AN ASSESSMENT OF A PROSPECTIVE MEASURE OF HEALTH SERVICES UTILIZATION AND THE COST OF ASTHMA

by

Wendy Joan Ungar

A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
Graduate Department of Health Administration
University of Toronto

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ABSTRACT

Introduction There is increasing concern with rising health care costs. Assessing cost-of-illness reveals the major determinants of costs to society. Weaknesses in current methodology include a lack of comprehensiveness, insufficient precision, the absence of information on reliability and validity and the omission of key stakeholders' perspectives. The objectives of this thesis were to assess the reliability of patient self-reports of health services utilization and to utilize a prospective model to generate a comprehensive and precise estimate of the cost of asthma per patient from multiple perspectives.

Methods The Pharmacy Medication Monitoring Program (PMMP) collects longitudinal data from patients recruited in community pharmacies. Respiratory patients reported medication consumption, health services use, out-of-pocket costs, quality-of-life and other information during 3 telephone interviews conducted at 1, 3 and 6 months after enrollment. Self-reports of health services utilization were compared to Ontario Health Insurance Plan (OHIP) records in 83 subjects and the cost of asthma was assessed in 1,279 patients.
Results A gradient in agreement between self-reports and OHIP records was observed, ranging from substantial for admissions to slight for emergency room visits. Age, disease severity and occupation were significant determinants of total costs. The annual cost to society among adults ranged from $1,633 per mildly ill patient (95% CI $1,282, $1,984) to $4,223 per severely ill patient (95% CI $3,849, $4,598). The costs in children under 4 years were higher than older children but lower than adults. Indirect costs were responsible for 43% of total costs. The largest components of direct costs were hospitalizations, 47%, and medications, 40%.

Conclusions Interventions aimed at reducing productivity losses and admissions may result in savings to society, the health care system and the patient. Estimates stratified by age, severity and occupation can serve as benchmarks and prove useful for case mix and capitation planning. The quality of clinical and health policy decision-making may be enhanced by cost-of-illness estimates that are comprehensive, precise and expressed from multiple perspectives. The PMMP is a potentially useful model for outcomes research and health economic assessments.
In Loving Memory

Mollie Cleman

walking in quiet strength,
breathing the speech of wisdom.
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<tr>
<td>ACE Inhibitor</td>
<td>Angiotensin Converting Enzyme Inhibitor</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
<td></td>
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<tr>
<td>95% CI</td>
<td>95% Confidence Interval</td>
<td></td>
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<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disorder</td>
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<tr>
<td>CPI</td>
<td>Consumer Price Index</td>
<td></td>
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<tr>
<td>CPS</td>
<td>Compendium of Pharmaceuticals and Specialties</td>
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</tr>
<tr>
<td>DRG</td>
<td>Diagnosis-related group</td>
<td></td>
</tr>
<tr>
<td>ER</td>
<td>Emergency Room</td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>Forced Expiratory Volume in 1 second</td>
<td></td>
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<tr>
<td>GP</td>
<td>General Practitioner</td>
<td></td>
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<tr>
<td>ICD-9-CM</td>
<td>International Classification of Diseases, 9th revision, Clinical Modification</td>
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<tr>
<td>LOS</td>
<td>Length of Stay</td>
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<td>MDI</td>
<td>Metered Dose Inhaler</td>
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<tr>
<td>NAEP</td>
<td>U.S. National Asthma Education Project</td>
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<td>NAMCS</td>
<td>U.S. National Ambulatory Medical Care Survey</td>
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<tr>
<td>NCHS</td>
<td>U.S. National Center for Health Statistics</td>
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<tr>
<td>NHANES</td>
<td>U.S. National Health and Nutrition Examination Survey</td>
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<td>NHDS</td>
<td>U.S. National Hospital Discharge Survey</td>
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<td>NHIS</td>
<td>U.S. National Health Interview Survey</td>
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<td>NHLBI</td>
<td>U.S. National Heart, Lung and Blood Institute</td>
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<td>NMES</td>
<td>U.S. National Medical Expenditures Survey</td>
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<td>NPHS</td>
<td>Canada National Population Heath Survey</td>
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<tr>
<td>NSAID</td>
<td>Non-steroidal Anti-inflammatory Drug</td>
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<tr>
<td>ODB</td>
<td>Ontario Drug Benefit program</td>
<td></td>
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<tr>
<td>OHIP</td>
<td>Ontario Health Insurance Plan</td>
<td></td>
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<tr>
<td>OTC</td>
<td>over the counter</td>
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<tr>
<td>PMMP</td>
<td>Pharmacy Medication Monitoring Program</td>
<td></td>
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<tr>
<td>QALY</td>
<td>Quality-adjusted Life Year</td>
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<tr>
<td>SOB</td>
<td>Shortness of breath</td>
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SYMBOLES

α  probability of committing a Type I error, failing to accept the null hypothesis
β  probability of committing a Type II error, inappropriately accepting the null hypothesis
κ  estimated kappa statistic
κa  estimated weighted kappa statistic
µg  microgram
p  probability
pm  pro re nata (as needed)
r  Spearman or Pearson correlation coefficient
INTRODUCTION
Chapter 1. INTRODUCTION

1.1 OVERVIEW

There is increasing public concern with the escalation of health care costs - a phenomenon that has resulted in dramatic health policy decisions across Canada aimed at curtailing costs to the public sector. Investigating the economic burden of specific diseases reveals the magnitude and variety of health resources consumed by patients with particular illnesses. Assessing the cost of illness can uncover key determinants of escalating costs to the health care system. Information gleaned from cost-of-illness studies may be used in comparative economic evaluations of health interventions and programs and may support clinical and health policy decision-making.

In recent years, approaches to cost-of-illness assessments have become more consistent, mainly as a result of efforts to establish methodological frameworks for these types of investigations (Rice 1967; Hodgson and Meiners 1982; Rice et al. 1985). Models employed by Rice and Hodgson have been replicated by Canadian and other investigators exploring the costs of specific illnesses as well as the overall cost of illness in a population (Wigle et al. 1991; Krahn et al. 1996; Chan et al. 1995; Harkness 1989). With the growing number of cost-of-illness studies employing similar analytical approaches appearing in the literature, certain inherent methodological weaknesses have become apparent. A major shortcoming of current cost-of-illness methodology is a lack of comprehensiveness. The use of retrospective techniques and reliance on secondary databases or health surveys not designed to measure economic outcomes result in a failure to capture many essential cost items (Roos et al. 1993; Strom 1992; Miller et
al. 1996). Frequently omitted items include patient out-of-pocket expenses, insurance-related costs and the cost of alternative health services. A second common weakness is a lack of precision. Population-based studies generate point estimates based on aggregate data where the population itself is the unit of analysis. A lack of sampling precludes the construction of meaningful indicators of precision, such as standard deviations or confidence intervals (O'Brien et al. 1994). The result is an unadjusted population-based average that provides no information on costs in clinically important sub-groups of the population or disease cohort. Cost-of-illness studies routinely rely on multiple data sources for generating utilization and cost estimates. A chronic problem for these types of investigations is the absence of information on the reliability and the validity of the methods used to extract data from each source (Iezzoni 1994; Goel et al. 1996; Fisher et al. 1992). Finally, while most cost-of-illness studies include a societal perspective, other viewpoints, such as the primary payer or patient are omitted. The methods and data sources employed often preclude the inclusion of other perspectives. Contrasting diverse perspectives provides insight into the perceptions of various key stakeholders and informs the public health policy-making process (Drummond and Stoddart 1984; Stoddart 1982).

Because of these limitations, researchers have begun to look for alternative study designs and models that will result in better quality cost-of-illness estimates (Chrischilles 1992; Lewis et al. 1993). Prospective epidemiological investigations offer the potential to overcome many of the current methodological limitations inherent in retrospective cost-of-illness assessments. Observational studies usually consist of large heterogeneous samples of patients and often rely on patient self-reports, mediated through questionnaires or interviews, to yield information on a broad range of utilization and economic variables (Kelsey et al. 1986). Prospective observational
studies have the potential to capture cost items lacking in other sources. Because data is collected at the patient level, variation in the point estimate can be quantified and summarized. The existence of alternative data sources for much of the self-reported information, including medical charts, pharmacy records and insurance claims files, facilitates the conduct of assessments of reliability and validity of patient self-reports. Collection of data directly from the patient also enables the presentation of costs from the patient perspective.

Careful attention must be paid to the process of measurement in applying epidemiological approaches to economic assessments. The multiple components of outcomes and costs that comprise an economic assessment may still require numerous information sources and diverse methods for collecting essential data. Research focusing on issues of comprehensiveness and precision in cost-of-illness assessment is needed to advance the methodology and to facilitate the interpretation of the results by policy makers and clinical decision-makers.

The goal of this thesis research is to present a study model that seeks to overcome the common limitations of cost-of-illness methodology discussed above. A prospective epidemiological approach is used to generate a comprehensive estimate of the cost-of-illness in a sample of patients with asthma, from the perspectives of society, the health care system and the patient.

Asthma is a chronic but rarely life-threatening disorder affecting approximately 4% of the population of Ontario (Decker et al. 1995). Chronic obstructive pulmonary disorder (COPD) and chronic bronchitis are estimated to afflict another 3% of the population (5% of those aged 65 and over) (Badley et al. 1993). The increasing prevalence, morbidity and mortality of respiratory
disorders have been noted in Canada and other developed countries (Wilkins and Mao 1993; Manfreda et al. 1993; Hogg et al. 1995; Gergen and Weiss 1992; Jackson et al. 1988; Weiss et al. 1993). The treatment of asthma and other respiratory disorders is characterized by controversy over the proper administration of inhaled bronchodilators (beta-agonists) and a complex array of therapeutic options (Sears et al. 1990; Holgate 1992; Hargrave et al. 1990). The standards for choosing medications continue to evolve rapidly as new information on existing and novel treatments becomes available. Although some reports have been compiled on the economic burden of asthma, the data sources are secondary and are based on treatment strategies that are no longer current (Krahn et al. 1996; Mellis et al. 1991; Weiss et al. 1992). Moreover, these studies estimate key cost components on an aggregated basis, rather than adopting a patient-level approach. The study of asthma would benefit from an investigation into the reliability of a prospective, observational approach to economic assessment.

Although preferable for chronic diseases such as asthma, epidemiological studies are often not considered because of time and cost constraints. The Pharmacy Medication Monitoring Program (PMMP) was established by the Centre for Evaluation of Medicines, McMaster University, in 1992 to monitor the health effects of different categories of prescription medications in a diverse patient population. In October 1994 the PMMP initiated the Inhaled Bronchial Medications project to monitor health outcomes in patients prescribed metered dose inhalers (MDIs) containing bronchodilators or anti-inflammatory agents. This project provided a valuable opportunity to investigate the reliability of a pharmacy-based surveillance model for prospectively assessing health care utilization and estimating the cost of asthma. This study was conducted as an independent extension to the PMMP Bronchial Inhalers project.
1.2 CONCEPTUAL FRAMEWORK

The reliability and validity of data collection methods and the consequent precision of point estimates, the comprehensiveness of data and the choice of perspective all pertain to the process of measurement. Attempts to measure all relevant cost items in a cost-of-illness analysis will result in an estimate with improved validity. The ability to assess the precision of a result depends on the measurement approach. Deterministic approaches to measurement rely on retrospective techniques to extract information from existing sources, sources that were not designed for the purpose of the evaluation. An example is the use of administrative billing databases of large payers such as Medicare in the U.S. or the Ontario Health Insurance Plan (OHIP) to generate aggregate estimates of utilization volume and costs. An aggregate estimate in a population is a summary measure - no information is provided on the variation of utilization and costs in the population. In contrast, a wholly stochastic approach to cost-of-illness analysis involves prospective collection of patient-level data on utilization and costs. With this approach, the distributions of utilization and costs can be obtained, permitting the determination of sample variance and the application of tests of statistical inference (Coyle et al. 1996; Mullahy 1996).

In reality, many economic assessments combine both of these approaches in a single study (O'Brien and Drummond 1994). Quasi-stochastic analyses may utilize surveys or completed clinical trials to collect patient-level utilization information which is then combined with standard unit cost data from fee schedules, price lists and other sources. The cost of each item is the product of its price multiplied by its volume of use. If variation is only associated with volume, then price is treated as a scalar, and all variation in cost is due to the variation in
volume. In other situations, variation in cost may be principally determined by variation in prices. Because cost-of-illness analyses require the measurement of multiple cost items, both stochastic and deterministic approaches can be employed for measuring both price and volume. These two basic approaches to economic assessment are summarized in Figure 1.

Figure 1. Approaches to Measurement in Economic Assessment

<table>
<thead>
<tr>
<th>DETERMINISTIC</th>
<th>STOCHASTIC</th>
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<tbody>
<tr>
<td>aggregate population summary estimate</td>
<td>population/sample parameter estimate</td>
</tr>
<tr>
<td>VOLUME</td>
<td>VOLUME</td>
</tr>
<tr>
<td>PRICE</td>
<td>PRICE</td>
</tr>
<tr>
<td>sensitivity analysis</td>
<td>confidence intervals</td>
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The critical difference between deterministic and stochastic approaches is how they deal with uncertainty. In wholly deterministic evaluations, uncertainty is a consequence of lack of knowledge. In the absence of comprehensive and reliable data, assumptions regarding probable values are made based on judgement. Deterministic evaluations rely on sensitivity analysis to represent the range of uncertainty and to test the robustness of conclusions. Some deterministic cost-of-illness studies present base-case summary measures along with minimum and maximum values. These values represent the lower and upper bounds resulting from the use of alternative
data sources or may represent extremes in values from a single data source (Krahn et al. 1996). In a simple sensitivity analysis, equally plausible values are substituted for a variable to explore the range of possible numeric outcomes (Briggs et al. 1994). The choice of values requires judgement however, and may reflect the investigator’s bias (O'Brien et al. 1992).

In stochastic approaches, uncertainty is reflected in the observed distribution of values for a particular variable. The variation can be quantified and expressed as a 95% confidence interval (CI). Presented alongside the point estimate, 95% CIs provide an indicator of precision. The sample or population variation is comprised of random and systematic components. Tests of inference can be applied to partition the variation and test hypotheses regarding the significance of observed differences between defined sub-groups. Multi-item cost-of-illness analyses can be viewed as a continuum between wholly deterministic and wholly stochastic approaches. The objective of methodological research in this field is to bring these analyses closer to a fully stochastic model which makes fewer assumptions, while improving comprehensiveness and establishing the reliability and validity of the data collection methods.

In this project, a prospective observational study model, relying on patient self-report of utilization and some costs, was used to generate a comprehensive estimate of the overall cost-of-illness in a sample of asthmatic patients. A quasi-stochastic approach was taken to permit statistical comparison of key clinical sub-groups and to generate 95% CIs around point estimates of total costs. Analyses were undertaken from multiple perspectives, including society, the health care system and the patient. Prior to undertaking the cost-of-illness assessment, an evaluation of the reliability of self-reported health services utilization was conducted.
BACKGROUND AND LITERATURE REVIEW
Chapter 2. BACKGROUND AND LITERATURE REVIEW

The rationale and methodology employed in this research project draw on several disciplines, including health economics, health services research, epidemiology and respirology. The background and literature review section focuses on those aspects of these disciplines that pertain to the process of measurement. This section describes the process of measurement in economic assessment, defines and discusses the key issues of measurement and characterizes the conventional sources of data used in observational approaches to economic assessment. Background information is also provided on the epidemiology and management of asthma. Completed investigations of the cost-of-illness of asthma are reviewed.

2.1 ECONOMIC ASSESSMENT

Although economic assessment methods have long been employed in the field of engineering to evaluate large-scale construction projects, it was not until the mid-1960s that economic assessment was applied to health care. In 1967 Dorothy Rice published a methodological framework for calculating annual costs of illness, disability and mortality associated with the eight principal diagnostic groups specified in the International Classification of Diseases (ICD) (Rice 1967). The potential usefulness of employing economic assessments to inform health services allocation decisions was soon realized. In 1977 a landmark paper was published describing how cost-benefit analysis and cost-effectiveness analysis could be used to compare two or more interventions to optimize allocative efficiency in health care decision-making (Weinstein and Stason 1977). Since then the field has expanded to included the measurement of
quality-adjusted life years (QALYs) and healthy-year equivalents (Mehrez and Gafni 1992) for the estimation of utility. Recently, effort has been devoted to standardizing the valuation techniques of economic evaluations (Gold, 1996; Drummond et al. 1993; Luce 1993).

While the objectives of a cost-of-illness assessment and a comparative study differ, both types of investigations require a careful delineation of costs. In economic terms, costs are the value of the resources that are foregone as a result of the allocation decision and are termed the opportunity costs (Drummond et al. 1987). These costs are preferred to accounting costs, charges, prices or reimbursements, which do not reflect the actual value of the resources consumed because of cross-subsidization (Freund and Dittus 1992). Costs are categorized as direct costs, indirect costs and psychosocial costs. Although these components have been combined in different groups by Hodgson and Meiners (1982), Rice (1985) and Drummond et al. (1987), their definition and composition are generally agreed upon. Despite different groupings, inter-study comparisons are possible as long as individual components are evaluated and presented separately.

2.1.1 Direct Costs

According to Rice (1966), the direct costs of illness consist of "the expenditures for prevention, detection, treatment, rehabilitation, research, training and capital investment in medical facilities. In terms of services or type of medical expenditure, direct costs include amounts spent for hospital or nursing home care, physicians and other medical professional services, drugs, medical supplies, research training and other non-personal services." In this definition, distinctions are not made between payers, i.e. the health care system, the insurer or the patient.
Hodgson and Meiners (1982) more clearly separate health care sector costs and patient costs. Direct health care sector costs include expenditures for medical care such as diagnosis, treatment, continuing care, rehabilitation and palliative treatment as well as expenditures for non-medical care which are required as a result of illness. Other health care sector costs relate to research, training, construction and administration carried out by public and private agencies for the treatment and prevention of illness. Direct patient costs are those borne by patients and others for transportation to health care providers, for certain household expenditures, homemaker services, relocation and property losses.

Drummond et al. (1987) distinguish between health care sector costs and patient/family costs. Health care sector costs are the organization and operating costs and include the costs of health care services, supplies, equipment and capital costs. Patient and family costs consist of out-of-pocket expenses and the value of patient and family inputs to the treatment of disease.

2.1.2 Indirect Costs
Exclusively measuring direct costs will fail to capture the full economic impact of a particular disease because they do not incorporate the productivity loss associated with disability and premature mortality. Rice expounds a clear method for imputing the value of productivity losses by multiplying workdays lost by age and sex-specific average wages. This is known as the human capital method. Both Rice and Hodgson have recognized the difficulties with this approach. One must use only year-round pre-tax full-time earnings. Transfer payments, such as taxes, and non-labour income are excluded. The true productivity loss depends on labour force participation rates. Recent studies of methods for appraising indirect costs consider labour force
participation rates and the acute versus chronic nature of disease (Koopmanschap and van Ineveld 1992; Koopmanschap and Rutten 1994). The human capital method is also potentially biased by asymmetry between the labour force demographic composition and the demographics of the patient population. Using age- and sex-specific wage rates which are influenced by the predominance of white middle-aged males in the work force will not accurately reflect the productivity losses of patients who possess lower socioeconomic status or who are older.

Since salaries are reported only by employed persons, valuing the opportunity cost of time of the non-employed as zero would seriously underestimate the indirect costs of these individuals. In applying the human capital approach to homemakers, a large segment of the population, Rice advocates substituting the value of the homemaker's time with the wage of a domestic worker, the market value approach. Hodgson also suggests the possibility of using the wage that the housekeeper could earn if working, the opportunity cost approach. In the opportunity cost approach, the indirect costs of unpaid labour have conventionally been assessed by assigning a wage and applying a weight, such as 0.4 (Glied 1996, Torgerson et al. 1994, Hodgson and Meiners 1982). Applying the same weight to different categories, such as persons caring for children and retirees may not be reasonable, as the opportunity costs of time differ among these groups. The value also depends on the perspective of the analysis, since the perspective determines which losses are counted. The human capital approach can be combined with a sensitivity analysis to test different assumptions regarding the value of the productivity loss for employed individuals, persons caring for children and persons at leisure. (Torgerson et al. 1994). The loss in leisure time also represents an indirect cost but there is less agreement on how to attribute a cost to this loss. Similarly, how one values the time of retirees, pensioners, students
and the unemployed has not been clearly defined.

In addition to the indirect costs associated with losses in work and leisure time, one must consider the time spent travelling to and waiting for health care services. Costs are associated with missed workdays, lost leisure time, travel and waiting time by family members and caregivers as well as the patient. Gold et al. (1996) distinguish between morbidity-related work absence and treatment-related travel and waiting time and view the latter as a direct non-medical cost, rather than an indirect cost. As both result in production losses that are measured the same way, morbidity-related work absence and travel/waiting time are frequently added together in the calculation of indirect costs (Drummond et al. 1987; Hodgson and Meiners 1982; Stoddart 1982; Krahn et al. 1996).

2.1.3 Intangible Costs

Other costs include those associated with the pain and suffering of disease. These have been labelled in the literature as intangible costs (Freund and Dittus 1992), psychosocial costs (Rice et al 1985; Hodgson and Meiners 1982) or psychic costs (Drummond et al. 1987). Because of the difficulty in quantifying these costs in monetary units, they are frequently absent from cost-of-illness estimates, although they have been evaluated through the measurement of quality of life.

Unlike clinical measures of disease, quality of life assessment reflects the patient's perceptions of the multi-faceted impact of a disease on one's well-being. Despite recognition that quality of life is wide-ranging and must be assessed from the patient's perspective, some clinical investigators measure only health-related quality of life (Torrance 1987; Guyatt et al. 1991,
O'Brien 1994). Both generic health status and disease-specific measurement instruments have been developed for the measurement of health-related quality of life. Multi-dimensional instruments assess several domains such as physical and social functioning, emotions and effects on behaviour. While general instruments such as the Sickness Impact Profile and the short-form (SF)-36 (Bergner et al. 1987, Ware 1993) allow a comparison of scores between groups suffering from different illnesses, they are considered insensitive to small changes to a specific health state caused by an intervention or over time (Guyatt et al. 1989). Ideally, a study would include both generic and disease-specific indices to allow inter- and intra-group comparisons.

The field of asthma treatment would benefit from quality of life assessment for several reasons. Controversy exists over the relevance of laboratory measures of respiratory responsiveness to a patient's ability to function and cope with the disease (Walker 1992). Asthma is a chronic condition which, unlike many other illnesses, relies on education, behaviour modification and self-monitoring. The increasing prevalence and morbidity of asthma have caused public concern regarding the burden of illness, economic and otherwise, it places on society.

The last few years have seen the publication of four asthma-specific quality of life questionnaires (Marks et al. 1992, 1993; Juniper et al.1992, 1993; Hyland 1991; Hyland et al. 1991; Hyland and Jones 1991; Quirk and Jones 1990; Quirk et al. 1991; Elegant 1991; Jones et al. 1992). In addition to these questionnaires, other measurement techniques touching on some aspect of quality of life in asthma have appeared in the literature (Thunedborg 1992; Creer 1992; Venables 1993). Only accumulated experience with each one of them will testify as to their reliability and validity in diverse sub-groups of asthmatic patients.
2.1.4 Perspective and Measurement

Precisely which costs should be measured and included in a cost-of-illness estimate depends on the perspective selected. In a welfare economics approach, all costs are counted, independent of the payer, representing the societal viewpoint (Stoddart 1982). Depending on the study purpose, it may be important to include the viewpoint of the health care system, a particular payer, such as a provincial government, or the patient. The choice of different perspectives may result in varying cost estimates and have important implications for decision and policy-making. Drummond et al. (1987) advocate the inclusion of the societal viewpoint in all economic assessments. The principal cost categories and their components are presented in Table 1.

<table>
<thead>
<tr>
<th>Category</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Costs</td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>family physician services</td>
</tr>
<tr>
<td></td>
<td>specialist services</td>
</tr>
<tr>
<td></td>
<td>clinic/emergency room services</td>
</tr>
<tr>
<td></td>
<td>inpatient services</td>
</tr>
<tr>
<td></td>
<td>laboratory services</td>
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<tr>
<td></td>
<td>medication dispensing fees</td>
</tr>
<tr>
<td></td>
<td>prescription and non-prescription medications</td>
</tr>
<tr>
<td></td>
<td>medical supplies and devices</td>
</tr>
<tr>
<td></td>
<td>alternative and non-insured services</td>
</tr>
<tr>
<td></td>
<td>transportation</td>
</tr>
<tr>
<td></td>
<td>babysitters and informal care</td>
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<tr>
<td>Patient /Family</td>
<td>days missed from usual activities</td>
</tr>
<tr>
<td></td>
<td>compromised days</td>
</tr>
<tr>
<td></td>
<td>waiting time to access health care</td>
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<tr>
<td></td>
<td>travel time to access health care</td>
</tr>
<tr>
<td>Indirect Costs</td>
<td>quality of life</td>
</tr>
<tr>
<td>Psychosocial Costs</td>
<td></td>
</tr>
</tbody>
</table>
The measurement of the various items within the categories of indirect, direct and intangible costs poses unique challenges to economic assessment. The measurement of direct medical costs requires information regarding both variable and fixed costs (Luce and Simpson 1993). Variable costs reflect the changing volume in the delivery of health care services, while fixed costs, such as hospital labour and capital remain constant over the range of service volume. Estimation of variable medical costs requires access to information on the utilization of specific types of health services and the charges for these services and procedures. Estimation of fixed costs rely on sophisticated case costing and allocation methods (Drummond et al. 1987).

Ascertaining patient-related direct costs, such as out-of-pocket expenditures, may be difficult as the sole source of information for many of these items is the patient self-report. The determination of indirect costs usually relies on a combination of previously compiled data (salary and wage statistics) and patient self-report (missed workdays, travel and waiting times). In long-term studies, direct and indirect costs must be discounted to assess the present value and adjustments for charges and transfer payments may have to be made (Katz and Welch 1993; Freund and Dittus 1992).

Psychosocial costs, represented by the measurement of health-related quality of life, can only be assessed through patient interviews and rating scales, although some assessments include proxies and the global opinions of health care professionals (McCusker and Stoddard 1984).

Due to the difficulty in identifying some costs precisely, e.g. indirect costs, sensitivity analysis is often employed (Briggs et al. 1994). By inserting a range of plausible values, upper and lower
limits of total costs may be defined. Because certain costs may be impossible to specify in monetary units, e.g. psychosocial costs, Hodgson warns that cost estimates may be understated (Hodgson and Meiners 1982). Examples of asthma cost-of-illness evaluations are presented in section 2.5.

2.2 MEASUREMENT ISSUES

Given the potential for bias and random error to influence measurement in economic assessments, it is important to establish the validity and reliability of any instrument or method used to elicit health services utilization and to identify potential sources of bias. Although conceptually qualitative, the attributes of validity and reliability can be measured quantitatively to characterize the method for eliciting information on health services utilization. Bias is defined as "any process at any stage of inference which tends to produce results or conclusions that differ systematically from the truth" (Murphy 1976), thus reducing the validity of the measurement. Validity is defined as the extent to which an instrument actually measures what it is supposed to measure and is sometimes termed the "accuracy" of a measurement instrument. Reliability is the consistency of the measurement, i.e. how well the measurement can be replicated (McDowell and Newell 1987).

2.2.1 Bias

Although bias can be introduced at every step of the research process from hypothesis-generation to publication of the results (Sackett 1979), only those biases associated with collection of data are discussed. Information on health services utilization may be biased if
certain types of patients or health care consumers are routinely excluded from the data collection process, such as non-English speakers and persons who are mentally or physically handicapped.

Another form of selection bias, volunteer bias, occurs when sampling is achieved through volunteer recruitment. Persons with a particular condition or high utilization of health services may be over- or under-represented. Interviewer bias occurs if the interviewer, cognizant of the study hypothesis and patient outcomes, does not obtain information objectively or induces the respondent to answer in a certain manner. Recall bias occurs when a patient with a particular condition or exposure ruminates to a greater extent on their use of health services than a healthy person, who may systematically under-report utilization. The tendency of patients to exaggerate or hide a problem is a recognized pitfall of measurement instruments that rely on subjective recall (McDowell and Newell 1987). Respondent bias occurs when an individual responds in a socially desirable way or is motivated to please the investigator. In a cost-of-illness study, interviewer, recall and response bias may result in over- or under-estimation of health services utilization and overall costs.

In addition to bias, which will systematically under- or over-estimate a measurement, the result can be affected by random error. Random variation occurs within subjects (and within interviewers). It is distinct from the true variation in responses that occurs between subjects. Random error can be reduced by the use of questionnaires and methodology that demand a high degree of precision, such as structured interviewing and exact phrasing. The extent of random plus true variation in the measurements is reflected in the size of the standard deviation or confidence interval of the point estimate.
2.2.2 Agreement

Measurement reliability between two raters, or two data sources, is usually expressed in terms of the observed agreement between the two sources (Fleiss 1981). The assessment of agreement extends beyond detecting a correlation. Correlation analysis, which makes use of indices including the Pearson coefficient \( r \), the regression coefficient \( b \) and the Spearman coefficient, measures how much one variable changes in response to variations in another. While indices of correlation are useful for measuring *association*, they are inadequate markers of *agreement*, since two variables may be perfectly correlated and yet never agree (Kramer and Feinstein 1981). Such is the case for two raters who exhibit the same magnitude of change in instrument scores between subjects, but one rater scores consistently higher or lower than the second rater (Streiner and Norman 1989).

A number of measures are available for quantifying agreement between dichotomous variables. These include the percent observed agreement, chi-square and kappa. The percent observed agreement is commonly reported in the literature and provides an intuitive and easy to interpret indication of the extent of agreement between two sources. Unfortunately, this measure does not correct for chance agreement. In contrast, the chi-square statistic tests whether or not the observed distributions of the dichotomous variables are significantly different from that expected by chance alone. The use of chi-square is inappropriate in reliability studies however, because it does not distinguish between significant agreement or disagreement (Kramer and Feinstein 1981). It is also important to note that using the difference in means between two measures as an index of agreement is incorrect. The lack of a significant difference does not imply agreement because only the *average* group difference is measured and not agreement for
individual subjects (Streiner and Norman 1989). The optimal measurement of agreement for
dichotomous variables remains the kappa statistic ($\kappa$), which is a ratio of the difference between
observed and chance-expected agreement and the potential agreement beyond chance. When $\kappa$
is $> 0$, the observed agreement is greater than that expected by chance. Landis and Koch (1977)
graded kappa scores, stating that values between 0.41 and 0.60 represented "moderate"
agreement, values between 0.61 and 0.80 "substantial agreement" and values between 0.81 and
1.00 "almost perfect" agreement. The use of the kappa statistic can be problematic in certain
cases, however. Feinstein and Cicchetti (1990) demonstrated that the value of kappa depends on
the marginal totals. As the marginal totals deviate from 0.5 of the total sample size, the kappa
value is paradoxically increased or decreased. When the imbalance is asymmetrical, i.e. row and
column marginals deviate in opposite directions, then kappa is artificially increased. When the
imbalance is symmetrical, i.e. row and column marginals deviate in the same direction, then the
agreement expected by chance is very high. This results in a reduced value for kappa.

An additional limitation to the simple kappa statistic is that it measures the frequency of exact
agreement, rather than the amount of partial agreement (Maclure and Willett 1987). Because of
this property, kappa calculations lose meaning for variables with more than two response
categories. For ordinal data, the probability of agreement by chance decreases as the number of
response groups increases. The resultant kappa is arbitrarily decreased. The solution to this
problem is the application of a weighted kappa, where the weight reflects the magnitude of
discordance (Cohen 1968). By convention, quadratic weights are applied, which are equivalent
to the square of the deviation of the observed response pair from exact agreement. Cohen (1968)
has shown that kappa calculated in this manner is equivalent to the intra-class correlation
To distinguish between within-patient and between-patient differences, a reliability coefficient, such as the intraclass correlation coefficient, is used to assess reliability of instruments measuring continuous variables. In the study of health services utilization reporting, multiple methods of reporting are often compared, rather than multiple raters using the same instrument. Such is the case in comparisons of self-report information to data in medical charts or to data abstracted from administrative sources. The same methods used to measure validity and reliability described above have been applied in these situations.

2.3 DATA SOURCES

It is clear from the above discussion that an economic assessment requires access to multiple data sources and for some items, no information may be retrievable. Economic assessments traditionally rely on secondary administrative databases and surveys (self-reports). How much information is retrieved from any particular source depends on the objective and scope of the study. Each data source possesses unique problems regarding accuracy and comprehensiveness and they differ with respect to the cost, feasibility and timeliness of data retrieval. Ultimately the quality of the raw data will determine the quality of the economic assessment.

2.3.1 Administrative Databases

Administrative databases are large, computerized files characterized by a systematic collection of data. Frequently, the primary purpose is to compile information on health services for billing
and reimbursement (Mitchell et al. 1994). These databases may contain records of an entire population, e.g. the U.S. Medicare Provider Analysis and Review File, or may be limited to a smaller geographic region, such as the OHIP database, or to a single institution. Records on health services provided to a segment of the population are also maintained by private insurers. Other types of administrative databases used in epidemiological and outcomes research include clinical databases, disease registries and vital statistic records.

