of NS-NSAID prescribing, there is no significant difference between those who reach the defined level of adoption immediately, and those who reach the same level of adoption later. Spearman correlation and segment profiles in this sample are presented in Appendix 7.12.

Table 7.1 provides a summary of the support for these hypotheses, relative to the three approaches to analysis taken to define the prescribing profiles of Nova Scotia physicians.

---

[13] Where adopters are defined as those individuals whose combined monthly prescription total of COX-2s and/or NS-NSAIDs averaged 8 or more, immediate adopters were a sub-segment of this sample, where 33% or more of the total prescriptions were COX-2s for at least the first 3 consecutive months of provincial coverage.

Table 7.1:

Summary of Hypotheses Support Based on Simple Correlation Analysis of Quartiles Relative to the Adoption Variable Definition

Hypothesis	Total Prescribing	Relative Prescribing	Immediate Adoption
H1: Influence of Journal Advertising and Detailing	No significant correlation between advertising and detailing for new or established drugs – Reject		
H2: Prescribing from new drug categories is a function of the presence of relative conditions within the practice's patient population	Fail to Reject	Reject	Fail to Reject
H3: Urban practices are more inclined to use new products	Reject	Fail to Reject	Reject
H4: Older physicians are less likely to prescribe from new drug categories	Reject	Fail to Reject	Reject
H5: Physicians who actively prescribe are more likely to prescribe new drug categories	Fail to Reject	Reject	Reject
H6: Male physicians are more likely to prescribe from new drug categories than female physicians	Fail to Reject	Reject	Reject

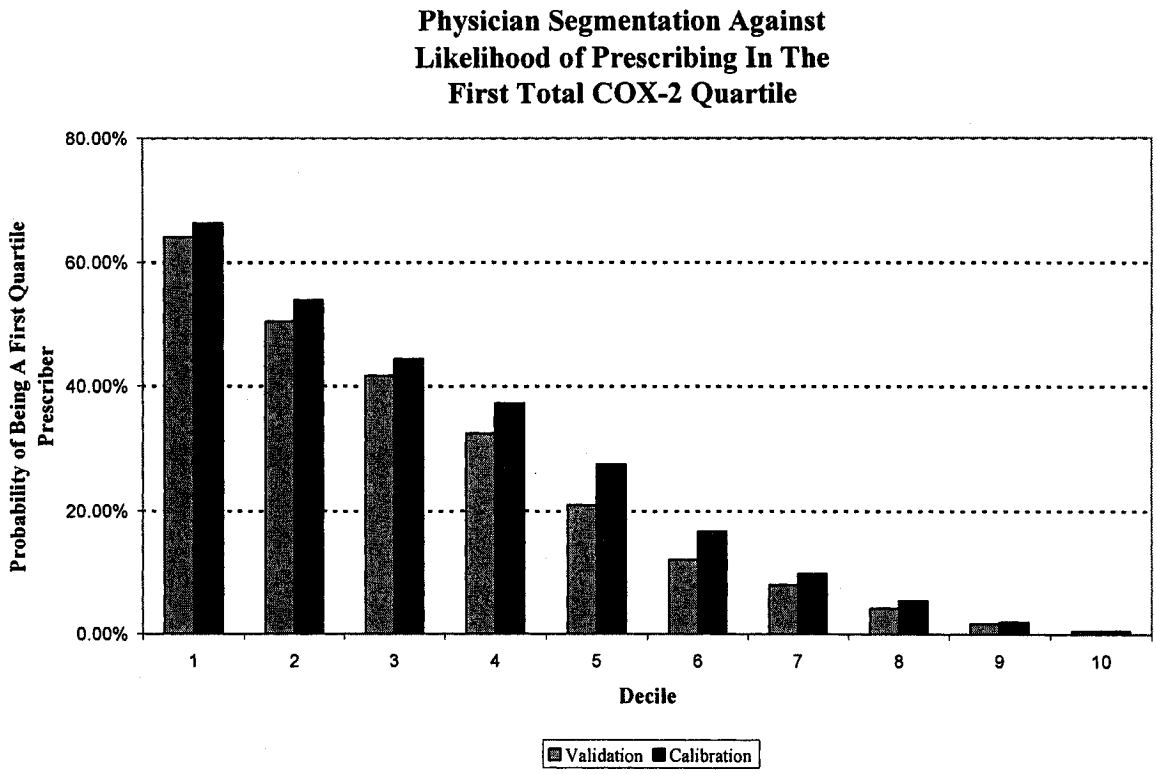
***Total Prescribing** – hypotheses are considered given the total number of prescriptions written during a set period of time, **Relative Prescribing** – hypotheses are considered given the ratio of COX-2s prescribed relative to COX-2s plus NS-NSAIDs prescribed in a given period, and **Immediate Adopters** - individuals who average 8 or more combined COX-2 or NS-NSAID prescriptions per month, where 33% or more of the total prescriptions were COX-2s for at least the first 3 consecutive months of provincial coverage.

7.3 Multivariate Analysis and Modeling

While the results of the multivariate analysis have been addressed throughout the discussion of the hypotheses, it is worthwhile to consider the graphical representation of the two equations, Y_{TWD} and Y_{RWD}. The first equation, where $Y_{TWD} = \beta_0 + \beta_1$ (general practitioner) + β_2 (rural based general practitioner) + β_3 (year of graduation) + β_4 (male general practitioner) + β_5 (born in Nova Scotia) + ε, has an adjusted R-square of 0.3348 and a concordant value of 81.1, where β_0 is the intercept, β_n is a regression coefficient on the independent variable Y_{TWD}, and ε is the residual or error value. When applied against the validation sample of physicians from our data set, the graphical representation would look like Figure 7.1, where decile 1 represents that percentage of physicians in the top 10% of our validation sample who meet the criteria of the regression equation.

That is, using this equation to rank the physician population into deciles or bins, the individuals in the first decile have a 65% probability of being a first quartile total prescriber, with the deciles decreasing incrementally to decile 10, where the individuals there have a close to 0% chance of being a first quartile total prescriber.

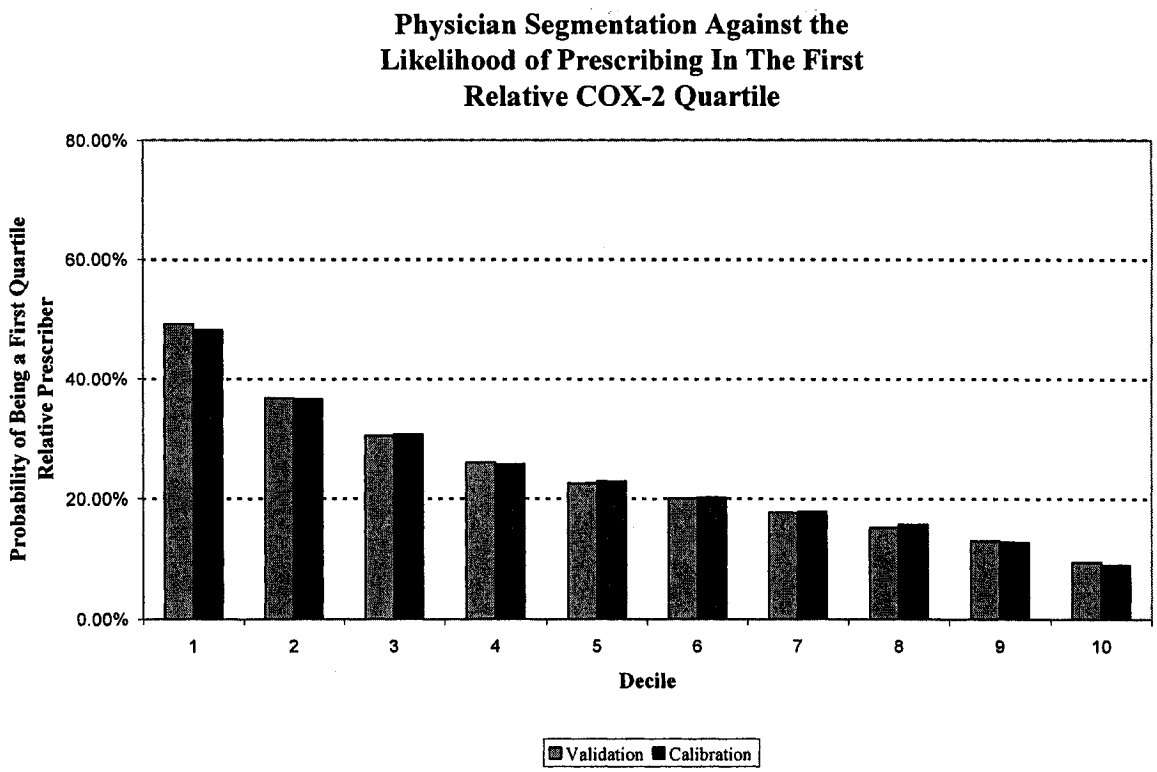
Figure 7.1:



The approach to the calculation of a predictive equation identifying those individuals likely to appear in the first quartile of the relative COX-2 prescribers was the same. As has been discussed previously, the variable defined as the ratio of average monthly cox-2 prescriptions over the total of average monthly prescriptions for the other three drug categories in the study dominated the original regression equation, allowing little opportunity to evaluate the physician demographics. To this end, this variable was removed to determine the influence of the other variables, resulting in $Y_{RWD} = ß_0 + ß_1$ (general practitioner) + $ß_2$ (physician age) + $ß_3$ (city based general practitioner) + ε, with an adjusted R-Square of 0.1031 and a concordant value of 66.9, where $ß_0$ is the intercept, $ß_n$ is a regression coefficient on the independent variable Y_{RWD}, and ε is the residual or error value.

Graphically, this regression equation, applied against the validation sample of physicians from our data set, would look like Figure 7.2. Decile 1 represents that percentage of physicians in the top 10% of our physician validation sample who meet the criteria of the regression. Using this equation to rank the physician population into deciles or bins, the individuals in the first decile have a 50% probability of being a first quartile relative prescriber, with the deciles decreasing incrementally to decile 10, where the individuals there have a close to a 10% chance of being a first quartile total prescriber.

Figure 7.2:



The shallower slope and lack of definition between the deciles in Figures 7.1 and 7.2 are a function of the decline in the predictive power of Y_R over Y_T, where we have a larger portion of the variance accounted for in Y_T (R-Sq = 0.2287, Concordant = 80.9%), than we do for Y_R (R-Sq = 0.0687, Concordant = 66.4%).

7.4 Theoretical Model and The Research Statement

7.4.1 Diffusion and Adoption

In addition to the hypotheses previously discussed, the objective of this research was to develop insight into whether or not differences exist between innovators/early adopters and late adopters, and if they do, to what extent. As a first step in this process, two approaches were taken to define and ultimately identify adopters, and to create parameters against which the population could be profiled.

The first approach separated the physician population into groups who either prescribed COX-2s in the first 25 months of availability (early prescribers) or prescribed COX-2s in the next 25 months of availability (late prescribers). These two groups were further evaluated against the likelihood of prescribing large volumes of COX-2s as well as against the likelihood of having a high level of COX-2 prescribing, relative to the total volume of COX-2s and NS-NSAIDS prescribed.

Appendices 6.8 and 6.10 present the relationships between the drug and demographic variables and the likelihood of prescribing in the upper quartile of total or relative COX-2 prescribers, respectively. Within the group of total COX-2 prescribers, with the exception of slightly higher average prescription rates of all drugs(Appendix 6.9), there is very little difference between the early and late prescribers within the upper quartile of total COX-2 prescribers. With respect to the upper quartile of relative COX-2 prescribers, general practitioners are more likely to be among the early prescribers, yet the later prescribers have almost double the general drug prescribing rates over their early counterparts (Appendix 6.11).

Given that the correlation between the independent variables and prescribing activity in both the early and late prescribing groups is similar, an attempt was made to cross-profile the upper and lower quartiles of physicians from both the relative and total COX-2 prescribing universe. Table 6.7 indicates that less than 4.6% of the total physician population is categorized as both an upper quartile relative prescriber and an upper quartile total prescriber, but 54.7% appear in the combined lower three quartiles of relative and total prescribers. These percentages are constant when comparing the early prescribers (Table 6.8), as well as the late prescribers(Table 6.9).

Given the lack of separation among adopters segmented against the early and late definitions of prescribing, a narrower working definition of adoption was created. This was done in an effort to establish unique profiles for those first to prescribe a new drug (early adopters) and those who prescribe at a later date. The first step in the creation of this universe was to subjectively assign the average number of monthly prescriptions that must occur in a given category before switching to an alternative (comparable) intervention can be considered trial. The number selected was 8 as this provided an adequate sample size (N = 295), and, while group represented 31.9% of the sample universe, they accounted for 76.9% of the total COX-2 prescriptions and 74.9% of the total NS-NSAID prescriptions written by the 925 physicians over the 50 month period of the study.

Despite the narrower focus of this strategy, once again, none of the independent variables appeared more strongly correlated with the immediate adopters or the late adopters.

While these results may not support the traditional five category classification model of adoption proposed by Rogers (19), or Coleman et al's incremental medical diffusion model (54), it does provide us with insight into the concept of adoption in a world of instant communication, mass and targeted marketing, and multiple media channels to which this target audience is exposed daily. Furthermore, this research supports the role that the nature of the innovation plays in adoption (as previously discussed, COX-2s would be a dynamically continuous variable).

Given the broad level of acceptance and the lack of separation between the early prescribers and the later prescribers (Table 6.6), it may be more appropriate to consider the adoption model proposed by Assael, namely innovators, late adopters and non-adopters (185). In this study, immediate adopters would be considered innovators, all other prescribers would be considered late adopters, and individuals who either didn't prescribe the drug, regardless of their reason, would be categorized as non-adopters. In many respects, Assael's model is a compression of the traditional five stage model, and this compression is driven to the point of product introduction by creating anticipation and preliminary demand.

7.4.2 Theoretical Considerations

While the model of diffusion and adoption provides general insight into understanding the basis of trial and adoption of new drug based interventions, and the subsequent influence of physician, practice and patient characteristics, much of what we see with respect to prescribing behaviour is explained through additional theoretical considerations. The applications of the evolving models of adoption were discussed in the

previous section, but the relevance of the other theoretical models proposed in Chapter 4, and their contribution to our understanding of the influence of physicians' characteristics, and their subsequent relationship to marketing activity, is worthy of further discussion.

The research statement for this thesis proposed that "The likelihood of a physician prescribing from a new drug category to a sample of his/her patient population is affected by marketing activity, practice characteristics and physician profile". At the fundamental level, our ability to gather data and develop insight into this process is a function of agency theory, such that one party depends on another party to perform some action on the principal's behalf. In this case, the physician, acting as an agent, performs an action (checkup, diagnosis and possible intervention/prescription) on behalf of the principal or patient. Additionally, if a significant proportion of prescribing behaviour is explained by physician characteristics, then we have demonstrated further support for agency theory. While the physician variables measured in this study were by no means inclusive, we do see correlation at both the bivariate and multivariate level of the physician demographic characteristics that were included in our set of independent variables. At the next level, however, the question remains, to what extent is each unique transaction or exchange influenced by the individual variables (in addition to all the variables we cannot measure), and how might one interpret this transaction in light of the supporting theories?

The theory of planned behaviour, which suggests that behavioural intentions are influenced by attitudes, subjective norms and perceived behavioural control, is an appropriate place to begin. Given the key elements of this theory, first and foremost we have seen the variance between the total and relative prescribers, which supports the attitude element of this equation. That is, the degree to which a physician has a

favourable or unfavorable attitude toward prescribing in general will influence their trial/adoption of a new category of drugs, and their subsequent volume of prescribing. This was aptly demonstrated by prescribing activity of the physicians in the universe of immediate adopters. In reality there was no period of trial and adoption, quite simply, individuals who anticipated the availability of a new drug, in consideration of the nature of their patient population, adopted and prescribed the drug as soon as it was available.

A second element within the context of the theory of planned behaviour is a function of the influence of subjective norms, namely, the expectation (pressure) to perform according to some group or socially defined stereotype. This can manifest itself in something as simple as writing a prescription for a patient, an action that is viewed as an expected professional behaviour, rather than simply lifestyle advice. This may explain the large volume of COX-2s that are prescribed in environments where a large number of NS-NSAIDs are prescribed. It presents an alternative that may lead to greater perceived performance by the physician in the eyes of the patient, and it reinforces the physicians' position as a seeker and communicator of new, effective technology/chemistry. Conversely, the same may be true of low volume COX-2 prescribers, that is, the expectation among some peers and patients may be anticipation of lifestyle advice as the key behavioural element.

Still within the context of the theory of planned behaviour, consider perceived behavioural control, which is a function of behaviour, in that it reflects past experience (product knowledge) while anticipating future hurdles. Again, the COX-2s, as presented, posed minimal risk, while affording the physician the opportunity to expand on past experience with a patient population in need of a viable alternative. The role of past

behaviour in the capacity of an "active prescriber" also manifests itself in this final function.

Role theory is also worthy of further discussion. Given that this theory is defined in the context of behaviours that are characteristic of persons operating in certain environments, physicians become the classic theoretical role model. The prescribing of a new drug category, an innovation whose adoption is considered "unlikely to have a significant impact on established use patterns", affords the physician the opportunity to live up to his or her "role". This is effectively the scenario physicians found themselves in with COX-2s, namely, prescribing for NS-NSAID targeted conditions with a new innovation (which may explain, in part, the 36.6% increase in category prescriptions the year after introduction). This action reinforced the physician's role, while strengthening their "role image" held by their patients, and, as mentioned earlier, provided them with the ability to reinforce their expected professional behaviour with their patients (and peers).