Because administrative databases contain detailed information on the utilization of health care services, they enable the assessment of direct medical costs. Utilization information is extracted by querying the diagnostic and procedural codes used to enter the raw data. A number of coding schemes are in use to classify diagnoses and procedures, including the International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM), the Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures and provincial physician fee schedules. The specificity and precision of each of these schemes vary and do not always follow a logical clinical pattern (Feinstein 1988). Depending on the condition, the codes entered may be vague or reflect the uncertainty of the clinician. Coding of specific procedures may be incomplete because of truncation or bundling or because some services were rendered at another institution or by other health care professionals. Coding is subject to entry errors by the health professional and transcription errors by the data abstractors. The link between diagnostic coding and budget allocation has also been responsible for "diagnosis-related group (DRG) creep", the tendency to overstate the severity of cases (Iezzoni 1994). Protocols for coding may differ between institutions (Ontario Hospital Association 1991). The greatest limitation of administrative databases is that they often lack information on risk factors, utilization of drugs
and non-insured services, as well as other important variables such as physical functioning and quality of life (Strom 1992; Romano and Mark 1994; Fisher et al. 1992; Iezzoni 1994).

Although administrative databases are used for economic assessments, it should be noted that they contain information on charges and payments, not true costs or resources consumed. Frequently, charges can be converted to costs by using cost-to-charge ratios (Lewis et al. 1993).

A major advantage of using administrative databases is the cost of conducting the study and the speed with which it can be completed compared to other methods (Strom 1992). Another advantage is the ability to electronically link files with other databases, such as medication/pharmacy records and vital statistics to achieve greater comprehensiveness and to study a wider range of services and outcomes in a large population (Roos and Wajda 1991; Shannon et al. 1989). Some databases, such as those of private insurers, may be more comprehensive than government-maintained systems. However these may be limited to a select, e.g. employed, segment of the population and may therefore not be sufficiently representative (Lewis et al. 1993). For longstanding databases, studies can cover a long period of time and follow individuals longitudinally (Roos et al. 1987). The use of administrative databases allows true population research, facilitating the observation of rare events. Recall bias and interviewer bias are non-existent with electronically compiled data although the entries are subject to "contact" bias, i.e. the inclination of the patient to make contact with the health care system. The presence of contact bias precludes the use of administrative databases for estimating the incidence and prevalence of any illness that can be manifested in a mild form.
Advancements in computer technology and the need for efficient claims systems have led to a growth in the availability of computerized claims files for research. The growing use of administrative databases for epidemiological, outcomes and economic assessments underscores the importance of ascertaining the accuracy, comprehensiveness and quality of these data.

2.3.2 Patient Self-reports

A self-report is the direct reporting by an individual on any issue. In the health field, it relates to health care, including prior medical history, demographic information, the use of specific services, out-of-pocket expenditures, health status and quality of life. Self-reporting may be mediated by face-to-face surveys or telephone interviews with a researcher or by mailed questionnaires. Participants may report on their own experiences, may serve as a proxy for others (children, elderly) or may report on behalf of a larger unit, such as a family or household. Data collection is accomplished by a variety of techniques ranging from a structured sequence of questions to an open-ended qualitative approach (Kelsey et al. 1986). Depending on the study design, self-reports may be cross-sectional or repeated over a specified period. The self-report describes health services use and expenditures that have occurred in the past. Depending on the study objective, the reports may be limited to the immediate past or extend over months or years.

and Linet 1989; Glandon et al. 1992). These studies evaluated screening procedures (Pap smear, mammography and photofluorography), surgery (hysterectomy and oophorectomy) and general health services utilization (ambulatory services and hospital admissions). Agreement was measured by comparing patient responses to information independently recorded in a second source, usually a medical record.

These studies demonstrated that the reliability of the self-report is not stable across different types of health services utilization. Within the same category of procedure, e.g. screening, the reliability of recall appeared higher for more distinct procedures. A mammogram, unlike a Pap smear or screening for stomach cancer, cannot be confused with other procedures. The reliability of the patient self-report was extremely high for prominent surgical procedures. Women appeared more aware of past hysterectomies than oophorectomies. Recall of hospitalizations within the past year was also high across several studies, with a positive relationship between the length of stay and the sensitivity of the self-report. However, self-reports of outpatient and inpatient hospital services in the elderly demonstrated significant under-reporting.

Several of the studies demonstrated that case-control status, race, education and socioeconomic status do not influence recall of health service utilization. Accuracy in recall appeared to be enhanced through the use of very precise wording. In a questionnaire examining recall of drug use in pregnancy, Mitchell et al (1986) found that recall was significantly enhanced when drug brand names were itemized, compared to an open-ended question regarding general drug exposure. The studies described above also demonstrated that the reliability of self-reports was inversely related to the length of the recall period, particularly in the elderly.
Only one study (Norrish et al. 1994) included confidence intervals around the point estimates. In addition, none of the researchers addressed the problem of using kappa when the proportion of observed events is significantly greater or less than 50%. Thus the reported kappas may be under-estimated and should be interpreted with caution (Maclure and Willett 1987).

All of the authors recognized the possible incompleteness of the data source used for comparison with the self-report, remarking that the quality of the medical record depends on the variable being measured. Medical records that incompletely record the provision of particular health services or interventions would reduce the observed level of agreement. With the exception of Horwitz (1986), none of the researchers sought to measure the extent of missing data or the level of accuracy in the medical records.

The use of self-reports for measuring health service utilization remains an important contribution to the methodology used to evaluate the costs and quality of health care services. The optimal use of self-reports of health services utilization may be as a complement to a variety of other sources of data. Mossey et al (1981) described how information obtained from personal interviews concerning sociodemographic factors, health status, health care needs and quality of life augment detailed health services information obtained from pre-validated administrative sources. The combination of self-report and administratively-derived data can be used to conduct longitudinal follow-up evaluations for particular cohorts, focusing on a wide range of outcomes and exposures. Combining the best available data from sources that include self-reports, physician records, hospital charts, insurance files and administrative databases will enhance the quality of health care services research and economic assessments.
2.4 THE EPIDEMIOLOGY OF ASTHMA

While medicine has succeeded in reducing the burden and improving the outcome of many chronic disorders such as diabetes and coronary artery disease, the incidence of negative health outcomes related to asthma continues to grow. Increases in the prevalence of asthma and its morbidity and mortality have been reported in North America, New Zealand, Australia and several European countries over the last 10-20 years (Anderson 1992; Becklake 1990; Burney 1993; Burr 1993; Gergen and Weiss 1992; Jackson et al. 1985; McFadden and Gilbert 1992; Weiss and Wagener 1990; Weiss et al.1993). The discussion of the epidemiology of asthma will commence with the challenge of defining asthma and measuring its occurrence with the use of patient self-reports, mediated through surveys and questionnaires. In section 2.4.2, asthma prevalence statistics will be presented, including information on existing sources of data in the U.S. and Canada. Reports of changing asthma morbidity and mortality will be reviewed in section 2.4.3, focusing on asthma-related hospitalizations as a marker for morbidity. Section 2.4.4 briefly reviews the overall goals of asthma management followed by discussion of available pharmacological interventions and current prescribing guidelines.

2.4.1 Definition of Asthma

The key challenge in accurately documenting the prevalence of asthma is achieving consensus on an operational case definition of the illness. Without such a definition, comparisons of international epidemiological reports are problematic and little can be surmised regarding global trends. Such a definition would facilitate accurate diagnoses by health care professionals, permit more reliable measurements by researchers and improve record-keeping and statistics
maintained by government health agencies. The International Consensus Report on diagnosis and management of asthma (NHLBI 1992) offers the following definition:

Asthma is a chronic inflammatory disorder of the airways in which many cells play a role, including mast cells and eosinophils. In susceptible individuals this inflammation causes symptoms which are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment, and causes an associated increase in airway responsiveness to a variety of stimuli.

This definition is more conceptual than operational. Published epidemiological studies have utilized diverse methods to document the occurrence of asthma, thereby limiting the value of international comparisons. Simple surveys ask patients whether they have ever been told by a physician that they have asthma. Aside from the possible recall bias and the dependence on access to medical care, this method assumes the physician is able to diagnose the disorder accurately and shares the diagnosis with the patient. Other questionnaires require evidence of symptoms, such as breathlessness and wheezing, which may not satisfy rigorous clinical definitions of asthma that depend on laboratory measurements of lung function. Symptom questionnaires also vary in the reference time frame (e.g. presently/in the last year/ever). Clinical studies of asthma interventions have the advantage of thorough patient examinations where the diagnosis of asthma is based on multiple clinical criteria, including the presence of symptoms and the results of laboratory pulmonary function tests (Ernst et al. 1996).

2.4.2 Asthma Prevalence

The results of the 1978-79 Canada Health Survey suggested an asthma prevalence of 2% in Canada (Mao et al. 1987). More recently, the 1990 Ontario Health Survey reported an average prevalence rate of 3.8% based on self-reports of asthma. The highest rate by age group, 5.6%,
was found in children aged 12 to 14 years (Decker et al. 1995). There was considerable area variation in self-reported prevalence in children under 15 years, ranging from 9.0% in the Toronto-East York Public Health Unit to 2.7% in the Bruce Public Health Unit (Chalk 1996). Asthma was ranked as the fifth most frequent chronic health problem affecting Ontarians, after allergies, skin problems, back pain and arthritis/rheumatism (Badley et al. 1993). The most recent Canadian survey, the 1994 National Population Health Survey (NPHS), reported a national prevalence of 6.3% (Trakas et al. 1997). The 6.8% prevalence recorded for Ontario by the NPHS was slightly higher than the national average.

U.S. data on the prevalence of asthma are maintained by the National Centre for Health Statistics. Several cross-sectional surveys are conducted periodically to collect U.S. national prevalence data on numerous diseases including asthma. These include the National Health Interview Survey (NHIS), the National Health and Nutrition Examination Survey (NHANES), the National Hospital Discharge Survey (NHDS) and the National Ambulatory Medical Care Survey (NAMCS). Mortality data are maintained by the National Vital Statistics System. This heterogeneous group of surveys include patient self-reports, face-to-face interviews with health providers, physician claims data and hospital discharge data. These sources indicate that the prevalence of asthma in the U.S. has been rising steadily in the last thirty years and the disease now affects 9-12 million people. NHANES estimated that the prevalence of asthma averaged between 6-10% in 1976-1980 (Weiss and Wagener 1990). Cross-sectional surveys performed in the 1980s in the UK estimated an adult prevalence rate of 2.2% and provided evidence of urban-rural differences similar to those in the U.S. (Weiss and Sullivan 1993). Asthma prevalence rates in New Zealand and Australia were estimated at 6 to 9% in the early 1980s.
Studies examining age differences indicate that prevalence rates are highest in persons under 18 years. During childhood more males than females are affected but this difference disappears in adulthood (Mellis et al. 1993, Burr 1993). The 1988 U.S. National Health Interview Survey revealed a 40% increase in asthma prevalence in children and adolescents between 1981 and 1988. Prevalence was higher in Blacks, people with low socioeconomic status and those living in inner city areas (Weiss and Sullivan 1993). While it is likely that elevated detection rates and improved diagnostic procedures may explain a portion of the observed increase, a Mayo Clinic retrospective community-based study revealed a 55% rise in asthma incidence between 1964 - 1983 while applying uniform detection and diagnostic criteria to the entire cohort. The incidence rate was highest in male children (Yunginger et al. 1992).

The increased incidence of asthma may be explained by numerous risk factors. Altered host susceptibility as a result of exposure to increasing concentrations of outdoor air pollution and indoor airborne allergens, including cigarette smoke and irritant gases, is possible. An increased allergic sensitivity to dust mites, cats and cockroaches resulting from exposure during the first few years of life has also been suggested. Viral infections may play a role in triggering childhood onset of asthma and may themselves be more prevalent due to the growing use of communal day care. The increased survival rate of premature and low birth weight infants with inferior respiratory function at birth may also contribute to the increased incidence of asthma (Gergen and Weiss 1992; Burney 1993; Anderson 1992; Weiss and Wagener 1990; Burr 1993; Weiss et al. 1993).
2.4.3 Asthma Morbidity and Mortality

In the last two decades researchers have examined hospital admission rates as a marker for morbidity to explore changes in disease severity over time. In Canada, pediatric hospitalizations due to asthma have increased four-fold since the 1960s (Mitchell 1985; Gergen 1990). Recent Canadian data indicate that between 1980-1988 the asthma admission rate increased 40% with an average annual increase of 4.3% (Wilkins and Mao 1993). Over this period the rate in persons aged 15 to 34 years rose from 75 to 110 asthma-related admissions per 100,000 population, with higher rates in women compared to men. While the largest increase, 46%, was in the 15-34 age group, the rate in children aged less than 15 years was five-fold higher than the rate seen in adults throughout the study period. In children, the asthma admission rate in boys was 750 per 100,000 population in 1988 and was more than 50% higher than the rate in girls, 450 per 100,000. During the same period, the average length of stay decreased from 4.5 to 3.5 days.

Considerable inter-provincial variation was observed in the age-standardized 1988 rates of admission for children under 15. The highest rate of 1,932 admissions per 100,000 population was observed in PEI compared to the low rate of 355 in Manitoba, resulting in an extremal quotient (EQ) of 5.4 and a coefficient of variation (CV) of 0.6. (Excluding the outlier PEI value, the EQ was 2.6 and the CV was 0.29 in children in 1988.) The rate in Ontario for children under 15 years increased from 495 to 665 per 100,000 between 1980 and 1988. The most recent evidence suggests that the pediatric rate of asthma-related admissions in Ontario may be declining, with a rate of 519 per 100,000 observed for 1991 (Chalk 1996) and 460 per 100,000 for 1994/95 (Goel et al. 1996). In the 15 to 34 age group, the admission rate in Ontario increased from 86 to 127 per 100,000 between 1980 and 1988. Inter-provincial variation was evident in
1988 in adults, the EQ was 3.3 and the CV, 0.32.

In the U.S., the discharge rate for asthmatics of all ages increased nearly three-fold between 1970-1987, a period during which overall hospitalization rates declined greatly (NCHS 1991). This period includes the 1979 introduction of ICD-9 which reclassified asthmatic bronchitis (ICD-8 code 492) to asthma (ICD-9 code 493). This "diagnostic shift" (Anderson 1992) may explain some of the increase. Enough data has been collected since 1979 to examine trends in morbidity under uniform coding criteria. Overall asthma admission rates increased from 157 in 1979 to 188 per 100,000 population in 1987. This rise in admissions was associated with increased disease severity and may also be partly due to increased self-referral. Twice as many hospitalizations occurred in Blacks compared to Caucasians (NHLBI 1991). The greatest increase occurred in children under 15 years, which in 1987 was close to 300 per 100,000, with children under age 5 responsible for most of the increase (Weiss et al. 1993). As these children aged, their hospitalization rate declined, indicating the absence of a birth cohort effect.

The accuracy of mortality data may be compromised by miscoding on death certificates. Validation studies conducted in Canada, New Zealand, the U.K. and the U.S. found that accuracy rates were close to 100% for deaths of persons aged 35 and under but decreased to 50% for deaths of 70-year-olds (Weiss et al. 1994; Sweet et al. 1992). Because of the rarity of other fatal respiratory disorders in persons aged under 35 years, most international reports of asthma mortality rates are restricted to this group (Weiss et al. 1994, Burr 1993). In contrast to the morbidity data, mortality rates in Canada displayed some fluctuation but no net change between 1980-1988 (Wilkins and Mao 1993). Asthma mortality remains rare in Canada with an average
of 58 deaths per year during the 1980s. The rate in children under 15 years was approximately twice that of persons aged 15-34 years. No sex-related differences were found in pediatric mortality rates but rates in adult males exceeded those in adult females. Inter-provincial mortality rates ranged from a high of 0.7 per 100,000 in Saskatchewan and Alberta to 0.2 per 100,000 in Newfoundland. The apparent stability in death rates may be due to the 9-year study period. When plotted over a 45-year period, death rates in Canada exhibited a marked decline in the 1950s and 1960s followed by a gradual increase beginning in the 1970s (Hogg et al. 1995).

In contrast to Canada, mortality in the U.S. due to asthma increased by 31% between 1980 - 1988 with overall rates at 0.2-0.3 per 100,000 (NHLBI 1991). Although overall rates remain low compared to coronary artery disease and lung cancer, the continued rise, particularly in Black men and women, is of concern. A study of geographic differences in the U.S. revealed that 21% of all deaths from asthma occurred in inner city neighbourhoods, although these locations accounted for only 7% of the susceptible population (McFadden and Gilbert 1992). In the UK, asthma deaths nearly doubled between 1978 to 1988 and similar increases have been reported in New Zealand, Germany and Scandinavia. Increases of 20% during the 1980s were recorded in Japan, Finland, the U.S., the Netherlands and France (Jackson et al. 1988). These studies on trends did not include statistical tests of significance.

The major findings of international epidemiological reports are summarized as follows:

1. Asthma prevalence increased steadily during the 1980s, with children and adolescents responsible for most of this trend.
2. Morbidity, as defined by hospitalizations, has also increased during the same period, with young children (under 5 years) accounting for most hospitalizations.
3. Asthma mortality has increased since the 1970s. Data on adults over 35 years should be interpreted with caution.

Several factors have been suggested as explanations for these trends. One reason for the rise in mortality may be inadequate control and management of the disease. Both patients and physicians may underestimate the severity of the illness, which if poorly or improperly treated, may quickly deteriorate, resulting in a fatal or near-fatal episode (NHLBI 1991). Inadequate management in the U.S. may be related to socioeconomic status, which has been found to play a significant role in access to medical care as well as small area variations in hospitalization and mortality rates (Weiss et al. 1993).

Another explanation for the increases in asthma morbidity and mortality relates to significant changes in the pharmacological treatment of the disorder, particularly the use (and potential for over-use) of MDIs. Although intended to be an efficacious treatment for asthma-associated bronchoconstriction, one of the earliest available inhaled beta-agonists, isoprenaline 'forte', was removed from the market in the 1960s when sharp increases in asthma deaths were noted in New Zealand, the U.K. and other countries. Although the cause was not fully explained, removal of the high dose product from the market and more cautious utilization of other MDIs caused mortality rates to return to pre-epidemic levels (Inman and Adelstein 1969). A second epidemic occurred in New Zealand in the 1970s and a number of case-control studies implicated fenoterol, a short-acting beta-agonist MDI which delivered doses twice the strength of salbutamol, another commonly available short-acting beta-agonist (Crane et al. 1989; Pearce et al. 1990). The odds ratio of asthma death for patients prescribed fenoterol MDI was 1.99. This rose to 9.82 in a subgroup of severe asthmatics (Pearce et al. 1990). Case-control studies documenting the rise and
fall of asthma deaths in New Zealand due to fenoterol suggested that patients developed an over-
reliance on the MDI. The inhaler offered immediate attenuation of bronchoconstriction without
reducing hypoxia. The potent bronchodilation offered by fenoterol may have delayed patients in
seeking medical attention. In the presence of hypoxia, these drugs may cause cardiotoxicity. The
bronchodilation could paradoxically facilitate the inhalation of allergens, thereby stimulating a
rapid and possibly fatal exacerbation (Crane et al. 1989; Burr 1993).

2.4.4 Asthma Management

The choice and dosage of medication for the treatment of asthma depend on the disease severity.
The mainstay of asthma therapy is dual treatment with bronchodilators and anti-inflammatory
agents. Classes of bronchodilating compounds such as beta-agonists, methylxanthines
(theophylline) and anticholinergics dilate the airways by relaxing bronchial smooth muscle.
Anti-inflammatory agents such as corticosteroids and sodium cromoglycate prevent and/or
control the development of inflammation in the airways. The current understanding of asthma as
an inflammatory rather than an allergic disorder has prompted widespread use of inhaled
corticosteroids. Prevailing medical opinion dictates that these agents be topically administered
as first-line therapy to control underlying inflammation with concomitant administration of beta-
agonist bronchodilator MDIs to control symptoms when necessary (McFadden and Gilbert
1992). Given in this manner, physicians can monitor the number of puffs of inhaled beta-agonist
required daily as a signal of worsening or improvement of the underlying pathophysiology.

In Table 2, Hargreave et al. (1990) suggest a concise treatment plan that calls for increases in
dosage and the introduction of more potent medications with increases in the level of severity.
More recently, the Canadian Asthma Consensus Conference (Ernst et al. 1996) was convened to re-address the management of asthma. Clinical experts were concerned that the stepped care approach featured in previous guidelines was too rigid in linking therapy recommendations to severity levels. The current preference is to view asthma on a disease continuum, thereby encouraging a more flexible approach to treatment that allows pharmacotherapy to be tailored to the disease severity with ongoing adjustments made to ensure good control. The primary goal is to obtain the best management possible in terms of symptoms, the need for bronchodilators, pulmonary function, diurnal variation, adverse drug reactions and quality of life. Because of the epidemiological studies linking inhaled beta-agonists with increased asthma mortality and concerns regarding the long-term use of all anti-asthmatic medications, the guidelines advocate reducing medications to the lowest possible doses required to achieve good control. (Hargreave et al. 1990, Ernst et al. 1996).

Table 2. Levels of Treatment

<table>
<thead>
<tr>
<th>Level</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inhaled beta-agonist as needed with or without inhaled anti-inflammatory (cromoglycate)</td>
</tr>
<tr>
<td>2</td>
<td>Level 1 plus regular cromoglycate or low-dose inhaled corticosteroid</td>
</tr>
<tr>
<td>3</td>
<td>Level 1 plus high-dose inhaled corticosteroid with or without sustained release theophylline or Level 1 plus high-dose inhaled corticosteroid with or without long-acting beta-agonist with or without inhaled ipratropium bromide</td>
</tr>
<tr>
<td>4</td>
<td>Level 3 plus oral prednisone</td>
</tr>
</tbody>
</table>

from Hargreave et al. (1990)
2.5  THE COST-OF-ILLNESS OF ASTHMA

If the prevalence of asthma and its attending morbidity are increasing, it is important to estimate the economic burden of illness and monitor changes over time as well as between sub-populations and regions. Measuring the cost-of-illness assists regulators and policy-makers to make decisions regarding the allocation of health resources and provides insight into the potential impact of novel therapeutic strategies (Buxton 1991). The full economic burden of a disease includes direct medical and patient costs, indirect costs such as loss of productivity, leisure activities and premature mortality and intangible costs related to loss in quality of life (Weiss and Sullivan 1993). In the prevalence approach to a cost-of-illness study, costs incurred by individual asthmatics during a specified period, e.g. one year, are measured.

A number of cost-of-illness studies pertaining to asthma have been completed in the U.S., Sweden, the U.K., Australia and Canada. The key design features and results of these studies are summarized in Table 3.
Table 3. Summary of Population-based Asthma Cost-of-illness Studies

<table>
<thead>
<tr>
<th>Place</th>
<th>Author &amp; Year</th>
<th>Study Year</th>
<th>Viewpoint</th>
<th>Economic Costs</th>
<th>% of GDP&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Direct Medical</td>
<td>Indirect</td>
</tr>
<tr>
<td>US</td>
<td>US NHLI 1972</td>
<td>1967</td>
<td>societal</td>
<td>$US 243 million</td>
<td>$US 272 million</td>
</tr>
<tr>
<td>US</td>
<td>Vance and Taylor 1971</td>
<td>1967-69</td>
<td>family</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Sweden</td>
<td>Thompson 1981</td>
<td>1975</td>
<td>societal</td>
<td>SEK 218 million</td>
<td>SEK 618 million</td>
</tr>
<tr>
<td>US</td>
<td>Marion et al. 1985</td>
<td>1977-80</td>
<td>family</td>
<td>$US 940 per family</td>
<td>$US 147 per family</td>
</tr>
<tr>
<td>US</td>
<td>Ross 1988</td>
<td>1988</td>
<td>societal</td>
<td>$US 8.7 billion</td>
<td>$US 2.2 billion</td>
</tr>
<tr>
<td>UK</td>
<td>Action Asthma 1990</td>
<td>1988</td>
<td>NHS</td>
<td>£ 344 million</td>
<td>£ 499 million</td>
</tr>
<tr>
<td>NSW</td>
<td>Mellis et al. 1991</td>
<td>1989</td>
<td>societal</td>
<td>$A 142 million</td>
<td>$A 67 million</td>
</tr>
<tr>
<td>Canada</td>
<td>Krahm et al 1996</td>
<td>1990</td>
<td>societal</td>
<td>$Cdn 306 million</td>
<td>$Cdn 198 million</td>
</tr>
<tr>
<td>US</td>
<td>Smith et al 1997</td>
<td>1994</td>
<td>societal</td>
<td>$US 5.15 billion</td>
<td>$US 6.73 billion</td>
</tr>
</tbody>
</table>


* Projected from 1985 data.

Abbreviations: NSW = New South Wales; NHLI = National Heart and Lung Institute (now the National Heart, Lung and Blood Institute); N/A = not available.
All of the studies took a prevalence approach. Direct costs ranged from 26% to 80% (average - 54%) of total costs. The largest component of medical costs was hospital expenditures (60%). Medications accounted for 30% and physician services, 10% (Weiss and Sullivan 1993).

The Canadian study determined that the total cost of asthma in Canada was $504 million in 1990 Canadian dollars, with direct costs accounting for $306 million and indirect costs $198 million respectively. Medications were the single largest cost component, $124 million and 41% of total costs (Krahn et al. 1996). It is probable that tertiary care costs are limited to severe asthmatics. Only a cost-of-illness assessment that includes appropriate indicators of disease severity would be able to determine the costs associated with degrees of morbidity. This information is important for health care planning as well the design of comparative economic evaluations.

All of these cost-of-illness investigations suffer from several important methodological weaknesses. Because the studies were conducted retrospectively, the estimates may have been based on utilization patterns that were not current. The reliance on general surveys and secondary databases did not allow for assessment of all relevant costs and excluded an evaluation of health-related quality of life. The accuracy of the results depends upon the validity and completeness of the databases used. The population approach permitted only an aggregate estimate of the economic burden in the entire cohort and did not allow for stochastic analyses or sub-group estimates that may be useful for decision-making at the patient or community level. The Australian study calculated a cost per asthmatic by dividing total costs by a rough prevalence estimate (Mellis et al. 1991) rather than measuring costs at the patient level. The high level of imprecision associated with ascertaining asthma prevalence (see section 2.4.1, 2.4.2)
cautions against this type of data manipulation. Similarly, Krahn et al. (1996) calculated per capita costs in the U.S. and Canada based on population size. Expressing costs per capita when only a segment of the population has asthma is of questionable value. Some of the estimates of cost components were subjective (based on expert opinion) and their inclusion reduces the quality of the overall estimate. Assumptions were made regarding the frequency of specific asthma-related services. This uncertainty was dealt with by presenting upper and lower bounds. This approach may result in a large range between upper and lower limits, diminishing the utility of the findings.

The assessment of costs for cost-of-illness and comparative economic evaluations could be much improved through the use of a prospective model designed to capture all relevant costs. In addition to collecting comprehensive information on the use of insured and non-insured health services, such an approach would permit a more accurate and precise estimation of indirect costs because detailed information on productivity losses of individual patients and caregivers could be obtained along with relevant socioeconomic characteristics. Sufficient information on medical histories and symptoms could be collected to improve the disease severity classification of asthmatics. Furthermore, information on demographics, medical history and medications could be used to provide patient-level cost-of-illness estimates. These estimates can be stratified by age, sex and disease severity and can be adjusted for other explanatory variables, providing for increased precision over estimates derived from aggregate population data. Prospective data collection also allows for analysis from multiple perspectives. Prospective patient interviews also facilitate the measurement of the impact of asthma on health-related quality of life, contributing to the development of general and disease-specific measures.
The authors of the previously completed assessments of the cost of asthma uniformly claimed that their results were under-estimates of the true cost of illness. Furthermore, there is a conviction among many health professionals that asthma is under-diagnosed and under-treated in large segments of the population (NHLBI 1991). The veracity of this assertion can only be tested by measuring the impact of treatment, education and other intervention programs on health outcomes. The treatment of asthma is currently evolving at a rapid rate. Theophylline administration is being replaced by routine administration of inhaled corticosteroids and beta-agonist usage is being curtailed (Ernst et al. 1996). New classes of therapeutic agents such as the leukotriene receptor antagonists and 5-lipoxygenase inhibitors are currently in development (Howell et al. 1995; Welch et al. 1994; Wensing et al. 1994). The impact of these changes in the pharmacotherapy and management of asthma must be closely monitored through the conduct of high quality economic assessments to ensure that optimal patient outcomes occur at a minimal cost to individual patients and to society.

2.6 SUMMARY

In societies faced with rapidly growing health care costs, demonstrations of the economic benefits of new treatments and procedures are vital. Comparative economic evaluations and cost-of-illness assessments share the need for a careful delineation of costs. While there is general agreement among researchers on what constitutes direct, indirect and intangible costs, the methods used to collect cost and utilization information require further research and development.
Conventional sources of data for economic assessments include secondary administrative databases and general population surveys. Each of these sources of data possess unique problems with respect to data quality and comprehensiveness. Data collection methods relying on each of these sources must be subjected to appropriate validity and reliability assessment, including identification of all sources of potential bias. Direct costs derived solely from administrative databases and general surveys are frequently incomplete and the data may not be accurate. Using the human capital method to measure productivity losses for the calculation of indirect costs may fail to capture the true opportunity costs of time lost. Moreover, the measurement of productivity losses of persons who are neither employed nor homemakers has not been addressed with this method. Current economic assessment methodology has resulted in the omission of intangible costs, i.e. the impact of illness on health-related quality of life.

Traditionally, calculation of costs for cost-of-illness assessments proceeds in a retrospective fashion from existing sources, resulting in a population-based summary value of average costs. Missing data and the need to make assumptions regarding opportunity costs reduce the precision of the result and diminish its value to health professionals and policy-makers.

In the field of epidemiology, prospective cohort studies are designed to measure the occurrence of specified outcomes in a pre-defined patient sample. Observational study designs hold promise for economic assessments which require accurate measurements of costs and the utilization of health care resources. Such an approach offers the potential to overcome the limitations of current cost-of-illness methods. Data on a full range of relevant economic variables may be collected, along with important disease and demographic information. Precision may be
increased through the application of stochastic statistical methods and the results may be stratified into clinically meaningful categories. Costs can be expressed at the patient level and from multiple perspectives, facilitating interpretation and application to clinical decision-making. Research is required to assess the reliability of a prospective observational approach, which depends on patient self-reports, for conducting economic assessments of a wide range of medical treatments and procedures.

Public health officials and health care professionals are increasingly concerned about the rising prevalence and morbidity of asthma. The segment of the population demonstrating the greatest increases in incidence and hospital admissions are children under 15 years of age. These increases appear to be part of a trend in developed countries around the world and the reasons are not fully understood. A complex array of therapeutic options are now available for the treatment of asthma with the aim of reducing symptoms and preventing disease progression. The near future will see the introduction of several new classes of anti-asthmatic medications to combat the increasing morbidity. New interventions must be subjected to careful health economic evaluations to ensure that health budgets are optimally allocated. Although the economic burden of asthma has been investigated in a number of cost-of-illness assessments, these studies are constrained by the methodological limitations of the retrospective study designs and reflect past medical practices. Given the changing epidemiological nature of asthma, high quality prospective economic assessments are required to monitor changes in the costs associated with this disease.
STUDY OBJECTIVES AND RESEARCH QUESTIONS
Chapter 3. STUDY OBJECTIVES AND RESEARCH QUESTIONS

The two principle study objectives were:

1. To assess the reliability of patient self-reports of health services utilization in a sample of patients with respiratory disease.

2. To use a prospective observational study design to assess the costs of asthma at the patient level from various perspectives.

Specific research questions pertaining to each of these two objectives were grouped separately for the assessments of the patient self-report and the cost-of-illness.

Assessment of Patient Self-Report

1. What types of health services utilization can be measured with patient self-reports?

2. What are the utilization rates for each category of health services as measured by patient self-report and by OHIP fee claims?

3. For each category of health service utilization (respiratory-related physician visits, emergency room/clinic visits and hospitalizations), what is the level of agreement between self-reports and OHIP fee service claims data?

4. Is the level of agreement for utilization reported during the 6-month follow-up period different than the level of agreement for utilization reported at baseline that occurred during the 6-12 month period before the study?
Cost-Of-Illness Assessment

1. Can asthma-related expenditures that are not routinely available from administrative databases be obtained from patient self-reports?

2. What are the annual direct and indirect costs of asthma expressed from the perspectives of a) society, b) the health care system and c) the patient?

3. Within each perspective, what are the average annual per patient costs associated with the treatment of asthma, for patients with mild, moderate and severe disease?

4. What are the severity-specific costs in patients aged 0-4 years, 5-14 years and 15 years and older?

5. What sociodemographic variables are significant predictors of total costs?

6. What are the differences in health-related quality of life between males and females, between severity levels and between age groups in patients with asthma?
Chapter 4. METHODS

This chapter explains the Pharmacy Medication Monitoring Program (section 4.1) and reports the sample sizes required and the methods used to recruit subjects (section 4.2). Section 4.3 describes the collection and management of data for the self-report assessment and section 4.4 expounds the process for developing the cost-of-illness question set. Section 4.5 describes the statistical techniques employed in the self-report and cost-of-illness assessments. This section also includes the methods used to define asthma, stratify by disease severity and assign a perspective to the cost-of-illness analysis. All data sources are described. The last section pertains to ethical issues in the conduct of this research project.

4.1 THE PHARMACY MEDICATION MONITORING PROGRAM

The Pharmacy Medication Monitoring Program is a pharmacoepidemiologic surveillance project established in 1992 by the Centre for Evaluation of Medicines, St. Joseph's Hospital, McMaster University (Willison et al. 1995). The primary purpose of the PMMP is to monitor the day-to-day beneficial and adverse effects of various categories of prescription medications in a diverse outpatient population.

This program is characterized by the use of community pharmacists to recruit patients at the point of drug purchase. Individuals consenting to the project undergo telephone interviews at 1-, 3- and 6-months after registration. Although the patients are not randomly selected, the PMMP offers several advantages over conventional observational or clinical trial study designs. The use
of pharmacists as an intermediary in recruitment facilitates access to a wide-ranging population. The sample of patients is more representative of actual users of the target medication compared to patients enrolled in randomized clinical trials. Pharmacy records permit the assessment of eligibility and the calculation of enrollment rates and allow a limited comparison of participants to non-participants. The program allows for observation of drug effects at doses and for indications beyond those studied in clinical trials, facilitating an evaluation of the effectiveness of the medication. Details of the methods used to recruit pharmacies and maintain stable patient enrollment in the program have been published elsewhere (Willison et al. 1995).

To date, the PMMP has completed several projects including assessments of angiotensin converting enzyme (ACE) inhibitors, nicotine replacement therapies and non-steroidal anti-inflammatory drugs (NSAIDs) (Levine et al. 1994; Gaebel et al. 1995). For each project, the interview consists of fixed and variable components. The fixed component, common to all projects, includes questions on demographics, concomitant medication usage, utilization of health services and quality of life (SF-36). The project-specific variable component collects information regarding target medication utilization, symptoms and risk factors. The Inhaled Bronchial Medications project was launched in October 1994. A pilot phase recruited 277 subjects between October and December 1994 at 8 Hamilton pharmacies. These individuals were followed until June 1995. In May 1995 the main Bronchial Inhalers project was launched with the participation of 34 community pharmacies. Participating pharmacies included stores within 60 kilometers of Hamilton, spanning St. Catharines, Hamilton, Burlington, Oakville, Mississauga, Brampton, Guelph and Kitchener. The telephone interviews in the main project were supplemented with questions on economic endpoints for the cost-of-illness assessment.
4.2 SUBJECTS

4.2.1 Sample Size Calculation

Donner and Eliasziw (1987) published power contours for determining sample sizes for reliability studies testing different hypotheses. In a study that has two 'raters' (i.e. the patient self-report and OHIP), it is desirable to have sufficient power to detect the presence of substantial agreement. Because the statistical measurement is agreement between individual reports, the desired sample size does not depend on the specified outcome variable's distribution, i.e. standard deviation from the mean. Multiple outcomes can be treated as independent variables in an agreement analysis. Kappa is a statistical measure of agreement used in inter-rater reliability assessments. A study that is designed to test the hypothesis that kappa is greater than 0.60 (which according to Landis and Koch (1977) represents substantial agreement) requires a sample size of 42 subjects at $\alpha = 0.05$ and $\beta = 0.20$.

The sample size estimate for the cost-of-illness assessment was predicated on collecting sufficient cost data on the most rare type of health services utilization - asthma-related hospital admissions. The literature reports mean hospitalization rates in respiratory patients ranging from 1% to 3% per year (Weiss et al. 1993; Lanes et al. 1994; Feeney et al. 1993; Mellis et al. 1991; Vollmer et al. 1994). Assuming the probability ($p$) of asthma-related hospitalization is rare in this cohort ($p = 0.01$), enrolling 500 subjects would result in approximately 5 hospitalizations per year, with a standard deviation $\pm 0.0044$. Thus a stable cost-of-illness estimate requires a minimum enrollment of 500 asthmatic subjects.
4.2.2 Recruitment

The Bronchial Inhalers study consisted of a pilot project (used for the self-report assessment) and the Main project (used for the cost-of-illness assessment). Both projects followed the standard PMMP procedures which are detailed below. Pharmacists and technicians employed at participating pharmacies were trained in the recruitment procedures by PMMP research staff. Recruitment for the pilot phase of the Bronchial Inhalers project proceeded from October 3 to December 31, 1994 during which 277 subjects were enrolled. The main project recruited 2,078 subjects from May 8 to October 8, 1995. During the recruitment periods, English-speaking customers filling a prescription for a metered dose inhaler for any indication were given verbal and written information regarding the project by the participating pharmacist. If a prescription was being filled by proxy or was being delivered, written information was included with the prescription. Interested patients were asked to fill out and sign a 3-part carbonless consent form. The form recorded the person's sex, date of birth, address, telephone number and health card number (Appendix 1). One copy of the consent form was returned to the study coordinator at the PMMP office. Each subject was telephoned within 3 weeks of registration for the baseline interview. If the patient was unable to undergo the interview at the time of telephone contact, another more convenient time was scheduled. If the interviewer could not reach a subject by telephone within 3 weeks post-registration, a registered letter was mailed to the address on the consent form requesting confirmation of the patient's willingness to participate. Patients responding positively to the registered letter were telephoned and the first interview was scheduled. Patients not responding were classified as lost-to-follow-up.

Subjects who participated in the pilot project had a variety of respiratory conditions. These
individuals were deemed eligible for the assessment of the self-report of health services utilization, the first thesis study objective, if they were 18 years of age or more and were residents of Ontario. Eligible subjects were mailed a cover letter and duplicate consent form describing the reliability study and requesting their health card number and permission to view their OHIP and hospital records (Appendix 2). These individuals were asked to read the information, to indicate their intention or refusal to participate and to return one copy of the consent form in the stamped envelope provided. Initially, letters were mailed to 205 potentially eligible candidates. This was followed 6 weeks later by a second mailing to 128 individuals who had not responded to the first mailing. Four weeks later telephone follow-up of the remaining non-responders commenced. Two attempts were made to contact each non-responder by telephone. Of the 197 subjects who were ultimately deemed eligible, 83 consented in writing.

The second study objective, an asthma cost-of-illness assessment, focused on patients recruited into the main Bronchial Inhalers project. This project recruited 2,078 subjects between May and October 1995 and 1,588 subjects successfully completed their 6-month interview by March 31, 1996. The same PMMP pharmacy procedures for recruiting patients described above were used in the main project. As no OHIP data were required for the cost-of-illness assessment, a second consent form was not distributed. The 1-, 3- and 6-month interviews of the main project were supplemented with economic questions.
4.2.3 Study Timeline

The timeline for recruiting subjects and undertaking the self-report assessment and the economic evaluation is portrayed below.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct 93 - Dec 94</td>
<td>1</td>
<td>Enrollment of 277 patients into pilot phase of PMMP Bronchial Inhalers project. 83 eligible subjects from pilot project volunteered for self-report assessment.</td>
</tr>
<tr>
<td>Oct 93 - June 95</td>
<td>2</td>
<td>Period for self-report assessment of 83 subjects, included a 3-month enrollment period, a 1-year pre-study recall period and a 6-month follow-up of health services utilization.</td>
</tr>
<tr>
<td>May 95 - Oct 95</td>
<td>3</td>
<td>2,078 subjects enrolled into main Bronchial Inhalers project which included the economic assessment.</td>
</tr>
<tr>
<td>May 95 - March 96</td>
<td>4</td>
<td>After 5-month recruitment period + 6-month follow-up period, 1,588 of 2,078 subjects completed the main Bronchial Inhalers study.</td>
</tr>
</tbody>
</table>
4.3 ASSESSMENT OF PATIENT SELF-REPORT

The assessment of the reliability of patient self-reports was conducted using data collected from Ontario residents aged 18 years or more who enrolled in the McMaster University PMMP from October 3 to December 31 1994. The specific variables and data sources that were compared in this evaluation are summarized below.

Table 4. Utilization Variables and Data Sources Compared

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>DATA SOURCES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PMMP questionnaire (patient self-report)</td>
</tr>
<tr>
<td>GP visits</td>
<td>✓</td>
</tr>
<tr>
<td>specialist visits</td>
<td>✓</td>
</tr>
<tr>
<td>ER/clinic visits</td>
<td>✓</td>
</tr>
<tr>
<td>hospitalizations</td>
<td>✓</td>
</tr>
</tbody>
</table>

✓ indicates data were extracted from specified source
✓ indicates data were not extracted from specified source

The reliability of patient self-reports of general practitioner (GP) and specialist visits, emergency room (ER) or clinic visits and hospitalizations was assessed by comparing these reports to OHIP data on the identical cohort. Self-reports of hospital admissions was also verified against hospital records, as described below in section 4.3.3.
4.3.1 PMMP Data Collection

4.3.1.1 Data Entry

Information collected from consent forms completed by patients in the recruiting pharmacies included basic demographics, such as name, date of birth, sex, address and health card number. These data were entered into a Paradox® spreadsheet by PMMP personnel (Paradox® 1994).

The telephone interviews for the PMMP Bronchial Inhaler Pilot Project were conducted using the Info Zero Un® questionnaire software program version 3.4 (Info Zero Un® 1994). This software allows real-time data entry during telephone interviews and permits the designation of fixed response options and logical skip patterns. The skip patterns, response options and acceptable parameters for each question were programmed by the PMMP Research Coordinator prior to the study. The questionnaire program was pre-tested by telephone by PMMP staff to test the performance of the skip patterns, the clarity of the response options and the ordering of the questions.

Two PMMP employees conducted the pilot project telephone interviews with the questionnaire software. Incorrect data entry or illogical character specification was signalled by a computer beep. Necessary changes could be made to any answers during the same session. Items requiring further clarification or elaboration by the patient, such as a medication dosage or hospital address, were noted on a written log maintained by the interviewer. This allowed an uninterrupted flow of questioning. All items noted on the log corresponded to specific question numbers. Missing information was entered from the log into the database at the end of the interview.
4.3.1.2 Interviews

Individuals signing consent forms were contacted within one month after registration for the baseline interview with follow-up interviews scheduled at 3 and 6 months after registration.

<table>
<thead>
<tr>
<th>Time</th>
<th>Registration</th>
<th>Baseline Interview</th>
<th>1-month Follow-up Interview</th>
<th>3-month Follow-up Interview</th>
<th>6-month Follow-up Interview</th>
</tr>
</thead>
</table>

All interviews were conducted by professionally trained interviewers employed by the PMMP and the same interviewer conducted all the interviews for an individual patient. Information collected on the consent form was verified at the start of the baseline interview.

The interview questions followed a closed-ended, structured format. In most cases response options were read aloud to the respondent. The exceptions were items requiring a frequency response, e.g. frequency of medication administration and frequency of physician visits.

At the initial telephone interview, detailed information was collected on:

- **demographics**: sex, date of birth, education, employment
- **smoking status**: type, amount, duration, years since quitting
- **medical problems**
- **symptoms**: frequency, duration, diurnal variation, seasonal variation of shortness of breath, wheeze and recurrent cough
- **medications**: type, dosage, prescription and compliance for prescription and non-prescriptions drugs
- **health-related quality of life**: SF-36 measurement of physical functioning, role
limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and, mental health.

- health services utilization: visits to family/general practitioner, specialist, emergency room/clinic, hospital admissions

During follow-up interviews conducted at 3- and 6-months post-registration, patients were asked about changes in their medications, symptoms, health status and quality of life and were asked to report their utilization of health services. The specific types of health services information that were collected as part of the PMMP project are listed below.

Baseline Questionnaire:

1. Respiratory-related visits to general or family practitioners in previous 6 months
2. Visits to lung specialist (allergist, respirologist) in previous 12 months
3. Visits to emergency room or clinics for any reason since registration
4. Admissions to hospital for any reason since registration
5. Respiratory-related admissions to hospital in 12 months prior to registration

3-month and 6-month Questionnaire:

6. Respiratory-related visits to family physician since last interview
7. Visits to lung specialist (allergist, respirologist) since last interview
8. Visits to emergency rooms or clinics for any reason since last interview
9. Respiratory- and non-respiratory-related admissions to hospital since last interview

The length of the recall period chosen for reporting each type of health service utilization was based on prior projects and the medical literature. Since patients were asked at baseline about respiratory-related hospital admissions that occurred in the previous 12 months, the overall recall period extended from October 1993 until June 1995.
4.3.1.3 Data Management

Data collected through telephone interviews from the pilot Bronchial Inhalers project were used in the assessment of the patient self-report. Raw data were converted to three ASCII text files (baseline, 3-month and 6-month) and downloaded from tape provided by the PMMP to a personal computer hard disk. No information identifying patients was included with the data files. The ASCII files were converted to SAS data sets using SAS v. 6.10 (SAS Institute 1993). Only variables relevant to the analysis were included in the SAS data sets. The raw data were examined for illogical entries. Minimal data cleaning was required and all corrections to the data were noted in a log. SAS programs were written to generate descriptive statistics, to compare consenters to non-consenters and to create variables for measuring types of health services utilization (see section 4.5.1). The three files were merged to perform the agreement analysis.

4.3.2 OHIP Data Collection

Identifying information for each subject providing written consent to participate in the evaluation of the self-report was provided to the Information Planning and Evaluation Branch of the Ontario Ministry of Health. A deterministic record linkage was conducted using the following variables: health card number, name, sex and date of birth. The initial linkage resulted in a 94% percent match. The five outstanding records were later matched by including the home address, resulting in a final match rate of 100%. The linkage was used to extract all OHIP fee service claims codes for these individuals for services that were delivered between October 1, 1993 and June 30 1995. The information extracted for each individual included date of birth, sex, service dates, number of services for each service date, fee schedule codes for each service date, diagnosis associated with each service code, amount paid, physician number, physician
specialty code, physician name, hospital admission date and hospital number. The data were delivered in three ASCII text files corresponding to 1993, 1994 and 1995. Diskettes were accompanied by detailed file specifications (Appendix 3). Each of the three OHIP data files was converted to a SAS data set in the same manner as the interview data files and the three data sets were merged.

4.3.3 Hospital Charts Verification

Subjects who agreed to participate in the assessment of the self-report provided written consent for viewing their hospital charts (Appendix 2). In addition, the approval of the Ethics Committee of the Chedoke-McMaster Hospitals for viewing hospital charts of PMMP participants was obtained (see section 4.6.2). Institutional regulations pertaining to access to charts and confidentiality were followed. Hospitalization is an infrequent event among patients with respiratory disease (Weiss et al. 1993; Lanes et al. 1994; Feeney et al. 1993; Melllis et al. 1991; Vollmer et al. 1994). This facilitated the verification of self-report information. The Ontario hospitals where patients reported pre-study and on-study admissions were contacted by letter by the PMMP staff. A copy of the patient's written consent to view their hospital charts was enclosed and the hospital was requested to return a copy of the chart face sheet. The face sheet information was used to verify the date and place of each admission.

4.4 COST-OF-ILLNESS ASSESSMENT

The PMMP was used as a platform to develop a set of telephone interview questions for capturing data on the cost of asthma that are not readily available from administrative sources.
The set of questions met several criteria. They were:

1. focused on "missing" economic data concerning
   - utilization of all health services, including care not publicly insured
   - health products and services requiring out-of-pocket payment
   - co-payments for drugs and devices
   - transportation costs to gain access to care
   - absenteeism and reduced productivity at work and at other activities
   - travel and waiting time

2. limited to data not already collected as part of principal questionnaire

3. clear and simple enough for telephone interview

4. structured and closed-ended to facilitate reliable responses

5. brief enough to add to the standard 30-minute telephone interview

4.4.1 Item Selection

A list of items for possible inclusion in the set of questions was compiled. The list was based on:

1. Literature review of articles describing
   i) the measurement of economic burden of illness,
   ii) the measurement of productivity losses,
   iii) the development and validation of asthma and respiratory disease symptom questionnaires.

2. Consultation with two pulmonologists, two nurses and a patient educator regarding
   the products and services that patients may purchase for controlling their asthma.

3. Discussions with nineteen asthma patients at the Firestone Clinic, St. Joseph's
   Hospital, Hamilton, and the Asthma Centre, Toronto Hospital. Patients were
   asked specifically about out-of-pocket expenses for products, services and travel,
   about extended health insurance coverage and about how asthma affects their
   productivity.
4.4.2 Item Reduction

Experienced researchers and professional interviewers were consulted to determine which items were suitable for inclusion based on the requirements listed in section 4.4. Initial versions of the questions were pre-tested with asthma patients at the Asthma Centre, Toronto Hospital, and at the Firestone Clinic, St. Joseph's Hospital, Hamilton. Pre-testing was completed with 19 face-to-face patient interviews (12 at the Asthma Centre and 7 at the Firestone Clinic). The clarity, relevance and practicality of each question was assessed by asking individual respondents to comment on their comprehension, their comfort in answering the question, their ease of recall and the question's relevance to their condition.

Items that appeared redundant, irrelevant or too difficult to answer accurately were deleted. Deleted questions included those regarding the installation of special appliances in the home or office, such as air conditioners or dehumidifiers, the purchase of educational materials, subscription to newsletters or membership in organizations, the name of the private health insurance carrier and the amount of annual premiums and/or deductibles. The wording of many questions was simplified to improve comprehension, e.g. reference to "asthma" was replaced with "breathing problems".

No resistance or refusal to answer questions was encountered. Pre-testing, including de-briefing took approximately 5-10 minutes. Subsequent to pre-testing, draft baseline and follow-up questions were prepared for field testing.
4.4.3 Field Testing

Telephone field testing of baseline economic questions was conducted to ensure proper wording and clarity prior to widespread implementation. Field testing was performed by a single PMMP interviewer with 24 pilot project participants at their 6-month interview. Nineteen adult patients and 5 parents of pediatric patients were included. The interviewer encountered no resistance or refusal to answer questions. The economic questions required approximately 2-3 minutes.

4.4.4 Implementation

After field testing was completed, the economic questions were incorporated at appropriate points into the main baseline, 3- and 6-month questionnaires. The question set developed for the thesis is included as Appendix 4. Data entry and interviews were carried out by five trained PMMP interviewers as described in sections 4.3.1.1 and 4.3.1.2. Subjects were recruited over a 5-month period and telephone interviews were conducted over a 6-month follow-up period.

4.4.5 Data Management

The same procedures that were followed for managing the data from the pilot Bronchial Inhalers project (section 4.3.1.3) were used for the main project data for the cost-of-illness analysis.

4.4.6 Item Analysis

Correlations between selected response items of the questions set, e.g. the number of doctors visits and days missed from work/usual activities and between disease severity and expenditures and indicators of health services utilization (frequency of office visits), were calculated by Spearman's correlation coefficient.
4.5 MEASUREMENT AND STATISTICAL ANALYSIS

The definitions of variables, the decision rules followed in ordering the data and the specific statistical tests used to evaluate the patient self-report and to assess the cost-of-illness are described below. Data management and statistical tests were carried out on an IBM compatible 486DX 66 MHZ personal computer using SAS 6.10 (SAS Institute 1993). Spreadsheets were maintained on Excel version 5.0.

4.5.1 Assessment of Patient Self-reports

This section describes the statistical tests used to compare the characteristics of participants to non-participants, the techniques used to define and operationalize the health services utilization variables and the inferential tests employed in the measure of agreement.

4.5.1.1 Comparison of Study Participants to Non-Participants

The samples of patients consenting and declining to participate in the reliability assessment of health services utilization were characterized according to age, sex, employment status, educational level, medications, self-reported diagnosis, smoking status, symptoms, health service use and quality of life variables. Because of wording errors in the telephone interview version of the SF-36, the social functioning domain could not be analysed. Where observed differences between respondents and non-respondents exceeded the difference deemed "clinically" significant for the purpose of the assessment, two-tailed t-tests for unpaired data and chi-square tests were performed to determine the statistical significance of the observed differences. For proportional data, Fishers Exact test was used when unstable cell counts
precluded the use of the chi-square. Contiguous categories were combined where appropriate to increase stability. Because of the small sample sizes, post-hoc power calculations were conducted to assess the statistical power of these tests.

4.5.1.2 Definition of Health Services Utilization Variables

Health services used 6-12 months prior to the study may not be recalled as accurately as services used during the 6-month follow-up period. Because of possible differences in recall accuracy, pre-study and follow-up health services utilization were analyzed separately. The different categories of resource utilization were also analyzed separately. The seven variables that were evaluated are defined in Table 5.

<table>
<thead>
<tr>
<th>Var. No.</th>
<th>Type of Service/Visit</th>
<th>Period</th>
<th>Level of Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>prior respiratory-related GP</td>
<td>6 months prior to baseline</td>
<td>dichotomous</td>
</tr>
<tr>
<td>2</td>
<td>prior respiratory specialist</td>
<td>12 months prior to baseline</td>
<td>dichotomous</td>
</tr>
<tr>
<td>3</td>
<td>respiratory-related admissions</td>
<td>12 months prior to registration</td>
<td>ordinal</td>
</tr>
<tr>
<td>4a</td>
<td>respiratory-related GP</td>
<td>6-month follow-up</td>
<td>dichotomous ordinal</td>
</tr>
<tr>
<td>4b</td>
<td></td>
<td></td>
<td>ordinal</td>
</tr>
<tr>
<td>5a</td>
<td>respiratory specialist</td>
<td>6-month follow-up</td>
<td>dichotomous ordinal</td>
</tr>
<tr>
<td>5b</td>
<td></td>
<td></td>
<td>ordinal</td>
</tr>
<tr>
<td>6a</td>
<td>ER/clinics</td>
<td>6-month follow-up</td>
<td>dichotomous ordinal</td>
</tr>
<tr>
<td>6b</td>
<td></td>
<td></td>
<td>ordinal</td>
</tr>
<tr>
<td>7a</td>
<td>admission for any reason</td>
<td>6-month follow-up</td>
<td>dichotomous ordinal</td>
</tr>
<tr>
<td>7b</td>
<td></td>
<td></td>
<td>ordinal</td>
</tr>
</tbody>
</table>

The sequence of registration and follow-up interviews and the utilization information collected at each interview are described in section 4.3.1.2. Variables 1 and 2 were analysed as
dichotomous data, indicating the presence/absence of one or more visits. Variable 3, prior respiratory admissions, was analysed as ordinal data\(^1\) based on the reported frequencies of admissions. Variables 4 - 7 were analysed dichotomously (presence/absence of service) and also ordinarily (the reported frequency of the service).

4.5.1.3 Operationalization of Health Services Utilization Variables

Prior to receipt of the raw data, the variables listed in Table 5 were operationalized based on the wording of specific interview questions and on the procedure and diagnostic codes used by the Ministry of Health to code health services.

The OHIP fee service manual was used to select codes pertaining to specific types of health services utilization (Ontario Ministry of Health 1992). The Ministry of Health uses 4-digit alphanumeric codes to classify consultations and visits, diagnostic and therapeutic procedures, surgical procedures and laboratory tests by specialty. Algorithms were created to assign OHIP fee codes to five general types of health services utilization. In the interview, patients were asked about visits to their "family physician". To be consistent with expected patients' perceptions, visits to a general practitioner, family physician or general internist were viewed as visits to a "family physician", while visits to a respirologist, a physician who performs allergy diagnostic tests (G codes) or pulmonary function testing (J codes) were equated with visits to a "lung and chest specialist". Some misclassification may have occurred due to family physicians billing for spirometry and respiratory specialists who file claims as general internists. All codes with an H

\(^1\) Evenly spaced ordinal data that is divisible is also referred to as ratio level data (McDowell and Newell 1987).
prefix were used to designate emergency care. C codes were used to designate hospitalizations. C codes associated with examinations by family practitioners and general internists indicated admissions for any reason while C codes associated with respirology consultations signified respiratory-related admissions. The coding algorithms that were used are displayed in Table 6.

Table 6. Mapping of OHIP Fee Claims Codes to Health Services

<table>
<thead>
<tr>
<th>Type of Utilization</th>
<th>OHIP Fee Service Claim Codes¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. examination by GP;</td>
<td>A001, A003, A004, A005, A006, A007, A008, A901, A905, A945, K017</td>
</tr>
<tr>
<td>by general internist;</td>
<td>A133, A134, A135, A136, A138, A435</td>
</tr>
<tr>
<td>2. examination by respirologist; allergy testing;</td>
<td>A473, A474, A475, A476, A478, A525, A623, A624, A625, A626, A628, A575</td>
</tr>
<tr>
<td>pulmonary function testing</td>
<td>G197, G206, G207, G208, G209, G213</td>
</tr>
<tr>
<td></td>
<td>J301, J304, J307, J311, J324, J327, J330*, J333, J335, J340</td>
</tr>
<tr>
<td>4. hospitalization for any reason; attended by general internist</td>
<td>C003, C004, C005, C006, C905, C132*, C133, C134, C135, C136, C435</td>
</tr>
<tr>
<td>5. hospitalization due to respiratory disorder</td>
<td>C472*, C473, C474, C475, C476, C575</td>
</tr>
</tbody>
</table>

¹ All fee service claim codes possess an A suffix (attending physician only)

These codes were used to extract information regarding health services utilization occurring during the study and recall periods from the OHIP fee claims record for each patient. Subsequent to receipt of the OHIP data files and perusal of the raw data, the algorithms were modified to include four additional relevant codes (indicated by *) to improve the accuracy of the mapping process. The specification of each selected code appears in Appendix 5.
The Ministry of Health uses 3-digit diagnostic codes to label each service. The codes pertaining to the respiratory system, 460-519 and 786, are similar to ICD-9 codes and were used to specify a GP visit as respiratory-related. The appearance of at least one such code on any service date was required to label that visit as respiratory-related. Each code is defined in Appendix 6.

Decision rules were used to attribute questionnaire items to each of the seven health services utilization variables. Similarly, precise conditions had to be met to qualify the OHIP claims as a specific type of utilization. The decision rules used for converting the interview and OHIP data into each health service category are summarized in Table 7. For each variable, all of the OHIP conditions had to be met.
Table 7. Decision Rules for Guiding Interview and OHIP Data Extraction

<table>
<thead>
<tr>
<th>Var. No.</th>
<th>Type of Service/Visit</th>
<th>Interview Questions</th>
<th>OHIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>prior respiratory-related GP</td>
<td><em>Baseline interview:</em> 1. &quot;Have you seen your family physician in the last 6 months about your breathing?&quot;</td>
<td>1. Procedure codes associated with examination by GP or general internist</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Service date within 183 days of date of baseline interview</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. OHIP diagnostic code 460-519, 786 (respiratory system)</td>
</tr>
<tr>
<td>2</td>
<td>prior respiratory specialist</td>
<td><em>Baseline interview:</em> 1. &quot;Have you seen a lung and chest specialist in the last year?&quot;</td>
<td>1. Procedure codes associated with examination by respirologist OR diagnostic test codes for allergy testing or pulmonary function testing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Service date within 365 days of date of baseline interview</td>
</tr>
<tr>
<td>3</td>
<td>respiratory-related hospitalizations</td>
<td><em>Baseline interview:</em> 1. &quot;In the last year, prior to registering in our program, were you ever hospitalized for your breathing problems?&quot; 2. &quot;Did you stay for more than 24 hours?&quot; (response must be &quot;yes&quot;) (up to 3 respiratory admissions per patient)</td>
<td>1. Procedure codes associated with hospital examination by respirologist</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Service date within 365 days of registration date</td>
</tr>
<tr>
<td>4</td>
<td>respiratory-related GP</td>
<td><em>3-month and 6-month interviews:</em> 1. &quot;Have you seen your family physician about your breathing since we last spoke on ...?&quot; 2. &quot;How many times have you been to their office?&quot;</td>
<td>1. Procedure codes associated with examination by GP or general internist</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Service date between baseline and 6-month interview</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. OHIP diagnostic code 460-519, 786 (respiratory system)</td>
</tr>
<tr>
<td>Var. No.</td>
<td>Type of Service/Visit</td>
<td>Interview Questions</td>
<td>OHIP</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------</td>
<td>----------------------</td>
<td>------</td>
</tr>
<tr>
<td>5</td>
<td>respiratory specialist</td>
<td>3-month and 6-month interviews: 1. &quot;Have you seen a lung and chest specialist about your breathing since we last spoke on...?&quot; 2. &quot;How many times have you visited the specialist?&quot;</td>
<td>1. Procedure codes associated with examination by respirologist OR diagnostic test codes for allergy testing or pulmonary function testing 2. Service date between baseline and 6-month interview</td>
</tr>
<tr>
<td>6</td>
<td>ER/clinics</td>
<td>Baseline, 3-month and 6-month interviews: 1. &quot;Have you had any new health problems since registering/last spoke?&quot; (response must be &quot;yes&quot;) 2. &quot;Did you go to the hospital?&quot; (response must be &quot;yes&quot;) 3. &quot;Did you stay for longer than 24 hours?&quot; (response must be &quot;no&quot;) (up to 5 entries per patient)</td>
<td>1. Procedure codes associated with emergency care 2. Service date between registration and 6-month interview</td>
</tr>
<tr>
<td>7</td>
<td>any hospitalization</td>
<td>Baseline, 3-month and 6-month interviews: 1. &quot;Have you had any new health problems since registering/last spoke?&quot; (response must be &quot;yes&quot;) 2. &quot;Did you go to the hospital?&quot; (response must be &quot;yes&quot;) 3. &quot;Did you stay for longer than 24 hours?&quot; (response must be &quot;yes&quot;) (up to 5 entries per patient)</td>
<td>1. Procedure codes associated with hospital examination by GP, general internist or respirologist 2. Service date between registration and 6-month interview</td>
</tr>
</tbody>
</table>
These decision rules were chosen to achieve maximum objectivity and accuracy in the measurement of each health services utilization variable.

4.5.1.4 Measurement of Agreement

The frequencies of health services utilization as determined by self-report and by OHIP were summarized in 2 x 2 (self-report vs. OHIP) contingency tables for dichotomous variables (variables 1, 2, 4a, 5a, 6a and 7a) and in multi-level contingency tables for ordinal variables (variables 3, 4b, 5b, 6b and 7b).

The proportion of observed agreement between the patient self-report and OHIP claims, $P_{oa}$, was calculated for each of the seven health services variables. For the dichotomous variables, agreement between the self-report and OHIP was measured using a simple (unweighted) kappa statistic (Fleiss 1981). The standard error and 95% confidence intervals were calculated for each unweighted kappa value as a measure of the precision of the estimate of agreement.

For ordinal variables, agreement between the self-report and OHIP-recorded frequencies was measured using a quadratic weighted kappa statistic (Streiner and Norman 1989). Weighting permits the consideration of partial agreement in the calculation of the kappa statistic. In quadratic weighting, the weight is the square of the discrepancy, with maximum weight assigned to maximum disagreement. The quadratic weighted kappa statistic is mathematically equivalent to the intra-class correlation coefficient (MacLure and Willett 1987; Kramer and Feinstein 1981). To increase the size of the cell counts and improve the power of the calculation, response levels were combined for variables 4a and 5a. The combined response groups consisted of 0, 1-
3, 4-6 and 7 or more visits. As long as \( N \geq 2g^2 \), where \( N \) represents the total sample size and \( g \) represents the number of response levels, a standard error and 95% confidence intervals can be calculated for a weighted kappa (Kramer and Feinstein 1981). Thus, indicators of precision are also presented for the ordinal variables. In accordance with Landis and Koch (1977), kappa values less than 0.40 were considered poor to fair, 0.41-0.60 moderate, 0.61-0.80 substantial and 0.81-1.00 almost perfect. The formulae for the kappa statistics, standard errors and 95% confidence intervals are displayed in Appendix 7.

The kappas for dichotomous variables 1 and 2, pre-study visits to a GP and respiratory specialist, were compared to those of variables 4 and 5, on-study visits to a GP and respiratory specialist, to determine whether the length of the recall period had an effect on the level of agreement.

4.5.2 Cost-of-illness of Asthma

4.5.2.1 Case Definition

The cost-of-illness was assessed in participants of the main Bronchial Inhalers project who were classified as asthmatic. The following criteria were applied to identify asthmatic subjects:

Inclusion Criteria

1. Prescription for an inhaled anti-asthmatic (bronchodilator, anti-inflammatory) medication in the last 4 weeks.
2. Shortness of breath (SOB), wheeze or recurrent cough reported to have ever occurred in the past.
3. Completed baseline, 3-month and 6-month interviews.
Exclusion Criteria

1. Patient was using oxygen.
2. Patient was over 55 and had a smoking history greater or equal to 20 pack-years
   (e.g. 1 pack/day x 20 years; 3 packs/day x 6.67 years)

The baseline interview questions pertaining to these inclusion/exclusion criteria are listed in Appendix 8.

4.5.2.2 Stratification

Subjects eligible for inclusion were stratified according to disease severity. Each patient was assigned to a single disease severity stratum based on his/her reported medication usage over the six-month study period. Medication information has been used previously to measure asthma disease severity but past methods were usually limited to counting the number of concomitant respiratory medications (Nguyen et al. 1996, NHLBI 1991, ATS 1986, Anie et al. 1996). Severity strata were developed based on clinical expert opinion and published Canadian prescribing guidelines (Hargreave et al. 1990). The severity strata were defined as:

**Mild**

1. Patient received bronchodilator monotherapy. Inhaled bronchodilator use did not exceed 4 puffs/day over the study period.

**Moderate**

1. Bronchodilator monotherapy exceeded 4 puffs/day during the study period
   OR
2. Inhaled anti-inflammatory (budesonide, beclomethasone, flunisolide, triamcinolone, fluticasone, cromolyn or nedocromil) monotherapy did not exceed 800 µg/day during the study period
3. The patient received two types of medication during the study period, neither of which was an oral corticosteroid. If one or both medications were inhaled anti-inflammatory agents, the combined dose did not exceed 800 $\mu$g/day.