Advertising theory, of course, establishes the premise of trial initiated through promotion, and the role this plays in accelerating the adoption process cannot be underestimated. While a product may achieve its own level of consumption through the process of diffusion, as was demonstrated previously, such was not the case with the COX-2s. While advertising serves to introduce and reinforce on a much broader scale, the lack of any correlation between marketing activity (detailing and journal advertising) and prescribing of new and existing categories of drugs, really supports the model of compressed adoption of the COX-2s. That is, the relationship between trial, adoption and

marketing activity is compressed into the period of initial drug availability, and following that point, appears to have no measurable influence on subsequent prescribing activity.

In summary, the physician, acting in their capacity as an agent (for the patient), is assigned a level of adoption (innovator, late adopter, non adopter). This level of adoption, is a function of the physician's profile, attitude, subjective norms (the way they see themselves in their role), and attitude toward prescribing, all of which are driven by their perceived behavioural control. Interestingly, it is this behavioural control (regardless of whether they choose to acknowledge it) that is ultimately influenced by the elements of advertising theory, namely, the pharmaceutical manufacturer's pursuit of increased return on advertising dollar spent, by targeting their message more effectively.

7.5 Strengths and Limitations

While many of the strengths and limitations associated with this study have been identified or inferred throughout this dissertation, this section will serve to consolidate and address these considerations.

7.5.1 Strengths

Given that behaviour is not simply defined by any single environment or characteristic, this research afforded the opportunity to study the relationship between a number of independent variables relative to physician prescribing behaviour. While there may be a number of limitations to this study, one of the key features of this research, and one of its greatest strengths, is that this study is based on actual transactional data (ie

physician visits resulting in a dispensed prescription). Given the nature of the data, this study is of great value to the disciplines of marketing, pharmaceutical management and health policy, offering insight and observation that are genuinely actionable.

This analysis was not based on survey data, or situational vignettes designed to study reactions and response within a simulated environment. To this end, the data reflects the realities of a physician's practice, including the influences associated with the external environment, marketing and regulatory activities, the nuances of individual patients as well as the personality and behavioural traits of the physician's themselves.

This research is also reflective of prescribing activity within a relatively homogenous patient population, namely Nova Scotia seniors 65 years of age or older. The Nova Scotia seniors' Pharmacare administrative health claims database provided Medicare (including prescription activity, excluding hospital visits), physician profile data as well as a number of relational independent variables which provide influencing characteristics from which to develop prescribing profiles.

Finally, to my knowledge, this study is one of two known Canadian studies to have considered multiple IMS Health Canada data sets, and the related independent variables, relative to their influence on prescribing activity. The other being the work by Tamblyn et al on physician and practice characteristics associated with prescribing new drugs in Quebec (122). While this data provided a number of approaches to interpret pharmaceutical manufacturer's detail activity, it had some limitations which are addressed in the next section.

7.5.2 Limitations

A common approach in evaluating physician prescribing activity and drug utilization is to consider using the WHO ATC DDD system (DDD) of drugs prescribed (227, 228). Given the fact that this research is focused on trial leading to adoption, the approach taken was to simply measure the occurrence of a prescription within a given category. While this does not accurately reflect the total DDDs of prescribing within a category by a physician, it provides indication of trial with respect to prescribing of drugs from the category (ie one prescription for a patient, regardless of the amount prescribed). While the number of prescriptions was selected rather than the DDD, the data did not take into account new prescriptions versus renewals. Although this may further delineate adopters versus non-adopters, the actual measure critical to analysis and interpretation in this study was total prescriptions written.

Another limitation of this study is the inability to identify whether the physician operates in a solo practice or a group/clinic environment. This is relevant given that, as presented in the literature review, there is some suggestion that the prescribing practices of physicians operating in a clinic or group environment are not independent. This may result in higher or lower prescribing activity among individuals working together, driven by independent variables that may not be significant among the solo practitioner population. In addition to the lack of information on the nature of their practice, the profile of their patient base is also unknown. Information on patient demographics (age, gender) and disease conditions may have provided further insight with respect to the appropriateness of COX-2 prescribing, as well as their prescribing activity (relative, absolute, immediate).

With respect to the identification of the universe of early COX-2 adopters, the database only provides information on those prescriptions written that were provincially reimbursed. It does not identify those physicians or their prescriptions that may have occurred prior to provincial reimbursement, individuals whose private coverage paid for the drugs after provincial coverage, or those individuals who refused the prescription, given the provincial co-pay requirements[14]. Additionally, the analysis did not account for prescriptions of synthetic prostaglandins, often prescribed in conjunction with NS-NSAIDS to protect the mucosal lining of the stomach. It did, however, include drugs in which these products had already been pre-formulated with NS-NSAIDs (ie diclofenac).

The administrative drug claims database used for this study shows prescriptions dispensed for a given product, it does not show the volume of drug samples passed along to patients that represent a full prescribing cycle (30 days, 60 days). Additionally, while it is possible to estimate prescribing based on prescriptions dispensed, patient use or non-use of these prescriptions or prescriptions prescribed but not dispensed cannot be known. That is, we are unable to obtain the data on drugs that are prescribed and not dispensed.

With respect to the IMS data, the level of drug detailing was determined through feedback from a panel of physicians from across Canada. Thus, while it provides a relative measure of the detailing activity for each drug, it is not province specific. Similarly, the advertising was also calculated on a national level, as typically these

---

[14] In Nova Scotia, if you do not receive a guaranteed income supplement, you must pay a premium of up to $400 a year for Pharmacare coverage. The co-payment (the portion of the prescription cost an individual pays to the pharmacy when a prescription is filled) is 33% of the total prescription cost to a maximum of $30 for each prescription, with an annual maximum of $360 (minimum co-payment of $3.00/prescription). Once the $360 in co-payments has been reached, Pharmacare covers 100% of the remaining prescriptions for the year(234).

journals would not offer regional advertising rates for markets as small as the province of Nova Scotia. Additionally, while panel data might infer that all physicians report all interactions in detail, this is unlikely. Furthermore, there is no information as to how these physicians are selected and to what degree they truly represent the prescribing physician population across Canada.

While detailing and professional journal advertising were the primary marketing variables considered in this study, the main marketing activity utilized by the pharmaceutical industry, sampling, is not part of this analysis. While it is recognized as one of the most critical pharmaceutical activities leading to trial (229), it was not captured in the IMS data that was obtained for this study. To this end, while its impact as an influencing variable is recognized, it was consciously not included in the study, given that the actual process of detailing typically involves the exchange of a sample between the pharmaceutical representative and the physician. To this end, detailing was considered as a representative surrogate for sampling.

7.6 Conclusions and Future Research

This research has contributed to our understanding of current models of adoption and physician profiles among populations of relative prescribers and total prescribers. Furthermore, it has provided insight into their subsequent impact on the interdisciplinary elements which served as the foundation for this research. The insights realized have varying degrees of relevance to the three disciplines which served as the focus of this research, namely, policy, marketing and pharmaceutical management. Additionally, given the cross-relevance of the findings, it is difficult to develop an exclusive

relationship between a given insight and a particular area or specialty. To this end, the results are discussed in general terms, recognizing that they may have different meanings, applications and relevance to individuals from the respective disciplines.

7.6.1 Immediate Adoption

While adoption is not the exclusive tenet of marketing, marketing strategy and its related activities have much to do with the rates of diffusion and uptake of new products and technologies. This thesis has established the fact that, within the realm of a specific type of new prescription drug, the process of adoption doesn't exist in its previously defined state. Given the insights gathered through this research, traditional adoption has been reconfigured as the compressed adoption curve. This new concept of adoption is supported by a number of findings from this study. The 36.6% immediate increase in category prescribing followed by a rapid decline in the growth of net category prescribing over the subsequent three years suggests that product growth accelerates and matures in a much narrower period of time than previously reported. Through a combination of public relations, media relations and strategic placement of peer reviewed articles and related research, the universe of physicians expected to adopt a new drug has effectively been pre-selected before the drug is even available.

This concept of a "pre-selected" audience of adopters is further reinforced by the distinct lack of new prescribers, that is, very few net new individuals appear to be prescribing the drug category following its introductory period. The absence of differentiation between immediate and later adopters, further suggests that the historically proposed profiles of the different stages of adoption have not been confirmed for this

drug class, leaving us with adopters and non-adopters, a delineation of adoption even more narrowly categorized than that proposed by Assael (185).

The impact of this insight on the discipline of marketing is significant, given that this compression of the adoption process effectively influences the structure of the product lifecycle, concentrating the stages of introduction, growth and maturity into a narrow window, followed by a long period of late maturity/decline. This impacts all elements of marketing strategy and the traditional approach to the prescription drug market.

While one might propose that this result should be of great concern/interest to public policy and its related activity, the reality is that there is little that can be done to arrest the diffusion of information that establishes the initial universe of adopters. This research considered these results in the context of policy, but the convergence of media, sources of information, passive DTC advertising influence from the US, together with a more demanding health care consumer, limits what can be done to prevent this spread of information. In fact, the rise of the "drug savvy patient" presents its own challenges to formularies across all jurisdictions, as they are now subjected to lobbies from a number of sources. The greater the demand created by the manufacturers among the end users, the greater the pressure on governments to approve new products. Given the impact of this approach on the reduction in adoption time among physicians, it is possible that there may be increasing demand from patients and physicians to reduce time within governments on the drugs' benefit status (ie compressed adoption for physicians leads to a compressed approval cycle for formularies). Policy implications are discussed further in Chapter 7.6.4.1.

7.6.2 Inter and Other Discipline Relevance and Cross-Functional Generalization

One of the keys to the relevance of this research to the disciplines of marketing, pharmaceutical management and health policy relates to the nature of the data, namely, detailed recording of actual prescribing activity paired with actual profile information of the prescribers. The conclusions presented in this thesis were a function of the analysis of real activities, namely, physician prescribing in an environment replete with outside market influences, competition, unpredictable influences including public relations, government regulations, passive third party patient influences, and irregular drug sampling and industry directed marketing activity.

While the influences of "many unplanned factors" may reduce the correlation between the independent and target variables (ie physician profile and likelihood of prescribing), it lends itself to a real-world scenario, one that is more relevant to the development of public policy and pharmaceutical management strategy, than the insights realized through analysis of vignettes or surveys. To this end, these results and their related insights are genuinely actionable, providing a realistic basis for the development of policy and educational strategies.

The significance of this work has been discussed relative to our understanding of the relationship between COX-2s and NS-NSAIDs. Given this, the second level of consideration is the extent to which these insights may lead to generalization relative to other "block-buster" prescription drug categories, and finally we must consider the insights from this research relative to their generalization outside the pharmaceutical industry, specifically to continuous or dynamic technological introductions either within or outside of the professional health management fields. That is, what are the product

categories and what are the circumstances under which insight arising from this research may be applied.

Within the context of these three levels of generalization, there is the additional consideration of relative and total adoption, and its occurrence in other areas where the diffusion and adoption of innovations is market critical.

7.6.2.1 Inter-Discipline Relevance

Generalization to other "block-buster" drugs in many respects is intuitive, given the impact (and the dependency) that multi-media, instant messaging and the Internet has had on message diffusion. Consider the five attributes of innovations, namely; 1)relative advantage, 2)compatibility, 3)complexity , 4)trial-ability and 5)observability, and one is left with the realization that all five of these attributes are influenced to some degree by the evolution of media and communications. To this end, the same series of events that led to immediate adoption of the COX-2s, and the categorization of adopters into total adopters and relative adopters applies to other prescription drug adoption cycles. Consequently, one might anticipate a similar market entry and adoption profile for subsequent "block-buster" drugs.

In the United States, Roughead et al found that states with more generous insurance coverage were more likely to prescribe COX-2s, even in situations where NS-NSAIDs were considered appropriate (230). This study went on to suggest that if greater restrictions, either through prior authorization or other approaches were implemented at introduction, there would have been a $256 million savings to pharmaceutical budgets in 2003 alone. In Australia, Kerr et al also found high discretionary use of COX-2s, where

between 37% and 61% of patients receiving COX-2s hadn't received any pain medication in the previous 12 months (90). In Northern Ireland, Girvin et al discovered a 26% increase in prescribing volume of anti-inflammatory agents over a three-year period following the introduction of rofecoxib and celecoxib (231), and in Finland, Helin-Salmivaara demonstrated that two years following their launch, COX-2s had gained the status of standard NSAIDs (158)among physicians.

Given the similarity of adoption of COX-2s in other jurisdictions (United States, Australia, Northern Ireland, Finland), to this research, we can see the international generalization of these findings. These results in turn lend credence to the proposal that the levels and rates of adoption that we have demonstrated with the COX-2s would most likely be repeated with the introduction of other "block-buster" drugs.

7.6.2.2 Relevance to Other Disciplines or Sectors

In consideration of the final level of generalization relating to the relevance of these findings outside the category of prescription drugs, I have selected two product categories in which to discuss the concepts of total and relative adoption. Within the category of agricultural products, consider the sub-category of herbicides, and within the category of consumer products, consider the sound recording industry. Given our three categories of innovation (continuous, dynamic and discontinuous[15]) (64), consider Table

---

[15] The three forms of innovation may be defined as: continuous innovation where there is little change in the technology or the behaviour or consumers toward it, 2) dynamic continuous innovation where there is change in the technology, but little change required in the consumers' behaviour toward the product's use, and finally, 3) discontinuous innovation, where consumers must learn new or changed behaviour.

7.2, which compares the nature of the innovation to each of three categories, 2,4-D, COX-2s and recorded sound. The purpose of this table is to simply demonstrate that within any product category, there are, by definition, relative product examples at each stage of the innovation cycle.

Table 7.2

Comparison of Three Product Categories and Their Evolution, Relative to the Three Main Classifications of Innovation

Innovation/Category	Joint/Pain Relief	Weed Control	Sound Recording
Discontinuous	Acetylsalicylic Acid (Aspirin)	Phenoxy-acetic Acid	Studio Mono Recording
Dynamic Continuous	COX-2	2,4-D (2,4 Dichlorophenoxy acetic acid)	Cassette Stereo Recording
Continuous	Generic COX-2s (a likely future development)	Generic 2,4 – D	Digital Stereo Recording and CD storage/retrieval

While some of the early work in understanding the fundamentals of adoption took place in the field of agriculture (evaluating adoption of new plant genetics, mechanization, weed and insect control, crop health and propagation (19)), the findings from this research have broad applications into the adoption of new technological developments in many commercial fields. That is, given the information and communication media similarities between most commercial organizations, with the introduction of any dynamically continuous innovation, we could anticipate its rate of adoption to be analogous to what we have seen with the COX-2s. While Table 7.2 presents a retrospective look at the relevance of these findings in other categories, it is likely representative of what we would expect in a present or future market application. That is, considering the definition of a dynamically continuous innovation, it is realistic

for us to assume a similar rate and level of adoption both among total users (large commercial entities) as well among relative users (small, medium enterprises).

A final application of this research is within the area of consumer adoption. Unlike commercial and health profession related applications, we are unlikely to see relative and total adoption profiles, but, given the parallels between communication media in the consumer and commercial arena, we would anticipate a similar cycle of compressed adoption.

7.6.2.3 Relative versus Total Adoption

While the recognition that this research is generalizable, and relevant to both commercial (business to business) l and consumer (business to consumer) product introduction, its contribution may be even greater, given the identification of two unique categories of adoption, namely, relative adopters and total or volume adopters. In this research, total adopters were considered within the context of the volume of a drug category prescribed during a set period of time (average number of prescriptions written for a specific drug category per month), whereas relative adopters were considered within the context of the prescribing of a new drug. In the latter case, adoption is presented as a relative value, namely, the new drug amount relative to the new drug plus the recommended alternatives (An expanded discussion of this definition may be found in Chapter 6.2.1).

The impact of this insight is further discussed in Chapter 7.5.3, but the question remains, why are these two groups different.

Physicians classified as high total prescribers were those individuals who had a large volume of prescriptions in the COX-2 category shortly after introduction. What makes these individuals different from the remaining physicians in the study? While this research indicates that the upper quartile of total prescribers are older, male, general practitioners, operating in rural practices, it also indicates that they have a larger number of prescriptions in many categories. Conversely, the upper quartile relative prescribers may be best classified as younger physicians with urban practices, they are more likely to be female and are a mix of both general practitioners and specialists. Additionally, they have a small number of prescriptions across many categories.

These results may infer a number of key points that the data don't emphatically state. Consider the following for high volume and high relative prescribing physicians:

- The large volume of prescriptions across a number a categories and the rural profile of the total prescribers suggest that this segment of physicians may have an older population of patients, and most likely a larger patient load than their urban counterparts.
- Given a practice that typically sees a larger volume of patients than the provincial average, these physicians may be more inclined to write a prescription, rather than spend additional time addressing lifestyle issues, attempting to resolve their patient's condition with a non-drug intervention.
- The higher presence of females among the high relative adopters may suggest that they spend more time considering the relevance of the

intervention to their patient base, and, while they are selective, are less inclined to consider a prescription as the first choice for therapy.

- The lower volume of prescribing among the relative group may be a function of a younger patient base, perhaps a part-time practice, or even a more holistic approach to therapy than their high total prescribing counterparts.

The lack of overlap between these two categories of adopters (prescribers) supports these considerations, but additional research is required to further confirm and validate these observations. Policy and market implications associated with these adoption profiles are discussed in the following sections.

7.6.3 Relative Prescribers and Volume Prescribers

This research, as indicated in the previous section, has identified two different groups of prescribers, and has further classified them as relative prescribers and volume or total prescribers. Volume prescribers are identified as individuals who may be inclined to prescribe heavily from a new drug category, whereas high relative prescribers are identified as individuals whose ratio of new drug prescribing is high relative to the alternatives. While the theoretical considerations, relative to our general understanding of adoption were discussed in Chapter 7.4.2, it is appropriate to revisit these theoretical considerations, and determine the extent of their relevance to our observations with respect to relative and total prescribers.

Consider that the major role of theory is to increase scientific understanding through systematized structures that provide the ability to both explain and predict

phenomena. Ideally, we would anticipate that the theories considered support our findings and assist in the development of relevant policy or marketing direction. That is, the theory represents an interlacing of principles, ideas and observations which in turn can be used to guide future human action. There are many theoretical theses that relate to the nature of the physician, patient, pharmaceutical industry relationship. Of the original five proposed, role theory, the theory of planned behaviour and diffusion-adoption theory are worthy, at this point, of further comment.

Role theory relates to the study of the behaviour of individuals within specific contexts, and it goes on to suggest that individuals act according to how the recipient of their actions within these various scenarios expects them to act. Considering the profile of our volume prescribers, this may be appropriate. An older audience (typical of a rural versus an urban market) with traditional expectations relative to a physician's role may expect a prescription to result from a visit to a clinic, and may be less inclined to consider lifestyle changes as a valid therapeutic intervention. Additionally, this may support the rural – older – male model given expectations and traditional values (physicians were almost always male). Conversely, the urban profile and role aligns with the urban patient profile, younger, non-traditional models, open to different approaches, non-traditional interest and insight into personal health, and quite possibly better informed about the alternatives. All of these perspectives serve to influence the urban patient's role expectations, leading to a different physician role behaviour, a key element of which is their approach to prescribing (relative prescribers).

The theory of planned behaviour also offers an interesting perspective relative to the results of this study. While role theory may support the geographic segmentation of

physicians (male-rural, female-urban), the theory of planned behaviour suggests that behaviour is influenced by attitudes, subjective norms resulting from clinic, patient or peer expectations, as well as perceived behavioural control (ease of implementation)). Among males and/or rural physicians, there may be a greater propensity to exhibit a behaviour (writing a prescription for a "new" drug) that they feel re-enforces their position/role, and is the expected activity among a possibly smaller peer group (that may include pharmaceutical representatives) than their urban conterparts. Additionally, given the influence of attitudes on behaviour, and that attitudes are influenced by education, culture, and beliefs, it is possible that all three of these influencing elements are significantly different between urban and rural practitioners.

Finally, consider diffusion-adoption theory, which relates knowledge of a product and an individual profile to the likelihood of trial leading to adoption. In many respects this is the cornerstone of this research, and it too has provided support to both explain and predict market phenomena. Given that it relates knowledge of a product, and the profile of an individual to the likelihood of trial leading to adoption, this research has demonstrated the presence of unique segments within the physician universe that are more likely than not to be considered either high relative or high total prescribers. It has identified a compressed adoption model supported by the literature, as well as a model of prescribers in both categories, that has been confirmed in validation tests with both responder segments.

Within the diffusion-adoption theory we see support for elements within both role theory, where expected physician role may manifest itself either through their actions as an innovator or early adopter, as well as within the theory of planned behaviour, where

the defined profile of an early adopter (relative or total) is reinforced by the profile of the high relative and total prescribers presented. The identification of these two segments of prescribing physicians has implications for health policy and most certainly for marketing (or approach to market). Academic detailing and other parties involved with continuing medical education are going to be interested in which group is likely to have the greatest long-term impact on product adoption. While it may be important to influence large volume prescribers to realize a monetary impact, it will be critical to meet with peer and opinion leaders who may be best identified through high relative prescribing (but not necessarily a supporting high volume of prescriptions). Peer leaders, while they may not necessarily be high volume prescribers, have the capacity to influence a large volume of prescribing (and prescribers) and thus need to be identified and communicated with accordingly.

Given their different profiles and approaches to prescribing, the approach to communicate with each segment will be different. From a policy perspective, internal metrics will determine which approach will have the greatest impact on population health while maximizing jurisdictional health spending returns.

Marketers, however, will be more interested in the share of category a product realizes within a given jurisdiction, as well as the relative value (ratio) of prescriptions to physicians. This research demonstrates a viable approach to identifying both categories of physicians, and the validity associated with each profile.

7.6.4 Implications For New Products and Policy

7.6.4.1 Policy

Policy makers are interested in the mid and long term impact of their actions on population health, budgets, and relationships between all of the stakeholders influenced by their actions. This concern may be summarized by four words; quality, efficacy, safety and cost. In consideration of the policy implications arising from this research, the real question to address here is, "Knowing what we know, would this change anything?". An alternate approach to this discussion might be, "What do our findings have to say to policy makers with respect to the introduction and adoption of new drugs?".

Consider a general approach which addresses the way in which public policy is served through drug approval and regulation. As stated earlier, once a drug has met the submission requirements of the Therapeutics Product Directorate, and is approved for use in Canada, it in turn receives a Notice of Compliance (NOC). Following receipt of the NOC, there several steps that a drug manufacturer may be follow prior to getting the product to market in a particular jurisdiction (province). Some of these steps include:

- Additional testing by the manufacturer to support unique situations that are incremental to the NOC guidelines
- Manufacturer submission to the respective formulary with resultant notification to all relevant parties indicating the extent of the coverage, reimbursement and any nuances with respect to maximum allowable costs and co-pay
- Direct to physician marketing activities (advertising in professional journals, corporate detailing, samples and various circular material) begin in earnest

Any one of these steps following NOC may be subject to various elements of health policy/regulation. While the approach to promotion of a product within a given jurisdiction may be limited or restricted until the associated formulary acknowledges coverage, some of the elements of the actual marketing campaign (spillover from other jurisdictions) are impossible to restrict. Consider a "block-buster" drug approved on the formulary in another jurisdiction. Product information would be available through a number of sources including the World Wide Web, through conferences and out of jurisdiction continuing medical education events, personal communication with peers and opinion leaders, the media, patients, and in some circumstances, through their own company.

The information on the product will be available to physicians, regardless of provincial pharmacare status. Ultimately, for policy to impact the communication/awareness element of new prescription drugs, the entire process associated with the way drugs go to market (including post-marketing surveillance) in developed nations would have to be addressed collectively. Given that this is highly unlikely, consider the policy alternatives:

- Counter detailing
    - academic detailing targeted at physicians identified as either upper quartile relative or upper quartile total adopters
    - targeted detailing strategies designed to communicate a specific message to a specific segment of the physician population, as defined by their collective demographics and the nature of their level of adoption

- Drug insurance programs such as increasing the co-pay (this would most likely drive the distribution of drug samples to individuals who could not afford the co-pay)
- Formulary amendments such as implementing prior authorization policies at market entry before prescribing habits for new drugs are formed (the key limitation here, however, is that many private payers typically add new drugs to their formularies as soon as the NOC is granted, thus facilitating the development of prescribing habits even before provincial formulary listing

Regardless of the approach, this research has provided us with delineation between those individuals who adopt a new product and prescribe it generously, and those who adopt a new product such that it becomes their product of choice for a set of conditions (but doesn't necessarily imply that large volumes of the product will be prescribed). With respect to the development of policy designed to more effectively regulate and anticipate budgetary implications, options are available, but primarily through the application of prescribing restrictions and subsequent efforts at changing prescribing behaviour before it becomes established.

7.6.4.2 New Products

The pharmaceutical industry would most likely be interested in finding and reaching those large volume practitioners who represent the upper 70 to 80% of all prescriptions written in a target category. This research moves us closer to identifying these unique physician segments, while providing insights into which marketing elements

are likely to produce the best return, given the target audience and their likely response to the message.

Consider the detailing of a new drug category to a group of physicians. From the perspective of the pharmaceutical industry, they are going to be interested in targeting those physicians who are likely to prescribe a large volume of the product. Given the results presented in Table 6.7, if only high relative prescribers are considered, they will fail to communicate with over 80% of the top quartile of total or volume prescribers.

If we consider the communication of a targeted message from an academic or public policy perspective, there may be greater interest in focusing the message on either a high or low relative prescriber audience, namely, a group who appears to be more focused on the integration of lifestyle and drug intervention in effecting the desired results for their patients. For high relative prescribers, it may be about reinforcing best practices, while within the segment of low relative prescribers, there may be issues of training or education that need to be addressed. Given this, there will still be a likelihood that academic detailers will also want to focus on those individuals who are high volume prescribers, as this would be most likely to generate the desired outcomes resulting in a reduction of inappropriate (ie using a more expensive intervention when there are less expensive alternatives) prescribing.

In both of these situations, however, one ultimately would like to start with that segment of the physician population that is in the first quartile of relative prescribing and the first quartile of total volume prescribing. These would be the physicians who would most likely have the larger practices, which may subsequently result in the greatest return on marketing dollar spent, and, by virtue of the size of their practice, may have the

greater likelihood of generating peer influence. However, having said this, it should be acknowledged that high volume is not always associated with prescribing the most expensive drugs. That is, some family physicians may have a high volume of prescriptions, but specialists, with a smaller patient base, may prescribe more expensive products as they may be more appropriate for their specific circumstances.

7.6.5 Future Research

While this research provided insight into the lack of a relationship between two marketing activities (journal advertising and detailing) and the prescribing of new and existing drug categories, there are many questions that remain to be answered in this area. Of particular significance is the fact that while this study considered pharmaceutical industry detailing, an important variable that was outside of the scope of this research relates to the role that prescription drug samples play in influencing prescribing. The physicians surveyed collectively felt that COX-2s were one of the most heavily sampled drugs they had ever experienced, and believed (albeit reluctantly and off the record) that this did have an impact on their prescribing behaviour. Thus, while detailing provided some insight, the residual value of the actual detailing even may be more a function of the samples left behind, rather than the message or the event.

While this research demonstrated no significant correlation between marketing activity and prescribing, the question remains, what role does marketing play in maintaining an established prescribing level among the immediate adopters? More importantly, are there levels and approaches to physician interaction that result in a decline in prescribing? While this has received some attention in the literature, it needs

to be further explored in an attempt to identify optimal levels of detailing influence. This stands to have a significant impact in areas of both pharmaceutical marketing and academic detailing.

One of the more substantial variables influencing physician behaviour is the patient, and subsequently, factors that influence the patient's approach to a physician-patient exchange stand to greatly influence the outcome of that meeting. While there has been extensive research into the impact of direct to consumer marketing and the subsequent patient influence on prescribing in the United States, there has been very little done in Canada in this regard. To this end, much work needs to be done to determine the extent to which direct to consumer advertising influences the Canadian patient, and subsequently the prescribing activity of Canadian physicians.

While this research established the separate populations of high relative prescribers and high total prescribers, an area worthy of further consideration is the relationship between these two groups, and their subsequent relevance to the proposed theoretical models. Are these two types of prescribing a function of the physician's practice, training, peer influences, patient demographics, physician demographics, or a combination of all five? Are new drugs prescribed to reinforce the physician's role or is prescribing a function of their environment? To what extent does the will of the patient, physician's formal training, peer pressure or relationships with the pharmaceutical representative have on prescribing?

This research identified and defined the compressed model of adoption. To this end, further work needs to be done to confirm the viability of this model within other drugs and drug classes, and furthermore, to establish its relevance within populations of

new physicians who start their careers at the mature and declining stages of drug product lifecycles.

Finally, given the theoretical considerations proposed in Chapter 4, the real question is, through analysis and subsequent validation, the extent to which the proposed theoretical models provide additional insight into the relationship between the patient, the physician and the numerous external variables that influence the prescribing decision. Furthermore, to what extent can this knowledge complement our efforts to educate and develop best practices among prescribing physicians?

APPENDICES

Appendix 5.1
Physician Survey and Results

Appendix 5.1.1
Physician Survey - Convenience Sample

Background

My name is Kent Groves, and I am a PhD Student at Dalhousie University, working toward completion of my dissertation in the area of *Pharmaceutical Marketing Strategy, and Its Influence on Physician Prescribing Behaviour*. The data for my research comes from two sources, namely, the Nova Scotia Population Health Research Unit (PHRU) and IMS Health Canada.

This research is unique in that it is being conducted by an Atlantic Canadian through an Atlantic Canadian Institution, and is multidisciplinary in its approach, with a focus on policy, marketing and pharmaceutical management. Through your involvement, you have an opportunity to gain a greater appreciation for the influence of pharmaceutical marketing on prescribing, the development of formulary policy, and contribute to our collective insight on pharmaceutical marketing activities such as detailing, sampling and journal advertising. While the summation of this research will be in the format of a PhD Dissertation, a final copy will be made available to participants, as will copies of all publications arising through this work.

The individuals to whom I am forwarding this survey are a small convenience sample of physicians from across the province. The responses will be summarized and aggregated, and the individual responders will remain anonymous, known only to the primary researcher (Kent Groves). While the results will not be incorporated into the final study, they will provide a litmus test, if you will, of the individual hypotheses that I list below.

Questions:

General Background Information
(please circle the appropriate answer, or fill in the blank)

1) What is the nature of your practice?
   a. -Specialist, (type of specialty_____)

      -Family or General Practitioner

   b. Solo practitioner -Member of a clinic?

2) If you are a member of a clinic, how many physicians are there in your clinic?

3) How long have you been a practicing physician (excluding residency)?

4) What is your gender? Male Female

5) How would you describe your practice?

Patients: Rural_____% + Urban_____% = Total 100%

Male_____% + Female_____% = Total 100%

<65_____% + >65_____% = Total Patients 100%

6) How many patients would you see in your office in a typical week (This excludes hospital visits and surgery)?

0 to 25
26 to 50
51 to 75
76 to 100
>100

7) How would you rate this volume of patient visits relative to your peers across Nova Scotia?

-Very High -Above Average -Average -Below Average -Very Low

Research Statement and Hypotheses

In this section, I have provided my research statement, 6 hypotheses (which are being tested) and 3 assumptions (not being tested). I would appreciate your comments on each of these. They can be a simple as saying "I agree", "I disagree", "This makes sense", or something more elaborate. Again, all information is confidential, as I am primarily interested in your thoughts about each statement, and the (what does practicing mean in this context? Can it be deleted? validity of my research.

My research statement is;

The likelihood of a physician prescribing from a new drug category to a sample of his/her patient population is affected by marketing activity, practice characteristics and physician profile.

Comments:

Six Hypotheses

H7. The probability of prescribing a drug category is a function of the volume of detailing (corporate or academic) and other commercial sources of information targeted toward the physician for that specific drug category.

Comments:

H8. "The number of opportunities available in which one may prescribe from a new drug category, will influence the consideration for and subsequent trial of a new product.

Comments:

H9. Physicians with practices in urban settings are more likely to prescribe new drugs than are physicians practicing in rural environments.

Comments:

H10. *Older physicians are less likely than younger physicians to prescribe from new drug categories. (In this case, older is somewhat subjective to the individual, but will probably relate to physicians over and under 50 years old)*

Comments:

H11. *Physicians with a history of active prescribing, are more likely to prescribe from new drug categories.*

Comments:

H12. Male physicians are more likely thatn female physicians to prescribe from new drug categories. The probability of prescribing from a new drug category is greater among male than female physicians.

Comments:

Assumptions

A1. The likelihood of a physician prescribing from a new drug category is a function of the demographics and geo-demographics of the patient. (ie where they live, their gender, their age, their lifestyle and social background)

Comments:

A2. The probability of prescribing a drug is a function of the intensity of commercial marketing efforts targeted directly at the consumer.

Comments:

A3. Physicians operating in group practices are more likely to prescribe from new drugs categories than are solo practitioners.

Comments:

Thank you for your time and consideration!

You may return this survey by e-mail to kgroves@dal.ca

OR

You may fax it to Kent Groves, School of Business, Fax 494-1107

OR

You may mail it to:

Kent Groves,
School of Business, Faculty of Management
Dalhousie University
6100 University Avenue,
Halifax NS B3H 3J5

Appendix 5.1.2

Physician Survey Results

Summary of Respondent Comments

The following summarized the number of patients each physician indicated they saw on a weekly basis and their perception as to that number's relevance to their peers typical patient visit load.

001 – 76 to 100; average
002 – 51 to 75; below average
003 – 26 to 50; average
004 – >200; above average (comment, >100 would be well below average for an average gp)
005 – 76 to 100; below average
006 - >100; average
007 – non practicing
008 – 0-25; below average
009 - >100; above average

Research Statement and Hypotheses
My research statement is;

The likelihood of a physician prescribing from a new drug category to a sample of his/her patient population is affected by marketing activity, practice characteristics and physician profile.

Comments:

001 – total influence on prescribing activity can be assigned 10 % to marketing activity, 30% to practice characteristics and 70% to physician profile.

002-agree; I have to say that because we are in an economically depressed area. Samples are very important

003 – I agree, but varies from one physician to another

004 – This is true

005 – It is affected by marketing activity as well as practice characteristics and physician profile

006- Assuming that "affected by" includes both positively and negatively I agree. No man is an island – we are all affected by external factors.

007 – I am not sure what you mean by physician profile, but I agree with the other two.

008 – I would agree, although most physicians do not believe they are affected by marketing, ie. Strategies include availability of sample drugs and easy to remember trade names.

009 - agree

Six Hypotheses

H1. The probability of prescribing a drug category is a function of the volume of detailing (corporate or academic) and other commercial sources of information targeted toward the physician for that specific drug category.

Comments:

001 – disagree; we have become evidence based and conservative about new wonder drugs just like the general public. Publications in peer reviewed reputable journals with RCT are the only source of dependable information safe enough to make clinical decisions upon.