Severe

1. The patient received one or two medications during the study period, where one was an inhaled anti-inflammatory drug with a dosage greater than 800 $\mu$g/day

OR

2. The patient received three or more types of medication during the study period, where one was an inhaled anti-inflammatory

OR

3. The patient received oral corticosteroids during the study period.

This disease severity stratification method was evaluated by calculating Spearman correlation coefficients between severity level and the number of prescriptions, medication costs, GP visits, specialist visits, the number of pulmonary function tests, admissions and the number of ER/clinic visits. The statistical significance of differences in the adjusted annual average number of prescriptions, medication costs and number of visits to GPs and specialists between severity strata were assessed with the Kruskal-Wallis test. The significance of observed differences between severity strata in the proportions of patients reporting visits to GPs and specialists, admissions and ER/clinic visits, pulmonary function tests and the use of spacers and peak flow meters was evaluated with the chi-square statistic.

4.5.2.3 Delineation of Costs

Within each severity classification, descriptive statistics were used to construct an estimate of the average annual cost of asthma from the perspectives of society, the health care system and
the patient. A cost-of-illness model was constructed to evaluate *respiratory-related* direct (medical and patient) and indirect costs from each perspective.

Costs were calculated by multiplying utilization volume by the best available cost estimate. Economic costs are preferred because accounting costs, charges, prices or reimbursements may not reflect the actual value of the resources consumed because of cross-subsidization (Freund and Dittus 1992). Since true economic costs were not available for most services and products, prices and fees (excluding taxes) were used.

Direct and indirect costs were summed to provide an overall estimate of the average annual per patient costs. Psychosocial or intangible costs were not included in the total cost-of-illness estimate, but were presented separately as quality of life results.

At the first interview, patients recalled the use of health services, out-of-pocket expenses and productivity losses over a 6 to 12 month pre-study period. Thus most cost items were measured over a 12- to 18-month duration. Assessments of medication consumption and dispensing fees were limited to the 6-month study period. All items were adjusted to annual averages.

The cost items and sources of information used in the cost-of-illness calculation for each of the three perspectives are summarized in the table below. Table 8a lists the items included in the societal perspective. Table 8b reflects the patient's out-of-pocket and indirect costs and omits health care system costs. Table 8c reflects only costs incurred to the health care system. The derivation of each cost item is explained following Table 8.
<table>
<thead>
<tr>
<th>Category</th>
<th>Item</th>
<th>Cost Information Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Costs - Medical</td>
<td>family physician visits</td>
<td>OHIP fee schedule</td>
</tr>
<tr>
<td></td>
<td>specialist visits</td>
<td>OHIP fee schedule</td>
</tr>
<tr>
<td></td>
<td>clinic/emergency room visits</td>
<td>Chedoke-McMaster Hospital</td>
</tr>
<tr>
<td></td>
<td>hospital admissions</td>
<td>Ontario case costing project</td>
</tr>
<tr>
<td></td>
<td>laboratory services</td>
<td>OHIP fee schedule</td>
</tr>
<tr>
<td></td>
<td>(pulmonary function testing)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>medication dispensing fees</td>
<td>ODB formulary, College of Pharmacists</td>
</tr>
<tr>
<td></td>
<td>prescription medications</td>
<td>ODB formulary, drug/device wholesaler</td>
</tr>
<tr>
<td></td>
<td>medical devices</td>
<td>drug/device wholesaler</td>
</tr>
<tr>
<td></td>
<td>alternative health services</td>
<td>OHIP fee schedule patient self-report</td>
</tr>
<tr>
<td>Direct Costs - Patient</td>
<td>transportation</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>babysitters and home care services</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>special recreation/exercises</td>
<td>patient self-report</td>
</tr>
<tr>
<td>Indirect Costs</td>
<td>days missed from usual activities</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>compromised days</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>travel and waiting time to access health care</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>annual wages</td>
<td>patient self-report (employed)</td>
</tr>
</tbody>
</table>
Table 8b. Cost-of-illness Assessment - Health Care System Perspective

<table>
<thead>
<tr>
<th>Category</th>
<th>Item</th>
<th>Cost Information Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Costs - Medical</td>
<td>family physician visits</td>
<td>OHIP fee schedule</td>
</tr>
<tr>
<td></td>
<td>specialist visits</td>
<td>OHIP fee schedule</td>
</tr>
<tr>
<td></td>
<td>clinic/emergency room visits</td>
<td>Chedoke-McMaster Hospital</td>
</tr>
<tr>
<td></td>
<td>hospital admissions</td>
<td>Ontario case costing project</td>
</tr>
<tr>
<td></td>
<td>laboratory services</td>
<td>OHIP fee schedule</td>
</tr>
<tr>
<td></td>
<td>medication dispensing fees</td>
<td>ODB formulary</td>
</tr>
<tr>
<td></td>
<td>prescription medications</td>
<td>ODB formulary</td>
</tr>
<tr>
<td></td>
<td>insured alternative health services</td>
<td>OHIP fee schedule</td>
</tr>
</tbody>
</table>

Table 8c. Cost-of-illness Assessment - Patient Perspective

<table>
<thead>
<tr>
<th>Category</th>
<th>Item</th>
<th>Cost Information Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct - Medical</td>
<td>prescription medications (includes</td>
<td>patient self-report, ODB formulary, drug</td>
</tr>
<tr>
<td></td>
<td>deductibles, co-payments and dispensing</td>
<td>wholesaler, College of Pharmacists</td>
</tr>
<tr>
<td></td>
<td>fees)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>medical devices</td>
<td>drug/device wholesaler</td>
</tr>
<tr>
<td></td>
<td>non-insured health services</td>
<td>patient self-report</td>
</tr>
<tr>
<td>Direct Costs - Patient</td>
<td>transportation</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>babysitters and home care services</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>special recreation/exercises</td>
<td>patient self-report</td>
</tr>
<tr>
<td>Indirect Costs</td>
<td>days missed from usual activities</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>compromised days</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>travel and waiting time to access health</td>
<td>patient self-report</td>
</tr>
<tr>
<td></td>
<td>care</td>
<td></td>
</tr>
<tr>
<td></td>
<td>annual wages</td>
<td>patient self-report (employed)</td>
</tr>
</tbody>
</table>
Direct Costs

Physician Services

The fees for general assessments recorded in the 1992 Ontario Schedule of Benefits were used to calculate the costs of physician visits (Ontario Ministry of Health 1992). These were $51.40 for the first family/general practitioner visit (consultation, code A005) in a 12-month period and $16.25 for subsequent visits (minor assessment, code A001). Specialist outpatient services were estimated at $105.40 for the first visit (consultation, code A475) and $23.10 for subsequent visits (partial assessment, code A478).

Respiratory Admissions

Costs for respiratory admissions were obtained from the Ontario case-costing project (Ontario Case Costing Project 1996). Average direct and total costs and average lengths of stay (LOS) were obtained for ICD9-CM diagnostic codes representing extrinsic asthma without status asthmaticus, code 493.00, and with status asthmaticus, code 493.01 (U.S. Department of Health and Human Services 1980). The costs were based on one year of data collected from 11 of 13 participating hospitals from October 1, 1993 to September 30, 1994. Direct costs represented the costs to the hospital for treating respiratory cases and include nursing services, laboratory and diagnostic tests and social work but excluded physician services paid for directly by OHIP. The fee charged for an inpatient specialist consultation ($105.40, code C475) was therefore added to the direct cost estimate for each admission. Total admission costs are the sum of the direct costs and indirect costs, the latter consisting of hospital overhead, housekeeping, etc. To estimate total costs, the OCCP allocated indirect costs to the direct cost centres using the Simultaneous Equation Allocation Method (OHA 1996). Both direct and total costs were used in the analysis.
and are represented as the minimum and maximum costs of respiratory admission. Since total admission costs were used in the base case cost-of-illness analysis, the admission costs in the base case cost-of-illness analysis are equivalent to the admission costs in the maximum analysis.

For each diagnostic code, costs were broken down by hospital type (teaching vs. non-teaching) and by age (0-4 years, 5-14 years, 15-70 years and 70 years and older). These age groups were selected on the basis of presumed differences in admission costs. For code diagnostic 493.00, OCCP estimates were based on 381 cases with an average inpatient total cost of $606.57 per diem. Only 16 cases of diagnostic code 493.01 were available for analysis, with an average inpatient total cost of $627.40 per diem. The number of cases of code 493.01 were too few to allow stratification of costs by hospital teaching status and age group. Thus the values associated with code 493.00 were used for all calculations.

As there was little difference in the total per diem costs between teaching and non-teaching hospitals ($585.33 vs. $607.02), the two groups were combined to improve the stability of the estimates. Average costs per diem and lengths of stay differed by age group. The following values were used in the analysis:

<table>
<thead>
<tr>
<th>Age Group (n)</th>
<th>Average LOS</th>
<th>Direct Cost Per Diem ($)</th>
<th>Total Cost Per Diem ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 4 (232)</td>
<td>2.53</td>
<td>417.55</td>
<td>631.38</td>
</tr>
<tr>
<td>5 - 14 (106)</td>
<td>2.54</td>
<td>439.92</td>
<td>626.54</td>
</tr>
<tr>
<td>15 - 70 (42)</td>
<td>3.38</td>
<td>341.54</td>
<td>487.10</td>
</tr>
<tr>
<td>70 and older</td>
<td>2.65</td>
<td>410.72</td>
<td>606.57</td>
</tr>
</tbody>
</table>

Data for only 1 case was available in the 70 and older category. As the costs of older patients could not be determined, the average costs across all age groups were substituted for this age
Patients self-reported lengths of stay were used for admissions reported at baseline. Since subsequent interviews did not record LOS information, age-specific OCCP figures were used.

ER/clinic Visits

The OCCP does not possess data on the costs of ER visits that do not result in hospital admissions. The average total cost of an emergency room visit at Chedoke-McMaster Hospital was previously estimated at $120.00 (Krahn et al. 1996). This amount includes all overhead and ancillary costs but excludes medications. No information is available on the cost of medications delivered in an emergency room/clinic setting. However, since these ER/clinic visits did not result in an admission, any drugs prescribed in the ER/clinic and filled in an outpatient pharmacy would be counted under the medication costs.

Laboratory Services

Laboratory costs consisted of pulmonary function testing (flow volume loop studies), code J304 in the 1992 OHIP Schedule of Benefits. Since they are exempt from the Independent Health Facilities Act, flow studies can be performed in the offices of general and family practitioners as well as respiratory specialists. The fee for this procedure was calculated by summing the professional component, $13.30, and the technical component, $18.60. The cost of laboratory services was calculated by multiplying the total fee, $31.90, by the number of visits to a GP and to a specialist for patients who reported "breathing into a machine" during a visit.

Dispensing Fees

Dispensing fees were assessed separately from the drug cost component for the societal and
health care system analyses. The usual and customary dispensing fees of the pharmacies where
the patients reported purchasing their medications were obtained from the College of
Pharmacists. All fees remained constant over the study period. For each reported medication, the
number of study period prescriptions was multiplied by the dispensing fee. For patients over 65
years of age, the Ontario Drug Benefits (ODB) dispensing fee of $6.11 was used. These fees
were summed to calculate the total cost of dispensing fees per patient during the study.

Medication Costs

The calculation of medication costs included all treatments that were reportedly used for
breathing disorders. These included a small number of reports for over the counter (OTC) cough,
cold and allergy medications as well as prescription antibiotics, anti-ulcer drugs and anti-
hypertensives. These constituted fewer than 5% of the total number of medications reported. The
cost calculations incorporated information provided on drug switching and new drugs added to
the patients' regimens during the study period. Drug prices were obtained from the 1995 ODB
formulary and from Drug Trading Inc., a drug wholesaler. For the latter, the purchase price from
the manufacturer at the time of the study was used. Each patient's medication costs were
calculated as follows:

1) The duration of medication consumption was determined for each drug. Although start and
end dates were not supplied, patients were asked whether they remained on or discontinued each
medication at every interview. Patients who reported commencing (ending) a treatment were
assigned a start (end) date that was halfway between the current and the last interview. The
duration was expressed in days.

2) For each medication, the size of the drug supply per prescription was estimated after
consultation with pharmacists and clinical experts. One inhaler per prescription was assumed. A one-month rule was used for nebulizer solutions and oral bronchodilators. A 10-day rule was followed for antibiotics and a 7-day rule for oral corticosteroids. The number of prescriptions for each drug was determined by multiplying the doses per day by the consumption duration and dividing by the doses per prescription. The number of prescriptions for each medication was rounded up to the next highest whole number to indicate payment for a prescription prior to consumption.

3) The cost of each medication over the course of the study was calculated by multiplying the number of prescriptions for the medication by the cost per prescription.

4) The costs for each medication were summed to yield the total medication costs per patient. As the ODB permits a 10% upcharge for retail pricing, 10% was added to the total cost of medications to reflect retail prices (Ontario Ministry of Health 1995).

Limited information was available on the dosage strength. Also, the number of doses per day was sometimes reported as a range. Minimum and maximum medication costs were therefore determined for each patient who reported the use of a drug that was available in multiple, differently-priced preparations or who reported a dose range. For the 18 reports of "prn" (as needed) usage, a dose range was determined based on the product monograph recommendations in the Compendium of Pharmaceuticals and Specialties (CPS).

Medical Devices

Medical devices consisted of spacers and peak flow meters. 1995 wholesale pricing information was procured from Drug Trading Inc. The prices used were those of the lowest priced product available. These were $21.73 for an adult peak flow meter, $38.32 for a pediatric (age under 10 years) peak flow meter, $23.13 for an adult spacer and $37.00 for an infant (age under 3 years)
 spacer. No information was collected on payments for home nebulizers.

Alternative Health Care Services

Out-of-pocket patient and health care system costs were calculated for alternative health services. Out-of-pocket costs were estimated by multiplying the number of sessions by the cost per session reported by the patient. The costs to the health care system for chiropractor and physiotherapist services were assessed by multiplying the number of visits by the OHIP basic fee of $9.65 for chiropractor care and $12.20 for physiotherapy. Out-of-pocket costs and health care system costs were summed to determine the total cost of alternative health services per patient.

Direct Patient Costs

The cost of transportation to access health care was based solely on patient reports and pertained to travel to the offices of GPs and specialists. The cost of recreation and exercise devoted to ameliorating the patient's respiratory condition was based on reported annual recreation membership fees. The costs of home care, housekeeping and child care services were based on self-reports of the number of days assistance was required and out-of-pocket payments for those services. Patients were not asked directly about provincially-funded home care services.

Indirect Costs

Indirect costs reflect the productivity loss associated with the disease. This loss was measured in days lost from productive activity as follows:
Productivity loss = \# days missed from work or usual activities + (# compromised days) \times (1 - \% level of functioning) + travel time (fraction of day) + waiting time (fraction of day)

The measurement of indirect costs requires assumptions regarding the value of the productivity loss. In the human capital method, a person's annual wage (excluding benefits) is used as a surrogate measure for the opportunity cost of time lost (Hodgson and Meiners 1982). Indirect costs are thus measured by multiplying the productivity loss days by the person's daily wages. Wages per day were estimated by dividing the reported 1995 annual salary by the number of potentially productive days per year. This was estimated by subtracting vacation time (10 work days) and legal holidays (10 work days) from the number of work days per year (260), resulting in 240 potentially productive days per year. Time spent waiting and travelling to access care was measured in hours and converted to days by dividing by 8, assuming 8 productive hours per day.

The indirect costs of unpaid labour have conventionally been assessed by assigning a wage and applying a weight, such as 0.4 (Glied 1996, Torgerson et al. 1994, Hodgson and Meiners 1982). The weight value also depends on the perspective of the analysis, since the perspective determines which losses are counted. The human capital approach was combined with a sensitivity analysis to test different assumptions regarding the value of the productivity loss for employed individuals, homemakers and other occupation categories. The impact of various weights on the opportunity cost of time was explored from the perspectives of society and the patient. The weights applied are listed below.
### Table 9a. Productivity Loss Weighting Schemes - Societal Perspective

<table>
<thead>
<tr>
<th>Occupation Category</th>
<th>Societal Perspective Indirect Cost Weighting Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method 1</td>
</tr>
<tr>
<td>Employed, no loss of pay</td>
<td>1.0</td>
</tr>
<tr>
<td>Employed, loss of pay</td>
<td>1.0</td>
</tr>
<tr>
<td>unemployed, students, retirees, disability pensioners</td>
<td>0.4</td>
</tr>
<tr>
<td>homemakers</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Method 1 represents the base case human capital method for both perspectives. From the patient perspective, the weight for the 'no loss of pay' category equals zero since the patient incurs no personal wage loss. However, for non-employed persons, the indirect costs stemming from morbidity are incurred by the patient.

At the baseline interview, employed subjects reported their annual salary within a $10,000 range, rather than the actual amount. For each subject, the median of the reported range was used in the
calculation. Wages were imputed for other non-employed individuals. Statistics Canada 1995 average annual wages were 8 to 10% lower than the sex- and age-specific means of the study sample (Statistics Canada 1994). Moreover, the study sample patient characteristics may not resemble the demographic profile upon which national average wages are based. Thus the sex- and age-specific means of the study sample were used to impute values for non-labour categories. For parent respondents (whose age and sex were unknown), the mean salary of the reported occupation category was used.

*Multi-variate Analyses*

Separate sub-group analyses were performed on persons aged 0-4 years, 5-14 years and 15 years or more. The indirect costs of pediatric patients were associated with the parent and/or caregiver rather than the patient. For the cost-of-illness analysis for subjects 0-4 years and 5-14 years, all parent/caregiver costs were assigned to the patient.

Within each of the three perspectives, multi-variate general linear models were generated to explore the potential significance of other explanatory variables on total costs. These variables included disease severity, sex, education, availability of a drug plan, smoking status and SF-36 scores. The effect of occupation was excluded from the societal and patient perspective multi-variate analyses. This variable was not an independent predictor of total costs because of its function in the calculation of indirect costs. In addition, the month of the baseline interview was assessed to determine whether season of participation influenced the total cost of asthma. Where main effects were significant, the Duncan test was used to perform pair-wise tests of significance between sub-groups (Cody and Smith 1991).
4.5.2.4 Quality of life Assessment

Psychosocial costs were expressed in terms of the impact of asthma on health-related quality of life and were represented by the eight SF-36 dimension scores. Dimensions of the SF-36 relate to physical function, social function, physical role, bodily pain, general health, vitality, emotional role and mental health. Only scores of subjects aged 18 years and older were analysed. Although the proxy responses of parents were used for the estimates of the direct and indirect costs of children, no evidence is available on the suitability of proxy SF-36 responses to permit inclusion of these data in the quality of life assessment of children.

The impact of sex, age group and disease severity on quality of life were examined in bivariate analyses. These variables were chosen to enable comparisons with population norms and published studies. Using a formula by Cohen (1988) and the observed variance of each sub-scale score in the U.S. population, Ware et al. (1993) determined samples sizes required to detect differences in scores (effect sizes) ranging from 2 to 20. In addition, Ware assessed the criterion validity of each domain by examining the effect sizes associated with clinically important differences in independent measures. Interpretation of a clinically important difference depends upon the research question and may also depend on the scale level. For example, Ware found that small differences at the lower end of the mental health scale had greater clinical significance than small changes at higher values. While Ware stated that a "clinically and socially relevant" difference for the SF-36 may be considered to be a score difference of 5 or more, he also cautions that interpretation must await the outcome of studies of small differences (Ware et al. 1993). Given the results of published SF-36 criterion validity studies and the sample sizes in this thesis research, a difference of 5 or more was considered clinically significant.
The effects of age group (18-34 years, 35-54 years, 55-64 years, 65-74 years and 75 years and older) and disease severity on SF-36 dimension scores were investigated separately using one-way ANOVA. Pairs of sub-groups were compared to reveal where differences occurred. The Duncan test was used to control for multiple comparisons. A Wilcoxon rank-sum test was used to test for differences in scores by sex. The means and standard deviations for the baseline, 3-month and 6-month scores were determined for each domain and differences between interviews were evaluated using one-way ANOVA for repeated measures. As the differences over time were not clinically significant, the average of the baseline, 3-month and 6-month scores for each domain were used in the analysis.

The relationship between quality of life and self-reported health services utilization was explored by examining correlations between SF-36 sub-scale scores and the frequency of physician visits as well as total costs.

4.6 ETHICS

4.6.1 Patient Consent

All individuals consenting to participate in the PMMP pilot or main Bronchial Inhalers project signed a written consent form after being provided with information about the project by the pharmacist (Appendix 1). This generic consent form granted permission to the researchers to view the patient's pharmacist, doctor, clinic and hospital records. Subjects enrolled in the pilot PMMP project who were eligible for the self-report assessment were mailed a cover letter, an information sheet/consent form in duplicate and a stamped self-addressed envelope (Appendix 2). All documents were geared to a 6-8th grade reading level. Subjects were asked to return one
copy of the form indicating their consent or refusal and to retain the second as an information sheet. Non-respondents were mailed a second form after 6 weeks. Those not responding 10 weeks after the initial mailing were telephoned by the individual who conducted the original PMMP interviews. All correspondence used the PMMP Centre for Evaluation of Medicines letterhead. A copy of the cover letter, consent form and information sheet was provided to the Information Planning and Evaluation Branch of OHIP with notification of the location of the signed forms. Subjects who participated in the cost-of-illness assessment provided written informed consent to participate upon registration in the main project (Appendix 1). While pharmacists were remunerated for recruiting patients into the Bronchial Inhalers Project, no compensation was offered to the subjects participating in the PMMP projects or this study.

4.6.2 Ethics Committee Approval

Approval for the PMMP was received on Dec. 3, 1992 from the McMaster Research Project Advisory Committee. In addition, approval was received on Jan. 13, 1995 from the Chedoke-McMasters Hospitals Medical Advisory Committee, permitting the viewing of hospital charts at all hospitals in the Chedoke-McMaster system. These approvals covered the basic program protocol, the consent form and the information sheet which are used in all PMMP projects. The augmentation of the PMMP with this research study did not require any changes to the protocol or original consent form. The additional study-specific cover letters and consent form and information sheet used in the assessment of the patient self-report are attached in Appendix 2. These documents, the Ph.D. study proposal and the PMMP consent form/information sheet were approved by the University of Toronto Human Subjects Review Committee on March 20, 1995. Copies of all Ethics Committee approvals from McMaster University, Chedoke-McMasters
4.6.3 Confidentiality

The names, dates of birth, sex and health card numbers of consenting subjects were released only to the OHIP research officer responsible for extracting the requested claims records. The OHIP data identified the subjects by their study numbers only. These number were used to link the OHIP claims to the interview data. During all analyses the subjects were identified only by code. Only the PMMP personnel and the investigator had access to the data and the names and health card numbers of subjects participating in the assessment of the self-report. After completion of data collection, the original signed consent forms and all documents identifying study participants were transferred to the PMMP office for storage and safe-keeping. No identifying information on subjects participating in the cost-of-illness assessment was obtained. Copies of the data and this report were made for security purposes only and were not accessible to other individuals. The confidentiality of all data generated and used in the analysis was preserved. After all analysis required for the Ph.D. dissertation and publications is completed, study data will be removed from the investigator's personal computer and downloaded to disk. Raw data diskettes and tapes will be retained in a secure place for the period stipulated by the University of Toronto, after which they will be placed in a research archive. The results of this study will form the basis of the Ph.D. dissertation. In addition to the thesis publication, the results will be submitted for presentation at a suitable health care conference and for publication in an appropriate journal. No patients are identified in the thesis or will be in any publications or presentations emanating from this study. All consenting subjects are assured of strict adherence to confidentiality in the written consent form and information sheet.
RESULTS
Chapter 5. RESULTS

The results for the assessments of the patient self-report of health services utilization and the cost of asthma are presented in separate sections of this chapter.

5.1 ASSESSMENT OF PATIENT SELF-REPORT

The assessment of the patient self-report includes an examination of patient characteristics and an analysis of the agreement between the self-report and OHIP claims data for several types of health services utilization.

5.1.1 Study Sample Characteristics

The Bronchial Inhalers pilot project enrolled 303 of 488 eligible patients who filled inhaler prescriptions at the 8 participating pharmacies between October to December 1994, resulting in an enrollment rate of 62%. Of these, 277 completed the pilot project. Of 197 participants who were eligible for the assessment of the patient self-report, 83 consented in writing, 67 declined verbally or in writing, 40 could not be reached (did not answer telephone, were out of town, address changed or telephone not-in-service) and 7 accepted verbally but did not provide written consent. Persons declining in writing cited concerns regarding confidentiality and release of the health card number, an unwillingness to participate in further research and a belief that the use of health services was insufficient to warrant inclusion.

Only subjects who provided written consent were included in the self-report assessment.
Complete baseline information was available for all 83 consenting subjects. Seventy-eight subjects completed the 3-month interview and 76 completed the 6-month interview, resulting in a drop-out rate of 8% over the 6-month follow-up period. The baseline demographics of patients consenting to participate were compared to those declining, to detect the presence of selection bias. The results are displayed in Table 10.

Table 10. Comparison of Consenters to Non-consenters

<table>
<thead>
<tr>
<th></th>
<th>Consenters (n = 83)</th>
<th>Non-consenters (n = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>males</td>
<td>32 (39 %)</td>
<td>46 (40 %)</td>
</tr>
<tr>
<td>females</td>
<td>51 (61 %)</td>
<td>68 (60 %)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>51.9 ± 19</td>
<td>47.2 ± 20</td>
</tr>
<tr>
<td><strong>Work Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>employed</td>
<td>37 (45 %)</td>
<td>50 (44 %)</td>
</tr>
<tr>
<td>retired</td>
<td>28 (34 %)</td>
<td>28 (24 %)</td>
</tr>
<tr>
<td>homemaker</td>
<td>8 (10 %)</td>
<td>14 (12 %)</td>
</tr>
<tr>
<td>student</td>
<td>6 (7 %)</td>
<td>17 (15 %)</td>
</tr>
<tr>
<td>disability pension</td>
<td>2 (2 %)</td>
<td>3 (3 %)</td>
</tr>
<tr>
<td>unemployed</td>
<td>2 (2 %)</td>
<td>2 (2 %)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>university graduate</td>
<td>16 (19 %)</td>
<td>13 (11 %)</td>
</tr>
<tr>
<td>college graduate</td>
<td>14 (17 %)</td>
<td>10 (9 %)</td>
</tr>
<tr>
<td>some university/college</td>
<td>20 (24 %)</td>
<td>25 (22 %)</td>
</tr>
<tr>
<td>secondary graduate</td>
<td>13 (16 %)</td>
<td>30 (26 %)</td>
</tr>
<tr>
<td>some secondary</td>
<td>15 (18 %)</td>
<td>27 (24 %)</td>
</tr>
<tr>
<td>primary</td>
<td>5 (6 %)</td>
<td>9 (8 %)</td>
</tr>
<tr>
<td><strong>Current smokers</strong></td>
<td>15 (18 %)</td>
<td>24 (21 %)</td>
</tr>
<tr>
<td><strong>Smoking duration (years)</strong></td>
<td>32 ± 16</td>
<td>26 ± 15</td>
</tr>
<tr>
<td><strong>Asthma self-diagnosis</strong></td>
<td>54 (65 %)</td>
<td>76 (67 %)</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOB</td>
<td>55 (75 %)</td>
<td>83 (90 %)</td>
</tr>
<tr>
<td>wheeze</td>
<td>44 (64 %)</td>
<td>68 (74 %)</td>
</tr>
<tr>
<td>recurrent cough</td>
<td>33 (67 %)</td>
<td>35 (69 %)</td>
</tr>
</tbody>
</table>
## Table 10. Comparison of Consenters to Non-consenters - cont’d

<table>
<thead>
<tr>
<th></th>
<th>Consenters (n = 83)</th>
<th>Non-consenters (n = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quality of Life (SF-36)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>physical function</td>
<td>80.7 ± 21.4</td>
<td>83.2 ± 17.4</td>
</tr>
<tr>
<td>role-physical</td>
<td>76.2 ± 36.2</td>
<td>78.7 ± 33.3</td>
</tr>
<tr>
<td>bodily pain</td>
<td>74.9 ± 23.9</td>
<td>79.9 ± 25.6</td>
</tr>
<tr>
<td>general health</td>
<td>69.2 ± 23.7</td>
<td>69.1 ± 25.1</td>
</tr>
<tr>
<td>vitality</td>
<td>57.9 ± 19.1</td>
<td>60.0 ± 19.2</td>
</tr>
<tr>
<td>role-emotional</td>
<td>89.6 ± 26.0</td>
<td>84.8 ± 30.4</td>
</tr>
<tr>
<td>mental health</td>
<td>79.3 ± 14.6</td>
<td>76.4 ± 18.8</td>
</tr>
<tr>
<td><strong>Respiratory Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Number (%) of prescriptions</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BD</td>
<td>85 (54 %)</td>
<td>107 (52 %)</td>
</tr>
<tr>
<td>IAI</td>
<td>72 (45 %)</td>
<td>95 (46 %)</td>
</tr>
<tr>
<td>OS</td>
<td>2 (1 %)</td>
<td>4 (2 %)</td>
</tr>
<tr>
<td><em>Number (%) of patients</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BD alone</td>
<td>14 (17 %)</td>
<td>27 (24 %)</td>
</tr>
<tr>
<td>BD + IAI</td>
<td>57 (69 %)</td>
<td>62 (54 %)</td>
</tr>
<tr>
<td>IAI alone</td>
<td>10 (12 %)</td>
<td>21 (18 %)</td>
</tr>
<tr>
<td>BD + IAI + OS</td>
<td>1 (1 %)</td>
<td>4 (4 %)</td>
</tr>
<tr>
<td>BD + OS</td>
<td>1 (1 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td><strong>Health Services Utilization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pre-study</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP visit in last 6 months</td>
<td>46 (55 %)</td>
<td>65 (57 %)</td>
</tr>
<tr>
<td>specialist visit in last year</td>
<td>28 (34 %)</td>
<td>36 (32 %)</td>
</tr>
<tr>
<td>respiratory admission in last year</td>
<td>3 (4 %)</td>
<td>5 (4 %)</td>
</tr>
<tr>
<td><em>On-study</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP visit</td>
<td>26 (33 %)</td>
<td>37 (35 %)</td>
</tr>
<tr>
<td>specialist visit</td>
<td>14 (18 %)</td>
<td>16 (15 %)</td>
</tr>
<tr>
<td>emergency room visit</td>
<td>16 (19 %)</td>
<td>21 (18 %)</td>
</tr>
<tr>
<td>admission (any reason)</td>
<td>4 (5 %)</td>
<td>5 (4 %)</td>
</tr>
</tbody>
</table>

Values are expressed as numbers of persons (percentage in parentheses) or as means ± standard deviations.

Abbreviations: SOB = shortness of breath; BD = bronchodilator; IAI = inhaled anti-inflammatory; OS = oral steroid; GP = general practitioner

1. Symptoms reported in 6 months prior to study start
2. The SF-36 is a generic health status instrument which measures functional status and well-being according to 8 multi-item domains. The social functioning domain was omitted because of wording errors in the questionnaire.
3. Number of persons reporting

Due to the small group sizes, there was insufficient power to assess the statistical significance of observed differences between the two groups at the β=0.20 level. However, all observed
differences were small and below the threshold of a "clinically" important difference, i.e. one that would be expected to affect the recall of health services utilization.

The 5-year difference in age between the consenters and non-consenters in this age range was not expected to result in significantly different recall of health services utilization. The work status distribution were similar; there was a higher proportion of retired persons in the study sample and a slightly smaller proportion of students. It appeared that the consenters achieved higher levels of education. This may have had an impact on the recall of health services utilization. The consenters reported fewer asthma symptoms in the last 6 months. Although the observed difference in the frequency of shortness of breath was statistically significant, the difference was small and would not be expected to result in less utilization of health services among consenters. Use of anti-asthmatic medications and the reported pre-study and on-study use of health services were similar between the two groups. The on-study use of emergency room/outpatient clinics was similar to the frequency of patients reporting visits to a respiratory specialist. Few patients reported pre-study respiratory admissions or on-study admissions for any reason.

5.1.2 Self-report of Hospital Admissions

Seven patients self-reported pre-study respiratory admissions or on-study admissions for any reason. The date and place of each admission were checked against information on the hospital chart face sheet. If the month, year and place of admission matched the information on the face sheet, the self-report was deemed confirmed. These admissions are described in Table 11.
Table 11. Validation of Self-reported Hospital Admissions

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Interview Date</th>
<th>Self-report Place</th>
<th>Type of Admission</th>
<th>Hospital Face Sheet Date</th>
<th>Confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>797</td>
<td>baseline</td>
<td>94/10/10</td>
<td>England</td>
<td>N/A</td>
<td>no</td>
</tr>
<tr>
<td>1116</td>
<td>baseline</td>
<td>94/08/04</td>
<td>St. Joseph's, Hamilton</td>
<td>93/12/21 bronchoscopy</td>
<td>uncertain*</td>
</tr>
<tr>
<td>1300</td>
<td>baseline</td>
<td>94/06/01</td>
<td>McMaster</td>
<td>94/6/11</td>
<td>yes</td>
</tr>
<tr>
<td>255</td>
<td>baseline</td>
<td>94/11/01</td>
<td>Joseph Brant</td>
<td>94/11/03</td>
<td>yes</td>
</tr>
<tr>
<td>1144</td>
<td>baseline</td>
<td>94/12/11</td>
<td>Henderson</td>
<td>94/12/11</td>
<td>yes</td>
</tr>
<tr>
<td>212</td>
<td>6-month</td>
<td>95/03/13</td>
<td>Joseph Brant</td>
<td>95/03/09</td>
<td>yes</td>
</tr>
<tr>
<td>1117</td>
<td>6-month</td>
<td>95/03/31</td>
<td>Chedoke-McMaster</td>
<td>95/03/20</td>
<td>yes</td>
</tr>
</tbody>
</table>

N/A = not available
* study no. 1116 pre-study respiratory admission on 94/08/04 was confirmed by OHIP claims records.