002 - agree

003 – I agree

004 – No. The decision as to what category of medication should be and most often is a function of ongoing continuing medical education. This particular decision should not be influenced by pharmaceutical marketing, which is inherently biased. Academic detailing per se is not delivered by pharmaceutical reps and therefore should apply here.

005 – no comment

006 – disagree. May influence choice of drug within the category but not the prescribing of the category

007 – Agree – but corporate and academic detailing may tend to move prescribing in opposite directions

008 – Yes, I would agree. There are many examples of this effect in the medical literature.

009 - agree

H2. "The number of opportunities available in which one may prescribe from a new drug category, will influence the consideration for and subsequent trial of a new product.

Comments:

001 – no

002 - true

003 – I agree

004 – I agree

005 – more

006 – yes

007 – maybe. If it is a common condition and currently used meds that sometimes don't work, the new one may be tried

008 – I don't understand this question

009 - agree

H3. Physicians with practices in urban settings are more likely to prescribe new drugs than are physicians practicing in rural environments.

Comments:

001 – not necessarily

002 – I am not sure why this would be

003 – I disagree

004 – No. There is no rationale that I can see for this hypothesis. Rural physicians are as up to date as their urban counterparts. Most physicians don't rely on pharmaceutical company marketing/advertising for their major prescribing decisions, therefore distance translating to fewer pharmaceutical company representative visits should make a difference

005- I do not think so

006 – Quite likely. (more likely to be detailed first. I presume pharmaceutical companies see more bang for their buck in urban centres)

007 – Disagree. I don't see why this would be so.

008 – not sure that I agree with this. New drug information is widely available and marketing and CME is available in most small communities.
009 – don't know

H4. *Older physicians are less likely than younger physicians to prescribe from new drug categories. (In this case, older is somewhat subjective to the individual, but will probably relate to physicians over and under 50 years old)*

Comments:
001 – partly agree
002 – "old school" would likely stick to older prescribing practices
003 – I agree, they follow practice experience rather than evidence based medicine
004 – True to a degree, but many exceptions exist. Many older physicians are "slow adopters" in this regard, preferring to have more evidence built up before they try a new product (& often with good reason)
005 - yes
006- not necessarily
007 – disagree – we are all subject to the same forces
008 – Not sure I agree – depends more on learning philosophy of physicians
009 - probably

H5. *Physicians with a history of active prescribing, are more likely to prescribe from new drug categories.*

Comments:
001 – don't know
002 – true
003 – not always
004 – what does active prescribing mean
005 – yes
006 – would make sense

007 – not sure of the term, active prescribing

008 – not sure if we know enough about this link, depends on what exactly we mean by active prescribing.

009 - agree

H6. Male physicians are more likely thatn female physicians to prescribe from new drug categories. The probability of prescribing from a new drug category is greater among male than female physicians.

Comments:

001 – don't know, would not think so

002 – I am not sure that I agree with this, it doesn't make sense

003 – don't know

004 – I don't believe that this would be so.

005 – don't know

006 – I have no idea if this is true

007 – disagree – don't see why this would be

008 – I am not sure what data is on this. Male physicians tend to work longer hours and have larger practices, which may be a factor.

009 – don't know

Assumptions

A4. The likelihood of a physician prescribing from a new drug category is a function of the demographics and geo-demographics of the patient. (ie where they live, their gender, their age, their lifestyle and social background)

Comments:

001 – agree

002 – true

003 – I agree

004 – I don't believe that this would be true. This would depend more on a physician's knowledge relating to a specific field and higher comfort zone treating these illnesses.

005 – no comment

006 – I suspect influenced by but not strong enough to say " a function of"

007 – most likely factor is their economic status

008 – I do not know enough about geo-demographics to comment

009 - agree

A5. The probability of prescribing a drug is a function of the intensity of commercial marketing efforts targeted directly at the consumer.

Comments:

001 – partly, patient direct requests for specific products has increased in the last 10-15 years

002 – agree

003 – I agree

004 – I disagree. For the majority of physicians who keep up to date and who are intent on basing their decisions on unbiased information (as opposed to what comes from drug companies) this would not be true. As well, being bombarded would likely turn us away from a given product.

005 – no comment

006 – would not be a major factor in my patient population but if it were no true why would pharma wasted millions on marketing?

007 – not sure. I don't know the data. It's possible

008 – I absolutely agree with this. Consumers will pressure their doctor for new drugs that are not as effective or appropriate

009 - agree

A6. Physicians operating in group practices are more likely to prescribe from new drugs categories than are solo practitioners.

Comments:

001 – yes; discussions with colleagues increase awareness of products. We are always concerned re. safety and if a colleague feels a new drug is safe and useful, it increases the chance of you trying it. Attending conferences is another good way to learn about new products.

002 – may be true. Talk amongst physicians

003 – I agree

004 – I don't agree. Are you making an assumption that solo MDs don't keep up to date as much or they are less capable in treating certain disease entities than their colleagues in clinics?

005 – no comment

006 – I would have thought less likely (greater extent of peer review would likely maek physicians more conservative in their prescribing)

007 - disagree. I don't see why this would be so.

008 – I would think the opposite is true. Group practices tend to have rounds, medi-consultants to discuss therapies. The sole practitioner is at the mercy of marketing effects

009 – probably.

Appendix 5.2

PHRU Data Extraction
Project Title: The Influence of Pharmaceutical Marketing Strategy on Physician Prescribing Behaviour

Investigator: Kent Groves

Method of Extraction

1. Pharmacare data were extracted for the calendar years 1999–2003. Records were retained if the DINs matched those provided by the investigator. It should be noted that the field 'Specialty' is not part of the Pharmacare database. There is a field called DOCTYPE that identifies the prescriber as a physician, dentist, optometrist or nurse practitioner, but does not indicate the specialty of the physician.

   NOTE: These files contain more than one record per person.

2. The study population was determined as a unique list of individuals in the extracted Pharmacare data. This is a list of individuals who had a prescription at any time from 1999-2003.

3. Physician billings data were extracted for all individuals identified in the study population for the calendar years 1999–2003. In other words, an individual may have had a prescription in 2001 but would be included in all years of the physician billings data.

   NOTE: These files contain more than one record per person.

   The variable quantity is not regularly used by PHRU. The summary that follows may provided a better understanding of the use of this field.

   This field is used to indicate either the number of services performed (number of lesions), the length of time (eg. 15 minute time blocks, detention, counseling) or the percentage of the body (burns) or surface area (eg. sq. inches). If the number exceeds that indicated for the health service code, the maximum for that code will pay.

4. Patient demographic data were extracted for all individuals in the study population for the calendar years 1999-2003. Individuals in the study population were liked to the MSI patient master file to determine their postal code within a given year. Health card number and postal code were then used to extract census data. In some cases, health card number and postal codes combinations could not be matched to the census data. This is usually due to new postal codes that had not been matched to an enumeration area.
   These files contain <u>one</u> record per person.

5. Unique physician IDs were determined from each physician and pharmacare year file. These IDs were then used to create yearly physician demographic files (i.e. Unique physician IDs from MED2002 and PHARM2002 where used to create the DOCS2002 file). It should be noted that many physicians have more than one specialty. In such cases, the record would be repeated for each specialty. Graduation year and medical school variables would be relevant to the given specialty.

   Physician demographic data extracted for the calendar year 2003 may not be as complete as the previous years. Physician registry and demographic data usually lag by one year, so that the physician data for 2004 would contain complete information for those physicians registered in 2003. This is only a problem for physicians who were newly registered in the latter half of 2003, as PHRU data are organized on a fiscal year basis.

General Notes:

1. Patient, physician and pharmacy identifiers have been replaced by study IDs.
2. Date of birth has been provided on the physician billing (med), pharmacare (pharm) and physician demographics (docs) files. To convert date of birth to age in a given year, you can use the following calculation:

   ```
   AGE=int((mdy(6,30,YEAR)-DOB)/365.25); /* calculates age at mid-year */
   ```

   Where MDY is a SAS function representing month, day and year.
3. Value labels have been provided on the following pages.

---Alphabetic List of Variables and Attributes---						
#	Variable	Type	Len	Pos	Format	Label
10	DOC_ID	Num	8	0		Doctor Study ID
1	MED_SCH	Char	6	20		Medical School Location
2	OPTIN	Num	4	8		Physician Registration Initiation Date
3	OPTOUT	Num	4	12		Physician Registration Termination Date
7	bplace	Num	3	33	BPLACEF.	Place of Birth
5	dcounty	Char	2	27	$COUNTYF.	Provider County
6	dob	Num	4	16		Date of Birth
8	dspecial	Char	4	29	$DSPECF.	Specialty Received
9	gradyear	Num	3	36		Year of Graduation
4	sex	Char	1	26	$SEXF.	Provider Gender

physician Demographics, 2003

----Sort Information----	
Sortedby:	DOC_ID
Validated:	YES
Character Set:	ASCII

Physician Billings, 2003

Data Set Name:	MED2003	**Observations:**	1484968
Member Type:	DATA	**Variables:**	9
Engine:	V8	**Indexes:**	0
Created:	15:33 Wednesday, October 13, 2004	**Observation Length:**	48
Last Modified:	15:33 Wednesday, October 13, 2004	**Deleted Observations:**	0
Protection:		**Compressed:**	NO
Data Set Type:		**Sorted:**	YES
Label:			

Data Set Name:	DOCS2003	**Observations:**	2427
Member Type:	DATA	**Variables:**	10
Engine:	V8	**Indexes:**	0
Created:	14:44 Wednesday, October 13, 2004	**Observation Length:**	40
Last Modified:	14:44 Wednesday, October 13, 2004	**Deleted Observations:**	0
Protection:		**Compressed:**	NO
Data Set Type:		**Sorted:**	YES
Label:			

Pharmacare, 2003

Data Set Name:	PHARM2003	**Observations:**	427722
Member Type:	DATA	**Variables:**	11
Engine:	V8	**Indexes:**	0
Created:	16:00 Wednesday, October 13, 2004	**Observation Length:**	56
Last Modified:	16:00 Wednesday, October 13, 2004	**Deleted Observations:**	0

-----Alphabetic List of Variables and Attributes-----

#	Variable	Type	Len	Pos	Format	Label
9	DOC_ID	Num	8	8		Doctor Study ID
8	STUDY_ID	Num	8	0		Patient Study ID
6	dob	Num	4	16		Date of Birth
2	dspecial	Char	4	25	$DSPECF.	Provider (Main) Specialty
3	dxcode1	Char	5	29		ICD9CM Diagnostic Code 1
7	dxdate	Num	4	20		Date of Service
4	postcode	Char	6	34		Patient Postal Code
5	quantity	Num	3	40		Quantity of Treatment
1	sex	Char	1	24	$SEXF.	Patient Gender

Protection:		**Compressed:**	NO
Data Set Type:		**Sorted:**	YES
Label:			

-----Sort Information-----	
Sortedby:	STUDY_ID
Validated:	YES
Character Set:	ASCII

----Alphabetic List of Variables and Attributes----						
#	Variable	Type	Len	Pos	Format	Label
10	DOC_ID	Num	8	8		Doctor Study ID
11	PHARM_ID	Num	8	16		Pharmacy ID
9	STUDY_ID	Num	8	0		Patient Study ID
2	atc	Char	7	37		Anatomical Therapeutic Class
1	compound	Char	1	36	$YESNOF.	Compound Indicator
4	daysupp	Num	3	45		Days Supply
5	din	Num	5	48		Drug ID Number
7	dob	Num	4	28		Date of Birth
6	qty	Num	4	24		Quantity Dispensed
8	rxdate	Num	4	32	MMDDYY10.	Prescription Date
3	sex	Char	1	44	$SEXF.	Patient Gender

-----Sort Information-----	
Sortedby:	STUDY_ID
Validated:	YES
Character Set:	ASCII

Patient Demographics, 2003

Data Set Name:	DEMOG2003	Observations:	75423
Member Type:	DATA	Variables:	6
Engine:	V8	Indexes:	0
Created:	16:22 Wednesday, October 13, 2004	Observation Length:	24
Last Modified:	16:22 Wednesday, October 13, 2004	Deleted Observations:	0
Protection:		Compressed:	NO
Data Set Type:		Sorted:	YES
Label:			

----Alphabetic List of Variables and Attributes----						
#	Variable	Type	Len	Pos	Format	Label
2	AVGFAMIN	Num	4	8		Avg 1996 EA family income
1	DWELLING	Char	1	12	$DWELLF.	Collective Dwelling Type
3	NUMFAMS	Num	3	13		Num families in EA (1996)
4	NUMHHS	Num	3	16		Num households in EA (1996)
5	POP96	Num	3	19		Total EA pop. (1996)
6	STUDY_ID	Num	8	0		Patient Study ID

----Sort Information----	
Sortedby:	STUDY_ID
Validated:	YES
Character Set:	ASCII

Birth Place Value Labels (BPLACE – Physician Demographics)

FORMAT NAME: BPLACEF LENGTH: 23 NUMBER OF VALUES: 153
MIN LENGTH: 1 MAX LENGTH: 40 DEFAULT LENGTH 23 FUZZ: STD

START	END	LABEL (VER. 8.2 25NOV2003:11:35:10)
11	11	AMHERST
12	12	ANNAPOLIS MUNICIPALITY
13	13	ANNAPOLIS ROYAL
14	14	ANTIGONISH MUNICIPALITY
15	15	ANTIGONISH TOWN
18	18	BERWICK
20	20	BRIDGEWATER
22	22	CAPE BRETON
23	23	CHESTER
26	26	COLCHESTER
27	27	CUMBERLAND
28	28	DARTMOUTH
29	29	DIGBY MUNICIPALITY
30	30	DIGBY TOWN
31	31	DOMINION
32	32	GLACE BAY
33	33	GUYSBOROUGH
34	34	HALIFAX CITY
35	35	HALIFAX MUNICIPALITY
41	41	KENTVILLE
42	42	KINGS
43	43	LIVERPOOL
46	46	LUNENBURG MUNICIPALITY
47	47	LUNENBURG TOWN
49	49	MIDDLETON
51	51	NEW GLASGOW
52	52	NEW WATERFORD
53	53	NORTH SYDNEY
54	54	OXFORD
55	55	PARRSBORO
56	56	PICTOU MUNICIPALITY
57	57	PICTOU TOWN
58	58	PORT HAWKESBURY
59	59	QUEENS
60	60	RICHMOND
61	61	SHELBURNE MUNICIPALITY
64	64	STELLARTON
65	65	STEWIACKE
67	67	SYDNEY CITY
68	68	SYDNEY MINES
70	70	TRURO
71	71	VICTORIA
72	72	WESTVILLE
73	73	WINDSOR
74	74	WOLFVILLE
75	75	YARMOUTH MUNICIPALITY
76	76	YARMOUTH TOWN
99	99	NOVA SCOTIA UNKNOWN
100	100	NEWFOUNDLAND
101	101	PRINCE EDWARD ISLAND
102	102	NEW BRUNSWICK
103	103	QUEBEC
104	104	ONTARIO
105	105	MANITOBA
106	106	SASKATCHEWAN
107	107	ALBERTA
108	108	BRITISH COLUMBIA
110	110	YUKON TERRITORY

111	111	CANADA UNKNOWN
120	120	USA
130	130	MEXICO
140	140	ARGENTINA
141	141	BOLIVIA
142	142	BRAZIL
144	144	COLUMBIA
145	145	CUBA
146	146	ECUADOR
148	148	PERU
150	150	VENEZUELA
160	160	OTHER AMERICA
170	170	ENGLAND
171	171	SCOTLAND
172	172	NORTHERN IRELAND
173	173	UNITED KINGDOM
175	175	IRELAND
200	200	AUSTRIA
201	201	BELGIUM
202	202	BULGARIA
203	203	CZECHOSLOVAKIA
205	205	FINLAND
206	206	FRANCE
207	207	GERMANY
208	208	GREECE
209	209	HUNGARY
211	211	ITALY
212	212	LATVIA
213	213	MALTA
214	214	NETHERLANDS
215	215	NORWAY
216	216	POLAND
217	217	PORTUGAL
218	218	RUMANIA
219	219	SPAIN
220	220	SWEDEN
221	221	SWITZERLAND
222	222	YUGOSLAVIA
240	240	EUROPE - OTHER
251	251	BURMA
252	252	SRI LANKA
253	253	CHINA
254	254	INDIA
255	255	INDONESIA
256	256	IRAN
257	257	IRAQ
258	258	ISRAEL
259	259	JAPAN
260	260	KOREA
261	261	LEBANON
262	262	MALAYSIA
263	263	PAKISTAN / BANGLADESH
264	264	PHILLIPINES
265	265	SYRIA
267	267	TURKEY
268	268	VIETNAM
269	269	ASIA - OTHER
301	301	EGYPT (U.A.R.)
302	302	GHANA
303	303	KENYA
304	304	NIGERIA
305	305	UNION OF SOUTH AFRICA
306	306	EAST AFRICA
307	307	AFRICA - OTHER
308	308	SAUDI ARABIA
400	400	AUSTRALIA
401	401	NEW ZEALAND

402	402	U.S.S.R.
403	403	WEST INDIES
499	499	OTHER OR UNKNOWN
500	500	INVERNESS
501	501	BADDECK
502	502	SPRINGHILL
503	503	HONG KONG
504	504	MIDDLE MUSQUODOBOIT
505	505	JAMAICA
506	506	SYDNEY
507	507	EGYPT
508	508	ABERDEEN
509	509	WASHINGTON DC
510	510	MONTREAL
511	511	MAURITIUS
512	512	CROATIA
513	513	UNKNOWN
514	514	ARICHAT
515	515	NOVA SCOTIA
517	517	MONCTON
518	518	KARACHI
519	519	KIRKUK
520	520	ILLINOIS
521	521	NELLORE INDIA
522	522	WINNIPEG
523	523	TRINIDAD / TOBAGO
527	527	LIBYA
528	528	BOSNIA/HERZEGOVINA

Provider County Value Labels (DCOUNTY – Physician Demographics)

FORMAT NAME: $COUNTYF LENGTH: 17 NUMBER OF VALUES: 24
MIN LENGTH: 1 MAX LENGTH: 40 DEFAULT LENGTH 17 FUZZ: 0

START	END	LABEL (VER. 8.2 25NOV2003:11:35:08)
00	00	Unknown
01	01	Annapolis
02	02	Antigonish
03	03	Cape Breton
04	04	Colchester
05	05	Cumberland
06	06	Digby
07	07	Guysborough
08	08	Halifax County
09	09	Hants
10	10	Inverness
11	11	Kings
12	12	Lunenberg
13	13	Pictou
14	14	Queens
15	15	Richmond
16	16	Shelburne
17	17	Victoria
18	18	Yarmouth
19	19	City of Halifax
20	20	City of Dartmouth
21	21	Sydney
33	33	Sackville, N.B.
99	99	Out-of-Province

Gender Value Labels (SEX - Physician Demographics, Physician Billings, Pharmacare)

FORMAT NAME: $SEXF LENGTH: 6 NUMBER OF VALUES: 4		
MIN LENGTH: 1 MAX LENGTH: 40 DEFAULT LENGTH 6 FUZZ: 0		
START	END	LABEL (VER. 8.2 25NOV2003:11:35:08)
1	1	Male
2	2	Female
F	F	Female
M	M	Male

Physician Specialty (DSPECIAL - Physician Demographics, Physician Billings)

FORMAT NAME: $DSPECF LENGTH: 31 NUMBER OF VALUES: 53		
MIN LENGTH: 1 MAX LENGTH: 40 DEFAULT LENGTH 31 FUZZ: 0		
START	END	LABEL (VER. 8.2 24MAR2004:15:14:22)
ANAE	ANAE	Anaesthetist
ANPA	ANPA	Anatomical Pathology
CARD	CARD	Cardiology
CASG	CASG	Cardiovasc/Thoracic Surgery
CLIA	CLIA	Clinical Immunology and Allergy
COMD	COMD	Community Medicine
DENT	DENT	Dental General Practitioner
DERM	DERM	Dermatology
DIRD	DIRD	Diagnostic Radiology
EMMD	EMMD	Emergency Medicine
ENDO	ENDO	Endodontics
ENME	ENME	Endocrinology and Metabolism
GAST	GAST	Gastroenterology
GEMD	GEMD	Geriatric Medicine
GENP	GENP	General Practitioner
GNSG	GNSG	General Surgery
HAGY	HAGY	Haematology
HAPA	HAPA	Haematology Pathology
HUGE	HUGE	Human Genetics
INDI	INDI	Infectious Diseases
INMD	INMD	Internal Medicine
MDON	MDON	Medical Oncology
MEBI	MEBI	Medical Biochemistry
MEGE	MEGE	Medical Genetics
MEMI	MEMI	Medical Microbiology
NCMD	NCMD	Nuclear Medicine
NEPA	NEPA	Neuropathology
NEPE	NEPE	Neurology Paediatric
NEPH	NEPH	Nephrology
NEUR	NEUR	Neurology
NUSG	NUSG	Neurosurgery
OBGY	OBGY	Obstetrics & Gynaecology
ODON	ODON	Orthodontics
OPHT	OPHT	Opthalmology
OPTO	OPTO	Optometry
ORAL	ORAL	Oral Surgery
ORTH	ORTH	Orthopaedic Surgery
OTOL	OTOL	Otolaryngology
PATH	PATH	General Pathology
PEDI	PEDI	Pediatrics
PEDO	PEDO	Pedodontics
PERI	PERI	Periodontics
PHMD	PHMD	Physical Medicine & Rehab

PLAS	PLAS	Plastic Surgery
PROS	PROS	Prosthodontics
PSYC	PSYC	Psychiatry
RADI	RADI	Diagnostic & Ther Radiology
RDON	RDON	Radiation Oncology
RHEU	RHEU	Rheumatology
RSMD	RSMD	Respiratory Medicine
THSG	THSG	Thoracic Surgery
UROL	UROL	Urology
VASG	VASG	Vascular Surgery

Dwelling Value Labels (Patient Demographics)

FORMAT NAME: $DWELLF LENGTH: 43 NUMBER OF VALUES: 9
MIN LENGTH: 1 MAX LENGTH: 43 DEFAULT LENGTH 43 FUZZ: 0

START	END	LABEL (VER. 8.2 27APR2004:11:47:42)
1	1	Hotels, School Res, Hostels, Campground
2	2	Work Camps, Merchant Marine
3	3	Religious Insitutions
4	4	Orphanages And Children's Homes
5	5	Nurs & Old Age Homes, Chronic Care, Srs
6	6	Hospitals, Psychiatric, Phys Handicapped
7	7	Hutterite Colonies
8	8	Juvenile Delinquent Homes, Jails
9	9	Milit Camps, Single Quarters, Army/Navy

Appendix 5.3
Drug Category and Respective ATC Codes

ATC Codes for Kent Groves
Jan 01, 1999-Dec 31, 2003

Drug Category	ATC codes
Calcium channel blockers	
Amlodipine (Norvasc)	C08CA01
Felodipine (Plendil, Renedil)	C08CA02
Nifedipine (Adalat and generics)	C08CA05
Verapamil (Isoptin and generics)	C08DA01
Diltiazem (Cardizem and generics)	C08DB01
ACE inhibitors without diuretics	
Captopril (Capoten and generics)	C09AA01
Enalapril (Vasotec and generics)	C09AA02
Lisinopril (Prinivil, Zestril and generics)	C09AA03
Perindopril (Coversyl)	C09AA04
Ramipril (Altace)	C09AA05
Quinapril (Accupril)	C09AA06
Benazepril (Lotensin)	C09AA07
Cilazapril (Inhibace and generics*)	C09AA08
Fosinopril (Monopril and generics)	C09AA09
Trandolapril (Mavik)	C09AA10
ACE inhibitors with diuretics	
Enalapril and diuretics (Vaseretic)	C09BA02
Lisinopril and diuretics (Prinizide, Zesteretic)	C09BA03
Perindopril and diuretics (Coversyl Plus)	C09BA04
Quinapril and diuretics (Accuretic)	C09BA06
Cilazapril and diuretics (Inhibace Plus)	C09BA08
Trandolapri and diuretics (Tarka)	C09BA10
Cholesterol reducing agents	
Simvastatin (Zocor and generics*)	C10AA01
Lovastatin (Mevacor and generics)	C10AA02
Pravastatin (Pravacol and generics)	C10AA03
Fluvastatin (Lesecol)	C10AA04
Atorvastatin (Lipitor)	C10AA05
Cerivastatin (Baycol)	C10AA06
Rosuvastatin (Crestor)	C10AA07
Clofibrate (Clariplex and generics)	C10AB01
Bezafibrate (Benzalip and generics*)	C10AB02
Gemfibrozil (Lopid and generics)	C10AB04
Fenofibrate (Lipidil and generics)	C10AB05
Colestyramine (Questran and generics)	C10AC01

Colestipol (Colestid)	C10AC02
Probucol (Lorelco)	C10AX02
Ezetimibe (Ezetrol)	C10AX09
NSAIDS	
Indomethacin (Indocid and generics)	M01AB01
Sulindac (generics only)	M01AB02
Tolmetin (Tolectin and generics)	M01AB03
Diclofenac (Voltaren, Arthrotec, and generics)	M01AB05
Etodolac (Ultradol and generics)	M01AB08
Ketorolac (Toradol and generics)	M01AB15
Piroxicam (Feldene and generics only)	M01AC01
Tenoxicam (Mobiflex generics only)	M01AC02
Ibuprofen (Motrin, Advil and generics)	M01AE01
Naproxen (Naprosyn and generics)	M01AE02
Ketoprofen (Orudis, Rhodis and generics)	M01AE03
Fenoprofen (Nalfon and generics)	M01AE04
Flurbiprofen (Froben and generics)	M01AE09
Tiaprofenic acid (Surgam and generics)	M01AE11
Oxaprozin (Daypro and generics)	M01AE12
Nabumetone (Relafen and generics)	M01AX01
Cox-2 Inhibitors	
Celecoxib	M01AH01
Rofecoxib	M01AH02
Valdecoxib	M01AH03
Meloxicam (Mobicox and generics)	M01AC06

Appendix 5.4
IMS Health: Canadian Promotional Audit
Circulation Numbers For Canadian Journals

	JOURNAL NAME	ISSUE	CIRCULATION
MEDICAL			
	Canadian Family Physician	Monthly	31,417
	Canadian Healthcare Manager	7 x year	9,822
	Chronicle of Skin & Allergy	8 x year	6,150
	Cdn.Jrl. of Rural Medicine	Quarterly	7,130
	Le Clinicien	Monthly	12,038
	Canadian Medical Association Journal	Bi-weekly	58,886
	Cdn. Jrl. of Diagnosis	Monthly	37,233
	Doctor's Review	Monthly	39,457
	Gastroenterology Canada	Quarterly	10,041
	Geriatrics & Aging	10 x year	18,767
	Cdn. Jrl. of C.M.E.	Monthly	37,507
	L'Actualite Medicale	Weekly	16,565
	Le Medecin du Quebec	Monthly	18,171
	Med Actuel-FMC	Bi-monthly	8,999
	Geriatrics Today	Quarterly	17,298
	*MD Canada	10 x year	30,985
	New England Jrl. of Medicine (Cdn. Ed.)	Weekly	4,363
	*National Review of Medicine	Semi-monthly	4,761
	Obstetrics & Gynaecology	Quarterly	9,721
	Ontario Medical Review	11 x year	23,164
	Patient Care	Monthly	27,257
	Physicians' Chronicle	Quarterly	31,564
	Stitches	Monthly	25,564
	Perspectives in Cardiology	10 x year	15,270
	Parkhurst Exchange	Monthly	39,277
	Medical Post	Weekly	43,468

SPECIALTY

Cdn. Jrl. of Anesthesia	10 x year	3,821
Chronicle of Cardio. & Internal Medicine	Bi-monthly	5,821
Clinical & Surgical Ophthalmology	Monthly	1,500
Cdn. Jrl. of Emergency Medicine	Bi-monthly	6,590
Cdn. Jrl. of Infectious Diseases	Bi-monthly	8,799
Cdn. Jrl. of Neurological Sciences	Quarterly	858
Cdn. Jrl. of Cardiology	Monthly	14,663
Cdn. Jrl. of Gastroenterology	Monthly	15,459
Cdn. Jrl. of Psychiatry	11 x year	6,715
Cdn. Jrl. of Surgery	Bi-monthly	2,326
Cdn. Jrl. of Urology	Bi-monthly	2,444
Chronicle of Neurology & Psychiatry	8 x year	6,037
Canadian Respiratory Journal	8 x year	13,805
Chronicle of Urology & Sexual Medicine	Bi-monthly	5,184
Dermatology Times of Canada	Bi-monthly	6,800
Journal of Otolaryngology	8 x year	911
Cdn. Jrl. of Ophthalmology	8 x year	862
Journal of Rheumatology	Monthly	1,048
Jrl. of Psychiatry and Neuroscience	Bi-monthly	7,013
L'Optometriste	Bi-monthly	3,868
Paediatrics and Child Health	10 x year	14,996
Clinical & Refractive Optometry	Monthly	2,379
Pain Research & Management	Quarterly	15,500
Journal JOGC	Monthly	12,464
Urology Times of Canada	Bi-monthly	4,800

NURSING

Canadian Onclolgy Nursing Journal	4 x year	903

PHARMACY

Canadian Journal of Hospital Pharm	7 x year	3,025
Canadian Pharmaceutical Journal	10 x year	12,040
L'Actualite Pharmaceutique	Monthly	5,060
Pharmacy Practice	Monthly	20,053
Pharmactuel	5 x year	1,300
Pharmacy Post	Monthly	17,457
Quebec Pharmacie	10 x year	7,194

JOURNALS ADDED IN 2004

MD Canada (February)
National Review of Medicine (April)

JOURNALS DELETED IN 2004

Annals of the Royal College of Physicians & Surgeons
Canadian Journal of Allergy and Clinical Immunology
Canadian Journal of Clinical Pharmacology
Canadian Journal of Diabetes
Journal of Geriatric Care
Journal of Sexual and Reproductive Medicine
PLein Soleil
Prix Galien

JOURNALS CHANGED NAME IN 2004

Ophthalmic Practice CCOP = Clinical & Surgical Ophthalmology
Practical Optometry PROP = Clinical & Refractive Optometry
Physicians' Computing Chronicle = Physicians' Chronicle

CIRCULATION FIGURES REPRESENT CIRCULATION TO:

Physicians,
Interns, Residents
Nurses, Dentists
Hospitals and Clinics

Excluded are:

Pharmaceutical manufacturers, distributors and representatives,
Educational institutions,
Libraries,
Government officials,

JOURNALS ADDED IN 2005

MD Canada (February)
National Review of Medicine (April)

Appendix 5.5
IMS Drug Categories, Common Names and Drug Identification Numbers

Product Category	Brand Name	Drug Identification Number
COX-2 INHIBITORS		
	BEXTRA	02246621, 02246622
	CELEBREX(CPA)	02239941, 02239942
	MOBICOX	02242785,
	VIOXX	02241109, 02241107, 02241108
NS-NSAIDS		
	APO-DICLO	02243433, 02162814, 02091194, 00839175, 00839183
	ARTHROTEC	01917056,
	ARTHROTEC(CPA)	02229837,
	DAYPRO	02027860,
	FROBEN	02223066, 02223074, 02223082
	MOTRIN	02187124, 01983873, 02186934
	NAPROSYN	02162431,
	NAPROSYN E	02162792, 02162415, 02162423
	NAPROSYN SR	02162466,
	ORUDIS SR	01926373,
	PENNSAID	02247265,
	VOLTAREN	00632732, 00632724, 00514012
	VOLTAREN SR	00590827, 00782459

Product Category	Brand Name	Drug Identification Number
ACE INHIBITORS		
	ACCUPRIL	01947664, 01947672, 01947680, 01947699
	ALTACE	02221829, 02221853, 02221837, 02221845
	COVERSYL	02246624, 02123274, 02123282
	INHIBACE	01911465, 01911473, 01911481
	MAVIK	02231457, 02231459, 02231460, 02239267
	LOTENSIN	00885843, 00885851, 00885835
	MONOPRIL	01907107, 01907115
	PRINIVIL(CPA)	00839396, 00839418, 00839388
	VASOTEC	01923846, 00670901, 00851795, 00670928, 00708879
	ZESTRIL	02049276, 02049384, 02049333
ACE INHIBITORS W/DIURETI		
	ACCURETIC	02237367, 02237368, 02237369
	COVERSYL PLUS	02246569,
	INHIBACE PLUS	02181479,
	PRINZIDE	02108194, 00884413, 00884421
	VASERETIC	02242826, 00657298
	ZESTORETIC	02103729, 02045737, 02045729

CHOLESTEROL REDUCE

BAYCOL	02243223, 02241466, 02237325, 02237326
BEZALIP	2083523
CRESTOR	02247162, 02247163, 02247164
EZETROL	02247521,
LESCOL	02250527
LIN-PRAVASTATIN	02237374
LIPIDIL MICRO	02146959, 02230283
LIPIDIL SUPRA	02241601, 02241602
LIPITOR	02230711, 02230713, 02230714, 02243097
MEVACOR	00795860, 00795852
PRAVACHOL	00893749, 00893757, 02222051
QUESTRAN	01918486, 00634093, 00464880
ZOCOR	00884332, 00884340, 00884359, 00884324, 02240332

Appendix 5.6:

Variable Names, Labels and Definitions

BPLACE	Place of Birth
DOB	Date of Birth
DOC_ID	Doctor Study ID
GRADYEAR	Year of Graduation
Brthcnnova	Birth Place: Nova Scotia
Brthcnothr	Birth Place: Other Canadian Province
Brthothrcn	Birth Place: Other Country
Cnbirthdoc	Birth Place: Canada
City	Practice County: City
Dage	Doctor age up to mid 2003
Dcountym	Practice County: unknown
Dsex	Doctor Gender 1: Female, 0: Male
Genp	Doctor type: general practice
Citygenp	General practitioners who work in urban clinics
Ruralgenp	General practitioners who work in rural clinics
Malgenp	Male general practitioners
Femgenp	Female general practitioners
Citysp	Specialists who work in urban clinics
Ruralsp	Specialists who work in rural clinics
Femsp	Female specialists
Malsp	Male specialists
Lentime	Years in Practice
Lgtime	Log transformation to duration of practice
Medcdn	Medical school: Canadian
cox2othr3	Relative monthly COX-2 prescribing over the average monthly prescribing of COX-2s, Calcium Channel Blockers, ACE Inhibitors and Cholesterol Lowering Agents
Nsaids	Non Specific - Non-Steroidal Anti Inflammatories
Avrgnsaids	Average monthly prescription volumes of non-specific NSAIDs
Choles	Cholesterol Reducing Drugs
Ace	Acetycholinesterase Inhibitors
Calcium	Calcium Channel Blockers
Cox-2	Cyclo-Oxygenase-2 Inhibitors
avrgothr3	Average monthly prescription volumes of Calcium Channel Blockers, ACE Inhibitors and Cholesterol Lowering Agents

Appendix 6.1:
Expanded Physician Profiles and Demographics

Variable	Sub Segment Size	Category Size
General Practitioner	835	
Specialist	371	
Total		***1206***
City Practice	567	
Rural Practice	639	
Total		***1206***
Gender- Female	343	
Gender - Male	863	
Total		***1206***
Canadian Med School Graduate	947	
Non-Canadian Med School Graduate	259	
Total		***1206***
City General Practitioner	347	
Rural General Practitioner	488	
City Specialist	220	
Rural Specialist	151	
Total		***1206***
Female General Practitioner	270	
Female Specialist	73	
Male General Practitioner	565	
Male Specialist	298	
Total		***1206***
Mean Graduation Year	1979.2	
Mean Physician Age	49.95	
Mean Number of Years in Practice	23.82	

Appendix 6.2:

Correlation Analysis for Selected Independent Variables* and the Likelihood of Prescribing in the Upper Quartile of the Total COX-2 Prescribers

	Correlation Coefficient	p Value
Dsex Doctor Gender1: Female 0: Male	-0.2570	<0.0001
Dage Doctor age up to mid 2003	0.1046	0.0014
GRADYEAR Year of Graduation	-0.1070	0.0011
Genp Doctor Type: general practice	0.2515	<0.0001
medcdn Medical school: Canadian	-0.0264	0.4225
City Practice County: city	-0.2612	<0.0001
Lentime Years of Practice	0.1070	0.0011
avrgnsaids Average Monthly NS-NSAID Prescriptions	0.6647	<0.0001
avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.6560	<0.0001
avrgace Average Monthly ACE Inhibitor Prescriptions	0.7071	<0.0001
avgcal Average Monthly Calcium Channel Blocker Prescriptions	0.6979	<0.0001
avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.71079	<0.0001
brthcnnova Birth Place: Nova Scotia	0.0248	0.4510
brthcnothr Birth Place: Other Canadian Province	-0.0645	0.0497
brthothrcn Birth Place: Other Country	0.0074	0.8220
cnbirthdoc Birth Place: Canada	-0.0350	0.2877

*Independent variables are further defined in Appendix 5.6.