Of the three reported pre-study respiratory admissions, confirmation was attempted only for the two that took place in Ontario. Although the admission of subject number 1116 on 94/08/04 was not confirmed by the hospital chart face sheet, the admission date was recorded in the OHIP claims records for this patient.

Two of the four on-study admissions were reported at baseline and took place in the 1-month interval between registration and the baseline interview. All four admissions were confirmed. The slight discrepancies between patient reports of admission dates and information on the hospital face sheet may be due to the fact that patients were reporting discharge dates or the dates of the significant hospital procedure while the face sheet recorded the date of admission. In all cases, the month was correct.
5.1.3 Agreement Analysis

The inter-rater reliability of patient self-reports of health services utilization was assessed by measuring the agreement between patient responses and OHIP fee claims data. Although linkage of patient health card numbers and basic identification resulted in a 100% match with the OHIP claims database, there was one subject for whom no claims were reported during the study period, despite self-reports of health services usage. This subject was retained in the analysis.

The agreement between patient self-reports and the OHIP claims records for each of the 7 health services utilization variables displayed in Table 10 was expressed as observed agreement, $P_o$, and the proportion of chance-corrected agreement, kappa. Values of $P_o$ and kappa were estimated from contingency tables depicting the frequency distributions for each category of health services. Each contingency table, displayed as Figures 2 - 8b, represents the measurement of health services utilization using the two data sources - self-report and OHIP.

Figure 2. Variable 1. Reports of one or more respiratory-related visits to a family physician/general practitioner in the 6 months prior to baseline interview

<table>
<thead>
<tr>
<th>Self-report</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>38</td>
</tr>
</tbody>
</table>

The reports of 32 of the 46 subjects who recalled one or more visits to a GP in the six months prior to the study were confirmed by OHIP records. Complete agreement between the two data sources was found for 56 of 83 subjects, resulting in a $P_o$ of 0.67. There were similar amounts of
under- and over-reporting. Chance-corrected agreement was fair but significantly better than
chance alone, with kappa equal to 0.34, and a 95% CI of [0.14, 0.55].

Figure 3. Variable 2. Reports of one or more visits to a respiratory specialist in the 12
months prior to baseline interview

<table>
<thead>
<tr>
<th></th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Self-report</td>
<td>28</td>
<td>55</td>
</tr>
<tr>
<td>Yes</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>No</td>
<td>6</td>
<td>49</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>53</td>
</tr>
</tbody>
</table>

The agreement was better for pre-study visits to a respiratory specialist than to a GP. The
observed agreement, \( P_o \), was 0.88 while kappa demonstrated substantial agreement, 0.74 with
95% CI [0.58, 0.89]. There were similar amounts of under-and over-reporting.

Figure 4. Variable 3. Reports of respiratory-related admissions in Ontario in 12 months
prior to registration

<table>
<thead>
<tr>
<th>No. Visits</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Self-report</td>
<td>81</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>2</td>
</tr>
</tbody>
</table>

Examination of the 2 pre-study respiratory-related admissions reported to occur in Ontario
revealed perfect agreement between the two data sources, with both \( P_o \) and kappa equal to 1.00.

The remaining variables pertained to on-study use of health services that occurred during the 6-
month follow-up period. The reports of on-study visits to GPs, respiratory specialists, ER/clinics and admissions were analysed dichotomously and ordinally. The analysis of the on-study variables was limited to the 76 subjects who completed the 6-month interviews.

Figure 5a. Variable 4a. Reports of one or more respiratory-related visits to a family physician/general practitioner between the baseline and 6-month interviews

<table>
<thead>
<tr>
<th>Self-report</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>36</td>
</tr>
</tbody>
</table>

Only 26 subjects reported one or more on-study visits to a GP; 22 of these were confirmed by OHIP. The sizable observed agreement, 0.71, conceals considerable under-reporting. Eighteen subjects (24%) who did not report a respiratory-related GP visit were documented to have had one according to their OHIP claims. This deviation from high observed agreement is evident in the moderate value for kappa, 0.43, with a 95% CI of [0.23, 0.63].

Figure 5b represents the frequency distributions for the number of reported respiratory-related visits to a GP during the prospective follow-up period. The diagonal, representing perfect agreement, is in boldface and the off-diagonal cells are shaded. To improve cell stability, response groups were combined into 1-3 visits, 4-6 visits and 7 or more visits. (Increasing the number of response groups results in a loss of power - the confidence intervals exceed 1.00 as the cell counts are reduced and weighted disagreement is increased.)
Figure 5b. Variable 4b. Reports of respiratory-related visits to a family physician/general practitioner between the baseline and 6-month interviews

<table>
<thead>
<tr>
<th>Self-report</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-1</td>
<td>2-4</td>
</tr>
<tr>
<td>0</td>
<td>32</td>
<td>18</td>
</tr>
<tr>
<td>1-3</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>4-6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>34</td>
</tr>
</tbody>
</table>

The values of the marginals and the location of most of the shaded cells above the diagonal suggest under-reporting of visits. Two patients who reported 6 and 11 respiratory-related GP visits experienced 8 and 12 visits respectively according to OHIP records and data extraction criteria. The observed agreement between the two data sources was 0.65 and the weighted kappa was only fair, 0.24 with 95% CI [0, 0.48].

Figure 6a. Variable 5a. Reports of one or more visits to a respiratory specialist between the baseline and 6-month interviews

<table>
<thead>
<tr>
<th>Self-report</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
<td>58</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>59</td>
</tr>
</tbody>
</table>

Like the pre-study respiratory specialist visits, on-study visits displayed high levels of agreement, with $P_e$ equal to 0.93 and kappa equal to 0.80, 95% CI [0.63, 0.97], representing substantial agreement. Only four patients did not report visits that were documented in the OHIP database.
Figure 6b represents the frequency distributions for on-study visits to a respiratory specialist. The diagonal, representing perfect agreement, is in boldface and the off-diagonal cells are shaded. To preserve cell stability and power, response groups were combined into 1-3 visits, 4-6 visits and 7 or more visits.

The boldface diagonal indicates a $P_o$ of 0.92 for the frequency of on-study visits to a respiratory specialist. Despite the high observed agreement, the weighted kappa was only 0.47, 95% CI[0.16, 0.78] indicating a moderate but significant level of agreement between the two data sources. The kappa value was lowered by one patient who self-reported 8 visits to a respiratory specialist but was observed to have none according to the patient's OHIP records. Upon closer examination, the OHIP data revealed that this patient did have numerous physician visits, but they could not be classified as visits to a respiratory specialist because they lacked the designated specialist or diagnostic test code specified by the data extraction criteria (Table 7). A second patient who reported 11 visits had only 7 visits recorded in the OHIP claims database.
Figure 7a. Variable 6a. Reports of one or more ER/clinic visits for any reason between registration and the 6-month interview

<table>
<thead>
<tr>
<th>Self-report</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>70</td>
</tr>
</tbody>
</table>

While the on-study recall of visits to an ER/clinic demonstrated reasonable observed agreement with $P_o$ equal to 0.76, the kappa estimate of agreement was only slightly better than chance, 0.08 with 95% CI [-0.30, 0.45]. Thirteen percent more patients self-reported an ER/visit than was evident from OHIP claims data. In addition, Feinstein and Cichetti (1990) have shown that when the marginals are symmetrically unbalanced, as they are in this case, the kappa value is artificially reduced.

Figure 7b. Variable 6b. Reports of ER/clinic visits for any reason between registration and the 6-month interview

<table>
<thead>
<tr>
<th>Self-report</th>
<th>No. Visits</th>
<th>OHIP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

Disaggregating the visits to ER/clinics into frequency distributions revealed similar results with $P_o$ and weighted kappa equal to 0.76 and 0.04, respectively, 95% CI [-0.46, 0.53].
Recall of hospital admission for any reason during the prospective follow-up demonstrated extremely good agreement with OHIP records. Observed agreement, P₀, was 0.97 and kappa was substantial, 0.74, with 95% CI [0.38, 1.10]. The small cell counts reduced the power of the calculation of the standard error of kappa, resulting in an upper 95% CI slightly exceeding 1.00.

As seen with the dichotomous variable, the observed agreement between the reported number of admissions and OHIP records was excellent, with P₀ equal to 0.96. The chance-corrected agreement was moderate with weighted kappa equal to 0.48. Because of the small cell counts, there was insufficient power to calculate a 95% CI.
The values of \( P_o \) and kappa for each health services variable are summarized in Table 12.

Table 12. Summary of Agreement Analysis

| Type of Service/Visit | Variable Type | \( P_o \) | \( \kappa \) | 95% CI | L&K Class
|----------------------|---------------|----------|------------|--------|------------------------
| prior respiratory-related GP | dichotomous | 0.67 | 0.34 | [0.14, 0.55] | fair |
| prior respiratory specialist | dichotomous | 0.88 | 0.74 | [0.58, 0.89] | substantial |
| prior respiratory admission | ordinal | 1.00 | 1.00 | [1.00, 1.00] | perfect |
| on-study respiratory-related GP | dichotomous | 0.71 | 0.43 | [0.23, 0.63] | moderate |
| on-study respiratory specialist | ordinal | 0.65 | 0.24* | [0.00, 0.48] | fair |
| on-study ER/clinic | dichotomous | 0.93 | 0.80 | [0.63, 0.97] | substantial |
| on-study admission | ordinal | 0.92 | 0.47* | [0.16, 0.78] | moderate |
| on-study admission | ordinal | 0.76 | 0.08 | [-0.30, 0.45] | slight |
| on-study admission | ordinal | 0.76 | 0.04* | [-0.46, 0.53] | slight |
| on-study admission | ordinal | 0.97 | 0.74 | [0.38, 1.10] | substantial |
| on-study admission | ordinal | 0.96 | 0.48* | | moderate |

1 Observed agreement, not corrected for chance
2 95% confidence interval that includes 0 indicates that agreement is not statistically significantly better than chance.
3 Landis & Koch classification of strength of observed agreement
  * quadratic weighted kappa

The proportions of observed agreement were strong for all variables except respiratory-related GP visits. Observed agreement was slightly better for on-study GP visits compared to pre-study visits (0.71 vs. 0.67). The lowest value of \( P_o \), 0.65, was observed with the reported frequency of on-study respiratory-related visits to GPs.
Five of seven health services utilization variables displayed values of kappa that were moderate or better. When the value of kappa was plotted against the type of health services utilization (Figure 9), a gradient in the level of agreement was apparent.

Figure 9. Health Services Utilization Agreement Gradient

In general, agreement was highest for those types of health services that were the most rare and significant from the patient's perspective, hospital admissions and visits to a respiratory specialist. One would expect these events to be recalled with greater accuracy than visits to a generalist. One might also have expected visits to an ER/clinic to demonstrate high agreement.
due to the significance of this health outcome, however, this was not observed in this study.

The on-study utilization variables measured the use of health services over the prospective follow-up period, with interviews at 1, 3 and 6 months after registration. The longest period of recall during the follow-up period was the 3-month interval between the 3- and 6-month interviews. In contrast, recall of prior use of health services extended 6-12 months, depending on the variable. P₀ and kappa were higher for variables pertaining to on-study visits to a respiratory specialist and GP compared to the pre-study recall of these types of health services. Although agreement for prior respiratory admissions was higher than on-study admissions, the wide confidence intervals around the weighted kappa for on-study admissions indicate that the difference was not significant.

5.2 ASTHMA COST-OF-ILLNESS ASSESSMENT

This section begins with an examination of the characteristics of the cost-of-illness study sample, followed by the results of the disease severity stratification. Subsequent sections are devoted to displaying the cost-of-illness results from the perspectives of society, the health care system and the patient. Finally, the psychosocial costs, expressed in terms of health-related quality-of-life measurements, are presented.

5.2.1 Study Sample Characteristics

During the main Bronchial Inhalers project, participating pharmacists approached 3,074 eligible study candidates, 2,078 subjects of whom consented to enroll, resulting in a 68% response rate.
A total of 1,588 inhaler users successfully completed the study between May 1995 and March 1996. To reduce the probability of including subjects with acute bronchitis or chronic obstructive pulmonary disease (COPD), 99 subjects who either had no asthma symptoms or were using oxygen were eliminated from the analysis. An additional 210 subjects who were older than 55 years and who reported at least 20 pack-years of smoking were eliminated, as these subjects were most likely suffering from COPD rather than asthma. This resulted in a study sample of 1279 subjects.

The characteristics of the study sample are summarized in Table 13.
Table 13. Cost-of-Illness Study Sample Characteristics in 1995-96

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>530 (41.4)</td>
</tr>
<tr>
<td>F</td>
<td>749 (58.6)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>4 years or less</td>
<td>88 (6.9)</td>
</tr>
<tr>
<td>5 to 14 years</td>
<td>251 (19.6)</td>
</tr>
<tr>
<td>15 to 34 years</td>
<td>342 (26.8)</td>
</tr>
<tr>
<td>35 to 54 years</td>
<td>361 (28.2)</td>
</tr>
<tr>
<td>mean age, years</td>
<td>34.2 ± 22.1</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>college graduate</td>
<td>253 (19.8)</td>
</tr>
<tr>
<td>some college</td>
<td>157 (12.3)</td>
</tr>
<tr>
<td>secondary graduate</td>
<td>249 (19.5)</td>
</tr>
<tr>
<td>some secondary</td>
<td>236 (18.5)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>employed full-time</td>
<td>481 (37.6)</td>
</tr>
<tr>
<td>employed part-time</td>
<td>192 (15.0)</td>
</tr>
<tr>
<td>homemaker</td>
<td>218 (17.0)</td>
</tr>
<tr>
<td>retired</td>
<td>156 (12.2)</td>
</tr>
<tr>
<td>1995 Annual salary, full- and part-time employed persons (n = 674)</td>
<td></td>
</tr>
<tr>
<td>less than $20,000</td>
<td>168 (25.0)</td>
</tr>
<tr>
<td>$20,001 to $30,000</td>
<td>130 (19.3)</td>
</tr>
<tr>
<td>$30,001 to $40,000</td>
<td>110 (16.3)</td>
</tr>
<tr>
<td>$40,001 to $50,000</td>
<td>69 (10.2)</td>
</tr>
<tr>
<td>$50,001 to $60,000</td>
<td>53 (7.9)</td>
</tr>
<tr>
<td>more than $60,000</td>
<td>42 (6.2)</td>
</tr>
<tr>
<td>refused to answer</td>
<td>102 (15.1)</td>
</tr>
<tr>
<td>Drug plan</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>1132 (88.5)</td>
</tr>
<tr>
<td>no</td>
<td>138 (10.8)</td>
</tr>
<tr>
<td>unknown</td>
<td>9 (0.7)</td>
</tr>
<tr>
<td>Drug plan that requires co-payment (n = 1132)</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>403 (35.6)</td>
</tr>
<tr>
<td>no</td>
<td>729 (64.4)</td>
</tr>
<tr>
<td>Medical History</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>current smoker</td>
<td>226 (17.7)</td>
</tr>
<tr>
<td>prior smoker</td>
<td>267 (20.9)</td>
</tr>
<tr>
<td>never smoked</td>
<td>786 (61.4)</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>shortness of breath</td>
<td>1108 (86.6)</td>
</tr>
<tr>
<td>wheeze</td>
<td>1089 (85.1)</td>
</tr>
<tr>
<td>cough</td>
<td>807 (63.1)</td>
</tr>
<tr>
<td>Disease Severity</td>
<td></td>
</tr>
<tr>
<td>mild</td>
<td>352 (27.5)</td>
</tr>
<tr>
<td>moderate</td>
<td>630 (49.3)</td>
</tr>
<tr>
<td>severe</td>
<td>297 (23.2)</td>
</tr>
</tbody>
</table>
Table 13. Cost-of-Illness Study Sample Characteristics - cont'd

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication consumption over 6-month study period</strong></td>
<td></td>
</tr>
<tr>
<td>bronchodilator alone</td>
<td>255 (19.9)</td>
</tr>
<tr>
<td>inhaled anti-inflammatory alone</td>
<td>119 (9.3)</td>
</tr>
<tr>
<td>bronchodilator and inhaled anti-inflammatory</td>
<td>849 (66.4)</td>
</tr>
<tr>
<td>inhaled anti-inflammatory and oral corticosteroid</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>bronchodilator and inhaled anti-inflammatory and oral corticosteroid</td>
<td>55 (4.3)</td>
</tr>
</tbody>
</table>

**Health Services Utilization**

<table>
<thead>
<tr>
<th>General/Family practitioner visits during prior 6 months and 6-month study period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>313 (24.5)</td>
</tr>
<tr>
<td>1 - 2</td>
<td>521 (40.7)</td>
</tr>
<tr>
<td>3 - 5</td>
<td>285 (22.3)</td>
</tr>
<tr>
<td>6 - 10</td>
<td>112 (8.8)</td>
</tr>
<tr>
<td>11 - 20</td>
<td>38 (3.0)</td>
</tr>
<tr>
<td>21 - 39</td>
<td>8 (0.6)</td>
</tr>
<tr>
<td>unknown</td>
<td>2 (0.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory specialist visit during prior year and 6-month study period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>893 (69.8)</td>
</tr>
<tr>
<td>1 - 2</td>
<td>253 (19.8)</td>
</tr>
<tr>
<td>3 - 5</td>
<td>90 (7.0)</td>
</tr>
<tr>
<td>6 - 10</td>
<td>32 (2.5)</td>
</tr>
<tr>
<td>11 - 20</td>
<td>9 (0.7)</td>
</tr>
<tr>
<td>21 - 39</td>
<td>2 (0.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Use of alternative health professional during prior year</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>yes</td>
<td>56 (4.4)</td>
</tr>
<tr>
<td>no</td>
<td>1223 (95.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory-related admissions during 12 months prior to study and 6-month study period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>1185 (92.7)</td>
</tr>
<tr>
<td>one admission</td>
<td>69 (5.4)</td>
</tr>
<tr>
<td>two admissions</td>
<td>17 (1.3)</td>
</tr>
<tr>
<td>three admissions</td>
<td>7 (0.5)</td>
</tr>
<tr>
<td>four admissions</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory-related ER/clinic visits during 12 months prior to study and 6-month study period</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>1166 (91.2)</td>
</tr>
<tr>
<td>one visit</td>
<td>96 (7.5)</td>
</tr>
<tr>
<td>two visits</td>
<td>17 (1.3)</td>
</tr>
</tbody>
</table>
The majority of patients were female (59%) and between 15 to 54 years (55%). Due to the inclusion of infants and children, the sample's mean age was quite young - 34 years. Fifty-three per cent were employed while homemakers comprised 17% of the sample. A large majority (89%) had insurance that paid for medications, although 36% of these patients were required to make co-payments.

Current or prior smokers comprised 39% of the sample and the asthma symptoms most frequently reported were shortness of breath and wheeze. Patients classified as mild asthmatics accounted for 28% of the sample, moderate asthmatics, 49%, and severe asthmatics, 23%. Most patients (66%) reported using both a bronchodilator and an inhaled anti-inflammatory medication, although 20% received bronchodilator monotherapy.

GP visits prior to or during the study were reported by 75% of the sample, with 41% reporting 1-2 visits. Only 31% of the sample reported a visit to a specialist in the year before or during the study period. Overall, 82% of the sample saw a GP or a specialist during the pre-study and follow-up periods. This is similar to the rate of 70% observed in the Ontario Health Survey for visits to physician in the prior 12 months (Decker et al. 1995). During the 18-month recall period, 94 patients (7%) reported 128 respiratory admissions. During the same period, 130 patients (9%) reported 113 ER clinic visits that did not result in a hospital admission.

5.2.2 Disease Severity Stratification

Table 14 indicates that disease severity was highly correlated with the number of prescriptions and medication costs.
Table 14. Correlations Between Utilization and Disease Severity

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N</th>
<th>Spearman Correlation Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of prescriptions</td>
<td>1279</td>
<td>0.69</td>
<td>0.0001</td>
</tr>
<tr>
<td>Medication costs ($)</td>
<td>1279</td>
<td>0.64</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of visits to specialist</td>
<td>1279</td>
<td>0.28</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of pulmonary function tests</td>
<td>1277</td>
<td>0.22</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of visits to general practitioner</td>
<td>1277</td>
<td>0.18</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of respiratory admissions</td>
<td>1279</td>
<td>0.14</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of admissions for any reason</td>
<td>1279</td>
<td>0.12</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of respiratory ER visits</td>
<td>1279</td>
<td>0.08</td>
<td>0.0025</td>
</tr>
<tr>
<td>No. of ER visits for any reason</td>
<td>1279</td>
<td>0.06</td>
<td>0.0265</td>
</tr>
</tbody>
</table>

The high correlation coefficients for these two variables are partly explained by the definition of asthma severity, which considers the number of different types of medications (but not the prescription volume for each drug). Evidence of the validity of the severity stratification scheme is suggested by the positive and significant correlations with various types of health services utilization, particularly visits to specialists. These results are summarized in Table 15 and Figures 10-12.
Table 15. Variation of Medication Utilization with Disease Severity

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Disease Severity Level</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild (N = 352)</td>
<td>Moderate (N = 630)</td>
</tr>
<tr>
<td>No. of prescriptions</td>
<td>5.0 ± 3.3</td>
<td>13.2 ± 9.4</td>
</tr>
<tr>
<td>Medication costs ($)</td>
<td>101.83 ± 152.20</td>
<td>324.94 ± 351.90</td>
</tr>
</tbody>
</table>

Values represent annual averages. P values are from Kruskal-Wallis test.

There was a five-fold difference in the mean number of prescriptions per patient per year between mild and severe patients. Medication costs increased approximately three-fold between each severity stratum, with average annual medication costs in severe patients reaching $837.

As seen in Figure 10, the average annual number of physician visits (GPs and specialists) per patient ranged from 2.2 in mild patients to 5.1 in severe asthmatics.

Figure 10. Annual Number of Physician Visits Stratified by Severity

The proportion of patients reporting respiratory-related health services utilization increased with severity for each type of health service (Figure 11).
The widest variation in reported usage was observed for specialist visits, which ranged from 15% of mild subjects to 48% of severe subjects. The occurrence of ER/clinic visits for the year prior to the study varied from 1% to 5% in mild and severe patients and the incidence of admissions for the year prior to the study ranged from 2% in mild patients to 11% in severe patients. These patients also reported severity-related increases in ER/clinic visits for any reason (21% to 27%) and admissions for any reason (4% to 14%). Figure 12 portrays the increased reliance on spacers and peak flow meters with increasing disease severity.

Figure 11. Respiratory-related Health Services Utilization Stratified by Severity

![Respiratory Health Services](image)

Figure 12. Use of Respiratory Devices Stratified by Severity

![Use of Respiratory Devices](image)
Differences between the proportions of patients in the severity strata depicted in Figures 10, 11 and 12 were statistically significant by chi-square tests.

5.2.3 Asthma Cost-of-Illness Results

The breakdown of each item in the overall cost-of-illness model is initially presented. Following this, the asthma cost-of-illness results are displayed separately for the societal, health care system and patient perspectives. Within each perspective, the cost components are presented as the proportions of direct and total costs in the sample. The average direct and indirect costs per patient per year are then presented, stratified by significant explanatory variables. The sections on the societal and patient perspectives include the results of sensitivity analyses on the value of indirect costs. The final section describes the psychosocial costs, in terms of SF-36 health-related quality of life scores, broken down by sex, age group and disease severity.

The cost-of-illness model consists of direct costs (medical and patient) and indirect costs. Direct medical costs include physician services, hospital admissions, pulmonary function tests, dispensing fees, drugs, devices and alternative health services. Direct patient costs consist of out-of-pocket expenses for transportation and parking to access care and recreational services purchased to alleviate the symptoms of asthma. Indirect costs are based on the value of days lost from work or other activities, restricted days and the travel and waiting time to access care. Each cost item, the number of patients reporting the item, the associated price or fee and the average annual utilization are summarized in Table 16.
Table 16. Average Price and Volume for Each Cost-of-Illness Item

<table>
<thead>
<tr>
<th>Category</th>
<th>Item</th>
<th># patients reporting (%)</th>
<th>Price or fee per service ($)</th>
<th>Utilization per person reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Costs - Medical</td>
<td>family physician visits</td>
<td>964 (75)</td>
<td>1st visit: 51.40</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>additional visits: 16.25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>specialist visits</td>
<td>386 (30)</td>
<td>1st visit: 105.40</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>additional visits: 23.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>clinic/emergency room visits</td>
<td>113 (9)</td>
<td>120</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>hospital admissions</td>
<td>94 (7)</td>
<td>per diem</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>laboratory services</td>
<td>413 (32)</td>
<td>direct: 342 - 440</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>total: 487 - 631</td>
<td></td>
</tr>
<tr>
<td></td>
<td>medication dispensing fees</td>
<td>1279 (100)</td>
<td>6.11 - 11.49</td>
<td>14.3</td>
</tr>
<tr>
<td></td>
<td>prescription medications ^1</td>
<td>1279 (100)</td>
<td>0.30 - 95.52</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>medical devices: spacer</td>
<td>357 (28)</td>
<td>23.10 - 37.00</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>peak flow monitor</td>
<td>109 (9)</td>
<td>21.73 - 38.32</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>alternative health services</td>
<td>56 (4)</td>
<td>3.00 - 100.00</td>
<td>18.8</td>
</tr>
<tr>
<td></td>
<td>out-of-pocket insured</td>
<td></td>
<td>9.65 - 12.20</td>
<td></td>
</tr>
<tr>
<td>Direct costs - Patient</td>
<td>transportation to access health care</td>
<td>227 (18)</td>
<td>0.25 - 32.00</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>special recreation/exercises</td>
<td>38 (3)</td>
<td>annual fee: 12.00</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12.00 - 1200.00</td>
<td></td>
</tr>
<tr>
<td>Indirect Costs</td>
<td>days missed from work/activities</td>
<td>767 (60)</td>
<td>17.66 - 254.17</td>
<td>21.1</td>
</tr>
<tr>
<td></td>
<td>travel - waiting time (days)</td>
<td>931 (73)</td>
<td>17.66 - 254.17</td>
<td>0.7</td>
</tr>
</tbody>
</table>

1 annual average
2 Utilization = number of prescriptions per patient
3 Price = range of prices for a medication. Utilization = number of different medications per person

The utilization represents the adjusted average annual volume in patients reporting the service or expense at baseline or subsequent interviews. Average hospital admissions and ER/clinic visits are less than one since they were adjusted from an 18-month to a 12-month period. There were, on average, 14 prescriptions filled per patient per year and each patient was treated with an average of 2 different types of medications. Among the small proportion of alternative health
care users (4% of the sample), patients reported an average of 19 sessions per year. Only 18% of the sample incurred transportation costs. These patients took an average of 5 round trips per year for physician services. The 767 patients (60%) reporting a work/usual activity loss, experienced an average of 21 lost days per year.

5.2.3.1 Societal Perspective

In the societal perspective, all costs are counted regardless of the payer. Including the societal perspective permits comparisons with other economic assessments of asthma and other diseases. The unadjusted average annual direct costs were $1,273 per patient. The relative contributions of the components of the direct costs to the cumulative costs of the whole sample are portrayed in Figure 13.

Figure 13.  Direct Cost Components - Societal Perspective

The largest cost component was hospital admissions, accounting for 47% of the direct costs of
the sample. Taken together, medications and dispensing fees contributed to 40% of direct costs. Physician services, which consisted of GP, specialist and ER/clinic visits, represented 9% of direct costs. The use of alternative health services and patient out-of-pocket costs together accounted for 3%. Patient out-of-pocket expenses included the costs of transportation to access care and annual fees for recreational services to improve symptom control. The patients in this sample did not report any costs for housekeeping and child care services.

In a sensitivity analysis of direct costs, minimum and maximum costs in the sample were calculated based on variations in two components - hospital admissions and medications. In the minimum cost model, the direct treatment-related costs of admission were used rather than the total cost of admission. The cost of medications was based on the lowest reported frequency of drug administration, and the lowest priced preparation, when a drug product was available in more than one strength, such as Pulmicort Turbuhaler. In the maximum cost model, the total cost of admission was used, the highest reported frequency of drug administration and the highest cost drug preparation, when multiple formulations were available. The unadjusted average minimum and maximum annual direct costs were $1,161 per patient and $1,350 per patient respectively. Figure 14 indicates that there was little variation in the relative contributions of the cost components between the minimum and maximum direct cost models.
Medications increased from 28% to 34% of the total direct costs. Although the absolute cost of admissions was higher, the proportion of the direct costs attributed to admissions decreased slightly to 44%. The direct cost of admissions represents 70% of the total cost. Thus the change in admission costs was small relative to the increase in medication costs between the minimum and maximum cost models.

The unadjusted average annual total costs per patient were $2,232. As displayed in Figure 15, direct costs contributed to 57% of the total costs of the patient sample.
The distribution of costs was highly skewed. Eighty-one percent of the sample (n=1036) experienced annual total costs less than $3000 per patient. The 19% of the sample with total costs greater or equal to $3000 accounted for 54% of the sample's cumulative costs. The 31 patients with annual costs exceeding $10,000 per patient accounted for 2% of the sample and 18% of the sample's cumulative costs.

It was of interest to examine the direct, indirect and total costs in general linear models adjusted for age group and disease severity. In addition to these factors, several other variables were studied to assess their potential as predictors of total costs. Education, smoking status and the SF-36 domains of physical function, physical role limitations and general health were significant predictors in bivariate analyses. However, all of these factors lost significance when added to models already containing severity and age group. Occupation was excluded as an independent variable in multi-variate models in the societal system analysis because of its function in
determining the value of indirect costs. The severity of asthma is known to fluctuate between seasons. The presence of a seasonal effect was tested by evaluating the relationship between total costs and month of study registration. No trends toward significance were observed.

The mean direct and indirect costs, adjusted for age group and severity are shown in Figure 16.

Figure 16. Annual Patient Costs - Societal Perspective

All three age groups demonstrated increasing costs with increasing severity. The coefficients associated with the main treatment effects of age group and severity in the model of total costs were statistically significant (p=0.0001). Slight interaction was evident suggesting that observed differences between severity strata depended on the age group. This is evident from the graph which depicts very little difference in direct, indirect or total costs between mild and moderately ill patients aged 0-4 years. The 5-14 years age group experienced the lowest costs. Total annual costs for mild patients in this age group were $777. Adults displayed the highest costs, with
severe patients costing an average of $4223 per year. Adults also displayed greater indirect costs compared to the other age groups. The adjusted annual means and 95% CIs, stratified by age group and severity, are summarized in Table 17.

Table 17. Adjusted Annual Total Costs per Patient - Societal Perspective

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>4 years or less</th>
<th></th>
<th></th>
<th>5 - 14 years</th>
<th></th>
<th></th>
<th>15 years and older</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>95% CI</td>
<td>n</td>
<td>Mean</td>
<td>95% CI</td>
<td>n</td>
<td>Mean</td>
</tr>
<tr>
<td>mild</td>
<td>18</td>
<td>1245</td>
<td>-74,2565</td>
<td>78</td>
<td>777</td>
<td>143,1411</td>
<td>255</td>
<td>1633</td>
</tr>
<tr>
<td>moderate</td>
<td>47</td>
<td>1252</td>
<td>435,2068</td>
<td>123</td>
<td>1231</td>
<td>726,1736</td>
<td>458</td>
<td>2303</td>
</tr>
<tr>
<td>severe</td>
<td>23</td>
<td>2352</td>
<td>1185,3519</td>
<td>49</td>
<td>1686</td>
<td>886,2486</td>
<td>223</td>
<td>4223</td>
</tr>
</tbody>
</table>

The negative lower 95% CI for mild patients aged 0 to 4 years is a consequence of skewed variation occurring in a small sub-sample of patients.

The characteristics of the sub-group of 94 patients reporting one or more respiratory hospital admissions were examined. This subset had the same proportions of males and females as found in the whole sample but demonstrated higher proportions of patients aged 0-4 years (19% vs. 7%) and 55 years or more (32% vs. 19%). Higher proportions of these patients were receiving concomitant therapy with bronchodilators, inhaled corticosteroids and oral corticosteroids (14% vs. 4%). The average annual total cost in this group was $5427 per patient, with admission costs alone accounting for $2036 per patient.