Appendix 6.3:

Correlation Analysis for Selected Independent Variables* and the Likelihood of Prescribing in the Upper Quartile of the Relative COX-2 Prescribers

	Correlation Coefficient	p Value
Dsex Doctor Gender1: Female 0: Male	0.0868	0.0082
Dage Doctor age up to mid 2003 (years)	-0.1087	0.0009
GRADYEAR Year of Graduation	0.1269	<0.0001
Genp Doctor Type: general practice	-0.0253	0.4421
Medcdn Medical school: Canadian	0.0196	0.5519
City Practice County: city	0.0747	0.0231
Lentime Years of Practice	-0.1269	<0.0001
Avrgnsaids Average Monthly NS-NSAID Prescriptions	-0.1613	<0.0001
avrgcox2 Average Monthly COX-2 Prescriptions	0.1198	0.0003
Avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.0075	0.8194
Avrgace Average Montly ACE Inhibitor Prescriptions	0.0094	0.7758
Avrgcal Average Monthly Calcium Channel Blocker Prescriptions	0.0020	0.9511
avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.0067	0.9511
Brthcnnova Birth Place: Nova Scotia	-0.0225	0.4942
Brthcnothr Birth Place: Other Canadian Province	0.0391	0.2343
Brthothrcn Birth Place: Other Country	0.0312	0.3425
Cnbirthdoc Birth Place: Canada	0.0145	0.6600

*Independent variables are further defined in Appendix 5.6.

Appendix 6.4:

Correlation Analysis for Selected Independent Variables and the Likelihood of Prescribing in the First Quartile of Total COX-2s for Older Physicians (>49 years)

	Correlation Coefficient	**p Value**
Dsex Doctor Gender1: Female 0: Male	-0.1582	0.0007
Dage Doctor age up to mid 2003	-0.0022	0.9633
GRADYEAR Year of Graduation	-0.0138	0.7693
Genp Doctor Type: general practice	0.3236	<0.0001
City Practice County: city	-0.2738	<0.0001
Lentime Years of Practice	0.0138	0.7693
Avrgnsaids Average Monthly NS-NSAID Prescriptions	0.67168	<0.0001
Avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.6568	<0.0001
Avrgace Average Monthly ACE Inhibitor Prescriptions	0.7202	<0.0001
Avgcal Average Monthly Calcium Channel Blocker Prescriptions	0.7104	<0.0001
Avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.7247	<0.0001

Appendix 6.5:

Correlation Analysis for Selected Independent Variables and the Likelihood of Prescribing in the First Quartile of Total COX-2s for Younger Physicians (<49 years)

	Correlation Coefficient	**p Value**
Dsex Doctor Gender1: Female 0: Male	-0.3116	<0.0001
Dage Doctor age up to mid 2003	0.0351	0.4463
GRADYEAR Year of Graduation	-0.0378	0.4117
Genp Doctor Type: general practice	0.2001	<0.0001
City Practice County: city	-0.2759	<0.0001
Lentime Years of Practice	0.0378	0.4117
avrgnsaids Average Monthly NS-NSAID Prescriptions	0.6476	<0.0001
Avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.6508	<0.0001
Avrgace Average Monthly ACE Inhibitor Prescriptions	0.6826	<0.0001
Avgcal Average Monthly Calcium Channel Blocker Prescriptions	0.6741	<0.0001
Avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.6866	<0.0001

Appendix 6.6:

Correlation Analysis for Selected Independent Variables and the Likelihood of Prescribing in the First Quartile of Total COX-2s for Female Physicians

	Correlation Coefficient	**p Value**
Dsex Doctor Gender1: Female 0: Male	na	Na
Dage Doctor age up to mid 2003	0.1519	0.0098
GRADYEAR Year of Graduation	-0.1734	0.0032
Genp Doctor Type: general practice	0.08867	0.1333
City Practice County: city	-0.1619	0.0059
Lentime Years of Practice	0.1734	0.0032
Avrgnsaids Average Monthly NS-NSAID Prescriptions	0.5253	<0.0001
Avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.5432	<0.0001
Avrgace Average Monthly ACE Inhibitor Prescriptions	0.5701	<0.0001
Avgcal Average Monthly Calcium Channel Blocker Prescriptions	0.5814	<0.0001
Avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.5894	<0.0001

Appendix 6.7:

Correlation Analysis for Selected Independent Variables and the Likelihood of Prescribing in the First Quartile of Total COX-2s for Male Physicians

	Correlation Coefficient	**p Value**
Dsex Doctor Gender1: Female 0: Male	na	na
Dage Doctor age up to mid 2003	0.0174	0.6613
GRADYEAR Year of Graduation	-0.01696	0.6692
Genp Doctor Type: general practice	0.3545	<0.0001
City Practice County: city	-0.2955	<0.0001
Lentime Years of Practice	0.0170	0.6692
Avrgnsaids Average Monthly NS-NSAID Prescriptions	0.6608	<0.0001
Avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.6512	<0.0001
Avrgace Average Monthly ACE Inhibitor Prescriptions	0.7058	<0.0001
Avgcal Average Monthly Calcium Channel Blocker Prescriptions	0.6933	<0.0001
Avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.7080	<0.0001

Appendix 6.8:

Correlation Analysis for Selected Independent Variables* and the Likelihood of Prescribing in the Upper Quartile of Total COX-2s Among Early and Late Prescribers

Independent Variable	Correlation Coefficient		p Value	
	< 25 months	> 25 months	< 25 months	>25 months
Dsex Doctor Gender1: Female 0: Male	-0.2557	-0.2781	<0.0001	<0.0001
Dage Doctor age up to mid 2003	0.1164	0.1130	0.0006	0.0010
GRADYEAR Year of Graduation	-0.1187	-0.1165	0.0004	0.0007
Genp Doctor Type: general practice	0.2214	0.2224	<0.0001	<0.0001
medcdn Medical school: Canadian	-0.0348	-0.0065	0.3038	0.8512
City Practice County: city	-0.2340	-0.2318	<0.0001	<0.0001
Lentime Years of Practice	0.1187	0.1165	0.0004	0.0007
avrgnsaids Average Monthly NS-NSAID Prescriptions	0.6387	0.5938	<0.0001	<0.0001
avrgchl Average Monthly Cholesterol Lowering Prescriptions	0.6307	0.6266	<0.0001	<0.0001
avrgace Average Monthly ACE Inhibitor Prescriptions	0.6708	0.6789	<0.0001	<0.0001
avgcal Average Monthly Calcium Channel Blocker Prescriptions	0.6722	0.6652	<0.0001	<0.0001
avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	0.6863	0.6778	<0.0001	<0.0001
brthcnnova Birth Place: Nova Scotia	0.0246	0.0588	0.4674	0.0874
brthcnothr Birth Place: Other Canadian Province	-0.0407	-0.0671	0.2289	0.0510
Birth Place: Other Country	0.0057	-0.0132	0.8657	0.7019
Birth Place: Canada	-0.0137	-0.0065	0.6848	0.8493

*Independent variables are further defined in Appendix 5.6

Appendix 6.9:

Comparison of Total Upper and Lower Quartile COX-2 Prescribers among Early and Late Prescribers

Independent Variable	Lower Quartile*		Upper Quartile	
	< 25 months	> 25 months	< 25 months	>25 months
Physician Gender Female	39%	40%	11%	10%
Doctor age up to mid 2003 (years)	48.7	48.7	51.4	51.3
Year of Graduation	1980.6	1980.6	1977.7	1977.8
Doctor Type: general practice	79%	81%	98%	99%
Medical school: Canadian	82%	81%	79%	81%
Practice County: city	48%	48%	22%	22%
Years of Practice	22.4	22.4	25.3	25.2
Average Monthly NS-NSAID Prescriptions	1.8	1.3	9.1	6.8
Average Monthly Cholesterol Lowering Prescriptions	5.4	7.2	25.0	32.3
Average Monthly ACE Inhibitor Prescriptions	7.1	8.1	34.4	39.5
Average Monthly COX-2 Prescriptions	NA	NA	NA	NA
Average Monthly Calcium Channel Blocker Prescriptions	6.1	6.7	29.2	31.7
Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	18.6	22.0	88.5	103.4
Birth Place: Nova Scotia	28%	27%	31%	33%
Birth Place: Other Canadian Province	28%	28%	23%	22%
Birth Place: Other Country	25%	25%	25%	24%
Birth Place: Canada	56%	55%	54%	54%

*All values presented are the mean values for each segment and characteristic.

Appendix 6.10:

Correlation Analysis for Selected Independent Variables* and the Likelihood of Prescribing in the Upper Quartile of the COX-2/COX-2+NS-NSAID Ratio Among Early and Late Prescribers

Independent Variable	Correlation Coefficient		p Value	
	< 25 months	> 25 months	< 25 months	>25 months
Dsex Doctor Gender1: Female 0: Male	0.0569	0.0589	0.0927	0.0870
Dage Doctor age up to mid 2003	-0.0692	-0.0871	0.0406	0.0113
GRADYEAR: Year of Graduation	0.0779	0.0946	0.0212	0.0059
Genp Doctor Type: general practice	-0.0778	0.0248	0.0214	0.4704
medcdn Medical school: Canadian	-0.0171	0.0724	0.6134	0.0352
City Practice County: city	0.0892	0.0767	0.0083	0.0256
Lentime :Years of Practice	-0.0779	-0.0946	0.0212	0.0059
avrgnsaids Average Monthly NS-NSAID Prescriptions	-0.1977	-0.1771	<0.0001	<0.0001
avrgchl Average Monthly Cholesterol Lowering Prescriptions	-0.0081	0.0438	0.8107	0.2029
avrgcox2 Average Monthly COX-2 Prescriptions	0.1200	0.1608	<0.0001	<0.0001
avrgace Average Monthly ACE Inhibitor Prescriptions	-0.0119	0.0461	0.7234	0.1807
avgcal Average Monthly Calcium Channel Blocker Prescriptions	-0.0203	0.0476	0.5483	0.1662
avrgothr3 – Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	-0.0141	0.0472	0.6771	0.1701
brthcnnova Birth Place: Nova Scotia	-0.0343	-0.0094	0.3105	0.7858
brthcnothr Birth Place: Other Canadian Province	0.0079	0.0968	0.8151	0.0048
brthothrcn Birth Place: Other Country	0.0751	-0.0432	0.0264	0.2088
cnbirthdoc Birth Place: Canada	-0.0242	0.0776	0.4740	0.0240

*Independent variables are further defined in Appendix 5.6

Appendix 6.11:

Comparison of Relative* Upper and Lower Quartile COX-2 Prescribers among Early and Late Prescribers

Independent Variable	Lower Quartile*		Upper Quartile	
	< 25 months	> 25 months	< 25 months	>25 months
Physician Gender Female	31%	29%	34%	35%
Doctor age up to mid 2003 (years)	49.8	50.5	48.1	48.3
Year of Graduation	1979.4	1978.7	1981.2	1981.4
Doctor Type: general practice	89%	86%	71%	85%
Medical school: Canadian	81%	78%	81%	84%
Practice County: city	37%	36%	56%	46%
Years of Practice	23.6	24.3	21.8	22.0
Average Monthly NS-NSAID Prescriptions	4.6	3.8	0.8	1.7
Average Monthly Cholesterol Lowering Prescriptions	11.6	13.2	6.1	14.4
Average Monthly ACE Inhibitor Prescriptions	15.9	15.9	7.9	16.6
Average Monthly COX-2 Prescriptions	3.1	3.3	4.7	5.0
Average Monthly Calcium Channel Blocker Prescriptions	13.6	13.0	6.8	13.4
Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	41.1	42.1	20.8	44.3
Birth Place: Nova Scotia	30%	28%	24%	28%
Birth Place: Other Canadian Province	25%	23%	30%	30%
Birth Place: Other Country	23%	26%	29%	24%
Birth Place: Canada	56%	52%	54%	58%

*COX-2 Prescribing Relative to Combined COX-2 + NS-NSAID Prescribers

**All values presented are the mean values for each segment and characteristic

Appendix 6.12:
Segment Profiles of COX-2 Adopting Physicians

Independent Variable	Segment 1	Segment 2	Segment 3	NS Physician Universe
	3 months	4 to 7 months	> 7 months	
Sample Size	143	44	109	925
Physician Gender Female	15%	14%	11%	31.1%
Doctor age up to mid 2003 (years)	50.9	50.6	52.1	49.6
Year of Graduation	1978.1	1979.3	1977.0	1979.6
Doctor Type: general practice	98%	100%	97%	81.5%
Medical school: Canadian	79%	84%	77%	80.4%
Practice County: city	24%	14%	21%	43.2%
Years of Practice	24.9	23.7	26.0	23.4
Average Monthly NS-NSAID Prescriptions	8.0	10.9	12.2	4.01
Average Monthly Cholesterol Lowering Prescriptions	29.1	31.9	27.3	12.7
Average Monthly ACE Inhibitor Prescriptions	37.5	40.0	37.7	16.2
Average Monthly COX-2 Prescriptions	11.0	9.0	7.5	3.7
Average Monthly Calcium Channel Blocker Prescriptions	31.8	34.4	31.0	13.7
Average combined monthly cholesterol lowering, ACE, Calcium channel blocker prescriptions	98.4	106.3	95.6	42.7
Birth Place: Nova Scotia	29%	32%	34%	28%
Birth Place: Other Canadian Province	25%	27%	16%	26.7%
Birth Place: Other	46%	41%	40%	45.3%

Appendix 6.13:

Analysis of Maximum Likelihood Estimates Using All Independent Variables and "rbest" as the Dependent Variable

Variable	Label	Estimates	p Value	Standardized Estimates	Standardized Odds Ratio
cox2othr3	Relative monthly COX-2 prescribing over COX-2s + all others	4.4373	<.0001	0.4369	1.55
Genp	General Practice	-0.6373	0.0573	-0.1341	0.87
Dage	Doctor Age	-0.0386	0.0014	-0.2141	0.81
Citygenp	General Practice in City Setting	0.6542	0.0079	0.168	1.18

Appendix 6.14:

Analysis of Maximum Likelihood Estimates Using All Independent Variables and "rbest" as the Dependent Variable

Variable	Label	Estimates	p Value	Standardized Estimates	Standardized Odds Ratio
cox2othr3	Relative monthly COX-2 prescribing over COX-2s + all others	4.4373	<.0001	0.4369	1.55
Genp	General Practice	-0.6373	0.0573	-0.1341	0.87
Dage	Doctor Age	-0.0386	0.0014	-0.2141	0.81
Citygenp	General Practice in City Setting	0.6542	0.0079	0.168	1.18

BIBLIOGRAPHY

1. IMS Health Canada. About IMS in Canada. 2004;2005(September 21, 2005).

2. Health Canada. Therapeutics Product Directorate: TPD-Web. 2005;2005(November 17).

3. IMS Health Canada. IMS Health, Canadian Disease and Therapeutic Index. 2005;.

4. Hepler CD, Grainger-Rousseau TJ. Pharmaceutical care versus traditional drug treatment. Is there a difference? Drugs 1995;49(1):1-10.

5. Rodham K. Role theory and the analysis of managerial work: The case of occupational health professionals. Journal of Applied Management Studies 2000;9(1):71.

6. Kotler P, Armstrong G and Cunningham PH. Principles of Marketing, 6th Canadian Edition. Toronto: Pearson, 2005.

7. Ajzen I. The theory of planned behavior. Organizational Behavior and Human Decision Processes 1991;50(2):179.

8. IMS Health Canada. Growth In Retail Prescriptions Slows in 2004. 2005(July 12).

9. WHO Collaborating Centre for Drug Statistics Methodology. About the ATC/DDD system. 2006;2006(February 28).

10. Health Canada. Drugs and Health Products - Drug Identification Number (DIN) Enforcement Policy (POL - 0040). 2005;2006(February/28).