*Indirect Costs Sensitivity Analysis*

In the base case analysis, the value of the morbidity-related time lost by employed persons is
given full weight while the time lost by others, such as homemakers, is weighted at 0.4 (Torgerson et al. 1994, Hodgson and Meiners 1982). While asthma is a chronic condition, asthma-related work absences result from acute exacerbations which may last no more than several days. It may not be reasonable to fully weight the time lost by employed persons who do not personally experience a pay loss. The true productivity loss would be small if the worker is replaced by internal or external labour pools during the period of acute exacerbation. In contrast, if a worker who is not paid during an absence is not replaced, a fully weighted productivity loss occurs. The opportunity cost of time lost by homemakers may also be underestimated, particularly if the women are involved in child care and are not easily replaced (Torgerson et al. 1994). The conventional assumptions of the human capital method were revisited in a sensitivity analysis in which a range of weights for persons in different occupations categories was applied. The analysis also distinguished between workers who lost pay during morbidity-related absences and those who did not (see Table 9a).

Because the productivity loss days, measured as absences from work or other usual activities and time spent waiting for health care, were not normally distributed, the results are expressed as quartile frequencies. Table 18 displays the distributions of productivity loss days and annual wages for persons in various occupation categories.
Table 18. Productivity Loss Days and Annual Wages

<table>
<thead>
<tr>
<th>Occupation Category (N)</th>
<th>Productivity Loss (days per year)</th>
<th>Annual Wages ($) *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absence from work or usual activities</td>
<td>Waiting for health services</td>
</tr>
<tr>
<td>all employed (673)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25% quartile</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50% quartile</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>75% quartile</td>
<td>7.6</td>
<td>0.5</td>
</tr>
<tr>
<td>no loss of pay (341)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25% quartile</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50% quartile</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>75% quartile</td>
<td>5.6</td>
<td>0.5</td>
</tr>
<tr>
<td>loss of pay (332)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25% quartile</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50% quartile</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>75% quartile</td>
<td>9.1</td>
<td>0.5</td>
</tr>
<tr>
<td>homemakers (229)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25% quartile</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>50% quartile</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>75% quartile</td>
<td>6.8</td>
<td>0.7</td>
</tr>
<tr>
<td>other (377) **</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25% quartile</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50% quartile</td>
<td>5.9</td>
<td>0.2</td>
</tr>
<tr>
<td>75% quartile</td>
<td>24.0</td>
<td>0.8</td>
</tr>
<tr>
<td>whole sample (1279)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25% quartile</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50% quartile</td>
<td>1.4</td>
<td>0.2</td>
</tr>
<tr>
<td>75% quartile</td>
<td>10.9</td>
<td>0.6</td>
</tr>
</tbody>
</table>

* The reported annual salaries were used for employed persons. For all other persons, age- and sex-specific sample mean salaries were used to impute annual wages (opportunity cost approach).
** 'Other' consists of unemployed persons, students, retirees and disability pensioners.

The annual median days lost from work was very small among employed persons (1.1 day).

Persons who lost pay during work absences had slightly longer absences than those not losing pay. Homemakers demonstrated the shortest absences from usual activities, 75% quartile, 6.8
days. The longest absences occurred in the 'other' category, which consisted of unemployed persons, students, retirees and disability pensioners. The 75% quartile in this group was 24 days. The differences between groups were statistically significant (Kruskal-Wallis test, $p = 0.0001$). Overall, the median work/usual activities days lost per year in the whole sample was 1.4 days. Time spent waiting for health services was similar across occupations and was short: the median was 0.2 days per year in the whole sample. The calculation of median annual wages was based on reported salaries for adult patients and caregivers' salaries for pediatric patients. The median annual wages were higher in the no loss of pay group than in the group experiencing pay loss during an absence. The imputed annual wages were smallest in the 'other' category, as this group drew from age group extremes which earn less than individuals aged 35-65 years. The median annual wage in the whole sample was $26,840.

Figure 17 demonstrates the change in median annual indirect costs for each occupation category as the weights are varied according to the methods in Table 9a.

Figure 17. Indirect Costs Sensitivity Analysis - Societal Perspective
In method 1, which represents the base case analysis, the indirect costs of all employed persons were weighted equally. In this scheme, employed persons with no pay loss demonstrated twice the annual indirect costs of employed persons with pay losses upon absence: $205 vs. $107. This method resulted in the lowest assessment of median annual indirect costs for homemakers, $42. Median annual indirect costs were much higher in the 'other' category, resulting from more productivity loss days in this group. In method 1, the median annual indirect costs in the whole sample were $122. Method 2, which weighted all categories fully and equally, resulted in the 'other' category demonstrating the highest median indirect costs, $449 per person per year. In this method, the costs of homemakers ($105) and employed persons with pay loss ($107) were almost identical. Method 3 reduced the weight of employed persons with no pay loss to 0.4, based on the premise that these individuals may be replaced resulting in a small true productivity loss. In this method, employed persons and homemakers experiences similar annual median indirect costs, $92 and $105 per person, respectively. Method 4 regarded the time of homemakers as more valuable than unemployed persons, students and others, reflecting the irreplaceability of child care services. Although this method reduced the median annual indirect costs of the 'other' category to $270 per person, this group persisted in demonstrating the highest indirect costs. Median annual indirect costs in the whole sample were $120 per person.

5.2.3.2 Health Care System Perspective

In the health care system perspective, total costs consist of the direct medical costs associated with publicly administered services, i.e. paid for by the province. Including the health care system perspective lends insight into the organization and funding of health services by a large single payer such as a provincial government. The unadjusted average annual cost to the health
The largest cost component by far was hospital admissions, accounting for 72% of the total costs. Physician services, which consisted of GP, specialist and ER/clinic visits, represented 14% of the costs while medications and dispensing fees together contributed 11%.

Multivariate modelling revealed that total costs varied significantly by severity and by occupation. The absence of age group as a main effect is suggested by Figure 16 which shows little variation in direct costs between age groups. Figure 19 displays the adjusted total costs, stratified by disease severity and occupation.
Unemployed persons demonstrated the lowest adjusted total costs, with an average of $655 per person per year. The average annual costs were similar in unemployed persons, employed persons and students. The most costly group was retired persons with adjusted annual costs ranging from $773 per person in mild patients to $2122 per person in severe patients. Total costs increased with increasing severity for all occupation categories except students and disability pensioners. In these two groups, the direct costs were more sensitive to differences between mild/moderate patients and severe patients than between mild and moderately ill patients. The similar results for mild and moderately ill patients among students and disability pensioners may be due to the small sub-sample sizes. The adjusted annual mean total costs per patient and 95% CIs, by occupation, are tabulated below.
Table 19. Adjusted Annual Total Costs per Patient - Health Care System

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Mild</th>
<th></th>
<th></th>
<th>Moderate</th>
<th></th>
<th></th>
<th>Severe</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>95% CI</td>
<td>n</td>
<td>Mean</td>
<td>95% CI</td>
<td>n</td>
<td>Mean</td>
<td>95% CI</td>
</tr>
<tr>
<td>unemployed</td>
<td>16</td>
<td>506</td>
<td>6,1006</td>
<td>29</td>
<td>537</td>
<td>166,909</td>
<td>14</td>
<td>922</td>
<td>388,1457</td>
</tr>
<tr>
<td>employed</td>
<td>206</td>
<td>517</td>
<td>378,657</td>
<td>335</td>
<td>635</td>
<td>525,744</td>
<td>132</td>
<td>889</td>
<td>714,1064</td>
</tr>
<tr>
<td>student</td>
<td>45</td>
<td>776</td>
<td>478,1074</td>
<td>64</td>
<td>620</td>
<td>368,872</td>
<td>16</td>
<td>959</td>
<td>459,1459</td>
</tr>
<tr>
<td>homemaker</td>
<td>47</td>
<td>592</td>
<td>300,883</td>
<td>112</td>
<td>768</td>
<td>579,957</td>
<td>59</td>
<td>1322</td>
<td>1072,1593</td>
</tr>
<tr>
<td>disability pensioner</td>
<td>10</td>
<td>830</td>
<td>197,1462</td>
<td>23</td>
<td>784</td>
<td>367,1201</td>
<td>15</td>
<td>1148</td>
<td>632,1665</td>
</tr>
<tr>
<td>retired</td>
<td>28</td>
<td>773</td>
<td>395,1151</td>
<td>67</td>
<td>1522</td>
<td>1278,1769</td>
<td>61</td>
<td>2122</td>
<td>1866,2378</td>
</tr>
</tbody>
</table>

5.2.3.3 Patient Perspective

In the patient perspective, those costs incurred directly by the patient are counted. These include out-of-pocket payments for transportation to access care and the cost of recreation memberships for improving symptom control. Also included are medication and device co-payments and deductibles for persons with drug plans and the full cost of medications and devices for persons with no coverage. Indirect costs, consisting of lost time from usual activities, are heavily incurred by patients and their families. The patient perspective provides insight into the range and cost of those health services required by asthma patients that are not covered by provincial health plans as well as the impact of indirect costs. The unadjusted average annual direct costs to the patient were $75. The relative contributions of the components of the direct costs are portrayed in Figure 20.
As expected, the largest cost component was medications, accounting for 73% of the direct costs of the patient sample. Personal out-of-pocket expenses for travel and recreation contributed 15% of the direct costs and the use of alternative health services 10%.

The unadjusted average total costs were $726 per patient. Thus, 90% of the total costs from the patient's perspective are indirect. The components of total cost are depicted in Figure 21. Proportions do not add to 100% due to rounding.
In the multivariate general linear model of total costs, both severity and age group demonstrated statistical significance as main effects. The mean direct and indirect costs, adjusted for severity and age group, are represented in Figure 22.

Figure 22. Annual Patient Costs - Patient Perspective

All three age groups demonstrated increasing costs with increasing severity. The 0-4 years age group experienced the lowest costs from the patient perspective. Adjusted annual costs for mild patients in this age group were $124 per patient. Adults displayed the highest costs, with severe patients costing an average of $1232 per patient per year. A higher proportion of the total costs in adults was due to indirect costs compared to the other age groups.

The adjusted annual mean total costs per patient and 95% CIs, stratified by age group and severity are displayed in Table 20. Negative lower confidence limits occurred for small sub-samples with skewed distributions of total costs.
Table 20. Adjusted Annual Total Costs per Patient - Patient Perspective

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>4 years or less</th>
<th>5 - 14 years</th>
<th>15 years and older</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>95% CI</td>
</tr>
<tr>
<td>mild</td>
<td>18</td>
<td>56</td>
<td>-458,325</td>
</tr>
<tr>
<td>moderate</td>
<td>47</td>
<td>81</td>
<td>-299,431</td>
</tr>
<tr>
<td>severe</td>
<td>22</td>
<td>234</td>
<td>-25,758</td>
</tr>
</tbody>
</table>

Indirect Costs Sensitivity Analysis

Figure 23 demonstrates the change in median annual indirect costs for each occupation category as the weights are varied according to the methods in Table 9b.

Figure 23. Indirect Costs Sensitivity Analysis - Patient Perspective

In all three patient perspective methods, the indirect costs of employed persons who did not lose pay during an absence were zero. In method 1, the base case analysis, the indirect costs of employed persons with pay loss were approximately twice the annual indirect costs of homemakers, $107 vs. $42 per person, respectively. Median annual indirect costs were highest in the 'other' category, $180 per person. This method produced the lowest estimate of indirect
costs for the whole sample, $26 per person per year. Method 2 weighted employed persons with loss of pay, homemakers and 'other' fully and equally. With this method, the 'other' category demonstrated the highest median annual indirect costs of $449 per person. In this method the costs of homemakers and employed persons with pay loss were almost identical, $105 and $107 per person, respectively. Method 3 valued the time of homemakers higher than unemployed persons, students and others. Although this method reduced the median annual indirect costs of the 'other' category to $270 per person, this group persisted in demonstrating the highest indirect costs. Median annual indirect costs in the whole sample were $37. Overall, varying the weighting scheme resulted in minor changes to the estimates of the whole sample.

5.2.4 Quality of life Assessment

A cost-of-illness assessment would not be complete without an evaluation of the intangible, psychosocial costs of the disease. The SF-36 health-related quality of life instrument was used to indicate the magnitude of quality of life impairment in the study sample. The quality of life analysis was limited to subjects 18 years or older, as no evidence is available regarding the validity of proxy respondents for children. Figure 29 depicts the mean SF-36 domain scores in males, females and the whole sample. Higher scores represent better quality of life and a difference of five or more is considered clinically important.
Figure 14. Quality of life in Males vs. Females

Males demonstrated higher scores than females for all domains, with clinically significant differences observed for physical function, physical role limitations, vitality and emotional role limitations. These differences were statistically significant (Mann-Whitney test, $p = 0.0001$). The largest sex difference was observed in physical role limitations, with males averaging 76 compared to 64 in females.

The relationship between disease severity and quality of life is represented in Figure 25.
Every domain demonstrated decreasing quality of life with increasing disease severity. All domains except emotional role limitations and mental health displayed statistically significant differences (1-way ANOVA, p<0.0001) between the mild and severe strata. Physical function, physical role limitations and general health demonstrated clinically important differences, i.e. score differences of 5 or more, between mild and moderate and between moderate and severe levels. These domains also demonstrated statistically significant correlations with severity (p<0.0001). Spearman correlations coefficients were equal to -0.23, -0.21 and -0.20 for physical function, general health and physical role limitations, respectively. Social function displayed clinically important reductions between moderate and severely ill patients. A two-way ANOVA with sex and severity revealed no interaction, i.e. differences between males and females and between severity levels were independent of the other factor.

The last analysis examined the effect of age on quality of life, summarized in Figure 26.
Only physical function displayed a clear reduction in quality of life with increasing age, with mean scores changing from 83 in 18 to 34 year-olds to 56 in persons aged 75 years or more. The differences between age groups were statistically significant by 1-way ANOVA, p=0.0001. The observed differences among age groups in the other domains were small and not considered clinically important.

The quality of life in the subset of 94 patients reporting hospital admissions was examined separately. These patients scored an average of 60 on physical function, 47 on physical role limitations and 52 on general health, well below the sample means of 76, 68 and 64 for the three domains respectively.
Chapter 6.  DISCUSSION

The discussions of the assessments of the patient self-report of health services utilization and the cost of asthma are presented in separate sections of this chapter.

6.1 ASSESSMENT OF PATIENT SELF-REPORT

The discussion of the assessment of the patient self-report begins with an examination of patient characteristics and follows with comments on the self-report of hospital admissions and the analysis of agreement. The discussion of the analysis of the agreement between the self-report and OHIP claims data focuses on the measurement of utilization, the accuracy of data and statistical techniques. The results are then compared to other published studies of agreement.

6.1 ASSESSMENT OF PATIENT SELF-REPORT

6.1.1 The Study Sample

Subjects for the assessment of the patient self-report of health services utilization were drawn from 197 eligible candidates from the PMMP Bronchial Inhalers pilot project enrollees. Only 83 consented, resulting in an enrollment rate of 42%. The low response rate is attributable to several factors. First, the PMMP policy was to curtail the process of soliciting informed consent after two letters and two phone calls by PMMP staff. This policy recognized the trade-off between achieving a high response rate for one study at the risk of jeopardizing involvement of volunteers and local pharmacies in future projects. As a result, there were 40 subjects who were not reached after the last phone call was made. Some individuals declined because they believed
their use of health services was insufficient to warrant inclusion. If many candidates declined for this reason, one would expect the average use of health services in the consenters to be higher than the non-consenters. In fact, the utilization in both groups was comparable (Table 10).

While more aggressive follow-up might have resulted in a better overall response rate, sufficient numbers were enrolled to provide the necessary power for the agreement analyses of the dichotomous variables. Moreover, enrolled subjects did not differ significantly from those who declined. The consenters were on average 5 years older than the non-consenters. While some studies have shown that recall of health services utilization decreases with age, these findings were in elderly subjects or across larger age increments (Brown and Adams 1992; Harlow and Linet 1989; Green et al. 1979; Norrish et al. 1994).

6.1.2 Self-report of Hospital Admissions

The high confirmation rate in this study suggests that patients accurately reported admissions that occurred in the prior year. One admission could not be confirmed by the hospital face sheet but was documented in OHIP claims for that patient. Hospital charts have been shown to miss certain types of data, such as co-morbidities, risk factors and medication information (van Walraven and Weinberg 1995; Iezzoni 1994). The hospital face sheet is frequently used in health services research to confirm diagnoses, admissions and lengths of stay. The failure of the face sheet to note the admission of this patient raises concern about its use as a gold standard for health services utilization. The combined use of hospital charts and an administrative database as the standard for comparison may be the best approach in studies assessing the validity of patient self-reports of hospital admissions.
6.1.3 Analysis of Agreement

Three principal factors affected the observed agreement in health services utilization between patient self-reports and OHIP fee claims: 1) the process of measuring utilization, 2) the sources of error and 3) the statistical techniques used to quantify agreement. The contribution of each of these factors is discussed separately. Following this, the overall findings of the agreement analysis are interpreted with respect to other studies.

6.1.3.1 Measurement of Utilization

Unlike inter-rater reliability assessments that measure the extent of agreement between two raters using the same instrument, an evaluation of agreement between two data sources involves measurement processes and constraints that are unique to each data source.

The data collected through telephone interviews was vulnerable to several potential sources of bias, including selection bias, recall bias, respondent bias and interviewer bias. While efforts to enroll all eligible candidates in the Bronchial Inhalers project at participating pharmacies may have attenuated selection bias in the pilot and main projects, some selection bias remained. The requirement for a bronchial inhaler prescription, the selection of pharmacies in southwestern Ontario and the lack of random sampling may have resulted in a study sample that was biased in its representation of respiratory patients. The absence of important differences between participants and non-participants suggests that volunteer bias was not a factor in this study. Recall bias, the tendency for individuals with a particular condition to ruminate to a greater extent on their use of health services than others, may have resulted in over-reporting. This was balanced however, by an individual's sensitivity to his/her possible overuse of services. The
closed-ended, structured format of the interview reduced the possibility of interviewer bias.

Measurement of utilization using the OHIP database was constrained by its coding classification system. The fee service codes were developed by the Ontario Ministry of Health to facilitate billing for particular procedures. The codes therefore do not classify health services in ways that may be meaningful to clinical, epidemiological or health economic researchers, such as the use of hospital outpatient clinics versus office practices for ambulatory care. An advantage of using the OHIP database to measure health services utilization was that the patient and researcher were not involved in the process of data generation. Thus respondent bias and interviewer bias were eliminated. However, since the OHIP data used in this study were restricted to subjects recruited into the pilot Bronchial Inhalers project, the same selection bias existed.

The choice of the seven variables examined in this analysis (Table 5) was guided by the requirements of a health economic assessment, which examines the volume of various types of physician services and inpatient care. The extent to which each variable was successfully operationalized influenced the degree of differential misclassification that may have occurred and the consequent level of observed agreement.

In the baseline, 3- and 6-month interviews, questions about the use of family physician services related specifically to the patient's 'breathing problems' and were not linked to a particular diagnosis. The respiratory association was made by linking services to any of the 3-digit OHIP respiratory system diagnostic codes (Appendix 6). Reliance on these diagnostic codes to designate a GP visit as respiratory-related may have contributed to the low level of agreement.
observed for pre- and on-study GP visits (kappa values of 0.34 and 0.43). Several studies have found that diagnosis codes in administrative databases are not as reliable as procedure codes (Romano and Mark 1994; Fisher et al. 1992; lezzone 1994; Hawker 1993). There is little incentive for the physician to indicate the diagnosis accurately on the claim form. Furthermore, the patient's perceptions of the reason for the visit may not match the physician's clinical observations and subsequent diagnoses entered on the claim form.

Substantial levels of agreement were observed for pre- and on-study respiratory specialist visits. A patient may perceive any physician who conducts pulmonary function testing as his/her "lung and chest physician" even if the physician is not a certified respirologist. The inclusion of diagnostic test codes pertaining to pulmonary function and allergy testing in the definition of a specialist visit enhanced the probability of agreement between the two data sources.

The existence of specific "C" codes for inpatient care permitted a straightforward extraction of respiratory-related admissions or hospital admissions for any reason from the OHIP database. The process for measuring admissions was more complex for the interview data. Patients were not asked directly whether they experienced an admission. Rather, this was inferred from a series of questions relating to 1) the incidence of health problems, 2) visits to a hospital and 3) 24-hour stays in a hospital. Despite the complex inference required for determining admissions from the interview data, perfect agreement was observed for prior respiratory admissions and substantial agreement was observed for on-study admissions. The high agreement likely reflects the significance of these events to the patient, resulting in accurate recall.
The agreement between the self-report and OHIP data for the occurrence of on-study ER/clinic visits was slight (kappa = 0.04). The poor agreement may be explained by the difficulties in specifying and operationalizing this variable. First, the wording of the interview questions, ("Have you been to any hospitals or clinics..."), necessitated combining emergency room visits, urgent care visits and hospital outpatient clinic visits in the same category. Emergency and urgent care represent a unique kind of care, provided in response to an acute episode. The measurement of this type of health service is important not only for economic assessments, but also for clinical studies measuring markers of morbidity and disease progression. In contrast, a hospital outpatient clinic visit may reflect routine supervision by a family practitioner or a specialist. Second, patients were not asked directly if they experienced emergency care. Patients who acknowledged visiting a hospital/clinic but who did not stay for more than 24 hours were assumed to have experienced an ER/clinic visit. Third, the measurement of ER/clinic visits was complicated by the lack of precise ER codes in the OHIP schedule of benefits. Existing "H" codes relate only to consultations by physicians on duty in the Emergency department. Assessments provided in an emergency room by other generalists or specialists cannot be distinguished from outpatient care services. The inability to discern emergency services accurately in OHIP claims data and the self-reporting of non-emergent clinic visits resulted in the high frequency of self-reports compared to OHIP claims.

Pre-study utilization of GPs and specialists were evaluated separately from on-study use of these health services. Studies have demonstrated that the accuracy of recall of health services decreases with the length of the recall period (Mancuso and Charlson 1995; Bradburn et al. 1987). In this study, the kappa values for pre-study visits to GPs and specialists recalled over 6 to
12 months were less than values corresponding to on-study recall over 2- to 3-month intervals. Hospital admissions occurring within 12 months of an interview have been shown to be reliably recalled (Harlow and Linet 1989; Norrish et al. 1994). The high level of agreement for admissions and specialist visits that took place within the prior year support this evidence.

6.1.3.2 Sources of Error

The biases that potentially affected the process of measuring of health services utilization were discussed above. In addition to these biases, random and systematic error may have resulted in imprecise and inaccurate data, both in the interview data files and the OHIP fee claims.

Interview Data

Errors in the interview data may have occurred due to faulty recall by the subject or data entry mistakes by the interviewer. The probability of inaccurate recall was minimized by the use of recall intervals shown to be reliable (Harlow and Linet 1989). On-study recall may also have been improved by a training effect, resulting from the subject's knowledge that he/she is being followed up and by gaining experience with answering the interview questions over the course of the study. The gradient in kappa values displayed in Figure 9, ranging from high agreement for admissions to moderate and slight agreement for visits to GPs and ER/clinics, can be explained by cognitive factors that affect the accuracy of recall and the direction and magnitude of recall biases. Survey questions that ask a patient to recall the frequency of an event, such as the number of visits to a doctor, are linked to two memory activities: retrieval and inference (Bradburn et al. 1987).
Several factors influence an individual's ability to retrieve factual information from memory (Mancuso and Charlson 1995). Some information is lost over time and cannot be retrieved, even with cues. The interview environment, such as a structured, closed-ended telephone interview that moves quickly from item to item, can adversely affect recall. While this type of questionnaire may demonstrate a high level of inter-rater reliability, construct validity may be sacrificed if important events cannot be remembered (Bradburn et al. 1987; Brown and Adams 1992). In addition, specific events are difficult to recall if there are numerous other similar events stored in memory. This last factor may explain why GP visits, less prominent in memory than specialist visits or admissions, were recalled less reliably.

When an individual relies on inference to answer a question, the response reflects the use of the "availability heuristic". This heuristic contends that the easier it is to bring an event to mind, the more frequently it will seem to have occurred (Mancuso and Charlson 1995). This suggests that over-reporting may have been more common in patients with higher levels of utilization.

Other factors that may have affected recall positively or negatively include illness severity, the level of discomfort or pain, the effects of medications, the presence of co-morbid conditions and mood. Personal characteristics including age, education and socio-economic status may also have influenced recall ability. In this study, patients completed the interviews before they were approached to participate in the self-report assessment. Thus, their recall was not biased by the knowledge that their responses would be compared to their OHIP claims.

Another potential source of error in the interview data was inaccurate data entry. Data entry
error was minimized by the use of real-time interview software that permitted the interviewer to enter the data as the patient was being interviewed, thus preventing transcription errors. The software was also programmed to disallow illogical entries.

*OHIP Data*

Administrative databases are not infallible, indeed studies have demonstrated that they may have inaccurate or missing data. (Roos et al. 1993; Roos et al. 1991; Iezzoni 1994) While the validity of several Canadian administrative databases has been assessed through comparisons with the contents of medical charts (Roos et al 1993; Ontario Hospital Association 1991; Hawker et al. 1997), this has not been done with the OHIP fee claims database. The quality of the data in the database depends on the accuracy of the consultation, procedure and diagnostic codes entered on the original claim form. Computerized billing practices reduce the probability of transcription errors. Despite this, it is possible that some insured health services utilization that occurred was not recorded in the OHIP database or was coded incorrectly.

The OHIP database does not include services that were rendered to Ontario residents outside of the province or services that were billed to other health insurance plans, such as the Workers Compensation Board. In addition, subjects may have reported utilization of alternative health professionals or other non-insured services. Subjects may have received care from physicians who were salaried or otherwise outside of the fee-for-service reimbursement system. Thus the OHIP database is not a complete record of health services provided to Ontario residents.
6.1.3.3 Statistical Techniques

Section 2.2.2 described the strengths and limitations of various measures used in reliability assessment. One of the limitations of the kappa statistic, the preferred measure of inter-rater reliability, is its dependence on the marginal totals (Feinstein and Cicchetti 1990). As the marginal totals deviate from 0.5 of the total sample size, the kappa value is paradoxically increased or decreased. When the imbalance is asymmetrical, i.e. row and column marginals deviate in opposite directions, then kappa is artificially increased. When the imbalance is symmetrical, i.e. row and column marginals deviate in the same direction, then the agreement expected by chance is very high. This results in a reduced value for kappa. An example of this effect can be seen in Figure 7a, ER/clinic visits. The skewed marginals deflated the value of kappa. The result, 0.08, was much lower than the observed agreement, $P_o = 0.76$.

The effect of the marginal totals on kappa is irrelevant when assessing the inter-rater reliability of ordinal data. For these data, a quadratic weighted kappa is conventionally used in the presence multiple response groups. The quadratic weighted kappa is mathematically equivalent to an intra-class correlation coefficient. Depending on the clinical relevance of the response categories, a quadratic weight may be an excessively conservative approach to measuring agreement. Moreover, unless the sample size is greater than or equal to twice the square of the number of response groups, there is insufficient power to calculate a standard error for kappa and the result may not be useful for interpretation (Kramer and Feinstein 1981). The power of the kappa calculation is also reduced by small unstable cell counts. A lack of power necessitated the combination of response categories for ordinal variables 4 and 5, representing on-study visits to GPs and to respiratory specialists.
The conservative nature of the weighted kappa and its power requirements are exemplified in Figures 8a and 8b, which presents the inter-source agreement for on-study hospital admissions. Progressing from the dichotomous to the ordinal analysis, the number of response groups was increased by one level - from a 2x2 to a 3x3 contingency table. This permitted a more refined analysis of the 3 patients who responded positively in both data sources. With only a 1-step increase in the number of response groups, the level of agreement decreased from 0.74 (substantial) to 0.48 (moderate). The small cell counts in Figure 8a resulted in a large standard error for kappa, evident from the wide 95% confidence intervals. In the ordinal analysis, the standard error for the weighted kappa was too large to permit the calculation of 95% confidence intervals. Thus, in this analysis of health services utilization, the application of a quadratic weight for kappa may have biased the measurement of agreement towards the null, where all observed agreement is due to chance (kappa = 0).

Correction for chance is a unique feature of kappa calculations that contributes to its popularity in epidemiological and health services research. Corrections for chance are not incorporated into assessments that measure sensitivity and specificity, even though chance agreement with a gold standard may occur. The reason for this is that assessments of validity presume that only objective measures, such as laboratory diagnostic tests, free from the influence of human subjectivity, are used as gold standards. All observed agreement is therefore "true" and none due to chance. This implies that the measures evaluated in inter-rater reliability assessments lack complete objectivity and a mechanism is required for correcting the "guesswork" that may occur. While this may be true in the case of two human raters using the same instrument, this assumption may not be tenable when two separate data sources are compared, where each
employs independent measurement processes. The need for chance correction may unfairly penalize the agreement result in this type of analysis (Feinstein and Cicchetti 1990). For this reason, and because of the unduly conservative nature of the weighted kappa, it is essential to convey both the chance-corrected (kappa) and uncorrected ($P_o$) agreement results for interpretation. Except for ER/clinic visits, the values for $P_o$ and kappa observed in this study were in reasonable proximity to each other. The kappa values and 95% confidence intervals for ER/clinic visits were close enough to 0 to suggest that all agreement between the two data source was due to chance. It is therefore conceivable that kappa over-corrects for chance when used to quantify agreement between two data sources that employ independent processes to measure health services utilization.

In epidemiology, the calculation of standard errors and 95% confidence intervals are considered minimum requirements in the presentation of statistics such as means and odds ratios. Confidence intervals reveal not only the significance of the result, but also the precision of the point estimate. Indicators of precision are necessary for drawing inferences regarding the credibility of study results and may point to weaknesses in study designs, such as a limited sample size. It follows that the utility of estimates of agreement such as kappa would be enhanced by the reporting of confidence intervals that indicate the precision of the point estimate. And yet, this is rare in the epidemiological and health services research literature. While the importance of the confidence interval may be subordinate to the value of the point estimate (Kramer and Feinstein 1987), its contribution to the interpretation of the result is of great relevance. The degree of precision reflected in a confidence interval may decide the difference between accepting an observed level of agreement as a trustworthy characterization of
inter-rater reliability or rejecting it as meaningless.

In this study, the width of the 95% confidence intervals varied depending on the variable. For the use of GP services, both pre-study and on-study unweighted kappa values displayed confidence intervals widths of 0.41 and 0.40, respectively. Of greater interest however, are the upper and lower limits. Agreement for GP visits was significantly greater than chance but never exceeded 0.63, displaying moderate agreement. Tighter confidence intervals were evident for the dichotomous variables associated with pre- and on-study visits to respiratory specialists. These intervals, with widths of 0.31 and 0.34 respectively, increase the confidence in the result. In contrast, the 95% confidence interval associated with the ordinal on-study specialist visits variable, 0.16-0.78, covered nearly the full spectrum of agreement. This diminishes the ability to conclude with certainty that the agreement was moderate, as suggested by the weighted kappa of 0.47. The confidence intervals related to ER/clinic visits include 0, suggesting that all agreement between the two data sources may have been due to chance. The problems in operationalizing this variable explain the poor agreement result. The weakness is compounded if kappa is over-correcting for chance as discussed above. The small cell counts for on-study hospital admissions reduced the power to measure agreement for this variable, resulting in large standard errors for both the dichotomous and ordinal variables.

6.1.3.4 Comparison to Previous Studies

A number of investigators have examined the agreement between patient self-reports of health services and a second source of data, usually medical records. Many of these investigations focused on specific medical procedures, including Pap smears (Walter et al. 1988; Sawyer et al.
1989; Bowman et al. 1991), mammography (Brown and Adams 1992; King et al. 1990),
hysterectomy and oophorectomy (Paganin-Hill and Ross 1982; Horwitz and Yu 1985; Horwitz
1986; Brett and Madans 1994) and stomach cancer screening (Tsubono et al. 1994). These
studies frequently described the validity of patient self-reports, expressed as sensitivity and
specificity, and regarded the medical record as a gold standard for comparison.

A few studies compared patient self-reports of outpatient visits and hospital admissions to
medical records. The earliest of these studies was performed by the U.S. National Centre for
Health Statistics (NCHS) in 1965. Information from household interviews conducted with 3,937
enrollees in the Health Insurance Plan of New York (NCHS 1965a) was compared to insurance
records. The recall of hospitalizations was high, with a sensitivity of 0.87. In interviews with a
different sample of 1,505 persons (NCHS 1965b), information on lengths of stay and dates of
admission were compared to hospital records. Sensitivities ranged from 0.74 for 1-day stays to
0.91 for stays greater than 4 days. Surgical admissions were recalled with greater accuracy than
non-surgical ones. In a third study, data from three versions of a questionnaire used to interview
patients were compared with hospital records (NCHS 1965c). As above, sensitivity was lowest
for 1-day stays (range 0.79-0.81) and highest for stays of 4 days or more (range 0.85-0.93) and
for surgical stays (range 0.88-0.94). While these results appear to support the findings in this
study for recall of admissions, the NCHS interviews were restricted to persons who had been
hospitalized in the past year. The results therefore cannot be extended to the general population
or to persons asked to recall admissions over a longer time period (Harlow and Linet 1989).

Green et al. (1979) studied the recall of outpatient and inpatient services in subjects aged 75
years and older. In his study, $P_o$ was 0.82 for GP visits in the prior 2 months, slightly higher than the 0.71 observed for on-study respiratory-related GP visits recalled over 2-3 months in this study. The observed agreement for surgery consultations in the last 2 months was 0.80, less than the value of 0.93 observed for on-study specialist visits in this study. $P_o$ for hospital admissions for any reason during the previous year was 0.88 in Green's study. The authors concluded that sensitivity may be improved by using a recall period of recall less than two months. For example, the sensitivity and specificity of the self-report for receipt of home services in the previous week were 97% and 92%, respectively. Whereas a shorter recall period may improve the results, it may not be compatible with the objectives of surveys and questionnaires that measure utilization over periods of several months. Few health care services are provided frequently enough to be captured in weekly rather than monthly recall periods. The under-reporting evident for recall periods of two months demonstrates the limited reliability of non-specific health service utilization reporting by the elderly. The data sources used to validate the self-reports were not described, nor was the abstraction process.

Norrish et al. (1994) assessed the validity of self-reported admissions in a random sample of 86 New Zealand residents who had documented prior hospital admissions. Fifty-eight percent of respondents recalled all admissions. There did not appear to be any differences in recall by age, sex or social class. As in the U.S. NCHS studies, longer lengths of stay were associated with better recall. Norrish speculated that the lower rate of recall evident in their study compared to the NCHS studies may have been due to a more complete hospital discharge database in New Zealand and the use of a longer (four-year) period of recall.
6.2 ASTHMA COST-OF-ILLNESS ASSESSMENT

The discussion of the asthma cost-of-illness assessment will begin with consideration of the study findings, following the sequence of the results. The findings will then be discussed in the context of other studies measuring health services utilization and the cost of asthma.

6.2.1 Study Sample Characteristics

While the study sample is not a random sample of asthmatics in the population, the demographic and medical characteristics reflect a range of diversity in age, education, occupation, disease severity and health services utilization. Such diversity permitted the testing of hypotheses regarding the key determinants of the cost of asthma. Because the sample may differ from the general population of asthmatics in the distributions of age, sex, education level, income and other important sociodemographic determinants of health and health services utilization, the average cost per patient in the sample may not be representative of 'average' asthma patient costs in the population. However, an unadjusted estimate of the 'average' cost per patient in a large diverse asthma patient population provides insufficient information on resource consumption and costs in sub-groups of clinical interest. This multi-variate cost-of-illness analysis generated estimates of total costs that controlled for factors of clinical relevance and factors that were found to be key determinants of cost, including age group and disease severity and occupation.

6.2.2 Asthma Disease Severity

The collection of detailed information on medication regimens permitted the development of a well-defined disease severity stratification scheme. Whereas prior schemes were limited to
counting the number of concomitant anti-asthmatic medications or inhalers puffs (Nguyen et al. 1996, NHLBI 1991, ATS 1986, Anie et al. 1996), the scheme employed in this study incorporated the dosage, types and number of different anti-asthmatic medications. The scheme is consistent with prescribing guidelines which recommend specific classes and dose ranges of medications for increasing levels of control. In practice, the selection of medications is based on a clinical assessment of severity. The Canadian Asthma Consensus Conference viewed asthma as a disease continuum and recommended that severity be defined according to "the frequency and chronicity of symptoms, the presence of persistent airflow limitation and the medication required to maintain control" (Ernst et al. 1996). The principle objective of "maintaining control" hints at the difficulty in distinguishing between the true extent of underlying disease and the degree of disease management. For example, patients with frequent symptoms may simply reflect inadequate control of mild disease rather than extensive underlying disease. The confounding of underlying severity with disease management is partly reflected in the correlations between severity and health services utilization variables displayed in Table 14. While all correlations were statistically significant, the coefficients were small for many utilization variables. Severe asthma that is appropriately managed will result in fewer exacerbations and a reduced need for health services. The higher coefficient for visits to a specialist compared to a GP or other acute forms of care may reflect the greater importance of regular follow-up visits in patients with greater disease severity.

The medications prescribed are a reflection of a physician's combined perceptions regarding a patient's underlying severity and his/her needs for achieving adequate control. Thus a stratification scheme based on medications rather than symptoms would be less likely to result
in misclassification. However, such a scheme assumes that physicians are prescribing appropriately. The observed correlation between severity level and the economic and utilization variables suggests that patients were, for the most part, receiving appropriate therapy.

The severity level distributions in this sample, 28% classified as mild, 49% moderate and 23% severe, may not represent the severity distribution in the population, where a significant burden of mild (and undiagnosed) disease may exist (Decker et al. 1995). Asthma management guidelines recommend that patients with severe disease be under the regular care of a respiratory specialist (Hargreave et al. 1990). Yet only 48% of patients classified as severe reported a visit to a specialist in the year before or during the 6 months of follow-up. Likewise, only 17% of these patients used a peak flow meter, important for self-monitoring and medication titration. These results may be due to the inclusion of moderately ill patients in the severe category, suggesting aggressive prescribing or misclassification. Alternatively, severely ill patients may be receiving appropriate medications but insufficient monitoring or education.

6.2.3 Asthma Cost-of-Illness Analysis

This study incorporated cost information that was derived from various sources, including physician fee schedules, drug formularies, administrative databases as well as patient self-reports. An ideal cost-of-illness assessment would measure the true economic costs, i.e. opportunity costs, of each item. It would also include methods for micro-costing events such as hospital admissions and ER visits (Gold et al. 1996). The purpose of the OCCP is to estimate the costs to Ontario hospitals of various types of admissions. Although the direct and average costs per admission provided by the OCCP did not pertain directly to the admissions reported by the
study subjects, they represent the best available data on the cost of respiratory admissions in Ontario. The OCCP per diem admission costs for asthma were stratified by hospital status (teaching vs. non-teaching) and age. The lengths of stay reported by study subjects were incorporated into the calculations of admission costs whenever possible. The admission cost determination used in this analysis represents an improvement in accuracy and precision over studies which rely on national averages. The most difficult item to evaluate was emergency room visits. The estimate of $120 used in this study is based on the average cost of ER services at Chedoke-McMaster hospital and was obtained from a 1990 study of the cost of asthma in Canada (Krahn et al. 1996). The OCCP does not have estimates for ER visits that do not result in admissions and figures were not available from the hospitals where patients reported ER/clinic visits. In a recent U.S. study, the average cost of non-urgent and semi-urgent visits were US $62 and US $159, respectively (Williams 1996). The cost for an ER visit in Alberta in 1992/93 was $69 and for a visit to a special ambulatory clinic, $183 (Jacobs et al. 1996). These estimates were not disease-specific however. The actual cost of an asthma-related ER visit remains unknown. Within physician services, ER/clinic visits accounted for 0.6% of direct costs, GP visits, 5.7% and specialist visits, 2.9%. The estimates of direct (and total) costs were not sensitive to variations in the estimated costs of ER/clinic costs.

In this sample, the societal analysis revealed that hospitalizations were the highest component of direct costs (47%), closely followed by medications and dispensing fees, which together accounted for 40%. Growing trends toward reduced lengths of stay and more aggressive therapy with costly inhaled corticosteroids may bring these two estimates closer together. The proportion of direct costs attributed to dispensing fees (10%) was estimated based on one prescription per
inhaler. This value was similar to self-reported physician services (9%). A key aspect of asthma disease management is adherence to medication regimens and action plans and correct inhaler technique. These results underscore the important role the pharmacist can play in the care and follow-up of asthma patients.

The analysis reveals the significant contribution of indirect costs to the overall economic burden of illness. Indirect costs included both productivity loss days and time spent travelling to and waiting for care. It is possible that double counting occurred if travel and waiting took place during absences from work/usual activities. The correlation between productivity loss days and the number of GP visits was equal to 0.30 and was significant (p=0.0001). However, the median number of days spent in travel and waiting per year was only 0.2 in the whole sample. Removing this measure from the calculation of indirect costs had little impact on the estimate of total costs.

The stratified analysis revealed that most indirect costs were incurred by adults. In the pediatric age groups, the respondent was a parent who was usually a homemaker or student. Using the base case human capital method, a weight of 0.4 was used to value the lost time of these individuals. It may be reasonable to weight the time of homemakers caring for asthmatic children at a higher level, based on the high opportunity cost of their time, i.e., the difficulty in replacing them. Doubling the weight to 0.8 led to a 10-15% increase in total costs per patient for these age groups and resulted in indirect costs exceeding direct costs in the societal analysis.

In the stratified analysis, 95% CIs were calculated alongside point estimates of total annual costs per patient. The larger sample size in the adult group resulted in relatively precise point estimates, i.e. narrow 95% confidence intervals.
The sensitivity analysis of indirect costs consistently displayed the highest costs for the 'other' category, which was comprised of unemployed persons, students, retirees and disability pensioners. Closer examination revealed that these costs were primarily due to disability pensioners. Among disability pensioners, the median number of days lost per year from usual activities was 18, compared with 3 in students, 5 in retirees and 3 in unemployed persons. Twenty-five per cent of disability pensioners experienced more than 57 productivity loss days per year and 10% reported more than 117 days. The median annual indirect costs were $1,047 per person in disability pensioners, $105 per person among students, $153 in retirees and $171 in unemployed persons. Disability pensioners may have occupational asthma that has caused a prolonged reduction in their day-to-day activities, resulting in the large observed indirect costs.

Patients in the 4 years and under age group had higher annual direct costs than those in the 5-14 years age group. The increasing incidence and morbidity of asthma in very young children is a growing public health concern. Parents of these children may seek out more health services than older children. Among the 94 subjects reporting hospital admissions, 20% were aged 4 years or less compared to 13% aged 5-14 years. The lack of distinction in costs between mildly and moderately ill children aged 4 years or less reflects the diagnostic uncertainty associated with this age group. Severity is difficult to assess since usual indicators of pulmonary function, including airflow measurements and the reliance on as-needed beta-agonists, cannot be used.

In a jurisdiction with a universal, publicly administered health care system, it is interesting to contrast the societal analysis with the health care system analysis. Since medications are not covered under universal health care (except for persons over 65 and on social assistance at the
time of this study), this component is downplayed in the health care system perspective. Most costs are related to hospital admissions, the most heavily targeted sector of recent government health care budget cuts. Conspicuous by its absence are the indirect costs. Health care planning and policy-making that is based on a health care system, rather than a societal perspective, overlooks the large contribution of lost productivity on the total economic burden of illness.

The multi-variate analysis from the health care system perspective provided evidence of the high annual direct costs of retirees, which averaged $1473 per patient, followed by disability pensioners, whose adjusted annual direct costs averaged $920 per patient. The high direct costs of retirees and disability pensioners may be associated with age-related deterioration of health.

The patient perspective analysis revealed which cost components of health care were directly absorbed by the patient. Despite the fact that 89% of patients had drug plans, many of these patients faced co-payments for drugs and devices. The analysis of total costs from the patient perspective excluded 38 patients (3% of the sample) who could not recall the amount of their co-payments. Adjusted average annual direct costs ranged from $38 per patient in mild patients to $115 per patient in severe patients. This study was completed prior to the introduction of co-payments and deductibles in the ODB, thus current out-of-pocket expenses for medications may be greater than these estimates. The total cost estimates in the pediatric age groups were relatively imprecise due to smaller sample sizes and skewed distributions of total costs.

The interviews included a question which asked patients if they ever delayed or not filled a prescription because of cost. Overall, 20% responded affirmatively, with no differences between
severity levels. This result is similar to the findings of a national hospital asthma outpatient survey in Ireland which found that 20% of adults reduced or stopped their medications because of cost (Feeney et al. 1993). While the average annual medication costs of persons delaying/avoiding drug purchase were slightly lower than persons not reporting a delay ($372 vs. $385), their use of GP services was significantly higher (3.4 vs. 2.8 visits per year, p = 0.01). The average direct costs were the same in both groups, but patients reporting delay/avoidance experienced significantly greater indirect costs. Their average total costs were consequently higher ($2,714 vs. $2,107 per patient per year, p = 0.004). There were significant differences in purchase avoidance behaviour between persons of various occupations. Unemployed persons responded with the highest cost-related purchase avoidance, 32%, followed by disability pensioners, at 25%. The group least likely to delay medication purchases were retirees, at 7%, as these patients received full prescription drug coverage at the time of the study.

The patient perspective analysis emphasizes the importance of measuring indirect costs and varying assumptions regarding the opportunity costs of time of persons in various occupations. With hospital admissions moving towards shorter lengths of stay, an increasing burden will be placed on family members to provide care and supervision of patients suffering from respiratory disease. The consequent productivity losses of these care providers must be recorded to document this shift of health care costs.

6.2.4 Quality-of-Life Assessment

The SF-36 is a general health status instrument that has been criticized for being unable to differentiate between patients of varying disease severity (Rothman and Revicki 1993; Richards
and Hemstreet 1994; Brazier and Dixon 1995). This contention was challenged in a study assessing the validity of the SF-36 instrument in clinically-diagnosed asthma patients (Bousquet et al. 1994). A group of 252 male and female patients aged 16 to 77 years with reversible airway obstruction of varying severity underwent pulmonary function testing and completed the SF-36 questionnaire by self-administration. The investigators found significant correlations between the percent predicted forced expiratory volume in 1 second (FEV1), a clinical measure of pulmonary function, and several of the instrument domains ($p < 0.0001$). The highest observed Pearson correlation coefficients were for physical function ($r = 0.47$), general health ($r = 0.41$), pain ($r = 0.36$) and physical role limitations ($r = 0.35$). One would expect pulmonary function to be most highly correlated with domains assessing aspects of physical function. In this thesis research, significant Spearman correlations were found between severity and physical function, general health and physical role limitations. Like Bousquet, higher SF-36 scores were observed in males in every domain. The mean scores in the whole sample were similar in the two studies for most domains; general health, emotional role limitations and mental health scores were lower in the Bousquet study, which may reflect a more restrictive selection of asthmatic patients.

In this study, a clear age trend was found only for physical function, which decreased with increasing age. SF-36 telephone interview norms for the U.S. population demonstrated decreases with age for physical function and physical role limitations (McHorney et al. 1994). Other domains did not display a linear relationship between age and domain score. Like the population norms, this thesis research observed higher mean scores in persons aged 55-64 compared to 45-54 years for general health, vitality, social function and mental health. In the U.S. population, persons aged 65 years and more had the lowest average scores for all domains.
6.2.5 Comparisons with Other Studies

There have been several studies examining the cost of asthma in the U.S., Canada and elsewhere (see Table 3). While some studies have attempted to evaluate the economic burden on large populations (Smith et al. 1997, Krahn et al. 1996, Weiss et al. 1992, Mellis et al. 1992, Action Asthma 1990, Ross 1988, Thompson 1981), others have sought to measure costs in defined samples of patients (Lanes et al. 1996, Carlson 1995, Feeney et al. 1993, Marion et al. 1985). Because the methods and approaches to economic assessment, as well as the sampling strategy, differ markedly between the population-based and small sample studies, the results cannot be compared directly and are discussed in separate sections.

*Population-based Cost-of-Asthma Studies*

A close examination of the most recent published studies reveals some of the principal limitations of population-based cost-of-illness methodology. The Australian, U.S. and Canadian studies (Mellis et al. 1991; Weiss et al. 1992, Krahn et al. 1996; respectively) were population-based retrospective estimates of the total economic burden of asthma from the societal perspective. While each study aimed to assess all direct and indirect cost components, each relied on qualitatively different sources of cost and utilization information. These differences are reflected in the estimates of the total and itemized costs. Table 21 presents the proportions of total costs associated with each component in the Canadian, U.S. and Australian studies.
Table 21. Comparison of Cost Components: Canada, Australia and the U.S.

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Proportion of Total Costs* (%)</th>
<th>Australia</th>
<th>US</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>inpatient care</td>
<td>10</td>
<td>24</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>emergency room</td>
<td>3</td>
<td>4.5</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>physician services</td>
<td>11.5</td>
<td>9.5</td>
<td>9.2</td>
<td></td>
</tr>
<tr>
<td>ambulance services</td>
<td>NE</td>
<td>NE</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>asthma drugs</td>
<td>41</td>
<td>16</td>
<td>24.6</td>
<td></td>
</tr>
<tr>
<td>asthma devices</td>
<td>2.5</td>
<td>NE</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>laboratory services</td>
<td>NE</td>
<td>NE</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>research</td>
<td>NE</td>
<td>NE</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>Patient out-of-pocket costs</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td></td>
</tr>
<tr>
<td><strong>Indirect Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total work days lost</td>
<td></td>
<td>15</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>outside employment</td>
<td>23</td>
<td>6</td>
<td>NE</td>
<td></td>
</tr>
<tr>
<td>homemaking</td>
<td>NE</td>
<td>9</td>
<td>NE</td>
<td></td>
</tr>
<tr>
<td>school days lost</td>
<td>NE</td>
<td>16</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td>travelling and waiting</td>
<td>9</td>
<td>NE</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>mortality</td>
<td>NE</td>
<td>15</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td><strong>Intangible Costs</strong></td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td></td>
</tr>
</tbody>
</table>

from Krahn et al. 1996; Mellis et al. 1991; Weiss et al. 1992
NE = not estimated
* numbers may not add to 100 because of rounding

The variability in the range and choice of outcomes measured influenced the estimate of total costs. The Australian study included more comprehensive estimates of the consumption of medical resources than the U.S. study but was less complete in its assessment of indirect costs.
The restriction of the cost-of-illness assessment to a discrete area of the country (New South Wales) allowed the Australian investigators to seek out diverse sources of utilization information, including hospital attendance records and annual reports and regional health department information. Claims files were used to estimate the volume of physician services along with University of Sydney outpatient audit information. The Australian Health Survey provided information on disability days of employed persons only. The paucity of survey information may explain the incomplete estimation of indirect costs.

The U.S. study relied heavily on surveys to measure utilization and tariff schedules to calculate costs. The frequency of hospital admissions was obtained from the National Hospital Discharge Survey. The cost of inpatient care was assessed using the expenses per day, independent of diagnosis. Utilization of emergency and hospital outpatient services was estimated from the National Health Interview Survey, the National Hospital Discharge Survey and the National Medical Care Utilization and Expenditure Surveys which provided information on the provision of asthma-related care. In the U.S., comprehensive population-based regional billing databases comparable to the provincial health plans do not exist. Information on physician services was therefore derived from the National Ambulatory Medical Care Survey. The U.S. study omitted the costs of ambulance and laboratory services, devices and research. Traveling and waiting time was excluded from the calculation of indirect costs and quality-of-life was not measured.

The largest two costs components, inpatient care and drugs, accounted for 24% and 16% of total costs respectively. These proportions are similar to the findings of this study, in which 27% of total costs were due to admissions and 17% to medications (excluding dispensing fees).
The Canadian study by Krahn et al. (1996) was the most comprehensive. This study obtained prevalence and utilization information from the 1978 Canada Health Survey and the 1990 Ontario Health Survey and medication usage information from the 1987 Canadian Disease and Therapeutic Index (IMS Canada 1987). While the Canada Health Survey data was adjusted for changes in population growth between 1979 and 1990, it is possible that utilization patterns and the prevalence of asthma in Canada changed over this period (Hogg et al. 1995; Mao et al. 1987; Wilkins and Mao 1993; Manfreda et al. 1993). The frequency of asthma-related admissions was obtained from Statistics Canada data. The cost of inpatient care was calculated by multiplying this frequency by the average cost per inpatient day for all types of admissions. As inpatient care was the second largest cost component and accounted for 17% of all costs, an inaccurate estimate would have a large impact on the overall estimate. Estimates of the frequencies of ambulance and laboratory services were derived from the opinions of asthma specialists. Indirect costs were calculated using the human capital method with salaries obtained from 1990 industrial average weekly earnings, adjusted for labour force participation. The cost of homemaking services was calculated using the market value approach. Missing from the Canadian cost-of-illness assessment were the costs of oral prescription drugs, non-prescription medications, patient out-of-pocket expenses and intangible costs.

In spite of their respective deficiencies, the Canadian and U.S. studies showed remarkably similar proportions of total costs for emergency services, physicians services and productivity losses. Taken together, the two largest cost components, inpatient care and drugs, accounted for a similar proportion of the total, 41% in Canada and 40% in the U.S. Their ranking is reversed however, with inpatient care leading in the U.S. and medications representing the largest
component in Canada. The extent to which this reversal is due to imprecision in estimating the costs versus differences in the health care systems is impossible to determine.

A recent U.S. population-based study by Smith et al. (1997) overcame some of the methodological difficulties encountered with the investigations described above by using a single source for cost and utilization information - the 1987 National Medical Expenditure Survey (NMES). Costs were adjusted to 1994 US dollars using the consumer price index (CPI) and wages were adjusted using annual changes in earnings. In his study, Smith found that admissions accounted for 54% of direct costs (49% of total) and medications, 16% (12% of total). Physician services contributed 29% of direct costs. Direct costs were US $5.15 billion, 95% CI US $3.32 billion, US $6.98 billion. Indirect costs were US $673 million, amounting to only 12% of total costs.

Glied (1996) recognized the problems associated with using previous data to project future foregone earnings and emphasized the difficulties in accurately assessing earnings growth over time. Moreover, CPI and earnings growth information adjusts only for monetary changes over time and does not consider demographic shifts in the population, changes in asthma prevalence and morbidity and changes to practice patterns and prescribing. In Smith's study, theophyllines were the most frequently prescribed anti-asthmatic medication (26% of patients) and inhaled corticosteroids were the least used (6% of patients). Since the National Asthma Education Project (NAEP) treatment guidelines were released in 1991, it is reasonable to speculate that this ranking has changed. More widespread and earlier treatment with inhaled corticosteroids would increase the overall costs of medications and may reduce the utilization of other health services.
Thus using 1987 data to estimate costs in 1994 may not be appropriate.

Smith relied on patient self-report of costs of medications and services. The NMES has been criticized as an unreliable source of cost information due to the error associated with patients' recall of medication expenses (Berk et al. 1990). As in the Canadian study, Smith assumed that all school loss and bed days resulted in a productivity loss day for a parent or caregiver and assigned a value of 0.5 to restricted activity days. In this thesis research, respondents who worked despite symptoms usually reported functional losses below 50%. These assumptions may have caused the indirect costs in the Smith and Krahn studies to be over-estimated. An important advantage of the Smith study was the inclusion of 95% confidence intervals for direct, indirect and total cost estimates. The 95% confidence interval for total costs was US $3.6 billion, US $8.1 billion. The US $4.5 billion difference between the upper and lower limits indicates considerable uncertainty and imprecision in the point estimate. It is essential to consider these intervals when judging the results and comparing them to the economic burden of other diseases.

There are several important methodological differences between this thesis research and the population-based assessments. First, this study took a micro-level approach to assessing costs, by determining the patient-specific costs of respiratory-related treatments. This approach is fundamentally different from studies which measure the aggregate costs of respiratory-related care using a probability sample as the unit of analysis. Second, this study focused on costs incurred to a sample of patients with asthma in a circumscribed geographic region in Southern Ontario. The results therefore reflect prevailing practice patterns and demographic behaviours in the region. Population-based studies extrapolate aggregate respiratory-related utilization and
costs to all members of a target disease population. Third, this study controlled for the effects of key explanatory variables in generating patient level estimates, stratifying by age group and severity. The population-based studies provided unadjusted average estimates without examining clinically important sub-groups of the population. Finally, these data were collected in 1995-1996 and therefore reflect more recent trends regarding pharmacotherapy and disease management. The results must also be viewed in the context of current health care trends and reforms that influence medication prescribing and pricing, use of emergency services, inpatient services and the use of alternative health care.

*Asthma Cost-of-Illness Studies in Defined Samples*

Several studies conducted on defined patient samples relied on computerized records and linked databases to generate cost and utilization estimates. Use of these records facilitated the generation of patient-level economic estimates.

Carlson (1995) compared the direct medical costs and health services utilization of asthmatics belonging to a managed care organization to those of a Medicaid population. Inpatient care and drug costs accounted for 30% and 37% of total medical costs respectively in the Medicaid population and 27% and 47% respectively in the managed care group. Medicaid patients had lower expenses for physician and ambulatory services than managed care patients.

A study of asthma patients from a single US outpatient clinic aimed to identify cost components that could be reduced through disease management. In this study, average direct costs per asthmatic were estimated at US $350. Medications and admissions were each responsible for
29% of total direct costs and physician services, 14% (Broshy et al. 1993).

Lanes et al. (1996) examined the claims files of 10,000 asthmatics registered in a group model health maintenance organization to assess health services utilization and direct medical costs from 1988 to 1991. The overall estimates reflect the demographics of the sample, 42% of which were under 15 years of age. The crude average direct cost was US $394 per person per year. As in this thesis research, the distribution of costs was skewed, with 10% of patients accounting for 42% of the costs. The average annual direct cost in the 10% most costly patients was US $2,104 per person. In this study, the average annual direct costs among the 13% most costly patients was US $2,561 (Cdn $3,560) per patient. In Lanes' study, medications accounted for 38% of total direct costs and admissions, 25%, compared to 40% and 47% in this sample.

Although the results of these studies cannot be extrapolated to the population as a whole, their comprehensive data sources permit them to make fewer assumptions in the calculation of the costs in the defined sample, resulting in more precise estimates. However, these studies are limited to estimates of medical costs and exclude the contribution of productivity losses, travel and waiting time and patient out-of-pocket costs, important components in the assessment of the total costs of asthma.

6.2.6 Implications for Measurement of the Cost-of-Illness

The population-based evaluations and the defined sample investigations consistently demonstrated the large contributions of hospital admissions and medications to direct costs.

However, a study that seeks only to measure direct costs or omits important components may be
misleading, as it fails to provide the proper perspective for interpreting the results. For example, studies focusing on the high cost of medications may ignore the even greater contribution of indirect costs. Population studies that measure direct and indirect costs fail to capture the impact of intangible costs, such as quality-of-life changes. Results that are expressed solely as a proportion of direct or total costs may facilitate inter-study comparisons, but can be deceptive if used as a basis for allocation decisions. Because of the 'balloon' effect, the proportions are not independent and are merely a consequence of the range of cost items measured. Only comprehensive estimates of absolute total costs can be used to establish benchmarks for gauging variation between regions or countries or change over time. These costs must be disaggregated into utilization and charges to identify the source of disparate results between regions or over time. Furthermore, estimates that ignore important sub-groups of the population are of limited usefulness for making health policy decisions regarding a population where the majority of expenses can be ascribed to a small segment of severely ill or poorly managed patients. Only stratified analyses can uncover which sub-groups and demographic factors are contributing to the total costs. These types of analyses are becoming increasingly important in jurisdictions moving toward capitated models of care that base budget planning on patient case-mix profiles.

All of the population-based and defined sample studies described above appropriately took a societal perspective. However, analyses undertaken from multiple viewpoints, such as the primary payer, the provider, the family and the patient, each offer unique insight into the process of interacting with the health care system. For example, the proportions of direct cost attributable to admissions varied from 47% to 72% between the societal and health care system perspectives. Whereas physician services and dispensing fees were comparable in the societal
perspective, they shifted to 14% and 2% respectively in the health care system analysis. Multi-perspective analyses facilitate understanding of the dynamic relationship between the payer-provider-patient triad and ensure that all interests are represented during debates concerning health care reform and allocation of scarce resources.

6.3 STUDY LIMITATIONS

6.3.1 Assessment of Patient Self-Report

The patients enrolled in the pilot Bronchial Inhalers project were not randomly selected from the population of bronchial inhaler users. The PMMP attempted to enroll all eligible subjects through aggressive recruitment at participating pharmacies and succeeded in achieving a 62% enrollment rate. It is possible that selection and volunteer bias occurred. Pharmacists may have preferentially approached patients who were likely to be good study candidates and avoided patients they perceived as unreliable or troublesome. It is therefore possible that the study candidates who volunteered had better recall accuracy than patients not enrolled.

While the sample size was adequate for examining overall agreement for each health service variable, a larger sample would have permitted subset analysis, such as examining under- and over-reporting of health services utilization in various sub-groups of patients. Age, sex, disease severity, extent of co-morbidity, prior use of health services and level of education may all influence recall and are potential predictors of agreement (Brown and Adams 1992). A larger sample would also have facilitated the application of the weighted kappa statistic to a greater number of response groups. An assessment of the reliability of the actual reported frequencies of
health service use, as opposed to clustered use, is important, as actual frequencies are the basis for assessing utilization volume in economic assessments.

In addition to patient characteristics, the level of observed agreement may have been affected by reports of utilization that occurred outside Ontario or that was not billed to OHIP. This study did not explore other sources of utilization information, such as insurance records or Worker's Compensation files.

The problems encountered in operationalizing ER/clinic visits and GP visits, and the potential for misclassification, have been discussed at length. These findings are important, as they point to the limitations associated with the PMMP questionnaire and the OHIP fee service coding process and indicate directions for improving the quality of the methodology.

6.3.2 Asthma Cost-Of-Illness Assessment
Like the pilot project, the main Bronchial Inhalers project from which the asthmatic cases were drawn, was not a random sample. This is only of consequence for extrapolating an overall sample average result to the general population. Since the sample was stratified by significant predictors of costs, i.e. age group, disease severity and occupation, cost-of-illness estimates in the sub-samples can be compared to other similarly defined sub-groups. The more important limitation was the difficulty in establishing an asthma case definition. This is a major weakness of large-scale epidemiological investigations that assess health and disease status in the absence of clinical information. Despite the inclusion requirement of asthma symptoms and the exclusion of probable cases of COPD, it is possible that cases of acute bronchitis and mild
COPD were included. The former would result in an underestimate of the total costs, while the latter could cause costs to be over-estimated.

The interview questionnaire did not distinguish between incident and prevalent cases of asthma. It is possible that pharmacists enrolled mostly prevalent cases. If utilization and costs are lower for newly diagnosed patients, and mostly prevalent cases were included, then the cost-of-illness results may be over-estimated. However, it is difficult to determine onset of asthma, as patients may remain symptomatic for long durations prior to being diagnosed clinically. The study design was biased in that a prescription for an inhaler was required. The costs of asthmatics who have not been diagnosed or who were not prescribed an anti-asthmatic medication were not reflected.

This analysis was limited to a one-year period. Asthma is a chronic disease and the economic consequences of long-term disability may be substantial. Likewise, the costs associated with premature mortality, although rare, were omitted. These costs were estimated at 11% of total annual costs in the Canadian population-based study (Krahn et al. 1996).

The quality of estimates of total direct and indirect costs is only as good as the quality of each component. Each item requires specification of both the individual costs and the volume of utilization. For all items, prices, charges and fees were used as surrogates for the opportunity costs. This limits the ability of these estimates to represent the true economic costs of asthma and is a common weakness of health economic evaluations.

Measurements of volume were derived from patient self-reports for all cost items. The
assessment of the patient self-report suggested that ER/clinik visits and GP visits may not have been reported with great accuracy. The problem with costing ER/clinik visits was further complicated by a lack of pricing information. However, this service accounted for less than 1 per cent of total costs. Although hospital admissions demonstrated very good reporting reliability, the estimate of the costs of admissions was based on the OCCP sample, rather than actual study patients' admissions. The accounting methods used by OCCP to derive direct and total admission were limited by the hospitals' management information systems, which continue to evolve.

While accurate prices could be obtained for medications, decision rules were followed for determining total consumption. Because of uncertainty in estimating the costs of medication, upper and lower bounds were calculated. These bounds were not substantially different from the base case estimate.

A number of items were missing from the cost-of-illness analysis. Although study participants were asked about home care and babysitting services, no expenses were reported. Patients were not asked about ambulance services or in-home nebulizers. Only the costs associated with flow studies were included as a laboratory expense, although patients may have undergone other types of lung function testing, such as plethysmography, exercise tests and methacholine challenges. During field testing, patients had difficulty reporting the costs of educational activities associated with their illness and this item was dropped from the questionnaire. Because of these omissions, the overall cost-of-illness may be under-estimated.

The use of the human capital method has been questioned as the optimal method for assessing the indirect costs of illness. Research is ongoing to improve this method by reducing its inherent
assumptions (Torgerson et al. 1994, Koopmanschap and Rutten 1996). This study overcame some of the biases associated with the human capital approach by using self-reported earned income to value the lost time of individuals rather than relying on national wage statistics. In addition, a sensitivity analysis of the weights used to value the opportunity cost of time of diverse groups was conducted.

Finally, the measurement of the intangible costs of asthma was undertaken with a general health status instrument. It may have been preferable to use a disease-specific index which would be more sensitive to quality-of-life changes precipitated by asthma. As yet, no disease-specific instrument has been validated for telephone interviews. Although the SF-36 is classified as a general health status questionnaire, it succeeded in discriminating between levels of disease severity. Its use also permitted comparisons with population norms and results from other studies. As the SF-36 is not applicable to children or parent proxy respondents, the measurement of quality-of-life was limited to adult subjects.
CONCLUSION
Chapter 7. CONCLUSION

This final chapter summarizes the key findings of the research, draws conclusions on the significance and implications of the study results and presents recommendations for application of the findings and directions for future research.

Prior to conducting a prospective cost-of-illness assessment relying on patient self-reports, an assessment of the reliability of patient self-reports of health services utilization was undertaken. Self-reports of hospital admissions and visits to respiratory specialists demonstrated substantial agreement with OHIP fee service claims data. GP visits displayed moderate agreement and ER/clinic visits, slight agreement. Agreement was slightly higher for utilization occurring during the study period compared to utilization reported to occur 6 to 12 months prior to the study.

The prospective approach used in this cost-of-illness assessment permitted the inclusion of many cost items not routinely available from other sources, resulting in a comprehensive total cost estimate. These items included insurance-related costs such as medication co-payments and deductibles, transportation costs to access care, recreation costs, costs associated with the use of alternative health care and inputs to indirect costs, such as travel and waiting time, earned income, productivity loss days, compromised days and level of compromised functioning.