11. Majumdar SR, Lipton HL and Soumerai SB. Evaluating and Improving Physician Prescribing. In: Strom BL, eds. Pharmacoepidemiology. 4th ed. West Sussex, England: Wiley & Sons, 2005:419-437.

12. Lazarou J, Pomeranz BH and Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998;279(15):1200-5.

13. Avorn G. Powerful Medicines: The Benefits, Risks and Costs of Prescription Drugs. New York: Alfred A Knopf, 2005.

14. Morgan S. Canadian prescription drug costs surpass 18 billion dollars. CMAJ 2005;172(10):1323-4.

15. Morgan S. Drug spending in Canada: recent trends and causes. Med Care 2004;42(7):635-42.

16. Canadian Institute For Health Information. Health Care In Canada, 2004. Ottawa, Canada: , 2004.

17. Government of Nova Scotia. Health Care Cost Drivers. 2004;2005(July 12):2.

18. Government of Nova Scotia. Nova Scotia Budget for the Fiscal Year 2005/2006. 2005;2005(July 12).

19. Rogers EM. Diffusion of Innovations. New York: The Free Press, 1983.

20. Faculty of Graduate Studies. Interdisciplinary PhD Programme: Student Handbook. 2005;2005(November 1).

21. Groves K, Flanagan P and MacKinnon N. Why physicians start or stop prescribing a drug: literature review and formulary implications. Formulary 2002;37(April):186-94.

22. Segal R, Wang F. Influencing physician prescribing. Pharm Pract Manag Q 1999;19(3):30-50.

23. Gill PS, Makela M and Vermeulen KM, et al. Changing doctor prescribing behaviour. Pharm World Sci 1999;21(4):158-67.

24. Sbarbaro JA. Can we influence prescribing patterns? Clin Infect Dis 2001;33 Suppl 3:S240-4.

25. Parrino TA. Controlled trials to improve antibiotic utilization: a systematic review of experience, 1984-2004. Pharmacotherapy 2005;25(2):289-98.

26. Pippalla RS, Riley DA and Chinburapa V. Influencing the prescribing behaviour of physicians: a metaevaluation. J Clin Pharm Ther 1995;20(4):189-98.

27. Wilson AL. Influencing prescribers. Top Hosp Pharm Manage 1994;14(3):40-6.

28. Hepler CD, Segal R and Freeman RA. How physicians choose the drugs they prescribe. Top Hosp Pharm Manage 1981;1(3):23-44.

29. Raisch DW. A model of methods for influencing prescribing: Part II. A review of educational methods, theories of human inference, and delineation of the model. DICP 1990;24(5):537-42.

30. Raisch DW. A model of methods for influencing prescribing: Part I. A review of prescribing models, persuasion theories, and administrative and educational methods. DICP 1990;24(4):417-21.

31. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. Lancet 2003;362(October 11):1225-30.

32. Anderson GM, Lexchin J. Strategies for improving prescribing practice. CMAJ 1996;154(7):1013-7.

33. Carter AO, Strachan D and Appiah Y. Physician prescribing practices: what do we know? where do we go? how do we get there? CMAJ 1996;154(11):1649-53.

34. Vuckovic N, Nichter M. Changing patterns of pharmaceutical practice in the United States. Soc Sci Med 1997;44(9):1285-302.

35. Bradley CP. Uncomfortable prescribing decisions: a critical incident study. BMJ 1992;304(6822):294-6.

36. Weiss MC, Fitzpatrick R, Scott DK and Goldacre MJ. Pressures on the general practitioner and decisions to prescribe. Fam Pract 1996;13(5):432-8.

37. Einarson TR. The Authority/Pharmacotherapy Care model: an explanatory model of the drug use process in primary care. Research in Social and Administrative Pharmacy 2005;1:101-17.

38. Gonul FF, Carter F, Petrova E and Srinivasan K. Promotion of prescription drugs and its impact on physicians' choice behavior. J Market 2001;65(July):79-90.

39. Rosenthal MB, Berndt ER, Donohue JM, Epstein AM and Frank RG. Demand effects of recent changes in prescription drug promotion. Menlo Park, CA: Henry J. Kaiser Family Foundation, 2003.

40. Horton LR. Some relationships between personality and consumer decision making. JMR 1979;16(2):233.

41. Olshavsky RW, Granbois DH. Consumer decision making--fact or fiction? JCR 1979;6(2):93.

42. Turley, W L, LeBlanc and P R. Evoked sets: A dynamic process model. Journal of Marketing Theory and Practice 1995;3(2):28.

43. Solomon M, Zaichkowsky J and Polegato R. Consumer Behaviour. Toronto: Prentice-Hall, 2004.

44. Rochaix L. The physician as perfect agent: a comment. Soc Sci Med 1998;47(3):355-6.

45. Mooney G, Ryan M. Agency in health care: getting beyond first principles. J Health Econ 1993;12(2):125-35.

46. Mott DA, Schommer JC, Doucette WR and Kreling DH. Agency theory, drug formularies, and drug product selection: implications for public policy. Journal of Public Policy and Marketing 1998;17(2):287-95.

47. MacLeod SM. Improving physician prescribing practices: bridge over troubled waters. CMAJ 1996;154(5):675-7.

48. McTavish JR. What did Bayer do before aspirin? Pharm Hist 1999;41(1):3-15.

49. Angus DE, Karpetz HM. Pharmaceutical policies in Canada. Issues and challenges. Pharmacoeconomics 1998;14 Suppl 1:81-96.

50. Health Canada. Therapeutics Product Directorate: TPD-Web. 2003;2005(July 19).

51. Nova Scotia Department of Health. Who makes the decisions regarding the benefit status of medications listed in the Nova Scotia Formulary? 2004;2005(19 July).

52. McPhee J. Role of The Atlantic Common Drug Review in Provincial Pharmacare Coverage. 2005;.

53. Greenhalgh T, Robert G, MacFarlane F, Bate P and Kyriakidou O. Diffusion of innovations in service organizations: systematic review and recommendations. The Millbank Quarterly 2004;82(4):581-629.

54. Coleman J, Katz E and Menzel H. Medical Innovation: A Diffusion Study. Indianapolis: Bobbs-Merrill Co., 1966.

55. Van den Bulte, Christophe, Lilien GL. Medical innovation revisited: social contagion versus marketing effort. AJS 2001;106(5):1409-35.

56. Peay MY, Peay ER. Innovation in high risk drug therapy. Soc Sci Med 1994;39(1):39-52.

57. Waarts E, Everdingen YMv and Hillegersberg Jv. The dynamics of factors affecting the adoption of innovations. The Journal of Product Innovation Management 2002;19(6):412.

58. Ma J, Stafford RS, Cockburn IM and Finkelstein SN. A statistical analysis of the magnitude and composition of drug promotion in the United States in 1998. Clin Ther 2003;25(5):1503-17.

59. Wozniak, D G. Joint information acquisition and new technology adoption: Late versus early adoption. The Review of Economics and Statistics 1993;75(3):438.

60. Olshavsky, W R, Spreng and A R. An exploratory study of the innovation evaluation process. The Journal of Product Innovation Management 1996;13(6):512.

61. Dybdahl T, Andersen M, Sondergaard J, Kragstrup J and Kristiansen IS. Does the early adopter of drugs exist? A population-based study of general practitioners' prescribing of new drugs. Eur J Clin Pharmacol 2004;60(9):667-72.

62. Shih C, Venkatesh A. Beyond adoption: development and application of a use-diffusion model. J Market 2004;68(1):59.

63. Marinova D. Actualizing innovation effort: the impact of market knowledge diffusion in a dynamic system of competition. J Market 2004;68(3):1.

64. Robertson ST. The process of innovation and the diffusion of innovation. J Market 1967;31(1):14.

65. McDonald H, Corkindale D and Sharp B. Behavioral versus demographic predictors of early adoption: a critical analysis and comparative test. Journal of Marketing Theory and Practice 2003;11(3):84.

66. Granovetter M. Threshold models of collective behavior. AJS 1978;83:1420-43.

67. Valente TW. Social network thresholds in the diffusion of innovations. Social Networks 1996;18(1):69-89.

68. Carpenter GS, Nakamoto K. Consumer preference formation and pioneering advantage. JMR 1989;26(3):285.

69. Boulding W, Christen M. Sustainable pioneering advantage? Profit implications of market entry order. Marketing Science 2003;22(3):371.

70. Vargo SL, Lusch RF. Evolving to a new dominant logic for marketing. J Market 2004;68(1):1.

71. Scharitzer D, Kollarits HC. Satisfied customers: Profitable customer relationships: Pharmaceutical marketing: How pharmaceutical sales representatives can achieve

economic success through relationship management with settled general practitioners-an empirical study. Total Quality Management 2000;11(7):S955.

72. Mintzes B, Barer ML and Kravitz RL, et al. How does direct-to-consumer advertising (DTCA) affect prescribing? A survey in primary care environments with and without legal DTCA. CMAJ 2003;169(5):405-412.

73. Revzan DA. Comment. J Market 1950;15(1):101.

74. Groves KE, Sketris I and Tett SE. Prescription drug samples--does this marketing strategy counteract policies for quality use of medicines? J Clin Pharm Ther 2003;28(4):259-71.

75. Marks JL, Kamins AM. The use of product sampling and advertising: effects of sequence of exposure and degree of advertising claim exaggeration on consumers' belief strength, belief confidence and attitudes. JMR 1988;25(3):266.

76. Rosenthal MB, Berndt ER, Donohue JM, Frank RG and Epstein AM. Promotion of prescription drugs to consumers. N Engl J Med 2002;346(7):498-505.

77. Hawkins SA, Hoch SJ. Low-involvement learning: memory without evaluation. JCR 1992;19(2):212-25.

78. Prosser H, Almond S and Walley T. Influences on GPs' decision to prescribe new drugs-the importance of who says what. Fam Pract 2003;20(1):61-8.

79. Avorn J, Chen M and Hartley R. Scientific versus commercial sources of influence on the prescribing behavior of physicians. Am J Med 1982;73(1):4-8.

80. Guldal D, Semin S. The influences of drug companies' advertising programs on physicians. Int J Health Serv 2000;30(3):585-95.

81. Watkins C, Harvey I, Carthy P, Moore L, Robinson E and Brawn R. Attitudes and behaviour of general practitioners and their prescribing costs: a national cross sectional survey. Qual Saf Health Care 2003;12(1):29-34.

82. Muijrers PE, Grol RP, Sijbrandij J, Janknegt R and Knottnerus JA. Differences in prescribing between GPs. Impact of the cooperation with pharmacists and impact of visits from pharmaceutical industry representatives. Fam Pract 2005;.

83. Jacoby A, Smith M and Eccles M. A qualitative study to explore influences on general practitioners' decisions to prescribe new drugs. Br J Gen Pract 2003;53(487):120-5.

84. Jiang P. The role of brand name in customization decisions: A search vs experience perspective. Journal of Product and Brand Management 2004;13(2):73-83.

85. Gorecki KP. The importance of being first - The case of prescription drugs in canada. International Journal of Industrial Organization 1986;4:371-395.

86. Leffler KB. Persuasion or information? The economics of prescription drug advertising. Journal of Law and Economics 1981;24:45-74.

87. Jones MI, Greenfield SM and Bradley CP. Prescribing new drugs: qualitative study of influences on consultants and general practitioners. BMJ 2001;323(7309):378-81.

88. Watkins C, Moore L, Harvey I, Carthy P, Robinson E and Brawn R. Characteristics of general practitioners who frequently see drug industry representatives: national cross sectional study. B M J 2003;326(May 31, 2003):1178-1179.

89. Majumdar SR, McAlister FA and Soumerai SB. Synergy between publication and promotion: comparing adoption of new evidence in Canada and the United States. A J M 2003;115(October 15):467-472.

90. Kerr SJ, Mant A, Horn FE, McGeechan K and Sayer GP. Lessons from early large-scale adoption of celecoxib and rofecoxib by Australian general practitioners. Med J Aust 2003;179(8):403-7.

91. Mizik N, Jacobson R. Are physicians "easy marks"? Quantifying the effects of detailing and sampling on new prescriptions. Management Science 2004;50(12):1704.

92. Hanssens, Marnik G. Dekimpe, Dominique M. The persistence of marketing effects on sales. Marketing Science 1995;14(1):1.

93. Gonul FF, Carter F and Wind J. What kind of patients and physicians value direct-to-consumer advertising of prescription drugs. Health Care Manag Sci 2000;3(3):215-26.

94. Manchanda P, Chintagunta PK. Responsiveness of physician prescription behavior to salesforce effort: An individual level analysis. Marketing Letters 2004;15(2-3):129-45.

95. Coenen S, Van Royen P, Michiels B and Denekens J. Optimizing antibiotic prescribing for acute cough in general practice: a cluster-randomized controlled trial. J Antimicrob Chemother 2004;54(3):661-72.

96. Solomon DH, Van Houten L and Glynn RJ, et al. Academic detailing to improve use of broad-spectrum antibiotics at an academic medical center. Arch Intern Med 2001;161(15):1897-902.

97. Zwar N, Wolk J, Gordon J, Sanson-Fisher R and Kehoe L. Influencing antibiotic prescribing in general practice: a trial of prescriber feedback and management guidelines. Fam Pract 1999;16(5):495-500.

98. Jones M, Greenfield S and Bradley C. A survey of the advertising of nine new drugs in the general practice literature. J Clin Pharm Ther 1999;24(6):451-60.

99. Schumock GT, Walton SM and Park HY, et al. Factors that influence prescribing decisions. Ann Pharmacother 2004;38(4):557-62.

100. Hurwitz AM, Caves ER. Persuasion or information? Promotion and the shares of brand name and generic pharmaceuticals. Journal of Law and Economics 1988;31(2):299.

101. Stafford RS, Furberg CD, Finkelstein SN, Cockburn IM, Alehegn T and Ma J. Impact of clinical trial results on national trends in alpha-blocker prescribing, 1996-2002. JAMA 2004;291(1):54-62.

102. Scott IA. On the need for probity when physicians interact with industry. Intern Med J 2006;36(4):265-9.

103. Roth MS. Media and message effects on DTC prescription drug print advertising awareness. J Adv Res 2003;43(2):180-93.

104. Schwartz RK, Soumerai SB and Avorn J. Physician motivations for nonscientific drug prescribing. Soc Sci Med 1989;28(6):577-82.

105. Peyrot M, Alperstein NM, Van Doren D and Poli LG. Direct-to-consumer ads can influence behavior. Advertising increases consumer knowledge and prescription drug requests. Mark Health Serv 1998;18(2):26-32.

106. Mehta A, Purvis SC. Consumer response to print prescription drug advertising. J Adv Res 2003;43(2):194-206.

107. Zachry WM3, Shepherd MD, Hinich MJ, Wilson JP, Brown CM and Lawson KA. Relationship between direct-to-consumer advertising and physician diagnosing and prescribing. A J H P 2002;59(1):42-9.

108. Vogel RJ, Ramachandran S and Zachry WM. A 3-stage model for assessing the probable economic effects of direct-to-consumer advertising of pharmaceuticals. Clin Ther 2003;25(1):309-29.

109. Donohue JM, Berndt ER, Rosenthal M, Epstein AM and Frank RG. Effects of pharmaceutical promotion on adherence to the treatment guidelines for depression. Med Care 2004;42(12):1176-85.

110. Stevenson FA, Greenfield SM, Jones M, Nayak A and Bradley CP. GP's perceptions of patient influence on prescribing. Fam Pract 1999;16(3):255-61.

111. Britten N, Ukoumunne OC and Boulton MG. Patients' attitudes to medicines and expectations for prescriptions. Health Expect 2002;5(3):256-69.

112. Skelly A. Prescribing habits linked to patient income. The Medical Post 2002;38(20):May 30, 2005.

113. Soumerai SB, Avorn J, Ross-Degnan D and Gortmaker S. Payment restrictions for prescription drugs under Medicaid. Effects on therapy, cost, and equity. N Engl J Med 1987;317(9):550-6.

114. Tamblyn R, Laprise R and Hanley JA, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. JAMA 2001;285(4):421-9.

115. Stewart RE, Vroegop S, Kamps GB, van der Werf GT and Meyboom-de Jong B. Factors influencing adherence to guidelines in general practice. Int J Technol Assess Health Care 2003;19(3):546-54.

116. World Health Organization. World Health Organization of Experts On The Rational Use of Drugs. 1987;.

117. Barber N. What constitutes good prescribing? BMJ 1995;310(6984):923-5.

118. McKinlay JB, Lin T, Freund K and Moskowitz M. The unexpected influence of physician attributes on clinical decisions: Results of an experiment. Journal of Health and Social Behavior 2002;43(1):92.

119. Bradley CP. Factors which influence the decision whether or not to prescribe: the dilemma facing general practitioners. Br J Gen Pract 1992;42(364):454-8.

120. McKinlay JB, Potter DA and Feldman HA. Non-medical influences on medical decision-making. Soc Sci Med 1996;42(5):769-76.

121. Bennett K, Teeling M and Feely J. "Selective" switching from non-selective to selective non-steroidal anti-inflammatory drugs. Eur J Clin Pharmacol 2003;59(8-9):645-9.

122. Tamblyn R, McLeod P, Hanley JA, Girard N and Hurley J. Physician and practice characteristics associated with the early utilization of new prescription drugs. Med Care 2003;41(8):895-908.

123. Cutts C, Tett SE. Doctors perceptions of the influences on their prescribing: a comparison of general practitioners based in rural and urban Australia. Eur J Clin Pharmacol 2003;58(11):761-6.