In addition to extensive collection of economic data, important information regarding potential predictors of cost was collected. Age group, disease severity and occupation were found to be significant determinants of total costs. Severity was correlated with health services utilization
and differences in utilization between severity levels were statistically significant.

The societal perspective analysis revealed that the annual total costs of asthma in adult patients ranged from $1,633 per patient (95% CI $1,282, $1,984) in mildly ill patients to $4,223 per patient (95% CI $3,849, $4,598) in severely ill patients. The costs of children under 4 years of age were higher than children aged 5-14 years, but were lower than adult costs. Annual total costs in moderately ill children under 4 years of age were $1,252 per patient (95% CI $435, $2,068). Indirect costs were responsible for 43% of total costs. The largest components of direct costs were admissions, accounting for 47%, closely followed by medications and dispensing fees, which together accounted for 40% of direct costs.

The analysis from the health care system perspective excluded private insurance-related costs, out-of-pockets expenses and indirect costs. In this analysis, occupation was a significant predictor of total costs. Retirees demonstrated the highest annual total costs, ranging from $773 per patient (95% CI $395, $1,151) in mildly ill patients to $2,122 per patient (95% CI $1,866, $2,378) in severely ill patients. The costs of the other occupations were comparable. Annual costs in employed persons ranged from $517 per patient (95% CI $378, $657) in mildly ill patients to $889 per patient (95% CI $714, $1,064) in severely ill patients. The largest contribution to health care system costs was admissions, accounting for 72% of the total.

The patient perspective analysis focused exclusively on out-of-pocket expenses and indirect costs incurred by the patient. Adults displayed the highest annual total costs, ranging from $706 per patient (95% CI $555, $930) in mildly ill patients to $1,232 per patient (95% CI $975,
$1,376) in severely ill patients. The largest direct cost component from the patient's point of view was medications, consisting of full payment by uninsured individuals and co-payments by persons with drug plans. While drugs were responsible for 73% of direct costs borne by patients, direct costs only accounted for 10% of total costs.

Despite its designation as a general health status instrument, the SF-36 successfully distinguished between levels of respiratory disease severity. Average SF-36 domains scores in this sample were comparable to those observed in a group of patients with clinically diagnosed asthma. Males demonstrated higher scores than females, but the differences were not significant. Except for physical function which declined with age, no clear relationship between quality-of-life and age group was observed.

By using a prospective observational study model, this study brought the measurement of the cost of asthma closer to a fully stochastic, assumption-free approach to economic assessment. Because sensitivity analysis and the construction of minimum and maximum cost models were required to deal with uncertainty related to the costs of medications, admissions and productivity losses, the model was not fully stochastic. Nevertheless, the variance in the volume of each cost item was measurable and inferential statistics were applied to test hypotheses regarding cost differences between clinically important sub-groups of patients. Summarizing the annual cost per patient according to age and disease severity permits a deeper understanding of the basis of the cost-of-asthma compared to aggregate models where no stratification is conducted.

The methodology employed in this study allowed the determination of 95% confidence intervals.
Clinical and health policy-decision making is greatly facilitated by point estimates that are accompanied by such indicators of precision. The analysis of the larger sub-groups, such as adults and employed persons, resulted in reasonably precise cost-of-illness estimates, with confidence intervals ranging from $300 to $700. Thus the point estimates of adults are precise - but are they accurate? The assessment of the patient self-report suggested that patients are reliable reporters of health services utilization. Moreover, the highest level of agreement was observed for the largest component of direct costs - hospital admissions.

By exposing the contributions of the various cost components, these results can facilitate health budget allocation decisions. The findings demonstrate that interventions aimed at reducing hospital admissions and drug costs may result in large savings to the health care system and to society. In addition, this analysis underscores the huge contribution of indirect costs to the patient and to society. Maintaining productivity is essential to good health and quality-of-life.

It is enlightening to contrast the results obtained from the three perspectives of society, the health care system and the patient. Societal perspectives are universally recommended in health economic evaluations to eliminate bias associated with representing a particular payer or interest group, thus facilitating inter-study and international comparisons. Members of a society with a universal, publicly administered health care system may presume that the government takes an impartial societal perspective in its planning decisions. The health care system analysis revealed that most costs were related to hospital admissions, the most heavily targeted sector of recent government health care budget cuts. Health care planning and policy-making that is based on a health care system, rather than a societal perspective, may overlook the large contribution of lost
productivity on the total economic burden of illness. The patient perspective stresses the fact that the health care system is accessed by individuals, not a collective. Personal perceptions regarding the strengths and failings of the health care system are based on the dynamic interaction between an individual and the system. Patients may view the problem of allocation and health care reform in a fundamentally different way than government, stemming from the fact that most of the costs confronted by an asthmatic patient are indirect ones, impacting greatly on a person's productive potential and quality-of-life.

Very little patient-level data is available on the costs of asthma. The actual costs observed in this study can be used as benchmarks in an environment marked by continuous change. In the future, the patient-level cost of asthma will be influenced by the increasing incidence, prevalence and morbidity of this disease, by changes in pharmacotherapy characterized by more aggressive treatment with inhaled corticosteroids and the introduction of leukotriene antagonists and 5-lipoxygenase inhibitors, by changes in practice patterns and disease management and by the restructuring of the health care system and the provision of services. Age- and severity-specific estimates of the cost of asthma may prove valuable as Ontario hospitals move from global budgeting to case mix models, and provider practices evolve from fee-for-service to capitation reimbursement. Current research initiatives into 'population health' must not neglect the importance of establishing meaningful patient-level estimates of illness and costs.

The methodology advanced in this research project would benefit from continued investigations. Research is needed to further assess the quality of the patient self-report by studying the impact of demographic, socioeconomic and medical characteristics on patient recall. Studies comparing
patient self-reports of symptoms and prescribed medications against medical and pharmacy records are necessary to assess the reporting reliability of these particular variables. The accuracy of data sources used for comparison, such as OHIP claims files, medical charts and pharmacy databases must be ascertained through thorough assessments of validity.

The elicitation of information from the patient can be improved through refinements to the PMMP questionnaire. Questions that clearly specified patients' prescribed drug formulations and start and stop dates would result in more precise estimates of the cost of medications. Assessment of ER/clinic visits would be facilitated by structured interview questions that asked the patient directly about the use of these services and that distinguished between emergency care and other forms of non-urgent care. The use of emergency services has been under increasing scrutiny by a cost-conscious public sector. These services, along with outpatient and walk-in-clinic are currently under study. While the Ontario Ministry of Health may not have immediate plans to introduce a more accurate coding system to the billing process, other quasi-government agencies, such as the OCCP, are beginning to look at emergency services and may generate higher quality data than is currently available from the OHIP fee claims database.

Further work is required to validate the disease severity stratification scheme by comparing it to clinical and other diagnostic measures of asthma severity. The scheme would have to evolve in parallel with prescribing guidelines that reflect advances in pharmacotherapy.

The cost-of-illness analysis revealed the significant contribution of indirect costs to the total cost of asthma. The quality of the human capital approach continues to evolve with greater
application of sensitivity analysis and exposition of inputs, resulting in more accurate estimates of indirect costs. Further research into this and other methods, including the friction cost method (Koopmanschap and van Ineveld 1992) and willingness-to-pay (Glied 1996) are required to improve the estimation of indirect costs.

Research is required to develop valid and reliable instruments for assessing quality-of-life in children, the group in which the incidence of asthma is highest. As a chronic disease, the study of asthma would also benefit from investigations of models for predicting lifetime costs.

The prospective approach taken in this project can be replicated for investigations of the costs associated with other illnesses. The scope can be broadened to include the measurement of specific health outcomes. Although this research focused on improving cost-of-illness methodology, this strategy for evaluating costs can also be applied to comparative economic assessments of medications, procedures, programs and services. Both randomized and observational comparative health economic assessments would benefit from a more comprehensive approach to assessing costs from multiple perspectives.

By involving community pharmacists, the Pharmacy Medication Monitoring Program forges a important link between health services research and the community. The PMMP is a potentially valuable model for performing cost-of-illness analyses, as well as comparative evaluations of the effectiveness and economic benefits of target medications. By improving the quality of estimates of the economic burden of illness, this methodology can lead to better health care decision-making and ultimately, to better health of Canadians.
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Chapter 8. REFERENCES


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APPENDICES
**APPENDIX I**

**PMMP Information Sheet and Consent Form**

**What is the PMMP?**

The Primary Methadone Management Program (PMMP) is a medication project designed to treat opioid addiction. It provides a stable supply of methadone to patients who have been prescribed for a specific period of time. The program aims to reduce the risk of overdose, improve treatment outcomes, and facilitate a safe and effective transition to a medication-free lifestyle.

**Why is this program needed?**

Many individuals living with opioid addiction find it challenging to manage their medication without the guidance of a healthcare provider. The PMMP offers a structured approach to ensure that patients receive the appropriate dose of methadone, which is crucial for their recovery.

**What do I need to do?**

To participate in the PMMP, you will need to undergo a comprehensive assessment to determine the appropriate dosage of methadone. This process may involve multiple visits to a healthcare provider. You will also need to follow the prescribed medication schedule and provide regular blood tests to monitor your progress.

**Why should I join the program?**

Joining the PMMP can be beneficial for individuals seeking a structured and supportive environment to manage their opioid addiction. The program provides a safe and controlled setting to help individuals reduce their dependency on opioids and improve their overall health.

**How long does the program last?**

The duration of the PMMP varies depending on individual needs and treatment goals. Typically, patients remain in the program for several months or years until they are ready to transition to a maintenance-free regimen.

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**Table: PMMP Information Sheet and Consent Form**

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
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<tbody>
<tr>
<td>Consent</td>
<td>X indicated that they understand and agree to the PMMP program terms.</td>
</tr>
<tr>
<td>Name</td>
<td>[Name]</td>
</tr>
<tr>
<td>Address</td>
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<tr>
<td>Other Providers</td>
<td>[Other Providers]</td>
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</table>

**TO BE COMPLETED BY PHARMACY**

- [ ] PMMP Initiation Date
- [ ] Date of Next Visit
- [ ] Dose of Methadone

**Other Information**

- [ ] Additional information or instructions

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**Appendix I continued...**
Cover Letter #1

PMMP letterhead

date
study candidate name
address

Dear __________,

As part of my Ph.D. program at the University of Toronto, I am conducting a research project about the use of health services by people with breathing problems. Visits to doctors, clinics and hospitals are examples of the health services that I will study.

To obtain the information I need to conduct this study, I depend on the cooperation of persons like yourself. This research is supported by the Medical Research Council of Canada and the Ontario Respiratory Care Society. The study is endorsed by the Pharmacy Medication Monitoring Program (PMMP) - a program in which you are now taking part.

The purpose of the study is to look at and compare different ways of collecting information about the use of health services. One way to collect information is by telephone interview with the PMMP. Other approaches are to collect information from hospital charts and from the Ontario Health Insurance Plan (OHIP). To see these files, I need your permission and your Ontario Health Card Number. All the information that is collected is confidential and only members of our research team will be able to see it. Your name will not appear in any report.

I sincerely hope you are interested in taking part in this important research project. If you are, please read the attached form which describes in detail the information that will be collected and how it will be handled. If you agree, write your Health Card Number on both copies, sign them, keep one copy and return the other in the envelope provided.

I thank you very much for your assistance.

Yours sincerely,

Wendy Ungar, M.Sc.
Ph.D. Candidate
APPENDIX 2  Cover letters 1 and 2 and Consent Form/Information Sheet - cont’d

Cover Letter #2

PMMP letterhead

date
study candidate name
address

Dear __________,

Several weeks ago I sent you a letter describing a research project I am doing as part of my Ph.D. program at the University of Toronto. This project concerns the use of health services by people with breathing problems. Visits to doctors, clinics and hospitals are examples of the health services that I will study.

To obtain the information I need to conduct this study, I depend on the cooperation of persons like yourself. This research is supported by the Medical Research Council of Canada and the Ontario Respiratory Care Society. The study is endorsed by the Pharmacy Medication Monitoring Program (PMMP) - a program in which you are now taking part.

The purpose of the study is to look at and compare different ways of collecting information about the use of health services. One way to collect information is by telephone interview with the PMMP. Other approaches are to collect information from hospital charts and from the Ontario Health Insurance Plan (OHIP). To see these files, I need your permission and your Ontario Health Card Number. All the information that is collected is confidential and only members of our research team will be able to see it. Your name will not appear in any report.

I sincerely hope you are interested in taking part in this important research project. Please read the attached form which describes in detail the information that will be collected and how it will be handled. If you agree, write your Health Card Number on both copies and sign them. Please indicate your agreement or refusal to participate, return one copy in the envelope provided and retain the second copy.

If you have any questions, please don’t hesitate to call Ms. Kathy Gaebel at the PMMP office at (905) 522-1155 ext. 4901, or leave a message for me and I will promptly return your call.

I thank you very much for your assistance.

Yours sincerely,

Wendy Ungar, M.Sc.
Ph.D. Candidate
The purpose of this research is to look at the best way to collect information about the use of health services. Visits to doctors, clinics and hospitals by persons with breathing problems are examples of health services that will be studied. One way to collect this information is by telephone interview. Another method is to look at Ontario Health Insurance Plan (OHIP) records. These are computerized records that contain information about visits to the doctor, such as the reason and what was done during the visit. A third method is to check the hospital chart. The only information that would be collected from the hospital chart is the date and reason for any hospitalization that may occur. The study will compare these 3 methods.

To take part, I only need to provide my Health Card Number and permission to view my OHIP and hospital records. My Health Card Number will be sent to OHIP to get information about the use of health services. Only information about my use of health services between October 1993 and July 1995 will be collected from OHIP and hospital records. No other information will be collected. After details about my use of health services have been recorded, my name and Health Card Number will be removed from the study files. All the information will be kept private and only members of the research team will be able to see it. My name will not appear in any report.

I understand that this is a separate project from the PMMP. Whether I agree or refuse to take part will not affect my involvement with the PMMP or any health services provided to me. My decision to provide my Health Card Number is completely voluntary and I may withdraw permission any time. If I have any questions, I can speak to Kathy Gaebel at the PMMP office or I can leave a message for Wendy Ungar by calling (905) 522-1155, ext. 4901.

☐ I agree to take part and give my permission for the researcher to look at my OHIP and hospital records. My Health Card Number is __ __ __ __ __ __ __

☐ I refuse to take part.

_________________________  _______________________
signature  date

(return one copy in the envelope provided and keep the other for your records)
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</table>
APPENDIX 4  Economic Assessment Question Set

Questionnaire No. 1  Post 1-month [baseline] Interview

1. Are you 65 or older?
   Yes - skip to Q2
   No

1a. Do you or a member of your family have a Drug Plan that pays for all or a part of your medications?
   Yes
   No - skip to Q2

1b. Do you pay for part of the cost of your inhalers?
   Yes
   No - skip to Q2

1c. How many inhalers did you buy in the last 6 months?
   no. ________  If zero, skip to Q2

1d. What was the cost to you for each inhaler, either in dollars or as a percentage of the price?
   $ ________  don't know / refused
   % ________  don't know / refused

2. Have you ever delayed or not filled a prescription because of cost?
   Yes
   No

3. How long does it take you to travel (one-way) to see the doctor(s) who look(s) after your breathing problem?
   ________  minutes  don't know / refused

4. How much do you spend on transportation or parking when you visit this doctor?
   $ ________
5. On average, how much time do you spend at the doctor's office, including waiting and examination?

_________ minutes / hours

(repeat 3, 4, 5 if > 1 doctor)

6. In the last year, did you receive care from an alternative health professional, such as a chiropractor or homeopath, for your breathing?

Yes
No - skip to Q7

6a. Was it:
   a) a chiropractor
   b) a homeopath
   c) other ____________ (specify)

6b. How many sessions did you have in the last year?

_________ # of sessions

6c. How much did you pay per session?

$ _________ don't know / refused

7. How many hours per week do you devote to exercise specifically to help your breathing?

_________ hours If zero, skip to Q8

7a. Are these exercises done at a health club or recreation centre?

Yes
No - skip to Q8

7b. How much is your yearly membership?

$ _________ don't know / refused

(inserted into the section on hospitalizations.)

8. How many days were you in the hospital? (general)
9. How many days were you in the hospital? (related to breathing problems)

_________ days

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<th>EMPLOYED</th>
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<tr>
<td>Part-time?</td>
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<tr>
<td>UNEMPLOYED, RETIRED, DISABILITY, STUDENT</td>
<td>Go to Q11</td>
</tr>
<tr>
<td>HOMEMAKER</td>
<td>Go to Q12</td>
</tr>
</tbody>
</table>

10a. How many days in the last 6 months did you miss work because of your breathing problems?

_________ days

10b. When you miss a day of work, do you still get paid?

    Yes
    No

10c. How many days in the last 6 months did you continue to work even though your breathing problems were worse than usual?

_________ days

If zero, skip to 10e.

10d. On those days, at what level did you function, on a scale from 0 to 100%?

_________ 0-100
don't know / refused

10e. The last question is about your salary and you don't have to answer it if you choose not to. However, if we have this information, then we can estimate the value of your time. Would you please tell me which category your annual salary falls into:

1- less than or equal to $20,000
2- $20,001 - $30,000
3- $30,001 - $40,000
4- $40,001 - $50,000
5- $50,001 - $60,000
6- greater than $60,000
7- refused to answer

Close
11. How many days in the last 6 months were your breathing problems bad enough to interfere with your usual daytime activities?

_______ days  If zero, skip to Close

11a. On those days, at what level did you function, on a scale from 0 to 100%?

_______ 0-100  don't know / refused

Close

12. How many days in the last 6 months were your breathing problems bad enough to interfere with your usual daytime activities?

_______ days  If zero, skip to Close

12a. On those days, at what level did you function, on a scale from 0 to 100%?

_______ 0-100  don't know / refused

12b. How many days in the last 6 months did you have someone help you because your breathing problems interfered with your usual activities? (in addition to your usual housekeeper or babysitting arrangements)

_______ days  If zero, skip to Close

12c. How many of those days did you pay someone to help you?

_______ days  If zero, skip to Close

12d. How much did you pay them per day?

$ ________  don't know / refused

Close
APPENDIX 4  Economic Assessment Question Set - cont'd  206

Questionnaire No. 2  3-month and 6-month Interviews

(inserted into the section on hospitalizations.)
How many days were you in the hospital?

_________  (days)

1. Did you buy any inhalers since the last interview?
   Yes
   No - skip to Q3

1a. How many inhalers did you buy?
   no.  ________  don't know / refused

__________________________________________________________

EMPLOYED  Go to Q2
UNEMPLOYED, RETIRED, DISABILITY, STUDENT  Go to Q3
HOMEMAKER  Go to Q4

__________________________________________________________

2. How many days since the last interview did you miss work because of your breathing problems?
   _________  days

2a. How many days since the last interview did you continue to work even though your breathing problems were worse than usual?
   _________  days  If zero, skip to Close.

2b. On those days, at what level did you function, on a scale from 0 to 100%?
   _________  0-100  don't know / refused

Close

__________________________________________________________

3. How many days since the last interview were your breathing problems bad enough to interfere with your usual daytime activities?
   _________  days  If zero, skip to Close.
3a. On those days, at what level did you function, on a scale from 0 to 100%?

_________ 0-100 don't know / refused

4. How many days since the last interview were your breathing problems bad enough to interfere with your usual daytime activities?

_________ days If zero, skip to Close

4a. On those days, at what level did you function, on a scale from 0 to 100%?

_________ 0-100 don't know / refused

4b. How many days since the last interview did you have someone help you because your breathing problems interfered with your usual activities? (in addition to your usual housekeeper or babysitting arrangements)

_________ days If zero, skip to Close

4c. How many of those days did you pay someone to help you?

_________ days If zero, skip to Close

Close
APPENDIX 4  Economic Assessment Question Set - cont'd

1a. Do you or a member of your family have a Drug Plan that pays for all or a part of (name)'s medications?

   Yes
   No - skip to Q2

1b. Do you pay for part of the cost of the inhalers?

   Yes
   No - skip to Q2

1c. How many inhalers did you buy in the last 6 months?

   no.  ________  If zero, skip to Q2

1d. What was the cost to you for each inhaler, either in dollars or as a percentage of the price?

   $  ________  don't know / refused
   %  ________  don't know / refused

2. Have you ever delayed or not filled a prescription because of cost?

   Yes
   No

3. How long does it take you to travel (one-way) to see the doctor(s) who look(s) after (name)'s breathing problem?

   ________ minutes  don't know / refused

4. How much do you spend on transportation or parking when you visit this doctor?

   $  ________

5. On average, how much time do you spend at the doctor's office?

   ________ minutes / hours

(repeat 3,4,5 if > 1 doctor)
6. In the last year, did (name) receive care from an alternative health professional, such as a chiropractor or homeopath, for his/her breathing?

Yes
No - skip to Q7

6a. Was it: a) a chiropractor
       b) a homeopath
       c) other ____________________ (specify)

6b. How many sessions did (name) have in the last year?

________ # of sessions

6c. How much did you pay per session?

$ ________ don't know / refused

7. How many hours per week do you supervise (name) in exercises specifically to help (name)'s breathing?

________ hours If zero, skip to Q8

7a. Are these exercises done at a recreation centre?

Yes
No - skip to Q8

7b. How much is the yearly membership?

$ ________ don't know / refused

(inserted into the section on hospitalizations)

8. How many days was (name) in the hospital? (general)

________ days

9. How many days was (name) in the hospital? (related to breathing problems)

________ days
10a. How many days in the last 6 months did you miss work because you had to care for (name)'s breathing problems?

_______ days

10b. When you miss a day of work, do you still get paid?

Yes
No

10c. The last question is about your salary and you don't have to answer it if you choose not to. However, if we have this information, then we can estimate the value of your time. Would you please tell me which category your annual salary falls into:

1- less than or equal to $20,000
2- $20,001 - $30,000
3- $30,001 - $40,000
4- $40,001 - $50,000
5- $50,001 - $60,000
6- greater than $60,000
7- refused to answer

Close

11. How many days in the last 6 months were your usual daytime activities interrupted because you had to care for (name)'s breathing problems?

_______ days

Close
12. How many days in the last 6 months were your usual daytime activities interrupted because you had to care for (name)'s breathing problems?

_________ days

13. How many days in the last 6 months did someone besides you look after (name) when he/she stayed at home because of breathing problems? (in addition to your usual housekeeper or babysitting arrangements)

_________ days If zero, skip to Close

13a. How many of those days did you pay someone to help you?

_________ days If zero, skip to Close

13b. How much did you pay them per day?

$_________ don't know / refused

Close
APPENDIX 4  Economic Assessment Question Set - cont’d

Questionnaire No. 2P - 3-month and 6-month Interviews

(inserted into the section on hospitalizations.)
How many days was (name) in the hospital?

_______ (days)

1. Did you buy any inhalers for (name) since the last interview?

   Yes
   No - skip to Q3

1a. How many inhalers did you buy?

   no. ________  don't know / refused

______________________________

EMPLOYED Go to Q2
UNEMPLOYED, RETIRED, DISABILITY, STUDENT Go to Q3
HOMEMAKER Go to Q4

2. How many days since the last interview did you miss work because you had to care for (name)'s breathing problems?

   _________ days

Close

______________________________

3. How many days since the last interview were your usual daytime activities interrupted because you had to care for (name)'s breathing problems?

   _________ days

Close

______________________________

4. How many days since the last interview were your usual daytime activities interrupted because you had to care for (name)'s breathing problems?

   _________ days
5. How many days since the last interview did someone besides you look after (name) when he/she stayed at home because of breathing problems? (in addition to your usual housekeeper or babysitting arrangements)

__________ days  If zero, skip to Close

6. How many of those days did you pay someone to help you?

__________ days

Close
## APPENDIX 5  OHIP Fee Service Claim Codes

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<th>FSC Code</th>
<th>Category</th>
<th>Description</th>
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<td>Family Practice and practice in general (00)</td>
<td>minor assessment, general assessment, general re-assessment consultation, repeat consultation, intermediate assessment, mini assessment, housecall assessment, limited consultation, special palliative care consultation, annual health examination, general assessment, general re-assessment consultation, repeat consultation, partial assessment, limited consultation</td>
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<td>examination by general internist</td>
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<td>Internal Medicine (13)</td>
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<td>skin testing, patch test, bronchial provocative testing, bronchial provocative testing, skin testing, histamine or methacholine test</td>
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<td>Pulmonary Function Studies</td>
<td>Vital Capacity</td>
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<td>Flow Volume Loop</td>
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<td>Repeat J304 after bronchodilator</td>
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<th>Consultation in Emergency Medicine</th>
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<td>Emergency Medicine (12)</td>
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<table>
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<th>General Assessment</th>
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<td>C005</td>
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<td>Repeat Consultation</td>
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<td>C006</td>
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<td>Limited Consultation</td>
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<td>C007</td>
<td></td>
<td>Subsequent Visit up to 5 Weeks</td>
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<td>C132</td>
<td></td>
<td>General Assessment</td>
</tr>
<tr>
<td>C133</td>
<td></td>
<td>General Re-assessment</td>
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<tr>
<td>C134</td>
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<td>Consultation</td>
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<td>C135</td>
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<table>
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<th>Subsequent Visit up to 5 Weeks</th>
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<td>General Assessment</td>
</tr>
<tr>
<td>C473</td>
<td>General Re-assessment</td>
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<td>C476</td>
<td>Limited Consultation</td>
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<td>C575</td>
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</table>

1. All fee service claim codes possess an A suffix (attending physician only)
2. Emergency Department equivalent includes urgent care centres, walk-in clinics, after-hour clinics or other settings where a physician renders an emergency service.

Abbreviations: FSC = fee service claim; FRC = functional residual capacity
APPENDIX 6 OHIP Respiratory System Diagnostic Codes

460 common cold, acute nasopharyngitis
461 acute sinusitis
463 acute tonsilitis
464 acute laryngitis, tracheitis, croup, epiglottis
466 acute bronchitis
470 deviated nasal septum
471 nasal polyp
473 chronic sinusitis
474 hypertrophy or chronic infection of tonsils and/or adenoids
477 allergic rhinitis, hay fever
486 pneumonia - all types
487 influenza
491 chronic bronchitis
492 emphysema
493 asthma, allergic bronchitis
494 bronchiectasis
496 other chronic obstructive pulmonary disease
501 asbestosis
502 silicosis
511 pleurisy with or without effusion
512 spontaneous pneumothorax, tension pneumothorax
515 pulmonary fibrosis
518 atelectasis, other diseases of lung
519 other diseases of respiratory system
518 signs/symptoms not yet diagnosed - respiratory system - epitaxis, hemoptysis

Note: These codes are identical to 3-digit ICD-9 diagnostic codes
### Statistical Formulae

A sample 2x2 contingency table is shown below:

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<thead>
<tr>
<th>OHIP Database</th>
<th>Present</th>
<th>Absent</th>
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</thead>
<tbody>
<tr>
<td>Present</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Self-report</td>
<td>c</td>
<td>d</td>
</tr>
<tr>
<td>absent</td>
<td>c₁</td>
<td>c₂</td>
</tr>
<tr>
<td></td>
<td>r₁</td>
<td>r₂</td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Symbol | Description | Formula
--- | --- | ---
\(P_o\) | observed proportion of agreement | \frac{(a+d)}{N}
\(P_c\) | chance-expectaed proportion of agreement | \frac{r₁c₁ + r₂c₂}{N²}
\(\kappa\) | Kappa, chance-corrected agreement | \frac{P_o - P_c}{1 - P_c}
\(\sigma_\kappa\) | kappa standard error | \left[ \frac{P_o(1 - P_o)}{N(1 - P_c)^2} \right]^{1/2}
\(z\) | \(z\) test of standard normal distribution for kappa | \frac{\kappa}{\sigma_\kappa}
\(f_o\) | observed cell count | a, b, c or d
\(f_e\) | expected cell count | \(\frac{r₁c₁, r₂c₂, r₁c₂, r₂c₁}{N \ N \ N \ N \ N}\)
\(w\) | quadratic disagreement weight, square of the difference between the diagonal and the specified group | \( (d - g)^² \)
APPENDIX 7  Statistical Formulae - cont'd

$q_{wo}$  observed proportion of weighted disagreements  $(\Sigma w_{fo})/N$

$q_{wc}$  chance-expected proportion of weighted disagreements  $(\Sigma w_{fc})/N$

$k_w$  quadratic weighted kappa  $1 - (q_{wo}/q_{wc})$

$\sigma_{kw}$  weighted kappa standard error  $\frac{\sqrt{\frac{N(\Sigma w_{fo}^2) - (\Sigma w_{fo})^2}{N(\Sigma w_{fc})^2}}}{}$

$z$  $z$ test of standard normal distribution for weighted kappa  $k_w/\sigma_{kw}$

$z$  $z$ test of standard normal distribution to compare two values of kappa  $\frac{k_1 - k_2}{(\sigma^2_{k1} + \sigma^2_{k2})^{1/2}}$

95% CI  approximate 95% confidence intervals for $k$ or $k_w$  $[k - (1.96 \times \sigma_k), k + (1.96 \times \sigma_k)]$

coefficient of variation  measure of variation  standard deviation/sample mean

Extremal quotient  measure of (area) variation  maximum value/minimum value
APPENDIX 8  Cost-of-Illness Inclusion/Exclusion Criteria Interview Questions

Q2. This is _________ calling from the Pharmacy Medication Monitoring Program. Back on _______ you received a prescription from ________. At that time you agreed to participate in a study about medicines and how people respond to them. Is this a good time to answer a few questions about your health? It will take about 30 minutes. Yes/No

Q158. Have you ever experienced episodes of shortness of breath or breathlessness? Yes/No

Q166. Have you ever suffered from wheezing or whistling in the chest? Yes/No

Q174. Have you ever suffered from recurrent episodes of coughing? Yes/No

Q141. Do you ever use oxygen? Yes/No

Q147. Do you presently smoke cigarettes? Yes/No

Q148. How many cigarettes, on average, do you smoke in a day? Number

Q153. Have you ever smoked cigarettes or a pipe? Yes/No

Q154. How many cigarettes or pipes, on average, were you smoking per day? Number

Q155. What age were you when you began smoking regularly? Number

Q156. What age were you when you stopped smoking? Number
APPENDIX 9  Ethics Committee Approvals

University of Toronto

OFFICE OF RESEARCH SERVICES

Approval by Review Committee on the Use of Human Subjects

Principal Investigator: Dr. P. Coyte, Health Administration (W. Ungar)

Title: An Assessment of a Prospective Observational Study Model for Collecting Health Care Utilization Data and Measuring the Cost of Illness Pertaining to Patients with Respiratory Disease

Review Committee:
- Dr. M. Cohen, Health Administration
- Professor D. Craig, Nursing
- Dr. T. Girvan, Pharmacy
- Dr. D. Cockrell, Health Administration

Documents Submitted to Review Committee:
- A protocol, cover letter, consent form, information on the McMaster University Pharmacy Medical Monitoring Program, including the McMaster University Ethics Committee approval, revised protocol, a letter dated March 1, 1995 from Professor G. Goldsmith, a letter dated March 5, 1995 from W. Ungar, and a revised consent form/information sheet.

Subjects: Patients with respiratory disease who are using bronchial inhalers

Procedures: As described in the attached revised information and consent form.

Method for Obtaining Consent: Information and consent form, revised as attached. Patients are to be given a copy of the form to keep.

Remarks:

Date of Approval: March 20, 1995

*During the course of the research, any significant deviations from the approved protocol and/or any unanticipated developments within the research should be brought to the attention of the Office of Research Services.

*A copy of this approval form is available to Review Committee members upon request.

SP: veggies

cc: Profs. P. Leatt, Health Administration

Susan Pilon, Executive Officer
Human Subjects Review Committee

Simcoe Hall 27 King's College Circle Toronto Ontario M5S 1A1  Telephone 416/978-2163  Fax 416/971-2010
DATE: January 13, 1995

TO: Dr. D. Rosenbloom - MUMC-1E4
Co-Chairman, Research Advisory Group
Dr. D. Offord - CH-A
Co-Chairman, Research Advisory Group

cc - M/ Levine
C. Goldsmith

FROM: F. G. H. Baillie (5215)
Chairman, Medical Advisory Committee

RE: THE PHARMACY MEDICATION MONITORING PROGRAMME - A PHARMACY-BASED POSTMARKETING SURVEILLANCE NETWORK

This is to advise that the Medical Advisory Committee, at its meeting on January 5, 1995, approved the above research project.

By means of a copy of this memo, investigators in this project should be aware that they are responsible for ensuring that evidence of consent is inserted in the patient's health record. In the case of invasive or otherwise risky research, the investigator might consider the advisability of keeping personal copies.
DATE: December 3, 1992

TO: Dr. C. Goldsmith/Dr. M. Levine

FROM: D. Rosenbloom, Pharm.D.
Chair, Research Project Advisory Committee

This is to confirm that your project "The Pharmacy Medication Monitoring Programme" Project #92-118 was reviewed by the Research Advisory Committee on November 25, 1992 and approved.

This project will be forwarded to M.A.C. for hospital approval.

Please note that it is the responsibility of the researcher to ensure that evidence of consent is inserted in the patient’s health record. In the case of invasive or otherwise risky research, the researcher might consider the advisability of keeping personal copies.

D. Rosenbloom, Pharm.D.
Chair