124. Cutts C, Tett SE. Influences on doctors' prescribing: is geographical remoteness a factor? Aust J Rural Health 2003;11(3):124-30.

125. Baldwin LM, Rosenblatt RA, Schneeweiss R, Lishner DM and Hart LG. Rural and urban physicians: does the content of their Medicare practices differ? J Rural Health 1999;15(2):240-51.

126. Redelmeier DA, Tan SH and Booth GL. The treatment of unrelated disorders in patients with chronic medical diseases. N Engl J Med 1998;338(21):1516-20.

127. Howlett JG, Cox JL, Haddad H, Stanley J, McDonald M and Johnstone DE. Physician specialty and quality of care for CHF: different patients or different patterns of practice? Can J Cardiol 2003;19(4):371-7.

128. Buban GM, Link BK and Doucette WR. Influences on oncologists' adoption of new agents in adjuvant chemotherapy of breast cancer. J Clin Oncol 2001;19(4):954-9.

129. Coleman J, Menzel H and Katz E. Social processes in physicians' adoption of a new drug. J Chronic Dis 1959;9(1):1-19.

130. Bearden WO, Etzel MJ. Reference group influence on product and brand purchase decisions. J C R 1982;9(2):183.

131. Rosenstein AH, Shulkin D. Changing physician behavior is tool to reduce health care costs. Health Care Strateg Manage 1991;9(9):14-6.

132. Grimshaw J, Eccles M and Tetroe J. Implementing clinical guidelines: current evidence and future implications. J Contin Educ Health Prof 2004;24 Suppl 1:S31-7.

133. Steffensen FH, Sorensen HT and Olesen F. Diffusion of new drugs in Danish general practice. Fam Pract 1999;16(4):407-13.

134. Cranney M, Warren E, Barton S, Gardner K and Walley T. Why do GPs not implement evidence-based guidelines? A descriptive study. Fam Pract 2001;18(4):359-63.

135. Prosser H, Walley T. New drug uptake: qualitative comparison of high and low prescribing GPs' attitudes and approach. Fam Pract 2003;20(5):583-91.

136. Helin-Salmivaara A, Huupponen R, Klaukka T, Hoppu K and Steering Group of the ROHTO programme. Focusing on changing clinical practice to enhance rational prescribing--collaboration and networking enable comprehensive approaches. Health Policy 2003;66(1):1-10.

137. Maue SK, Segal R, Kimberlin CL and Lipowski EE. Predicting physician guideline compliance: an assessment of motivators and perceived barriers. Am J Manag Care 2004;10(6):383-91.

138. Pearson SA, Rolfe I and Smith T. Factors influencing prescribing: an intern's perspective. Med Educ 2002;36(8):781-7.

139. Denig P, Haaijer-Ruskamp FM, Wesseling H and Versluis A. Impact of clinical trials on the adoption of new drugs within a university hospital. Eur J Clin Pharmacol 1991;41(4):325-8.

140. Allery LA, Owen PA and Robling MR. Why general practitioners and consultants change their clinical practice: a critical incident study. BMJ 1997;314(7084):870-4.

141. Landon BE, Reschovsky J, Reed M and Blumenthal D. Personal, organizational, and market level influences on physicians' practice patterns: results of a national survey of primary care physicians. Med Care 2001;39(8):889-905.

142. O'Neill L, Kuder J. Explaining variation in physician practice patterns and their propensities to recommend services. Med Care Res Rev 2005;62(3):339-57.

143. Ashworth M, Armstrong D, Colwill S, Cohen A and Balazs J. Motivating general practitioners to change their prescribing: the incentive of working together. J Clin Pharm Ther 2000;25(2):119-24.

144. Carthy P, Harvey I, Brawn R and Watkins C. A study of factors associated with cost and variation in prescribing among GPs. Fam Pract 2000;17(1):36-41.

145. Soumerai SB, McLaughlin TJ and Gurwitz JH, et al. Effect of local medical opinion leaders on quality of care for acute myocardial infarction: a randomized controlled trial. JAMA 1998;279(17):1358-63.

146. Hemminki E. Review of literature on the factors affecting drug prescribing. Soc Sci Med 1975;9(2):111-6.

147. Mitchell V, Walsh G. Gender differences in german consumer decision-making styles. Journal of Consumer Behaviour 2004;3(4):331-46.

148. Sproles GB, Kendall EL. A methodology for profiling consumers' decision-making styles. Journal of Consumer Affairs 1986;20(2):267.

149. Sproles KE, Sproles BG. Consumer decision-making styles as a function of individual learning styles. Journal of Consumer Affairs 1990;24(1):134.

150. Chang J, Samuel N. Internet shopper demographics and buying behaviour in australia. Journal of American Academy of Business 2004;5(1/2):171.

151. Dholakia RR. Going shopping: key determinants of shopping behaviors and motivations. International Journal of Retail and Distribution Management 1999;27(4):154.

152. Fischer E, Arnold SJ. Sex, gender identity, gender role attitudes, and consumer behavior. Psychology and Marketing 1994;11(2):163.

153. Inman W, Pearce G. Prescriber profile and post-marketing surveillance. Lancet 1993;342(8872):658-61.

154. Duetz MS, Schneeweiss S, Maclure M, Abel T, Glynn RJ and Soumerai SB. Physician gender and changes in drug prescribing after the implementation of reference pricing in British Columbia. Clin Ther 2003;25(1):273-84.

155. Gilly MC, Zeithaml VA. The elderly consumer and adoption of technologies. J C R 1985;12(3):353-7.

156. Lacy BE, Crowell MD, Riesett RP and Mitchell A. Age, specialty, and practice setting predict gastroesophageal reflux disease prescribing behavior. J Clin Gastroenterol 2005;39(6):489-94.

157. Freiman MP. The rate of adoption of new procedures among physicians. The impact of specialty and practice characteristics. Med Care 1985;23(8):939-45.

158. Helin-Salmivaara A, Huupponen R, Virtanen A and Klaukka T. Adoption of celecoxib and rofecoxib: a nationwide database study. J Clin Pharm Ther 2005;30(2):145-52.

159. Tamayo-Sarver JH, Dawson NV, Cydulka RK, Wigton RS and Baker DW. Variability in emergency physician decision making about prescribing opioid analgesics. Ann Emerg Med 2004;43(4):483-93.

160. Armstrong D, Reyburn H and Jones R. A study of general practitioners' reasons for changing their prescribing behaviour. BMJ 1996;312(7036):949-52.

161. Denig P, Witteman CL and Schouten HW. Scope and nature of prescribing decisions made by general practitioners. Qual Saf Health Care 2002;11(2):137-43.

162. Nazareth I, Freemantle N, Duggan C, Mason J and Haines A. Evaluation of a complex intervention for changing professional behaviour: the Evidence Based Out Reach (EBOR) Trial. J Health Serv Res Policy 2002;7(4):230-8.

163. Jones MI, Greenfield SM, Jowett S, Bradley CP and Seal R. Proton pump inhibitors: a study of GPs' prescribing. Fam Pract 2001;18(3):333-8.

164. Nedungadi P. Recall and consumer consideration sets: influencing choice without altering brand evaluations. J C R 1990;17(3):263.

165. Krapfel, E. Robert Jr. An advocacy behavior model of organizational buyers' vendor choice. Journal of Marketing 1985;49(4):51.

166. Eisenhardt KM. Agency theory: an assessment and review. The Academy of Management Review 1989;14(1):57-74.

167. Broderick AJ. Role theory and the management of service encounters. The Service Industries Journal 1999;19(2):117.

168. Broderick AJ. Role theory, role management and service performance. The Journal of Services Marketing 1998;12(5):348.

169. Ajzen I. Nature and operation of attitudes. Annu Rev Psychol 2001;52:27-58.

170. Dorfman R, Steiner PO. Optimal advertising and optimal quality. The American Economic Review 1954;44(5):826-36.

171. Grimshaw J. Current evidence on changing behaviour of health care providers. Unpublished 2005;.

172. Shivers-Blackwell SL. Using role theory to examine determinants of transformational and transactional leader behavior. Journal of Leadership and Organizational Studies 2004;10(3):41.

173. Vakratsas D, Ambler T. How advertising works: What do we really know? Journal of Marketing 1999;63(1):26.

174. Petty RE, Cacioppo JT and Schumann D. Central and peripheral routes to advertising effectiveness: the moderating role of involvement. J C R 1983;10(2):135.

175. Kotler P. A generic concept of marketing. Journal of Marketing 1972;36(2):46-54.

176. Mowen CJ. Beyond consumer decision making. Journal of Consumer Marketing 1988;5(1):15.

177. Hoyer DW, Brown PS. Effects of brand awareness on choice for a common, repeat-purchase product. J C R 1990;17(2):141.

178. Sketris I, Bowles S and Manuel R. Canadian Public Policies and Practices Related to Drug Prices, Utilizatioin and Expenditures. Journal of Pharmaceutical Finance, Economics and Policy 2004;12(1):23-54.

179. Levy H, Simon JL. A generalization that makes useful the Dorfman-Steiner theorem with respect to advertising. Managerial and Decision Economics 1989;10(1):85.

180. Mitchell TR, James LR. Building better theory: Time and the specification of when things happen. The Academy of Management Review 2001;26(4):530.

181. Hawkey CJ. COX-2 inhibitors. Lancet 1999;353(9149):307-14.

182. Hawkey CJ. COX-2 chronology. Gut 2005;54(11):1509-14.

183. Anderson RL, Ortinau DJ. Exploring consumers' postadoption attitudes and use behaviors in monitoring the diffusion of a technology-based discontinuous innovation. Journal of Business Research 1988;17(3):283-300.

184. Foxall G. Consumer choice as an evolutionary process: an operant interpretation of adopter behavior. Advances In Consumer Research 1994;21:312-7.

185. Assael H. Consumer Behavior and Marketing Actions. In: 2nd ed. Boston: Kent Publishing Company, 1983:443-956.

186. Gatignon H, Roberston TS. A propositional inventory for new diffusion research. J C R11(4):849-69.

187. Katz E. The two-step flow of communication: an up-to-date report on an hypothesis. Public Opinion Quarterly 1957;21(1):61-78.

188. Eddy DM. Variations in physician practice: the role of uncertainty. Health Aff 1984;3(2):74-89.

189. Austin PC, Mamdani MM, Tu K and Zwarenstein M. Changes in prescribing patterns following publication of the ALLHAT trial. JAMA 2004;291(1):44-5.

190. Soumerai SB, Avorn J. Principles of educational outreach ('academic detailing') to improve clinical decision making. JAMA 1990;263(4):549-56.

191. Braybrook S, Walker R. Influencing prescribing in primary care: a comparison of two different prescribing feedback methods. J Clin Pharm Ther 1996;21(4):247-54.

192. Hunt SD, Arnett DB. Resource-advantage theory and embeddedness: Explaining R-A theory's explanatory success. Journal of Marketing Theory and Practice 2003;11(1):1.

193. Shin JH, Haynes RB and Johnston ME. Effect of problem-based, self-directed undergraduate education on life-long learning. CMAJ 1993;148(6):969-76.

194. Alreck PL. Consumer age role norms, then and now. Psychology and Marketing 2000;17(10):891.

195. Greco PJ, Eisenberg JM. Changing physicians' practices. N Engl J Med 1993;329(17):1271-3.

196. Avery AJ, Rodgers S and Heron T, et al. A prescription for improvement? An observational study to identify how general practices vary in their growth in prescribing costs. BMJ 2000;321(7256):276-81.

197. Sumpradit N, Fors SW and McCormick L. Consumers' attitudes and behavior toward prescription drug advertising. Am J Health Behav 2002;26(1):68-75.

198. Jackevicius C, Tu K, Filate W, Brien S and Tu J. Trends in cardiovasuclar drug utilization and drug expenditures in Canada between 1996 and 2001. Can J Cardiol 2003;19(12):1359-1366.

199. Thiels C, Linden M, Grieger F and Leonard J. Gender differences in routine treatment of depressed outpatients with the selective serotonin reuptake inhibitor sertraline. Int Clin Psychopharmacol 2005;20(1):1-7.

200. Kasje WN, Denig P, Stewart RE, de Graeff PA and Haaijer-Ruskamp FM. Physician, organisational and patient characteristics explaining the use of angiotensin converting enzyme inhibitors in heart failure treatment: a multilevel study. Eur J Clin Pharmacol 2005;61(2):145-51.

201. Sleath B, Shih YC. Sociological influences on antidepressant prescribing. Soc Sci Med 2003;56(6):1335-44.

202. Sambamoorthi U, Olfson M, Walkup JT and Crystal S. Diffusion of new generation antidepressant treatment among elderly diagnosed with depression. Med Care 2003;41(1):180-94.

203. The Henry J. Kaiser Family Foundation. Impact of direct-to-consumer advertising on prescription drug spending. Menlo Park, CA: The Henry J. Kaiser Family Foundation, 2003.

204. Population Health Research Unit. About The Population Health Research Unit. 2004;.

205. Population Health Research Unit - Department of Community Health and Epidemiology - Dalhousie University. About PHRU. 2005;2005(September 21, 2005).

206. Health Canada. Drug Product Database. 2005;2005(August, 22).

207. Altman DG, Schulz KF and Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001;134(8):663-94.

208. Mamdani M, Sykora K and Li P, et al. Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. BMJ 2005;330(7497):960-2.

209. Stats Canada. Population Urban and Rural, by Province and Territory. 2005;2005(November 17, 2005).

210. Apte CV, Hong SJ, Natarajan R, Pednault EPD, Tipu FS and Weiss SM. Data-intensive analytics for predictive modeling. IBM Journal of Research and Development 2003;47(1):17-23.

211. Rothschild LM, Gaidis CW. Behavioral learning theory: its relevance to marketing and promotions. Journal of Marketing 1981;45(2):70.

212. DiClemente DF, Hantula DA. Applied behavioral economics and consumer choice. Journal of Economic Psychology 2003;24(5):589.

213. Hair JF, Anderson RE, Tathan RL and Black WC. Multivariate Data Analysis. New Jersey: Prentice Hall, 1998.

214. Scott I, Heyworth R and Fairweather P. The use of evidence-based medicine in the practice of consultant physicians. Results of a questionnaire survey. Aust N Z J Med 2000;30(3):319-26.

215. Mayer J, Piterman L. The attitudes of Australian GPs to evidence-based medicine: a focus group study. Fam Pract 1999;16(6):627-32.

216. Young JM, Ward JE. Evidence-based medicine in general practice: beliefs and barriers among Australian GPs. J Eval Clin Pract 2001;7(2):201-10.

217. MacLean LC, Richman A. Physician practice style variations. Socio-Economic Planning Sciences 1989;23(6):361-71.

218. Hofmann DA. An overview of the logic and rationale of hierarchical linear models. Journal of Management 1997;23(6):723.

219. Wagner AK, Soumerai SB, Zhang F and Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther 2002;27(4):299-309.

220. Canadian Coordinating Office For Health Technology Assessment. Welcome To CCOHTA - Common Drug Review (CDR). 2005;2005(12/4).

221. Murthi BPS, Srinivasan K. Consumers' extent of evaluation in brand choice. The Journal of Business 1999;72(2):229.

222. Dillon, R W, Gupta and Sunil. A segment-level model of category volume and brand choice. Marketing Science 1996;15(1):38.

223. Dai C, Stafford RS and Alexander GC. National trends in cyclooxygenase-2 inhibitor use since market release: nonselective diffusion of a selectively cost-effective innovation. Arch Intern Med 2005;165(2):171-7.

224. Martinez B, Mathews AW, Lublin JS and Winslow R. Expiration date: Merck pulls Vioxx from market after link to heart problems; stock plunges amid questions about drug giant's future; loss of $2.5 billion in sales; arthritis patients' quandary. Wall Street Journal 2004;:A.1.

225. Hedner T, Himmelmann A. Cardiovascular complications of COX-2 selective inhibitors cause considerable concern. Blood Press 2004;13(5):260-1.

226. Hensley S. Pfizer is early winner as Vioxx users switch drugs. Wall Street Journal 2004;:D.13.

227. Cosentino M, Leoni O, Banfi F, Lecchini S and Frigo G. An approach for the estimation of drug prescribing using the defined daily dose methodology and drug dispensation data. Theoretical considerations and practical applications. Eur J Clin Pharmacol 2000;56(6-7):513-7.

228. Natsch S, Hekster YA, de Jong R, Heerdink ER, Herings RM and van der Meer JW. Application of the ATC/DDD methodology to monitor antibiotic drug use. Eur J Clin Microbiol Infect Dis 1998;17(1):20-4.

229. Groves, K. E. M., Pendlebury J. Prescription drug sampling - is the status quo about to change? CPJ 2005;138(6):60-6.

230. Roughead EE, Zhang F, Ross-Degnan D and Soumerai S. Differential effect of early or late implementation of prior authorization policies on the use of Cox II inhibitors. Med Care 2006;44(4):378-82.

231. Girvin B, Rafferty T, Stevenson MR and Johnston GD. Uptake of COX-2 selective inhibitors and influence on NSAID prescribing in Northern Ireland. Pharmacoepidemiol Drug Saf 2004;13(3):153-7.

232. Health Canada. Legislative Renewal - Issue Paper; Direct to Consumer Advertising (DTCA) of Prescription Drugs. Ottawa, ON: Government of Canada, 2003.

233. SAS Institute Inc. Logistic Regression Examples Using the SAS System. Cary, NC: SAS Institute Inc., 1995.

234. Nova Scotia Department of Health. Nova Scotia Seniors' Pharmacare Information. 2006;2006(April 15, 2006).